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(54) **ANTI-PACAP ANTIBODIES AND USES THEREOF**

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(57) **ABSTRACT**

The present invention is directed to antagonistic antibodies and antigen binding fragments thereof having binding specificity for PACAP. These antibodies inhibit, block or neutralize at least one biological effect associated with PACAP, e.g., vasodilation. In exemplary embodiments these antibodies and antigen binding fragments thereof may comprise specific V_H, V_L, and CDR polypeptides described herein. In some embodiments these antibodies and antigen binding fragments thereof bind to and/or compete for binding to specific epitope(s) on human PACAP. The invention is further directed to using these antagonistic anti-PACAP antibodies, and binding fragments thereof, for the diagnosis, assessment, and treatment of diseases and disorders associated with PACAP and conditions where antagonism of PACAP-related activities, such as vasodilation, mast cell degranulation, and/or neuronal activation, are therapeutically beneficial, e.g., headache and migraine indications.

Figure 1A

Antibody Variable Heavy Chain Protein Features

Sequence Name	FR1	CDR1	FR2	CDR2
Ab1	QSVEESGGRLVTPGTPLTLTCTVSGFSLS	SAVMN	WVRQAPGKGLEWIG	SIVASGTTYYASWANG
Ab1.H	EVQLVESGGGLVQPGGSLRLSCAASGFTVS	SAVMN	WVRQAPGKGLEWIG	SIVASGTTYYASSANG
Ab2	QSVEESGGRLVTPGTPLTLTCTVSGFSLS	GAAMN	WVRQAPGKGLEWIG	VIGNSGSTYYASWAKG
Ab3	QEQLVESGGGLVQPEGSLTLTCTASGFSFS	SSDYMC	WVRQAPGKGLEWIG	CIDAGSSGDTYFASWAKG
Ab4	QSVEESGGRLVTPGTPLTLTCTVSGFSLS	SYDMS	WVRQAPGKGLEYIG	IINTNDDTWYASWVKG
Ab5	QSVEESGGRLVTPGTPLTLTCTVSGFSLS	SYAMI	WVRQAPGKGLEWIG	IIYDNGDTYYASWAKG
Ab6	QQLEQSGGGAEGGLVKPGGSLELCCKASGFSLS	STYWMC	WVRQAPGKGLEWIG	CIYTGSGSTDYASWVNG
Ab7	QSVEESGGRLVTPGTPLTLTCTASGIDLS	GYAMG	WVRQAPGKGLEWIG	DISTYGTTDYASWVNG
Ab8	QQLEQSGGGAEGGLVKPGGSLELCCKASGFSLT	TSHWMC	WVRQAPGKGLNWIG	CISAGSGDADYATWVDA
Ab9	QQLEQSGGGAEGGLVKPGGSLKLSCKASGFTIS	RDYWIC	WVRQAPGKGLEWIG	CISAGGGSTDYANWVNG
Ab11	QSVEESGGRLVTPGTPLTLTCTASGFSLS	RYAMG	WVRQAPGKGLEWIG	DISTYGTTDYASWVNG
Ab12	QSVEESGGRLVTPGTPLTLTCTASGFSLS	SYAMG	WVRQAPGKGLEWIG	DISTYGTTDYASWVYG
Ab13	QSVEESGGRLVTPGTPLTLTCTVSGFSLS	SAAMN	WVRQAPGKGLEWIG	IIDNTAGTYYAPWAKG
Ab14	QSVEASGGRLVTPGTPLTLTCTVSGFSLS	SAAMN	WVRQAPGKGLEWIG	FIEYSKNIVYASWAKG
Ab15	QSVEASGGHLVTPGTPLTLTCTVSGFSLS	SAAMN	WVRQAPGKGLEWIG	SVDERQNKYYASWAKG
Ab16	QSVEESGGRLVTPGTPLTLTCTVSGFSLS	SAAMS	WVRQAPGKGLEWIG	IIDDSGNTYYASWAKA
Ab17	QSVEESGGRLVTPGTPLTLTCTVSGFSLS	SAAMN	WVRQAPGKGLEWIG	IFDPYSSTYYASWAKG
Ab18	QSVEESGGRLVTPGTPLTLTCTVSGFSLS	SAALS	WVRQAPGKGLEWIG	IIDKGVMSYYASWAKG
Ab19	QSVEASGGRLVTPGTPLTLTCTVSGFSLS	SATMN	WVRQAPGKGLEWIG	LIGGNDERYYASWAKG
Ab22	QEQLVESGGGLVQPEGSLTLTCTASGFDFS	SNAMC	WVRQAPGKGLEWIG	SIYNADGKNYYAIWAKG
Ab23	QSVEESGGRLVTPGTPLTLTCTVSGFSLN	NYAMS	WVRQAPGKGLEWIG	IMGVNDITYYASWAKG

Figure 1B

Antibody Variable Heavy Chain Protein Features Sequence

Name	FR3	CDR3	FR4	
Ab1	RFTISKTSSTTMDLKMTSPTTEDTATYFCAR	GGGEFFI	WGPGTLVTVSS	(SEQ ID NO: 2)
Ab1.H	RFTISRDNSKNTLYLQMNSLRAEDTAVYYCAR	GGGEFFI	WGQGTLVTVSS	(SEQ ID NO: 42)
Ab2	RFTISKTSSTTVDLKMTSPTTEDTATYFCAR	GGGEFFI	WGQGTLVTVSS	(SEQ ID NO: 82)
Ab3	RFTISKTSSTTVTLQMTSLTAADTATYFCAR	HLYGSITFAFGL	WGQGTLVTVSS	(SEQ ID NO: 682)
Ab4	RFTISKTSSTTVDLKMTSLTTEDTATYFCAR	ISDAYVFDYAYYFTL	WGQGTLVTVSS	(SEQ ID NO: 642)
Ab5	RFTISKTSTTVYLKIASPTTEDTATYFCAR	EPGSTTQNDL	WGQGTLVTVSS	(SEQ ID NO: 482)
Ab6	QFTLSRDIDQSTGCLQLNSLTVADTAMYYCTK	NFDL	WGPGTLVTVSS	(SEQ ID NO: 722)
Ab7	RFTISRTSTTVTLKMTSLTTEDTATYFCAR	DYWLSL	WGPGTLVTVSS	(SEQ ID NO: 522)
Ab8	QFTLSRDIDQNTGCLQLNSLTPADTAMYYCTI	NFEL	WGQGTLVTVSS	(SEQ ID NO: 762)
Ab9	RFTLSRDIDQSTGCLQLNSLTDADTAMYYCAG	NLEI	WGQGTLVTVSS	(SEQ ID NO: 802)
Ab11	RFTISRTSTTVTLKMTSLTTEDTATYFCAR	DYWLSL	WGQGTLVTVSS	(SEQ ID NO: 562)
Ab12	RFTISRTSTTVTLKMTSLTTEDTATYFCAR	DYWLSL	WGQGTLVTVSS	(SEQ ID NO: 602)
Ab13	RFTISKTSSTTVDLKMTSPTTEDTATYFCAR	GGGEFFI	WGPGTLVTVSS	(SEQ ID NO: 122)
Ab14	RFTISKVSSTTVDLKMTSPTTEDTATYFCAR	GGGEFFI	WGQGTLVTVSS	(SEQ ID NO: 162)
Ab15	RFTISRTSSTTVNLKMTSPTTEDTATYFCAR	GGGEFFI	WGQGTLVTVSS	(SEQ ID NO: 202)
Ab16	RFTISKTSSTTVDLKMTSPTTEDTATYFCAR	GGGEFFI	WGPGTLVTVSS	(SEQ ID NO: 242)
Ab17	RFTISKTSSTTVDLKMTSPTTEDTATYFCAR	GGGEFFI	WGPGTLVTVSS	(SEQ ID NO: 282)
Ab18	RFTISKTSSTTVDLKVTSPTTEDTATYFCAR	GGGEFFI	WGQGTLVTVSS	(SEQ ID NO: 322)
Ab19	RFTISKTSSTTVDLKMTSPTTEDTATYFCAR	GGGEFFI	WGPGTLVTVSS	(SEQ ID NO: 362)
Ab22	RFTISRTSSTTVTLQMTSLTAADTATYFCAR	DFDL	WGQGTLVTVSS	(SEQ ID NO: 882)
Ab23	RFTISKTSTTVDLKMTSLTTEDTATYFCTR	EIRDDGDSSDKL	WGPGTLVTVSS	(SEQ ID NO: 922)

Figure 2A

Antibody Variable Light Chain Protein Features

Sequence Name	FR1	CDR1	FR2	CDR2
Ab1	DPVMTQTPSSTSAAVGGTVTISC	QSSESVYSNYLS	WYQQKPGQPPNFLIY	QASNLAS
Ab1.H	DIQMTQSPSTLSASVGDRVTITC	QSSESVYSNYLS	WYQQKPGKAPKFLIY	QASNLAS
Ab2	AQVLTQTPSPVSAAVGGTVTINC	QSSESVYKNNYLS	WYQQKPGQPPKFLIY	QASNLAD
Ab3	AAVLTQTPSPVSAAVGGTVTINC	QASQSIGSDLA	WYQQKPGQPPKLLIY	DASTLAS
Ab4	ALVMTQTPSSVSAAVGGTVTINC	LASQNIYNSLA	WYQQKPGQPPKLLIY	RASTLAS
Ab5	DVVMTQTPASVSEPVGGTVTIKC	QASENIYNSLL	WYQQKPGQPPKLLIY	RASTLAS
Ab6	AQVLTQTPSSVSAAVGGTVTINC	QSSPSVYSNNYLS	WFQQKPGQPPKGLIA	DASTLAS
Ab7	AAVLTQTPSPVSAAVGGTVTIKC	QSSQSVYDNNALA	WYQQKPGQPPKLLIY	AASTLAS
Ab8	AQVLTQTPSSVSAAVGGTVTINC	QSSPSVYSSYLS	WFQQKPGQPPKFLIY	EASKLAS
Ab9	AQVLTQTPSSVSAAVGGTVTINC	QSSPSIYSGAFLS	WFQQKPGQPPKFLIY	EASKLAS
Ab11	AAVLTQTPSPVSAAVGGTVTIKC	QSSQSVYDNNALA	WYQQKPGQPPKLLIY	AASNLAS
Ab12	AAVLTQTPSPVSAAVGGTVTIKC	QSSQSVYDNNALA	WYQQKPGQPPKLLIY	AASTLAS
Ab13	AQVLTQTPSSVSAAVGGTVTINC	QSSQSVHDGSYLS	WYQQKPGQPPNFLIY	QASNLAS
Ab14	AQVLTQTPSSVSAAVGGTVTINC	QSSQSVYSNNRLS	YYQQKPGQPPKLLIY	EASSLAY
Ab15	AQVLTQTPSSVSAAVGGTVTINC	QSSQSVYSNNRLS	WYQQKPGQPPNLLIY	EASSLAS
Ab16	DPVLTQTPSSVSAAVGGTVTINC	QSSQSVYNNKWLS	WYQQKPGQSPKFLIY	QASNLAS
Ab17	AQVLTQTPSSVSAAVGGTVTINC	QSSQSVYKNKYLS	WYQQKVGQPPKFLIY	QASNLAS
Ab18	AQVLTQTPSSVSAAVGGTVTINC	QSSKSVYNNNWLS	WYQQKPGQPPKFLIY	QASNLAS
Ab19	AQVLTQTPSSVSAAVGGTVTINC	QSSESVYTNDRLS	WYQQKPGQPPKLLIY	EASKLAS
Ab22	AAVLTQTPSPVSAAVGGTVTINC	QSSQSVYDNDWLA	WFQQKPGQPPKLLIY	LTSTLAS
Ab23	AIKMTQTPSSVSAAVGGTVTINC	QASEDIYTNLA	WYQQKPGQPPNLLIY	DASDLAS

Figure 2B

Antibody Variable Light Chain Protein Features

Sequence Name	FR3	CDR3	FR4	
Ab1	GVPSRFKGSGSGTQFTLTITDLECDDAATYYC	AGGYSENIVG	FGGGTEVVVKR	(SEQ ID NO: 22)
Ab1.H	GVPSRFSGSGSGTEFTLTISSLQPDDFATYYC	AGGYSENIVG	FGGGTKVEIKR	(SEQ ID NO: 62)
Ab2	GVPSRFKGSGSGTQFTLTISDLECDDAATYYC	AGGYSTYMSG	FGGGTEVVVKR	(SEQ ID NO: 102)
Ab3	GVPSRFSGSGSGTQFTLTISGVQCDDAATYYC	QGTYYSSGWYTA	FGGGTEVVVKR	(SEQ ID NO: 702)
Ab4	GVSSRFKGSGSGTQFTLTISGVECADAATYYC	QQGAGADNIGNP	FGGGTEVVVKR	(SEQ ID NO: 662)
Ab5	GVSSRFKGSGSGTEFTLTISDLECADAATYYC	QNYYNIWTNGAA	FGGGTEVVVKR	(SEQ ID NO: 502)
Ab6	GVPSRFKGSGSGTQFTLTISGVQCDDAAAYYC	LGYYDCGSTDCHA	FGGGTEVVVKR	(SEQ ID NO: 742)
Ab7	GVPSRFKGSGSGTQFTLTINGVQCDDAATYYC	LGGYDDPADNA	FGGGTEVVVKR	(SEQ ID NO: 542)
Ab8	GVPSRFSGSGSGTQFTLTISGVQCSDAATYYC	LGAYDCGRTDCHA	FGGGTEVVVKR	(SEQ ID NO: 782)
Ab9	GVPSRFSGSGSGTQFTLTISDVQCDDAATYYC	LGFYDCSSVDCHA	FGGGTEVVVKR	(SEQ ID NO: 822)
Ab11	GVPDRFSGSGSGTQFTLTISGVQCDDAATYYC	LGGYDDAADNA	FGGGTEVVVKR	(SEQ ID NO: 582)
Ab12	GVPSRFSGSGSGTEFTLTISGVQCDDAATYYC	LGGYYDPADNA	FGGGTEVVVKR	(SEQ ID NO: 622)
Ab13	GVPSRFKGSGSGTQFTLTISDLECDDAATYYC	AGGYSSNICG	FGGGTEVVVKR	(SEQ ID NO: 142)
Ab14	GVPSRFKGSGSGTQFTLTISDLECDDAATYYC	AGAYSNSIYS	FGGGTEVVVKR	(SEQ ID NO: 182)
Ab15	GVPSRFSGSGSGTQFTLTISDLECDDAATYYC	AGAYNTGIYG	FGGGTEVVVKR	(SEQ ID NO: 222)
Ab16	GVPSRFKGSGSGTQFTLTISDLECDDGATYYC	AGGYRGNVCG	FGGGTEVVVKR	(SEQ ID NO: 262)
Ab17	GVPSRFKGSGSGTQFTLTISDLECDDAATYYC	AGGYSGNMVD	FGGGTEVVVKR	(SEQ ID NO: 302)
Ab18	GVPSRFKGSGSGTQFTLTISDLECDDAATYYC	AGGYSGNIVG	FGGGTEVVVKR	(SEQ ID NO: 342)
Ab19	GVPPRFSGSGSGTQFTLTISDLECDDAATYYC	AGAYSTSIHG	FGGGTEVVVKR	(SEQ ID NO: 382)
Ab22	GVPSRFSGSGSGTQFTLTISGVQCDDAATYYC	LGGYDEDGDTHV	FGGGTEVVVKR	(SEQ ID NO: 902)
Ab23	GVPSRFSGSGDGTQFTLTISAVQCEDAATYYC	QGVAWSSNTGYGSA	FGGGTEVVVKR	(SEQ ID NO: 942)

Figure 3A

Antibody Variable Heavy Chain DNA Features

Sequence Name	FR1
Ab1	cagtcggtggaggagtccgggggtcgcctggtcacgcctgggacacccctgacactcacctgcaccgtctctggat
Ab1.H	gaggtgcagcttgtggagtctgggggaggcttggtccagcctgggggggtccctgagactctcctgtgcagcctctg
Ab2	cagtcggtggaggagtccgggggtcgcctggtcacgcctgggacacccctgacactcacctgcaccgtctctggat
Ab3	caggagcagctggtggagtccgggggaggcctggtccagcctgagggatccctgacactcacctgcacagcctctg
Ab4	cagtcggtggaggagtccgggggtcgcctggtcacgcctgggacacccctgacactcacctgcaccgtctctggat
Ab5	cagtcggtggaggagtccgggggtcgcctggtcacgcctgggacacccctgacactcacctgcacagtctctggat
Ab6	cagcagctggagcagtccggaggaggagccgaaggaggcctggtcaagcctgggggatccctggaactctgctgca
Ab7	cagtcggtggaggagtccgggggtcgcctggtaacgcctgggacacccctgacactcacctgcacagcctctggaa
Ab8	cagcagctggagcagtccggaggaggagccgaaggaggcctggtcaagcctgggggatccctggaactctgctgca
Ab9	cagcagctggagcagtccggaggaggagccgaaggaggcctggtcaagcctgggggatccctgaaactctcctgca
Ab11	cagtcggtggaggagtctgggggtcgcctggtcacgcctgggacacccctgacactcacctgcacagcctctggat
Ab12	cagtcggtggaggagtccgggggtcgcctggtcacgcctgggacacccctgacactcacctgcacagcctctggat
Ab13	cagtcggtggaggagtccgggggtcgcctggtcacgcctgggacacccctgacactcacctgcaccgtctctggat
Ab14	cagtcggtggaggcgtccgggggtcgcctggtcacgcctgggacacccctgacactcacctgcaccgtctctggat
Ab15	cagtcggtggaggcgtccgggggtcacctagtcacgcctgggacacccctgacactcacctgcaccgtctctggat
Ab16	cagtcggtggaggagtccgggggtcgcctggtcacgcctgggacacccctgacactcacctgcaccgtctctggat
Ab17	cagtcagtggaggagtccgggggtcgcctggtcacgcctgggacacccctaacactcacctgcaccgtctctggat
Ab18	cagtcggtggaggagtccgggggtcgcctggtcacgcctgggacacccctgacactcacctgcaccgtctctggat
Ab19	cagtcggtggaggcgtccgggggtcgcctggtcacgcctgggacacccctgacactcacctgcaccgtctctggat
Ab22	caggagcagctggtggagtccgggggaggcctggtccagcctgagggatccctgacactcacctgcacagcctctg
Ab23	cagtcggtggaggagtccgggggtcgcctggtcacgcctgggacacccctgacactcacctgcaccgtctctggat

Figure 3B

Antibody Variable Heavy Chain DNA Features

Sequence Name	FR1	CDR1	FR2
Ab1	tctccctcagt	agcgctgtaatgaat	tgggtccgccaggctccagggaagggctggaat
Ab1.H	gattcaccgtcagt	agcgctgtaatgaat	tgggtccgtcaggctccagggaagggctggagt
Ab2	tctccctcagt	ggcgctgcgatgaac	tgggtccgccaggctccagggaagggctggaat
Ab3	gattctccttcagt	agcagcgactacatgtgc	tgggtccgccaggctccagggaagggctggagt
Ab4	tctccctcagc	agctacgacatgagc	tgggtccgccaggctccagggaaagggctggaat
Ab5	tctccctcagt	agctatgcgatgatc	tgggtccgccaggctccagggaagggctggaat
Ab6	aggcctctggattctccctcagt	agcacctactggatgtgc	tgggtccgccaggctccagggaagggctggagt
Ab7	tcgacctcagt	ggctatgcaatgggc	tgggtccgccaggctccagggaagggctggaat
Ab8	aagcctctggattctccctcact	acgagccactggatgtgt	tgggtccgccaggctccagggaagggctgaatt
Ab9	aagcctctggattcaccatcagt	agggactactggatatgt	tgggtccgccaggctccagggaagggctggagt
Ab11	tctccctcagt	agatatgcaatgggc	tgggtccgccaggctccagggaagggctggaat
Ab12	tctccctcagt	agctatgcaatgggc	tgggtccgccaggctccagggaagggctggaat
Ab13	tctccctcagt	agcgctgcaatgaac	tgggtccgccaggctccagggaagggctggaat
Ab14	tctccctcagt	agcgctgcaatgaac	tgggtccgccaggctccagggaagggctggaat
Ab15	tctccctcagt	agcgctgcaatgaac	tgggtccgccaggctccagggaagggctggaat
Ab16	tctccctcagt	agcgctgcaatgagc	tgggtccgccaggctccagggaagggctggaat
Ab17	tctccctcagt	agcgctgcaatgaac	tgggtccgccaggctccagggaagggctggaat
Ab18	tctccctcagt	agcgctgcattgagc	tgggtccgccaggctccagggaagggctggaat
Ab19	tctccctcagt	agcgctacaatgaac	tgggtccgccaggctccagggaagggctggaat
Ab22	gattcgacttcagt	agcaatgcaatgtgc	tgggtccgccaggctccagggaagggcctggagt
Ab23	tctccctcaat	aactatgcaatgagc	tgggtccgccaggctccagggaagggctggaat

Figure 3C

Antibody Variable Heavy Chain DNA Features

Sequence Name	FR2	CDR2
Ab1	ggatcgga	agtattgttgctagtggtaccacatactacgcgagctgggcgaacggc
Ab1.H	ggatcgga	agtattgttgctagtggtaccacatactacgctagcctctgctaacggc
Ab2	ggatcgga	gttattggtaatagtggtagcacatactacgcgtcctgggcgaaaggc
Ab3	ggatcgga	tgcattgatgctggtagtagtggtgacacttactacgcgagctgggcgaaaggc
Ab4	acatcggc	atcattaatactaatgatgacacatggtacgcgagctgggtgaaaggc
Ab5	ggatcgga	atcatttatgataaatggtgacacatactacgcgagctgggcgaaaggc
Ab6	ggattgga	tgcatttatactggtagtggtagcacagactacgcgagctgggtgaatggc
Ab7	ggatcgga	gacattagtacctatggtaccacagactacgcgagctgggtgaatggc
Ab8	ggattgga	tgcattagtgccggtagtggtgacgcagactacgcgacctgggtggatgcc
Ab9	ggattgga	tgcattagtgctggtggtggtagcacagactacgcgaactgggtgaatggc
Ab11	ggatcgga	gacattagtacttatggtaccacagactacgcgagctgggtgaatggc
Ab12	ggatcgga	gacattagtacttatggtaccacagactacgcgagctgggtgtatggc
Ab13	ggatcgga	attattgataatactgctggcacatattacgcgccctgggcgaaaggc
Ab14	ggatcgga	tttattgagtatagtaagaatatagtttacgcgtccctgggcgaaaggc
Ab15	ggatcgga	tcggttgatgagcgtcagaataaatattacgcgtcctgggcgaaaggc
Ab16	ggatcgga	attattgatgatagtggtaacacatactacgcgtcctgggcgaaagcc
Ab17	ggatcggt	attttgatccttatagtagtacatactacgcgtcctgggcgaaaggc
Ab18	ggatcgga	attattgataagggtgttatgtctttactacgcgtcctgggcgaaaggc
Ab19	ggatcggg	cttattggcggtaatgacgaaagatactacgcgtcctgggcgaaaggc
Ab22	ggatcgga	tccatttataatgctgatggtaagaattattacgcgatttgggcgaaaggc
Ab23	ggatcgga	atcatgggtgttaatgatatcacatactacgcgagctgggcgaaaggc

Figure 3D

Antibody Variable Heavy Chain DNA Features

Sequence Name	FR3
Ab1	cgattcaccatctccaaaacctcgtcgaccacgatggatctgaaaatgaccagtccgacaaccgaggacacggcca
Ab1.H	cgattcaccatctccagagacaattccaagaacaccctgtatcttcaaatgaacagcctgagagctgaggacactg
Ab2	cgattcaccatctccaaaacctcgtcgaccacggtggatctgaaaatgaccagtccgacaaccgaggacacggcca
Ab3	cgattcaccatctccaaaacctcgtcgaccacggtgactctgcaaatgaccagtctgacagccgcggacacggcca
Ab4	cgattcaccatctccaaaacctcgtcgaccacggtggatctgaaaatgaccagtctgacaaccgaggacacggcca
Ab5	cggttcaccatctccaaaacctcgaccacggtgtatctgaagatcgccagtccgacaaccgaggacacggccacct
Ab6	caattcactctctccagagacatcgaccagagcacaggttgcctacaactgaacagtctgacagtcgcggacacgg
Ab7	cgattcaccatctccagaacctcgaccacggtgactctgaaaatgaccagtctgacaaccgaggacacggccacct
Ab8	caattcactctctccagagacatcgaccagaacacaggttgcctacaattgaacagtctgacacccgcggacacgg
Ab9	cgattcactctctccagagacatcgaccagagcacaggttgccttcaactgaacagtctgacagacgcggacacgg
Ab11	cgattcaccatctccagaacctcgaccacggtgactctgaaaatgaccagtctgacaaccgaggacacggccacct
Ab12	cgattcaccatctccagaacctcgaccacggtgactctgaaaatgaccagtctgacaaccgaggacacggccacct
Ab13	cgattcaccatctccaaaacctcgtcgaccacggtggatctgaaaatgaccagtccgacaaccgaggacacggcca
Ab14	cgattcaccatctccaaagtctcgtcgaccacggtggatctgaaaatgaccagtccgacaaccgaggacacggcca
Ab15	cgattcaccatctccagaacctcgtcgaccacggtgaatctgaaaatgaccagtccgacaaccgaggacacggcca
Ab16	cgattcaccatctccaaaacctcgtcgaccacggtggatctgaaaatgaccagtccgacaaccgaggacacggcca
Ab17	cgattcaccatctccaaaacctcgtcgaccacggtggatctgaaaatgaccagtccgacaaccgaggacacggcca
Ab18	cgattcaccatctccaaaacctcgtcgaccacggtggatctaaaagtgaccagtccgacaaccgaggacacggcca
Ab19	cgattcaccatctccaaaacctcgtcgaccacggtggatctgaaaatgaccagtccgacaaccgaggacacggcca
Ab22	cgattcaccatctccagaacctcgtcgaccacggtgactctgcaaatgaccagtctgacagccgcggacacggcca
Ab23	cgattcaccatctccaaaacctcgaccacggtggatctgaaaatgaccagtctgacaaccgaggacacggccacct

Figure 3E

Antibody Variable Heavy Chain DNA Features

Sequence Name	FR3	CDR3
Ab1	cctatttctgtgccaga	gggggaggggaatttttcatc
Ab1.H	ctgtgtattactgtgctaga	gggggaggggaatttttcatc
Ab2	cctatttctgtgccaga	gggggaggggaatttttcatc
Ab3	cctatttctgtgcgaga	catctttatggtagtattactttcgcctttggcttg
Ab4	cctatttctgtgccaga	atatccgatgcttatgtttttgattatgcgtattactttactttg
Ab5	acttctgtgccaga	gagcctggtagtactactcagaatgacttg
Ab6	ccatgtattactgtacgaaa	aattttgacttg
Ab7	atttctgtgccaga	gactattggttgagcttg
Ab8	ccatgtattactgtacgata	aattttgagttg
Ab9	ccatgtattactgtgcggga	aatctagagatc
Ab11	atttctgtgccaga	gactattggttgagcttg
Ab12	atttctgtgccaga	gactattggttgagcttg
Ab13	cctatttctgtgccaga	gggggaggggaatttttcatc
Ab14	cctatttctgtgccagg	gggggaggggaatttttcatc
Ab15	cctatttctgtgccaga	gggggaggggaatttttcatc
Ab16	cctatttctgtgccaga	gggggaggggagtttttcatc
Ab17	cctatttctgtgccaga	gggggaggggaatttttcatc
Ab18	cctatttctgtgccaga	gggggggggggaatttttcatc
Ab19	cctatttctgtgccaga	gggggggggggaatttttcatc
Ab22	cctatttctgtgcgaga	gactttgacttg
Ab23	atttctgtactaga	gagatccgtgatgatggtgatagttctgataagttg

Figure 3F

Antibody Variable Heavy Chain DNA Features

Sequence Name	FR4	
Ab1	tggggcccggggaccctcgtcaccgtctcgagc	(SEQ ID NO: 12)
Ab1.H	tggggccaagggaccctcgtcaccgtctcgagc	(SEQ ID NO: 52)
Ab2	tggggccaagggaccctggtcaccgtctcgagc	(SEQ ID NO: 92)
Ab3	tggggccagggcaccctggtcaccgtctcgagc	(SEQ ID NO: 692)
Ab4	tggggccaggggaccctggtcaccgtctcgagc	(SEQ ID NO: 652)
Ab5	tggggccaagggaccctggtcaccgtctcgagc	(SEQ ID NO: 492)
Ab6	tggggcccgggcaccctggtcaccgtctcgagc	(SEQ ID NO: 732)
Ab7	tggggcccgggcaccctcgtcaccgtctcgagc	(SEQ ID NO: 532)
Ab8	tggggccaaggcaccctggtcaccgtctcgagc	(SEQ ID NO: 772)
Ab9	tggggccaagggaccctggtcaccgtctcgagc	(SEQ ID NO: 812)
Ab11	tggggccaaggcaccctcgtcaccgtctcgagc	(SEQ ID NO: 572)
Ab12	tggggccaaggcaccctggtcaccgtctcgagc	(SEQ ID NO: 612)
Ab13	tggggcccgggcaccctcgtcaccgtctcgagc	(SEQ ID NO: 132)
Ab14	tggggccaaggcaccctggtcaccgtctcgagc	(SEQ ID NO: 172)
Ab15	tggggccagggcaccctcgtcaccgtctcgagc	(SEQ ID NO: 212)
Ab16	tggggcccgggcaccctcgtcaccgtctcgagc	(SEQ ID NO: 252)
Ab17	tggggcccaggcaccctcgtcaccgtctcgagc	(SEQ ID NO: 292)
Ab18	tggggccagggcaccctcgtcaccgtctcgagc	(SEQ ID NO: 332)
Ab19	tggggcccgggcaccctggtcaccgtctcgagc	(SEQ ID NO: 372)
Ab22	tggggccagggcaccctcgtcaccgtctcgagc	(SEQ ID NO: 892)
Ab23	tggggcccgggcaccctcgtcaccgtctcgagc	(SEQ ID NO: 932)

Figure 4A

Antibody Variable Light Chain DNA Features

Sequence Name	FR1
Ab1	gaccctgtgatgacccagactccatcttccacgtctgcggctgtgggaggcacagtcaccatcagttgc
Ab1.H	gacatccagatgacccagtctccttccaccctgtctgcatctgtaggagacagagtcaccatcacttgt
Ab2	gcccaagtgctgacccagactccatccccagtgtctgcagctgtgggaggcaccgtcaccatcaattgc
Ab3	gcagccgtgctgacccagacaccatcgcccgtgtctgcagctgtgggaggcacagtcaccatcaattgc
Ab4	gcccttgtgatgacccagactccatcctccgtgtctgcagctgtgggaggcacagtcaccatcaattgc
Ab5	gatgttgtgatgacccagactccagcctccgtgtctgaacctgtgggaggcacagtcaccatcaagtgc
Ab6	gcccaagtgctgacccagactccatcctccgtgtctgcagctgtgggaggcacagtcaccatcaattgc
Ab7	gcagccgtgctgacccagacaccatcgcccgtgtctgcagctgtgggaggcacagtcaccatcaagtgc
Ab8	gcccaagtgctgacccagactccatcctccgtgtctgcagctgtgggaggcacagtcaccatcaattgc
Ab9	gcccaagtgctgacccagactccatcctccgtgtctgcagctgtgggaggcacagtcaccatcaattgc
Ab11	gcagccgtgctgacccagacaccatcgcccgtgtctgcagctgtgggaggcacagtcaccatcaagtgc
Ab12	gcagccgtgctgacccagacaccatcgcccgtgtctgcagctgtgggaggcacagtcaccatcaagtgc
Ab13	gcgcaagtgctgacccagactccatcgtccgtgtctgcagctgtgggaggcacagtcaccatcaattgc
Ab14	gcgcaagtgctgacccagactccatcgtccgtgtctgcagctgtgggaggcacagtcaccatcaattgc
Ab15	gcgcaagtgctgacccagactccatcgtccgtgtctgcagctgtgggaggcacagtcaccatcaattgc
Ab16	gaccctgtgctgacccagactccatcgtccgtgtctgcagctgtgggaggcacagtcaccatcaattgc
Ab17	gcccaagtgctgacccagactccatcgtccgtgtctgcagctgtgggaggcacagtcaccatcaattgc
Ab18	gcgcaagtgctgacccagactccatcgtccgtgtctgcagctgtgggaggcacagtcaccatcaattgc
Ab19	gcgcaagtgctgacccagactccatcgtccgtgtctgcagctgtgggaggcacagtcaccatcaattgc
Ab22	gcagccgtgctgacccagacaccatcgcccgtgtctgcagctgtgggaggcacagtcaccatcaattgc
Ab23	gccatcaaaatgacccagactccatcctccgtgtctgcagctgtgggaggcacagtcaccatcaattgc

Figure 4B

Antibody Variable Light Chain DNA Features

Sequence Name	CDR1	FR2
Ab1	cagtccagtgagagtgtttatagtaactacttatcc	tggtatcagcagaaaccagggcagcctcccaacttcc
Ab1.H	cagtccagtgagagtgtttatagtaactacttatcc	tggtatcagcagaaaccaggaaaagcccctaagttcc
Ab2	cagtccagtgagagtgtttataagaacaactacttatcc	tggtatcagcagaaaccagggcagcctcccaagttcc
Ab3	caggccagtcagagcattggtagcgacttagcc	tggtatcagcagaaaccagggcagcctcccaagctcc
Ab4	ctggccagtcagaacatttacaattctttagcc	tggtatcagcagaaaccagggcagcctcccaagctcc
Ab5	caggccagtgagaacatttacaactctttactc	tggtatcagcagaaaccagggcagcctcccaagctcc
Ab6	cagtccagtccgagtgtttatagtaacaactacttatcc	tggtttcagcagaaaccagggcagcctcccaaaggcc
Ab7	cagtccagtcagagtgtttatgataacaatgctttagcc	tggtatcagcagaaaccagggcagcctcccaagctcc
Ab8	cagtccagtccgagtgtttatagtagctacttatcc	tggtttcagcagaaaccagggcagcctcccaagttcc
Ab9	cagtccagtccgagtatttatagtggcgccttttttatcc	tggtttcagcagaaaccagggcagcctcccaagttcc
Ab11	cagtccagtcagagtgtttatgataacaatgctttagcc	tggtatcagcagaaaccaggacagcctcccaagctcc
Ab12	cagtccagtcagagtgtttatgataacaatgctttagcc	tggtatcagcagaaaccagggcagcctcccaagctcc
Ab13	cagtccagtcagagtgttcatgatggcagctacttatcc	tggtatcagcagaaaccagggcagcctcccaacttcc
Ab14	cagtccagtcagagtgtttatagtaacaaccggttatcg	tactatcagcagaaaccagggcagcctcccaagctcc
Ab15	cagtccagtcagagtgtttatagtaacaaccgcttatcc	tggtatcagcagaaaccagggcagcctcccaatctcc
Ab16	cagtccagtcagagtgtttataataacaagtggttatcc	tggtatcagcagaaaccaggacagtctcccaagttcc
Ab17	cagtccagtcagagtgtttataagaataagtacttatcc	tggtatcagcagaaagtagggcagcctcccaagttcc
Ab18	cagtccagtaagagtgtttataacaacaattggttatcc	tggtatcaacagaaaccagggcagcctcccaagttcc
Ab19	cagtccagtgagagtgtttatactaacgaccgcttatcc	tggtatcagcagaaaccagggcagcctcccaagctcc
Ab22	cagtccagtcagagtgtttatgataacgactggttagcc	tggttccagcagaaaccagggcagcctcccaagctcc
Ab23	caggccagtgaggacatttacaccaatttagcc	tggtatcagcagaaaccagggcagcctcccaacctcc

Figure 4C

Antibody Variable Light Chain DNA Features

Sequence Name	FR2	CDR2	FR3
Ab1	tgatctac	caggcatccaatttggcatct	ggggtcccatcgcggttcaaaggcagtggatctgggacacagttca
Ab1.H	tgatctat	caggcatccaatttggcatct	ggagtcccatcaaggttcagcggcagtggatctggaacagaattca
Ab2	tgatctac	caggcatccaatttggcagat	ggggtcccatcgcggttcaaaggcagtggatctgggacacagttca
Ab3	tgatctat	gatgcatccactctggcatct	ggggtcccatcgcggttcagcggcagtggatctgggacacagttca
Ab4	tgatctac	agggcatccactctggcatct	ggggtctcatcgcggttcaaaggcagtggatctgggacacagttca
Ab5	tgatctat	agggcatccactctggcatct	ggggtctcatcgcggttcaaaggcagtggatctgggacagagttca
Ab6	tgatcgct	gatgcatccactctggcatct	ggggtcccatcgcggttcaaaggcagtggatctgggacacagttca
Ab7	tgatctat	gctgcatccactctggcatct	ggggtcccatcgcggttcaaaggcagtggatctgggacacagttca
Ab8	tgatctac	gaagcatccaaactggcatct	ggggtcccatcgcggttcagcggcagtggatctgggacacagttca
Ab9	tgatctac	gaagcctccaaactggcatct	ggggtcccatcgcggttcagtggcagtggatctgggacacagttca
Ab11	tgatctat	gctgcatccaatctggcatct	ggggtcccagataggttcagcggcagtggatctgggacacagttca
Ab12	tgatctat	gctgcatccactctggcatct	ggggtcccatcgcggttcagtggcagtggatctgggacagagttca
Ab13	tgatctac	caggcatccaatttggcatct	ggggtcccatcgcggttcaaaggcagtggatctgggacacagttca
Ab14	tgatctac	gaagcatccagtctggcatat	ggggtcccatcgcggttcaaaggcagtggatctgggacacagttca
Ab15	tgatctac	gaagcatccagtctggcatct	ggggtcccatcgcggttcagcggcagtggatctgggacacagttca
Ab16	tgatttac	caggcatccaatttggcatct	ggggtcccatcgcggttcaaaggcagtggatctgggacacagttca
Ab17	tgatctac	caggcatccaatttggcatct	ggggtcccatcgcggttcaaaggcagtggatctgggacacagttca
Ab18	tgatctac	caggcatccaatttggcatct	ggggtcccgtcgcggttcaaaggcagtggatctgggacacagttca
Ab19	tgatctac	gaagcatccaagctggcatct	ggggtcccaccgcggttcagcggcagtggatctgggacacagttca
Ab22	tgatctat	ctgacatccactctggcatct	ggagtcccatcgcggttcagcggcagtggatctgggacacagttca
Ab23	tgatctat	gatgcatccgatctggcatct	ggggtcccgtcgcggttcagcggcagtggagatgggacacagttca

Figure 4D

Antibody Variable Light Chain DNA Features

Sequence Name	FR3	CDR3
Ab1	ctctcaccatcaccgacctggagtgtgacgatgccgccacttattactgt	gcaggcggttatagtgaaaacattg
Ab1.H	ctctcaccatcagcagcctgcagcctgatgattttgcaacttactactgt	gcaggcggttatagtgaaaacattg
Ab2	ctctcaccatcagcgacctggagtgtgacgatgccgccacttattactgt	gcaggcggttatagtacttatatgt
Ab3	ctctcaccatcagcggcgtgcagtgtgacgatgctgccacttactactgt	caaggcacttattatagtagtggtt
Ab4	ctctcaccatcagcggcgtggagtgtgccgatgctgccacttactactgt	caacagggtgctggtgctgataata
Ab5	ctctcaccatcagcgacctggagtgtgccgatgctgccacttactactgt	caaaactattataatatatggacta
Ab6	ctctcaccatcagcggcgtgcagtgtgacgatgctgccgcttactactgt	ctaggctattatgattgtggtagta
Ab7	ctctcaccatcaacggcgtgcagtgtgacgatgctgccacttactactgt	ctaggcggttatgatgatcctgctg
Ab8	ctctcaccatcagcggcgtgcagtgtagcgatgctgccacttactactgt	cttggcgcgtatgattgtggtcgta
Ab9	ctctcaccatcagcgacgtacagtgtgacgatgctgccacttactactgt	ctaggcttttatgattgtagcagtg
Ab11	ctctcaccatcagcggcgtgcagtgtgacgatgctgccacttactactgt	ctaggcggttatgatgatgctgctg
Ab12	ctctcaccatcagcggcgtgcagtgtgacgatgctgccacttactactgt	ctaggcggttattatgatcctgctg
Ab13	ctctcaccatcagcgacctggagtgtgacgatgccgccacttattactgt	gcaggcggttatagtagtaatattt
Ab14	ctctcaccatcagcgacctggagtgtgacgatgccgccacttattactgt	gcaggtgcctatagtaatagtattt
Ab15	ctctcaccatcagcgacctggagtgtgacgatgccgccacttattactgt	gcaggcgcttataatactgggattt
Ab16	ctctcaccatcagcgacctggagtgtgacgatggcgccacttattactgt	gcaggcggctaccgtggtaatgttt
Ab17	ctctcaccatcagcgacctggagtgtgacgatgccgccacttattactgt	gcaggcggttatagtggtaatatgg
Ab18	ctctcaccatcagcgacctcgagtgtgacgatgccgccacttattactgt	gcaggcggttatagtggtaatattg
Ab19	ctctcaccatcagcgacctggagtgtgacgatgccgccacttattactgt	gcaggcgcttatagtactagtatcc
Ab22	ctctcaccatcagtggtgtgcagtgtgacgatgctgccacttactactgt	ctaggcggctatgatgaagatggtg
Ab23	ctctcaccatcagcgccgtgcagtgtgaagatgctgccacttactactgt	caaggtgttgcttggagtagtaata

Figure 4E

Antibody Variable Light Chain DNA Features

Sequence Name	CDR3	FR4	
Ab1	ttggt	ttcggcggagggaccgaggtggtggtcaaacgt	(SEQ ID NO: 32)
Ab1.H	ttggt	ttcggcggaggaaccaaggtggaaatcaaacgt	(SEQ ID NO: 72)
Ab2	ctggt	ttcggcggagggaccgaggtggtggtcaaacgt	(SEQ ID NO: 112)
Ab3	ggtacactgct	ttcggcggagggaccgaggtggtggtcaaacgt	(SEQ ID NO: 712)
Ab4	ttggtaatcct	ttcggcggagggaccgaggtggtggtcaaacgt	(SEQ ID NO: 672)
Ab5	atggtgctgct	ttcggcggagggaccgaggtggtggtcaaacgt	(SEQ ID NO: 512)
Ab6	ctgattgtcatgct	ttcggcggagggaccgaggtggtggtcaaacgt	(SEQ ID NO: 752)
Ab7	ataatgct	ttcggcggagggaccgaggtggtggtcaaacgt	(SEQ ID NO: 552)
Ab8	ctgattgtcatgct	ttcggcggagggaccgaggtggtggtcaaacgt	(SEQ ID NO: 792)
Ab9	ttgattgccatgct	ttcggcggagggaccgaggtggtggtcaaacgt	(SEQ ID NO: 832)
Ab11	ataatgct	ttcggcggagggaccgaggtggtggtcaaacgt	(SEQ ID NO: 592)
Ab12	ataatgct	ttcggcggagggaccgaggtggtggtcaaacgt	(SEQ ID NO: 632)
Ab13	gtggt	ttcggcggagggaccgaggtggtggtcaaacgt	(SEQ ID NO: 152)
Ab14	atagt	ttcggcggagggaccgaggtggtggtcaaacgt	(SEQ ID NO: 192)
Ab15	atggt	ttcggcggagggaccgaggtggtggtcaaacgt	(SEQ ID NO: 232)
Ab16	gtggt	ttcggcggagggaccgaggtggtggtcaaacgt	(SEQ ID NO: 272)
Ab17	ttgat	ttcggcggagggaccgaggtggtggtcaaacgt	(SEQ ID NO: 312)
Ab18	ttggt	ttcggcggagggaccgaggtggtggtcaaacgt	(SEQ ID NO: 352)
Ab19	atggt	ttcggcggagggaccgaggtggtggtcaaacgt	(SEQ ID NO: 392)
Ab22	atacgcatgtt	ttcggcggagggaccgaggtggtggtcaaacgt	(SEQ ID NO: 912)
Ab23	ctggttatggttccgct	ttcggcggagggaccgaggtggtggtcaaacgt	(SEQ ID NO: 952)

Figure 5

Antibody Heavy Chain Protein Features

Sequence Name	Variable region coordinates	SEQ ID NO:	CDR1 coordinates	SEQ ID NO:	CDR2 coordinates	SEQ ID NO:	CDR3 coordinates	SEQ ID NO:
Ab1	1-113	2	30-34	4	49-64	6	96-102	8
Ab1.H	1-115	42	31-35	44	50-65	46	98-104	48
Ab2	1-113	82	30-34	84	49-64	86	96-102	88
Ab3	1-122	682	31-36	684	51-68	686	100-111	688
Ab4	1-121	642	30-34	644	49-64	646	96-110	648
Ab5	1-115	482	30-34	484	49-64	486	95-104	488
Ab6	1-117	722	34-39	724	54-70	726	103-106	728
Ab7	1-111	522	30-34	524	49-64	526	95-100	528
Ab8	1-117	762	34-39	764	54-70	766	103-106	768
Ab9	1-117	802	34-39	804	54-70	806	103-106	808
Ab11	1-111	562	30-34	564	49-64	566	95-100	568
Ab12	1-111	602	30-34	604	49-64	606	95-100	608
Ab13	1-113	122	30-34	124	49-64	126	96-102	128
Ab14	1-113	162	30-34	164	49-64	166	96-102	168
Ab15	1-113	202	30-34	204	49-64	206	96-102	208
Ab16	1-113	242	30-34	244	49-64	246	96-102	248
Ab17	1-113	282	30-34	284	49-64	286	96-102	288
Ab18	1-113	322	30-34	324	49-64	326	96-102	328
Ab19	1-113	362	30-34	364	49-64	366	96-102	368
Ab22	1-112	882	31-35	884	50-66	886	98-101	888
Ab23	1-117	922	30-34	924	49-64	926	95-106	928

Figure 6

Antibody Heavy Chain Protein Features

Sequence Name	FR1 coordinates	SEQ ID NO:	FR2 coordinates	SEQ ID NO:	FR3 coordinates	SEQ ID NO:	FR4 coordinates	SEQ ID NO:	Constant region coordinates	SEQ ID NO:
Ab1	1-29	3	35-48	5	65-95	7	103-113	9	114-443	10
Ab1.H	1-30	43	36-49	45	66-97	47	105-115	49	116-445	50
Ab2	1-29	83	35-48	85	65-95	87	103-113	89	114-443	90
Ab3	1-30	683	37-50	685	69-99	687	112-122	689	123-452	690
Ab4	1-29	643	35-48	645	65-95	647	111-121	649	122-451	650
Ab5	1-29	483	35-48	485	65-94	487	105-115	489	116-445	490
Ab6	1-33	723	40-53	725	71-102	727	107-117	729	118-447	730
Ab7	1-29	523	35-48	525	65-94	527	101-111	529	112-441	530
Ab8	1-33	763	40-53	765	71-102	767	107-117	769	118-447	770
Ab9	1-33	803	40-53	805	71-102	807	107-117	809	118-447	810
Ab11	1-29	563	35-48	565	65-94	567	101-111	569	112-441	570
Ab12	1-29	603	35-48	605	65-94	607	101-111	609	112-441	610
Ab13	1-29	123	35-48	125	65-95	127	103-113	129	114-443	130
Ab14	1-29	163	35-48	165	65-95	167	103-113	169	114-443	170
Ab15	1-29	203	35-48	205	65-95	207	103-113	209	114-443	210
Ab16	1-29	243	35-48	245	65-95	247	103-113	249	114-443	250
Ab17	1-29	283	35-48	285	65-95	287	103-113	289	114-443	290
Ab18	1-29	323	35-48	325	65-95	327	103-113	329	114-443	330
Ab19	1-29	363	35-48	365	65-95	367	103-113	369	114-443	370
Ab22	1-30	883	36-49	885	67-97	887	102-112	889	113-442	890
Ab23	1-29	923	35-48	925	65-94	927	107-117	929	118-447	930

Figure 7

Antibody Light Chain Protein Features

Sequence Name	Variable region coordinates	SEQ ID NO:	CDR1 coordinates	SEQ ID NO:	CDR2 coordinates	SEQ ID NO:	CDR3 coordinates	SEQ ID NO:
Ab1	1-110	22	24-35	24	51-57	26	90-99	28
Ab1.H	1-110	62	24-35	64	51-57	66	90-99	68
Ab2	1-111	102	24-36	104	52-58	106	91-100	108
Ab3	1-111	702	24-34	704	50-56	706	89-100	708
Ab4	1-111	662	24-34	664	50-56	666	89-100	668
Ab5	1-111	502	24-34	504	50-56	506	89-100	508
Ab6	1-114	742	24-36	744	52-58	746	91-103	748
Ab7	1-112	542	24-36	544	52-58	546	91-101	548
Ab8	1-113	782	24-35	784	51-57	786	90-102	788
Ab9	1-114	822	24-36	824	52-58	826	91-103	828
Ab11	1-112	582	24-36	584	52-58	586	91-101	588
Ab12	1-112	622	24-36	624	52-58	626	91-101	628
Ab13	1-111	142	24-36	144	52-58	146	91-100	148
Ab14	1-111	182	24-36	184	52-58	186	91-100	188
Ab15	1-111	222	24-36	224	52-58	226	91-100	228
Ab16	1-111	262	24-36	264	52-58	266	91-100	268
Ab17	1-111	302	24-36	304	52-58	306	91-100	308
Ab18	1-111	342	24-36	344	52-58	346	91-100	348
Ab19	1-111	382	24-36	384	52-58	386	91-100	388
Ab22	1-113	902	24-36	904	52-58	906	91-102	908
Ab23	1-113	942	24-34	944	50-56	946	89-102	948

Figure 8

Antibody Light Chain Protein Features

Sequence Name	FR1 coordinates	SEQ ID NO:	FR2 coordinates	SEQ ID NO:	FR3 coordinates	SEQ ID NO:	FR4 coordinates	SEQ ID NO:	Constant region coordinates	SEQ ID NO:
Ab1	1-23	23	36-50	25	58-89	27	100-110	29	111-216	30
Ab1.H	1-23	63	36-50	65	58-89	67	100-110	69	111-216	70
Ab2	1-23	103	37-51	105	59-90	107	101-111	109	112-217	110
Ab3	1-23	703	35-49	705	57-88	707	101-111	709	112-217	710
Ab4	1-23	663	35-49	665	57-88	667	101-111	669	112-217	670
Ab5	1-23	503	35-49	505	57-88	507	101-111	509	112-217	510
Ab6	1-23	743	37-51	745	59-90	747	104-114	749	115-220	750
Ab7	1-23	543	37-51	545	59-90	547	102-112	549	113-218	550
Ab8	1-23	783	36-50	785	58-89	787	103-113	789	114-219	790
Ab9	1-23	823	37-51	825	59-90	827	104-114	829	115-220	830
Ab11	1-23	583	37-51	585	59-90	587	102-112	589	113-218	590
Ab12	1-23	623	37-51	625	59-90	627	102-112	629	113-218	630
Ab13	1-23	143	37-51	145	59-90	147	101-111	149	112-217	150
Ab14	1-23	183	37-51	185	59-90	187	101-111	189	112-217	190
Ab15	1-23	223	37-51	225	59-90	227	101-111	229	112-217	230
Ab16	1-23	263	37-51	265	59-90	267	101-111	269	112-217	270
Ab17	1-23	303	37-51	305	59-90	307	101-111	309	112-217	310
Ab18	1-23	343	37-51	345	59-90	347	101-111	349	112-217	350
Ab19	1-23	383	37-51	385	59-90	387	101-111	389	112-217	390
Ab22	1-23	903	37-51	905	59-90	907	103-113	909	114-219	910
Ab23	1-23	943	35-49	945	57-88	947	103-113	949	114-219	950

Figure 9

Antibody Heavy Chain DNA Features

Sequence Name	Variable region coordinates	SEQ ID NO:	CDR1 coordinates	SEQ ID NO:	CDR2 coordinates	SEQ ID NO:	CDR3 coordinates	SEQ ID NO:
Ab1	1-339	12	88-102	14	145-192	16	286-306	18
Ab1.H	1-345	52	91-105	54	148-195	56	292-312	58
Ab2	1-339	92	88-102	94	145-192	96	286-306	98
Ab3	1-366	692	91-108	694	151-204	696	298-333	698
Ab4	1-363	652	88-102	654	145-192	656	286-330	658
Ab5	1-345	492	88-102	494	145-192	496	283-312	498
Ab6	1-351	732	100-117	734	160-210	736	307-318	738
Ab7	1-333	532	88-102	534	145-192	536	283-300	538
Ab8	1-351	772	100-117	774	160-210	776	307-318	778
Ab9	1-351	812	100-117	814	160-210	816	307-318	818
Ab11	1-333	572	88-102	574	145-192	576	283-300	578
Ab12	1-333	612	88-102	614	145-192	616	283-300	618
Ab13	1-339	132	88-102	134	145-192	136	286-306	138
Ab14	1-339	172	88-102	174	145-192	176	286-306	178
Ab15	1-339	212	88-102	214	145-192	216	286-306	218
Ab16	1-339	252	88-102	254	145-192	256	286-306	258
Ab17	1-339	292	88-102	294	145-192	296	286-306	298
Ab18	1-339	332	88-102	334	145-192	336	286-306	338
Ab19	1-339	372	88-102	374	145-192	376	286-306	378
Ab22	1-336	892	91-105	894	148-198	896	292-303	898
Ab23	1-351	932	88-102	934	145-192	936	283-318	938

Figure 10

Antibody Heavy Chain DNA Features

Sequence Name	FR1 coordinates	SEQ ID NO:	FR2 coordinates	SEQ ID NO:	FR3 coordinates	SEQ ID NO:	FR4 coordinates	SEQ ID NO:	Constant region coordinates	SEQ ID NO:
Ab1	1-87	13	103-144	15	193-285	17	307-339	19	340-1329	20
Ab1.H	1-90	53	106-147	55	196-291	57	313-345	59	346-1335	60
Ab2	1-87	93	103-144	95	193-285	97	307-339	99	340-1329	100
Ab3	1-90	693	109-150	695	205-297	697	334-366	699	367-1356	700
Ab4	1-87	653	103-144	655	193-285	657	331-363	659	364-1353	660
Ab5	1-87	493	103-144	495	193-282	497	313-345	499	346-1335	500
Ab6	1-99	733	118-159	735	211-306	737	319-351	739	352-1341	740
Ab7	1-87	533	103-144	535	193-282	537	301-333	539	334-1323	540
Ab8	1-99	773	118-159	775	211-306	777	319-351	779	352-1341	780
Ab9	1-99	813	118-159	815	211-306	817	319-351	819	352-1341	820
Ab11	1-87	573	103-144	575	193-282	577	301-333	579	334-1323	580
Ab12	1-87	613	103-144	615	193-282	617	301-333	619	334-1323	620
Ab13	1-87	133	103-144	135	193-285	137	307-339	139	340-1329	140
Ab14	1-87	173	103-144	175	193-285	177	307-339	179	340-1329	180
Ab15	1-87	213	103-144	215	193-285	217	307-339	219	340-1329	220
Ab16	1-87	253	103-144	255	193-285	257	307-339	259	340-1329	260
Ab17	1-87	293	103-144	295	193-285	297	307-339	299	340-1329	300
Ab18	1-87	333	103-144	335	193-285	337	307-339	339	340-1329	340
Ab19	1-87	373	103-144	375	193-285	377	307-339	379	340-1329	380
Ab22	1-90	893	106-147	895	199-291	897	304-336	899	337-1326	900
Ab23	1-87	933	103-144	935	193-282	937	319-351	939	352-1341	940

Figure 11

Antibody Light Chain DNA Features

Sequence Name	Variable region coordinates	SEQ ID NO:	CDR1 coordinates	SEQ ID NO:	CDR2 coordinates	SEQ ID NO:	CDR3 coordinates	SEQ ID NO:
Ab1	1-330	32	70-105	34	151-171	36	268-297	38
Ab1.H	1-330	72	70-105	74	151-171	76	268-297	78
Ab2	1-333	112	70-108	114	154-174	116	271-300	118
Ab3	1-333	712	70-102	714	148-168	716	265-300	718
Ab4	1-333	672	70-102	674	148-168	676	265-300	678
Ab5	1-333	512	70-102	514	148-168	516	265-300	518
Ab6	1-342	752	70-108	754	154-174	756	271-309	758
Ab7	1-336	552	70-108	554	154-174	556	271-303	558
Ab8	1-339	792	70-105	794	151-171	796	268-306	798
Ab9	1-342	832	70-108	834	154-174	836	271-309	838
Ab11	1-336	592	70-108	594	154-174	596	271-303	598
Ab12	1-336	632	70-108	634	154-174	636	271-303	638
Ab13	1-333	152	70-108	154	154-174	156	271-300	158
Ab14	1-333	192	70-108	194	154-174	196	271-300	198
Ab15	1-333	232	70-108	234	154-174	236	271-300	238
Ab16	1-333	272	70-108	274	154-174	276	271-300	278
Ab17	1-333	312	70-108	314	154-174	316	271-300	318
Ab18	1-333	352	70-108	354	154-174	356	271-300	358
Ab19	1-333	392	70-108	394	154-174	396	271-300	398
Ab22	1-339	912	70-108	914	154-174	916	271-306	918
Ab23	1-339	952	70-102	954	148-168	956	265-306	958

Figure 12

Antibody Light Chain DNA Features

Sequence Name	FR1 coordinates	SEQ ID NO:	FR2 coordinates	SEQ ID NO:	FR3 coordinates	SEQ ID NO:	FR4 coordinates	SEQ ID NO:	Constant region coordinates	SEQ ID NO:
Ab1	1-69	33	106-150	35	172-267	37	298-330	39	331-648	40
Ab1.H	1-69	73	106-150	75	172-267	77	298-330	79	331-648	80
Ab2	1-69	113	109-153	115	175-270	117	301-333	119	334-651	120
Ab3	1-69	713	103-147	715	169-264	717	301-333	719	334-651	720
Ab4	1-69	673	103-147	675	169-264	677	301-333	679	334-651	680
Ab5	1-69	513	103-147	515	169-264	517	301-333	519	334-651	520
Ab6	1-69	753	109-153	755	175-270	757	310-342	759	343-660	760
Ab7	1-69	553	109-153	555	175-270	557	304-336	559	337-654	560
Ab8	1-69	793	106-150	795	172-267	797	307-339	799	340-657	800
Ab9	1-69	833	109-153	835	175-270	837	310-342	839	343-660	840
Ab11	1-69	593	109-153	595	175-270	597	304-336	599	337-654	600
Ab12	1-69	633	109-153	635	175-270	637	304-336	639	337-654	640
Ab13	1-69	153	109-153	155	175-270	157	301-333	159	334-651	160
Ab14	1-69	193	109-153	195	175-270	197	301-333	199	334-651	200
Ab15	1-69	233	109-153	235	175-270	237	301-333	239	334-651	240
Ab16	1-69	273	109-153	275	175-270	277	301-333	279	334-651	280
Ab17	1-69	313	109-153	315	175-270	317	301-333	319	334-651	320
Ab18	1-69	353	109-153	355	175-270	357	301-333	359	334-651	360
Ab19	1-69	393	109-153	395	175-270	397	301-333	399	334-651	400
Ab22	1-69	913	109-153	915	175-270	917	307-339	919	340-657	920
Ab23	1-69	953	103-147	955	169-264	957	307-339	959	340-657	960

FIG. 13A

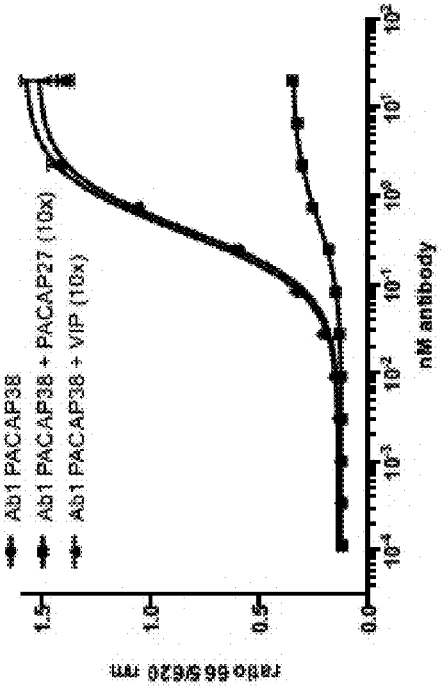


FIG. 13B

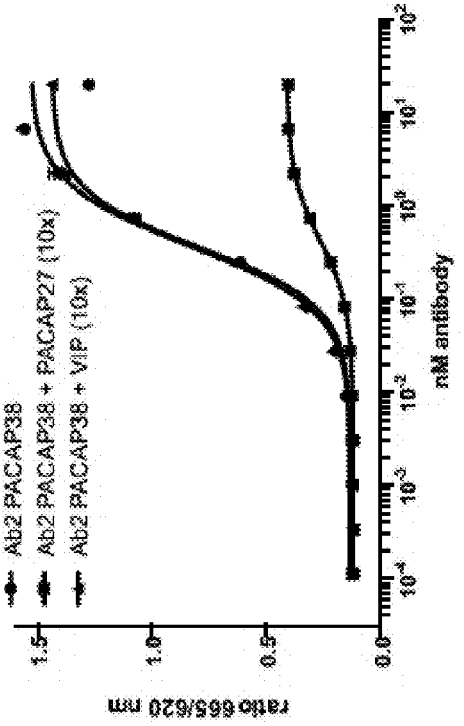


FIG. 13C

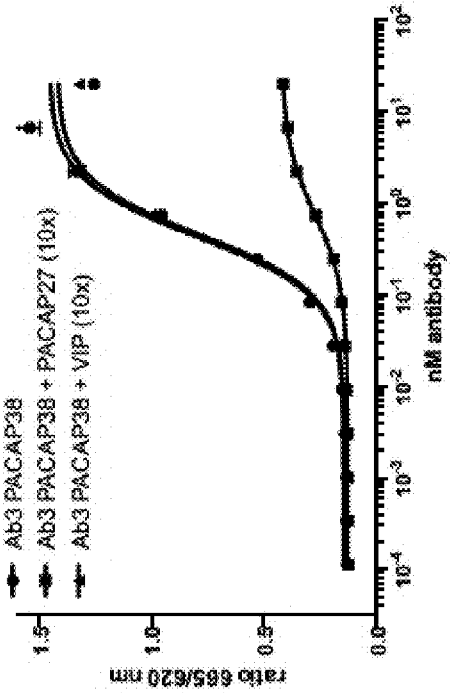


FIG. 13D

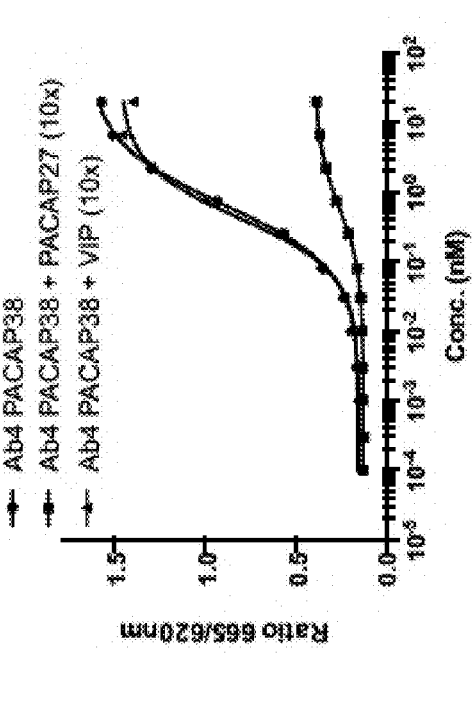


FIG. 13E

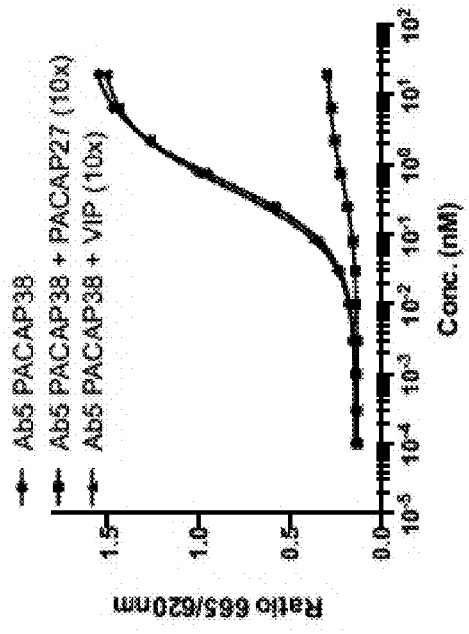


FIG. 13F

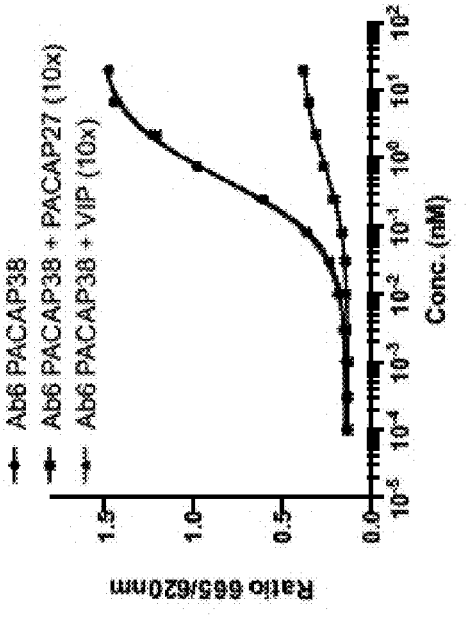


FIG. 13G

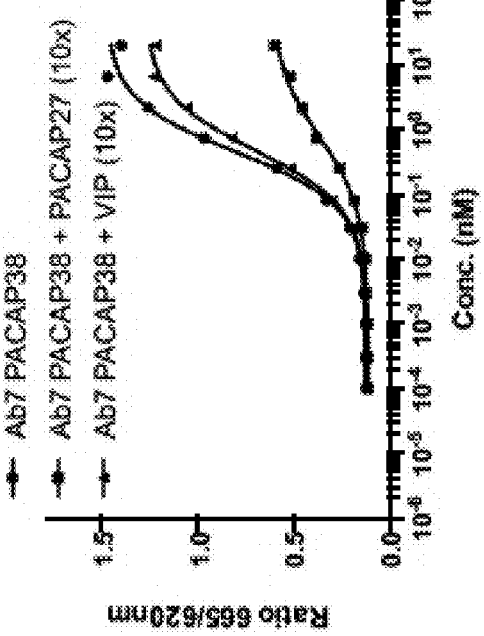
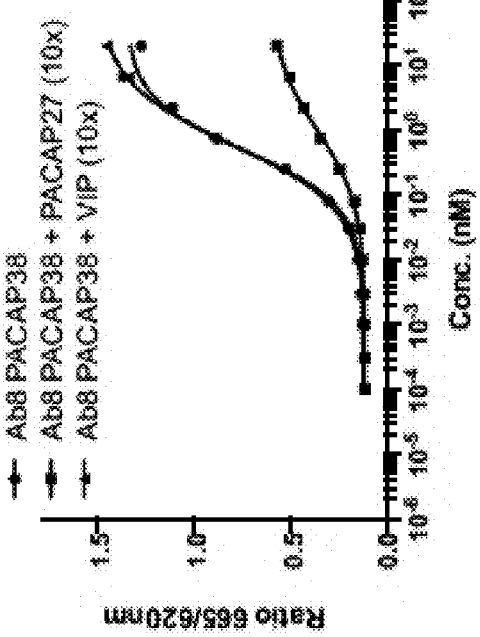


FIG. 13H



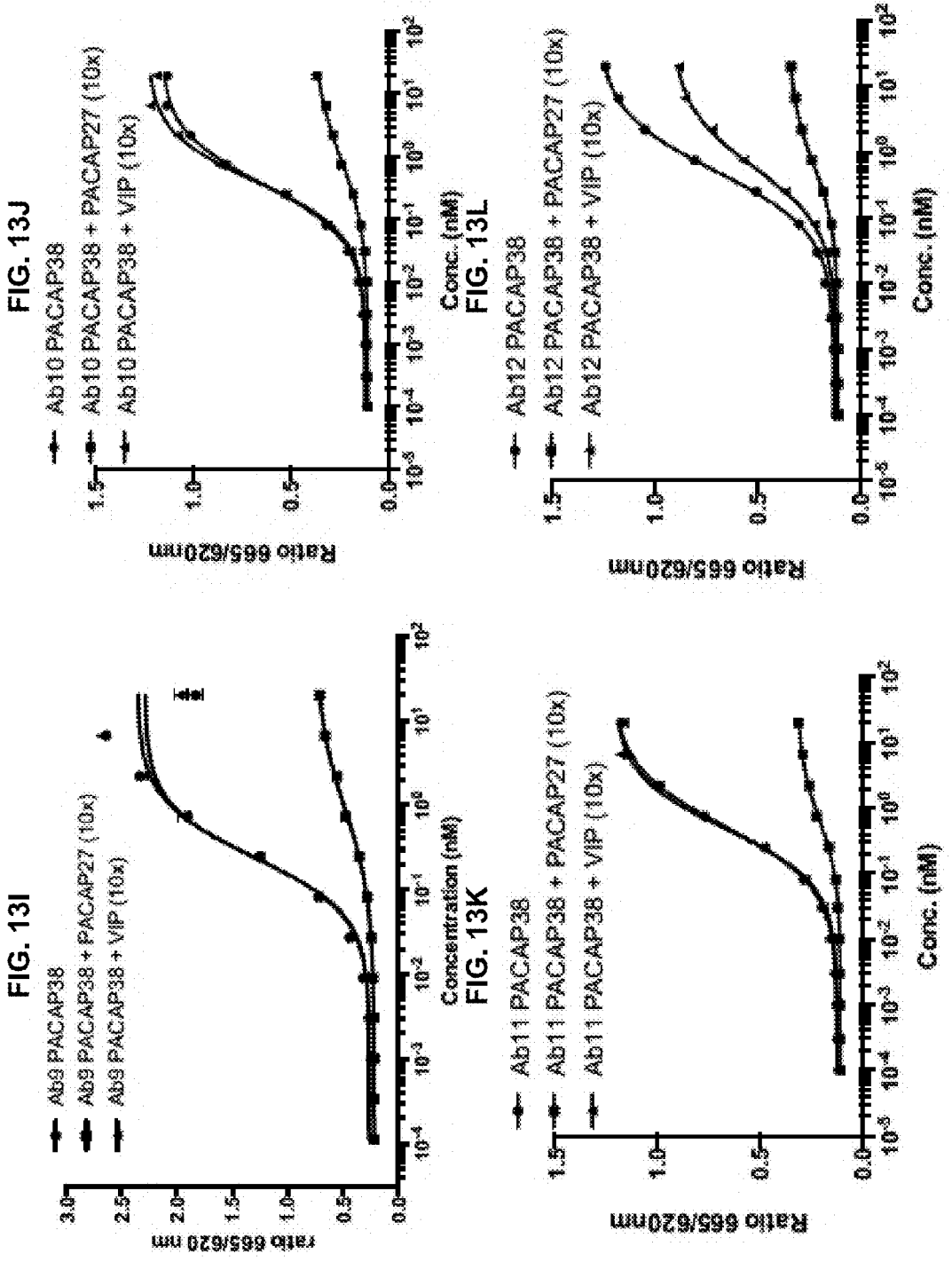


FIG. 13I

FIG. 13J

FIG. 13K

FIG. 13L

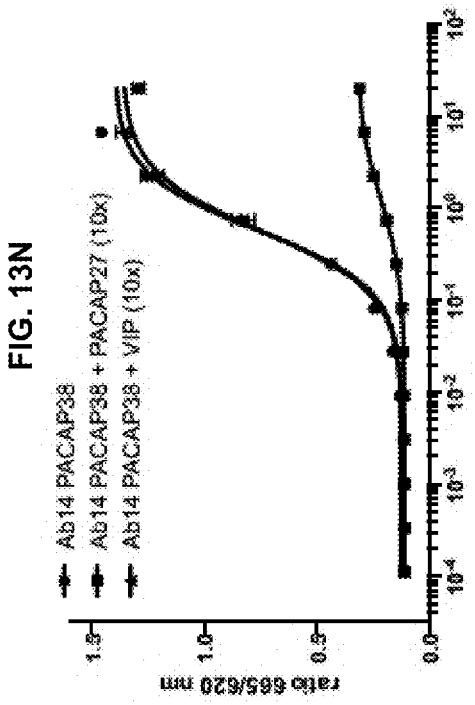


FIG. 13M

FIG. 13N

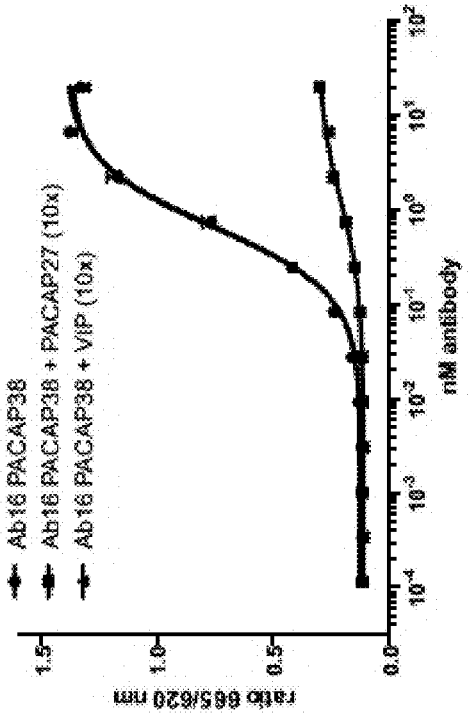


FIG. 13O

FIG. 13P

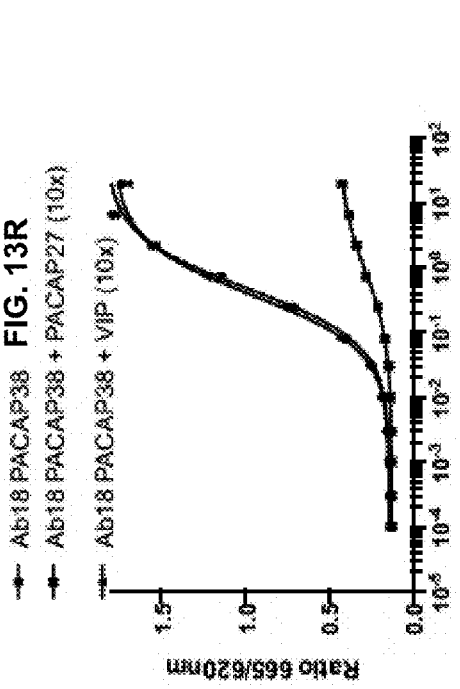


FIG. 13R

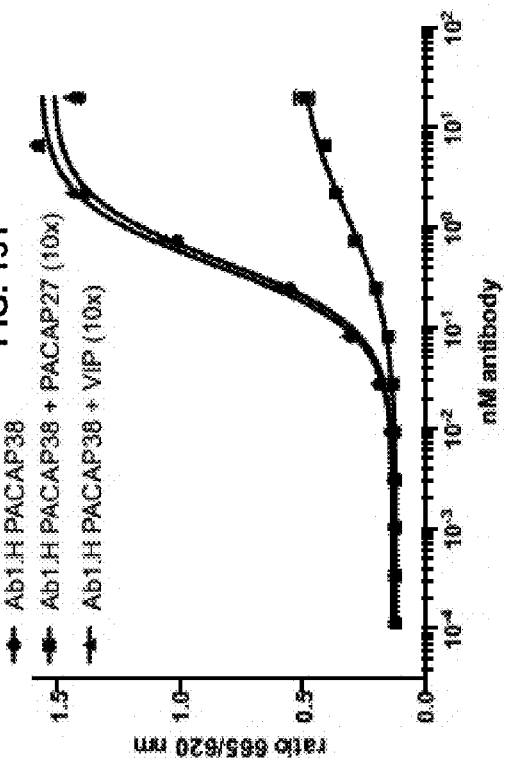


FIG. 13T

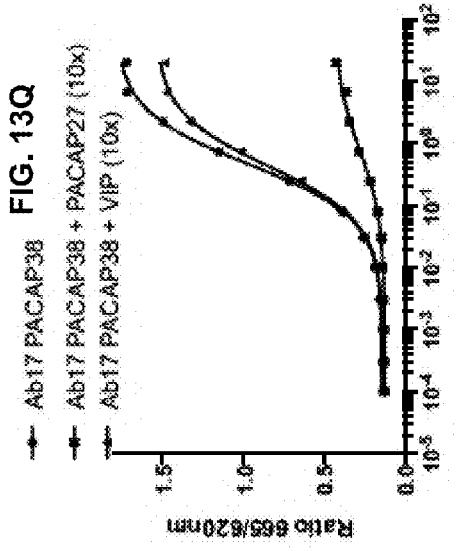


FIG. 13Q

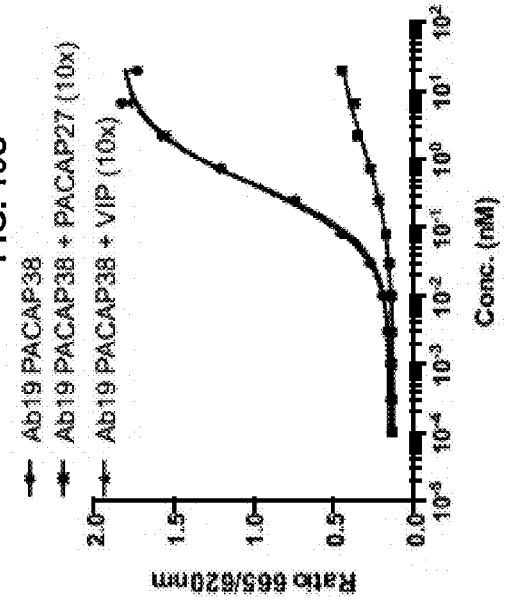


FIG. 13S

FIG. 13U

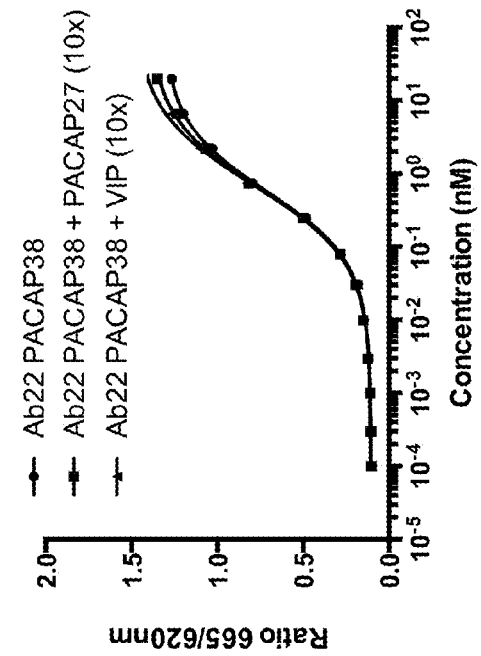


FIG. 13V

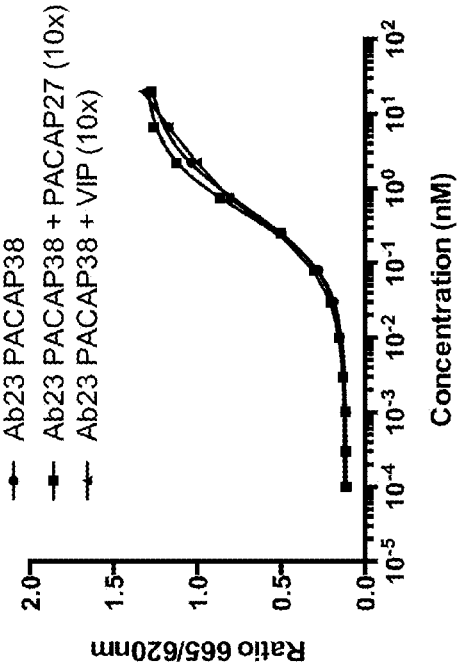


FIG. 14A

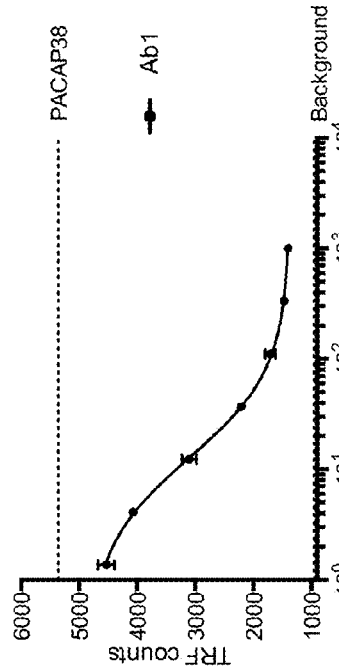


FIG. 14B

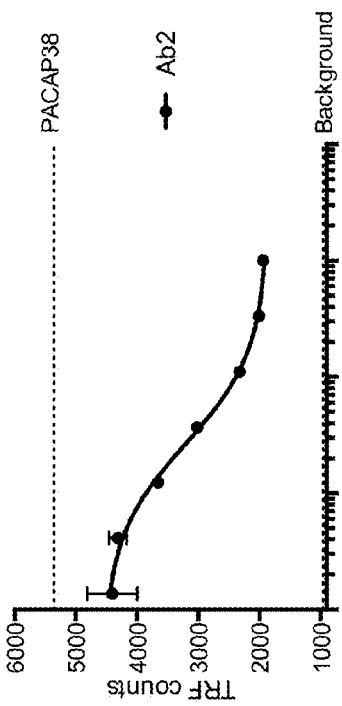


FIG. 14C

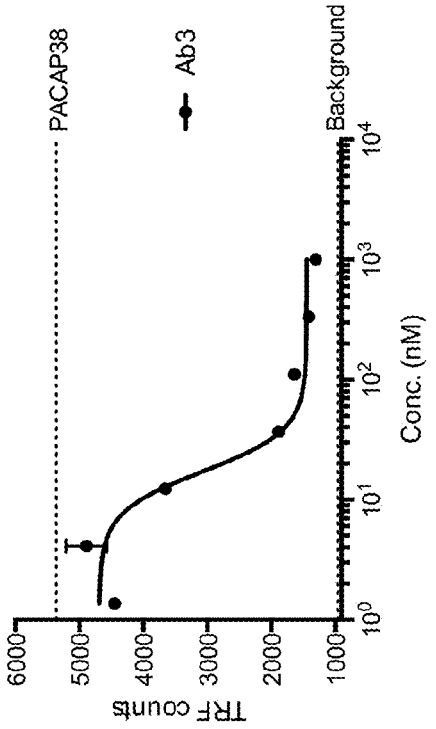


FIG. 14D

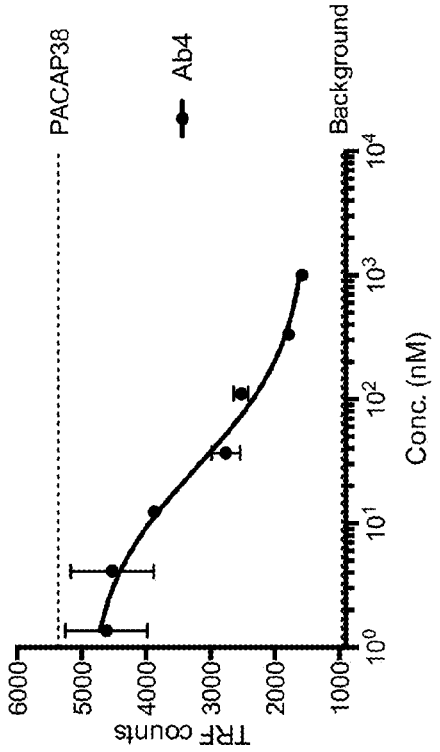


FIG. 14E

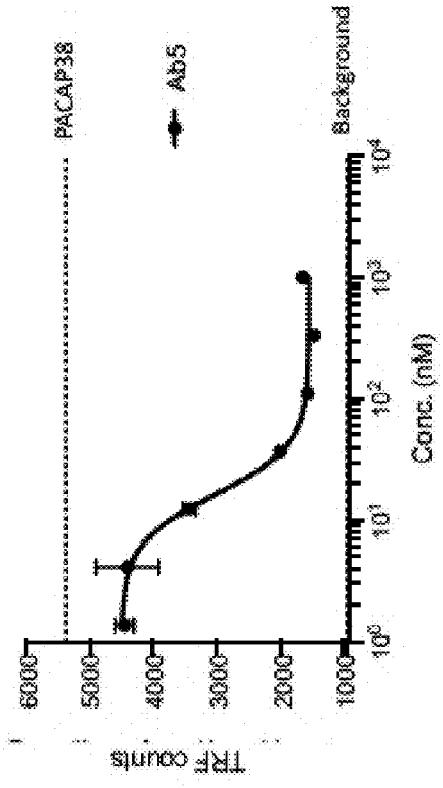


FIG. 14F

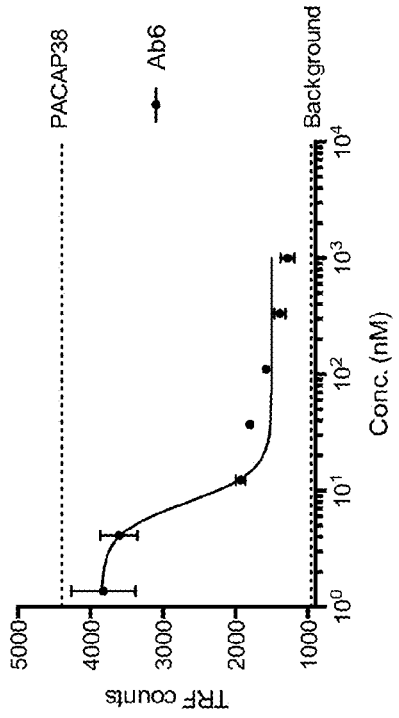


FIG. 14H

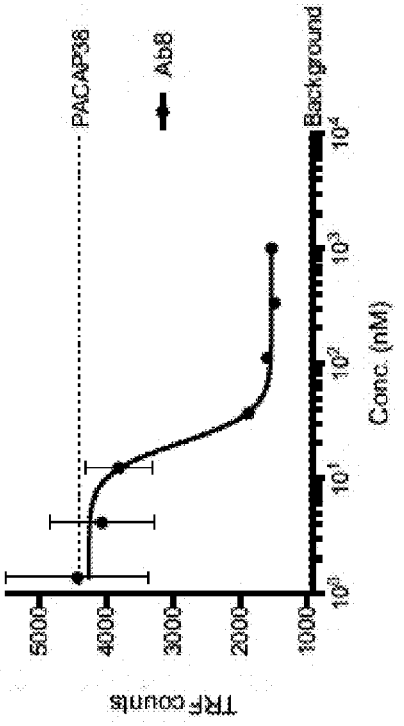


FIG. 14G

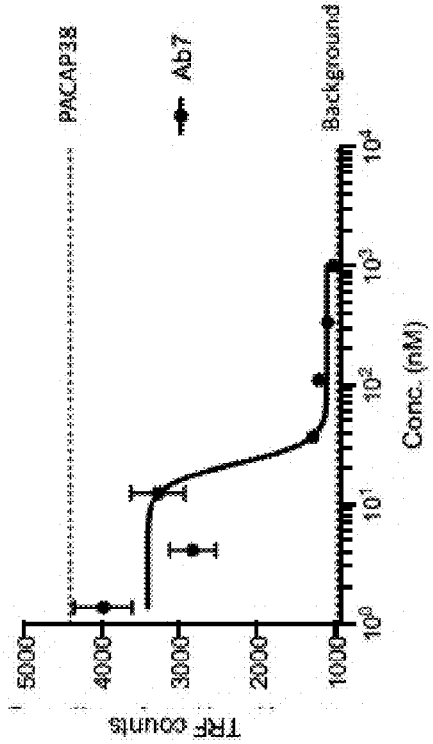


FIG. 14J

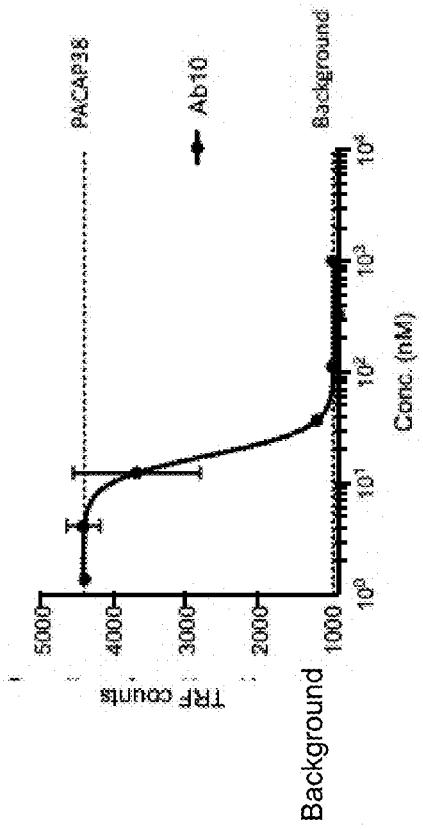


FIG. 14I

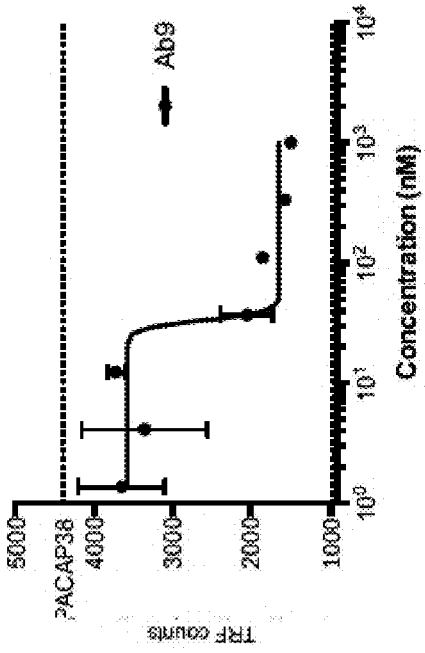


FIG. 14K

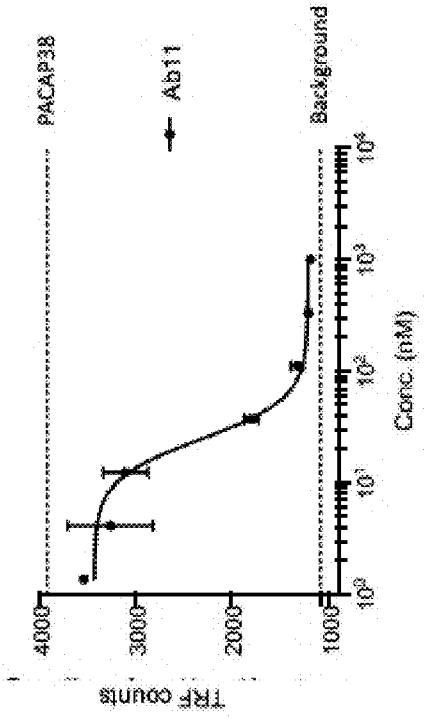


FIG. 14L

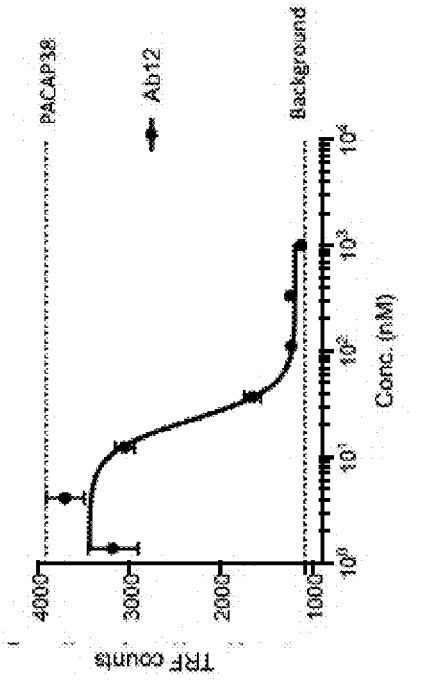


FIG. 14M

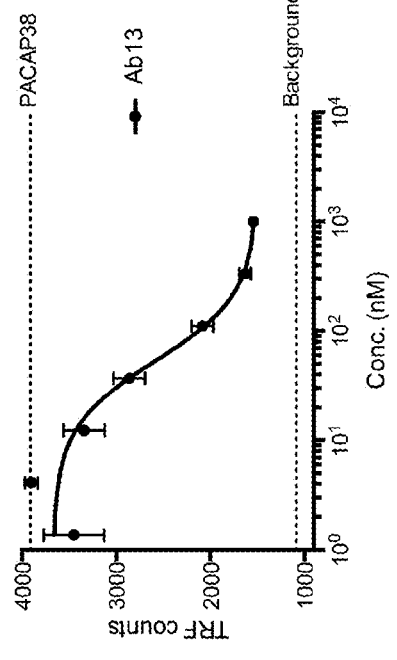


FIG. 14N

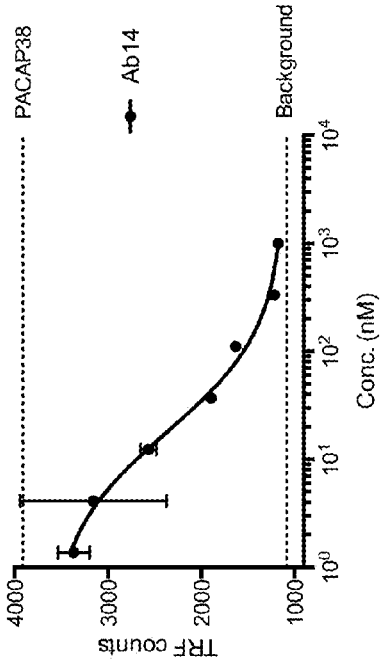


FIG. 14O

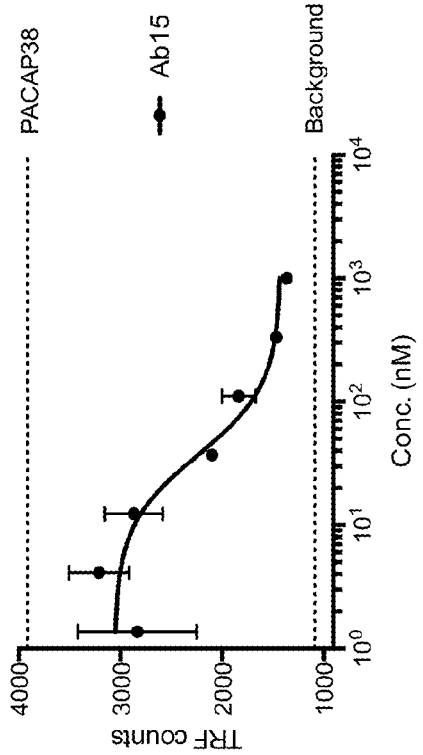


FIG. 14P

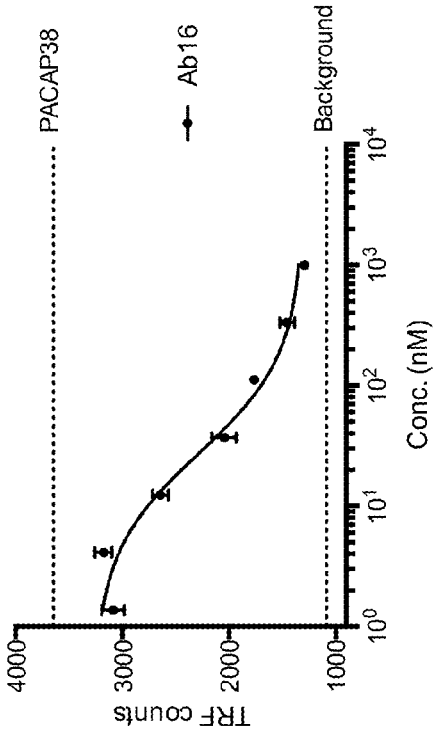


FIG. 14Q

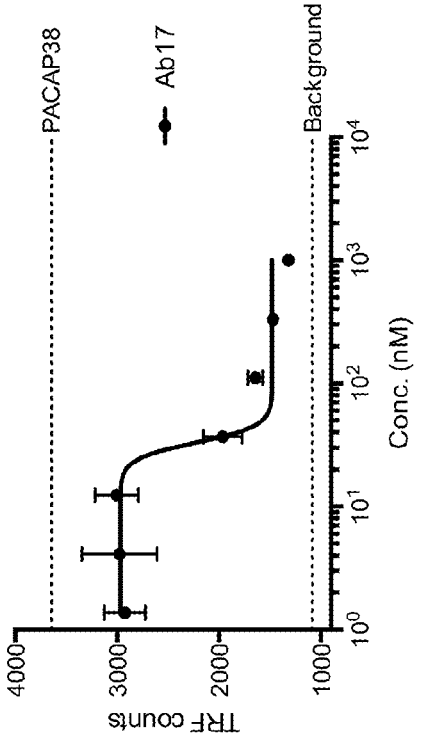
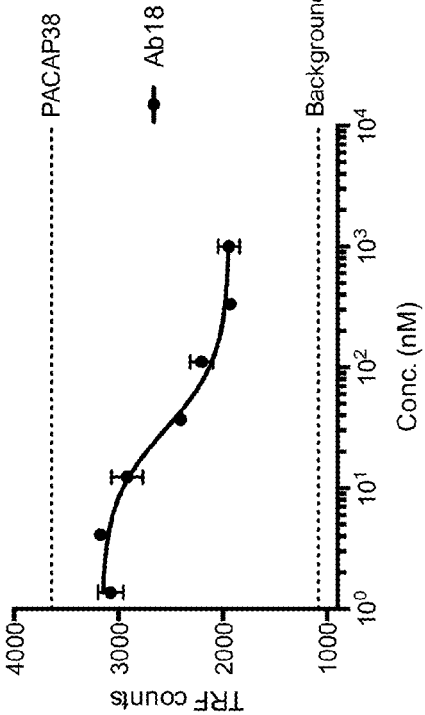


FIG. 14R



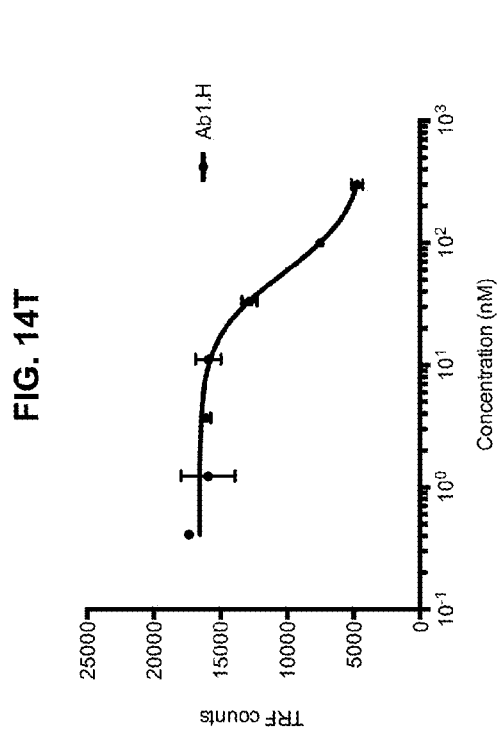


FIG. 14T

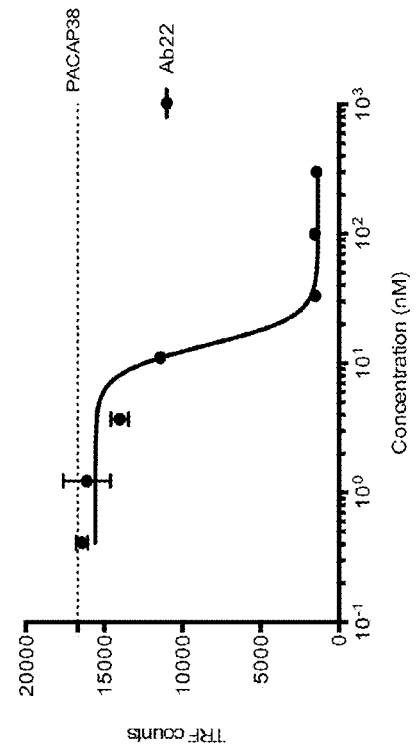


FIG. 14V

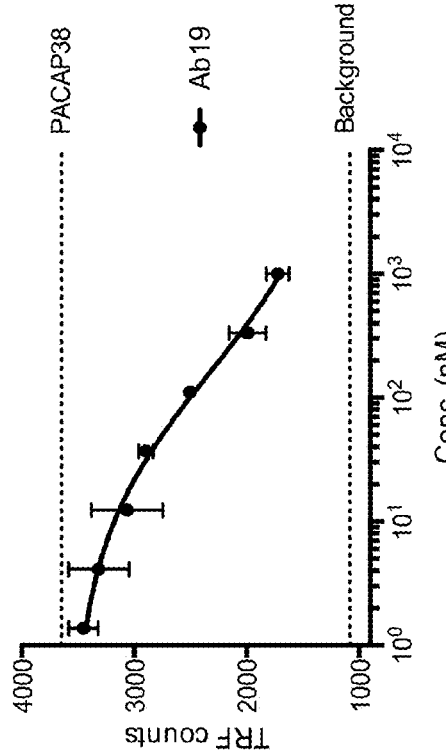


FIG. 14S

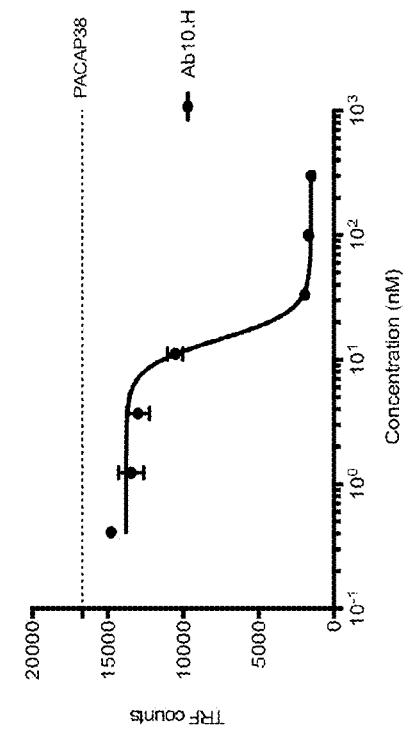


FIG. 14U

FIG. 14W

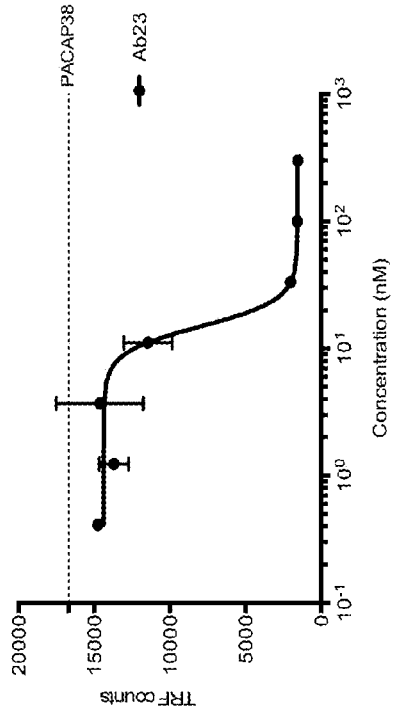


FIG. 14X

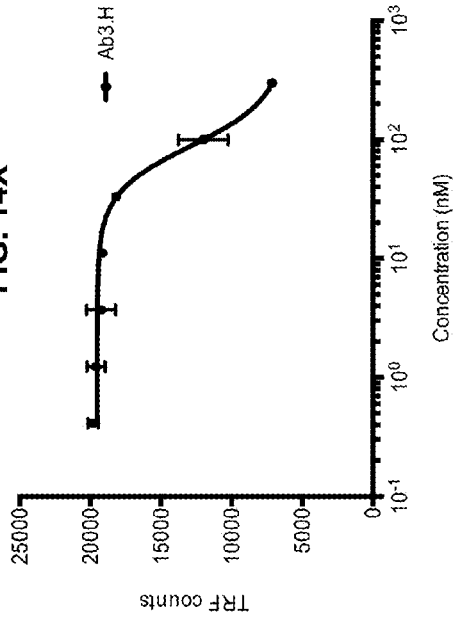


FIG. 14Y

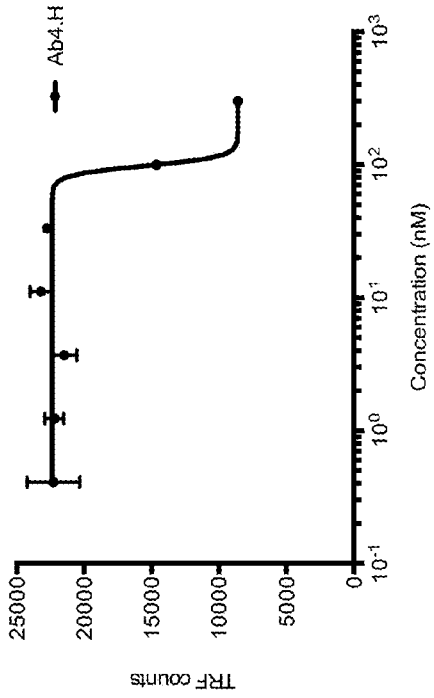


FIG. 14Z

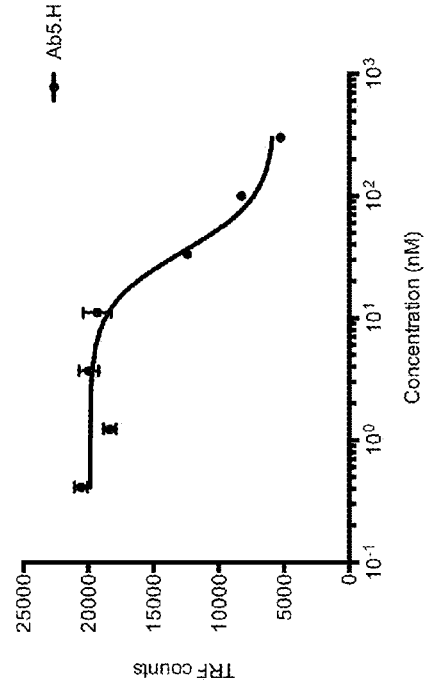


FIG. 14BB

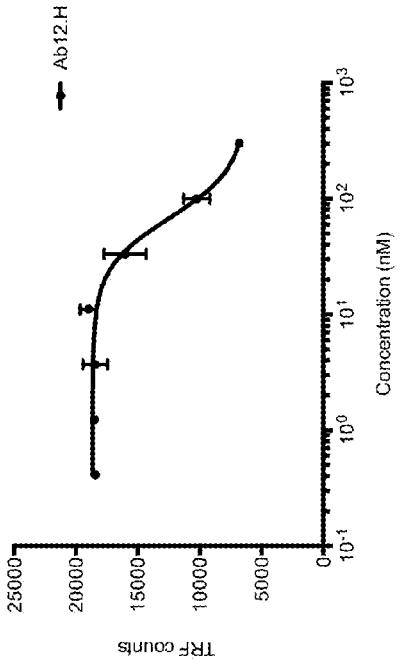


FIG. 14AA

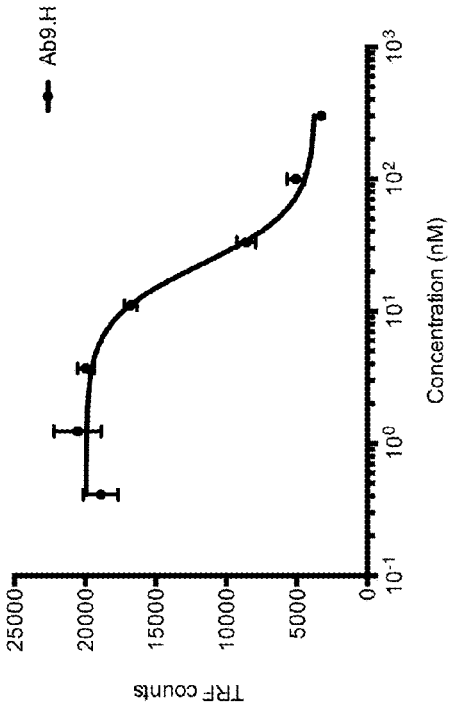


FIG. 15B

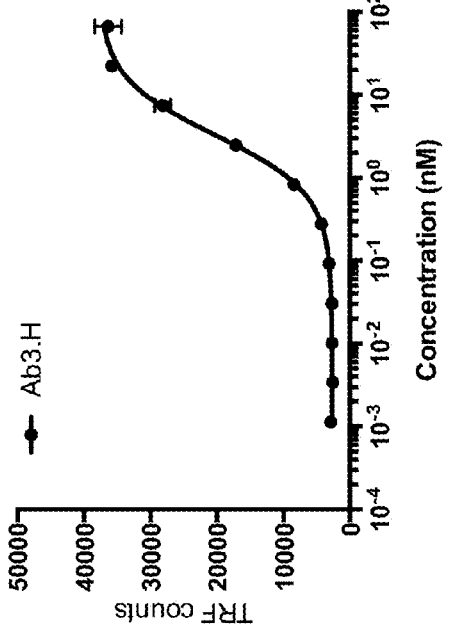


FIG. 15A

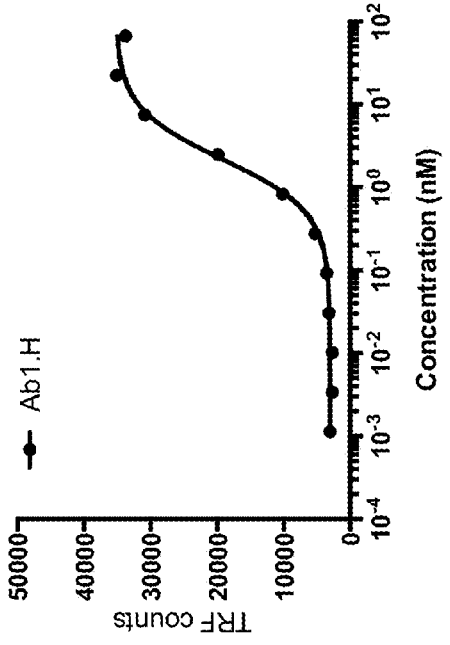


FIG. 15C

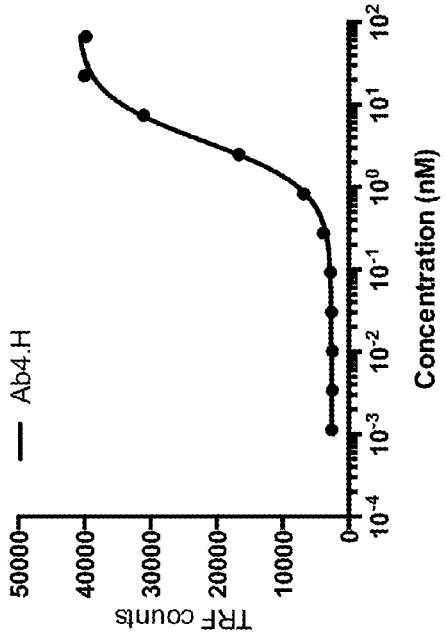


FIG. 15D

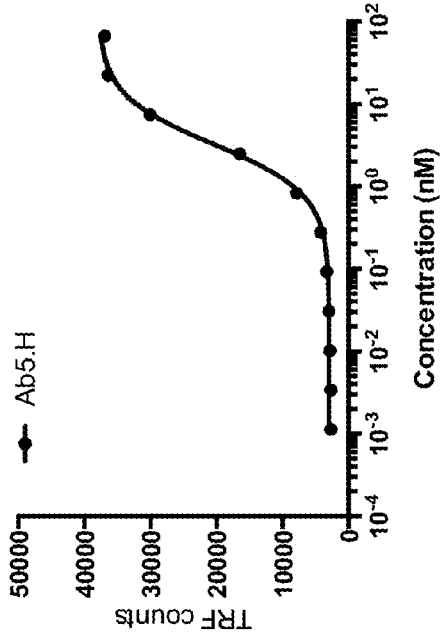


FIG. 15E

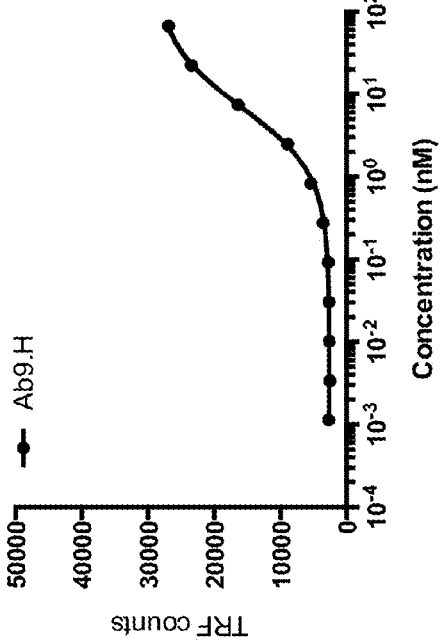


FIG. 15F

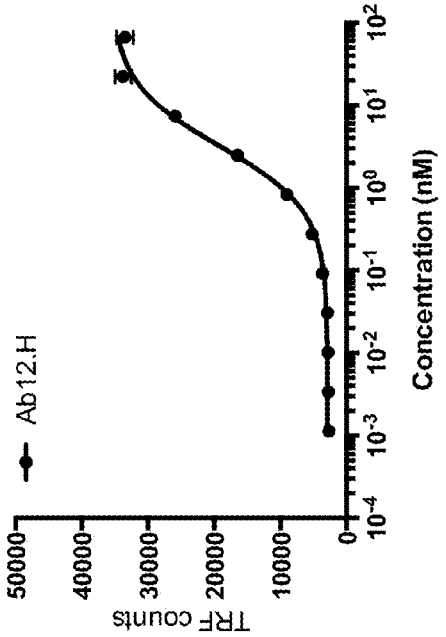


FIG. 15G

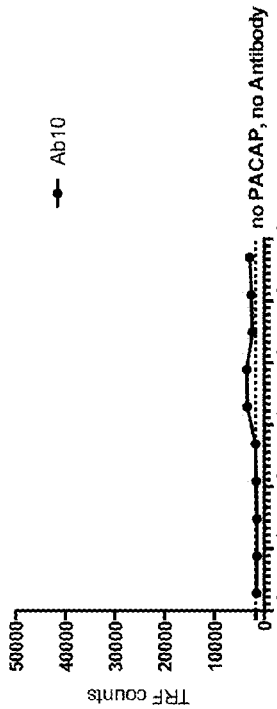


FIG. 15H

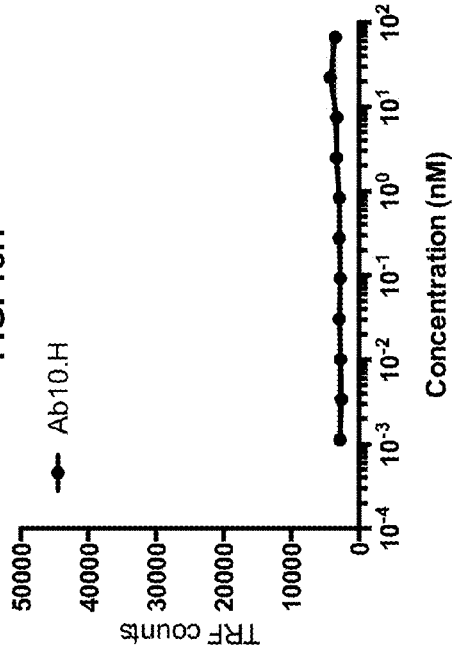


FIG. 15I

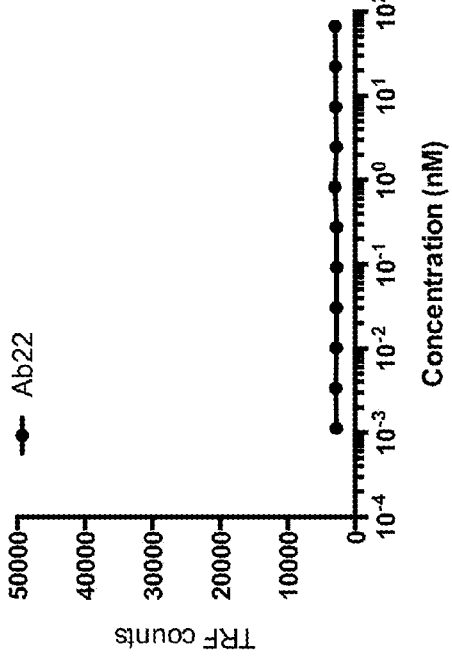
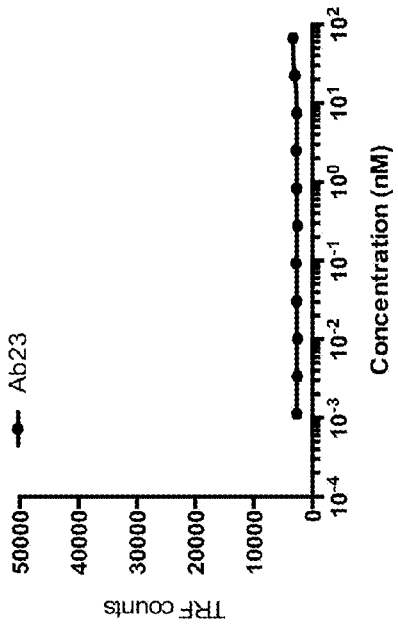
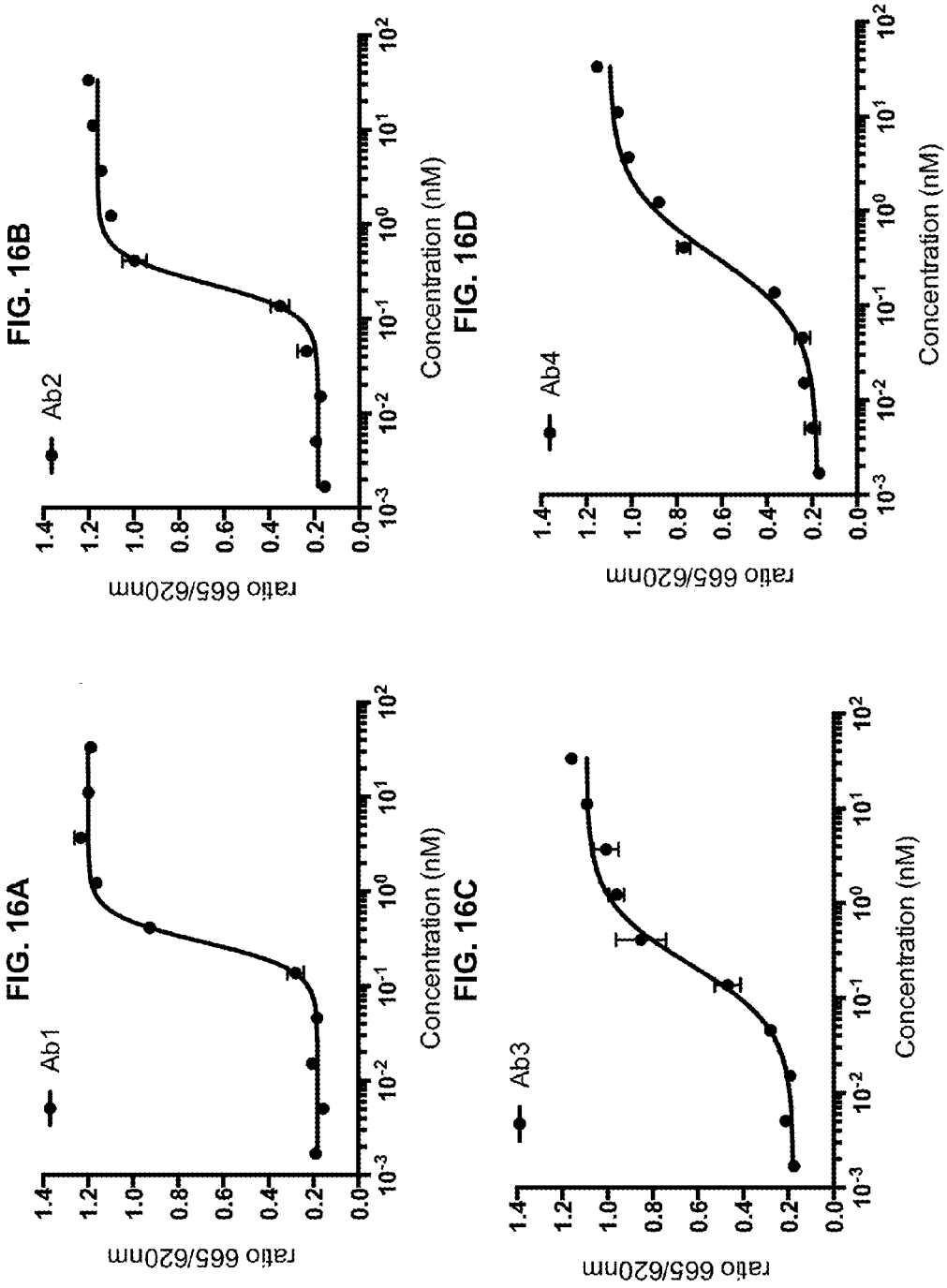


FIG. 15J




FIG. 16A
Ab1
ratio 665/620nm
Concentration (nM)
FIG. 16B
Ab2
ratio 665/620nm
Concentration (nM)
FIG. 16C
Ab3
ratio 665/620nm
Concentration (nM)
FIG. 16D
Ab4
ratio 665/620nm
Concentration (nM)

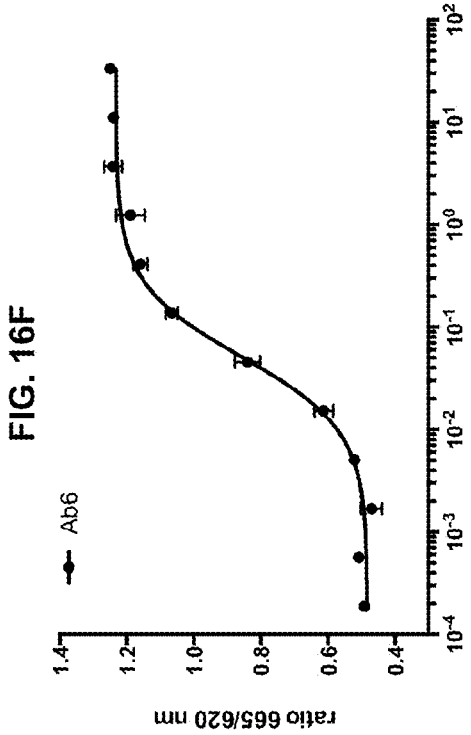


FIG. 16F

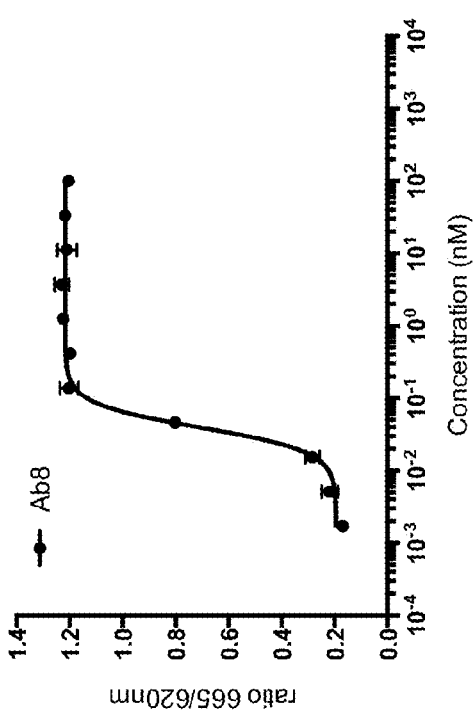


FIG. 16H

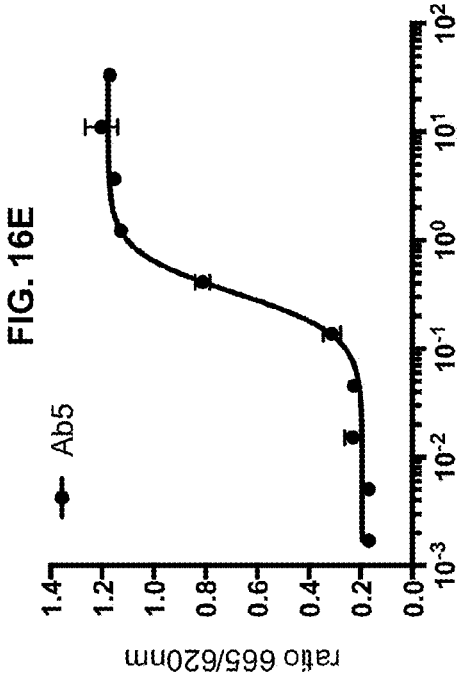


FIG. 16E

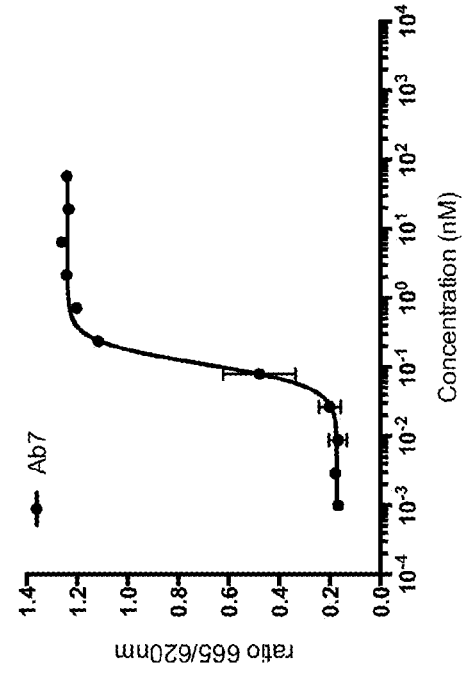


FIG. 16G

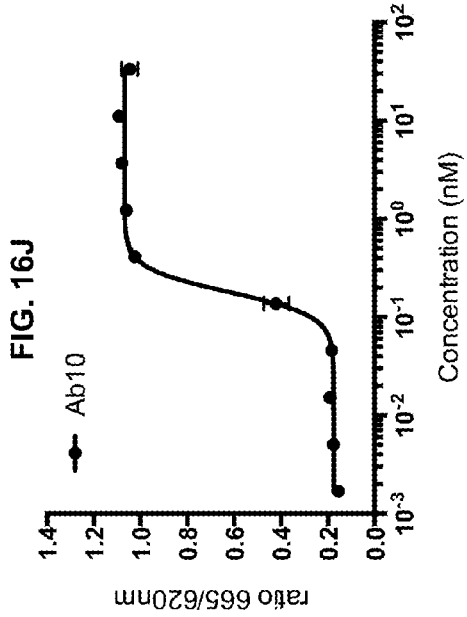


FIG. 16J

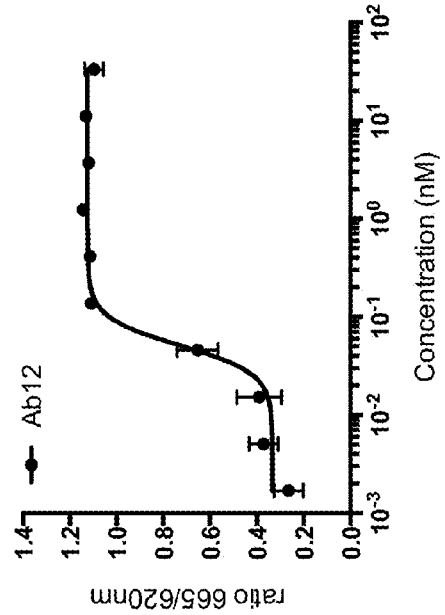


FIG. 16L

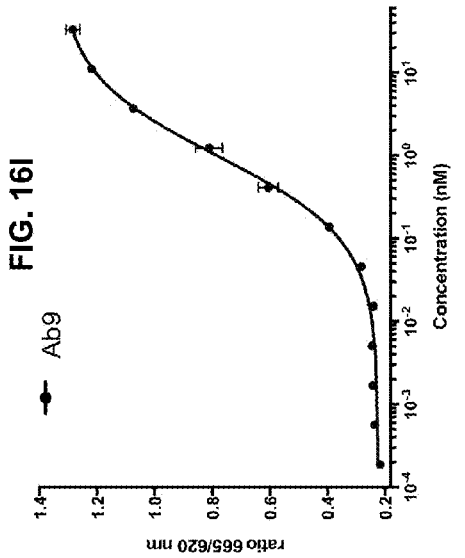


FIG. 16I

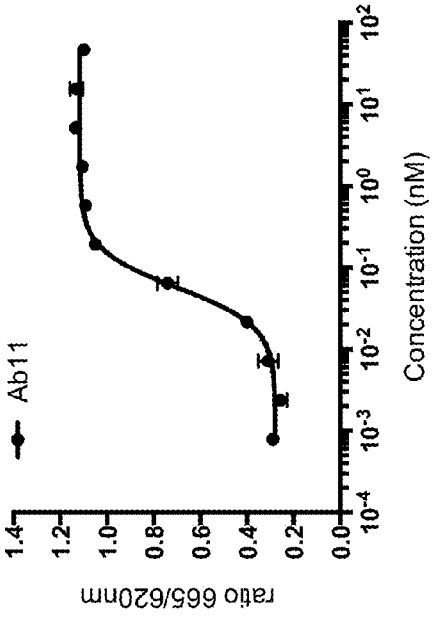


FIG. 16K

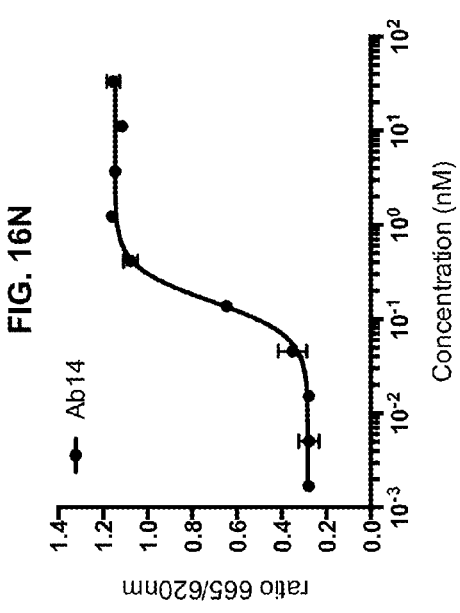


FIG. 16M

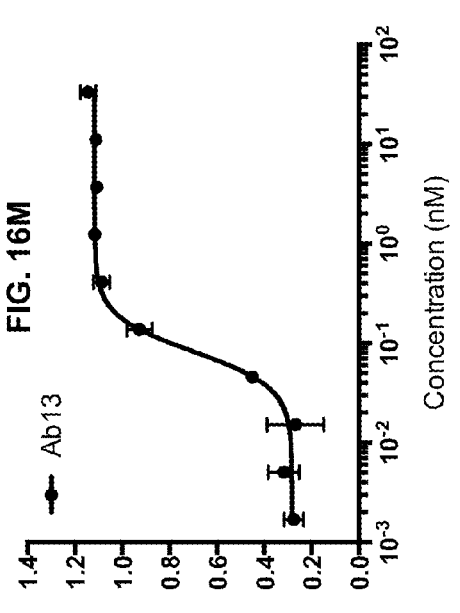


FIG. 16N

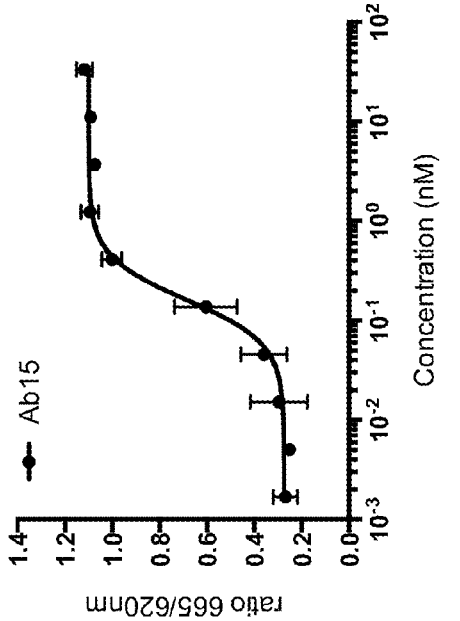


FIG. 16O

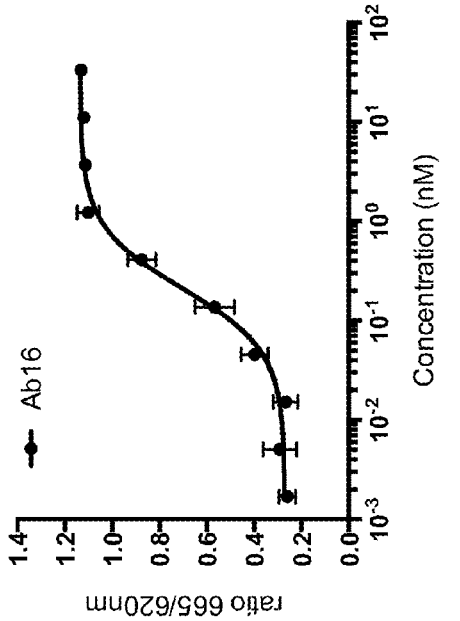


FIG. 16P

FIG. 16Q

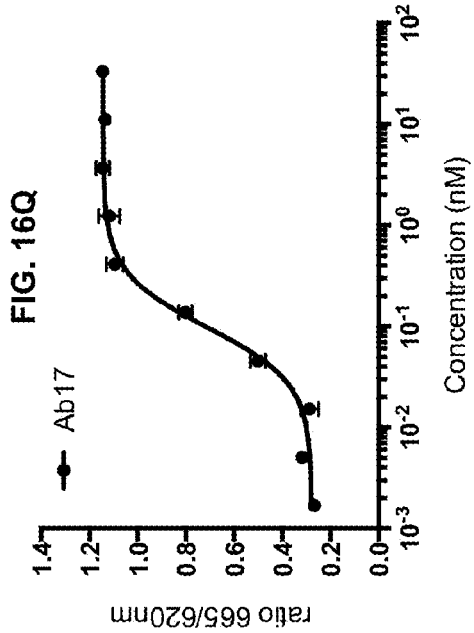


FIG. 16R

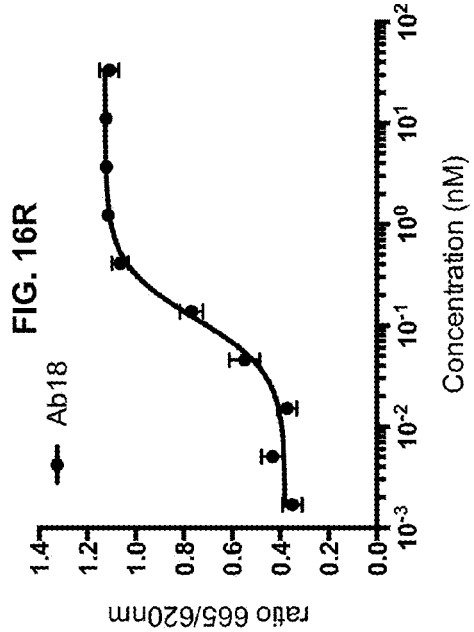


FIG. 16S

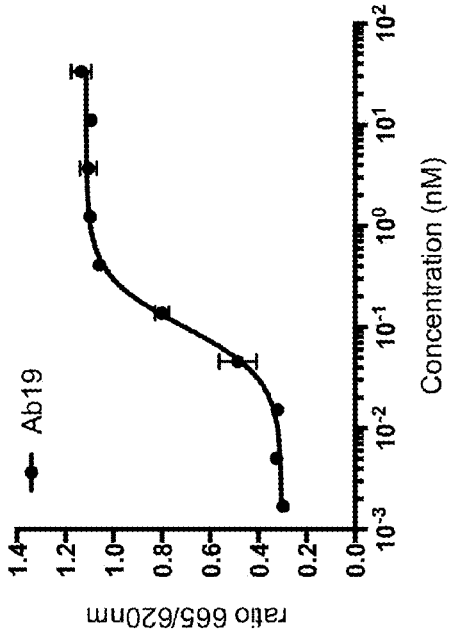


FIG. 16T

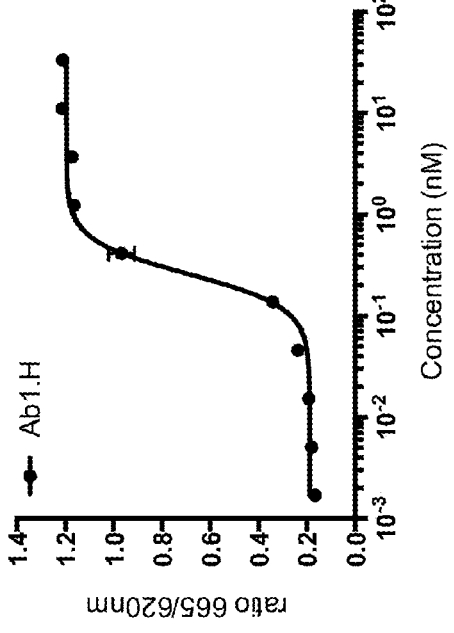


FIG. 16V

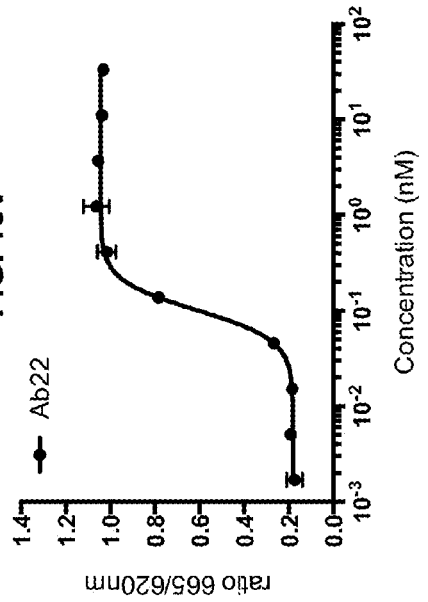


FIG. 16X

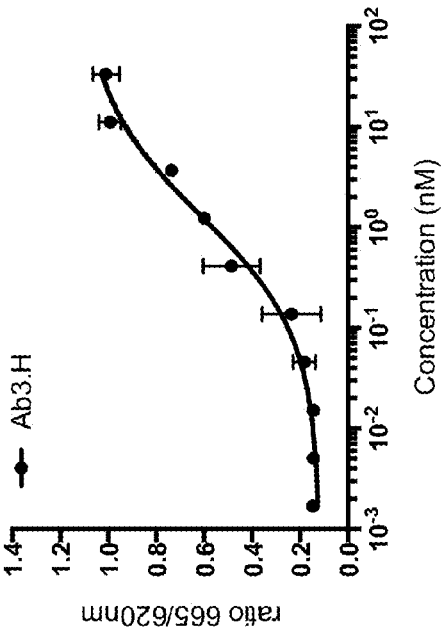


FIG. 16U

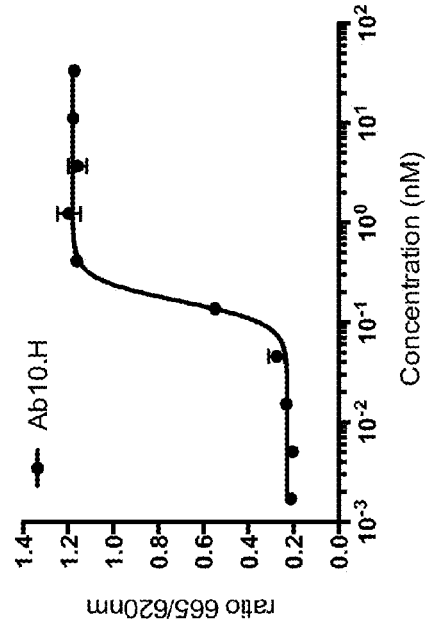
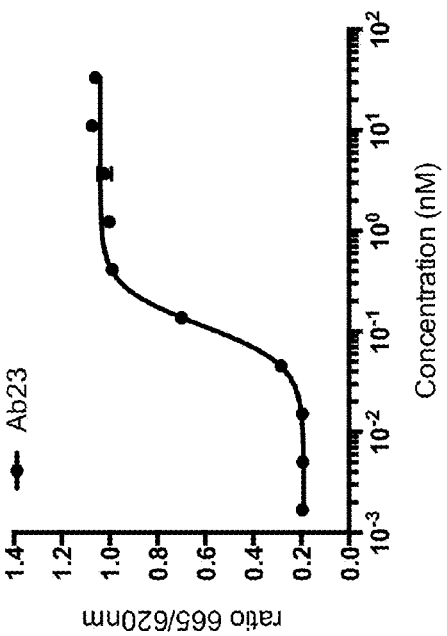


FIG. 16W



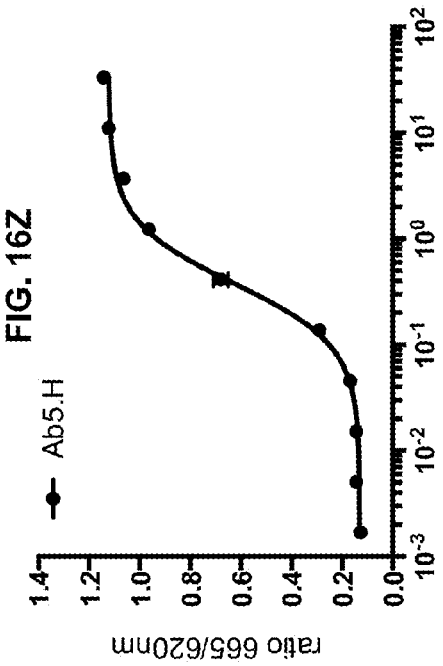


FIG. 16Z

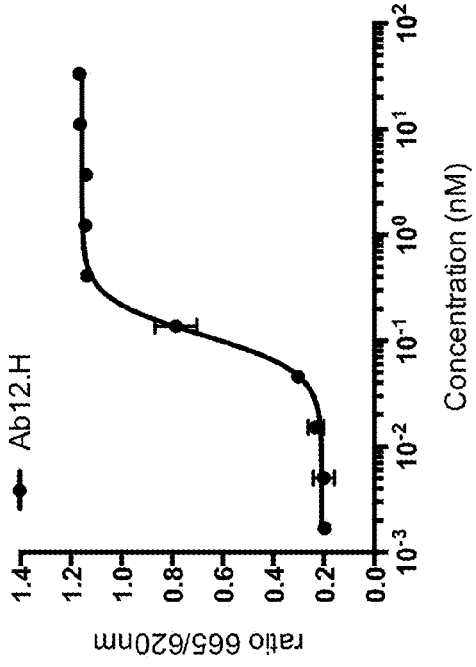


FIG. 16BB

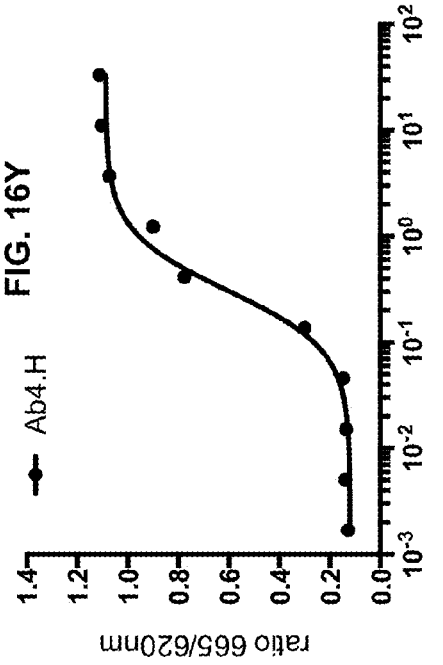


FIG. 16Y

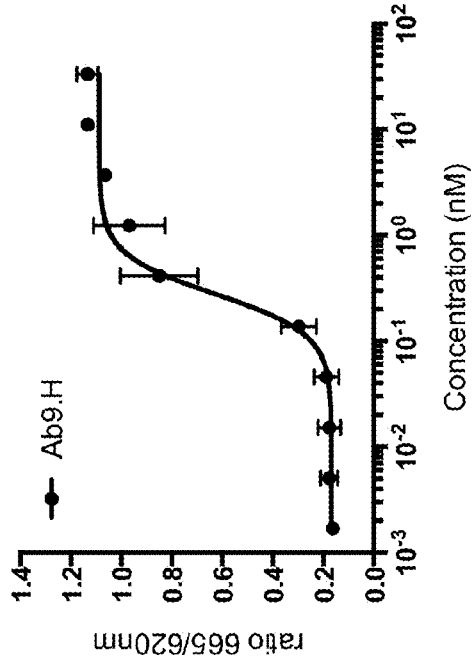


FIG. 16AA

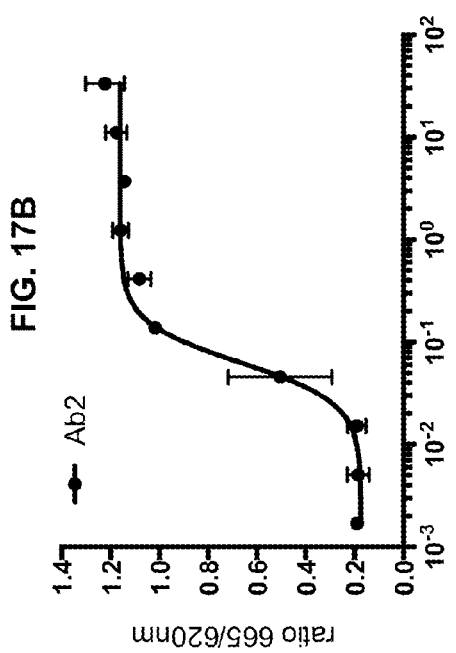


FIG. 17B

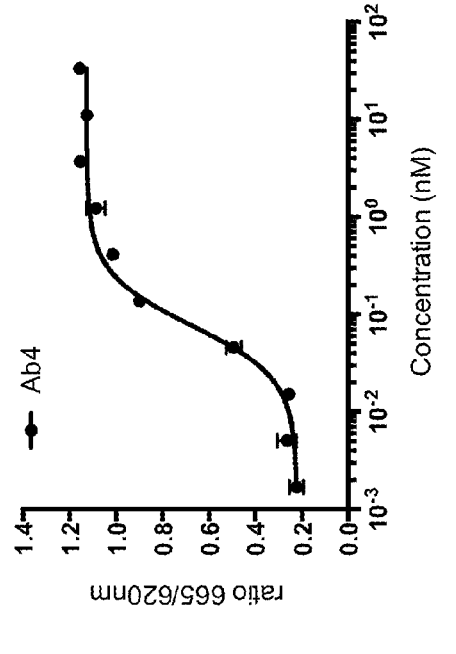


FIG. 17D

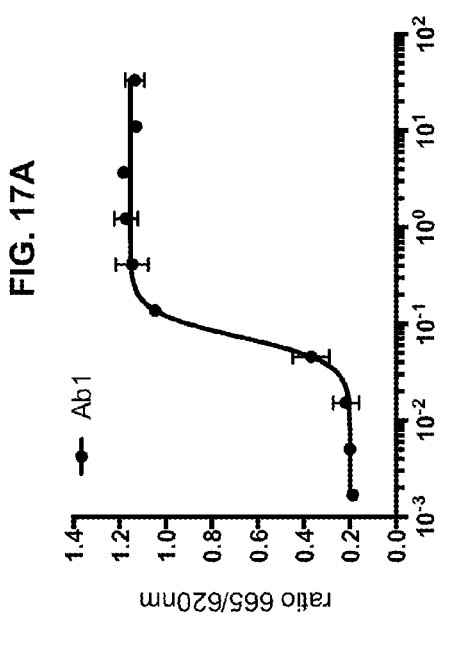


FIG. 17A

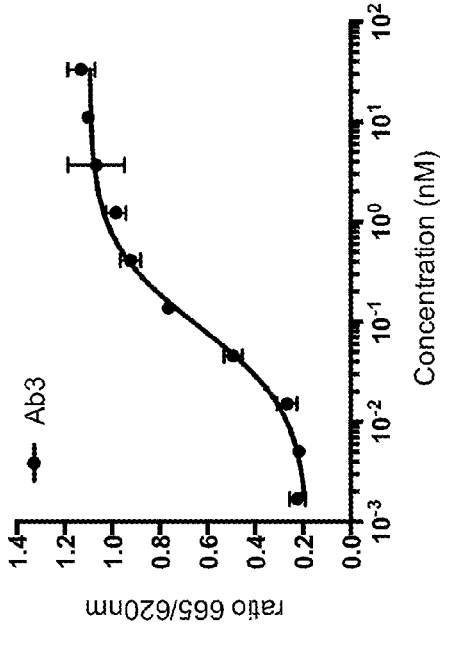


FIG. 17C

FIG. 17E

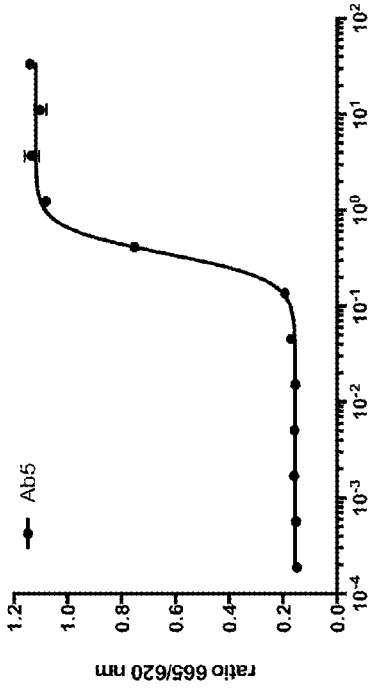


FIG. 17F

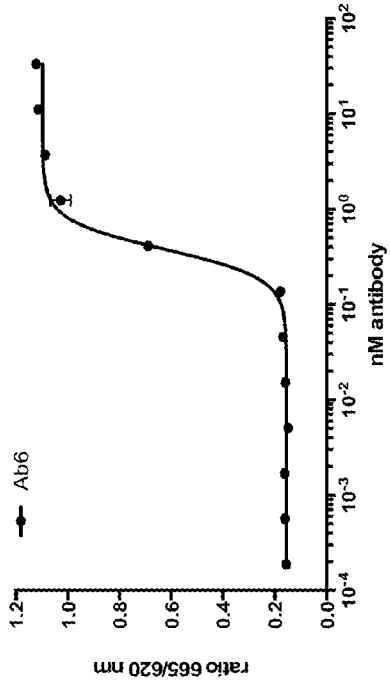


FIG. 17G

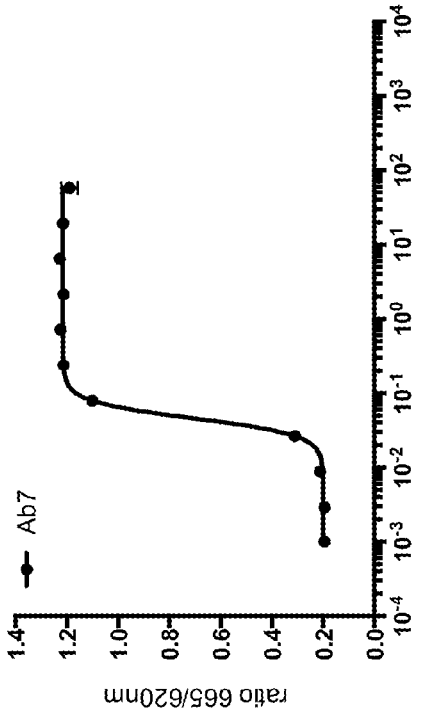
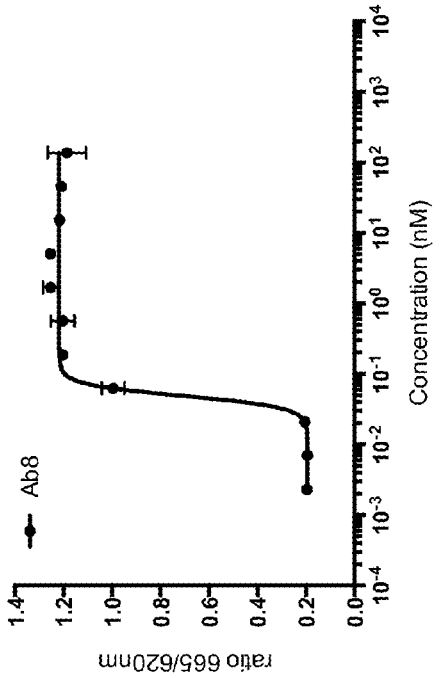
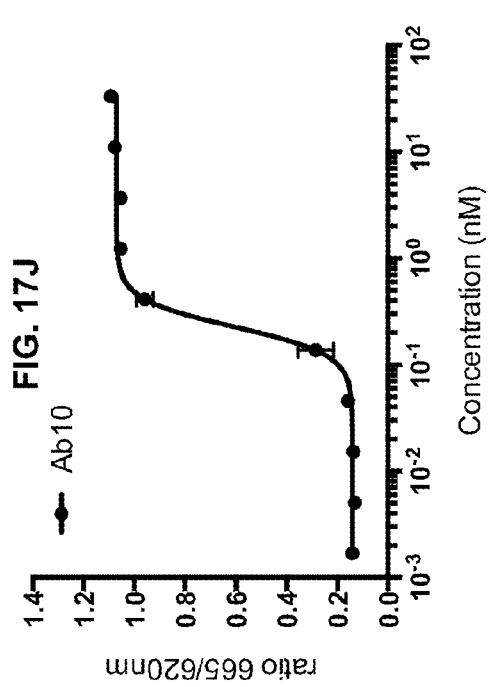
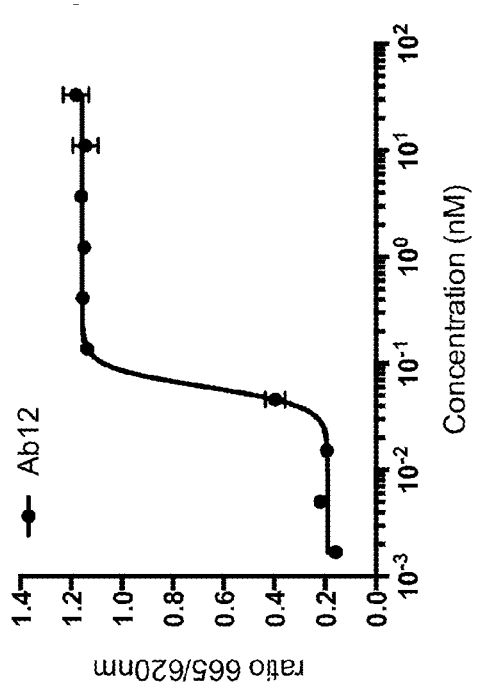
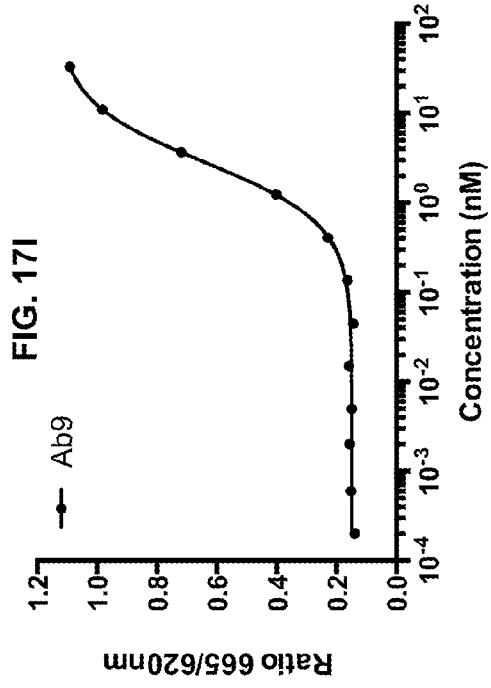


FIG. 17H




FIG. 17J
Ab10
ratio 665/620nm
Concentration (nM)


FIG. 17L
Ab12
ratio 665/620nm
Concentration (nM)


FIG. 17I
Ab9
Ratio 665/620nm
Concentration (nM)

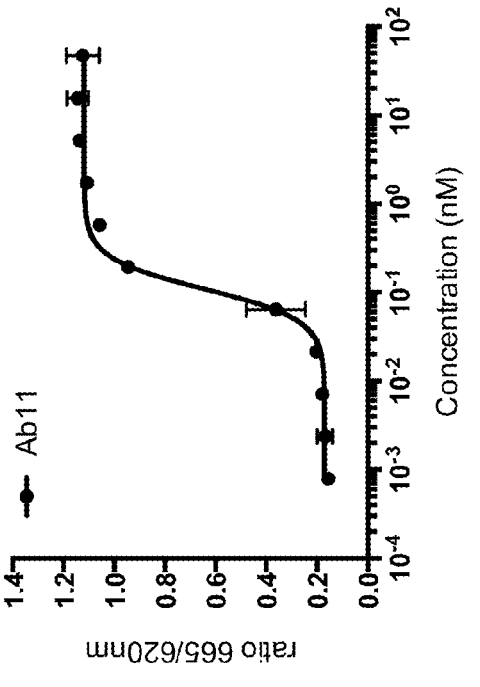

FIG. 17K
Ab11
ratio 665/620nm
Concentration (nM)

FIG. 17M

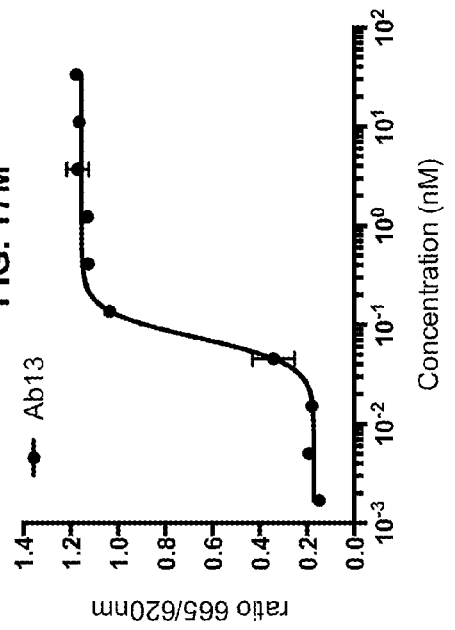


FIG. 17N

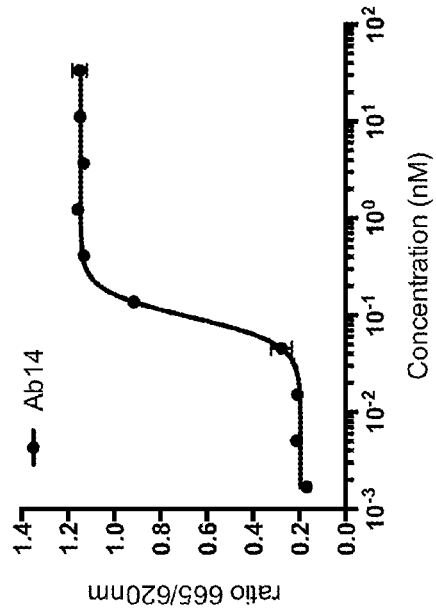


FIG. 17O

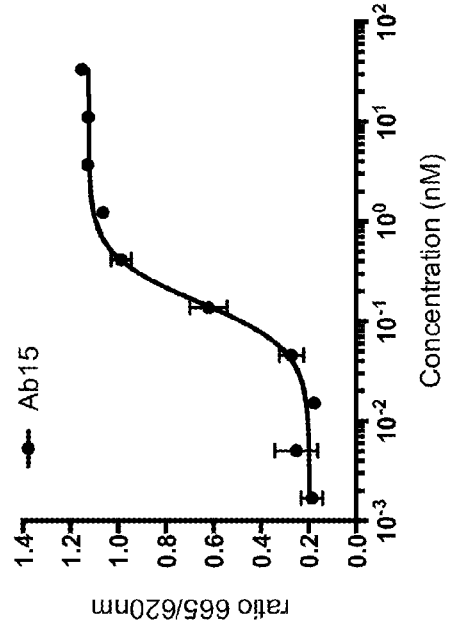


FIG. 17P

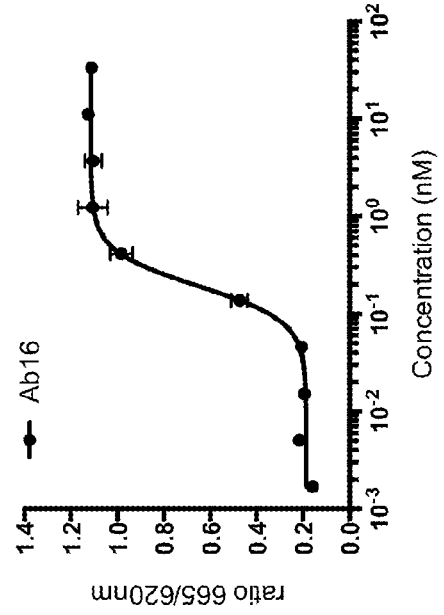


FIG. 17Q

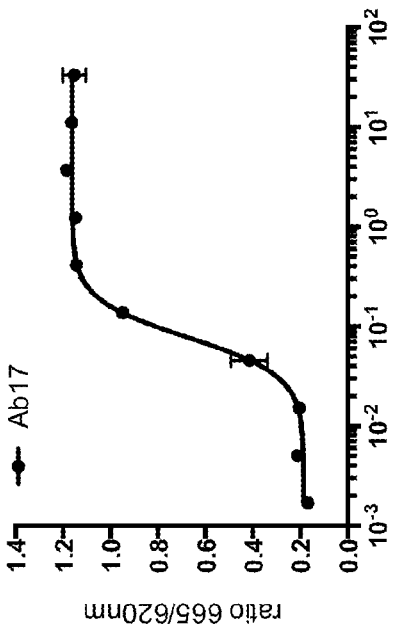


FIG. 17R

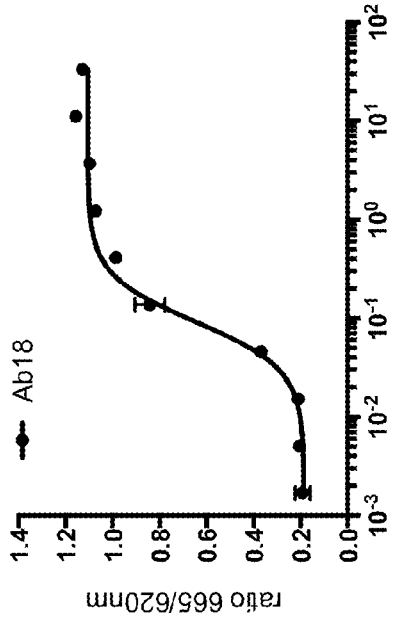


FIG. 17S

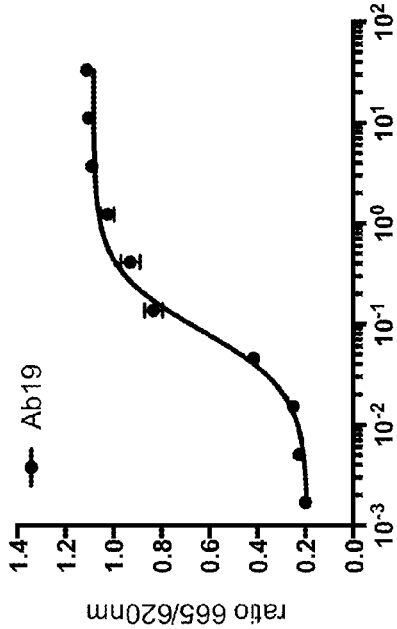


FIG. 17T

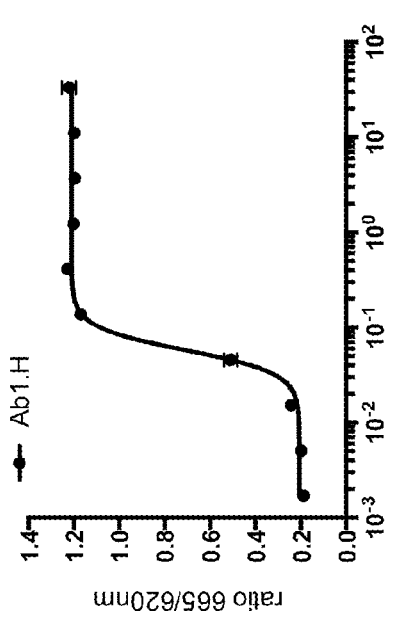


FIG. 17U

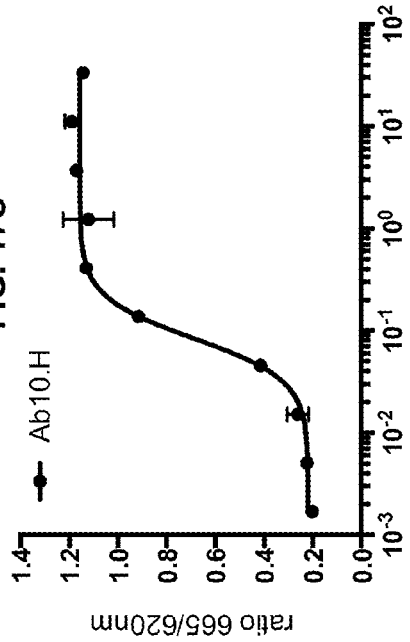


FIG. 17V

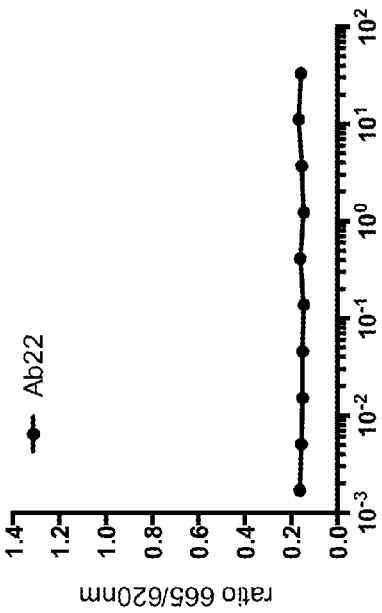


FIG. 17W

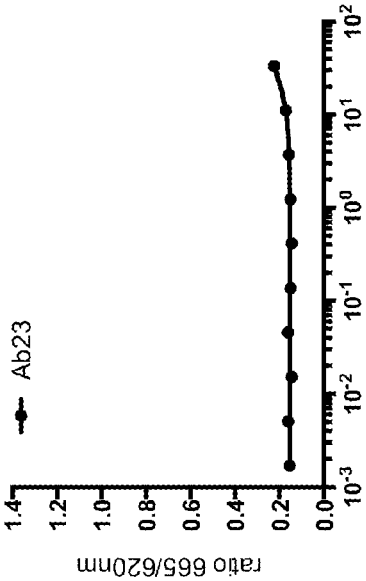
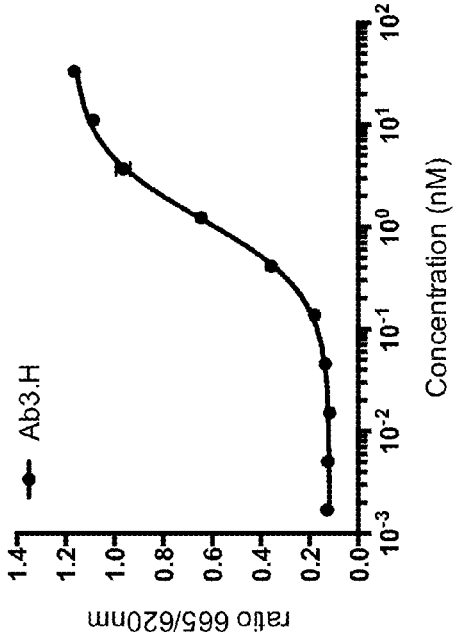


FIG. 17X



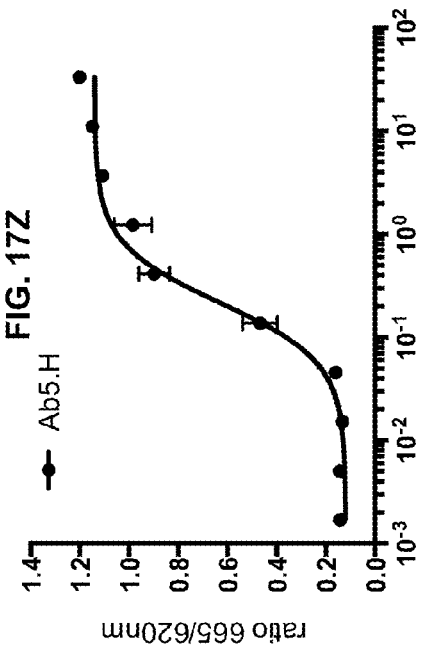


FIG. 17Z

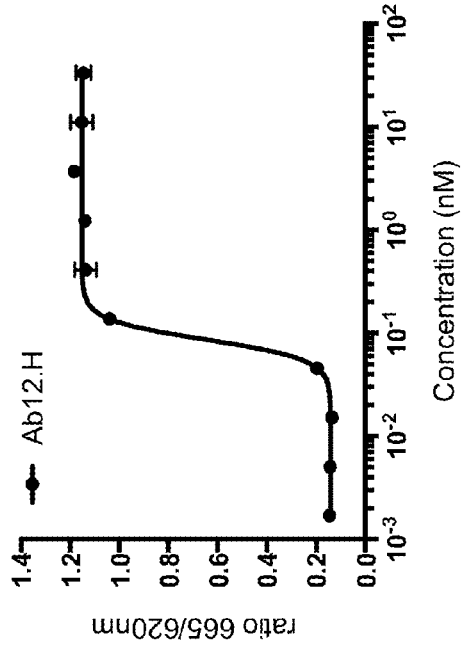


FIG. 17BB

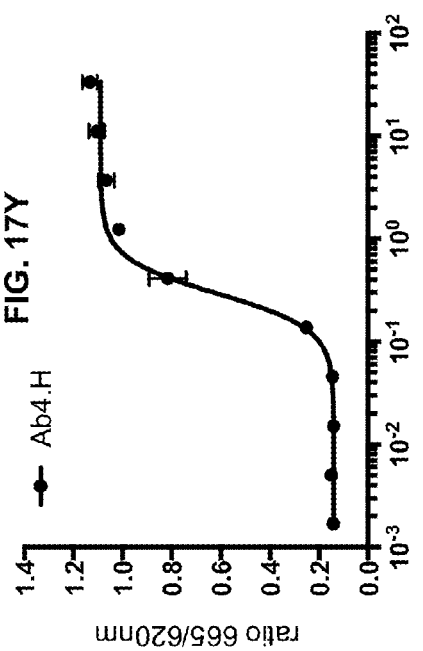


FIG. 17Y

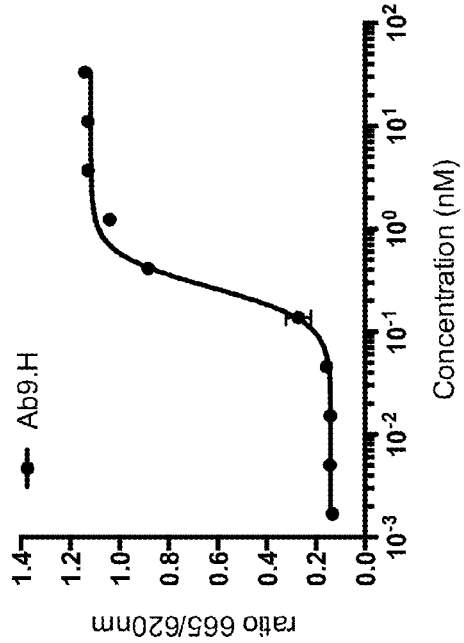


FIG. 17AA

FIG. 18A

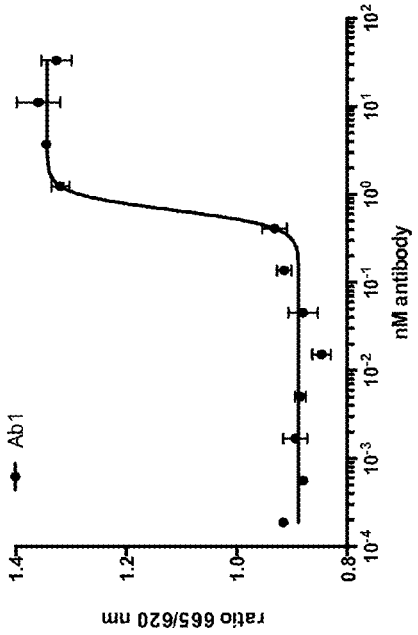


FIG. 18B

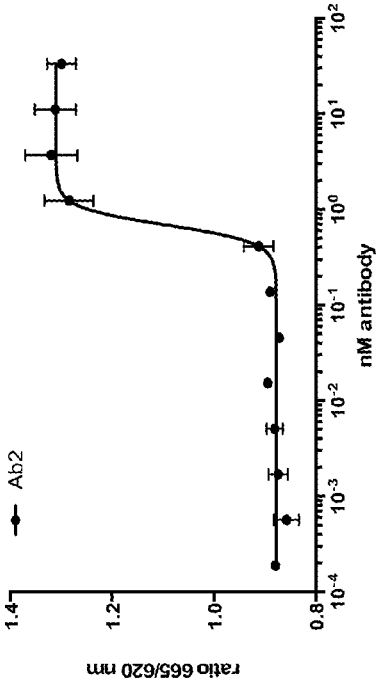


FIG. 18C

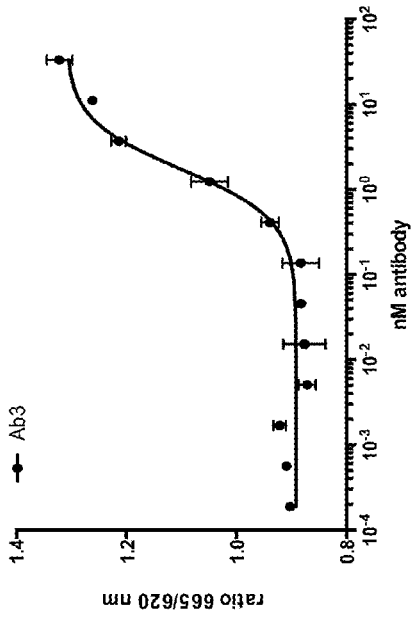


FIG. 18D

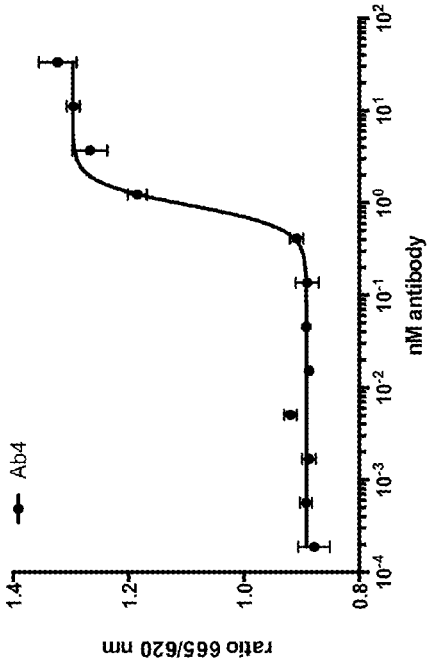


FIG. 18E

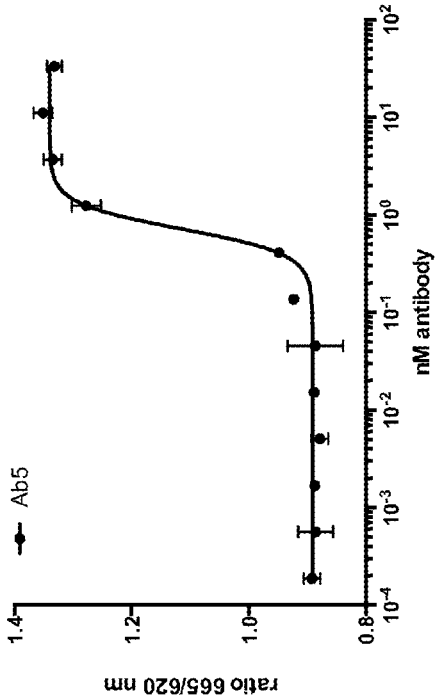


FIG. 18F

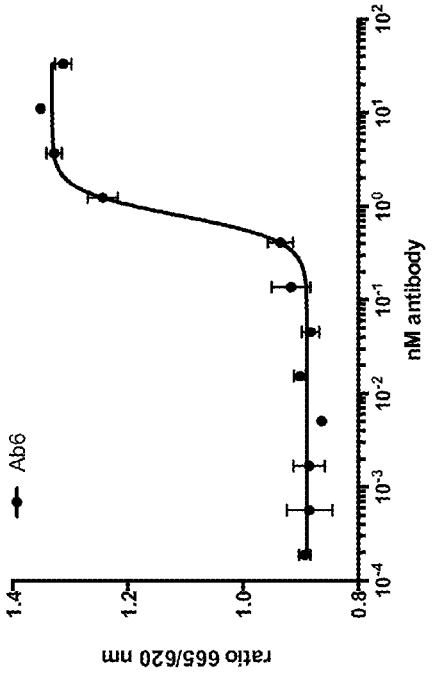


FIG. 18G

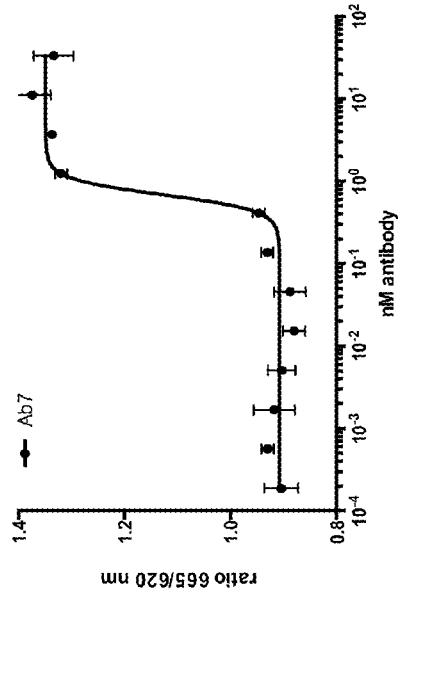


FIG. 18H

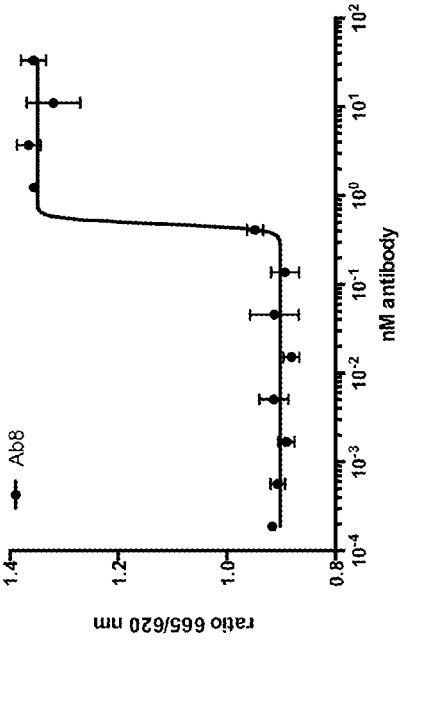


FIG. 18I

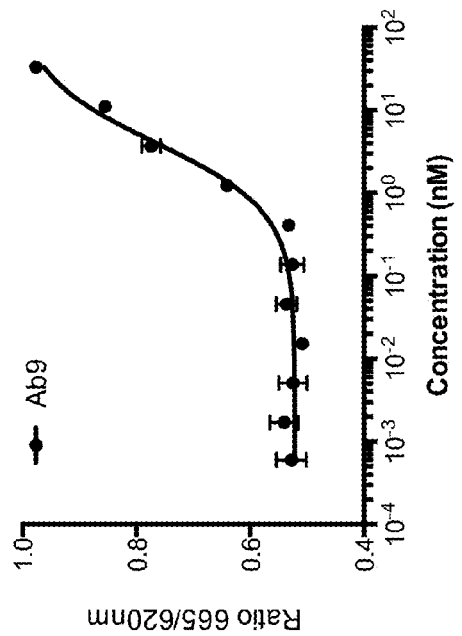


FIG. 18J

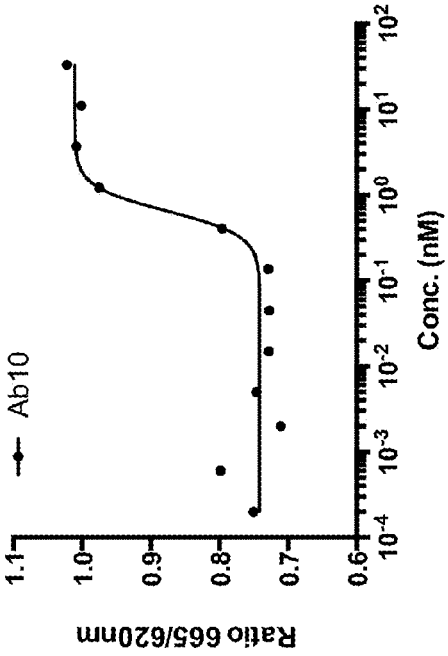


FIG. 18K

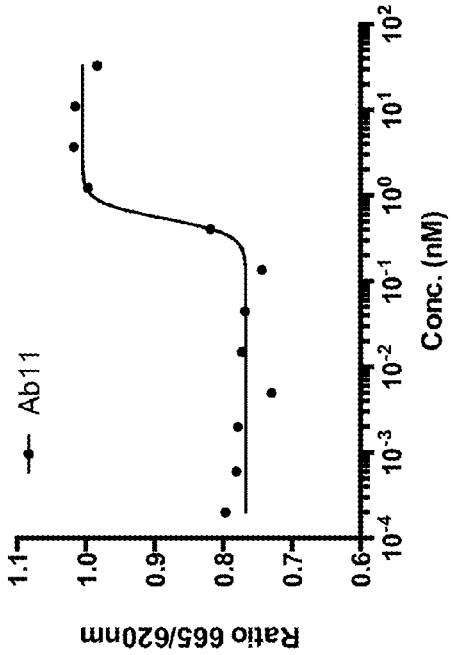


FIG. 18L

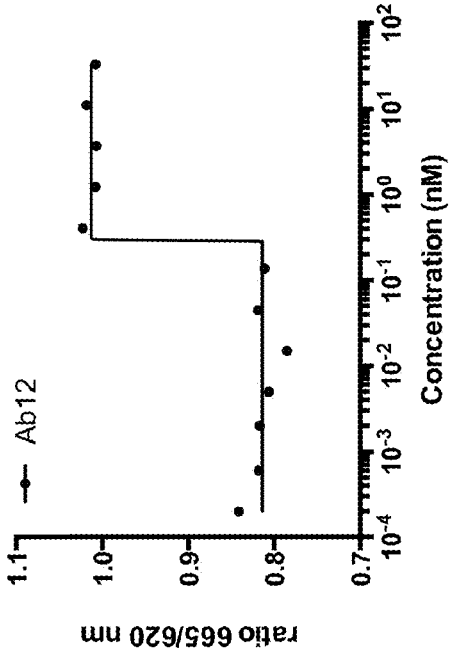


FIG. 18M

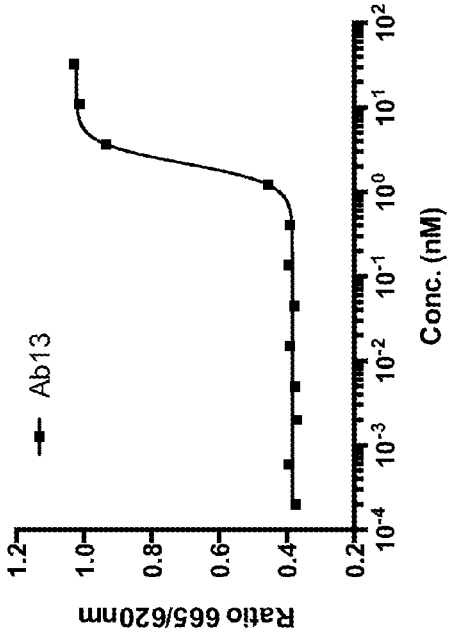


FIG. 18N

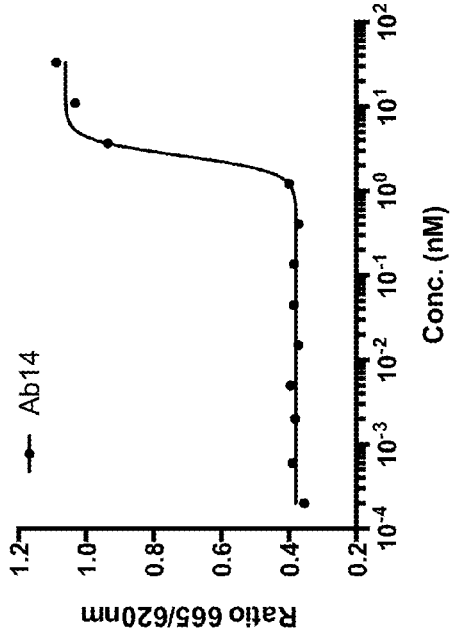


FIG. 18O

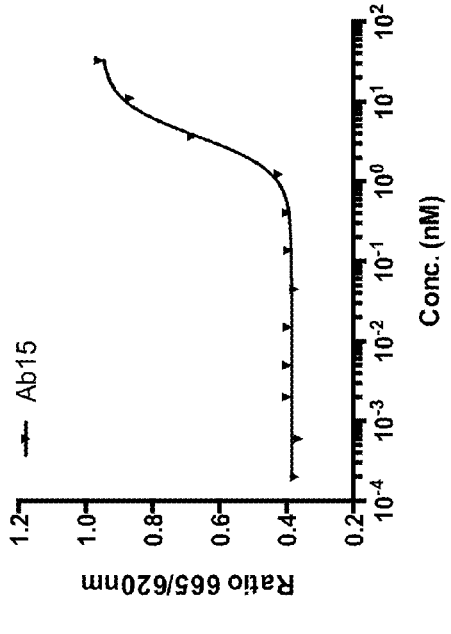


FIG. 18P

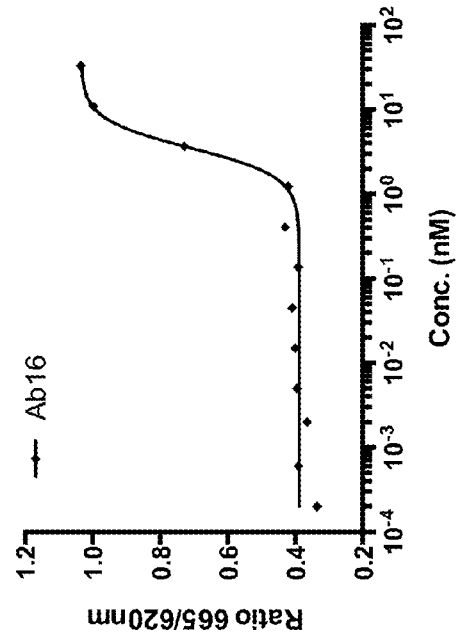


FIG. 18R

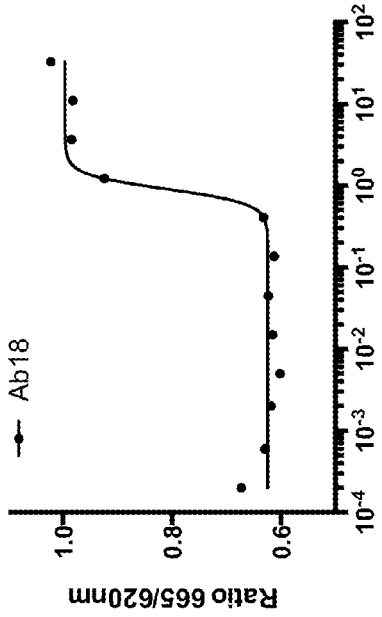


FIG. 18T

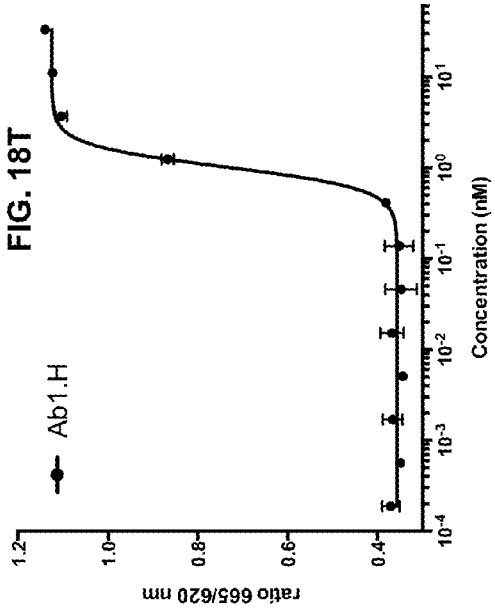


FIG. 18Q

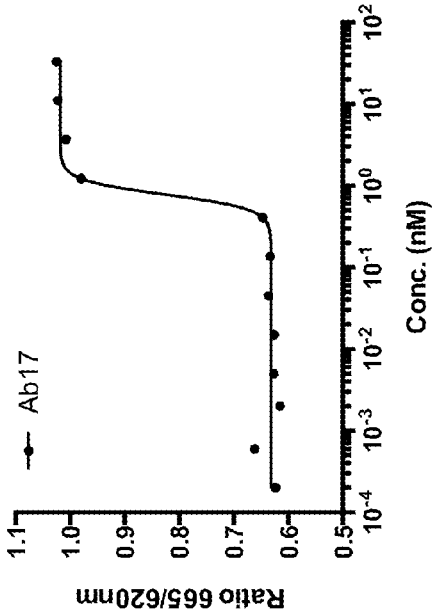


FIG. 18S

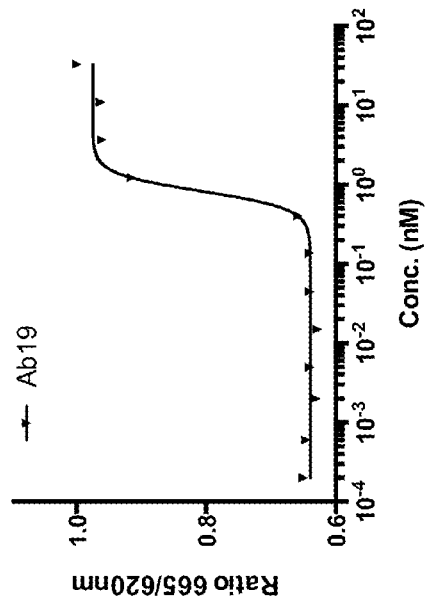


FIG. 18U

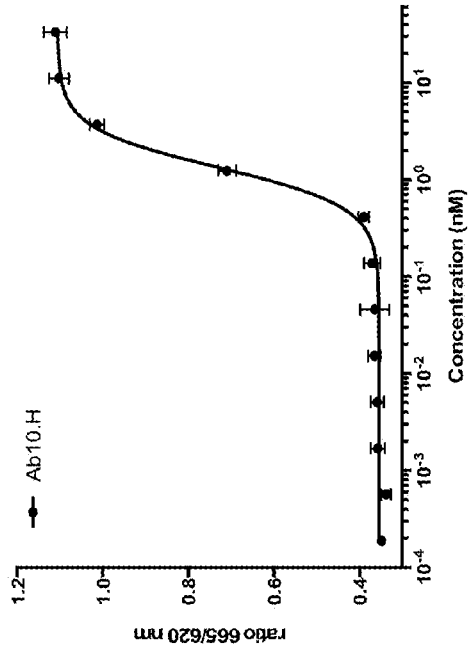


FIG. 18V

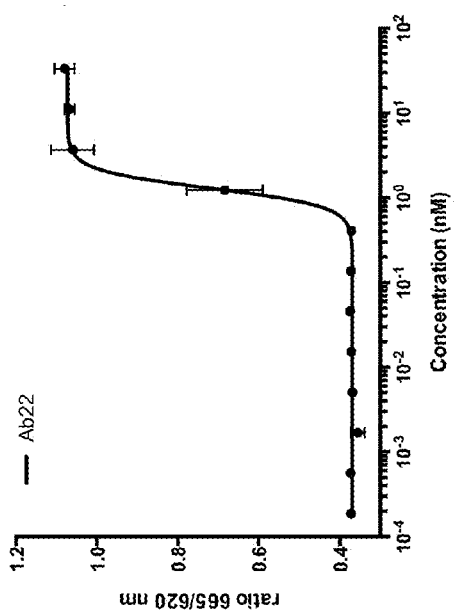


FIG. 18W

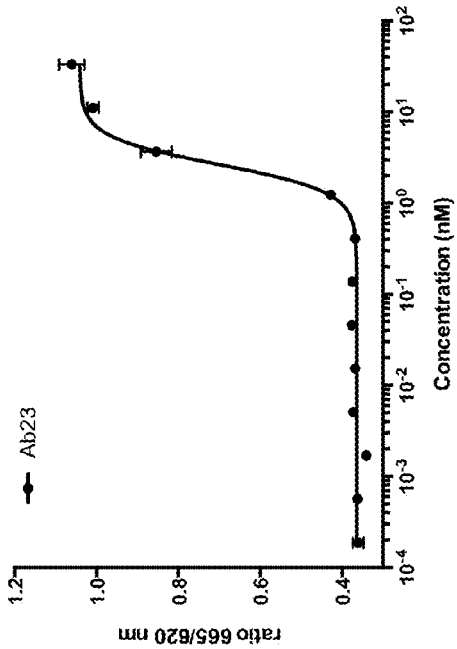
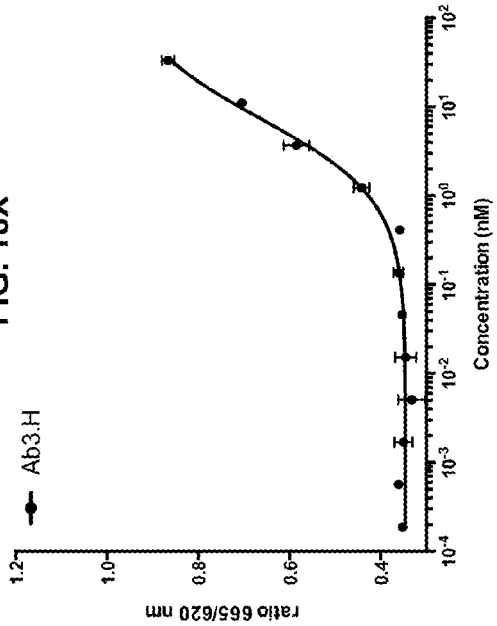


FIG. 18X



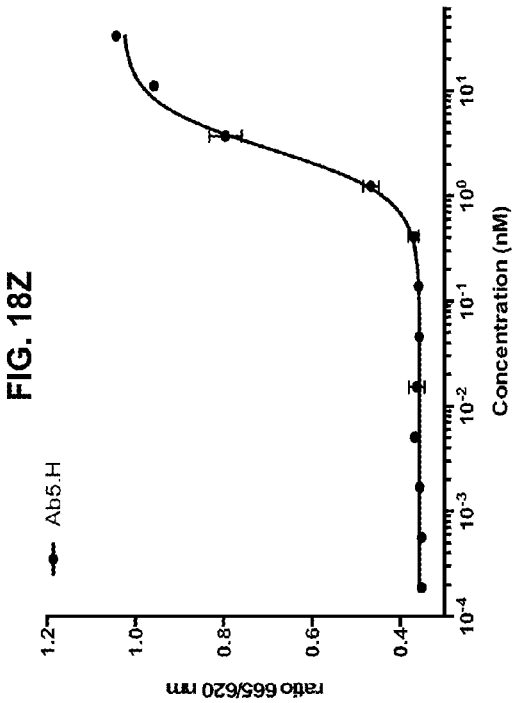


FIG. 18Z

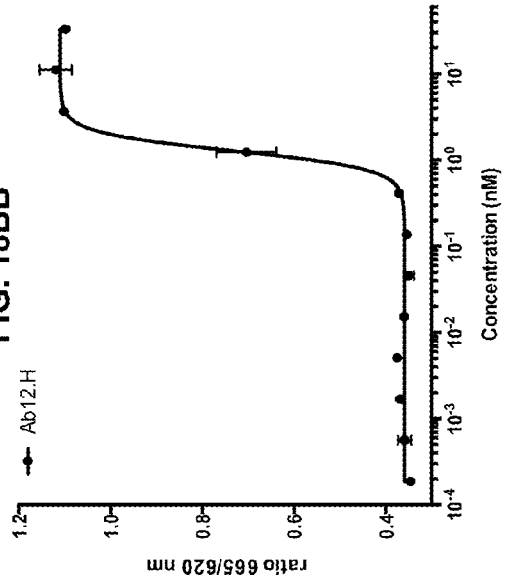


FIG. 18BB

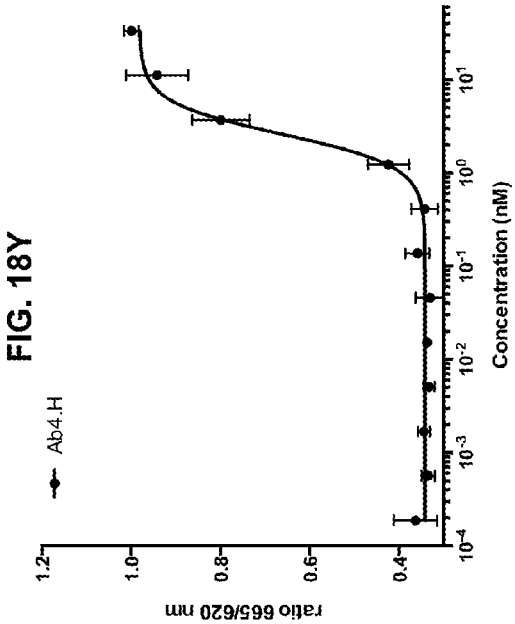


FIG. 18Y

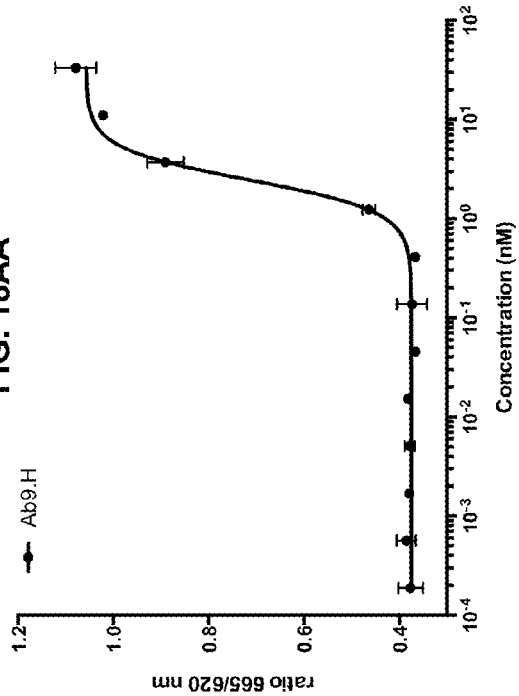


FIG. 18AA

FIG. 19A

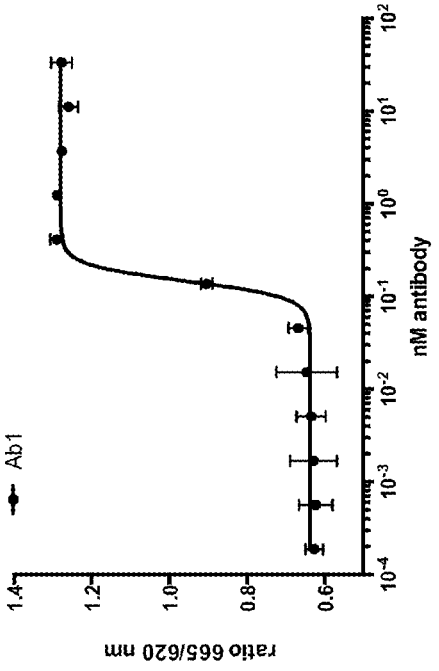


FIG. 19B

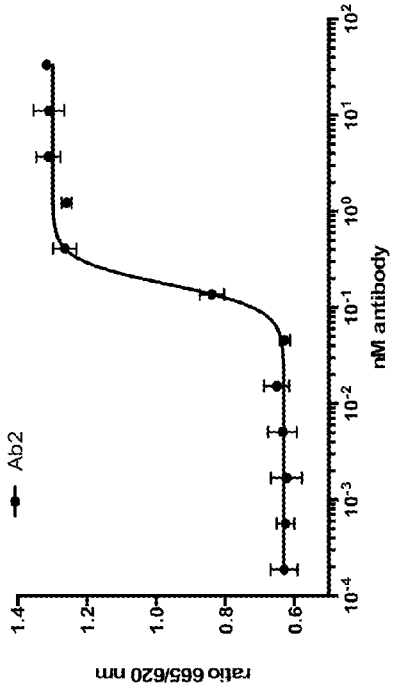


FIG. 19C

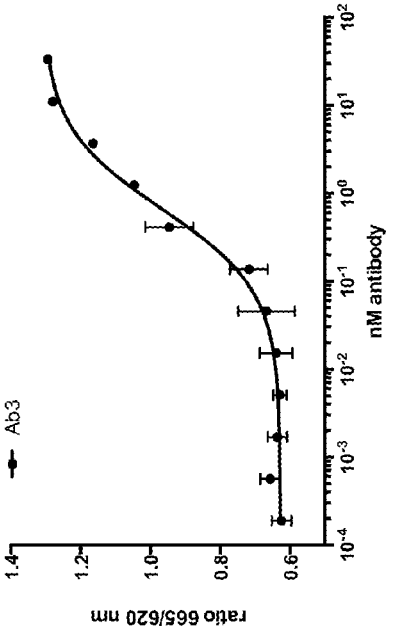


FIG. 19D

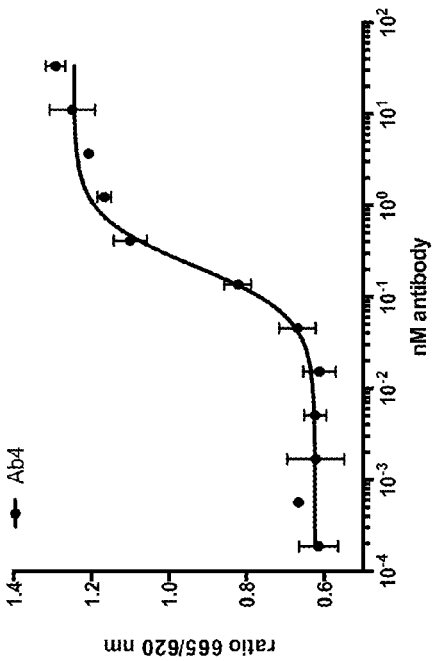


FIG. 19E

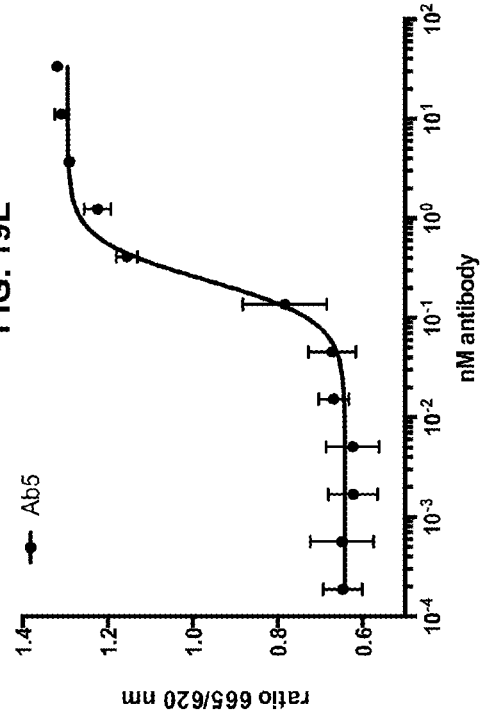


FIG. 19F

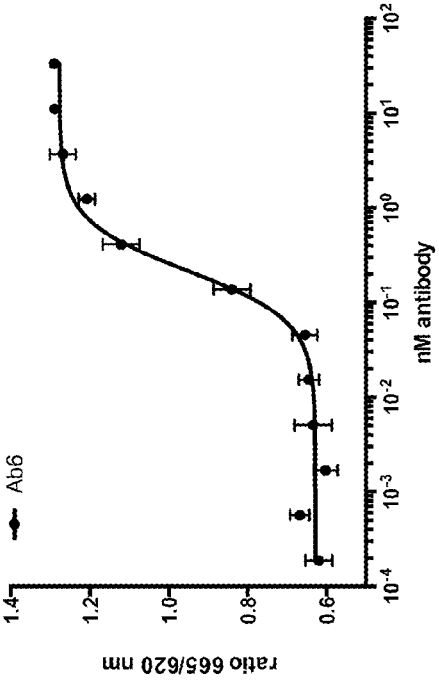


FIG. 19G

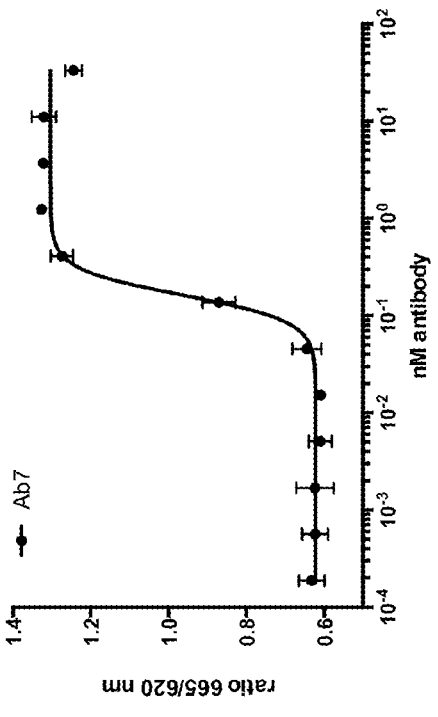
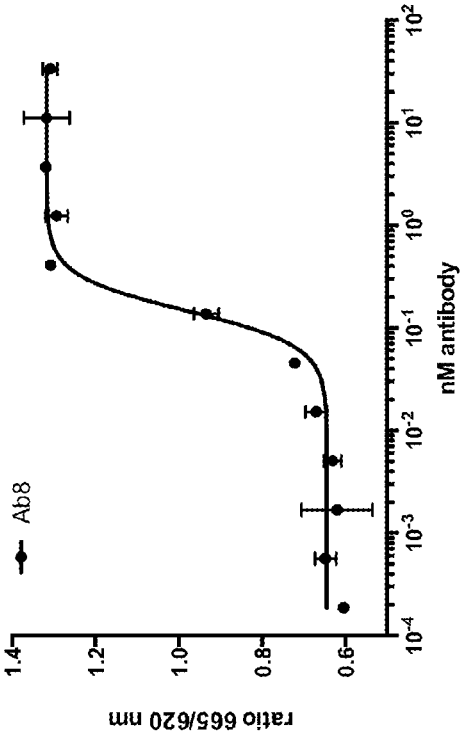
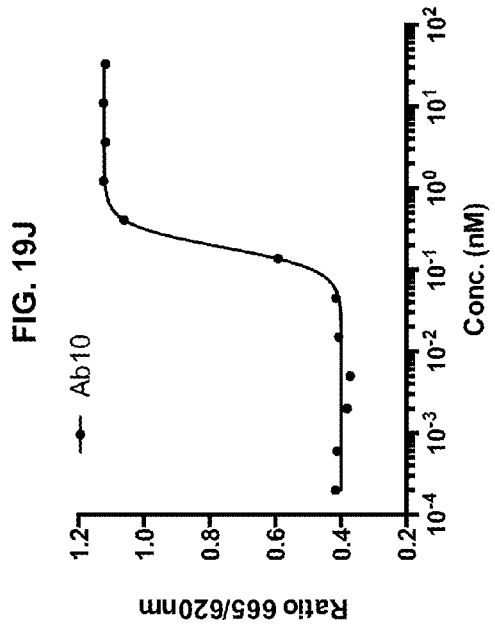
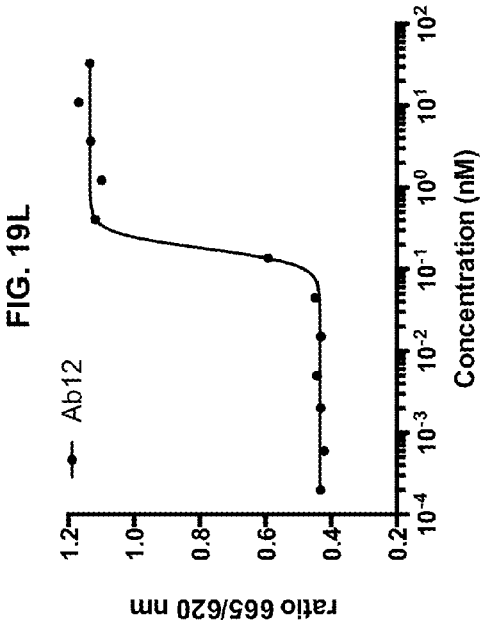
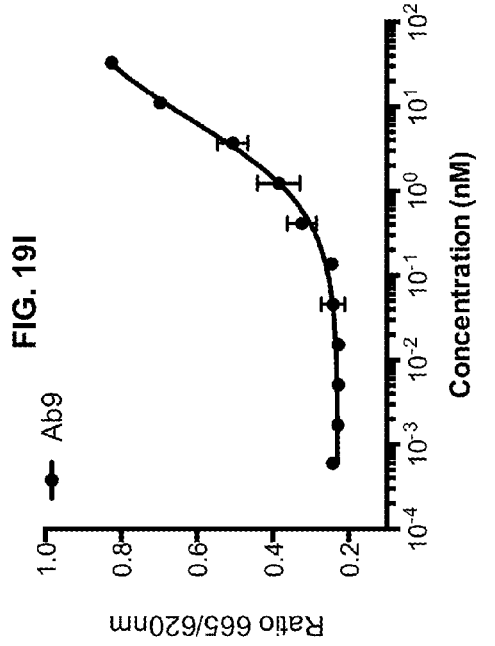


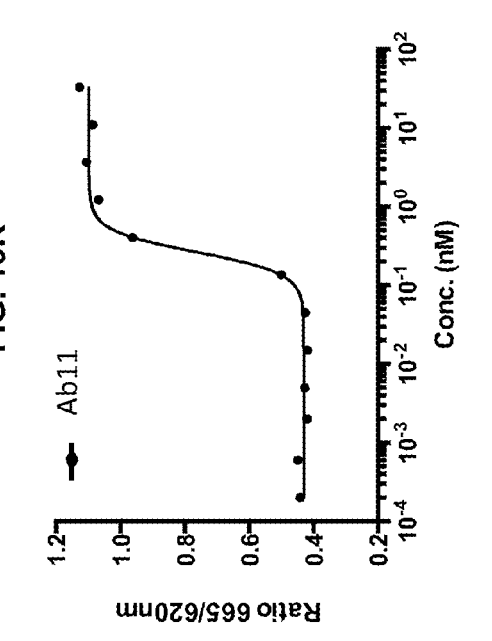
FIG. 19H

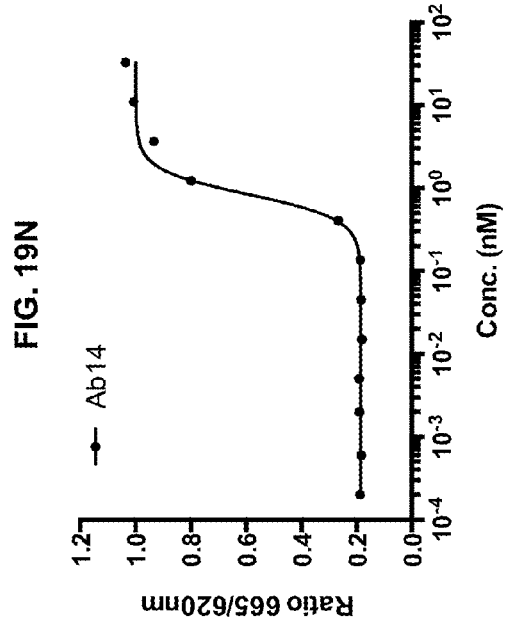


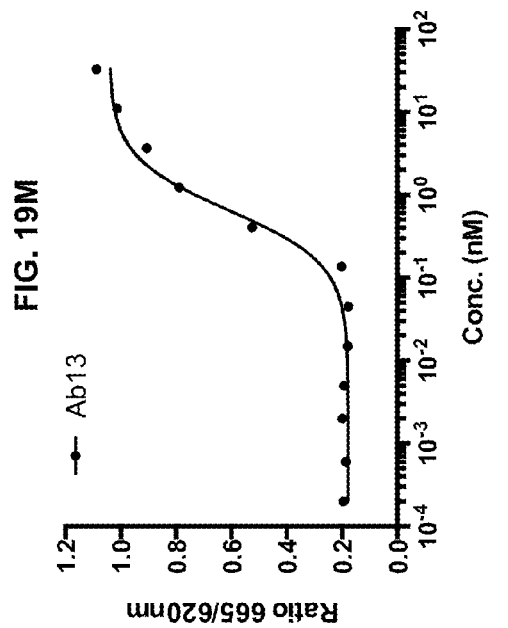

FIG. 19J
Ab10
Ratio 665/620nm
Conc. (nM)

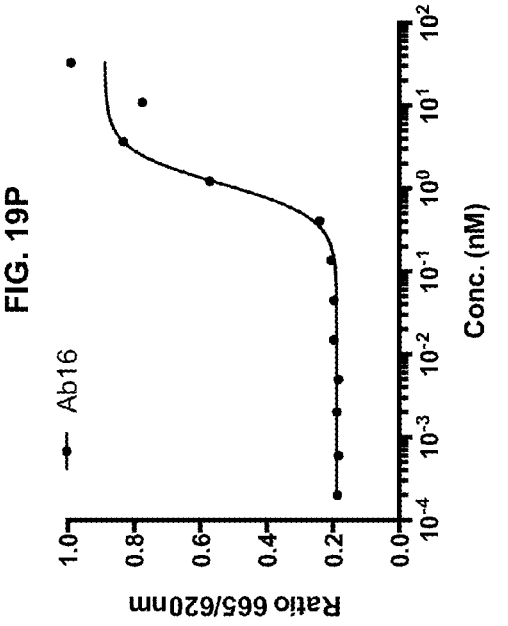

FIG. 19L
Ab12
ratio 665/620 nm
Concentration (nM)


FIG. 19I
Ab9
Ratio 665/620nm
Concentration (nM)


FIG. 19K
Ab11
Ratio 665/620nm
Conc. (nM)


FIG. 19N
Ab14
Ratio 665/620nm
Conc. (nM)


FIG. 19M
Ab13
Ratio 665/620nm
Conc. (nM)


FIG. 19P
Ab16
Ratio 665/620nm
Conc. (nM)

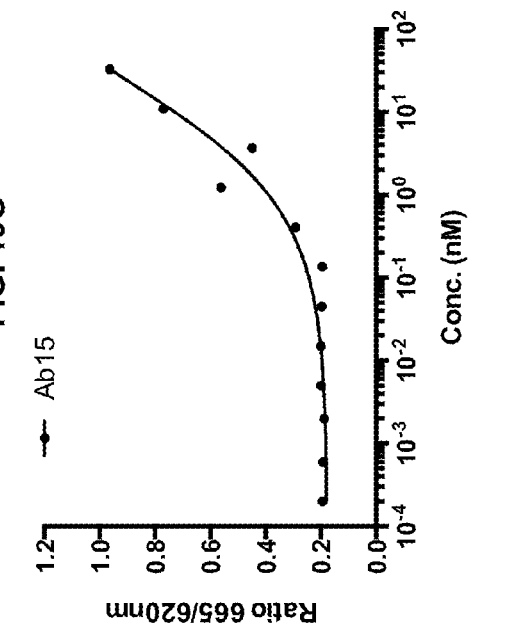

FIG. 19O
Ab15
Ratio 665/620nm
Conc. (nM)

FIG. 19Q

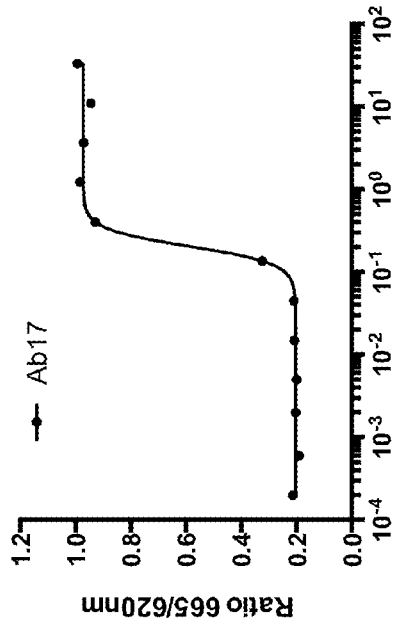


FIG. 19R

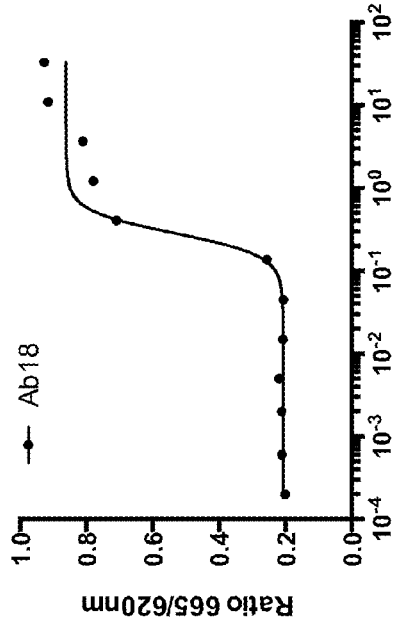


FIG. 19S

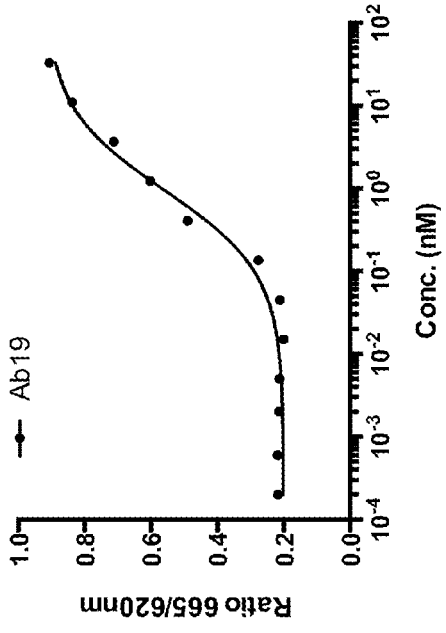
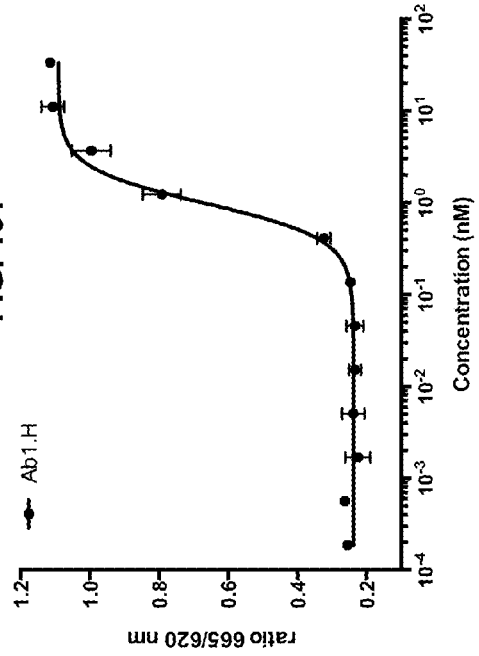
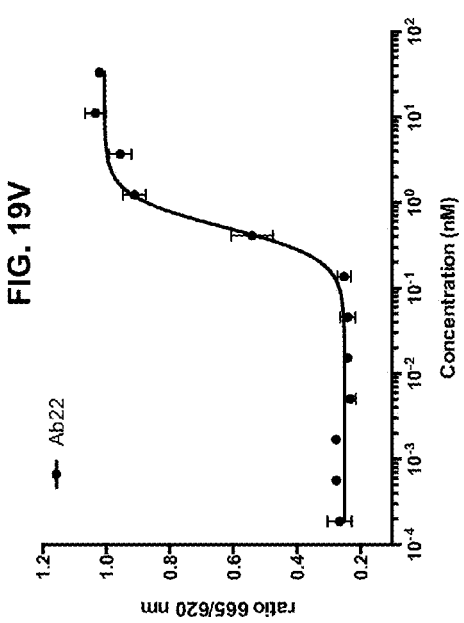
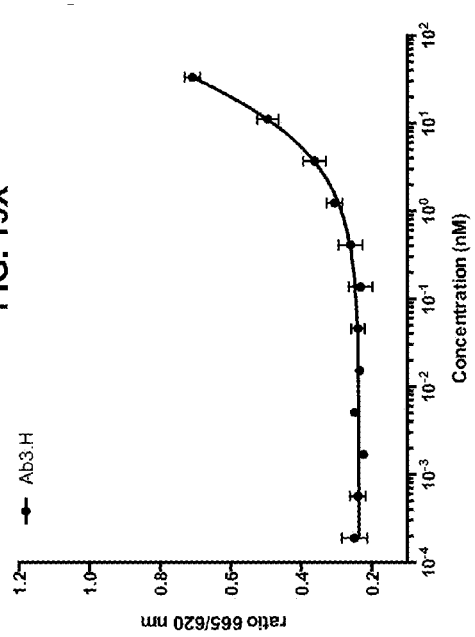
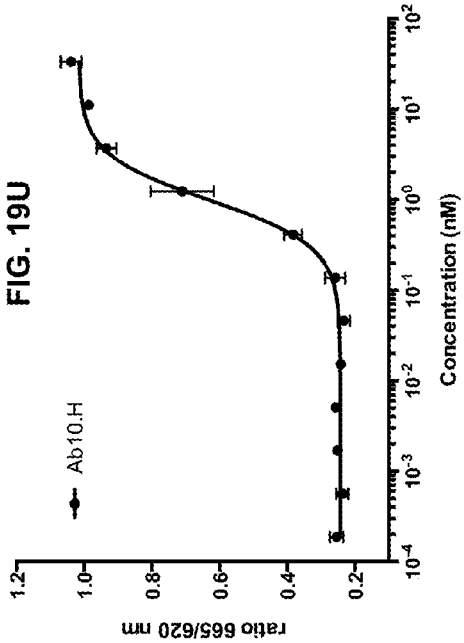


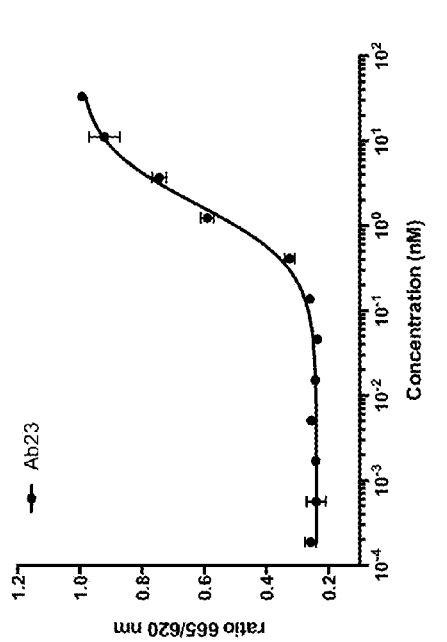
FIG. 19T




FIG. 19V
Ab22
ratio 665/620 nm
Concentration (nM)


FIG. 19X
Ab3.H
ratio 665/620 nm
Concentration (nM)


FIG. 19U
Ab10.H
ratio 665/620 nm
Concentration (nM)


FIG. 19W
Ab23
ratio 665/620 nm
Concentration (nM)

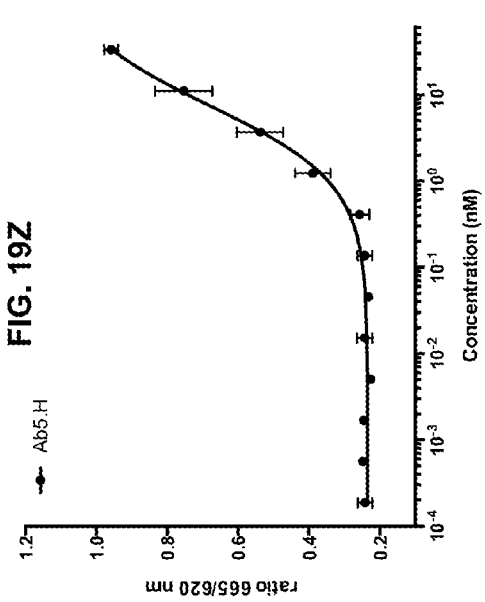


FIG. 19Z

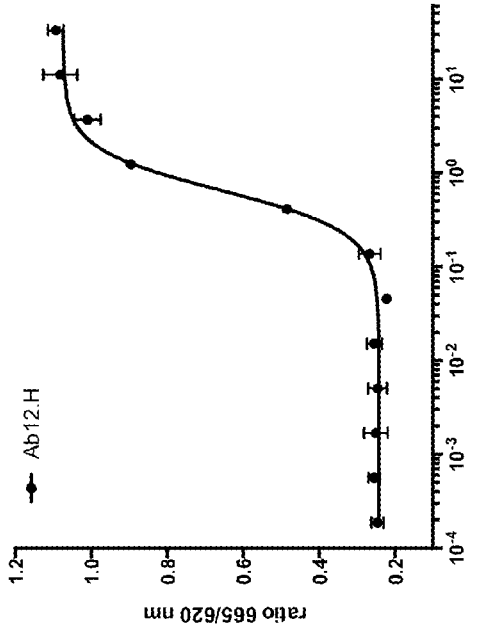


FIG. 19BB

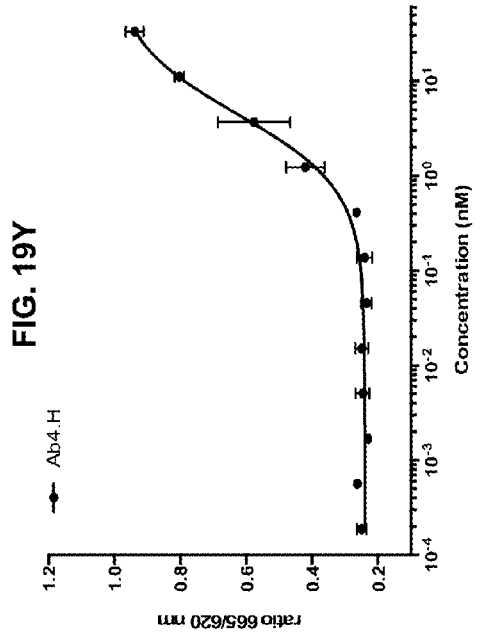


FIG. 19Y

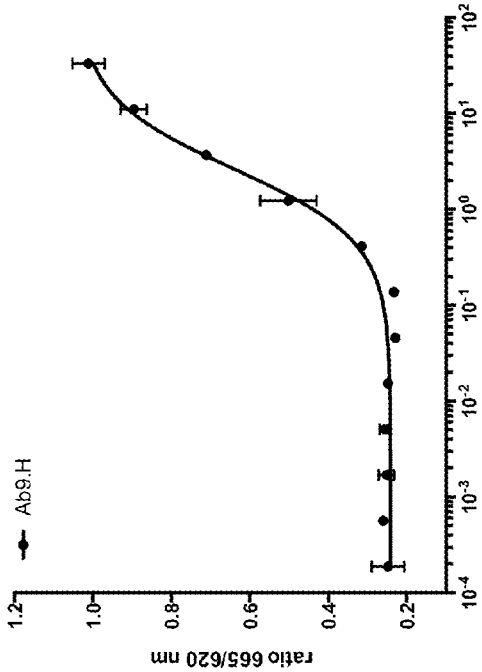


FIG. 19AA

FIG. 20

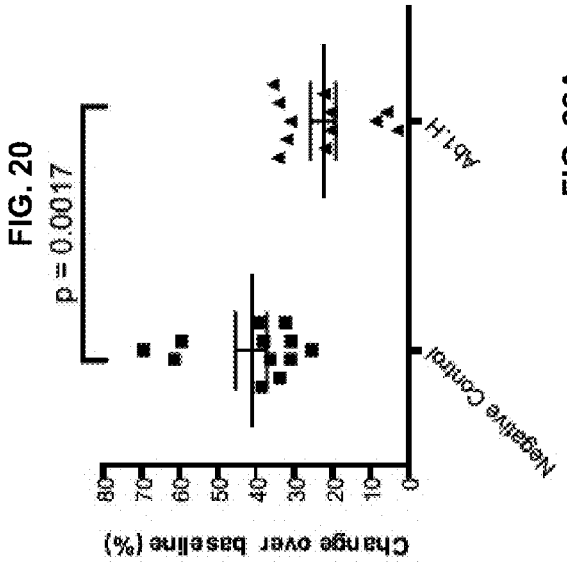


FIG. 21

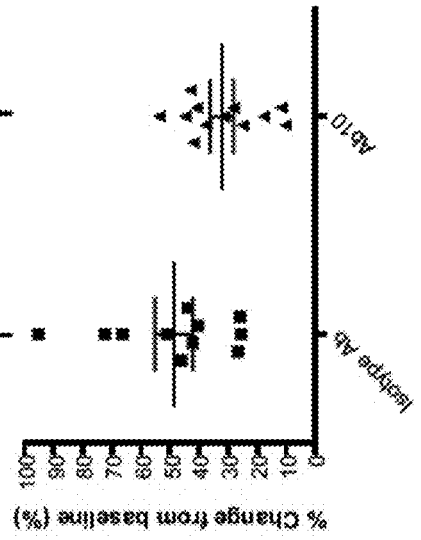


FIG. 22A

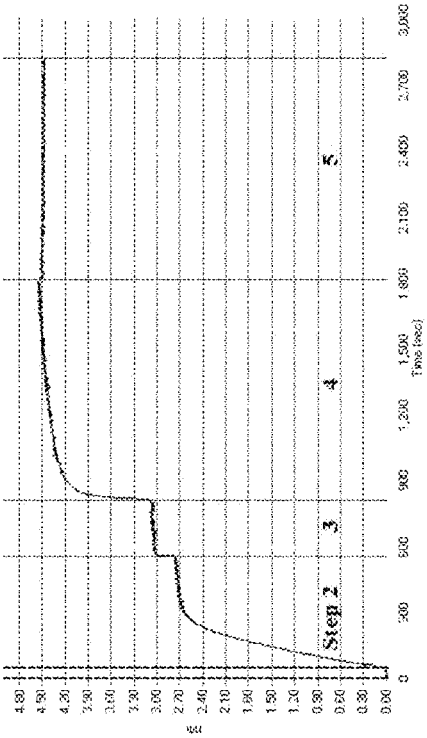


FIG. 22B

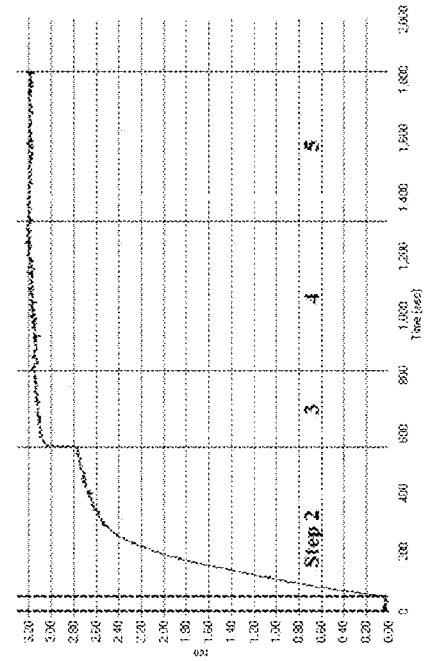


FIG. 23

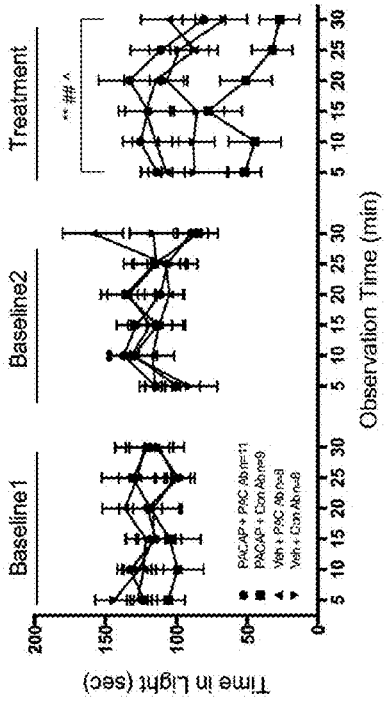
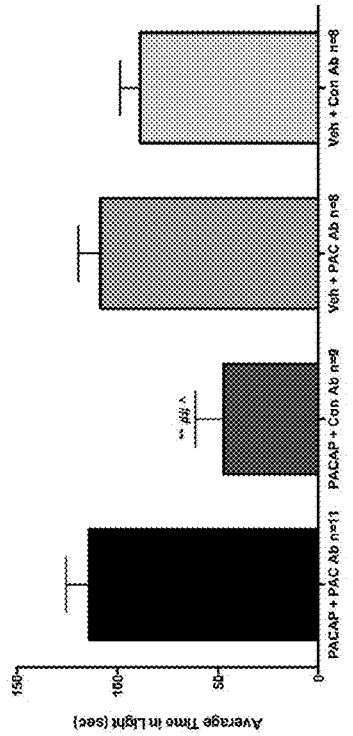


FIG. 24



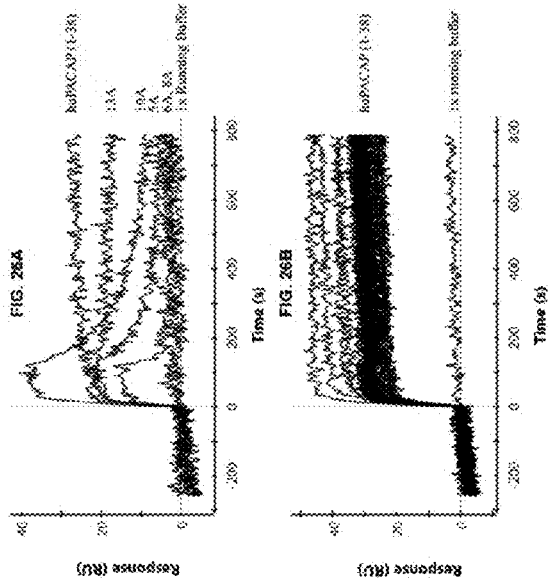
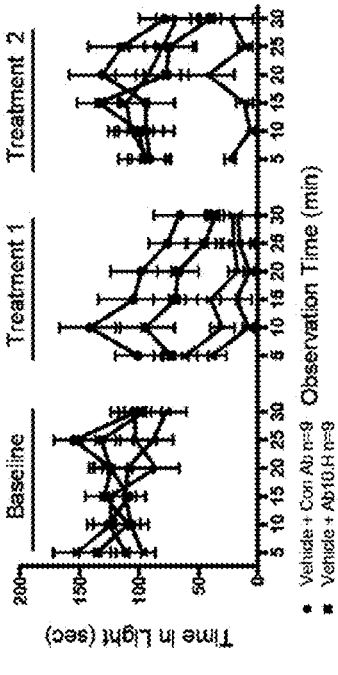
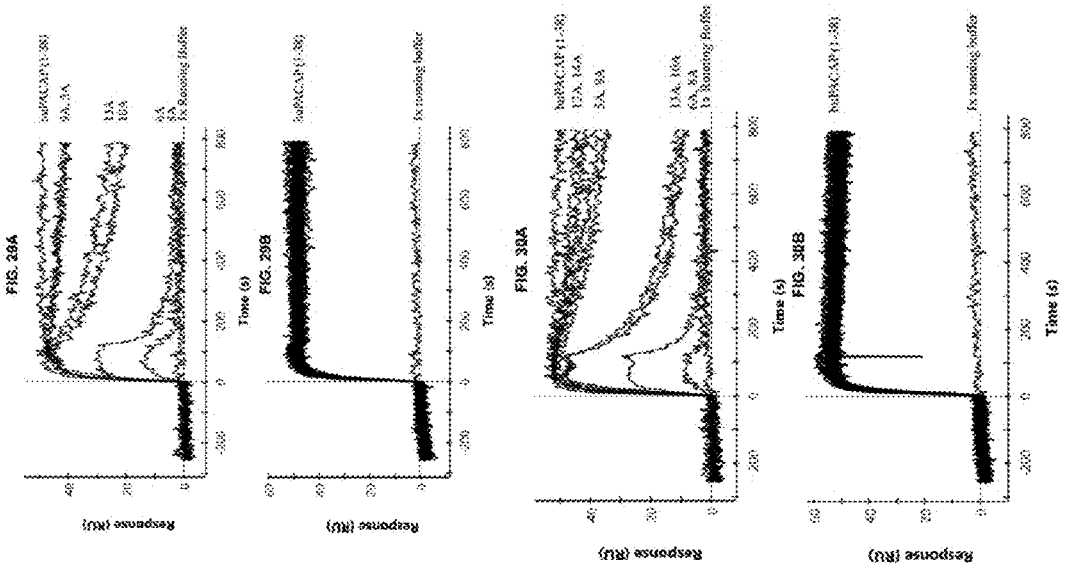
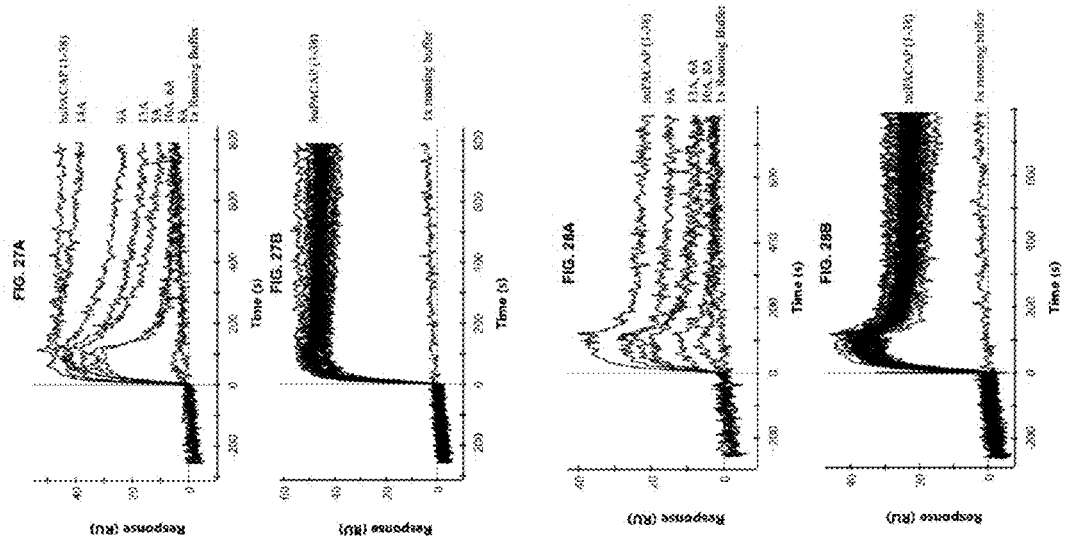
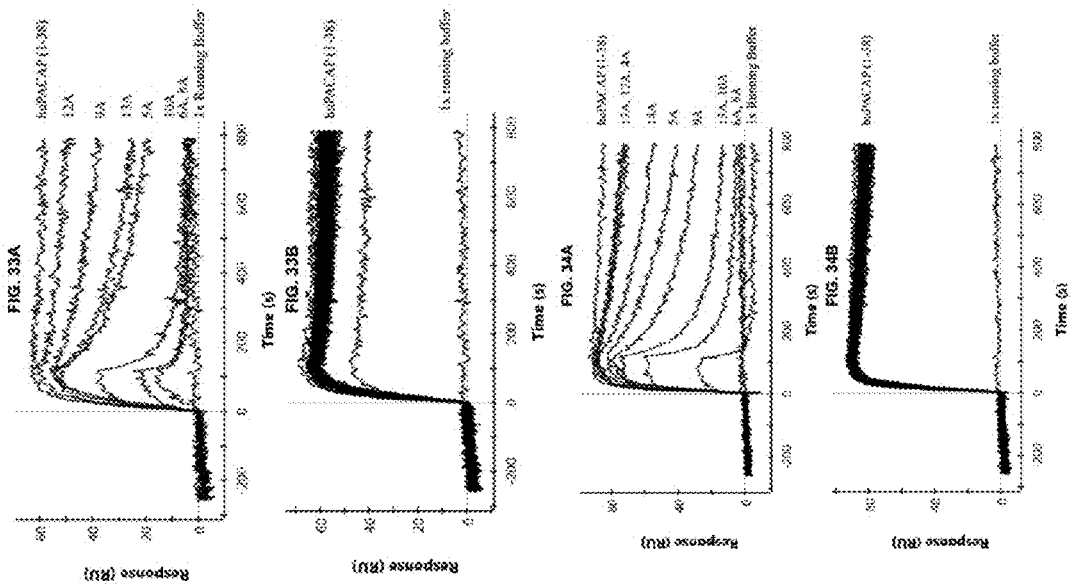


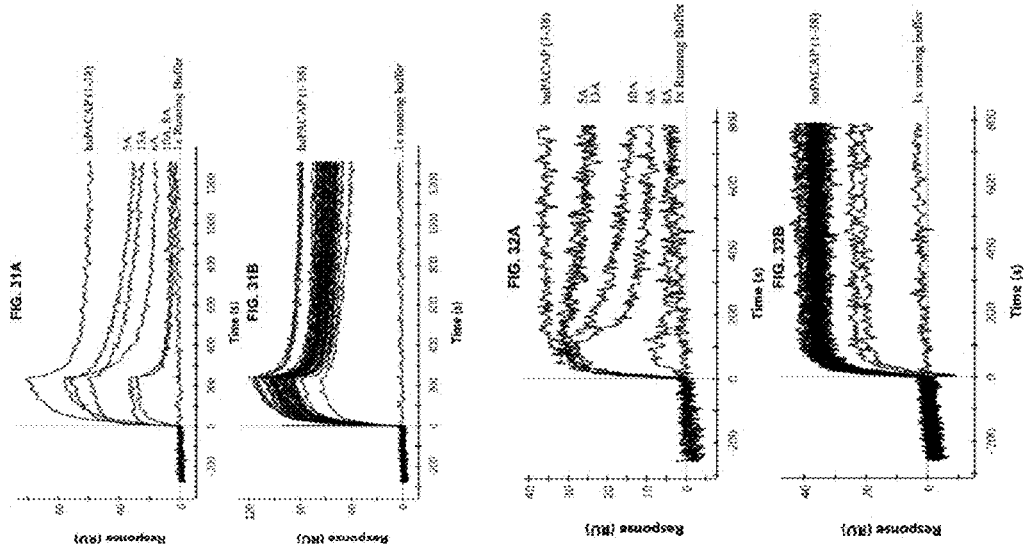
FIG. 25

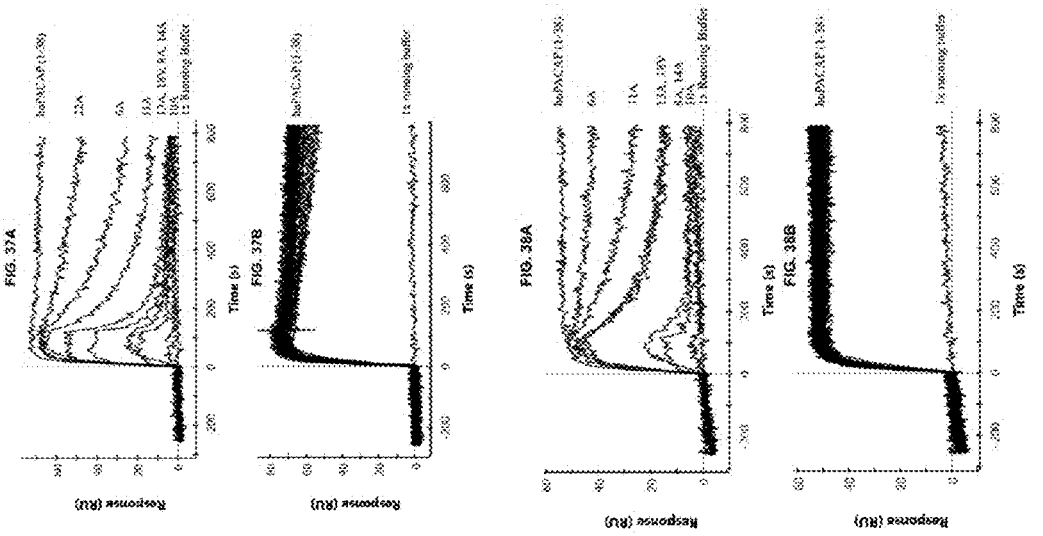


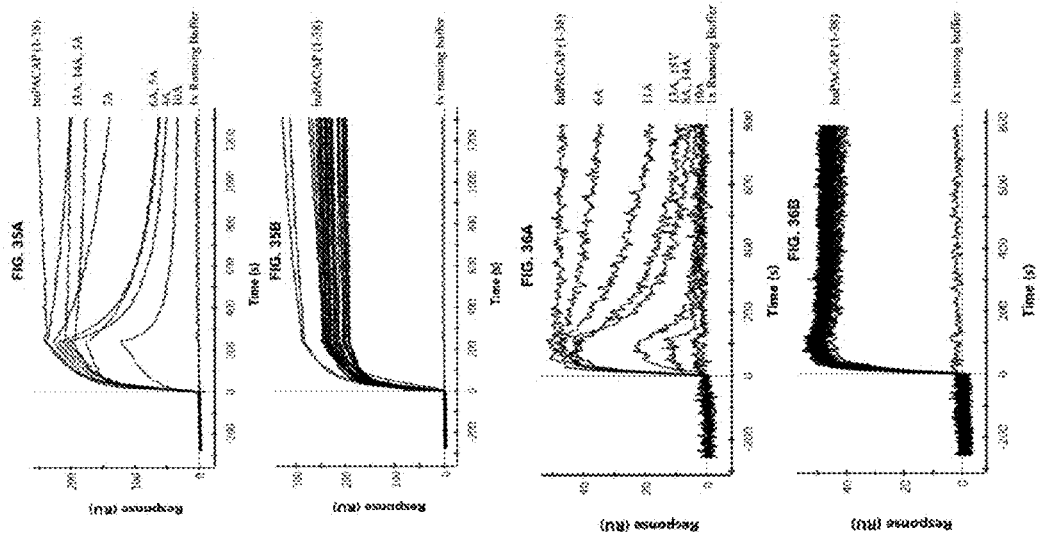

FIG. 26A
FIG. 26B
FIG. 32A
FIG. 32B
Response (RU)
Time (s)

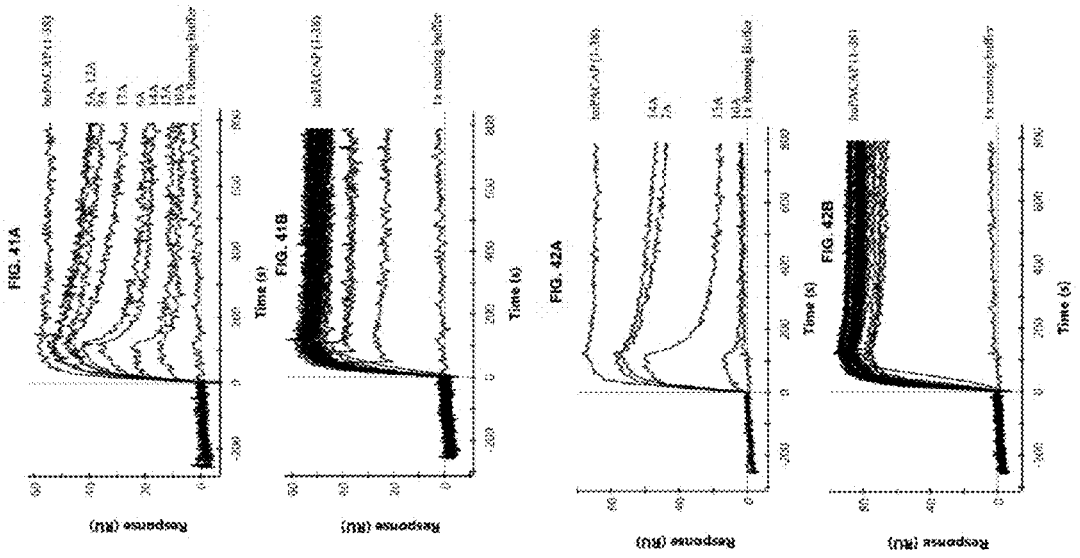

FIG. 27A
FIG. 27B
FIG. 28A
FIG. 28B
Response (RU)
Time (s)

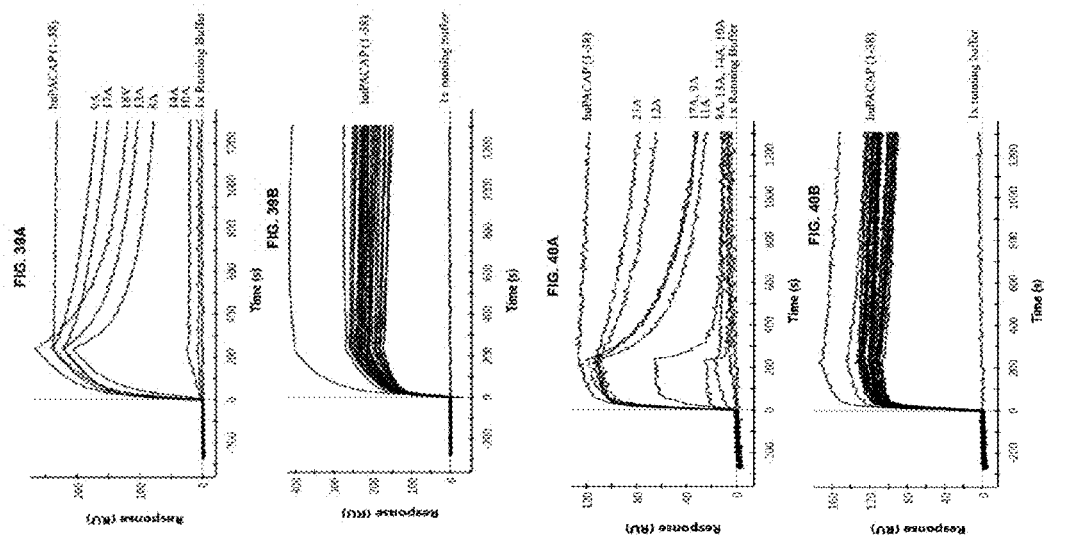

FIG. 33A
FIG. 33B
FIG. 34A
FIG. 34B
Response (RU)
Time (s)

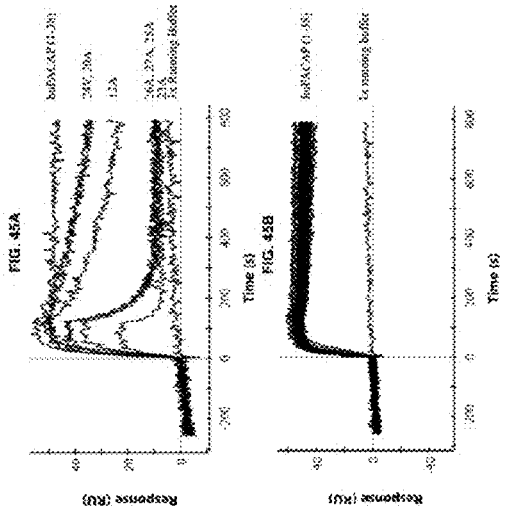

FIG. 31A
FIG. 31B
FIG. 32A
FIG. 32B
Response (RU)
Time (s)


FIG. 37A
FIG. 37B
FIG. 38A
FIG. 38B
Response (RU)
Time (s)
1x Running Buffer


FIG. 35A
FIG. 35B
FIG. 36A
FIG. 36B
Response (RU)
Time (s)
1x Running Buffer


FIG. 41A
FIG. 41B
FIG. 42A
FIG. 42B
Response (RU)
Time (s)
1x Running Buffer
1x running buffer


FIG. 38A
FIG. 38B
FIG. 40A
FIG. 40B
Response (RU)
Time (s)
1x Running Buffer
1x running buffer


FIG. 45A
FIG. 45B
Response (RU)
Time (s)

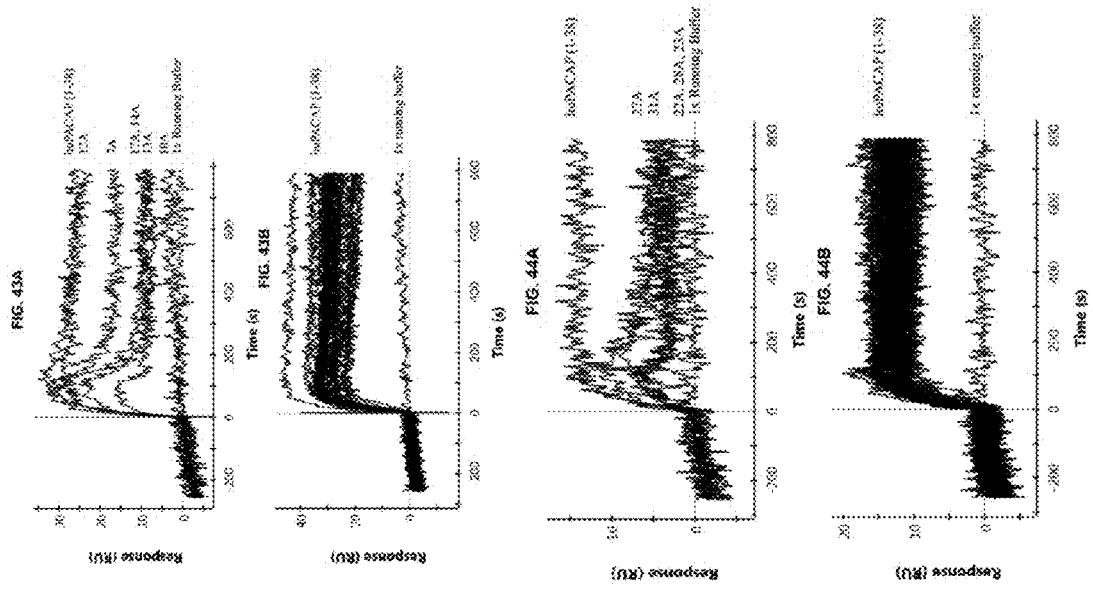

FIG. 43A
FIG. 43B
FIG. 44A
FIG. 44B
Response (RU)
Time (s)

FIG. 46A: Summary of Effects of PACAP Alanine Scanning Mutants on Antibody Binding

VIP	PACAP	#	Ab1	Ab2	Ab13	Ab14	Ab15	Ab16	Ab17	Ab18	Ab19
H	H	1									
S	S	2									
D	D	3									
A	G	4									4A
V	I	5	5A	5A		5A	5A	5A	5A	5A	5A
F	F	6	6A	6A	6A	6A	6A	6A	6A	6A	6A
T	T	7									
D	D	8	8A	8A	8A	8A	8A	8A	8A	8A	8A
N	S	9		9A	9A	9A	9A			9A	9A
Y	Y	10	10A	10A	10A	10A	10A	10A	10A	10A	10A
T	S	11									
R	R	12					12A			12A	12A
L	Y	13	13A	13A	13A	13A	13A	13A	13A	13A	13A
R	R	14		14A			14A				14A
K	K	15									
Q	Q	16									
M	M	17									17A
A	A	18									
V	V	19									
K	K	20									
K	K	21									
Y	Y	22									
L	L	23									
N	A	24									
S	A	25									
I	V	26									
L	L	27									

FIG. 46B: Summary of Effects of PACAP Alanine Scanning Mutants on Antibody Binding

VIP	PACAP	#	Ab1	Ab2	Ab13	Ab14	Ab15	Ab16	Ab17	Ab18	Ab19
N	G	28									
	K	29									
	R	30									
	Y	31									
	K	32									
	Q	33									
	R	34									
	V	35									
	K	36									
	N	37									
	K	38									

FIG. 47A: Summary of Effects of PACAP Alanine Scanning Mutants on Antibody Binding

VIP	PACAP	#	Ab5	Ab7	Ab11	Ab12	Ab4	Ab3	Ab6	Ab8	Ab9	Ab22	Ab23
H	H	1											
S	S	2											
D	D	3	3A										
A	G	4	4A										
V	I	5	5A						5A				
F	F	6	6A	6A	6A	6A			6A				
T	T	7	7A							7A	7A		
D	D	8		8A	8A	8A	8A	8A					
N	S	9					9A	9A	9A				
Y	Y	10	10A	10A	10A	10A	10A	10A	10A	10A	10A		
T	S	11		11A	11A	11A		11A					
R	R	12						12A	12A		12A		12A
L	Y	13	13A	13A	13A	13A	13A	13A	13A	13A	13A		
R	R	14	14A	14A	14A	14A	14A	14A	14A	14A	14A		
K	K	15											
Q	Q	16											
M	M	17					17A	17A	17A		17A		
A	A	18		18V	18V	18V	18V						
V	V	19											
K	K	20											20A
K	K	21						21A					
Y	Y	22			22A							22A	
L	L	23										23A	23A
N	A	24											24V
S	A	25											
I	V	26											26A
L	L	27										27A	27A

FIG. 47B: Summary of Effects of PACAP Alanine Scanning Mutants on Antibody Binding

VIP	PACAP	#	Ab5	Ab7	Ab11	Ab12	Ab4	Ab3	Ab6	Ab8	Ab9	Ab22	Ab23
N	G	28										28A	28A
	K	29											
	R	30											
	Y	31										31A	
	K	32											
	Q	33											
	R	34											
	V	35											
	K	36											
	N	37											
	K	38											

ANTI-PACAP ANTIBODIES AND USES THEREOF

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Application Ser. No. 62/148,550, filed Apr. 16, 2015, U.S. Provisional Application Ser. No. 62/148,557, filed Apr. 16, 2015, U.S. Provisional Application Ser. No. 62/148,562, filed Apr. 16, 2015, U.S. Provisional Application Ser. No. 62/148,596, filed Apr. 16, 2015, U.S. Provisional Application Ser. No. 62/148,643, filed Apr. 16, 2015, U.S. Provisional Application Ser. No. 62/148,583, filed Apr. 16, 2015, U.S. Provisional Application Ser. No. 62/148,640, filed Apr. 16, 2015, each of which is hereby incorporated by reference in its entirety.

SEQUENCE DISCLOSURE

[0002] This application includes as part of its disclosure an electronic sequence listing text file named "43257o5808.txt", having a size of 525,090 bytes and created on Feb. 29, 2016, which is hereby incorporated in its entirety.

FIELD OF THE INVENTION

[0003] This invention generally pertains to antibodies and antigen binding fragments thereof, preferably humanized, chimerized, and human antibodies and antigen binding fragments thereof, and compositions containing such antibodies and antigen binding fragments thereof, wherein such antibodies and antigen binding fragments thereof specifically bind to Pituitary Adenylate Cyclase-Activating Polypeptide ("PACAP") and therapeutic and diagnostic uses for the antibodies, antigen binding fragments, and compositions thereof.

BACKGROUND

[0004] Pituitary Adenylate Cyclase-Activating Polypeptide ("PACAP") is a member of the secretin/vasoactive intestinal peptide ("VIP")/growth hormone-releasing hormone ("GHRH") family. PACAP is a multifunctional vasodilatory peptide that exists in two α-amidated active forms, one with 38 amino acids (PACAP38; SEQ ID NO: 1241) and the other with 27 amino acids (PACAP27; SEQ ID NO: 1242). Both peptides have the same N-terminal 27 amino acids and are synthesized from the same precursor protein, preproPACAP (See, Moody et al., *Curr. Opin. Endocrinol. Diabetes Obes.,* 18(1):61-67, 2011). PACAP38 is the more prevalent active form, representing up to 90% of PACAP forms in mammalian tissues (See, Kaiser and Russo, *Neuropeptides,* 47:451-461, 2013). The sequence of PACAP38 is identical in all mammals and differs from the avian and amphibian orthologs by only one amino acid (See, Vaudry et al., *Pharmacol. Rev.,* 52:269-324, 2000). The secretin/VIP/GHRH family includes mammalian peptide histidine methioneamide ("PHM"), secretin, glucagon, glucagon-like peptide-1 ("GLP1"), glucagon-like peptide-2 ("GLP2"), glucose-dependent-insulinotrophic-polypeptide ("GIP"), and growth-hormone-releasing-factor ("GRF"). PACAP27 has 68% sequence identity to VIP at the amino acid level (See, Vaudry et al. 2000).

[0005] PACAP is widely distributed in the brain and peripheral organs, e.g., the endocrine system, gonads, sympathetic neurons, respiratory system, gastrointestinal tract, cardiovascular system, and urogenital tracts (See, Schytz et al., *Neurotherapeutics,* 7:191-196, 2010). In particular, PACAP is expressed throughout the nervous system, including a presence in the trigeminovascular system, trigeminal ganglia, spinal cord, hypothalamus, and pituitary. PACAP has roles in neurodevelopment, neuroprotection, neuromodulation, neurogenic inflammation, and nociception with multiple actions (See, Kaiser and Russo (2013)).

[0006] Consistent with its widespread distribution, PACAP exerts pleiotropic effects including modulation of neurotransmitter release, vasodilation, bronchodilation, and activation of intestinal motility, increase of insulin and histamine secretion, as well as stimulation of cell proliferation and/or differentiation. PACAP has been shown to act as a hormone, a neurohormone, a neurotransmitter, and a trophic factor in a number of tissues (See, Vaudry et al., *Pharmacological Rev.,* 52(2):269-324, 2000).

[0007] The biological effects of PACAP are mediated via three different G-protein coupled receptors: PAC1-R, vasoactive intestinal peptide receptor type 1 ("VPAC1-R"), and vasoactive intestinal peptide receptor type 2 ("VPAC2-R"). These receptors are expressed in diverse tissues. PAC1-R is particularly abundant in the nervous system (e.g., olfactory bulb, thalamus, hypothalamus, cerebellum, and spinal dorsal horn), pituitary, and adrenal glands. By contrast, VPAC1-R and VPAC2-R are expressed mainly in the lung, liver, and testis, although they have been detected in other tissues as well. VPAC1-R expression has been detected in the nervous system (e.g., cerebral cortex and hippocampus), smooth muscle cells of lung, liver, intestine, megakaryocytes, and platelets. VPAC1-R associates with receptor-associated membrane protein ("RAMP", specifically RAMP2) (See, Christopoulos et al., *J. Biol. Chem.,* 278:3293-3297, 2002). VPAC2-R expression profile includes the nervous (e.g., thalamus, hippocampus, brain stem, and dorsal root ganglia ("DRG")), cardiovascular system, gastrointestinal system, pancreas, and reproductive systems (See, Usdin et al., *Endocrin.,* 135:2662-2680, 1994; Sheward et al., *Neurosci.,* 67:409-418, 1995).

[0008] PAC1-R is selective for PACAP38 and PACAP27. In particular, PAC1-R binds to PACAP with 100-1000-fold greater affinity than VIP, i.e., K_D~0.5 nM for PACAP27/PACAP38 vs. K_D~500 nM for VIP. Conversely, VPAC1-R and VPAC2-R have equal affinities for PACAP and VIP (K_D~1 nM) (See Schytz et al. (2010)).

[0009] Upon activation, these receptors are all capable of causing downstream production of cyclic adenosine monophosphate ("cAMP"), and/or activation of phospholipase C ("PLC"), and/or modulation of phospholipase D ("PLD"). In particular, PAC1-R is coupled to dual signal transduction pathways acting through cAMP and Ca^{2+}, whereas VPAC1-R and VPAC2-R are coupled principally to adenylyl cyclase. PAC1-R is coupled to G_s protein, which activates adenylyl cyclase to form cAMP that in turn activates protein kinase A. PAC1-R also couples to Gq and thereby activates PLC, which produces inositol phosphate, which increases cytosolic calcium release from intra-cellular calcium stores. There is some evidence for a role of PAC1-R in PLD activation (See McCulloch et al., *Ann. N. Y. Acad. Sci.,* 921:175-185, 2000). Another PACAP signaling pathway results in the elevation of intra-cellular sodium levels via activation of nonselective cation channels (See Roy et al.,

American Journal of Physiology: Regulatory, Integrative and Comparative Physiology, 304(12):R1070-R1084, 2013).

[0010] PACAP is hypothesized to play a role in a multitude of diseases and disorders, including but not limited to migraine, headache, and pain, though such a role for PACAP has not been clinically demonstrated. Migraines are believed to have a neurovascular component. Migraines affect approximately 10% of the adult population in the U.S. and are typically accompanied by intense headaches. Approximately 20-30% of migraine sufferers experience aura, comprising focal neurological phenomena that precede and/or accompany the event. A role for PACAP in migraine has been suggested by several observations: (1) plasma levels of PACAP are elevated during migraine attacks (ictal), as compared to interictal levels, in humans (see, Tuka et al., *Cephalalgia,* 33(13):1085-1095, 2013); (2) an infusion of PACAP38 triggered headaches in healthy subjects, and headaches followed by migraine-like attacks in migraineurs (see, Schytz et al., *Brain,* 132:16-25 2009; and Amin et al., *Brain,* 137:779-794, 2014, respectively); (3) PACAP-induced vasodilation may play a role in neurogenic inflammation (see, Kaiser and Russo, *Neuropeptides,* 47:451-461, 2013); and (4) PACAP-induced migraines are associated with photophobia, phonophobia, nausea, and respond to triptans (see, Amin et al., *Brain,* 32:140-149 2012). PACAP has also been shown to induce vasodilation, photophobia, as well as mast cell degranulation and neuronal activation (See, Markovics et al., *Neurobiology of Disease,* 45:633-644 2012; Baun et al., *Cephalalgia,* 32(4):337-345, 2012; Chan et al., *Pharmacology & Therapeutics,* 129:332-351, 2011).

[0011] One effective treatment for migraines is the administration of triptans, which are a family of tryptamine-based drugs, including sumatriptan and rizatriptan. Members of this family have an affinity for multiple serotonin receptors, including 5-HT_{1B}, 5-HT_{1D}, and 5-HT_{1F}. Members of this family of drugs selectively constrict cerebral vessels, but also cause vasoconstrictive effects on coronary vessels (See Durham, *New Eng. J. Med.,* 350 (11):1073-75, 2004). There is a theoretical risk of coronary spasm in patients with established heart disease following administration, and cardiac events after taking triptans in rare instances may occur. Accordingly, they are contraindicated for some patients with coronary vascular disease.

[0012] Similarly, pain may often be addressed through the administration of certain narcotics or non-steroidal anti-inflammatory drugs ("NSAIDs"). However, the administration of these treatments often has negative consequences. NSAIDs have the potential to cause kidney failure, intestinal bleeding, and liver dysfunction. Narcotics have the potential to cause nausea, vomiting, impaired mental functioning, and addiction. Therefore, it is desirable to identify alternative treatments for pain in order to avoid certain of these negative consequences.

[0013] PACAP may also be involved in diseases and disorders other than migraine, headache, and pain. For example, PACAP may correlate to or even play a causal role in anxiety disorders (WO 2012/106407); thrombocytopenia (WO 2004/062684); and inflammatory skin diseases (WO 2010/007175). PACAP and PAC1-R polymorphisms are associated with post-traumatic stress syndrome ("PTSD") in females, major depressive disorder, and generalized anxiety disorder, suggesting a role for PACAP in these conditions. Further, supporting a role for PACAP in thrombocytopenia, trisomy 18 patients have excess PACAP and exhibit defective megakaryocyte maturation (See, Schytz et al. 2010; and Moody et al., *Curr. Opin. Endocrinol. Diabetes Obes.,* 18(1):61-67, 2011).

[0014] Also, PACAP and other neuropeptides, such as Calcitonin Gene-Related Peptide ("CGRP"), substance P, neurokinin A, bradykinin, and endothelin-1, are expressed in the lower urinary tract ("LUT") (see, Arms and Vizzard, *Handbook Exp. Pharmacol.,* 202:395-423 2011) and reportedly may play a role in LUT dysfunction and urinary tract disorders such as urinary tract infection ("UTI"), abnormal voiding, urinary urgency, nocturia, urinary incontinence, overactive bladder, and the pain associated with such conditions.

[0015] PACAP and PACAP receptors have also been suggested to modulate inflammatory and neuropathic pain and have been implicated in both pronociception and antinociception (See, Davis-Taber et al., *J. Pain,* 9(5):449-56 2008). PACAP has also been reported to be required for spinal desensitization and the induction of neuropathic pain (See, Mabuchi et al., *J. Neurosci.,* 24(33):7283-91, 2004). Additionally, morphine withdrawal behavior is reportedly modified in PACAP-receptor deficient mice further suggesting the role of PACAP in morphine withdrawal anxiolytic response (See, Martin et al., *Mol. Brain Res.,* 110(1):109-18 2003).

BRIEF SUMMARY OF THE INVENTION

[0016] In one aspect, the present invention in general relates to anti-PACAP antibodies and antigen binding fragments thereof, preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, that antagonize, inhibit, neutralize, or block at least one biological effect associated with human PACAP. In certain embodiments, the anti-PACAP antibodies and antigen binding fragments thereof inhibit or neutralize at least one biological effect elicited by PACAP, which includes PACAP27 and/or PACAP38, as discussed infra. In other embodiments, the anti-PACAP antibodies and antigen binding fragments thereof neutralize or inhibit PACAP activation of at least one of PAC1-R, VPAC1-R, and/or VPAC2-R; neutralize or inhibit PACAP activation of each of PAC1-R, VPAC1-R, and VPAC2-R; and/or neutralize or inhibit PACAP activation of PAC1-R; and/or inhibits PACAP binding to the cell surface, e.g., via a glycosaminoglycan ("GAG"). In yet other embodiments, the anti-PACAP antibodies and antigen binding fragments thereof are capable of inhibiting PACAP binding to at least one of PAC1-R, VPAC1-R, and/or VPAC2-R; are capable of inhibiting PACAP binding to each of PAC1-R, VPAC1-R, and/or VPAC2-R; or are capable of inhibiting PACAP binding to PAC1-R. In other embodiments, the anti-PACAP antibodies and antigen binding fragments thereof inhibit PACAP-induced cAMP production. In yet other embodiments, the anti-PACAP antibodies and antigen binding fragments thereof, alone or in combination, when administered to a subject, e.g., a human, reduce PACAP-induced vasodilation, photophobia, mast cell degranulation, and/or neuronal activation. In related embodiments, the human or humanized anti-PACAP antibodies and antigen binding fragments thereof are suitable for treating a human subject having an acute, episodic or chronic condition associated with increased vasodilation, photophobia, mast cell degranulation, and/or neuronal activation.

[0017] In another embodiment, the method provides a eukaryotic host cell that is mammalian selected from the group consisting of baby hamster kidney ("BHK") cells; chinese hamster ovary ("CHO") cells; mouse sertoli cells ("TM4" cells); African green monkey kidney cells ("VERO-76" cells); human cervical carcinoma ("HELA") cells; canine kidney cells ("MDCK"); buffalo rat liver ("BRL") cells; human lung cells; human liver ("Hep G2") cells; mouse mammary tumor ("MMT") cells; TRI cells; MRC 5 cells; and FS4 cells. Preferably, the mammalian host cell is a CHO cell. More preferably, the mammalian host cell is a CHO K1 cell.

[0018] In a preferred embodiment, the anti-PACAP antibodies and antigen binding fragments thereof do not substantially interact with (bind) to VIP. The present invention also encompasses the therapeutic use (as a monotherapy or combination therapy) and diagnostic use of such anti-PACAP antibodies and antigen binding fragments thereof.

[0019] More particularly, anti-PACAP antibodies and antigen binding fragments thereof according to the invention can include human, humanized, and chimerized antibodies and fragments thereof, as well as scFvs, camelbodies, shark antibodies, nanobodies, Immunoglobulin New Antigen Receptor ("IgNAR"), fragment antigen binding ("Fab") fragments, Fab' fragments, MetMab like antibodies, bispecific antibodies, monovalent antibody fragments, and $F(ab')_2$ fragments. Additionally, anti-PACAP antibodies and antigen binding fragments thereof according to the invention can substantially or entirely lack N-glycosylation and/or O-glycosylation. In one embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise a human constant domain, e.g., that of IgG1, IgG2, IgG3, or IgG4 antibody or a fragment thereof. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof may comprise an Fc region that has been modified to alter (enhance or impair) at least one of effector function, half-life, proteolysis, or glycosylation. For example, the Fc region may contain one or more mutations that alters or eliminates N- and/or O-glycosylation.

[0020] In some embodiments, anti-PACAP antibodies and antigen binding fragments thereof bind to PACAP with a K_D of less than or equal to 5×10^{-5} M, 10^{-5} M, 5×10^{-6} M, 10^{-6} M, 5×10^{-7} M, 10^{-7} M, 5×10^{-8} M, 10^{-8}M, 5×10^{-9}M, 10^{-9} M, 5×10^{-10} M, 10^{-10} M, 5×10^{-11} M, 10^{-11} M, 5×10^{-12} M, 10^{-12} M, 5×10^{-13} M, or 10^{-13} M, e.g., as determined by ELISA, bio-layer interferometry ("BLI"), Kinetic Exclusion Assay (KINEXA®, Sapidyne Instruments, Boise, Id.), or SPR, e.g., at 25° or 37° C. Preferably, the human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof bind to PACAP with a K_D of less than or equal to 5×10^{-10} M, 10^{-10} M, 5×10^{-11} M, 10^{-11} M, 5×10^{-12} M, or 10^{-12} M. Preferably, the human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof bind to PACAP with a K_D that is less than about 100 nM, less than about 40 nM, less than about 1 nM, less than about 100 pM, less than about 50 pM, or less than about 25 pM. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof bind to PACAP with a K_D that is between about 10 pM and about 100 pM. In another embodiment, the human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof bind to PACAP with an off-rate (k_{off}) of less than or equal to 5×10^{-4} s^{-1}, 10^{-4} s^{-1}, 5×10^{-5} s^{-1}, or 10^{-5} s^{-1}.

[0021] In yet another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof will specifically bind to the linear or conformational epitope(s) and/or compete for binding to the same linear or conformational epitope(s) on human PACAP as an anti-PACAP antibody selected from the group consisting of Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, or Ab1.H (the specific amino acid sequences of the variable and constant regions of these anti-PACAP antibodies, and the nucleic acids that encode for such variable and constant regions, and the epitopes bound thereby as determined using alanine scanning methods are disclosed infra). In particular, the invention embraces anti-PACAP antibodies and antigen binding fragments thereof that specifically bind to the same linear or conformational epitope(s) on human PACAP as an anti-PACAP antibody selected from the group consisting of Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, and Ab1.H. As disclosed infra, in exemplary embodiments, the epitope(s) are determined using alanine scanning mutation strategy.

[0022] In yet another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof include human, humanized or chimerized anti-PACAP antibodies or antibody fragments which bind to the identical epitopes as any one of Ab1, Ab2, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab1.H, Ab5, Ab7, Ab11, Ab12, Ab4, Ab3, Ab6, Ab8, and Ab9 or a binding fragment of any one of the foregoing.

[0023] In yet another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof include human, humanized or chimerized anti-PACAP antibodies or antibody fragments that specifically bind to an epitope on human PACAP or a fragment or variant thereof containing the corresponding amino acid residues wherein said epitope is selected from the group consisting of:

[0024] i. at least one of residues 7, 10, 13, and 14 of a human PACAP;

[0025] ii. at least one of residues 5, 6, 8, 10, and 13 of a human PACAP;

[0026] iii. at least one of residues 6, 8, 9, 10, and 13 of a human PACAP;

[0027] iv. at least one of residues 5, 6, 8, 9, 10, and 13 of a human PACAP;

[0028] v. at least one of residues 7, 10, 12, 13, 14, and 17 of a human PACAP;

[0029] vi. at least one of residues 5, 6, 8, 9, 10, 12, and 13 of a human PACAP;

[0030] vii. at least one of residues 5, 6, 8, 9, 10, 13, and 14 of a human PACAP;

[0031] viii. at least one of residues 6, 8, 10, 11, 13, 14, and 18 of a human PACAP;

[0032] ix. at least one of residues 8, 9, 10, 13, 14, 17, and 18 of a human PACAP;

[0033] x. at least one of residues 3, 4, 5, 6, 7, 10, 13, and 14 of a human PACAP;

[0034] xi. at least one of residues 5, 6, 8, 9, 10, 12, 13, and 14 of a human PACAP;

[0035] xii. at least one of residues 5, 6, 9, 10, 12, 13, 14, and 17 of a human PACAP;

[0036] xiii. at least one of residues 6, 8, 10, 11, 13, 14, 18, and 22 of a human PACAP;

[0037] xiv. at least one of residues 8, 9, 10, 11, 12, 13, 14, 17, and 21 of a human PACAP;

[0038] xv. at least one of residues 4, 5, 6, 8, 9, 10, 12, 13, 14, and 17 of a human PACAP;

[0039] xvi. at least two of the residues of any one of (i)-(xv);

[0040] xvii. at least three of the residues of any one of (i)-(xv);

[0041] xviii. at least four of the residues of any one of (i)-(xv);

[0042] xix. at least five of the residues of any one of (ii)-(xv);

[0043] xx. at least six of the residues of any one of (iv)-(xv);

[0044] xxi. at least seven of the residues of any one of (vi)-(xv);

[0045] xxii. at least eight of the residues of any one of (x)-(xv);

[0046] xxiii. at least nine of the residues of (xiv) or (xv);

[0047] xxiv. all ten residues of (xv);

[0048] In yet another embodiment of the invention, anti-PACAP antibodies or antigen binding fragments thereof include human, humanized or chimerized anti-PACAP antibodies or antibody fragments that specifically bind to an epitope on human PACAP, or a fragment or variant thereof that may contain the corresponding amino acid residues that may include residues 8 and/or 14 of human PACAP.

[0049] In yet another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof include human, humanized or chimerized anti-PACAP antibodies or antibody fragments that specifically bind to an epitope on human PACAP or a fragment or variant thereof containing the corresponding amino acid residues that is present in human wild-type PACAP38 but not human wild-type human PACAP27.

[0050] In yet another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof include human, humanized or chimerized anti-PACAP antibodies or antibody fragments that specifically bind to an which specifically binds to an epitope on human PACAP or a fragment or variant thereof containing the corresponding amino acid residues, wherein said epitope is identified by alanine scanning, e.g., as disclosed in Example 12 or another art-recognized method.

[0051] In yet another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof include human, humanized or chimerized anti-PACAP antibodies or antibody fragments that specifically bind to an epitope on human PACAP or a fragment or variant thereof containing the corresponding amino acid residues, wherein said epitope consists of the residues of any one of (i)-(xv) as described above.

[0052] In yet another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof include human, humanized or chimerized anti-PACAP antibodies or antibody fragments which specifically binds to an epitope on human PACAP or a fragment or variant thereof containing the corresponding amino acid residues that is present in human wild-type PACAP38 and in human wild-type human PACAP27.

[0053] In yet another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof include human, humanized or chimerized anti-PACAP antibodies or antibody fragments that specifically bind to human wild-type human PACAP38 but which does not bind or appreciably bind to human wild-type human PACAP27.

[0054] In yet another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof include human, humanized or chimerized anti-PACAP antibodies or antibody fragments which has a K_D for human PACAP38 which is at least 10 fold, 100 fold, 1,000 fold, 10,000 fold, or 100,000 fold lower (stronger) than the K_D of said antibody or antibody fragment to human PACAP27.

[0055] In yet another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof include human, humanized or chimerized anti-PACAP antibodies or antibody fragments which do not bind to or does not appreciably bind to human Vasoactive Intestinal Peptide ("VIP").

[0056] In yet another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof include human, humanized or chimerized anti-PACAP antibodies or antibody fragments which have a K_D for human PACAP which is at least 10, 100, 1,000, 10,000 or 100,000 fold less (weaker) than the K_D of said antibody or antibody fragment to human VIP.

[0057] In some embodiments, the present invention provides an anti-PACAP antibodies and antigen binding fragments thereof, are preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, comprising at least 2 complementarity determining regions ("CDRs"), or at least 3 CDRs, or at least 4 CDRs, or at least 5 CDRs, or all six CDRs of an anti-PACAP antibody selected from the group consisting of Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, and Ab1.H. In instances where all 6 CDRs are not present, preferably at least the V_H CDR3 and V_L CDR3 are present. In exemplary embodiments, the antibodies and antigen binding fragments thereof comprise the variable heavy ("V_H") chain and/or the variable light ("V_L") chain of one of Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, or Ab1.H.

[0058] In a specific embodiment, anti-PACAP antibodies and antigen binding fragments thereof according to the invention, comprise human, humanized, or chimerized anti-PACAP antibodies or antigen binding fragments thereof, which comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 4; a CDR2 sequence consisting of SEQ ID NO: 6; and a CDR3 sequence consisting of SEQ ID NO: 8; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 24; a CDR2 sequence consisting of SEQ ID NO: 26; and a CDR3 sequence consisting of SEQ ID NO: 28. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof may comprise (a) a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 2, and/or (b) a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 22. In a more specific embodiment, the anti-PACAP antibodies and antigen binding fragments thereof may comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 2, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 22. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 1, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 21.

[0059] In another specific embodiment, the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 44; a CDR2 sequence consisting of SEQ ID NO: 46; and a CDR3 sequence consisting of SEQ ID NO: 48; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 64; a CDR2 sequence consisting of SEQ ID NO: 66; and a CDR3 sequence consisting of SEQ ID NO: 68. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 42, and/or (b) a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 62. In another specific embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 42, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 62. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof may comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 41, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 61.

[0060] In another specific embodiment, anti-PACAP antibodies and antigen binding fragments thereof according to the invention, preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, may comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 84; a CDR2 sequence consisting of SEQ ID NO: 86; and a CDR3 sequence consisting of SEQ ID NO: 88; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 104; a CDR2 sequence consisting of SEQ ID NO: 106; and a CDR3 sequence consisting of SEQ ID NO: 108. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 82, and/or (b) a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 102. In another specific embodiment, the anti-PACAP antibodies and antigen binding fragments thereof may comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 82, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 102. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 81, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 101.

[0061] In another specific embodiment, the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, may comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 124; a CDR2 sequence consisting of SEQ ID NO: 126; and a CDR3 sequence consisting of SEQ ID NO: 128; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 144; a CDR2 sequence consisting of SEQ ID NO: 146; and a CDR3 sequence consisting of SEQ ID NO: 148. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof may comprise (a) a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 122 and/or (b) a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 142. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof may comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 122, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 142. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 121, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 141.

[0062] In another specific embodiment, the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, may comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 164; a CDR2 sequence consisting of SEQ ID NO: 166; and a CDR3 sequence consisting of SEQ ID NO: 168; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 184; a CDR2 sequence consisting of SEQ ID NO: 186; and a CDR3 sequence consisting of SEQ ID NO: 188. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 162, and/or (b) a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 182. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 162, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 182. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 161, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 181.

[0063] In another specific embodiment, the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, are preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, and comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 204; a CDR2 sequence consisting of SEQ ID NO: 206; and a CDR3 sequence consisting of SEQ ID NO: 208; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 224; a CDR2 sequence consisting of SEQ ID NO: 226; and a CDR3 sequence consisting of SEQ ID NO: 228. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 202 and/or (b) a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 222. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy

chain having the amino acid sequence of SEQ ID NO: 202, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 222. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 201, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 221.

[0064] In another specific embodiment, the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, are preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, and comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 244; a CDR2 sequence consisting of SEQ ID NO: 246; and a CDR3 sequence consisting of SEQ ID NO: 248; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 264; a CDR2 sequence consisting of SEQ ID NO: 266; and a CDR3 sequence consisting of SEQ ID NO: 268. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 242 and/or (b) a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 262. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 242, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 262. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 241, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 261.

[0065] In another specific embodiment, the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, are preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, and comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 284; a CDR2 sequence consisting of SEQ ID NO: 286; and a CDR3 sequence consisting of SEQ ID NO: 288; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 304; a CDR2 sequence consisting of SEQ ID NO: 306; and a CDR3 sequence consisting of SEQ ID NO: 308. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof can comprise a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 282, and/or a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 302. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 282, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 302. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 281, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 301.

[0066] In another specific embodiment, the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, are preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, and comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 324; a CDR2 sequence consisting of SEQ ID NO: 326; and a CDR3 sequence consisting of SEQ ID NO: 328; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 344; a CDR2 sequence consisting of SEQ ID NO: 346; and a CDR3 sequence consisting of SEQ ID NO: 348. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof can comprise a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 322, and/or a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 342. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 322, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 342. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 321, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 341.

[0067] In another specific embodiment, the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, are preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, and comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 364; a CDR2 sequence consisting of SEQ ID NO: 366; and a CDR3 sequence consisting of SEQ ID NO: 368; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 384; a CDR2 sequence consisting of SEQ ID NO: 386; and a CDR3 sequence consisting of SEQ ID NO: 388. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof can comprise a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 362, and/or a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 382. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 362, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 382. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 361, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 381.

[0068] In another specific embodiment, the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, are preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, and comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 484; a CDR2 sequence consisting of SEQ ID NO: 486; and a CDR3 sequence consisting of SEQ ID NO: 488; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 504; a CDR2 sequence consisting of SEQ ID NO: 506; and a CDR3 sequence consisting of SEQ ID NO: 508. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof can comprise a variable

heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 482, and/or a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 502. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 482, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 502. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 481, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 501.

[0069] In another specific embodiment, the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, are preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, and comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 524; a CDR2 sequence consisting of SEQ ID NO: 526; and a CDR3 sequence consisting of SEQ ID NO: 528; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 544; a CDR2 sequence consisting of SEQ ID NO: 546; and a CDR3 sequence consisting of SEQ ID NO: 548. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof can comprise a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 522, and/or a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 542. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 522, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 542. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 521, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 541.

[0070] In another specific embodiment, the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, are preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, and comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 564; a CDR2 sequence consisting of SEQ ID NO: 566; and a CDR3 sequence consisting of SEQ ID NO: 568; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 584; a CDR2 sequence consisting of SEQ ID NO: 586; and a CDR3 sequence consisting of SEQ ID NO: 588. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof can comprise a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 562, and/or a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 582. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 562, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 582. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 561, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 581.

[0071] In another specific embodiment, the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, are preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, and comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 604; a CDR2 sequence consisting of SEQ ID NO: 606; and a CDR3 sequence consisting of SEQ ID NO: 608; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 624; a CDR2 sequence consisting of SEQ ID NO: 626; and a CDR3 sequence consisting of SEQ ID NO: 628. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof can comprise a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 602, and/or a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 622. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 602, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 622. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 601, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 621.

[0072] In another specific embodiment, the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, are preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, and comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 644; a CDR2 sequence consisting of SEQ ID NO: 646; and a CDR3 sequence consisting of SEQ ID NO: 648; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 664; a CDR2 sequence consisting of SEQ ID NO: 666; and a CDR3 sequence consisting of SEQ ID NO: 668. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof can comprise a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 642, and/or a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 662. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 642, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 662. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 641, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 661.

[0073] In another specific embodiment, the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, are preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, and comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO:

684; a CDR2 sequence consisting of SEQ ID NO: 686; and a CDR3 sequence consisting of SEQ ID NO: 688; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 704; a CDR2 sequence consisting of SEQ ID NO: 706; and a CDR3 sequence consisting of SEQ ID NO: 708. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof can comprise a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 682, and/or a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 702. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 682, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 702. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 681, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 701.

[0074] In another specific embodiment, the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, are preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, and comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 724; a CDR2 sequence consisting of SEQ ID NO: 726; and a CDR3 sequence consisting of SEQ ID NO: 728; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 744; a CDR2 sequence consisting of SEQ ID NO: 746; and a CDR3 sequence consisting of SEQ ID NO: 748. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof can comprise a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 722, and/or a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 742. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 722, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 742. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 721, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 741.

[0075] In another specific embodiment, the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, are preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, and comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 764; a CDR2 sequence consisting of SEQ ID NO: 766; and a CDR3 sequence consisting of SEQ ID NO: 768; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 784; a CDR2 sequence consisting of SEQ ID NO: 786; and a CDR3 sequence consisting of SEQ ID NO: 788. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof fragment can comprise a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 762, and/or a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 782. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 762, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 782. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 761, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 781.

[0076] In another specific embodiment, the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, are preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, and comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 804; a CDR2 sequence consisting of SEQ ID NO: 806; and a CDR3 sequence consisting of SEQ ID NO: 808; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 824; a CDR2 sequence consisting of SEQ ID NO: 826; and a CDR3 sequence consisting of SEQ ID NO: 828. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof can comprise a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 802, and/or a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 822. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 802, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 822. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 801, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 821.

[0077] Also, in some embodiments the anti-PACAP antibodies and antigen binding fragments may comprise sequence variants of any of the disclosed antibodies which are modified by mutagenesis, e.g., affinity maturation to alter one or more properties such as binding affinity or immunogenicity.

[0078] In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof are directly or indirectly attached to another moiety, such as a detectable label or therapeutic agent.

[0079] In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof inhibit or neutralize at least one biological effect elicited by PACAP; neutralize or inhibit PACAP activation of at least one of PAC1-R, VPAC1-R, and/or VPAC2-R; neutralize or inhibit PACAP activation of each of PAC1-R, VPAC1-R, and VPAC2-R; neutralize or inhibit PACAP activation of PAC1-R; are capable of inhibiting PACAP binding to at least one of PAC1-R, VPAC1-R, and/or VPAC2-R; are capable of inhibiting PACAP binding to each of PAC1-R, VPAC1-R, and/or VPAC2-R; are capable of inhibiting PACAP binding to PAC1-R; and/or inhibits PACAP binding to the cell surface, e.g., via a GAG; inhibit PACAP-induced cAMP production; and/or when administered to a subject reduce PACAP-induced vasodilation, photophobia, mast cell degranulation, and/or neuronal activation.

[0080] In another embodiment, the human, or humanized, anti-PACAP antibodies and antigen binding fragments thereof are suitable for treating a human subject having an acute, episodic, or chronic condition associated with increased vasodilation, photophobia, mast cell degranulation, and/or neuronal activation.

[0081] In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof do not substantially interact with (i.e., bind to) VIP. Preferably, the anti-PACAP antibodies and antigen binding fragments thereof have stronger affinity for PACAP as compared to VIP, i.e., although there is some cross-reactivity, the antibodies preferentially bind to PACAP as compared to VIP. For example, the affinity of said antibodies and antigen binding fragments thereof to PACAP is at least 10-fold, 30-fold, 100-fold, 300-fold, 1000-fold, 3000-fold, 10000-fold, 30000-fold, 100000-fold, 300000-fold, 1000000-fold, 3000000-fold, 10000000-fold, 30000000-fold, or stronger than the affinity of said antibodies and antigen binding fragments thereof to VIP (e.g., the K_D of said antibody or fragment for binding to human PACAP is 10-fold, 30-fold, 100-fold, 300-fold, 1000-fold, 3000-fold, 10000-fold, 30000-fold, 100000-fold, 300000-fold, 1000000-fold, 3000000-fold, 10000000-fold, or 30000000-fold lower than the K_D for binding to VIP).

[0082] In one embodiment, the anti-PACAP antibodies and antigen binding fragments thereof are attached to at least one effector moiety, e.g., which comprises a chemical linker. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof are attached to one or more detectable moieties, e.g., which comprise a fluorescent dye, enzyme, substrate, bioluminescent material, radioactive material, chemiluminescent moiety, or mixtures thereof.

[0083] In one embodiment, the anti-PACAP antibodies and antigen binding fragments thereof are attached to one or more functional moieties.

[0084] The invention also contemplates antibodies, e.g., anti-idiotypic antibodies, produced against an anti-PACAP antibodies and antigen binding fragments thereof as described above. Furthermore, the invention provides a method of using the anti-idiotypic antibody to monitor the in vivo levels of said anti-PACAP antibodies and antigen binding fragments thereof in a subject or to neutralize said anti-PACAP antibody in a subject being administered said anti-PACAP antibody or antigen binding fragment thereof.

[0085] Moreover, the present invention encompasses a composition suitable for therapeutic, prophylactic, or a diagnostic use comprising a therapeutically, prophylactically, or diagnostically effective amount of at least one anti-PACAP antibody or antigen binding fragment as described herein. In particular, compositions and dosage forms containing the subject anti-PACAP antibodies or binding fragments thereof for use in treating or preventing migraine or other headache indications are provided herein. Also provided herein are dosage forms containing the subject anti-PACAP antibodies or binding fragments thereof for use in treating or preventing photophobia. The composition may be suitable for subcutaneous administration, intramuscular administration, and/or intravenous administration. The composition may be lyophilized. In some embodiments, the composition further comprises a pharmaceutically acceptable diluent, carrier, solubilizer, emulsifier, preservative, or mixture thereof.

[0086] Additionally, in some embodiments, the composition further comprises another active agent, e.g., a chemotherapeutic, an analgesic, an anti-inflammatory, an immunosuppressant, a cytokine, an antiproliferative, and an antiemetic. Preferably, the other therapeutic agent is an analgesic, e.g., an NSAID, an opioid analgesic, an antibody (e.g., an anti-human Nerve Growth Factor ("NGF") antibody or antibody fragment; or an anti-human CGRP or anti-human CGRP-receptor antibody or antibody fragment); or a non-antibody biologic, such as an NGF or CGRP polypeptide fragment or conjugate; or BOTOX® (Botulinum toxin). Suitable NSAIDs for use in combination with the subject anti-PACAP antibodies include, but are not limited to, a cyclooxygenase 1 and/or cyclooxygenase 2 inhibitor; propionic acid derivatives including ibuprofen, naproxen, naprosyn, diclofenac, and ketoprofen; acetic acid derivatives including tolmetin and sulindac; fenamic acid derivatives including mefenamic acid and meclofenamic acid; biphenylcarboxylic acid derivatives including diflunisal and flufenisal; and oxicams including piroxim, sudoxicam, and isoxicam. Suitable opioid analgesics for use in combination with the subject anti-PACAP antibodies include, e.g., codeine, dihydrocodeine, morphine or a morphine derivative or pharmaceutically acceptable salt thereof, diacetylmorphine, hydrocodone, hydromorphone, levorphanol, oxymorphone, alfentanil, buprenorphine, butorphanol, fentanyl, sufentanil, meperidine, methadone, nalbuphine, propoxyphene, and pentazocine, or pharmaceutically acceptable salts thereof. The combined administration of the opioid analgesic and the anti-PACAP antibody or antigen binding fragment thereof may increase the analgesic effect elicited thereby.

[0087] The present invention further contemplates an isolated nucleic acid sequence or nucleic acid sequences encoding an anti-PACAP antibody or antigen binding fragment described herein, as well as a vector or vectors containing these isolated nucleic acid sequence or sequences.

[0088] Additionally, the invention provides a host cell comprising these isolated nucleic acid sequence or sequences or the vector or set forth above. The host cell may be a eukaryotic host cell that is mammalian, selected from the group consisting of baby hamster kidney ("BHK") cells; chinese hamster ovary ("CHO") cells; mouse sertoli cells ("TM4" cells); African green monkey kidney cells ("VERO-76" cells); human cervical carcinoma ("HELA") cells; canine kidney cells ("MDCK"); buffalo rat liver ("BRL") cells; human lung cells; human liver ("Hep G2") cells; mouse mammary tumor ("MMT") cells; TRI cells; MRC 5 cells; and FS4 cells. Preferably, the mammalian host cell is a CHO cell. More preferably, the mammalian host cell is a CHO K1 cell. The host cell may be a prokaryotic cell, i.e., bacterial cell, or a eukaryotic cell, including a mammalian, fungal, yeast, avian, or insect cell. In one embodiment, the host cell is a filamentous fungus or is a yeast cell. Preferably, the yeast species is of the genus *Pichia*. Most preferably, the species of *Pichia* is selected from *Pichia pastoris, Pichia methanolica*, and *Hansenula polymorpha* (*Pichia angusta*).

[0089] The invention further provides a method of expressing anti-PACAP antibodies and antigen binding fragments thereof, typically human, humanized, or chimeric antibodies and antigen binding fragments thereof, the method comprising culturing the host cell described herein under conditions that provide for expression of said antibody or antigen binding fragment thereof. The host cell may be a cell culture, such as a Chinese hamster ovary ("CHO") cell or a polyploid yeast culture that stably expresses and

secretes into the culture medium at least 10-25 mg/liter of said antibody or antigen binding fragment thereof. The polyploid yeast may be made by a method that comprises: (i) introducing at least one expression vector containing one or more heterologous polynucleotides encoding said antibody operably linked to a promoter and a signal sequence into a haploid yeast cell; (ii) producing by mating or spheroplast fusion a polyploid yeast from said first and/or second haploid yeast cell; (iii) selecting polyploid yeast cells that stably express said antibody; and (iv) producing stable polyploid yeast cultures from said polyploid yeast cells that stably express said antibody into the culture medium. Preferably, the yeast species is of the genus *Pichia*.

[0090] In other embodiments, the mammalian cell culture may be made by a method that comprises: (i) introducing at least one expression vector containing one or more heterologous polynucleotides encoding said antibody operably linked to a promoter and a signal sequence into a mammalian cell; (ii) producing single cells for culturing to express one or more heterologous polynucleotides encoding said antibody; (iii) selecting a mammalian cell that stably expresses said antibody; and (iv) producing cell cultures from said mammalian cell that stably expresses said antibody into the culture medium. Preferably, the mammalian species are CHO cells.

[0091] The invention further relates to the therapeutic and diagnostic uses of anti-PACAP antibodies and antigen binding fragments thereof, preferably a human antibody, humanized antibody, or chimeric antibody, or a fragment thereof.

[0092] In one embodiment, the invention provides a method for blocking, inhibiting, or neutralizing one or more biological effects associated with PACAP in a subject comprising administering to a subject an effective amount of a human or humanized or chimerized anti-PACAP antibody or antigen binding fragment thereof that antagonizes, inhibits, neutralizes, or blocks at least one biological effect associated with human PACAP. In a specific embodiment, the method employs an anti-PACAP antibody or antigen binding fragment thereof that specifically binds to the same or overlapping linear or conformational epitope(s) and/or competes for binding to the same or overlapping linear or conformational epitope(s) on human PACAP as an anti-PACAP antibody selected from Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, and Ab1.H.

[0093] In another embodiment, the invention provides a method for blocking, inhibiting, or neutralizing one or more biological effects associated with PACAP in a subject comprising administering to a subject an effective amount of a human, humanized, or chimerized anti-PACAP antibody or antigen binding fragment thereof that antagonizes, inhibits, neutralizes, or blocks at least one biological effect associated with human PACAP and that does not substantially interact with (bind) VIP, e.g., the anti-PACAP antibody or antigen binding fragment thereof has stronger affinity for PACAP as compared to VIP, i.e., although there is some cross-reactivity, the antibodies preferentially bind to PACAP as compared to VIP. For example, the affinity of said antibody or antigen binding fragment thereof to PACAP is at least 10-fold, 30-fold, 100-fold, 300-fold, 1000-fold, 3000-fold, 10000-fold, 30000-fold, 100000-fold, 300000-fold, 1000000-fold, 3000000-fold, 10000000-fold, 30000000-fold, or higher than the affinity of said antibody or antigen binding fragment thereof to VIP (e.g., the K_D of said antibody or fragment for binding to human PACAP is 10-fold, 30-fold, 100-fold, 300-fold, 1000-fold, 3000-fold, 10000-fold, 30000-fold, 100000-fold, 300000-fold, 1000000-fold, 3000000-fold, 10000000-fold, 30000000-fold, or lower than the K_D for binding to VIP). In a specific embodiment, the method employs an anti-PACAP antibody or antigen binding fragment thereof that specifically binds to the same or overlapping linear or conformational epitope(s) and/or competes for binding to the same or overlapping linear or conformational epitope(s) on human PACAP as an anti-PACAP antibody selected from Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, and Ab1.H.

[0094] In yet another embodiment, the invention provides a method for blocking, inhibiting, or neutralizing one or more biological effects associated with PACAP in a subject comprising administering to a subject an effective amount of a human, humanized, or chimerized anti-PACAP antibody or antigen binding fragment thereof that inhibits or neutralizes at least one biological effect elicited by PACAP; neutralizes or inhibits PACAP activation of at least one of PAC1-R, VPAC1-R, and/or VPAC2-R; neutralizes or inhibits PACAP activation of each of PAC1-R, VPAC1-R, and VPAC2-R; neutralizes or inhibits PACAP activation of PAC1-R; is capable of inhibiting PACAP binding to at least one of PAC1-R, VPAC1-R, and/or VPAC2-R; is capable of inhibiting PACAP binding to each of PAC1-R, VPAC1-R, and/or VPAC2-R; is capable of inhibiting PACAP binding to PAC1-R; and/or is capable of inhibiting PACAP binding to the cell surface, e.g., via a GAG; inhibits PACAP-induced cAMP production; and/or when administered to a subject reduces PACAP-induced vasodilation, photophobia, mast cell degranulation, and/or neuronal activation. In a specific embodiment, the method employs an anti-PACAP antibody or antigen binding fragment thereof that specifically binds to the same or overlapping linear or conformational epitope(s) and/or competes for binding to the same or overlapping linear or conformational epitope(s) on human PACAP as an anti-PACAP antibody selected from Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, and Ab1.H.

[0095] In another embodiment, the invention provides a method for treating or preventing the onset, frequency, severity, or duration of headache or migraine in a subject comprising administering to a subject an effective amount of a human, humanized, or chimerized anti-PACAP antibody or antigen binding fragment thereof that inhibits or neutralizes at least one biological effect elicited by PACAP; neutralizes or inhibits PACAP activation of at least one of PAC1-R, VPAC1-R, and/or VPAC2-R; neutralizes or inhibits PACAP activation of each of PAC1-R, VPAC1-R, and VPAC2-R; neutralizes or inhibits PACAP activation of PAC1-R; is capable of inhibiting PACAP binding to at least one of PAC1-R, VPAC1-R, and/or VPAC2-R; is capable of inhibiting PACAP binding to each of PAC1-R, VPAC1-R, and/or VPAC2-R; is capable of inhibiting PACAP binding to PAC1-R; and/or is capable of inhibiting PACAP binding to the cell surface, e.g., via a GAG; inhibits PACAP-induced cAMP production; and/or when administered to a subject reduces PACAP-induced vasodilation, photophobia, mast cell degranulation, and/or neuronal activation. In another embodiment, the invention provides a method for treating or preventing in a human subject an acute, episodic, or chronic

condition associated with increased vasodilation, photophobia, mast cell degranulation, and/or neuronal activation.

[0096] In a specific embodiment, the method employs an anti-PACAP antibody or antigen binding fragment thereof that specifically binds to the same or overlapping linear or conformational epitope(s) and/or competes for binding to the same or overlapping linear or conformational epitope(s) on human PACAP as an anti-PACAP antibody selected from Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, and Ab1.H. The epitope can be identified using an alanine scanning mutation strategy, for example.

[0097] In a specific embodiment, the headache or migraine treated and/or prevented by administration of the subject anti-PACAP antibodies and antigen binding fragments thereof is selected from migraine with or without aura, hemiplegic migraine, cluster headache, migrainous neuralgia, chronic headache, and tension headache.

[0098] In another specific embodiment, the subject has a ocular disorder associated with photophobia selected from the group consisting of achromatopsia, aniridia, photophobia caused by an anticholinergic drug, aphakia (absence of the lens of the eye), buphthalmos (abnormally narrow angle between the cornea and iris), cataracts, cone dystrophy, congenital abnormalities of the eye, viral conjunctivitis ("pink eye"), corneal abrasion, corneal dystrophy, corneal ulcer, disruption of the corneal epithelium, ectopia lentis, endophthalmitis, eye trauma caused by disease, injury, or infection such as chalazion, episcleritis, glaucoma, keratoconus, or optic nerve hypoplasia, hydrophthalmos, or congenital glaucoma iritis, optic neuritis, pigment dispersion syndrome, pupillary dilation (naturally or chemically induced), retinal detachment, scarring of the cornea or sclera, and uveitis.

[0099] In another specific embodiment, the subject has a nervous system-related or neurological condition associated with photophobia selected from the group consisting of autism spectrum disorders, chiari malformation, dyslexia, encephalitis including myalgic encephalomyelitis (also known as "chronic fatigue syndrome"), meningitis, subarachnoid hemorrhage, tumor of the posterior cranial fossa, ankylosing spondylitis, albinism, ariboflavinosis, benzodiazepines (long term use of or withdrawal from benzodiazepines), chemotherapy, chikungunya, cystinosis, Ehlers-Danlos syndrome, hangover, influenza, infectious mononucleosis, magnesium deficiency, mercury poisoning, migraine, rabies, and tyrosinemia type II (also known as "Richner-Hanhart syndrome").

[0100] In another specific embodiment, the subject has a photophobia-associated disorder selected from the group consisting of migraine (with or without aura), iritis, uveitis, meningitis, depression, bipolar disorder, cluster headache or anther trigeminal autonomic cephalalgia ("TAC") or blepharospasm, depression, agoraphobia, Post-Traumatic Stress Disorder ("PTSD"), traumatic brain injury, and bipolar disorder.

[0101] In another embodiment, the invention provides a method for neutralizing PACAP-induced PAC1-R, VPAC1-R, and/or VPAC2-R signaling, comprising administering to a subject in need thereof an effective amount of an anti-PACAP antibody or antigen binding fragment thereof that specifically binds to the same or overlapping linear or conformational epitope(s) and/or competes for binding to the same or overlapping linear or conformational epitope(s) on human PACAP as an anti-PACAP antibody selected from Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, and Ab1.H.

[0102] In another embodiment, the invention provides a method for inhibiting PACAP-induced cAMP production, comprising administering to a subject in need thereof an effective amount of an anti-PACAP antibody or antigen binding fragment thereof that specifically binds to the same or overlapping linear or conformational epitope(s) and/or competes for binding to the same or overlapping linear or conformational epitope(s) on human PACAP as an anti-PACAP antibody selected from Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, and Ab1.H.

[0103] In yet another embodiment, the invention provides a method for inhibiting PACAP-induced vasodilation, photophobia, mast cell degranulation, and/or neuronal activation, comprising administering to a subject in need thereof an effective amount of an anti-PACAP antibody or antigen binding fragment thereof that specifically binds to the same or overlapping linear or conformational epitope(s) and/or competes for binding to the same or overlapping linear or conformational epitope(s) on human PACAP as an anti-PACAP antibody selected from Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, and Ab1.H.

[0104] In yet another embodiment, the invention provides a method for treating or preventing a condition associated with elevated PACAP levels in a subject, comprising administering to a subject in need thereof an effective amount of an anti-PACAP antibody or antigen binding fragment thereof that specifically binds to the same or overlapping linear or conformational epitope(s) and/or competes for binding to the same or overlapping linear or conformational epitope(s) on human PACAP as an anti-PACAP antibody selected from Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, and Ab1.H. The epitope can be identified using an alanine scanning mutation strategy, for example.

[0105] Exemplary anti-PACAP antibodies and antigen binding fragments thereof suitable for use in this invention comprise a V_H chain having an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, 99 or 100% sequence identity to a V_H chain selected from SEQ ID NOs: 2; 42; 82; 122; 162; 202; 242; 282; 322; 362; 482; 522; 562; 602; 642; 682; 722; 762; and 802, and/or a V_L chain having an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, 99, or 100% sequence identity to a V_L chain selected from selected from SEQ ID NOs: 22; 62; 102; 142; 182; 222; 262; 302; 342; 382; 502; 542; 582; 622; 662; 702; 742; 782; and 822, and/or at least 2, 3, 4, 5, or all 6 CDRs comprised therein.

[0106] In one embodiment, the anti-PACAP antibody or antigen binding fragment thereof employed in the methods binds to PACAP27 and/or PACAP38 and blocks PACAP27 and/or PACAP38 binding to PAC1-R, VPAC1-R, and/or VPAC2-R. In another embodiment, the anti-PACAP antibody or antigen binding fragment thereof employed in the methods binds to PACAP27 and/or PACAP38 and blocks PACAP27 and/or PACAP38 binding to each of PAC1-R, VPAC1-R, and VPAC2-R. Preferably, the anti-PACAP antibody or antigen binding fragment thereof binds to PACAP27 and/or PACAP38 and blocks PACAP27 and/or PACAP38 binding to PAC1-R.

[0107] More particularly, anti-PACAP antibodies and antigen binding fragments thereof employed in the methods according to the invention may include human, humanized, and chimerized antibodies and fragments thereof, as well as scFvs, camelbodies, shark antibodies, nanobodies, IgNAR, Fab fragments, Fab' fragments, MetMab like antibodies, bispecific antibodies, monovalent antibody fragments, and $F(ab')_2$ fragments. Additionally, the anti-PACAP antibody or antigen binding fragment thereof employed by the methods according to the invention may substantially or entirely lack N-glycosylation and/or O-glycosylation. In one embodiment, the anti-PACAP antibody or antigen binding fragment thereof used in the encompassed methods comprises a human constant domain, e.g., an IgG1, IgG2, IgG3, or IgG4 antibody. In another embodiment, the anti-PACAP antibody or antigen binding fragment thereof comprises an Fc region that has been modified to alter (enhance or impair) at least one of effector function, half-life, proteolysis, or glycosylation. For example, the Fc region may contain one or more mutations that alters or eliminates N- and/or O-glycosylation.

[0108] In one embodiment, the subject methods employ an anti-PACAP antibody or antigen binding fragment thereof that binds to PACAP with a K_D of less than or equal to 5×10^{-5} M, 10^{-5} M, 5×10^{-6} M, 10^{-6} M, 5×10^{-7} M, 10^{-7} M, 5×10^{-8} M, 10^{-8} M, 5×10^{-9} M, 10^{-9} M, 5×10^{-10} M, 10^{-10} M, 5×10^{-11} M, 10^{-11} M, 5×10^{-12} M, 10^{-12} M, 5×10^{-13} M, or 10^{-13} M. Preferably, the human, humanized, or chimerized anti-PACAP antibody or antigen binding fragment thereof binds to PACAP with a K_D of less than or equal to 5×10^{-10} M, 10^{-10} M, 5×10^{-11} M, 10^{-11} M, 5×10^{-12} M, or 10^{-12} M. More preferably, the methods employ a human, humanized, or chimerized anti-PACAP antibody or antigen binding fragment thereof that binds to PACAP with a K_D that is less than about 100 nM, less than about 40 nM, less than about 1 nM, less than about 100 pM, less than about 50 pM, or less than about 25 pM. Alternatively, the anti-PACAP antibody or antigen binding fragment thereof binds to PACAP with a K_D that is between about 10 pM and about 100 pM. In another embodiment, the human, humanized or chimerized anti-PACAP antibody or antigen binding fragment thereof binds to PACAP with an off-rate (k_{off}) of less than or equal to 5×10^{-4} s^{-1}, 10^{-4} s^{-1}, 5×10^{-5} s^{-1}, or 10^{-5} s^{-1}.

[0109] In another embodiment, the anti-PACAP antibody or antigen binding fragment thereof used in the subject methods is directly or indirectly attached to another moiety, such as a detectable label or therapeutic agent; is attached to at least one effector moiety, e.g., which comprises a chemical linker; and/or is attached to one or more detectable moieties, e.g., which comprises a fluorescent dye, enzyme, substrate, bioluminescent material, radioactive material, chemiluminescent moiety, or mixtures thereof; and/or is attached to one or more functional moieties.

[0110] In another embodiment, the method further comprises administering separately or co-administering another agent, e.g., selected from a chemotherapeutic, an analgesic, an anti-inflammatory, an immunosuppressant, a cytokine, an antiproliferative, and an antiemetic. Preferably, the other therapeutic agent is an analgesic, e.g., an NSAID (such as a cyclooxygenase 1 and/or cyclooxygenase 2 inhibitor; propionic acid derivatives including ibuprofen, naproxen, naprosyn, diclofenac, and ketoprofen; acetic acid derivatives including tolmetin and sulindac; fenamic acid derivatives including mefenamic acid and meclofenamic acid; biphenylcarboxylic acid derivatives including diflunisal and flufenisal; and oxicams including piroxim, sudoxicam, and isoxicam), an opioid analgesic (such as morphine or a morphine derivative or pharmaceutically acceptable salt thereof; codeine, dihydrocodeine, diacetylmorphine, hydrocodone, hydromorphone, levorphanol, oxymorphone, alfentanil, buprenorphine, butorphanol, fentanyl, sufentanil, meperidine, methadone, nalbuphine, propoxyphene and pentazocine or pharmaceutically acceptable salts thereof), another antibody (such as an anti-NGF antibody or antibody fragment or an anti-CGRP or anti-CGRP receptor ("anti-CGRP-R") antibody or antibody fragment), or a non-antibody biologic, e.g., BOTOX®.

[0111] In one embodiment, the combined administration of the opioid analgesic and the anti-PACAP antibody or antigen binding fragment thereof increase the analgesic effect as compared to either the opioid analgesic or the anti-PACAP antibody or antigen binding fragment thereof administered alone.

[0112] In another embodiment, the subject has previously been treated ("a treated subject") and received an anti-CGRP or anti-CGRP-R antibody or antibody fragment thereof. The treated subject may be a migraineur who did not adequately respond to anti-CGRP or anti-CGRP-R antibody treatment ("poor responder"). Alternatively, the treated subject may have previously received at least one anti-CGRP or anti-CGRP-R antibody or antibody fragment thereof administration, and has elicited an immune response to said antibody or antibody fragment thereof. Exemplary anti-CGRP and anti-CGRP-R antibodies and antibody fragments thereof are disclosed in U.S. Pat. Nos. 9,102,731; 9,115,194; 8,734,802; 8,623,366; 8,597,649; and 8,586,045; and U.S. Patent Application Publication No.'s 20120294822, 20120294802, and 20120294797, the contents of each which are incorporated by reference in their entireties herein.

[0113] An aspect of the present invention in general relates to anti-PACAP antibodies and antigen binding fragments thereof, preferably human, humanized, or chimerized anti-human PACAP antibodies or antibody fragments thereof that may antagonize, inhibit, neutralize or block at least one biological effect associated with human PACAP.

[0114] Moreover, the invention pertains to anti-PACAP antibodies and antigen binding fragments thereof that may include human, humanized or chimerized anti-PACAP antibodies or antibody fragments thereof that specifically compete for binding to human PACAP with an antibody selected from the group consisting of Ab1, Ab2, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab1.H, Ab5, Ab7, Ab11, Ab12, Ab4, Ab3, Ab6, Ab8, and Ab9, or an antigen-binding fragment thereof.

[0115] Additionally, the anti-PACAP antibodies and antigen binding fragments of the invention may include human, humanized or chimerized anti-PACAP antibodies or antibody fragments that may specifically bind to at least one linear or conformational epitope bound by an anti-PACAP antibody selected from the group consisting of Ab1, Ab2, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab1.H, Ab5, Ab7, Ab11, Ab12, Ab4, Ab3, Ab6, Ab8, and Ab9 or an antigen-binding fragment thereof. The epitope may be identified by alanine scanning, e.g., as disclosed in Example 12, or another art-recognized method. Also, in another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof of the invention may include human, humanized or chimerized anti-PACAP antibodies or antibody

fragments thereof which may bind to the identical epitopes as any one of Ab1, Ab2, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab1.H, Ab5, Ab7, Ab11, Ab12, Ab4, Ab3, Ab6, Ab8, and Ab9 or an antigen-binding fragment thereof. The epitope may be identified by alanine scanning, e.g., as disclosed in Example 12, or another art-recognized method.

[0116] In a further embodiment of the invention, the anti-PACAP antibodies or antigen binding fragments thereof of the invention may include human, humanized or chimerized anti-PACAP antibodies or antibody fragments which may specifically bind to an epitope on human PACAP or a fragment or variant thereof containing the corresponding amino acid residues wherein said epitope includes one or more of the following:

[0117] i. at least one of residues 7, 10, 13, and 14 of a human PACAP;

[0118] ii. at least one of residues 5, 6, 8, 10, and 13 of a human PACAP;

[0119] iii. at least one of residues 6, 8, 9, 10, and 13 of a human PACAP;

[0120] iv. at least one of residues 5, 6, 8, 9, 10, and 13 of a human PACAP;

[0121] v. at least one of residues 7, 10, 12, 13, 14, and 17 of a human PACAP;

[0122] vi. at least one of residues 5, 6, 8, 9, 10, 12, and 13 of a human PACAP;

[0123] vii. at least one of residues 5, 6, 8, 9, 10, 13, and 14 of a human PACAP;

[0124] viii. at least one of residues 6, 8, 10, 11, 13, 14, and 18 of a human PACAP;

[0125] ix. at least one of residues 8, 9, 10, 13, 14, 17, and 18 of a human PACAP;

[0126] x. at least one of residues 3, 4, 5, 6, 7, 10, 13, and 14 of a human PACAP;

[0127] xi. at least one of residues 5, 6, 8, 9, 10, 12, 13, and 14 of a human PACAP;

[0128] xii. at least one of residues 5, 6, 9, 10, 12, 13, 14, and 17 of a human PACAP;

[0129] xiii. at least one of residues 6, 8, 10, 11, 13, 14, 18, and 22 of a human PACAP;

[0130] xiv. at least one of residues 8, 9, 10, 11, 12, 13, 14, 17, and 21 of a human PACAP;

[0131] xv. at least one of residues 4, 5, 6, 8, 9, 10, 12, 13, 14, and 17 of a human PACAP;

[0132] xvi. at least two of the residues of any one of (i)-(xv);

[0133] xvii. at least three of the residues of any one of (i)-(xv);

[0134] xviii. at least four of the residues of any one of (i)-(xv);

[0135] xix. at least five of the residues of any one of (ii)-(xv);

[0136] xx. at least six of the residues of any one of (iv)-(xv);

[0137] xxi. at least seven of the residues of any one of (vi)-(xv);

[0138] xxii. at least eight of the residues of any one of (x)-(xv);

[0139] xxiii. at least nine of the residues of (xiv) or (xv); and

[0140] xxiv. all ten residues of (xv);

[0141] In a specific embodiment of the invention, anti-PACAP antibodies or antigen binding fragments thereof of the invention may include human, humanized or chimerized anti-PACAP antibodies or antibody fragments which specifically bind to an epitope on human PACAP, or a fragment or variant thereof that may contain the corresponding amino acid residues that may include residues 8 and/or 14 of human PACAP. Also, in another embodiment of the invention, the anti-PACAP antibodies or antigen binding fragments thereof may include a human, humanized or chimerized anti-PACAP antibodies or antibody fragments thereof, which specifically bind to an epitope on human PACAP (or a fragment or variant thereof containing the corresponding amino acid residues that may be present in human wild-type PACAP38) but not human wild-type human PACAP27. The epitope may be identified by alanine scanning, e.g., as disclosed in Example 12 or another art-recognized method.

[0142] In an additional embodiment of the invention, anti-PACAP antibodies or antigen binding fragments thereof of the invention may include human, humanized or chimerized anti-PACAP antibodies or antibody fragments thereof which may specifically bind to an epitope on human PACAP or a fragment or variant thereof that contain the corresponding amino acid residues, wherein said epitope may consist of the residues of any one of (i)-(xv) as described above. The epitope may be identified by alanine scanning, e.g., as disclosed in Example 12, or another art-recognized method.

[0143] Another aspect of the invention also embraces anti-PACAP antibodies or antigen binding fragments thereof that may include human, humanized or chimerized anti-PACAP antibodies or antibody fragment which specifically bind to an epitope on human PACAP (or a fragment or variant thereof that may contain the corresponding amino acid residues) that may be present in human wild-type PACAP38 and in human wild-type human PACAP27.

[0144] Additionally, the anti-PACAP antibodies or antigen binding fragments thereof may include human, humanized or chimerized anti-PACAP antibodies or antibody fragments thereof, which may specifically bind to human wild-type human PACAP38 but which may not bind or appreciably bind to human wild-type human PACAP27. The invention may also embody anti-PACAP antibodies or antigen binding fragments thereof that may include human, humanized or chimerized anti-PACAP antibodies or antibody fragments thereof which may specifically interact with residues 28 and 31 of human PACAP38. In another embodiment of the invention, the anti-PACAP antibodies and antigen binding fragments thereof of the invention may include human, humanized or chimerized anti-PACAP antibodies or antibody fragments thereof which may have a K_D for human PACAP38 which may be at least 10, 100, 1000, 10,000 or 100,000 fold lower (stronger) than the K_D of said antibody or antibody fragment to human PACAP27.

[0145] In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof of the invention may include human, humanized or chimerized anti-PACAP antibodies or antibody fragments thereof which do not bind to or do not appreciably bind to human Vasoactive Intestinal Peptide ("VIP"). Said anti-PACAP antibodies or antibody fragments thereof may have a KD for human PACAP which may be at least 10, 100, 1000, 10,000 or 100,000 fold lower (stronger) than the KD of said antibody or antibody fragment to human VIP.

[0146] In embodiments of the invention, a human, humanized or chimerized anti-PACAP antibody or antibody fragment as disclosed herein, may inhibit or may neutralize at least one biological effect elicited by human PACAP.

[0147] In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof of the invention may include human, humanized or chimerized anti-PACAP antibodies or antibody fragments thereof that may comprise one or more of the following properties: (a) inhibit, block or prevent PACAP activation of at least one of PAC1 receptor ("PAC1-R"), vasoactive intestinal peptide receptor type 1 ("VPAC1-R"), and/or vasoactive intestinal peptide receptor type 2 ("VPAC2-R"); (b) inhibit, block or prevent PACAP activation of each of PAC1-R, VPAC1-R, and VPAC2-R; (c) inhibit, block or prevent PACAP activation of PAC1-R; (d) are capable of inhibiting PACAP binding to at least one of PAC1-R, VPAC1-R, and/or VPAC2-R; (e) are capable of inhibiting PACAP binding to each of PAC1-R, VPAC1-R, and/or VPAC2-R; (f) may be capable of inhibiting PACAP binding to PAC1-R-expressing cells; (g) are capable of inhibiting PACAP binding to VPAC1-R-expressing cells; (h) are capable of inhibiting PACAP binding to VPAC2-R-expressing cells; (i) do inhibit PACAP binding to the cell surface, e.g. via a glycosaminoglycan ("GAG"); (j) do not inhibit PACAP-mediated binding of such antibody to the cell surface, e.g., via a GAG; (k) do inhibit PACAP-mediated binding of such antibody to the cell surface, e.g., via a glycosaminoglycan ("GAG"); (1) inhibit, block or prevent PACAP-induced cAMP production; and/or (m) when administered to a subject reduce PACAP-induced vasodilation, photophobia, mast cell degranulation and/or neuronal activation.

[0148] The invention may also pertain to anti-PACAP antibodies and antigen binding fragments thereof that may be preferably human, humanized or chimerized anti-PACAP antibodies or antibody fragments which may be substantially non-immunogenic in human subjects. The invention may also relate to anti-PACAP antibodies and antigen binding fragments thereof that may be preferably human, humanized or chimerized anti-PACAP antibodies or antibody fragments, which may be suitable for treating a human subject having an acute, episodic or chronic condition associated with increased vasodilation, photophobia, mast cell degranulation and/or neuronal activation.

[0149] The invention may also embody anti-PACAP antibodies and antigen binding fragments thereof that may be preferably human, humanized or chimerized anti-PACAP antibodies or antibody fragments that may comprise at least 2 complementarity determining regions ("CDRs") of an anti-PACAP antibody that may be selected from Ab1, Ab2, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab1.H, Ab5, Ab7, Ab11, Ab12, Ab4, Ab3, Ab6, Ab8, or Ab9, preferably including the VH CDR3 and/or the VL CDR3. Another additional embodiment of the invention may include anti-PACAP antibodies and antigen binding fragments thereof that may be preferably human, humanized or chimerized anti-PACAP antibodies or antibody fragments that may comprise at least 3, at least 4, at least 5, or all 6 CDRS of an anti-PACAP antibody selected from Ab1, Ab2, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab1.H, Ab5, Ab7, Ab11, Ab12, Ab4, Ab3, Ab6, Ab8, or Ab9. In instances where all 6 CDRs may not be present, preferably at least the VH CDR3 and the VL CDR3 may be present.

[0150] In another embodiment of the invention, anti-PACAP antibodies and antigen binding fragments thereof, preferably human, humanized or chimerized anti-PACAP antibodies or antibody fragments thereof, may comprise a sequence variant of any of the antibodies or antibody fragments of the invention that may contain one or more modifications that may putatively alter binding affinity or immunogenicity.

[0151] In a specific embodiment, anti-PACAP antibodies and antigen binding fragments thereof according to the invention, comprise human, humanized, or chimerized anti-PACAP antibodies or antigen binding fragments thereof, which comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 4; a CDR2 sequence consisting of SEQ ID NO: 6; and a CDR3 sequence consisting of SEQ ID NO: 8; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 24; a CDR2 sequence consisting of SEQ ID NO: 26; and a CDR3 sequence consisting of SEQ ID NO: 28. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof may comprise (a) a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 2, and/or (b) a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 22. In a more specific embodiment, the anti-PACAP antibodies and antigen binding fragments thereof may comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 2, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 22. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 1, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 21.

[0152] In another specific embodiment, the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 44; a CDR2 sequence consisting of SEQ ID NO: 46; and a CDR3 sequence consisting of SEQ ID NO: 48; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 64; a CDR2 sequence consisting of SEQ ID NO: 66; and a CDR3 sequence consisting of SEQ ID NO: 68. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 42, and/or (b) a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 62. In another specific embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 42, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 62. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof may comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 41, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 61.

[0153] In another specific embodiment, anti-PACAP antibodies and antigen binding fragments thereof according to the invention, preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, may comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 84; a CDR2 sequence consisting of SEQ ID NO: 86; and a CDR3

sequence consisting of SEQ ID NO: 88; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 104; a CDR2 sequence consisting of SEQ ID NO: 106; and a CDR3 sequence consisting of SEQ ID NO: 108. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 82, and/or (b) a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 102. In another specific embodiment, the anti-PACAP antibodies and antigen binding fragments thereof may comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 82, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 102. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 81, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 101.

[0154] In another specific embodiment, the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, may comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 124; a CDR2 sequence consisting of SEQ ID NO: 126; and a CDR3 sequence consisting of SEQ ID NO: 128; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 144; a CDR2 sequence consisting of SEQ ID NO: 146; and a CDR3 sequence consisting of SEQ ID NO: 148. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof may comprise (a) a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 122 and/or (b) a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 142. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof may comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 122, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 142. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 121, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 141.

[0155] In another specific embodiment, the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, may comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 164; a CDR2 sequence consisting of SEQ ID NO: 166; and a CDR3 sequence consisting of SEQ ID NO: 168; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 184; a CDR2 sequence consisting of SEQ ID NO: 186; and a CDR3 sequence consisting of SEQ ID NO: 188. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 162, and/or (b) a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 182. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 162, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 182. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 161, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 181.

[0156] In another specific embodiment, the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, are preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, and comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 204; a CDR2 sequence consisting of SEQ ID NO: 206; and a CDR3 sequence consisting of SEQ ID NO: 208; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 224; a CDR2 sequence consisting of SEQ ID NO: 226; and a CDR3 sequence consisting of SEQ ID NO: 228. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 202 and/or (b) a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 222. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 202, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 222. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 201, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 221.

[0157] In another specific embodiment, the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, are preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, and comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 244; a CDR2 sequence consisting of SEQ ID NO: 246; and a CDR3 sequence consisting of SEQ ID NO: 248; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 264; a CDR2 sequence consisting of SEQ ID NO: 266; and a CDR3 sequence consisting of SEQ ID NO: 268. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 242 and/or (b) a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 262. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 242, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 262. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 241, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 261.

[0158] In another specific embodiment, the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, are preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, and comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 284; a CDR2 sequence consisting of SEQ ID NO: 286; and a CDR3 sequence consisting of SEQ ID NO: 288; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 304; a CDR2 sequence consisting of SEQ ID NO: 306; and a CDR3 sequence consisting of SEQ ID NO: 308. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof can comprise a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 282, and/or a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 302. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 282, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 302. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 281, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 301.

[0159] In another specific embodiment, the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, are preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, and comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 324; a CDR2 sequence consisting of SEQ ID NO: 326; and a CDR3 sequence consisting of SEQ ID NO: 328; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 344; a CDR2 sequence consisting of SEQ ID NO: 346; and a CDR3 sequence consisting of SEQ ID NO: 348. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof can comprise a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 322, and/or a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 342. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 322, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 342. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 321, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 341.

[0160] In another specific embodiment, the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, are preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, and comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 364; a CDR2 sequence consisting of SEQ ID NO: 366; and a CDR3 sequence consisting of SEQ ID NO: 368; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 384; a CDR2 sequence consisting of SEQ ID NO: 386; and a CDR3 sequence consisting of SEQ ID NO: 388. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof can comprise a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 362, and/or a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 382. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 362, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 382. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 361, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 381.

[0161] In another specific embodiment, the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, are preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, and comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 484; a CDR2 sequence consisting of SEQ ID NO: 486; and a CDR3 sequence consisting of SEQ ID NO: 488; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 504; a CDR2 sequence consisting of SEQ ID NO: 506; and a CDR3 sequence consisting of SEQ ID NO: 508. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof can comprise a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 482, and/or a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 502. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 482, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 502. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 481, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 501.

[0162] In another specific embodiment, the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, are preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, and comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 524; a CDR2 sequence consisting of SEQ ID NO: 526; and a CDR3 sequence consisting of SEQ ID NO: 528; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 544; a CDR2 sequence consisting of SEQ ID NO: 546; and a CDR3 sequence consisting of SEQ ID NO: 548. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof can comprise a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 522, and/or a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 542. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain

having the amino acid sequence of SEQ ID NO: 522, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 542. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 521, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 541.

[0163] In another specific embodiment, the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, are preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, and comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 564; a CDR2 sequence consisting of SEQ ID NO: 566; and a CDR3 sequence consisting of SEQ ID NO: 568; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 584; a CDR2 sequence consisting of SEQ ID NO: 586; and a CDR3 sequence consisting of SEQ ID NO: 588. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof can comprise a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 562, and/or a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 582. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 562, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 582. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 561, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 581.

[0164] In another specific embodiment, the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, are preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, and comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 604; a CDR2 sequence consisting of SEQ ID NO: 606; and a CDR3 sequence consisting of SEQ ID NO: 608; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 624; a CDR2 sequence consisting of SEQ ID NO: 626; and a CDR3 sequence consisting of SEQ ID NO: 628. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof can comprise a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 602, and/or a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 622. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 602, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 622. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 601, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 621.

[0165] In another specific embodiment, the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, are preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, and comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 644; a CDR2 sequence consisting of SEQ ID NO: 646; and a CDR3 sequence consisting of SEQ ID NO: 648; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 664; a CDR2 sequence consisting of SEQ ID NO: 666; and a CDR3 sequence consisting of SEQ ID NO: 668. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof can comprise a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 642, and/or a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 662. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 642, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 662. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 641, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 661.

[0166] In another specific embodiment, the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, are preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, and comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 684; a CDR2 sequence consisting of SEQ ID NO: 686; and a CDR3 sequence consisting of SEQ ID NO: 688; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 704; a CDR2 sequence consisting of SEQ ID NO: 706; and a CDR3 sequence consisting of SEQ ID NO: 708. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof can comprise a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 682, and/or a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 702. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 682, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 702. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 681, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 701.

[0167] In another specific embodiment, the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, are preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, and comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 724; a CDR2 sequence consisting of SEQ ID NO: 726; and a CDR3 sequence consisting of SEQ ID NO: 728; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 744; a CDR2 sequence consisting of SEQ ID NO: 746; and a CDR3 sequence consisting of SEQ ID NO: 748. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof can comprise a variable

heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 722, and/or a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 742. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 722, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 742. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 721, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 741.

[0168] In another specific embodiment, the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, are preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, and comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 764; a CDR2 sequence consisting of SEQ ID NO: 766; and a CDR3 sequence consisting of SEQ ID NO: 768; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 784; a CDR2 sequence consisting of SEQ ID NO: 786; and a CDR3 sequence consisting of SEQ ID NO: 788. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof fragment can comprise a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 762, and/or a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 782. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 762, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 782. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 761, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 781.

[0169] In another specific embodiment, the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, are preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, and comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 804; a CDR2 sequence consisting of SEQ ID NO: 806; and a CDR3 sequence consisting of SEQ ID NO: 808; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 824; a CDR2 sequence consisting of SEQ ID NO: 826; and a CDR3 sequence consisting of SEQ ID NO: 828. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof can comprise a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 802, and/or a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 822. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 802, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 822. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 801, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 821.

[0170] Additionally, the anti-PACAP antibodies and antigen binding fragments of the invention may include human, humanized or chimerized anti-PACAP antibodies or antibody fragments wherein the antibodies or antibody fragments may be selected from the group consisting of scFvs, camelbodies, nanobodies, Immunoglobulin New Antigen Receptor ("IgNAR"), fragment antigen binding ("Fab") fragments, Fab' fragments, MetMab like antibodies, monovalent antibody fragments, and $F(ab')_2$ fragments. In another embodiment, the anti-PACAP antibodies and antigen binding fragments of the invention, preferably human, humanized or chimerized anti-PACAP antibodies or antibody fragments, may substantially or entirely lack N-glycosylation and/or O-glycosylation. Also, the invention embraces an embodiment of the invention wherein the anti-PACAP antibodies and antigen binding fragments of the invention, preferably human, humanized or chimerized anti-PACAP antibodies or antibody fragments, may comprise a human constant domain, e.g. that of an IgG1, IgG2, IgG3, or IgG4 antibody or fragment thereof.

[0171] An additional embodiment of the invention relates to anti-PACAP antibodies and antigen binding fragments, preferably human, humanized or chimerized anti-PACAP antibodies or antibody fragments, wherein said antibodies or antibody fragments may comprise an Fc region that may have been modified to alter at least one of effector function, half-life, proteolysis, or glycosylation, e.g., wherein the Fc region may contain one or more mutations that may alter or eliminate N- and/or O-glycosylation.

[0172] In yet another embodiment of the invention, anti-PACAP antibodies and antigen binding fragments, preferably human, humanized or chimerized anti-PACAP antibodies or antibody fragments, may bind to PACAP with a binding affinity (KD) of less than or equal to 5×10^{-5} M, 10^{-5} M, 5×10^{-6} M, 10^{-6} M, 5×10^{-7} M, 10^{-7} M, 5×10^{-8} M, 10^{-8} M, 5×10^{-9} M, 10^{-9} M, 5×10^{-10} M, 10^{-10} M, 5×10^{-11} M, 10^{-11} M, 5×10^{-12} M, 10^{-12} M, 5×10^{-13} M, or 10^{-13} M, e.g., as may determined by ELISA, bio-layer interferometry ("BLI"), KINEXA or surface plasmon resonance at 25° or 37° C. Also, another embodiment of the invention pertains to anti-PACAP antibodies and antigen binding fragments, preferably human, humanized or chimerized anti-PACAP antibodies or antibody fragments, wherein said antibodies or antibody fragments may bind to PACAP with a binding affinity (KD) of less than or equal to 5×10^{-10} M, 10^{-10} M, 5×10^{-11} M, 10^{-11} M, 5×10^{-12} M, or 10^{-12} M. Additionally, the anti-PACAP antibodies and antigen binding fragments, preferably human, humanized or chimerized anti-PACAP antibodies or antibody fragments, of the invention may include anti-PACAP antibodies or antibody fragments which bind to PACAP with an off-rate (k_{off}) of less than or equal to 5×10^{-4} s^{-1}, 10^{-4} s^{-1}, 5×10^{-5} s^{-1}, or 10^{-5} s^{-1}.

[0173] Another embodiment of the invention relates to anti-PACAP antibodies and antigen binding fragments, preferably human, humanized or chimerized anti-PACAP antibodies or antibody fragments, wherein said antibodies and antibody fragments may be directly or indirectly attached to a detectable label or therapeutic agent. An additional embodiment of the invention pertains to anti-PACAP antibodies and antigen binding fragments, preferably human,

humanized or chimerized anti-PACAP antibodies or antibody fragments that when administered to a subject may inhibit or may neutralize at least one biological effect elicited by PACAP. The anti-PACAP antibodies and antigen binding fragments, preferably human, humanized or chimerized anti-PACAP antibodies or antibody fragments, of the invention may neutralize or may inhibit PACAP activation of at least one of PAC1-R, VPAC1-R, or VPAC2-R; may neutralize or may inhibit PACAP activation of each of PAC1-R, VPAC1-R, and VPAC2-R; may neutralize or may inhibit PACAP activation of PAC1-R; may be capable of inhibiting or preventing PACAP binding to at least one of PAC1-R, VPAC1-R, or VPAC2-R; may be capable of inhibiting or preventing PACAP binding to each of PAC1-R, VPAC1-R, and VPAC2-R; may be capable of inhibiting or preventing PACAP binding to PAC1-R-expressing cells, VPAC1-R-expressing cells, and/or VPAC2-R-expressing cells; may inhibit or block PACAP-induced cAMP production; may, when administered to a subject, may reduce PACAP-induced vasodilation, photophobia, mast cell degranulation and/or neuronal activation.

[0174] In yet another embodiment of the invention, anti-PACAP antibodies and antigen binding fragments, preferably human, humanized or chimerized anti-PACAP antibodies or antibody fragments, may bind to PACAP with a K_D that may be less than about 100 nM; with a K_D that may be less than about 40 nM; with a K_D that may be less than about 100 pM; with a K_D that may be less than about 50 pM; with a K_D that may be less than about 25 pM; or with a K_D that may be between about 10 pM and about 100 pM. The invention also embraces anti-PACAP antibodies and antigen binding fragments, preferably human, humanized or chimerized anti-PACAP antibodies or antibody fragments, that may have stronger binding affinity for PACAP as compared to VIP and/or that may not bind to VIP, e.g., wherein said antibodies or antibody fragments thereof may have an affinity to PACAP that may be at least 10-fold, 30-fold, 100-fold, 300-fold, 1000-fold, 3000-fold, 10000-fold, 30000-fold, 100000-fold, 300000-fold, 1000000-fold, 3000000-fold, 10000000-fold, 30000000-fold or more stronger than the affinity of said antibody or antibody fragment to VIP.

[0175] In another embodiment, the invention pertains to anti-PACAP antibodies and antigen binding fragments, preferably human, humanized or chimerized anti-PACAP antibodies or antibody fragments, that may be attached to at least one effector moiety, e.g., wherein said effector moiety may comprise a chemical linker. In another embodiment, the invention pertains to anti-PACAP antibodies and antigen binding fragments, preferably human, humanized or chimerized anti-PACAP antibodies or antibody fragments, that may be attached to one or more detectable moieties, e.g., wherein said detectable moieties may comprise a fluorescent dye, enzyme, substrate, bioluminescent material, radioactive material, chemiluminescent moiety, and/or mixtures thereof. Also, the anti-PACAP antibodies and antigen binding fragments of the invention, preferably human, humanized or chimerized anti-PACAP antibodies or antibody fragments, may be attached to one or more functional moieties.

[0176] Another embodiment of the invention relates to anti-idiotypic antibodies that may be produced against anti-PACAP antibodies or antibody fragments, wherein said anti-idiotypic antibodies optionally may neutralize one or more biological effects of the anti-PACAP antibody to which it may bind. This embodiment of the invention may also relate to a method of using said anti-idiotypic antibody to monitor the in vivo levels of said anti-PACAP antibody or antibody fragment in a subject or to neutralize the in vivo effects of said anti-PACAP antibody in a subject.

[0177] In yet another embodiment, the invention pertains to a composition that may be suitable for therapeutic, prophylactic, or a diagnostic use, whereby the composition may comprise a therapeutically, prophylactically or diagnostically effective amount of at least one anti-PACAP antibody or antibody fragment or anti-idiotypic antibody, e.g., wherein the composition may be suitable for administration via injection, topical, oral, inhalation or transdermal; may be suitable for subcutaneous, intravenous, intramuscular, topical, oral, inhalatory, intranasal, intrabuccal, vaginal, anal, transdermal, intraperitoneal, or intrathecal administration; and/or wherein the composition may be suitable for subcutaneous intravenous or intramuscular administration. The invention also embraces an embodiment of the invention wherein said composition of at least one anti-PACAP antibody or antibody fragment or anti-idiotypic antibody may be lyophilized; and/or wherein said composition may comprise a pharmaceutically acceptable diluent, carrier, solubilizer, emulsifier, preservative, or mixture thereof. Said composition of the invention may further comprise at least one other active agent, e.g., wherein the other active agent may be selected from the group consisting of a chemotherapeutic, an analgesic, an anti-inflammatory, an immunosuppressant, a cytokine, an antiproliferative, an antiemetic and/or a cytotoxin. Said composition may also be lyophilized, stabilized, and/or may be formulated for administration by injection.

[0178] A further embodiment of the invention embraces an isolated nucleic acid sequence or nucleic acid sequences that may encode an anti-PACAP antibody or antibody fragment or anti-idiotypic antibody, and wherein said isolated nucleic acid sequence or nucleic acid sequences may be contained within a vector or vectors. Additionally, in an embodiment of the invention, a host cell may comprise said isolated nucleic acid sequence or sequences, wherein said host cell may be a mammalian, bacterial, fungal, yeast, avian, amphibian, plant or insect cell; and/or said host cell may be a filamentous fungus or a yeast. Wherein said host cell may be a yeast cell, the yeast may be selected from the following genera: *Arxiozyma; Ascobotryozyma; Citeromyces; Debaryomyces; Dekkera; Eremothecium; Issatchenkia; Kazachstania; Kluyveromyces; Kodamaea; Lodderomyces; Pachysolen; Pichia; Saccharomyces; Saturnispora; Tetrapisispora; Torulaspora; Williopsis; and Zygosaccharomyces*; or the yeast may be genus *Pichia*. In an embodiment of the invention, the yeast host cell may be selected from *Pichia pastoris, Pichia methanolica* and *Hansenula polymorpha* (*Pichia angusta*).

[0179] The invention also relates to a method of expressing an anti-PACAP antibody or antibody fragment that may comprise culturing any of but not limited to the host cells disclosed herein under conditions that may provide for expression of said antibody or antibody fragment. Additionally, the invention pertains to said method wherein the host cell may be a yeast cell or CHO cell that may stably express and may secrete said antibody or antibody fragment. For example, said yeast cell may be a polyploid yeast that may be made by a method that may comprise: (i) introducing at least one expression vector containing one or more heter-

ologous polynucleotides encoding said antibody operably linked to a promoter and a signal sequence into a haploid yeast cell; (ii) producing by mating or spheroplast fusion a polyploid yeast from said first and/or second haploid yeast cell; (iii) selecting polyploid yeast cells that stably express said antibody; and (iv) producing stable polyploid yeast cultures from said polyploid yeast cells that stably express said antibody into the culture medium; and said polyploid yeast may be of the genus *Pichia*. Additionally in another embodiment, the invention embraces a method of expressing an anti-PACAP antibody or antibody fragment that may comprise culturing a host cell wherein said host cell may be a mammalian cell, e.g., a CHO cell.

[0180] Additionally, the invention pertains to a method that may block, inhibit, block or neutralize one or more biological effects associated with PACAP in a subject that may comprise administering to said subject a therapeutically or prophylactically effective amount of a human, humanized or chimerized anti-PACAP antibody or antibody fragment that may antagonize, inhibit, neutralize or block at least one biological effect associated with human PACAP. Another aspect of the invention relates to a method that may block, inhibit, or neutralize one or more biological effects associated with PACAP in a subject that may comprise administering to a subject a therapeutically or prophylactically effective amount of a human, humanized or chimerized anti-PACAP antibody or antibody fragment that may antagonize, inhibit, neutralize or block at least one biological effect associated with human PACAP and that may not substantially interact with (bind) VIP.

[0181] Another aspect of the invention generally relates to a method that may block, inhibit, or neutralize one or more biological effects, e.g., vasomotor effects, associated with PACAP in a subject that may comprise administering to a subject a therapeutically or prophylactically effective amount of a human, humanized or chimerized anti-PACAP antibody or antibody fragment that may comprise one or more of the following: inhibits, blocks or neutralizes at least one biological effect elicited by PACAP; neutralizes or inhibits PACAP activation of at least one of PAC1-R, VPAC1-R, and/or VPAC2-R; inhibits, blocks or neutralizes PACAP activation of each of PAC1-R, VPAC1-R, and VPAC2-R; neutralizes or inhibits PACAP activation of PAC1-R; inhibits PACAP binding to at least one of PAC1-R, VPAC1-R, and/or VPAC2-R; inhibits PACAP binding to each of PAC1-R, VPAC1-R, and/or VPAC2-R; inhibits PACAP binding to PAC1-R-expressing cells; inhibits PACAP binding to VPAC1-R and/or VPAC2-R-expressing cells; does not inhibit PACAP-mediated binding of such antibody to the cell surface, e.g., via a glycosaminoglycan ("GAG"); inhibits PACAP binding to the cell surface, e.g. via a glycosaminoglycan ("GAG"); inhibits PACAP-induced cAMP production; and/or, when administered to a subject, reduces PACAP-induced vasodilation, photophobia, mast cell degranulation and/or neuronal activation.

[0182] Another embodiment of the invention relates to a method that may block, inhibit, or neutralize vasodilation, e.g., vasodilation of the dural arteries, which may be associated with or may be elicited by PACAP in a subject that may comprise administering to a subject a therapeutically or prophylactically effective amount of a human, humanized or chimerized anti-PACAP antibody or antibody fragment that may block, inhibit, or neutralize vasodilation associated with, or elicited by PACAP.

[0183] Yet another embodiment of the invention pertains to a method that may treat or prevent the onset, frequency, severity or duration of headache or migraine, e.g., wherein said headache or migraine may be selected from migraine with aura, migraine without aura, hemiplegic migraine, cluster headache, migrainous neuralgia, chronic headache, chronic migraine, medication overuse headache, and tension headache, in a subject that may comprise administering to a subject in need thereof an effective amount of a human, humanized or chimerized anti-human PACAP antibody or antibody fragment that may elicit one or more of the following effects: inhibits or neutralizes at least one biological effect elicited by PACAP; neutralizes or inhibits PACAP activation of at least one of PAC1-R, VPAC1-R, and/or VPAC2-R; neutralizes or inhibits PACAP activation of each of PAC1-R, VPAC1-R, and VPAC2-R; neutralizes or inhibits PACAP activation of PAC1-R; inhibits PACAP binding to at least one of PAC1-R, VPAC1-R, and/or VPAC2-R; inhibits PACAP binding to each of PAC1-R, VPAC1-R, and/or VPAC2-R; inhibits PACAP binding to PAC1-R-expressing cells; inhibits PACAP binding to VPAC1-R and/or VPAC2-R-expressing cells; does not inhibit PACAP-mediated binding of such antibody to the cell surface, e.g., via a GAG; inhibits PACAP binding to the cell surface, e.g. via a glycosaminoglycan ("GAG"); inhibits PACAP-induced cyclic adenosine monophosphate ("cAMP") production; and/or, when administered to a subject, reduces PACAP-induced vasodilation, photophobia, mast cell degranulation and/or neuronal activation.

[0184] Another embodiment of the invention relates to a method of treating a human subject that may have an acute, episodic or chronic condition that may be associated with at least one of increased vasodilation, photophobia, mast cell degranulation and neuronal activation or a combination of said conditions that may comprise administering to a subject in need thereof an effective amount of an antagonistic human, humanized or chimerized anti-human PACAP antibody or antibody fragment.

[0185] The invention also pertains to any of the methods disclosed herein that may be effected by the administration of a therapeutically or prophylactically effective amount of at least one human, humanized or chimerized anti-PACAP antibody or antibody fragment; and/or wherein said anti-PACAP antibody may be a human antibody or antibody fragment; and/or wherein said anti-PACAP antibody may be a humanized antibody or antibody fragment; and/or wherein said anti-PACAP antibody may be a chimeric antibody or antibody fragment.

[0186] Another embodiment of the invention also relates to a method wherein an anti-PACAP antibody or antibody fragment of the invention may bind to PACAP27 and/or PACAP38 and may block PACAP27 and/or PACAP38 binding to PAC1-R, VPAC1-R, and/or VPAC2-R. Another embodiment of the invention pertains to a method wherein said anti-PACAP antibody or antibody fragment may bind to PACAP27 and/or PACAP38 and may block PACAP27 and/or PACAP38 binding to each of PAC1-R, VPAC1-R, and VPAC2-R. Yet another embodiment of the invention relates to a method wherein said anti-PACAP antibody or antibody fragment may bind to PACAP27 and/or PACAP38 and may block PACAP27 and/or PACAP38 binding to PAC1-R-expressing cells. Additionally, said anti-PACAP antibody or antibody fragment of the invention may have an affinity to PACAP that may be at least 10-fold, 30-fold, 100-fold,

300-fold, 1000-fold, 3000-fold, 10000-fold, 30000-fold, 100000-fold, 300000-fold, 1000000-fold, 3000000-fold, 10000000-fold, 30000000-fold or more stronger than the affinity of said antibody or antibody fragment to VIP.

[0187] The invention embraces a method that may block, inhibit, block or neutralize one or more biological effects associated with PACAP in a subject that may comprise administering to said subject a therapeutically or prophylactically effective amount of a human, humanized or chimerized anti-PACAP antibody or antibody fragment that may antagonize, inhibit, neutralize or blocks at least one biological effect associated with human PACAP, and wherein said subject may have a condition selected from the group consisting of migraine with aura, migraine without aura, hemiplegic migraines, cluster headaches, migrainous neuralgia, chronic headaches, tension headaches, general headaches, hot flush, photophobia, chronic paroxysmal hemicrania, secondary headaches due to an underlying structural problem in the head, secondary headaches due to an underlying structural problem in the neck, cranial neuralgia, sinus headaches, headache associated with sinusitis, allergy-induced headaches, allergy-induced migraines, trigeminal neuralgia, post-herpetic neuralgia, phantom limb pain, fibromyalgia, reflex sympathetic dystrophy, pain, chronic pain, inflammatory pain, post-operative incision pain, post-surgical pain, trauma-related pain, lower back pain, eye pain, tooth pain, complex regional pain syndrome, cancer pain, primary or metastatic bone cancer pain, fracture pain, osteoporotic fracture pain, pain resulting from burn, gout joint pain, pain associated with sickle cell crises, pain associated with temporomandibular disorders, cirrhosis, hepatitis, neurogenic pain, neuropathic pain, nociceptic pain, visceral pain, menstrual pain, ovarialgia, osteoarthritis pain, rheumatoid arthritis pain, diabetic neuropathy, sciatica, dyspepsia, irritable bowel syndrome, inflammatory bowel disease, Crohn's disease, ileitis, ulcerative colitis, renal colic, dysmenorrhea, cystitis, interstitial cystitis, menstrual period, labor, menopause, pancreatitis, schizophrenia, depression, post-traumatic stress disorder ("PTSD"), anxiety disorders, autoimmune diabetes, Sjögren's syndrome, multiple sclerosis, overactive bladder, bronchial hyperreactivity, asthma, stroke, bronchitis, bronchodilation, emphysema, chronic obstructive pulmonary disease ("COPD"), inflammatory dermatitis, adenocarcinoma in glandular tissue, blastoma in embryonic tissue of organs, carcinoma in epithelial tissue, leukemia in tissues that form blood cells, lymphoma in lymphatic tissue, myeloma in bone marrow, sarcoma in connective or supportive tissue, adrenal cancer, AIDS-related lymphoma, anemia, bladder cancer, bone cancer, brain cancer, breast cancer, carcinoid tumors, cervical cancer, chemotherapy, colon cancer, cytopenia, endometrial cancer, esophageal cancer, gastric cancer, head cancer, neck cancer, hepatobiliary cancer, kidney cancer, leukemia, liver cancer, lung cancer, lymphoma, Hodgkin's disease, non-Hodgkin's, nervous system tumors, oral cancer, ovarian cancer, pancreatic cancer, prostate cancer, rectal cancer, skin cancer, stomach cancer, testicular cancer, thyroid cancer, urethral cancer, cancer of bone marrow, multiple myeloma, tumors that metastasize to the bone, tumors infiltrating the nerve and hollow viscus, tumors near neural structures, acne vulgaris, atopic dermatitis, urticaria, keloids, hypertrophic scars and rosacea, endothelial dysfunction, Raynaud's syndrome, coronary heart disease ("CHD"), coronary artery disease ("CAD"), heart failure, peripheral arterial disease ("PAD"), diabetes, pulmonary hypertension ("PH"), connective tissue disorder, allergic dermatitis, psoriasis, pruritus, neurogenic cutaneous redness, erythema, sarcoidosis, shock, sepsis, opiate withdrawal syndrome, morphine tolerance, and epilepsy. Additionally, said subject may have a condition selected from the group consisting of migraine, headache and a pain associated disease or condition, wherein said headache or migraine may selected from the group consisting of migraine with aura, migraine without aura, hemiplegic migraine, cluster headache, migrainous neuralgia, chronic headache, chronic migraine, medication overuse headache, and tension headache. Also, said subject may have a ocular disorder associated with photophobia that may be selected from the group consisting of achromatopsia, aniridia, photophobia caused by an anticholinergic drug, aphakia, buphthalmos, cataracts, cone dystrophy, congenital abnormalities of the eye, viral conjunctivitis, corneal abrasion, corneal dystrophy, corneal ulcer, disruption of the corneal epithelium, ectopia lentis, endophthalmitis, eye trauma caused by disease, eye trauma caused by injury, eye trauma caused by infection, chalazion, episcleritis, glaucoma, keratoconus, optic nerve hypoplasia, hydrophthalmos, congenital glaucoma iritis, optic neuritis, pigment dispersion syndrome, pupillary dilation, retinal detachment, scarring of the cornea, sclera and uveitis. Further, said subject may have a nervous system-related or neurological condition associated with photophobia that may be selected from the group consisting of autism spectrum disorders, Chiari malformation, dyslexia, encephalitis, meningitis, subarachnoid hemorrhage, tumor of the posterior cranial fossa, ankylosing spondylitis, albinism, ariboflavinosis, benzodiazepines, chemotherapy, chikungunya, cystinosis, Ehlers-Danlos syndrome, hangover, influenza, infectious mononucleosis, magnesium deficiency, mercury poisoning, migraine, rabies, and tyrosinemia type II. Additionally, said subject may have a photophobia associated disorder that may be selected from the group consisting of migraine with aura, migraine without aura, iritis, uveitis, meningitis, depression, bipolar disorder, cluster headache or anther trigeminal autonomic cephalalgia ("TAC") or blepharospasm, depression, agoraphobia and bipolar disorder.

[0188] The invention also embraces any of the methods disclosed herein wherein the method relates to an antibody or antibody fragment that may be a human, humanized, or chimerized anti-PACAP antibody or antibody fragment; and/or wherein the antibody or antibody fragment may a human, humanized, or chimerized anti-PACAP antibody or antibody fragment; and/or wherein the antibody or antibody fragment may be an anti-PACAP antibody or antibody fragment that may comprise the same CDRs as an anti-PACAP antibody that may be selected from Ab1, Ab2, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab1.H, Ab5, Ab7, Ab11, Ab12, Ab4, Ab3, Ab6, Ab8, or Ab9.

[0189] The invention also embraces any of the methods disclosed herein wherein the anti-PACAP antibodies and antigen binding fragments thereof according to the invention comprise human, humanized, or chimerized anti-PACAP antibodies or antigen binding fragments thereof, which comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 4; a CDR2 sequence consisting of SEQ ID NO: 6; and a CDR3 sequence consisting of SEQ ID NO: 8; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 24; a CDR2 sequence consisting of SEQ ID NO: 26; and a

CDR3 sequence consisting of SEQ ID NO: 28. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof may comprise (a) a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 2, and/or (b) a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 22. In a more specific embodiment, the anti-PACAP antibodies and antigen binding fragments thereof may comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 2, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 22. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 1, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 21.

[0190] The invention also embraces any of the methods disclosed herein wherein the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 44; a CDR2 sequence consisting of SEQ ID NO: 46; and a CDR3 sequence consisting of SEQ ID NO: 48; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 64; a CDR2 sequence consisting of SEQ ID NO: 66; and a CDR3 sequence consisting of SEQ ID NO: 68. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 42, and/or (b) a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 62. In another specific embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 42, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 62. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof may comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 41, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 61.

[0191] The invention also embraces any of the methods disclosed herein wherein the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, may comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 84; a CDR2 sequence consisting of SEQ ID NO: 86; and a CDR3 sequence consisting of SEQ ID NO: 88; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 104; a CDR2 sequence consisting of SEQ ID NO: 106; and a CDR3 sequence consisting of SEQ ID NO: 108. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 82, and/or (b) a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 102. In another specific embodiment, the anti-PACAP antibodies and antigen binding fragments thereof may comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 82, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 102. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 81, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 101.

[0192] The invention also embraces any of the methods disclosed herein wherein the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, may comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 124; a CDR2 sequence consisting of SEQ ID NO: 126; and a CDR3 sequence consisting of SEQ ID NO: 128; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 144; a CDR2 sequence consisting of SEQ ID NO: 146; and a CDR3 sequence consisting of SEQ ID NO: 148. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof may comprise (a) a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 122 and/or (b) a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 142. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof may comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 122, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 142. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 121, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 141.

[0193] The invention also embraces any of the methods disclosed herein wherein the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, may comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 164; a CDR2 sequence consisting of SEQ ID NO: 166; and a CDR3 sequence consisting of SEQ ID NO: 168; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 184; a CDR2 sequence consisting of SEQ ID NO: 186; and a CDR3 sequence consisting of SEQ ID NO: 188. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 162, and/or (b) a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 182. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 162, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 182. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid

sequence of SEQ ID NO: 161, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 181.

[0194] The invention also embraces any of the methods disclosed herein wherein the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, are preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, and comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 204; a CDR2 sequence consisting of SEQ ID NO: 206; and a CDR3 sequence consisting of SEQ ID NO: 208; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 224; a CDR2 sequence consisting of SEQ ID NO: 226; and a CDR3 sequence consisting of SEQ ID NO: 228. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 202 and/or (b) a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 222. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 202, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 222. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 201, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 221.

[0195] The invention also embraces any of the methods disclosed herein wherein the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, are preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, and comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 244; a CDR2 sequence consisting of SEQ ID NO: 246; and a CDR3 sequence consisting of SEQ ID NO: 248; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 264; a CDR2 sequence consisting of SEQ ID NO: 266; and a CDR3 sequence consisting of SEQ ID NO: 268. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 242 and/or (b) a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 262. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 242, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 262. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 241, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 261.

[0196] The invention also embraces any of the methods disclosed herein wherein the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, are preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, and comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 284; a CDR2 sequence consisting of SEQ ID NO: 286; and a CDR3 sequence consisting of SEQ ID NO: 288; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 304; a CDR2 sequence consisting of SEQ ID NO: 306; and a CDR3 sequence consisting of SEQ ID NO: 308. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof can comprise a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 282, and/or a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 302. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 282, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 302. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 281, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 301.

[0197] The invention also embraces any of the methods disclosed herein wherein the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, are preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, and comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 324; a CDR2 sequence consisting of SEQ ID NO: 326; and a CDR3 sequence consisting of SEQ ID NO: 328; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 344; a CDR2 sequence consisting of SEQ ID NO: 346; and a CDR3 sequence consisting of SEQ ID NO: 348. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof can comprise a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 322, and/or a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 342. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 322, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 342. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 321, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 341.

[0198] The invention also embraces any of the methods disclosed herein wherein the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, are preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, and comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 364; a CDR2 sequence consisting of SEQ ID NO: 366; and a CDR3 sequence consisting of SEQ ID NO: 368; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 384; a CDR2 sequence consisting of SEQ ID NO: 386; and a CDR3 sequence consisting of SEQ ID NO: 388. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof can comprise a variable heavy chain

comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 362, and/or a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 382. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 362, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 382. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 361, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 381.

[0199] The invention also embraces any of the methods disclosed herein wherein the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, are preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, and comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 484; a CDR2 sequence consisting of SEQ ID NO: 486; and a CDR3 sequence consisting of SEQ ID NO: 488; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 504; a CDR2 sequence consisting of SEQ ID NO: 506; and a CDR3 sequence consisting of SEQ ID NO: 508. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof can comprise a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 482, and/or a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 502. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 482, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 502. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 481, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 501.

[0200] The invention also embraces any of the methods disclosed herein wherein the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, are preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, and comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 524; a CDR2 sequence consisting of SEQ ID NO: 526; and a CDR3 sequence consisting of SEQ ID NO: 528; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 544; a CDR2 sequence consisting of SEQ ID NO: 546; and a CDR3 sequence consisting of SEQ ID NO: 548. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof can comprise a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 522, and/or a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 542. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 522, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 542. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 521, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 541.

[0201] The invention also embraces any of the methods disclosed herein wherein the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, are preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, and comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 564; a CDR2 sequence consisting of SEQ ID NO: 566; and a CDR3 sequence consisting of SEQ ID NO: 568; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 584; a CDR2 sequence consisting of SEQ ID NO: 586; and a CDR3 sequence consisting of SEQ ID NO: 588. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof can comprise a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 562, and/or a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 582. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 562, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 582. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 561, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 581.

[0202] The invention also embraces any of the methods disclosed herein wherein the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, are preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, and comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 604; a CDR2 sequence consisting of SEQ ID NO: 606; and a CDR3 sequence consisting of SEQ ID NO: 608; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 624; a CDR2 sequence consisting of SEQ ID NO: 626; and a CDR3 sequence consisting of SEQ ID NO: 628. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof can comprise a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 602, and/or a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 622. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 602, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 622. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 601, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 621.

[0203] The invention also embraces any of the methods disclosed herein wherein the anti-PACAP antibodies and

antigen binding fragments thereof according to the invention, are preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, and comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 644; a CDR2 sequence consisting of SEQ ID NO: 646; and a CDR3 sequence consisting of SEQ ID NO: 648; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 664; a CDR2 sequence consisting of SEQ ID NO: 666; and a CDR3 sequence consisting of SEQ ID NO: 668. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof can comprise a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 642, and/or a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 662. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 642, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 662. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 641, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 661.

[0204] The invention also embraces any of the methods disclosed herein wherein the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, are preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, and comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 684; a CDR2 sequence consisting of SEQ ID NO: 686; and a CDR3 sequence consisting of SEQ ID NO: 688; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 704; a CDR2 sequence consisting of SEQ ID NO: 706; and a CDR3 sequence consisting of SEQ ID NO: 708. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof can comprise a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 682, and/or a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 702. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 682, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 702. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 681, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 701.

[0205] The invention also embraces any of the methods disclosed herein wherein the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, are preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, and comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 724; a CDR2 sequence consisting of SEQ ID NO: 726; and a CDR3 sequence consisting of SEQ ID NO: 728; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 744; a CDR2 sequence consisting of SEQ ID NO: 746; and a CDR3 sequence consisting of SEQ ID NO: 748. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof can comprise a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 722, and/or a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 742. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 722, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 742. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 721, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 741.

[0206] The invention also embraces any of the methods disclosed herein wherein the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, are preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, and comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 764; a CDR2 sequence consisting of SEQ ID NO: 766; and a CDR3 sequence consisting of SEQ ID NO: 768; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 784; a CDR2 sequence consisting of SEQ ID NO: 786; and a CDR3 sequence consisting of SEQ ID NO: 788. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof fragment can comprise a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 762, and/or a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 782. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 762, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 782. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 761, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 781.

[0207] The invention also embraces any of the methods disclosed herein wherein the anti-PACAP antibodies and antigen binding fragments thereof according to the invention, are preferably human, humanized, or chimerized anti-PACAP antibodies and antigen binding fragments thereof, and comprise (a) a variable heavy chain comprising a CDR1 sequence consisting of SEQ ID NO: 804; a CDR2 sequence consisting of SEQ ID NO: 806; and a CDR3 sequence consisting of SEQ ID NO: 808; and/or (b) a variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 824; a CDR2 sequence consisting of SEQ ID NO: 826; and a CDR3 sequence consisting of SEQ ID NO: 828. Alternatively, the anti-PACAP antibodies and antigen binding fragments thereof can comprise a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 802, and/or a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99%

sequence identity to SEQ ID NO: 822. In another embodiment, the anti-PACAP antibodies and antigen binding fragments thereof comprise (a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 802, and/or (b) a variable light chain having the amino acid sequence of SEQ ID NO: 822. More specifically, the anti-PACAP antibodies and antigen binding fragments thereof can comprise (a) a heavy chain having the amino acid sequence of SEQ ID NO: 801, and/or (b) a light chain having the amino acid sequence of SEQ ID NO: 821.

[0208] The invention also relates to any of the methods disclosed herein wherein the anti-PACAP antibodies or antibody fragments may be selected from the group consisting of scFvs, camelbodies, nanobodies, Immunoglobulin New Antigen Receptor ("IgNAR"), fragment antigen binding ("Fab") fragments, Fab' fragments, MetMab like antibodies, monovalent antibody fragments, and $F(ab')_2$ fragments. Additionally, the invention relates to any of the methods disclosed herein wherein the anti-PACAP antibody or antibody fragment may substantially or entirely lack N-glycosylation and/or O-glycosylation. Also, the invention pertains to any of the methods disclosed herein wherein the anti-PACAP antibody or antibody fragment may comprise a human constant domain, e.g., that of an IgG1, IgG2, IgG3, or IgG4 antibody.

[0209] Another aspect of the invention pertains to any of the methods disclosed herein wherein the anti-PACAP antibody or antibody fragment may comprise an Fc region that may have been modified to alter at least one of effector function, half-life, proteolysis, or glycosylation, e.g., the Fc region may contain one or more mutations that alters or eliminates N- and/or O-glycosylation.

[0210] A further aspect of the invention relates to any of the methods disclosed herein wherein the anti-PACAP antibody or antibody fragment may bind to PACAP with a binding affinity (K_D) of less than or equal to 5×10^{-5} M, 10^{-5} M, 5×10^{-6} M, 10^{-6} M, 5×10^{-7} M, 10^{-7} M, 5×10^{-8} M, 10^{-8} M, 5×10^{-9} M, 10^{-9} M, 5×10^{-10} M, 10^{-10} M, 5×10^{-11} M, 10^{-11} M, 5×10^{-12} M, 10^{-12} M, 5×10^{-13} M, or 10^{-13} M. Also, said anti-PACAP antibody or antibody fragment of any of the methods disclosed herein may bind to PACAP with a binding affinity (K_D) of less than or equal to 5×10^{-10} M, 10^{-10} M, 5×10^{-11} M, 10^{-11} M, 5×10^{-12} M, or 10^{-12} M. Another embodiment of the invention pertains any of the methods disclosed herein wherein the anti-PACAP antibody or antibody fragment may bind to PACAP with an off-rate (k_{off}) of less than or equal to 5×10^{-4} s^{-1}, 10^{-4} s^{-1}, 5×10^{-5} s^{-1}, or 10^{-5} s^{-1}.

[0211] Moreover, the invention embraces any of the methods disclosed herein wherein the anti-PACAP antibody or antibody fragment may be directly or indirectly attached to a detectable label or therapeutic agent. Also, the invention relates to any of the methods disclosed herein wherein the anti-PACAP antibody or antibody fragment may bind to PACAP with a KD that may be less than about 100 nM, less than about 40 nM, less than about 1 nM, less than about 100 pM, less than about 50 pM, or less than about 25 pM. Also, the invention embraces any of the methods disclosed herein wherein the anti-PACAP antibody or antibody fragment may bind to PACAP with a KD that may be between about 10 pM and about 100 pM. The invention further pertains to any of the methods disclosed herein wherein the method may further comprise administering separately or co-administering another agent, e.g., wherein the other agent may be selected from a chemotherapeutic, an analgesic, an anti-inflammatory, an immunosuppressant, a cytokine, an anti-proliferative, an antiemetic or a cytotoxin. Also, the invention embraces any of the methods disclosed herein wherein the other therapeutic agent may be an analgesic, and said analgesic may be a non-steroidal anti-inflammatory drug ("NSAID"), an opioid analgesic, another antibody or a non-antibody biologic, and further wherein said other antibody may be an anti-NGF antibody or antibody fragment; and/or may be an anti-Calcitonin Gene-Related Peptide ("CGRP") antibody or antibody fragment and/or an anti-CGRP receptor antibody or antibody fragment. The invention also pertains to any of the methods disclosed herein wherein said NSAID may be a cyclooxygenase 1 and/or cyclooxygenase 2 inhibitor; and/or wherein said NSAID may be selected from the group consisting of (1) propionic acid derivatives including ibuprofen, naproxen, naprosyn, diclofenac, and ketoprofen; (2) acetic acid derivatives including tolmetin and sulindac; (3) fenamic acid derivatives including mefenamic acid and meclofenamic acid; (4) biphenylcarboxylic acid derivatives including diflunisal and flufenisal; and (5) oxicams including piroxim, sudoxicam, and isoxicam. The invention further relates to any of the methods disclosed herein wherein said opioid analgesic may be selected from the group consisting of codeine, dihydrocodeine, diacetylmorphine, hydrocodone, hydromorphone, levorphanol, oxymorphone, alfentanil, buprenorphine, butorphanol, fentanyl, sufentanil, meperidine, methadone, nalbuphine, propoxyphene, pentazocine, and pharmaceutically acceptable salts thereof; and/or wherein the opioid analgesic may be morphine or a morphine derivative or pharmaceutically acceptable salt thereof; and/or wherein the combined administration of the opioid analgesic and the anti-PACAP antibody or antigen binding fragment may increase the analgesic effect as compared to either the opioid analgesic or the anti-PACAP antibody or antigen binding fragment administered alone.

[0212] Furthermore, the invention relates to any of the methods disclosed herein wherein a subject of any of the methods disclosed herein may have previously received an anti-CGRP antibody or antibody fragment and/or an anti-CGRP receptor antibody or antibody fragment; and/or wherein said subject may be a migraineur who may have not adequately responded to anti-CGRP antibody and/or an anti-CGRP receptor antibody or antibody fragment treatment; and/or wherein said subject may have previously received at least one anti-CGRP antibody or antibody fragment and/or an anti-CGRP receptor antibody or antibody fragment administration that may have elicited an immune response to the anti-CGRP antibody or antibody fragment and/or the anti-CGRP receptor antibody or antibody fragment.

[0213] Moreover, the invention embraces any of the methods disclosed herein wherein the antibody or antigen binding fragment thereof of the invention may ameliorate or treat one or more conditions associated with PACAP expression in a subject in need thereof, said condition may be selected from the group consisting of: migraine with aura, migraine without aura, hemiplegic migraines, cluster headaches, migrainous neuralgia, chronic headaches, tension headaches, general headaches, hot flush, photophobia, chronic paroxysmal hemicrania, secondary headaches due to an underlying structural problem in the head, secondary headaches due to an underlying structural problem in the neck,

cranial neuralgia, sinus headaches, headache associated with sinusitis, allergy-induced headaches, allergy-induced migraines, trigeminal neuralgia, post-herpetic neuralgia, phantom limb pain, fibromyalgia, reflex sympathetic dystrophy, pain, chronic pain, inflammatory pain, post-operative incision pain, post-surgical pain, trauma-related pain, lower back pain, eye pain, tooth pain, complex regional pain syndrome, cancer pain, primary or metastatic bone cancer pain, fracture pain, osteoporotic fracture pain, pain resulting from burn, gout joint pain, pain associated with sickle cell crises, pain associated with temporomandibular disorders, cirrhosis, hepatitis, neurogenic pain, neuropathic pain, nociceptic pain, visceral pain, menstrual pain, ovarialgia, osteoarthritis pain, rheumatoid arthritis pain, diabetic neuropathy, sciatica, dyspepsia, irritable bowel syndrome, inflammatory bowel disease, Crohn's disease, ileitis, ulcerative colitis, renal colic, dysmenorrhea, cystitis, interstitial cystitis, menstrual period, labor, menopause, pancreatitis, schizophrenia, depression, post-traumatic stress disorder, anxiety disorders, autoimmune diabetes, Sjögren's syndrome, multiple sclerosis, overactive bladder, bronchial hyperreactivity, asthma, stroke, bronchitis, bronchodilation, emphysema, chronic obstructive pulmonary disease ("COPD"), inflammatory dermatitis, adenocarcinoma in glandular tissue, blastoma in embryonic tissue of organs, carcinoma in epithelial tissue, leukemia in tissues that form blood cells, lymphoma in lymphatic tissue, myeloma in bone marrow, sarcoma in connective or supportive tissue, adrenal cancer, AIDS-related lymphoma, anemia, bladder cancer, bone cancer, brain cancer, breast cancer, carcinoid tumors, cervical cancer, chemotherapy, colon cancer, cytopenia, endometrial cancer, esophageal cancer, gastric cancer, head cancer, neck cancer, hepatobiliary cancer, kidney cancer, leukemia, liver cancer, lung cancer, lymphoma, Hodgkin's disease, non-Hodgkin's, nervous system tumors, oral cancer, ovarian cancer, pancreatic cancer, prostate cancer, rectal cancer, skin cancer, stomach cancer, testicular cancer, thyroid cancer, urethral cancer, cancer of bone marrow, multiple myeloma, tumors that metastasize to the bone, tumors infiltrating the nerve and hollow viscus, tumors near neural structures, acne vulgaris, atopic dermatitis, urticaria, keloids, hypertrophic scars and rosacea, endothelial dysfunction, Raynaud's syndrome, coronary heart disease ("CHD"), coronary artery disease ("CAD"), heart failure, peripheral arterial disease ("PAD"), diabetes, pulmonary hypertension ("PH"), connective tissue disorder, allergic dermatitis, psoriasis, pruritus, neurogenic cutaneous redness, erythema, sarcoidosis, shock, sepsis, opiate withdrawal syndrome, morphine tolerance, and epilepsy.

[0214] In another embodiment of the invention, an anti-PACAP antibody or antibody fragment or a method as disclosed herein may inhibit the effects of PACAP on vasodilation; and/or may inhibit the effects of PACAP on cAMP production; and/or may inhibit the effects of PACAP on PLC resulting in reduced Ca++ and PLD levels; and/or may inhibit the effects of PACAP on adenylate cyclase activity; and/or may inhibit the effects of PACAP on its binding to any or all of PAC1-R, VPAC1-R or VPAC2-R; and/or may inhibit the effects of PACAP on neurodevelopment; may inhibit the effects of PACAP on neuroprotection; and/or may inhibit the effects of PACAP on neuromodulation; and/or may inhibit the effects of PACAP on neurogenic inflammation; and/or may inhibit the effects of PACAP on nociception; and/or may modulate the interaction of PACAP with binding the cell surface, e.g. via at least one GAG, e.g., wherein at least one said GAG may comprise one or more of heparin, chondroitin, keratin, and hyaluronic acid, and further wherein said antibody or antibody fragment or method may block or inhibit receptor-independent cellular uptake of PACAP3 8 and/or PACAP27 and/or may inhibit or may block GAG-dependent uptake of PACAP38 and/or PACAP27 by cells.

[0215] A further embodiment of the invention relates to method of therapy or prophylaxis that may comprise the administration of an anti-PACAP antibody or antibody fragment of the invention. Additionally, the invention pertains to a composition that may be used in human therapy that may contain an anti-PACAP antibody or antibody fragment of the invention. Said composition may contain another active agent, e.g., wherein the other agent may selected from a chemotherapeutic, an analgesic, an anti-inflammatory, an immunosuppressant, a cytokine, an antiproliferative, an antiemetic or a cytotoxin. Wherein said other agent may be an analgesic, said analgesic may be a NSAID, an opioid analgesic, another antibody or a non-antibody biologic. When said other agent may be an analgesic that may be another antibody, the other antibody may be an anti-NGF antibody or antibody fragment, and/or the other antibody may be an anti-Calcitonin Gene-Related Peptide ("CGRP") antibody or antibody fragment and/or an anti-CGRP receptor antibody or antibody fragment. Wherein said other agent may be a NSAID, said NSAID may be a cyclooxygenase 1 and/or cyclooxygenase 2 inhibitor; and/or said NSAID may be selected from the group consisting of (1) propionic acid derivatives including ibuprofen, naproxen, naprosyn, diclofenac, and ketoprofen; (2) acetic acid derivatives including tolmetin and sulindac; (3) fenamic acid derivatives including mefenamic acid and meclofenamic acid; (4) biphenylcarboxylic acid derivatives including diflunisal and flufenisal; and (5) oxicams including piroxim, sudoxicam, and isoxicam. Wherein said other agent may be an opioid analgesic, said opioid analgesic may be selected from the group consisting of codeine, dihydrocodeine, diacetylmorphine, hydrocodone, hydromorphone, levorphanol, oxymorphone, alfentanil, buprenorphine, butorphanol, fentanyl, sufentanil, meperidine, methadone, nalbuphine, propoxyphene, pentazocine, and pharmaceutically acceptable salts thereof; and/or said opioid analgesic may be morphine or a morphine derivative or pharmaceutically acceptable salt thereof; and/or said opioid analgesic and an anti-PACAP antibody or antigen binding fragment according to the invention may increase the analgesic effect as compared to either the opioid analgesic or the anti-PACAP antibody or antigen binding fragment administered alone.

[0216] In another embodiment of the invention, an anti-PACAP antibody or fragment or composition according to the invention, wherein the anti-PACAP antibody or fragment and another active agent may be combined therewith or may be administered in combination, may elicit a synergistic or additive effect on the treatment or prevention of a PACAP associated effect, e.g., migraine or on pain. Another embodiment of the invention additionally embraces an anti-PACAP antibody or fragment or composition according the invention that may be used in therapy or diagnosis, e.g., migraine treatment or prophylaxis. A further embodiment of the invention relates to an anti-PACAP antibody or fragment or composition according to the invention that may be used for treating one or more of hot flush, migraine with or without

aura, hemiplegic migraine, cluster headache, migrainous neuralgia, chronic headache, chronic migraine, medication overuse headache or tension headache.

[0217] Another embodiment of the invention pertains an anti-PACAP antibody or fragment or composition according to the invention that may be used for ameliorating, controlling, reducing incidence of, or delaying the development or progression of headache, e.g., migraine with or without aura, hemiplegic migraine, cluster headache, migrainous neuralgia, chronic headache, chronic migraine, medication overuse headache or tension headache. In an embodiment of the invention, the use may be for a subject who may have previously received or may be receiving an anti-CGRP antibody or antibody fragment and/or an anti-CGRP receptor antibody or antibody fragment, and further wherein said subject may be a migraineur who may not have adequately responded to anti-CGRP antibody or antibody fragment and/or anti-CGRP receptor antibody or antibody fragment treatment; and/or wherein said subject may have previously received at least one anti-CGRP antibody or antibody fragment and/or anti-CGRP receptor antibody or antibody fragment administration that may have elicited an immune response to the anti-CGRP antibody or antibody fragment and/or anti-CGRP receptor antibody or antibody fragment.

BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING

[0218] FIG. **1**A-**1**B provides the polypeptide sequences of the variable heavy chain region for antibodies Ab1, Ab1.H, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab22, and Ab23 (SEQ ID NOs: 2; 42; 82; 682; 642; 482; 722; 522; 762; 802; 562; 602; 122; 162; 202; 242; 282; 322; 362; 882; and 922, respectively) aligned by their FRs and CDRs.

[0219] FIG. **2**A-**2**B provides the polypeptide sequences of the variable light chain region for antibodies Ab1, Ab1.H, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab22, and Ab23 (SEQ ID NOs: 22; 62; 102; 702; 662; 502; 742; 542; 782; 822; 582; 622; 142; 182; 222; 262; 302; 342; 382; 902; and 942, respectively) aligned by their FRs and CDRs.

[0220] FIG. **3**A-**3**F provides the polynucleotide sequences encoding the variable heavy chain region for antibodies Ab1, Ab1.H, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab22, and Ab23 (SEQ ID NOs: 12; 52; 92; 692; 652; 492; 732; 532; 772; 812; 572; 612; 132; 172; 212; 252; 292; 332; 372; 892; and 932, respectively) aligned by their FRs and CDRs.

[0221] FIG. **4**A-**4**E provide the polynucleotide sequences encoding the variable light chain region for antibodies Ab1, Ab1.H, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab22, and Ab23 (SEQ ID NOs: 32; 72; 112; 712; 672; 512; 752; 552; 792; 832; 592; 632; 152; 192; 232; 272; 312; 352; 392; 912; and 952, respectively) aligned by their FRs and CDRs.

[0222] FIG. **5** provides the polypeptide sequence coordinates for certain antibody heavy chain protein sequence features including the variable region and CDRs of the heavy chain for antibodies Ab1, Ab1.H, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab22, and Ab23.

[0223] FIG. **6** provides the polypeptide sequence coordinates for certain antibody heavy chain protein sequence features including the constant region and framework regions FRs of the heavy chain for antibodies Ab1, Ab1.H, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab22, and Ab23.

[0224] FIG. **7** provides the polypeptide sequence coordinates for certain antibody light chain protein sequence features including the variable region and CDRs of the light chain for antibodies Ab1, Ab1.H, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab22, and Ab23.

[0225] FIG. **8** provides the polypeptide sequence coordinates for certain antibody light chain protein sequence features including the constant region and framework regions FRs of the light chain for antibodies Ab1, Ab1.H, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab22, and Ab23.

[0226] FIG. **9** provides the polynucleotide sequence coordinates for certain antibody heavy chain DNA sequence features including the variable region and CDRs of the heavy chain for antibodies Ab1, Ab1.H, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab22, and Ab23.

[0227] FIG. **10** provides the polynucleotide sequence coordinates for certain antibody heavy chain DNA sequence features including the constant region and FRs of the heavy chain for antibodies Ab1, Ab1.H, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab22, and Ab23.

[0228] FIG. **11** provides the polynucleotide sequence coordinates for certain antibody light chain DNA sequence features including the variable region and CDRs of the light chain for antibodies Ab1, Ab1.H, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab22, and Ab23.

[0229] FIG. **12** provides the polynucleotide sequence coordinates for certain antibody light chain DNA sequence features including the constant region and FRs of the light chain for antibodies Ab1, Ab1.H, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab22, and Ab23.

[0230] FIG. **13**A-V provides representative competitive binding data for Ab1 (FIG. **13**A), Ab2 (FIG. **13**B), Ab3 (FIG. **13**C), Ab4 (FIG. **13**D), Ab5 (FIG. **13**E), Ab6 (FIG. **13**F), Ab7 (FIG. **13**G), Ab8 (FIG. **13**H), Ab9 (FIG. **13**I), Ab10 (FIG. **13**J), Ab11 (FIG. **13**K), Ab12 (FIG. **13**L), Ab13 (FIG. **13**M), Ab14 (FIG. **13**N), Ab15 (FIG. **13**O), Ab16 (FIG. **13**P), Ab17 (FIG. **13**Q), Ab18 (FIG. **13**R), Ab19 (FIG. **13**S), Ab1.H, (FIG. **13**T), Ab22 (FIG. **13**U), and Ab23 (FIG. **13**V), respectively, obtained following the protocol in Example 1 infra.

[0231] FIG. **14**A-BB provides representative data showing Ab1-mediated (FIG. **14**A), Ab2-mediated (FIG. **14**B), Ab3-mediated (FIG. **14**C), Ab4-mediated (FIG. **14**D), Ab5-mediated (FIG. **14**E), Ab6-mediated (FIG. **14**F), Ab7-mediated (FIG. **14**G), Ab8-mediated (FIG. **14**H), Ab9-mediated (FIG. **14**I), Ab10-mediated (FIG. **14**J), Ab11-mediated (FIG. **14**K), Ab12-mediated (FIG. **14**L), Ab13-mediated (FIG. **14**M), Ab14-mediated (FIG. **14**N), Ab15-mediated (FIG. **14**O), Ab16-mediated (FIG. **14**P), Ab17-mediated (FIG. **14**Q), Ab18-mediated (FIG. **14**R), Ab19-mediated (FIG. **14**S), Ab1.H-mediated (FIG. **14**T), Ab10.H-mediated (FIG. **14**U), Ab22-mediated (FIG. **14**V), Ab23-mediated (FIG.

14W), Ab3.H-mediated (FIG. 14X), Ab4.H-mediated (FIG. 14Y), Ab5.H-mediated (FIG. 14Z), Ab9.H-mediated (FIG. 14AA), and Ab12.H-mediated (FIG. 14BB) inhibition of PACAP38 binding to PAC1-R-expressing PC-12 cells obtained following the protocol in Example 5 infra.

[0232] FIG. 15A-J provides representative data showing Ab1.H (FIG. 15A), Ab3.H (FIG. 15B), Ab4.H (FIG. 15C), Ab5.H (FIG. 15D), Ab9.H (FIG. 15E), Ab12.H (FIG. 15F), Ab10 (FIG. 15G), Ab10.H (FIG. 15H), Ab22 (FIG. 15I), and Ab23 (FIG. 15J) binding to PAC1-R-expressing PC-12 cells in the presence of PACAP38 obtained following the protocol in Example 6 infra.

[0233] FIG. 16A-BB provides representative data showing Ab1-mediated (FIG. 16A), Ab2-mediated (FIG. 16B), Ab3-mediated (FIG. 16C), Ab4-mediated (FIG. 16D), Ab5-mediated (FIG. 16E), Ab6-mediated (FIG. 16F), Ab7-mediated (FIG. 16G), Ab8-mediated (FIG. 16H), Ab9-mediated (FIG. 16I), Ab10-mediated (FIG. 16J), Ab11-mediated (FIG. 16K), Ab12-mediated (FIG. 16L), Ab13-mediated (FIG. 16M), Ab14-mediated (FIG. 16N), Ab15-mediated (FIG. 16O), Ab16-mediated (FIG. 16P), Ab17-mediated (FIG. 16Q), Ab18-mediated (FIG. 16R), Ab19-mediated (FIG. 16S), Ab1.H-mediated (FIG. 16T), Ab10.H-mediated (FIG. 16U), Ab22-mediated (FIG. 16V), Ab23-mediated (FIG. 16W), Ab3.H-mediated (FIG. 16X), Ab4.H-mediated (FIG. 16Y), Ab5.H-mediated (FIG. 16Z), Ab9.H-mediated (FIG. 16AA), and Ab12.H-mediated (FIG. 16BB) inhibition of PACAP38-driven cAMP production via PAC1-R-expressing PC-12 cells obtained following the protocol in Example 1 infra.

[0234] FIG. 17A-BB provides representative data showing Ab1-mediated (FIG. 17A), Ab2-mediated (FIG. 17B), Ab3-mediated (FIG. 17C), Ab4-mediated (FIG. 17D), Ab5-mediated (FIG. 17E), Ab6-mediated (FIG. 17F), Ab7-mediated (FIG. 17G), Ab8-mediated (FIG. 17H), Ab9-mediated (FIG. 17I), Ab10-mediated (FIG. 17J), Ab11-mediated (FIG. 17K), Ab12-mediated (FIG. 17L), Ab13-mediated (FIG. 17M), Ab14-mediated (FIG. 17N), Ab15-mediated (FIG. 17O), Ab16-mediated (FIG. 17P), Ab17-mediated (FIG. 17Q), Ab18-mediated (FIG. 17R), Ab19-mediated (FIG. 17S), Ab1.H-mediated (FIG. 17T), Ab10.H-mediated (FIG. 17U), Ab22-mediated (FIG. 17V), Ab23-mediated (FIG. 17W), Ab3.H-mediated (FIG. 17X), Ab4.H-mediated (FIG. 17Y), Ab5.H-mediated (FIG. 17Z), Ab9.H-mediated (FIG. 17AA), and Ab12.H-mediated (FIG. 17BB) inhibition of PACAP27-driven cAMP production via PAC1-R-expressing PC-12 cells obtained following the protocol in Example 1 infra.

[0235] FIG. 18A-BB provides representative data showing Ab1-mediated (FIG. 18A), Ab2-mediated (FIG. 18B), Ab3-mediated (FIG. 18C), Ab4-mediated (FIG. 18D), Ab5-mediated (FIG. 18E), Ab6-mediated (FIG. 18F), Ab7-mediated (FIG. 18G), Ab8-mediated (FIG. 18H), Ab9-mediated (FIG. 18I), Ab10-mediated (FIG. 18J), Ab11-mediated (FIG. 18K), Ab12-mediated (FIG. 18L), Ab13-mediated (FIG. 18M), Ab14-mediated (FIG. 18N), Ab15-mediated (FIG. 18O), Ab16-mediated (FIG. 18P), Ab17-mediated (FIG. 18Q), Ab18-mediated (FIG. 18R), Ab19-mediated (FIG. 18S), Ab1.H-mediated (FIG. 18T), Ab10.H-mediated (FIG. 18U), Ab22-mediated (FIG. 18V), Ab23-mediated (FIG. 18W), Ab3.H-mediated (FIG. 18X), Ab4.H-mediated (FIG. 18Y), Ab5.H-mediated (FIG. 18Z), Ab9.H-mediated (FIG. 18AA), and Ab12.H-mediated (FIG. 18BB) inhibition of PACAP38-driven cAMP production via VPAC1-R-expressing CHO-K1 cells obtained following the protocol in Example 3 infra.

[0236] FIG. 19A-BB provides representative data showing Ab1-mediated (FIG. 19A), Ab2-mediated (FIG. 19B), Ab3-mediated (FIG. 19C), Ab4-mediated (FIG. 19D), Ab5-mediated (FIG. 19E), Ab6-mediated (FIG. 19F), Ab7-mediated (FIG. 19G), Ab8-mediated (FIG. 19H), Ab9-mediated (FIG. 19I), Ab10-mediated (FIG. 19J), Ab11-mediated (FIG. 19K), Ab12-mediated (FIG. 19L), Ab13-mediated (FIG. 19M), Ab14-mediated (FIG. 19N), Ab15-mediated (FIG. 19O), Ab16-mediated (FIG. 19P), Ab17-mediated (FIG. 19Q), Ab18-mediated (FIG. 19R), Ab19-mediated (FIG. 19S), Ab1.H-mediated (FIG. 19T), Ab10.H-mediated (FIG. 19U), Ab22-mediated (FIG. 19V), Ab23-mediated (FIG. 19W), Ab3.H-mediated (FIG. 19X), Ab4.H-mediated (FIG. 19Y), Ab5.H-mediated (FIG. 19Z), Ab9.H-mediated (FIG. 19AA), and Ab12.H-mediated (FIG. 19BB) inhibition of PACAP38-driven cAMP production via VPAC2-R-expressing CHO-K1 cells obtained following the protocol in Example 4 infra.

[0237] FIG. 20 provides representative data showing a reduction in vasodilation obtained by administering Ab1.H following PACAP38 administration in a rabbit model, relative to a vehicle control, obtained following the protocol in Example 7 infra.

[0238] FIG. 21 provides representative data showing a reduction in vasodilation obtained by administering Ab10 following PACAP38 administration in a rabbit model, relative to an isotype antibody control, obtained following the protocol in Example 8 infra.

[0239] FIG. 22A provides epitope binning data for labeled Ab1 and unlabeled Ab10 obtained following the protocol in Example 9 infra.

[0240] FIG. 22B provides epitope binning data for unlabeled Ab1 and labeled Ab10 obtained following the protocol in Example 9 infra.

[0241] FIG. 23 provides representative data showing the in vivo effect of the administration of PACAP and an anti-PACAP antibody Ab1.H in a rodent photophobia model, which model detects the amount of time treated animals (mice) spend in the light per 5 minute intervals compared to appropriate control animals obtained following the protocol in Example 11 infra.

[0242] FIG. 24 provides representative data showing the in vivo effect of the administration of PACAP and anti-PACAP antibody Ab1.H in a rodent photophobia animal model, which detects the average amount of time treated animals (mice) spend in the light compared to appropriate control animals obtained following the protocol in Example 11 infra.

[0243] FIG. 25 provides representative data showing the in vivo effect of the administration of PACAP and an anti-PACAP antibody Ab10.H in a rodent photophobia model, which model detects the amount of time treated animals (mice) spend in the light compared to appropriate control animals obtained following the protocol in Example 11 infra

[0244] FIG. 26A presents results of surface plasmon resonance-based binding kinetics measurements for binding of anti-PACAP antibody Ab1 to PACAP alanine scanning mutants 5A, 6A, 8A, 10A, and 13A, along with controls including wild-type PACAP (labelled huPACAP (1-38))

(positive control) and 1× running buffer (negative control) obtained following the protocol in Example 12 infra.

[0245] FIG. **26**B presents results of surface plasmon resonance-based binding kinetics measurements for binding of anti-PACAP antibody Ab1 to PACAP alanine scanning mutants 1A-4A, 7A, 9A, 11A, 12A, and 14A-38A, along with controls including wild-type PACAP (labelled huPACAP (1-38)) (positive control) and 1× running buffer (negative control) obtained following the protocol in Example 12 infra.

[0246] FIG. **27**A presents results of surface plasmon resonance-based binding kinetics measurements for binding of anti-PACAP antibody Ab2 to PACAP alanine scanning mutants 5A, 6A, 8A, 9A, 10A, 13A, and 14A, along with controls including wild-type PACAP (labelled huPACAP (1-38)) (positive control) and 1× running buffer (negative control) obtained following the protocol in Example 12 infra.

[0247] FIG. **27**B presents results of surface plasmon resonance-based binding kinetics measurements for binding of anti-PACAP antibody Ab2 to PACAP alanine scanning mutants 1A-4A, 7A, 11A, 12A, and 15A-38A, along with controls including wild-type PACAP (labelled huPACAP (1-38)) (positive control) and 1× running buffer (negative control) obtained following the protocol in Example 12 infra.

[0248] FIG. **28**A presents results of surface plasmon resonance-based binding kinetics measurements for binding of anti-PACAP antibody Ab13 to PACAP alanine scanning mutants 6A, 8A, 9A, 10A, and 13A, along with controls including wild-type PACAP (labelled huPACAP (1-38)) (positive control) and 1× running buffer (negative control) obtained following the protocol in Example 12 infra.

[0249] FIG. **28**B presents results of binding kinetics measurements for binding of anti-PACAP antibody Ab13 to PACAP alanine scanning mutants 1A-5A, 7A, 11A, 12A, and 14A-38A, along with controls including wild-type PACAP (labelled huPACAP (1-38)) (positive control) and 1× running buffer (negative control) obtained following the protocol in Example 12 infra.

[0250] FIG. **29**A presents results of surface plasmon resonance-based binding kinetics measurements for binding of anti-PACAP antibody Ab14 to PACAP alanine scanning mutants 5A, 6A, 8A, 9A, 10A, and 13A, along with controls including wild-type PACAP (labelled huPACAP (1-38)) (positive control) and 1× running buffer (negative control) obtained following the protocol in Example 12 infra.

[0251] FIG. **29**B presents results of surface plasmon resonance-based binding kinetics measurements for binding of anti-PACAP antibody Ab14 to PACAP alanine scanning mutants 1A-4A, 7A, 11A, 12A, and 14A-38A, along with controls including wild-type PACAP (labelled huPACAP (1-38)) (positive control) and 1× running buffer (negative control) obtained following the protocol in Example 12 infra.

[0252] FIG. **30**A presents results of surface plasmon resonance-based binding kinetics measurements for binding of anti-PACAP antibody Ab15 to PACAP alanine scanning mutants 5A, 6A, 8A, 9A, 10A, 12A, 13A, and 14A, along with controls including wild-type PACAP (labelled huPACAP (1-38)) (positive control) and 1× running buffer (negative control) obtained following the protocol in Example 12 infra.

[0253] FIG. **30**B presents results of surface plasmon resonance-based binding kinetics measurements for binding of anti-PACAP antibody Ab15 to PACAP alanine scanning mutants 1A-4A, 7A, 11A, and 15A-38A, along with controls including wild-type PACAP (labelled huPACAP (1-38)) (positive control) and 1× running buffer (negative control) obtained following the protocol in Example 12 infra.

[0254] FIG. **31**A presents results of surface plasmon resonance-based binding kinetics measurements for binding of anti-PACAP antibody Ab16 to PACAP alanine scanning mutants 6A, 8A, 10A, and 13A, along with controls including wild-type PACAP (labelled huPACAP (1-38)) (positive control) and 1× running buffer (negative control) obtained following the protocol in Example 12 infra.

[0255] FIG. **31**B presents results of surface plasmon resonance-based binding kinetics measurements for binding of anti-PACAP antibody Ab16 to PACAP alanine scanning mutants 1A-5A, 7A, 9A, 11A, 12A, and 14A-38A, along with controls including wild-type PACAP (labelled huPACAP (1-38)) (positive control) and 1× running buffer (negative control) obtained following the protocol in Example 12 infra.

[0256] FIG. **32**A presents results of surface plasmon resonance-based binding kinetics measurements for binding of anti-PACAP antibody Ab17 to PACAP alanine scanning mutants 5A, 6A, 8A, 10A, and 13A, along with controls including wild-type PACAP (labelled huPACAP (1-38)) (positive control) and 1× running buffer (negative control) obtained following the protocol in Example 12 infra.

[0257] FIG. **32**B presents results of surface plasmon resonance-based binding kinetics measurements for binding of anti-PACAP antibody Ab17 to PACAP alanine scanning mutants 1A-4A, 7A, 9A, 11A, 12A, and 14A-38A, along with controls including wild-type PACAP (labelled huPACAP (1-38)) (positive control) and 1× running buffer (negative control) obtained following the protocol in Example 12 infra.

[0258] FIG. **33**A presents results of surface plasmon resonance-based binding kinetics measurements for binding of anti-PACAP antibody Ab18 to PACAP alanine scanning mutants 5A, 6A, 8A, 9A, 10A, 12A, and 13A, along with controls including wild-type PACAP (labelled huPACAP (1-38)) (positive control) and 1× running buffer (negative control) obtained following the protocol in Example 12 infra.

[0259] FIG. **33**B presents results of surface plasmon resonance-based binding kinetics measurements for binding of anti-PACAP antibody Ab18 to PACAP alanine scanning mutants 1A-4A, 7A, 11A, and 14A-38A, along with controls including wild-type PACAP (labelled huPACAP (1-38)) (positive control) and 1× running buffer (negative control) obtained following the protocol in Example 12 infra.

[0260] FIG. **34**A presents results of surface plasmon resonance-based binding kinetics measurements for binding of anti-PACAP antibody Ab19 to PACAP alanine scanning mutants 4A, 5A, 6A, 8A, 9A, 10A, 12A, 13A, 14A, and 17A, along with controls including wild-type PACAP (labelled huPACAP (1-38)) (positive control) and 1× running buffer (negative control) obtained following the protocol in Example 12 infra.

[0261] FIG. **34**B presents results of surface plasmon resonance-based binding kinetics measurements for binding of anti-PACAP antibody Ab19 to PACAP alanine scanning mutants 1A-3A, 7A, 11A, 15A, 16A, and 18V-38A, along

with controls including wild-type PACAP (labelled huPACAP (1-38)) (positive control) and 1× running buffer (negative control) obtained following the protocol in Example 12 infra.

[0262] FIG. **35**A presents results of surface plasmon resonance-based binding kinetics measurements for binding of anti-PACAP antibody Ab5 to PACAP alanine scanning mutants 3A, 4A, 5A, 6A, 7A, 10A, 13A, and 14A, along with controls including wild-type PACAP (labelled huPACAP (1-38)) (positive control) and 1× running buffer (negative control) obtained following the protocol in Example 12 infra.

[0263] FIG. **35**B presents results of surface plasmon resonance-based binding kinetics measurements for binding of anti-PACAP antibody Ab5 to PACAP alanine scanning mutants 1A, 2A, 8A, 9A, 11A, 12A, and 15A-38A, along with controls including wild-type PACAP (labelled huPACAP (1-38)) (positive control) and 1× running buffer (negative control) obtained following the protocol in Example 12 infra.

[0264] FIG. **36**A presents results of surface plasmon resonance-based binding kinetics measurements for binding of anti-PACAP antibody Ab7 to PACAP alanine scanning mutants 6A, 8A, 10A, 11A, 13A, 14A, and 18V, along with controls including wild-type PACAP (labelled huPACAP (1-38)) (positive control) and 1× running buffer (negative control) obtained following the protocol in Example 12 infra.

[0265] FIG. **36**B presents results of surface plasmon resonance-based binding kinetics measurements for binding of anti-PACAP antibody Ab7 to PACAP alanine scanning mutants 1A-5A, 7A, 9A, 12A, 15A-17A, and 19A-38A, along with controls including wild-type PACAP (labelled huPACAP (1-38)) (positive control) and 1× running buffer (negative control) obtained following the protocol in Example 12 infra.

[0266] FIG. **37**A presents results of surface plasmon resonance-based binding kinetics measurements for binding of anti-PACAP antibody Ab11 to PACAP alanine scanning mutants 6A, 8A, 10A, 11A, 13A, 14A, 18V, and 22A, along with controls including wild-type PACAP (labelled huPACAP (1-38)) (positive control) and 1× running buffer (negative control) obtained following the protocol in Example 12 infra.

[0267] FIG. **37**B presents results of surface plasmon resonance-based binding kinetics measurements for binding of anti-PACAP antibody Ab11 to PACAP alanine scanning mutants 1A-5A, 7A, 9A, 12A, 15A-17A, 19A-21A, and 23A-38A, along with controls including wild-type PACAP (labelled huPACAP (1-38)) (positive control) and 1× running buffer (negative control) obtained following the protocol in Example 12 infra.

[0268] FIG. **38**A presents results of surface plasmon resonance-based binding kinetics measurements for binding of anti-PACAP antibody Ab12 to PACAP alanine scanning mutants 6A, 8A, 10A, 11A, 13A, 14A, and 18V, along with controls including wild-type PACAP (labelled huPACAP (1-38)) (positive control) and 1× running buffer (negative control) obtained following the protocol in Example 12 infra.

[0269] FIG. **38**B presents results of surface plasmon resonance-based binding kinetics measurements for binding of anti-PACAP antibody Ab12 to PACAP alanine scanning mutants 1A-5A, 7A, 9A, 12A, 15A-17A, and 19A-38A, along with controls including wild-type PACAP (labelled huPACAP (1-38)) (positive control) and 1× running buffer (negative control) obtained following the protocol in Example 12 infra.

[0270] FIG. **39**A presents results of surface plasmon resonance-based binding kinetics measurements for binding of anti-PACAP antibody Ab4 to PACAP alanine scanning mutants 8A, 9A, 10A, 13A, 14A, 17A, and 18V, along with controls including wild-type PACAP (labelled huPACAP (1-38)) (positive control) and 1× running buffer (negative control) obtained following the protocol in Example 12 infra.

[0271] FIG. **39**B presents results of surface plasmon resonance-based binding kinetics measurements for binding of anti-PACAP antibody Ab4 to PACAP alanine scanning mutants 1A-7A, 11A, 12A, 15A, 16A, and 19A-38A, along with controls including wild-type PACAP (labelled huPACAP (1-38)) (positive control) and 1× running buffer (negative control) obtained following the protocol in Example 12 infra.

[0272] FIG. **40**A presents results of surface plasmon resonance-based binding kinetics measurements for binding of anti-PACAP antibody Ab3 to PACAP alanine scanning mutants 8A, 9A, 10A, 11A, 12A, 13A, 14A, 17A, and 21A, along with controls including wild-type PACAP (labelled huPACAP (1-38)) (positive control) and 1× running buffer (negative control) obtained following the protocol in Example 12 infra.

[0273] FIG. **40**B presents results of surface plasmon resonance-based binding kinetics measurements for binding of anti-PACAP antibody Ab3 to PACAP alanine scanning mutants 1A-7A, 15A, 16A, 18A-20A, and 22A-38A, along with controls including wild-type PACAP (labelled huPACAP (1-38)) (positive control) and 1× running buffer (negative control) obtained following the protocol in Example 12 infra.

[0274] FIG. **41**A presents results of surface plasmon resonance-based binding kinetics measurements for binding of anti-PACAP antibody Ab6 to PACAP alanine scanning mutants 5A, 6A, 9A, 10A, 12A, 13A, 14A, and 17A, along with controls including wild-type PACAP (labelled huPACAP (1-38)) (positive control) and 1× running buffer (negative control) obtained following the protocol in Example 12 infra.

[0275] FIG. **41**B presents results of surface plasmon resonance-based binding kinetics measurements for binding of anti-PACAP antibody Ab6 to PACAP alanine scanning mutants 1A-4A, 7A, 8A, 11A, 15A, 16A, and 18V-38A, along with controls including wild-type PACAP (labelled huPACAP (1-38)) (positive control) and 1× running buffer (negative control) obtained following the protocol in Example 12 infra.

[0276] FIG. **42**A presents results of surface plasmon resonance-based binding kinetics measurements for binding of anti-PACAP antibody Ab8 to PACAP alanine scanning mutants 7A, 10A, 13A, and 14A, along with controls including wild-type PACAP (labelled huPACAP (1-38)) (positive control) and 1× running buffer (negative control) obtained following the protocol in Example 12 infra.

[0277] FIG. **42**B presents results of surface plasmon resonance-based binding kinetics measurements for binding of anti-PACAP antibody Ab8 to PACAP alanine scanning mutants 1A-6A, 8A, 9A, 11A, 12A, and 15A-38A, along with controls including wild-type PACAP (labelled

huPACAP (1-38)) (positive control) and 1× running buffer (negative control) obtained following the protocol in Example 12 infra.

[0278] FIG. **43**A presents results of surface plasmon resonance-based binding kinetics measurements for binding of anti-PACAP antibody Ab9 to PACAP alanine scanning mutants 7A, 10A, 12A, 13A, 14A, and 17A, along with controls including wild-type PACAP (labelled huPACAP (1-38)) (positive control) and 1× running buffer (negative control) obtained following the protocol in Example 12 infra.

[0279] FIG. **43**B presents results of surface plasmon resonance-based binding kinetics measurements for binding of anti-PACAP antibody Ab9 to PACAP alanine scanning mutants 1A-6A, 8A, 9A, 11A, 15A, 16A, and 18V-38A, along with controls including wild-type PACAP (labelled huPACAP (1-38)) (positive control) and 1× running buffer (negative control) obtained following the protocol in Example 12 infra.

[0280] FIG. **44**A presents results of surface plasmon resonance-based binding kinetics measurements for binding of anti-PACAP antibody Ab22 to PACAP alanine scanning mutants 22A, 23A, 27A, 28A, and 31A, along with controls including wild-type PACAP (labelled huPACAP (1-38)) (positive control) and 1× running buffer (negative control) obtained following the protocol in Example 12 infra.

[0281] FIG. **44**B presents results of surface plasmon resonance-based binding kinetics measurements for binding of anti-PACAP antibody Ab22 to PACAP alanine scanning mutants 1A-21A, 24V-26A, 29A, and 30A, along with controls including wild-type PACAP (labelled huPACAP (1-38)) (positive control) and 1× running buffer (negative control) obtained following the protocol in Example 12 infra.

[0282] FIG. **45**A presents results of surface plasmon resonance-based binding kinetics measurements for binding of anti-PACAP antibody Ab23 to PACAP alanine scanning mutants 12A, 20A, 23A, 24V, 26A, 27A, and 28A, along with controls including wild-type PACAP (labelled huPACAP (1-38)) (positive control) and 1× running buffer (negative control) obtained following the protocol in Example 12 infra.

[0283] FIG. **45**B presents results of surface plasmon resonance-based binding kinetics measurements for binding of anti-PACAP antibody Ab23 to PACAP alanine scanning mutants 1A-11A, 13A-19A, 21A, 22A, 25V, and 29A-31A, along with controls including wild-type PACAP (labelled huPACAP (1-38)) (positive control) and 1× running buffer (negative control) obtained following the protocol in Example 12 infra.

[0284] FIG. **46**A presents a summary of the effects of PACAP alanine scanning mutants on antibody binding. In column 1 of FIG. **46**A, VIP residues are listed in the order of their spatial arrangement along the VIP primary sequence from amino acid residues 1-27. In column 2 of FIG. **46**A, PACAP residues are listed in the order of their spatial arrangement along the PACAP primary sequence from amino acid residues 1-27. Column 3 of 46A provides the number corresponding to each residue from 1-27 for both VIP and PACAP, as arranged spatially along their primary polypeptide sequences. In columns 4-12 of 46A, the antibodies Ab1, Ab2, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, and Ab19 tested during the alanine scanning studies, and the PACAP residues determined to contribute to PACAP/antibody binding (such as 5A, 6A, for example), are listed.

[0285] FIG. **46**B presents a summary of the effects of PACAP alanine scanning mutants on antibody binding. In column 1 of FIG. **46**B, VIP residue 28 is listed. In column 2 of FIG. **46**B, PACAP residues are listed in the order of their spatial arrangement along the PACAP primary sequence from amino acid residues 28-38. Column 3 of FIG. **46**B provides the number corresponding to residue 28 for VIP and each of residues 28-38 for PACAP, as arranged spatially along their primary polypeptide sequences. In columns 4-12 of FIG. **46**B, the antibodies Ab1, Ab2, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, and Ab19 tested during the alanine scanning studies, and the PACAP residues determined to contribute to PACAP/antibody binding (such as 5A, 6A, for example), are listed.

[0286] FIG. **47**A presents a summary of the effects of PACAP alanine scanning mutants on antibody binding. In column 1 of FIG. **47**A, VIP residues are listed in the order of their spatial arrangement along the VIP primary sequence from amino acid residues 1-27. In column 2 of 47A, PACAP residues are listed in the order of their spatial arrangement along the PACAP primary sequence from amino acid residues 1-27. Column 3 of FIG. **47**A provides the number corresponding to each residue from 1-27 for both VIP and PACAP, as arranged spatially along their primary polypeptide sequences. In columns 4-12 of FIG. **47**A, the antibodies Ab5, Ab7, Ab11, Ab12, Ab4, Ab3, Ab6, Ab8, Ab9, Ab22, and Ab23 tested during the alanine scanning studies, and the PACAP residues determined to contribute to PACAP/antibody binding (such as 5A, 6A, for example), are listed.

[0287] FIG. **47**B presents a summary of the effects of PACAP alanine scanning mutants on antibody binding. In column 1 of FIG. **47**B, VIP residue 28 is listed. In column 2 of FIG. **47**B, PACAP residues are listed in the order of their spatial arrangement along the PACAP primary sequence from amino acid residues 28-38. Column 3 of FIG. **47**B provides the number corresponding to residue 28 for VIP and for each of 28-38 for PACAP, as arranged spatially along their primary polypeptide sequences. In columns 4-12 of FIG. **47**B, the antibodies Ab5, Ab7, Ab11, Ab12, Ab4, Ab3, Ab6, Ab8, Ab9, Ab22, and Ab23 tested during the alanine scanning studies, and the PACAP residues determined to contribute to PACAP/antibody binding (such as 5A, 6A, for example), are listed.

DETAILED DESCRIPTION

Definitions

[0288] It is to be understood that this invention is not limited to the particular methodology, protocols, cell lines, animal species or genera, and reagents described, as such may vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only, and is not intended to limit the scope of the present invention, which will be limited only by the appended claims. As used herein the singular forms "a", "and", and "the" include plural referents unless the context clearly dictates otherwise. Thus, for example, reference to "a cell" includes a plurality of such cells and reference to "the protein" includes reference to one or more proteins and equivalents thereof known to those skilled in the art, and so forth. All technical and scientific terms used herein have the

same meaning as commonly understood to one of ordinary skill in the art to which this invention belongs unless clearly indicated otherwise.

[0289] Pituitary Adenylate Cyclase ActivatingPolypeptide (PACAP): As used herein, unless stated otherwise PACAP includes any mammalian form of PACAP, and in particular encompasses the following *Homo sapiens* PACAP27 and *Homo sapiens* PACAP38 amino acid sequences:

[0290] PACAP38:

[0291] HSDGIFTDSYSRYRKQMAVKKYLAAVLG-KRYKQRVKNK (SEQ ID NO: 1241), wherein the C-terminal lysine is amidated; but also any mutants, splice variants, isoforms, orthologs, homologs, and variants of this sequence.

[0292] PACAP27:

[0293] HSDGIFTDSYSRYRKQMAVKKYLAAVL (SEQ ID NO: 1242), wherein the C-terminal leucine is amidated; but also any mutants, splice variants, isoforms, orthologs, homologs, and variants of this sequence.

[0294] "Photophobia" herein refers to a symptom of abnormal intolerance to visual perception of light, sometimes additionally defined by abnormal or irrational fear of light, or by presence of actual physical photosensitivity of the eyes. In the present invention photophobia includes in particular light aversion associated with migraine, cluster headaches and other neurological causes of light aversive behavior that can trigger a migraine or cluster headache. Patients/subjects can develop photophobia as a result of several different medical conditions, related to the eye or the nervous system. Photophobia can be caused by an increased response to light starting at any step in the visual system such as: (i) too much light entering the eye, (ii) too much light can enter the eye if it is damaged, such as with corneal abrasion and retinal damage, or if a pupil(s) is unable to normally constrict (seen with damage to the oculomotor nerve), (iii) overstimulation of the photoreceptors in the retina, (iv) excessive electric impulses to the optic nerve, and (v) excessive response in the central nervous system.

[0295] "Effective treatment or prevention of photophobia" herein refers to inhibiting light aversive behavior or photophobia or inhibiting the onset of light aversive behavior or photophobia in a subject in need thereof, e.g., a subject having an active migraine attack or cluster headache or a subject prone to migraine or cluster headaches, or one of the other photophobia-associated disorders identified herein after administration of an effective amount of an anti-PACAP antibody or antigen binding fragment thereof according to the invention. The treatment may be effected as a monotherapy or in association with another active agent such as topiramate or dihydroergotamine by way of example.

[0296] The term "migraine" refers to a complex and disabling neurological disorder that may progress during four stages: prodrome, aura, headache, and postdrome. A migraine is defined by the International Headache Society as a headache that lasts for 4-72 hours and is characterized by at least two of the following: unilateral localization, pulsating quality, moderate to severe pain intensity; and aggravation by movement such as walking. In addition, the headache must be accompanied by at least one of the following: nausea and/or vomiting, photophobia, or phonophobia. A migraine may also be accompanied by aura, which typically precedes the deadline during the premonition or prodrome phase, and often results in visual changes, e.g., a scintillating scotoma that moves across the visual field. The prodrome may also be accompanied by other symptoms, e.g., fatigue, gastrointestinal issues, and mood changes. A migraineur is often incapacitated for extended periods of time. The postdrome is the final phase and occurs after the attack, during which time the migraineur may feel exhausted or mildly euphoric.

[0297] The term "headache" refers to pain in any region of the head. Headaches may occur on one or both sides of the head, be isolated to a certain location, radiate across the head from one point, or have a vise-like quality. A headache may be a sharp pain, throbbing sensation or dull ache. Headaches may appear gradually or suddenly, and they may last less than an hour or for several days.

[0298] The term "pain associated disease or condition" refers to any disease or condition defined, in whole or in part, by acute and/or chronic pain. Pain is generally defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage. Pain may be classified as neurogenic, neuropathic, inflammatory, or nociceptic.

[0299] The term "opioid analgesic" herein refers to all drugs, natural or synthetic, with morphine-like actions. The synthetic and semi-synthetic opioid analgesics are derivatives of five chemical classes of compound: phenanthrenes; phenylheptylamines; phenylpiperidines; morphinans; and benzomorphans, all of which are within the scope of the term. Exemplary opioid analgesics include codeine, dihydrocodeine, diacetylmorphine, hydrocodone, hydromorphone, levorphanol, oxymorphone, alfentanil, buprenorphine, butorphanol, fentanyl, sufentanil, meperidine, methadone, nalbuphine, propoxyphene, and pentazocine, or pharmaceutically acceptable salts thereof.

[0300] The term "NSAID" refers to a non-steroidal anti-inflammatory compound. NSAIDs are categorized by virtue of their ability to inhibit cyclooxygenase. Cyclooxygenase 1 and cyclooxygenase 2 are two major isoforms of cyclooxygenase and most standard NSAIDs are mixed inhibitors of the two isoforms. Most standard NSAIDs fall within one of the following five structural categories: (1) propionic acid derivatives, such as ibuprofen, naproxen, naprosyn, diclofenac, and ketoprofen; (2) acetic acid derivatives, such as tolmetin and sulindac; (3) fenamic acid derivatives, such as mefenamic acid and meclofenamic acid; (4) biphenylcarboxylic acid derivatives, such as diflunisal and flufenisal; and (5) oxicams, such as piroxim, sudoxicam, and isoxicam. Another class of NSAID has been described that selectively inhibit cyclooxygenase 2. COX-2 inhibitors have been described, e.g., in U.S. Pat. Nos. 5,616,601; 5,604,260; 5,593,994; 5,550,142; 5,536,752; 5,521,213; 5,475,995; 5,639,780; 5,604,253; 5,552,422; 5,510,368; 5,436,265; 5,409,944; and 5,130,311, all of which are hereby incorporated by reference. Certain exemplary COX-2 inhibitors include celecoxib (SC-58635), DUP-697, flosulide (CGP-28238), meloxicam, 6-methoxy-2 naphthylacetic acid (6-MNA), rofecoxib, MK-966, nabumetone (prodrug for 6-MNA), nimesulide, NS-398, SC-5766, SC-58215, T-614; or combinations thereof.

[0301] As used herein, "treatment" is an approach for obtaining beneficial or desired clinical results. For purposes of this invention, beneficial or desired clinical results include, but are not limited to, one or more of the following: improvement in any aspect of PACAP-related conditions such as migraine or headache. For example in the context of

headache or migraine treatment this includes lessening severity, alleviation of pain intensity, and other associated symptoms, reducing frequency of recurrence, increasing the quality of life of those suffering from the headache, and decreasing dose of other medications required to treat the headache. For migraine, other associated symptoms include, but are not limited to, nausea, vomiting, and sensitivity to light, sound, and/or movement. For cluster headache, other associated symptoms include, but are not limited to swelling under or around the eyes, excessive tears, red eye, rhinorrhea or nasal congestion, and red flushed face.

[0302] "Reducing incidence" or "prophylaxis" or "prevention" means any of reducing severity for a particular disease, condition, symptom, or disorder (the terms disease, condition, and disorder are used interchangeably throughout the application). Reduction in severity includes reducing drugs and/or therapies generally used for the condition by, for example, reducing the need for, amount of, and/or exposure to drugs or therapies. Reduction in severity also includes reducing the duration, and/or frequency of the particular condition, symptom, or disorder (including, for example, delaying or increasing time to next episodic attack in an individual).

[0303] "Ameliorating" headache or one or more symptoms of headache or migraine or other PACAP-related condition means a lessening or improvement of one or more symptoms of the condition, e.g., headache or migraine as compared to not administering an anti-PACAP antagonist antibody. "Ameliorating" also includes shortening or reduction in duration of a symptom.

[0304] As used herein, "controlling headache" or "controlling migraine" or "controlling" another PACAP-related condition refers to maintaining or reducing severity or duration of one or more symptoms of the condition, e.g., headache or migraine or frequency of headache or migraine attacks in an individual (as compared to the level before treatment). For example, the duration or severity of head pain, or frequency of attacks is reduced by at least about any of 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or 100% in the individual as compared to the level before treatment. The reduction in the duration or severity of head pain, or frequency of attacks can last for any length of time, e.g., 2 weeks, 4 weeks (1 month), 8 weeks (2 months), 16 weeks (3 months), 4 months, 5 months, 6 months, 9 months, 12 months, etc.

[0305] As used therein, "delaying" the development of a PACAP-related condition such as migraine or headache means to defer, hinder, slow, retard, stabilize, and/or postpone progression of the condition or disease. This delay can be of varying lengths of time, depending on the history of the condition or disease and/or individuals being treated. As is evident to one skilled in the art, a sufficient or significant delay can, in effect, encompass prevention, in that the individual does not develop headache (e.g., migraine). A method that "delays" development of the symptom is a method that reduces probability of developing the symptom in a given time frame and/or reduces extent of the symptoms in a given time frame, when compared to not using the method. Such comparisons are typically based on clinical studies, using a statistically significant number of subjects.

[0306] "Development" or "progression" of a PACAP-related condition such as migraine or headache means initial manifestations and/or ensuing progression of the disorder. Development of headache or migraine can be detectable and assessed using standard clinical techniques as well known in the art. However, development also refers to progression that may be undetectable. For purpose of this invention, development, or progression refers to the biological course of the symptoms. "Development" includes occurrence, recurrence, and onset. As used herein "onset" or "occurrence" of a condition such as headache or migraine includes initial onset and/or recurrence.

[0307] As used herein, an "effective dosage" or "effective amount" of drug, compound, or pharmaceutical composition is an amount sufficient to effect beneficial or desired results. For prophylactic use, beneficial or desired results include results such as eliminating or reducing the risk, lessening the severity, or delaying the outset of the disease, including biochemical, histological, and/or behavioral symptoms of the disease, its complications and intermediate pathological phenotypes presenting during development of the disease. For therapeutic use, beneficial or desired results include clinical results such as reducing pain intensity, duration, or frequency of headache attack, and decreasing one or more symptoms resulting from headache (biochemical, histological, and/or behavioral), including its complications and intermediate pathological phenotypes presenting during development of the disease, increasing the quality of life of those suffering from the disease, decreasing the dose of other medications required to treat the disease, enhancing effect of another medication, and/or delaying the progression of the disease of patients. An effective dosage can be administered in one or more administrations. For purposes of this invention, an effective dosage of drug, compound, or pharmaceutical composition is an amount sufficient to accomplish prophylactic or therapeutic treatment either directly or indirectly. As is understood in the clinical context, an effective dosage of a drug, compound, or pharmaceutical composition may or may not be achieved in conjunction with another drug, compound, or pharmaceutical composition. Thus, an "effective dosage" may be considered in the context of administering one or more therapeutic agents, and a single agent may be considered to be given in an effective amount if, in conjunction with one or more other agents, a desirable result may be or is achieved.

[0308] A "suitable host cell" or "host cell" generally includes any cell wherein the subject anti-PACAP antibodies and antigen binding fragments thereof can be produced recombinantly using techniques and materials readily available. For example, the anti-PACAP antibodies and antigen binding fragments thereof of the present invention can be produced in genetically engineered host cells according to conventional techniques. Suitable host cells are those cell types that can be transformed or transfected with exogenous DNA and grown in culture, and include bacteria, fungal cells (e.g., yeast), and cultured higher eukaryotic cells (including cultured cells of multicellular organisms), particularly cultured mammalian cells, e.g., human or non-human mammalian cells. In an exemplary embodiment these antibodies may be expressed in CHO cells. Techniques for manipulating cloned DNA molecules and introducing exogenous DNA into a variety of host cells are disclosed by Sambrook et al., *Molecular Cloning: A Laboratory Manual,* 2nd ed., Cold Spring Harbor, N.Y.: Cold Spring Harbor Laboratory Press (1989), and *Current Protocols in Molecular Biology*, Ausubel et al., editors, New York, N.Y.: Green and Wiley and Sons (1993).

[0309] In some exemplary embodiments the antibodies may be expressed in mating competent yeast, e.g., any haploid, diploid or tetraploid yeast that can be grown in culture. Yeast useful in fermentation expression methods may exist in a haploid, diploid, or other polyploid form. The cells of a given ploidy may, under appropriate conditions, proliferate for an indefinite number of generations in that form. Diploid cells can also sporulate to form haploid cells. Sequential mating can result in tetraploid strains through further mating or fusion of diploid strains. The present invention contemplates the use of haploid yeast, as well as diploid or other polyploid yeast cells produced, for example, by mating or spheroplast fusion. By way of example, such yeast may include members of the Saccharomycetaceae family, which includes the genera *Arxiozyma; Ascobotryozyma; Citeromyces; Debaryomyces; Dekkera; Eremothecium; Issatchenkia; Kazachstania; Kluyveromyces; Kodamaea; Lodderomyces; Pachysolen; Pichia; Saccharomyces; Saturnispora; Tetrapisispora; Torulaspora; Williopsis*; and *Zygosaccharomyces*. Other types of yeast potentially useful in the invention include *Yarrowia; Rhodosporidium; Candida; Hansenula; Filobasium; Sporidiobolus; Bullera; Leucosporidium* and *Filobasidella.*

[0310] In a preferred exemplary embodiment of the invention, the mating competent yeast used for antibody expression may comprise a member of the genus *Pichia*. In a further preferred exemplary embodiment of the invention, the mating competent yeast of the genus *Pichia* is one of the following species: *Pichia pastoris, Pichia methanolica*, and *Hansenula polymorpha* (*Pichia angusta*). In a particularly preferred embodiment of the invention, the mating competent yeast of the genus *Pichia* is the species *Pichia pastoris.*

[0311] A "selectable marker" herein refers to a gene or gene fragment that confers a growth phenotype (physical growth characteristic) on a cell receiving that gene as, for example through a transformation event. The selectable marker allows that cell to survive and grow in a selective growth medium under conditions in which cells that do not receive that selectable marker gene cannot grow. Selectable marker genes generally fall into several types, including positive selectable marker genes such as a gene that confers on a cell resistance to an antibiotic or other drug, temperature when two temperature sensitive ("ts") mutants are crossed or a is mutant is transformed; negative selectable marker genes such as a biosynthetic gene that confers on a cell the ability to grow in a medium without a specific nutrient needed by all cells that do not have that biosynthetic gene, or a mutagenized biosynthetic gene that confers on a cell inability to grow by cells that do not have the wild type gene; and the like. Suitable markers include but are not limited to: ZEO; G418; LYS3; MET1; MET3a; ADE1; ADE3; URA3; and the like.

[0312] An "expression vector" herein refers to DNA vectors containing elements that facilitate manipulation for the expression of a foreign protein within the target host cell, e.g., a bacterial, insect, yeast, plant, amphibian, reptile, avian, or mammalian cell, and most typically a yeast or mammalian cell, e.g., a CHO cell. Conveniently, manipulation of sequences and production of DNA for transformation is first performed in a bacterial host, e.g. *E. coli*, and usually vectors will include sequences to facilitate such manipulations, including a bacterial origin of replication and appropriate bacterial selection marker. Selection markers encode proteins necessary for the survival or growth of transformed host cells grown in a selective culture medium. Host cells not transformed with the vector containing the selection gene will not survive in the culture medium. Typical selection genes encode proteins that (a) confer resistance to antibiotics or other toxins, (b) complement auxotrophic deficiencies, or (c) supply critical nutrients not available from complex media. Exemplary vectors and methods for transformation of yeast are described, for example, in Burke, D., Dawson, D., & Stearns, T., *Methods in yeast genetics: a Cold Spring Harbor Laboratory course manual*, Plainview, N.Y.: Cold Spring Harbor Laboratory Press (2000). Expression vectors for use in the methods of the invention may include yeast or mammalian specific sequences, including a selectable auxotrophic or drug marker for identifying transformed host strains. A drug marker may further be used to amplify copy number of the vector in a yeast host cell.

[0313] The polypeptide coding sequence of interest is operably linked to transcriptional and translational regulatory sequences that provide for expression of the polypeptide in the desired host cells, e.g., yeast or mammalian cells. These vector components may include, but are not limited to, one or more of the following: an enhancer element, a promoter, and a transcription termination sequence. Sequences for the secretion of the polypeptide may also be included, e.g. a signal sequence, and the like. An origin of replication, e.g., a yeast origin of replication, is optional, as expression vectors are often integrated into the host cell genome. In one embodiment of the invention, the polypeptide of interest is operably linked, or fused, to sequences providing for optimized secretion of the polypeptide from yeast diploid cells.

[0314] Nucleic acids are "operably linked" when placed into a functional relationship with another nucleic acid sequence. For example, DNA for a signal sequence is operably linked to DNA for a polypeptide if it is expressed as a preprotein that participates in the secretion of the polypeptide; a promoter or enhancer is operably linked to a coding sequence if it affects the transcription of the sequence. Generally, "operably linked" means that the DNA sequences being linked are contiguous, and, in the case of a secretory leader, contiguous and in reading frame. However, enhancers do not have to be contiguous. Linking is accomplished by ligation at convenient restriction sites or alternatively via a PCR/recombination method familiar to those skilled in the art (GATEWAY® Technology; Invitrogen, Carlsbad Calif.). If such sites do not exist, the synthetic oligonucleotide adapters or linkers are used in accordance with conventional practice.

[0315] Promoters are untranslated sequences located upstream (5') to the start codon of a structural gene (generally within about 100 to 1000 bp) that control the transcription and translation of particular nucleic acid sequences to which they are operably linked. Such promoters fall into several classes: inducible, constitutive, and repressible promoters (that increase levels of transcription in response to absence of a repressor). Inducible promoters may initiate increased levels of transcription from DNA under their control in response to some change in culture conditions, e.g., the presence or absence of a nutrient or a change in temperature.

[0316] The promoter fragment may also serve as the site for homologous recombination and integration of the expression vector into the same site in the host cell, e.g., yeast cell, genome; alternatively, a selectable marker may be

used as the site for homologous recombination. *Pichia* transformation is described in Cregg et al., *Mol. Cell. Biol.,* 5:3376-3385 (1985). Suitable promoters for use in different eukaryotic and prokaryotic cells are well known and commercially available.

[0317] The polypeptides of interest may be produced recombinantly not only directly, but also as a fusion polypeptide with a heterologous polypeptide, e.g. a signal sequence or other polypeptide having a specific cleavage site at the N-terminus of the mature protein or polypeptide. In general, the signal sequence may be a component of the vector, or it may be a part of the polypeptide coding sequence that is inserted into the vector. The heterologous signal sequence selected preferably is one that is recognized and processed through one of the standard pathways available within the host cell, e.g., a mammalian cell, an insect cell, or a yeast cell. Additionally, these signal peptide sequences may be engineered to provide for enhanced secretion in expression systems. Secretion signals of interest also include mammalian and yeast signal sequences, which may be heterologous to the protein being secreted, or may be a native sequence for the protein being secreted. Signal sequences include pre-peptide sequences, and in some instances may include propeptide sequences. Many such signal sequences are known in the art, including the signal sequences found on immunoglobulin chains, e.g., K28 preprotoxin sequence, PHA-E, FACE, human MCP-1, human serum albumin signal sequences, human Ig heavy chain, human Ig light chain, and the like. For example, see Hashimoto et. al., *Protein Eng.,* 11(2):75 (1998); and Kobayashi et. al., *Therapeutic Apheresis,* 2(4):257 (1998)).

[0318] Transcription may be increased by inserting a transcriptional activator sequence into the vector. These activators are cis-acting elements of DNA, usually about from 10 to 300 bp, which act on a promoter to increase its transcription. Transcriptional enhancers are relatively orientation and position independent, having been found 5' and 3' to the transcription unit, within an intron, as well as within the coding sequence itself. The enhancer may be spliced into the expression vector at a position 5' or 3' to the coding sequence, but is preferably located at a site 5' from the promoter.

[0319] Expression vectors used in eukaryotic host cells may also contain sequences necessary for the termination of transcription and for stabilizing the mRNA. Such sequences are commonly available from 3' to the translation termination codon, in untranslated regions of eukaryotic or viral DNAs or cDNAs. These regions contain nucleotide segments transcribed as polyadenylated fragments in the untranslated portion of the mRNA.

[0320] Construction of suitable vectors containing one or more of the above-listed components employs standard ligation techniques or PCR/recombination methods. Isolated plasmids or DNA fragments are cleaved, tailored, and religated in the form desired to generate the plasmids required or via recombination methods. For analysis to confirm correct sequences in plasmids constructed, the ligation mixtures are used to transform host cells, and successful transformants selected by antibiotic resistance (e.g. ampicillin or Zeocin) where appropriate. Plasmids from the transformants are prepared, analyzed by restriction endonuclease digestion, and/or sequenced.

[0321] As an alternative to restriction and ligation of fragments, recombination methods based on specific attachment ("att") sites and recombination enzymes may be used to insert DNA sequences into a vector. Such methods are described, for example, by Landy, *Ann. Rev. Biochem.,* 58:913-949 (1989); and are known to those of skill in the art. Such methods utilize intermolecular DNA recombination that is mediated by a mixture of lambda and *E. coli*—encoded recombination proteins. Recombination occurs between att sites on the interacting DNA molecules. For a description of att sites see Weisberg and Landy, *Site-Specific Recombination in Phage Lambda*, in *Lambda II*, p. 211-250, Cold Spring Harbor, N.Y.: Cold Spring Harbor Press (1983). The DNA segments flanking the recombination sites are switched, such that after recombination, the att sites are hybrid sequences comprised of sequences donated by each parental vector. The recombination can occur between DNAs of any topology.

[0322] Att sites may be introduced into a sequence of interest by ligating the sequence of interest into an appropriate vector; generating a PCR product containing att B sites through the use of specific primers; generating a cDNA library cloned into an appropriate vector containing att sites; and the like.

[0323] Folding, as used herein, refers to the three-dimensional structure of polypeptides and proteins, where interactions between amino acid residues act to stabilize the structure. While non-covalent interactions are important in determining structure, usually the proteins of interest will have intra- and/or intermolecular covalent disulfide bonds formed by two cysteine residues. For naturally occurring proteins and polypeptides or derivatives and variants thereof, the proper folding is typically the arrangement that results in optimal biological activity, and can conveniently be monitored by assays for activity, e.g. ligand binding, enzymatic activity, etc.

[0324] In some instances, for example where the desired product is of synthetic origin, assays based on biological activity will be less meaningful. The proper folding of such molecules may be determined on the basis of physical properties, energetic considerations, modeling studies, and the like.

[0325] The expression host may be further modified by the introduction of sequences encoding one or more enzymes that enhance folding and disulfide bond formation, i.e. foldases, chaperonins, etc. Such sequences may be constitutively or inducibly expressed in the yeast host cell, using vectors, markers, etc. as known in the art. Preferably the sequences, including transcriptional regulatory elements sufficient for the desired pattern of expression, are stably integrated in the yeast genome through a targeted methodology.

[0326] For example, the eukaryotic protein disulfide isomerase ("PDI") is not only an efficient catalyst of protein cysteine oxidation and disulfide bond isomerization, but also exhibits chaperone activity. Co-expression of PDI can facilitate the production of active proteins having multiple disulfide bonds. Also of interest is the expression of immunoglobulin heavy chain binding protein ("BIP"); cyclophilin; and the like. In one embodiment of the invention, each of the haploid parental strains expresses a distinct folding enzyme, e.g. one strain may express BIP, and the other strain may express PDI or combinations thereof.

[0327] Cultured mammalian cells are also preferred exemplary hosts for production of the disclosed anti-PACAP antibodies and antigen binding fragments thereof. As men-

tioned CHO cells are particularly suitable for expression of antibodies. Many procedures are known in the art for manufacturing monoclonal antibodies in mammalian cells. (See, Galfre, G. and Milstein, C., *Methods Enzym.,* 73:3-46, 1981; Basalp et al., *Turk. J. Biol.,* 24:189-196, 2000; Wurm, F. M., *Nat. Biotechnol.,* 22:1393-1398, 2004; and Li et al., *mAbs,* 2(5):466-477, 2010). As mentioned in further detail infra, common host cell lines employed in mammalian monoclonal antibody manufacturing schemes include, but are not limited to, human embryonic retinoblast cell line PER.C6® (Crucell N.V., Leiden, The Netherlands), NS0 murine myeloma cells (Medical Research Council, London, UK), CV1 monkey kidney cell line, 293 human embryonic kidney cell line, BHK baby hamster kidney cell line, VERO African green monkey kidney cell line, human cervical carcinoma cell line HELA, MDCK canine kidney cells, BRL buffalo rat liver cells, W138 human lung cells, HepG2 human liver cells, MMT mouse mammary tumor cells, TRI cells, MRC5 cells, Fs4 cells, myeloma or lymphoma cells, or Chinese Hamster (*Cricetulus griseus*) Ovary (CHO) cells, and the like. Many different subclones or sub-cell lines of CHO cells known in the art that are useful and optimized for production of recombinant monoclonal antibodies, such as the DP12 (CHO K1 dhfr-) cell line, NS0 cells are a non-Ig secreting, non-light chain-synthesizing subclone of NS-1 cells that are resistant to azaguanine. Other Chinese Hamster and CHO cells are commercially available (from ATCC, etc.), including CHO-DXB11 (CHO-DUKX), CHO-pro3, CHO-DG44, CHO 1-15, CHO DP-12, Lec2, M1WT3, Lec8, pgsA-745, and the like, all of which are genetically altered to optimize the cell line for various parameters. Monoclonal antibodies are commonly manufactured using a batch fed method whereby the monoclonal antibody chains are expressed in a mammalian cell line and secreted into the tissue culture medium in a bioreactor. Medium (or feed) is continuously supplied to the bioreactor to maximize recombinant protein expression. Recombinant monoclonal antibody is then purified from the collected media. In some circumstances, additional steps are needed to reassemble the antibodies through reduction of disulfide bonds, etc. Such production methods can be scaled to be as large as 10,000 L in a single batch or more. It is now routine to obtain as much as 20 pg/cell/day through the use of such cell lines and methodologies, providing titers as high as 10 g/L or more, amounting to 15 to 100 kg from bioreactors of 10 kL to 25 kL. (Li et al., 2010). Various details of this production methodology, including cloning of the polynucleotides encoding the antibodies into expression vectors, transfecting cells with these expression vectors, selecting for transfected cells, and expressing and purifying the recombinant monoclonal antibodies from these cells are provided below.

[0328] For recombinant production of an anti-PACAP antibody or antigen binding fragment in mammalian cells, nucleic acids encoding the antibody or fragment thereof are generally inserted into a replicable vector for further cloning (amplification of the DNA) or for expression. DNA encoding the antibody is readily isolated or synthesized using conventional procedures (e.g., by using oligonucleotide probes that are capable of binding specifically to DNAs encoding the heavy and light chains of the antibody). The vector components generally include, but are not limited to, one or more of the following: a signal sequence, an origin of replication, one or more marker genes, an enhancer element, a promoter, and a transcription termination sequence. Selection of promoters, terminators, selectable markers, vectors, and other elements is a matter of routine design within the level of ordinary skill in the art. Many such elements are known in the art and are available through commercial suppliers.

[0329] The antibodies of this invention may be produced recombinantly not only directly, but also as a fusion polypeptide with a heterologous polypeptide, which is preferably a signal sequence or other polypeptide having a specific cleavage site at the N-terminus of the mature protein or polypeptide. The homologous or heterologous signal sequence selected preferably is one that is recognized and processed (i.e., cleaved by a signal peptidase) by the host cell. In mammalian cell expression, mammalian signal sequences as well as viral secretory leaders, for example, the herpes simplex gD signal, are available.

[0330] Such expression vectors and cloning vectors will generally contain a nucleic acid sequence that enables the vector to replicate in one or more selected host cells. Typically, in cloning vectors this sequence is one that enables the vector to replicate independently of the host chromosomal DNA, and includes origins of replication or autonomously replicating sequences. Such sequences are well known for a variety of bacteria, yeast, and viruses, e.g., the origin of replication from the plasmid pBR322 is suitable for most Gram-negative bacteria, the 2mu plasmid origin is suitable for yeast, and various viral origins (Simian Virus 40 ("SV40"), polyoma, adenovirus, vesicular stomatitis virus ("VSV"), or bovine papillomavirus ("BPV") are useful for cloning vectors in mammalian cells. Generally, the origin of replication component is not needed for mammalian expression vectors (the SV40 origin may typically be used only because it contains the early promoter).

[0331] These vectors will also typically contain a selection gene, also termed a selectable marker. Typical selection genes encode proteins that (a) confer resistance to antibiotics or other toxins, e.g., ampicillin, neomycin, methotrexate, or tetracycline, (b) complement auxotrophic deficiencies, or (c) supply critical nutrients not available from complex media, e.g., the gene encoding D-alanine racemase for Bacilli.

[0332] One example of a selection scheme utilizes a drug to arrest growth of a host cell. Drug selection is generally used to select for cultured mammalian cells into which foreign DNA has been inserted. Such cells are commonly referred to as "transfectants". Cells that have been cultured in the presence of the selective agent and are able to pass the gene of interest to their progeny are referred to as "stable transfectants." Examples of such dominant selection use the drugs neomycin, mycophenolic acid, and hygromycin. An exemplary selectable marker is a gene encoding resistance to the antibiotic neomycin. Selection is carried out in the presence of a neomycin-type drug, such as G-418 or the like. Those cells that are successfully transformed with a heterologous gene produce a protein conferring drug resistance and thus survive the selection regimen.

[0333] Selection systems can also be used to increase the expression level of the gene of interest, a process referred to as "amplification." Amplification of transfectants typically occurs by culturing the cells in the presence of a low level of the selective agent and then increasing the amount of selective agent to select for cells that produce high levels of the products of the introduced genes. Exemplary suitable selectable markers for mammalian cells are those that enable the identification of cells competent to take up the antibody

nucleic acid, such as dihydrofolate reductase ("DHFR"), thymidine kinase, metallothionein-I and -II, preferably primate metallothionein genes, adenosine deaminase, ornithine decarboxylase, etc.

[0334] For example, an amplifiable selectable marker for mammalian cells is dihydrofolate reductase, which confers resistance to methotrexate. Other drug resistance genes (e.g. hygromycin resistance, multi-drug resistance, puromycin acetyltransferase) can also be used. Cells transformed with the DHFR selection gene are first identified by culturing all of the transformants in a culture medium that contains methotrexate ("MTX"), a competitive antagonist of DHFR. An appropriate host cell when wild-type DHFR is employed is the Chinese hamster ovary ("CHO") cell line deficient in DHFR activity.

[0335] Alternatively, host cells (particularly wild-type hosts that contain endogenous DHFR) transformed or co-transformed with DNA sequences encoding antibody, wild-type DHFR protein, and another selectable marker such as aminoglycoside 3'-phosphotransferase ("APH") can be selected by cell growth in medium containing a selection agent for the selectable marker such as an aminoglycosidic antibiotic, e.g., kanamycin, neomycin, or G-418. See U.S. Pat. No. 4,965,199.

[0336] These vectors may comprise an enhancer sequence that facilitates transcription of a DNA encoding the antibody. Many enhancer sequences are known from mammalian genes (for example, globin, elastase, albumin, alpha-feto-protein, and insulin). A frequently used enhancer is one derived from a eukaryotic cell virus. Examples thereof include the SV40 enhancer on the late side of the replication origin (bp 100-270), the cytomegalovirus early promoter enhancer, the polyoma enhancer on the late side of the replication origin, and adenovirus enhancers (See, Yaniv, *Nature,* 297:17-18, 1982, on enhancing elements for activation of eukaryotic promoters). The enhancer may be spliced into the vector at a position 5' or 3' to the antibody-encoding sequence, but is preferably located at a site 5' from the promoter.

[0337] Expression and cloning vectors will also generally comprise a promoter that is recognized by the host organism and is operably linked to the antibody nucleic acid. Promoter sequences are known for eukaryotes. Virtually all eukaryotic genes have an AT-rich region located approximately 25 to 30 bases upstream from the site where transcription is initiated. Another sequence found 70 to 80 bases upstream from the start of transcription of many genes is a CNCAAT region where N may be any nucleotide. At the 3' end of most eukaryotic genes is an AATAAA sequence that may be the signal for addition of the poly A tail to the 3' end of the coding sequence. All of these sequences are suitably inserted into eukaryotic expression vectors.

[0338] Antibody transcription from vectors in mammalian host cells is controlled, for example, by promoters obtained from the genomes of viruses such as polyoma virus, fowlpox virus, adenovirus (such as Adenovirus 2), BPV, avian sarcoma virus, cytomegalovirus, a retrovirus, hepatitis-B virus, and most preferably SV40, from heterologous mammalian promoters, e.g., the actin promoter or an immunoglobulin promoter, from heat-shock promoters, provided such promoters are compatible with the host cell systems.

[0339] The early and late promoters of the SV40 virus are conveniently obtained as an SV40 restriction fragment that also contains the SV40 viral origin of replication. The immediate early promoter of the human cytomegalovirus is conveniently obtained as a HindIII E restriction fragment. A system for expressing DNA in mammalian hosts using the BPV as a vector is disclosed in U.S. Pat. No. 4,419,446. A modification of this system is described in U.S. Pat. No. 4,601,978. See also Reyes et al., *Nature,* 297:598-601 (1982) on expression of human beta-interferon cDNA in mouse cells under the control of a thymidine kinase promoter from herpes simplex virus. Alternatively, the rous sarcoma virus long terminal repeat can be used as the promoter.

[0340] Strong transcription promoters can be used, such as promoters from SV40, cytomegalovirus, or myeloproliferative sarcoma virus. See, e.g., U.S. Pat. No. 4,956,288 and U.S. Patent Publication No. 20030103986. Other suitable promoters include those from metallothionein genes (U.S. Pat. Nos. 4,579,821 and 4,601,978) and the adenovirus major late promoter. Expression vectors for use in mammalian cells include pZP-1, pZP-9, and pZMP21, which have been deposited with the American Type Culture Collection, 10801 University Blvd., Manassas, Va. USA under accession numbers 98669, 98668, and PTA-5266, respectively, and derivatives of these vectors.

[0341] Expression vectors used in eukaryotic host cells (yeast, fungus, insect, plant, animal, human, or a nucleated cell from other multicellular organism) will also generally contain sequences necessary for the termination of transcription and for stabilizing the mRNA. Such sequences are commonly available from the 5' and, occasionally 3', untranslated regions of eukaryotic or viral DNAs or cDNAs. These regions contain nucleotide segments transcribed as polyadenylated fragments in the untranslated portion of the mRNA encoding the antibody. One useful transcription termination component is the bovine growth hormone polyadenylation region. See WO 94/11026 and the expression vector disclosed therein.

[0342] Suitable host cells for cloning or expressing the subject antibodies include prokaryote, yeast, or higher eukaryote cells described above. However, interest has been greatest in vertebrate cells, and propagation of vertebrate cells in culture has become a routine procedure. Examples of useful mammalian host cell lines are monkey kidney CV1 line transformed by SV40 (COS-1 (ATCC No. CRL 1650); and COS-7, ATCC CRL 1651); human embryonic kidney line (293 or 293 cells subcloned for growth in suspension culture, (ATCC No. CRL 1573; Graham et al., *J. Gen. Virol.,* 36:59-72 (1977)); baby hamster kidney cells (BHK, ATCC CCL 10, ATCC No. CRL 1632; BHK 570, ATCC No. CRL 10314); CHO cells (CHO-K1, ATCC No. CCL 61; CHO-DG44, Urlaub et al., *Proc. Natl. Acad. Sci. USA,* 77:4216-4220 (1980)); mouse sertoli cells (TM4, *Mather, Biol. Reprod.,* 23:243-251 (1980)); monkey kidney cells (CV1 ATCC CCL 70); African green monkey kidney cells (VERO-76, ATCC CRL-1587); human cervical carcinoma cells (HELA, ATCC CCL 2); canine kidney cells (MDCK, ATCC CCL 34); buffalo rat liver cells (BRL 3A, ATCC CRL 1442); human lung cells (W138, ATCC CCL 75); human liver cells (Hep G2, HB 8065); mouse mammary tumor (MMT 060562, ATCC CCL51); TRI cells (Mather et al., *Annals N.Y. Acad. Sci.,* 383:44-68 (1982)); MRC 5 cells; FS4 cells; and a human hepatoma line (Hep G2). Additional suitable cell lines are known in the art and available from public depositories such as the American Type Culture Collection, Manassas, Va.

[0343] Host cells are transformed with the above-described expression or cloning vectors for antibody production and cultured in conventional nutrient media modified as appropriate for inducing promoters, selecting transformants, or amplifying the genes encoding the desired sequences as discussed supra.

[0344] The mammalian host cells used to produce the antibody of this invention may be cultured in a variety of media. Commercially available media such as Ham's F10 (Sigma-Aldrich Corporation, St. Louis, Mo.), Minimal Essential Medium (("MEM" (Sigma-Aldrich Corporation, St. Louis, Mo.), Roswell Park Memorial Institute-1640 medium ("RPMI-1640", Sigma-Aldrich Corporation, St. Louis, Mo.), and Dulbecco's Modified Eagle's Medium (("DMEM" Sigma-Aldrich Corporation, St. Louis, Mo.) are suitable for culturing the host cells. In addition, any of the media described in Ham et al., Meth. Enz., 58:44 (1979), Barnes et al., Anal. Biochem., 102:255 (1980), U.S. Pat. Nos. 4,767,704; 4,657,866; 4,927,762; 4,560,655; or 5,122,469; WO 90/03430; WO 87/00195; or U.S. Patent Reexam No. 30,985 can be used as culture media for the host cells. Any of these media may be supplemented as necessary with hormones and/or other growth factors (such as insulin, transferrin, or epidermal growth factor), salts (such as sodium chloride, calcium, magnesium, and phosphate), buffers (such as HEPES), nucleotides (such as adenosine and thymidine), antibiotics (such as Gentamycin drug), trace elements (defined as inorganic compounds usually present at final concentrations in the micromolar range), and glucose or an equivalent energy source. Any other necessary supplements may also be included at appropriate concentrations that would be known to those skilled in the art. The culture conditions, such as temperature, pH, and the like, are those previously used with the host cell selected for expression, and will be apparent to the ordinarily skilled artisan. Methods of development and optimization of media and culture conditions are known in the art (See, Gronemeyer et al., Bioengineering, 1(4):188-212, 2014).

[0345] After culture conditions are optimized and a preferred cell line clone is selected, these cells are cultured (either adherent cells or suspension cultures) most typically in a batch-fed process in a bioreactor (many models are commercially available) that involves continuously feeding the cell culture with medium and feed, optimized for the particular cell line chosen and selected for this purpose. (See, Butler, M., *Appl. Microbiol. Biotechnol.,* 68:283-291, 2005; and Kelley, B., *mAb,* 1(5):443-452, 2009). Perfusion systems are also available in which media and feed are continuously supplied to the culture while the same volume of media is being withdrawn from the bioreactor. (Wurm, 2004). Synthetic media, also commercially available, are available for growing cells in a batch-fed culture, avoiding the possibility of contamination from outside sources, such as with the use of animal components, such as bovine serum albumin, etc. However, animal-component-free hydrolysates are commercially available to help boost cell density, culture viability and productivity. (Li et al., 2010). Many studies have been performed in an effort to optimize cell culture media, including careful attention to head space available in roller bottles, redox potentials during growth and expression phases, presence of reducing agents to maintain disulfide bonds during production, etc. (See, for instance, Hutterer et al., *mAbs,* 5(4):608-613, 2013; and Mullan et al., *BMC Proceed.,* 5(Suppl 8):P110, 2011). Various methodologies have been developed to address the possibility of harmful oxidation during recombinant monoclonal antibody production. (See, for example, U.S. Pat. No. 8,574,869). Cultured cells may be grown by feeding nutrients continuously or as separately administered amounts. Often various process parameters such as cell concentration, pH, temperature, CO_2, dO_2, osmolality, amount of metabolites such as glucose, lactate, glutamine and glutamate, and the like, are monitored by the use of probes during the cell growth either on-line by direct connection to calibrated analyzers or off-line by intervention of operators. The culturing step also typically involves ensuring that the cells growing in culture maintain the transfected recombinant genes by any means known in the art for cell selection.

[0346] Following fermentation, i.e., upon reaching maximum cell growth and recombinant protein expression, the culturing step is typically followed by a harvesting step, whereby the cells are separated from the medium and a harvested cell culture media is thereby obtained. (See, Liu et al., *mAbs,* 2(5):480-499, 2010). Typically various purification steps, involving column chromatography and the like, follow culturing to separate the recombinant monoclonal antibody from cell components and cell culture media components. The exact purification steps needed for this phase of the production of recombinant monoclonal antibodies depends on the site of expression of the proteins, i.e., in the cytosol of the cells themselves, or the more commonly preferred route of protein excreted into the cell culture medium. Various cell components may be separated using techniques known in the art such as differential centrifugation techniques, gravity-based cell settling, and/or size exclusion chromatograph/filtration techniques that can include tangential flow micro-filtration or depth filtration. (See, Pollock et al., *Biotechnol. Bioeng.,* 110:206-219, 2013, and Liu et al., 2010). Centrifugation of cell components may be achieved on a large scale by use of continuous disk stack centrifuges followed by clarification using depth and membrane filters. (See, Kelley, 2009). Most often, after clarification, the recombinant protein is further purified by Protein A chromatography due to the high affinity of Protein A for the Fc domain of antibodies, and typically occurs using a low pH/acidification elution step (typically the acidification step is combined with a precautionary virus inactivation step). Flocculation and/or precipitation steps using acidic or cationic polyelectrolytes may also be employed to separate animal cells in suspension cultures from soluble proteins. (Liu et al., 2010). Lastly, anion- and cation-exchange chromatography, hydrophobic interaction chromatograph ("HIC"), hydrophobic charge induction chromatograph (HCIC), hydroxyapatite chromatography using ceramic hydroxyapatite ($Ca_5(PO_4)_3OH)_2$, and combinations of these techniques are typically used to polish the solution of recombinant monoclonal antibody. Final formulation and concentration of the desired monoclonal antibody may be achieved by use of ultracentrifugation techniques. Purification yields are typically 70 to 80%. (Kelley, 2009).

[0347] The terms "desired protein" or "desired antibody" are used interchangeably and refer generally to a parent antibody specific to a target, i.e., PACAP or a chimeric or humanized antibody or a binding portion thereof derived therefrom as described herein. The term "antibody" is intended to include any polypeptide chain-containing molecular structure with a specific shape that fits to and recognizes an epitope, where one or more non-covalent

binding interactions stabilize the complex between the molecular structure and the epitope. The archetypal antibody molecule is the immunoglobulin, and all types of immunoglobulins, IgG, IgM, IgA, IgE, IgD, etc., from all sources, e.g. human, rodent, rabbit, cow, sheep, pig, dog, other mammals, chicken, other avians, etc., are considered to be "antibodies." A preferred source for producing antibodies useful as starting material according to the invention is rabbits. Examples thereof include chimeric antibodies, human antibodies and other non-human mammalian antibodies, humanized antibodies, single chain antibodies (such as scFvs), camelbodies, nanobodies, IgNAR (single-chain antibodies which may be derived from sharks, for example), small-modular immunopharmaceuticals ("SMIPs"), and antibody fragments such as Fabs, Fab', $F(ab')_2$, and the like (See Streltsov et al., *Protein Sci.,* 14(11):2901-9 (2005); Greenberg et al., *Nature,* 374(6518):168-73 (1995); Nuttall et al., *Mol. Immunol.,* 38(4):313-26 (2001); Hamers-Casterman et al., *Nature,* 363(6428):446-8 (1993); Gill et al., *Curr. Opin. Biotechnol.*, (6):653-8 (2006)).

[0348] For example, antibodies or antigen binding fragments thereof may be produced by genetic engineering. In this technique, as with other methods, antibody-producing cells are sensitized to the desired antigen or immunogen. The messenger RNA isolated from antibody producing cells is used as a template to make cDNA using PCR amplification. A library of vectors, each containing one heavy chain gene and one light chain gene retaining the initial antigen specificity, is produced by insertion of appropriate sections of the amplified immunoglobulin cDNA into the expression vectors. A combinatorial library is constructed by combining the heavy chain gene library with the light chain gene library. This results in a library of clones that co-express a heavy and light chain (resembling the Fab fragment or antigen binding fragment of an antibody molecule). The vectors that carry these genes are co-transfected into a host cell. When antibody gene synthesis is induced in the transfected host, the heavy and light chain proteins self-assemble to produce active antibodies that can be detected by screening with the antigen or immunogen.

[0349] Antibody coding sequences of interest include those encoded by native sequences, as well as nucleic acids that, by virtue of the degeneracy of the genetic code, are not identical in sequence to the disclosed nucleic acids, and variants thereof. Variant polypeptides can include amino acid ("aa") substitutions, additions, or deletions. The amino acid substitutions can be conservative amino acid substitutions or substitutions to eliminate non-essential amino acids, such as to alter a glycosylation site, or to minimize misfolding by substitution or deletion of one or more cysteine residues that are not necessary for function. Variants can be designed so as to retain or have enhanced biological activity of a particular region of the protein (e.g., a functional domain, catalytic amino acid residues, etc.). Variants also include fragments of the polypeptides disclosed herein, particularly biologically active fragments and/or fragments corresponding to functional domains. Techniques for in vitro mutagenesis of cloned genes are known. Also included in the subject invention are polypeptides that have been modified using ordinary molecular biological techniques so as to improve their resistance to proteolytic degradation or to optimize solubility properties or to render them more suitable as a therapeutic agent.

[0350] Chimeric antibodies may be made by recombinant means by combining the V_L and V_H regions, obtained from antibody producing cells of one species with the constant light and heavy chain regions from another. Typically chimeric antibodies utilize rodent or rabbit variable regions and human constant regions, in order to produce an antibody with predominantly human domains. The production of such chimeric antibodies is well known in the art, and may be achieved by standard means (as described, e.g., in U.S. Pat. No. 5,624,659, incorporated herein by reference in its entirety). It is further contemplated that the human constant regions of chimeric antibodies of the invention may be selected from IgG1, IgG2, IgG3, and IgG4 constant regions.

[0351] Humanized antibodies are engineered to contain even more human-like immunoglobulin domains, and incorporate only the complementarity determining regions of the animal-derived antibody. This is accomplished by carefully examining the sequence of the hyper-variable loops of the variable regions of the monoclonal antibody and fitting them to the structure of the human antibody chains. Although facially complex, the process is straightforward in practice. See, e.g., U.S. Pat. No. 6,187,287, incorporated fully herein by reference.

[0352] In addition to entire immunoglobulins (or their recombinant counterparts), immunoglobulin fragments comprising the epitope binding site (e.g., Fab', $F(ab')_2$, or other fragments) may be synthesized. "Fragment" or minimal immunoglobulins may be designed utilizing recombinant immunoglobulin techniques. For instance "Fv" immunoglobulins for use in the present invention may be produced by synthesizing a fused variable light chain region and a variable heavy chain region. Combinations of antibodies are also of interest, e.g. diabodies, which comprise two distinct Fv specificities. In another embodiment of the invention, small molecule immunopharmaceuticals ("SMIPs"), camelbodies, nanobodies, and IgNAR are encompassed by immunoglobulin fragments.

[0353] Immunoglobulins and fragments thereof may be modified post-translationally, e.g. to add effector moieties such as chemical linkers, detectable moieties, such as fluorescent dyes, enzymes, toxins, substrates, bioluminescent materials, radioactive materials, chemiluminescent moieties, and the like, or specific binding moieties, such as streptavidin, avidin, or biotin, and the like may be utilized in the methods and compositions of the present invention. Examples of additional effector molecules are provided infra.

[0354] A polynucleotide sequence "corresponds" to a polypeptide sequence if translation of the polynucleotide sequence in accordance with the genetic code yields the polypeptide sequence (i.e., the polynucleotide sequence "encodes" the polypeptide sequence), one polynucleotide sequence "corresponds" to another polynucleotide sequence if the two sequences encode the same polypeptide sequence.

[0355] A "heterologous" region or domain of a DNA construct is an identifiable segment of DNA within a larger DNA molecule that is not found in association with the larger molecule in nature. Thus, when the heterologous region encodes a mammalian gene, the DNA flanking the gene usually does not flank the mammalian genomic DNA in the genome of the source organism. Another example of a heterologous region is a construct where the coding sequence itself is not found in nature (e.g., a cDNA where the genomic coding sequence contains introns or synthetic

sequences having codons different than the native gene). Allelic variations or naturally-occurring mutational events do not give rise to a heterologous region of DNA as defined herein.

[0356] A "coding sequence" is an in-frame sequence of codons that correspond to or encode a protein or peptide sequence. Two coding sequences correspond to each other if the sequences or their complementary sequences encode the same amino acid sequences. A coding sequence in association with appropriate regulatory sequences may be transcribed and translated into a polypeptide. A polyadenylation signal and transcription termination sequence will usually be located 3' to the coding sequence. A "promoter sequence" is a DNA regulatory region capable of initiating transcription of a downstream (3' direction) coding sequence, and typically contain additional sites for binding of regulatory molecules, e.g., transcription factors, that affect the transcription of the coding sequence. A coding sequence is "under the control" of the promoter sequence or "operatively linked" to the promoter when RNA polymerase binds the promoter sequence in a cell and transcribes the coding sequence into mRNA, which is then in turn translated into the protein encoded by the coding sequence.

[0357] The general structure of antibodies in vertebrates now is well understood. See Edelman, G. M., *Ann. N.Y. Acad. Sci.,* 190:5 (1971). Antibodies consist of two identical light polypeptide chains of molecular weight approximately 23,000 daltons (the "light chain"), and two identical heavy chains of molecular weight 53,000-70,000 (the "heavy chain"). The four chains are joined by disulfide bonds in a "Y" configuration wherein the light chains bracket the heavy chains starting at the mouth of the "Y" configuration. The "branch" portion of the "Y" configuration is designated the F_{ab} region; the stem portion of the "Y" configuration is designated the F_C region. The amino acid sequence orientation runs from the N-terminal end at the top of the "Y" configuration to the C-terminal end at the bottom of each chain. The N-terminal end possesses the variable region having specificity for the antigen that elicited it, and is approximately 100 amino acids in length, there being slight variations between light and heavy chain and from antibody to antibody.

[0358] The variable region is linked in each chain to a constant region that extends the remaining length of the chain and that within a particular class of antibody does not vary with the specificity of the antibody (i.e., the antigen eliciting it). There are five known major classes of constant regions that determine the class of the immunoglobulin molecule (IgG, IgM, IgA, IgD, and IgE corresponding to γ, μ, α, δ, and ϵ (gamma, mu, alpha, delta, or epsilon) heavy chain constant regions). The constant region or class determines subsequent effector function of the antibody, including activation of complement (see Kabat, E. A., *Structural Concepts in Immunology and Immunochemistry,* 2nd Ed., p. 413-436, New York, N.Y.: Holt, Rinehart, Winston (1976)), and other cellular responses (see Andrews et al., *Clinical Immunology*, pp. 1-18, W. B. Sanders, Philadelphia, Pa. (1980); Kohl et al., *Immunology,* 48:187 (1983)); while the variable region determines the antigen with which it will react. Light chains are classified as either κ (kappa) or λ (lambda). Each heavy chain class can be prepared with either kappa or lambda light chain. The light and heavy chains are covalently bonded to each other, and the "tail" portions of the two heavy chains are bonded to each other by covalent disulfide linkages when the immunoglobulins are generated either by hybridomas or by B-cells.

[0359] The expression "variable region" or "VR" refers to the domains within each pair of light and heavy chains in an antibody that are involved directly in binding the antibody to the antigen. Each heavy chain has at one end a variable domain (V_H) followed by a number of constant domains. Each light chain has a variable domain (V_L) at one end and a constant domain at its other end; the constant domain of the light chain is aligned with the first constant domain of the heavy chain, and the light chain variable domain is aligned with the variable domain of the heavy chain.

[0360] The expressions "complementarity determining region," "hypervariable region," or "CDR" refer to one or more of the hyper-variable or complementarity determining regions ("CDRs") found in the variable regions of light or heavy chains of an antibody (See Kabat et al., *Sequences of Proteins of Immunological Interest,* 4^{th} ed., Bethesda, Md.: U.S. Dept. of Health and Human Services, Public Health Service, National Institutes of Health (1987)). These expressions include the hypervariable regions as defined by Kabat et al., (*Sequences of Proteins of Immunological Interest*, NIH Publication No. 91-3242, Bethesda, Md.: U.S. Dept. of Health and Human Services, National Institutes of Health (1983)) or the hypervariable loops in 3-dimensional structures of antibodies (Chothia and Lesk, *J. Mol. Biol.,* 196: 901-917 (1987)). The CDRs in each chain are held in close proximity by framework regions ("FRs") and, with the CDRs from the other chain, contribute to the formation of the antigen binding site. Within the CDRs there are select amino acids that have been described as the selectivity determining regions ("SDRs") that represent the critical contact residues used by the CDR in the antibody-antigen interaction (see Kashmiri et al., *Methods,* 36(1):25-34 (2005)).

[0361] An "epitope" or "binding site" is an area or region on an antigen to which an antigen-binding peptide (such as an antibody) specifically binds. A protein epitope may comprise amino acid residues directly involved in the binding (also called immunodominant component of the epitope) and other amino acid residues, which are not directly involved in the binding, such as amino acid residues that are effectively blocked by the specifically antigen binding peptide (in other words, the amino acid residue is within the "footprint" of the specifically antigen binding peptide). The term epitope herein includes both types of amino acid binding sites in any particular region of PACAP, i.e., PACAP38 and PACAP27, that specifically binds to an anti-PACAP antibody. PACAP may comprise a number of different epitopes, which may include, without limitation, (1) linear peptide antigenic determinants, (2) conformational antigenic determinants that consist of one or more non-contiguous amino acids located near each other in a mature PACAP conformation; and (3) post-translational antigenic determinants that consist, either in whole or part, of molecular structures covalently attached to a PACAP protein such as carbohydrate groups. In particular, the term "epitope" includes the specific residues in a protein or peptide, e.g., PACAP, which are involved in the binding of an antibody to such protein or peptide as determined by known and accepted methods such as alanine scanning techniques. Such methods are exemplified herein.

[0362] The phrase that an antibody (e.g., first antibody) binds "substantially" or "at least partially" the same epitope

as another antibody (e.g., second antibody) means that the epitope binding site for the first antibody comprises at least 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, or more of the amino acid residues on the antigen that constitutes the epitope binding site of the second antibody. Also, that a first antibody binds substantially or partially the same or overlapping epitope as a second antibody means that the first and second antibodies compete in binding to the antigen, as described above. Thus, the term "binds to substantially the same epitope or determinant as" a monoclonal antibody means that an antibody "competes" with the antibody.

[0363] The phrase "binds to the same or overlapping epitope or determinant as" an antibody of interest means that an antibody "competes" with said antibody of interest for at least one, (e.g., at least 2, at least 3, at least 4, at least 5) or all residues on PACAP to which said antibody of interest specifically binds. The identification of one or more antibodies that bind(s) to substantially or essentially the same epitope as the monoclonal antibodies described herein can be readily determined using alanine scanning. Additionally, any one of variety of immunological screening assays in which antibody competition can be assessed. A number of such assays are routinely practiced and well known in the art (see, e.g., U.S. Pat. No. 5,660,827, issued Aug. 26, 1997, which is specifically incorporated herein by reference). It will be understood that actually determining the epitope to which an antibody described herein binds is not in any way required to identify an antibody that binds to the same or substantially the same or overlapping epitope as the monoclonal antibody described herein.

[0364] For example, where the test antibodies to be examined are obtained from different source animals, or are even of a different Ig isotype, a simple competition assay may be employed in which the control antibody is mixed with the test antibody and then applied to a sample containing PACAP. Protocols based upon ELISAs, radioimmunoassays, Western blotting, and the use of BIACORE® (GE Healthcare Life Sciences, Marlborough, Mass.) analysis are suitable for use in such simple competition studies.

[0365] In certain embodiments, the control anti-PACAP antibody is pre-mixed with varying amounts of the test antibody (e.g., in ratios of about 1:1, 1:2, 1:10, or about 1:100) for a period of time prior to applying to the PACAP38 or PACAP27 antigen sample. In other embodiments, the control and varying amounts of test antibody can simply be added separately and admixed during exposure to the PACAP38 or PACAP27 antigen sample. As long as bound antibodies can be distinguished from free antibodies (e.g., by using separation or washing techniques to eliminate unbound antibodies) and control antibody from the test antibody (e.g., by using species specific or isotype specific secondary antibodies or by specifically labeling the control antibody with a detectable label) it can be determined if the test antibody reduces the binding of the control antibody to the PACAP38 or PACAP27 antigens, indicating that the test antibody recognizes substantially the same epitope as the control anti-PACAP antibody. The binding of the (labeled) control antibody in the presence of a completely irrelevant antibody (that does not bind PACAP) can serve as the control high value. The control low value can be obtained by incubating the labeled control antibody with the same but unlabeled control antibody, where competition would occur and reduce binding of the labeled antibody. In a test assay, a significant reduction in labeled antibody reactivity in the presence of a test antibody is indicative of a test antibody that recognizes substantially the same epitope, i.e., one that competes with the labeled control antibody. For example, any test antibody that reduces the binding of the control antibody to PACAP38 or PACAP27 by at least about 50%, such as at least about 60%, or more preferably at least about 70% (e.g., about 65-100%), at any ratio of test antibody between about 1:1 or 1:10 and about 1:100 is considered to be an antibody that binds to substantially the same or overlapping epitope or determinant as the control antibody.

[0366] Preferably, such test antibody will reduce the binding of the control antibody to PACAP38 or PACAP27 antigen preferably at least about 50%, at least about 60%, at least about 80%, or at least about 90% (e.g., about 95%) of the binding of the control antibody observed in the absence of the test antibody.

[0367] A simple competition assay in which a test antibody is applied at saturating concentration to a surface onto which PACAP38 or PACAP27 is immobilized also may be advantageously employed. The surface in the simple competition assay is preferably a BIACORE® (GE Healthcare Life Sciences, Marlborough, Mass.) chip (or other media suitable for surface plasmon resonance ("SPR") analysis). The binding of a control antibody that binds PACAP38 or PACAP27 to the PACAP-coated surface is measured. This binding to the PACAP38- or PACAP27-containing surface of the control antibody alone is compared with the binding of the control antibody in the presence of a test antibody. A significant reduction in binding to the PACAP38- or PACAP27-containing surface by the control antibody in the presence of a test antibody indicates that the test antibody recognizes substantially the same epitope as the control antibody such that the test antibody "competes" with the control antibody. Any test antibody that reduces the binding of control antibody by at least about 20% or more, at least about 40%, at least about 50%, at least about 70%, or more, can be considered to be an antibody that binds to substantially the same epitope or determinant as the control antibody. Preferably, such test antibody will reduce the binding of the control antibody to PACAP38 or PACAP27 by at least about 50% (e.g., at least about 60%, at least about 70%, or more). It will be appreciated that the order of control and test antibodies can be reversed; i.e. the control antibody can be first bound to the surface and then the test antibody is brought into contact with the surface thereafter in a competition assay. Preferably, the "sandwich-style" binding assay exemplified in Example 9 infra is used. Alternatively, the antibody having greater affinity for PACAP38 or PACAP27 antigen is bound to the PACAP38- or PACAP27-containing surface first, as it will be expected that the decrease in binding seen for the second antibody (assuming the antibodies are competing) will be of greater magnitude. Further examples of such assays are provided in e.g., Saunal and Regenmortel, *J. Immunol. Methods,* 183:33-41 (1995), the disclosure of which is incorporated herein by reference.

[0368] In addition, whether an antibody binds the same or overlapping epitope(s) on PACAP as another antibody or the epitope bound by a test antibody may in particular be determined using a Western-blot based assay. In this assay a library of peptides corresponding to the antigen bound by the antibody, the PACAP protein, is made, that comprise overlapping portions of the protein, typically 10-25, 10-20, or 10-15 amino acids long. These different overlapping amino acid peptides encompassing the PACAP sequence are

synthesized and covalently bound to a PEPSPOTS' nitrocellulose membrane (JPT Peptide Technologies, Berlin, Germany). Blots are then prepared and probed according to the manufacturer's recommendations.

[0369] Essentially, the immunoblot assay then detects by fluorometric means what peptides in the library bind to the test antibody and thereby can identify what residues on the antigen, i.e., PACAP, interact with the test antibody. (See U.S. Pat. No. 7,935,340, incorporated by reference herein).

[0370] Various epitope mapping techniques are known in the art. By way of example, X-ray co-crystallography of the antigen and antibody; NMR; SPR (e.g., at 25° or 37° C.); array-based oligo-peptide scanning (or "pepscan analysis"); site-directed mutagenesis (e.g., alanine scanning); mutagenesis mapping; hydrogen-deuterium exchange; phage display; and limited proteolysis are all epitope mapping techniques that are well known in the art (See, e.g., *Epitope Mapping Protocols: Second Edition, Methods in Molecular Biology*, editors Mike Schutkowski and Ulrich Reineke, 2nd Ed., New York, N.Y.: Humana Press (2009), and *Epitope Mapping Protocols, Methods in Molecular Biology*, editor Glenn Morris, 1st Ed., New York, N.Y.: Humana Press (1996), both of which are herein incorporated by referenced in their entirety).

[0371] The identification of one or more antibodies that bind(s) to substantially or essentially the same epitope as the monoclonal antibodies described herein, e.g., Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, or Ab1.H, can be readily determined using any one of variety of immunological screening assays in which antibody competition can be assessed. A number of such assays are routinely practiced and well known in the art (see, e.g., U.S. Pat. No. 5,660,827, issued Aug. 26, 1997, which is incorporated herein by reference). It will be understood that determining the epitope to which an antibody described herein binds is not in any way required to identify an antibody that binds to the same or substantially the same epitope as the monoclonal antibody described herein.

[0372] For example, where the test antibodies to be examined are obtained from different source animals, or are even of a different Ig isotype, a simple competition assay may be employed in which the control antibody (one of Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, or Ab1.H, for example) is mixed with the test antibody and then applied to a sample containing either or both PACAP38 and PACAP27, each of which is known to be bound by Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab1.H. Protocols based upon ELISAs, radioimmunoassays, Western blotting, and BIACORE® (GE Healthcare Life Sciences, Marlborough, Mass.) analysis (as described in the Examples section herein) are suitable for use in such simple competition studies.

[0373] In certain embodiments, the method comprises pre-mixing the control antibody with varying amounts of the test antibody (e.g., in ratios of about 1:1, 1:2, 1:10, or about 1:100) for a period of time prior to applying to the PACAP antigen sample. In other embodiments, the control and varying amounts of test antibody can be added separately and admixed during exposure to the PACAP antigen sample. As long as bound antibodies can be distinguished from free antibodies (e.g., by using separation or washing techniques to eliminate unbound antibodies) and control antibody from the test antibody (e.g., by using species specific or isotype specific secondary antibodies or by specifically labelling the control antibody with a detectable label), the method can be used to determine that the test antibody reduces the binding of the control antibody to the PACAP antigen, indicating that the test antibody recognizes substantially the same epitope as the control antibody (e.g., Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, or Ab1.H). The binding of the (labeled) control antibody in the presence of a completely irrelevant antibody (that does not bind PACAP) can serve as the control high value. The control low value can be obtained by incubating the labeled control antibody with the same but unlabeled control antibody, where competition would occur and reduce binding of the labeled antibody. In a test assay, a significant reduction in labeled antibody reactivity in the presence of a test antibody is indicative of a test antibody that recognizes substantially the same epitope, i.e., one that competes with the labeled control antibody. For example, any test antibody that reduces the binding of Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, or Ab1.H to both of PACAP38 and PACAP27 antigens by at least about 50%, such as at least about 60%, or more preferably at least about 70% (e.g., about 65-100%), at any ratio of control Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, or Ab1.H:test antibody or Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, or Ab1.H:test antibody between about 1:1 or 1:10 and about 1:100 is considered to be an antibody that binds to substantially the same epitope or determinant as Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, or Ab1.H, respectively. Preferably, such test antibody will reduce the binding of Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, or Ab1.H to at least one, preferably each, of the PACAP38 and PACAP27 antigens preferably at least about 50%, at least about 60%, at least about 80% or at least about 90% (e.g., about 95%) of the binding of Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, or Ab1.H observed in the absence of the test antibody. These methods can be adapted to identify and/or evaluate antibodies that compete with other control antibodies.

[0374] A simple competition assay in which a test antibody is applied at saturating concentration to a surface onto which either PACAP38 or PACAP27, or both, are immobilized also may be advantageously employed. The surface in the simple competition assay is preferably of a media suitable for OCTET® and/or PROTEON®. The binding of a control antibody (e.g., Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, or Ab1.H) to the PACAP-coated surface is measured. This binding to the PACAP-containing surface of the control antibody alone is compared with the binding of the control antibody in the presence of a test antibody. A significant reduction in binding to the PACAP-containing surface by the control antibody in the presence of a test antibody indicates that the test antibody recognizes substantially the same epitope as the control antibody such that the test antibody "competes" with the control antibody. Any test

antibody that reduces the binding of control antibody (such as Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, or Ab1.H) to both of PACAP38 and PACAP27 antigens by at least about 20% or more, at least about 40%, at least about 50%, at least about 70%, or more, can be considered to be an antibody that binds to substantially the same epitope or determinant as the control antibody (e.g., Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, or Ab1.H). Preferably, such test antibody will reduce the binding of the control antibody (e.g., Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, or Ab1.H) to the PACAP antigen by at least about 50% (e.g., at least about 60%, at least about 70%, or more). It will be appreciated that the order of control and test antibodies can be reversed; i.e. the control antibody can be first bound to the surface and then the test antibody is brought into contact with the surface thereafter in a competition assay. Preferably, the antibody having higher affinity for PACAP38 and PACAP27 is bound to the PACAP-containing surface first, as it will be expected that the decrease in binding seen for the second antibody (assuming the antibodies are competing) will be of greater magnitude. Further examples of such assays are provided in, e.g., Saunal and Regenmortel, *J. Immunol. Methods,* 183:33-41 (1989), the disclosure of which is incorporated herein by reference.

[0375] Determination of whether an antibody, antigen binding fragment thereof, or antibody derivative binds within one of the epitope regions defined above can be carried out in ways known to the person skilled in the art. In another example of such mapping/characterization methods, an epitope region for an anti-PACAP antibody may be determined by epitope "footprinting" using chemical modification of the exposed amines/carboxyls in the PACAP38 and PACAP27 protein. One specific example of such a foot-printing technique is the use of hydrogen-deuterium exchange detected by mass spectrometry ("HXMS"), wherein a hydrogen/deuterium exchange of receptor and ligand protein amide protons, binding, and back exchange occurs, wherein the backbone amide groups participating in protein binding are protected from back exchange and therefore will remain deuterated. Relevant regions can be identified at this point by peptic proteolysis, fast microbore high-performance liquid chromatography separation, and/or electrospray ionization mass spectrometry (See, e.g., Ehring H., *Analytical Biochemistry,* 267(2):252-259 (1999) and Engen, J. R. & Smith, D. L., *Anal. Chem.,* 73:256A-265A (2001)). Another example of a suitable epitope identification technique is nuclear magnetic resonance epitope mapping ("NMR"), where typically the position of the signals in two-dimensional NMR spectres of the free antigen and the antigen complexed with the antigen binding peptide, such as an antibody, are compared. The antigen typically is selectively isotopically labeled with ^{15}N so that only signals corresponding to the antigen and no signals from the antigen binding peptide are seen in the NMR-spectrum. Antigen signals originating from amino acids involved in the interaction with the antigen binding peptide typically will shift position in the spectres of the complex compared to the spectres of the free antigen, and the amino acids involved in the binding can be identified that way, See, e.g., *Ernst Schering Res. Found. Workshop*, (44):149-67 (2004); Huang et al., *J. Mol. Biol.,* 281(1):61-67 (1998); and Saito and Patterson, *Methods,* 9(3):516-24 (1996)). Epitope mapping/characterization also can be performed using mass spectrometry ("MS") methods (See, e.g., Downard, *J. Mass Spectrom.,* 35(4):493-503 (2000) and Kiselar and Downard, *Anal. Chem.,* 71(9):1792-801 (1999)).

[0376] Protease digestion techniques also can be useful in the context of epitope mapping and identification. Antigenic determinant-relevant regions/sequences can be determined by protease digestion, e.g. by using trypsin in a ratio of about 1:50 to PACAP38 or PACAP27 overnight ("o/n") digestion at 37° C. and pH 7-8, followed by mass spectrometry ("MS") analysis for peptide identification. The peptides protected from trypsin cleavage by the anti-PACAP antibody can subsequently be identified by comparison of samples subjected to trypsin digestion and samples incubated with antibody and then subjected to digestion by e.g. trypsin (thereby revealing a footprint for the antibody). Other enzymes like chymotrypsin or pepsin can be used in similar epitope characterization methods. Moreover, enzymatic digestion can provide a quick method for analyzing whether a potential antigenic determinant sequence is within a region of PACAP in the context of a PACAP-binding polypeptide. If the polypeptide is not surface exposed, it is most likely not relevant in terms of immunogenicity/antigenicity (See, e.g., Manca, *Ann. Ist. Super. Sanità,* 27(1):15-9 (1991) for a discussion of similar techniques).

[0377] Site-directed mutagenesis is another technique useful for characterization of a binding epitope. For example, in "alanine-scanning" site-directed mutagenesis (also known as alanine scanning, alanine scanning mutagenesis, alanine scanning mutations, combinatorial alanine scanning, or creation of alanine point mutations, for example), each residue within a protein segment is replaced with an alanine residue (or another residue such as valine where alanine is present in the wild-type sequence) through such methodologies as direct peptide or protein synthesis, site-directed mutagenesis, the GENEART™ Mutagenesis Service (Thermo Fisher Scientific, Waltham, Mass. U.S.A.) or shotgun mutagenesis, for example. A series of single point mutants of the molecule is thereby generated using this technique; the number of mutants generated is equivalent to the number of residues in the molecule, each residue being replaced, one at a time, by a single alanine residue. Alanine is generally used to replace native (wild-type) residues because of its non-bulky, chemically inert, methyl functional group that can mimic the secondary structure preferences that many other amino acids may possess. Subsequently, the effects replacing a native residue with an alanine has on binding affinity of an alanine scanning mutant and its binding partner can be measured using such methods as, but not limited to, SPR binding experiments. If a mutation leads to a significant reduction in binding affinity, it is most likely that the mutated residue is involved in binding. Monoclonal antibodies specific for structural epitopes (i.e., antibodies that do not bind the unfolded protein) can be used as a positive control for binding affinity experiments to verify that the alanine-replacement does not influence the overall tertiary structure of the protein (as changes to the overall fold of the protein may indirectly affect binding and thereby produce a false positive result). See, e.g., Clackson and Wells, *Science,* 267:383-386 (1995); Weiss et al., *Proc. Natl. Acad. Sci. USA,* 97(16):8950-8954 (2000); and Wells, *Proc. Natl. Acad. Sci. USA,* 93:1-6 (1996). In Example 12 alanine scanning methods are used to identify the specific epitope or

residues of PACAP which specifically interact with the anti-PACAP antibodies disclosed herein.

[0378] Electron microscopy can also be used for epitope "footprinting". For example, Wang et al., *Nature,* 355:275-278 (1992) used coordinated application of cryoelectron microscopy, three-dimensional image reconstruction, and X-ray crystallography to determine the physical footprint of a Fab-fragment on the capsid surface of native cowpea mosaic virus.

[0379] Other forms of "label-free" assay for epitope evaluation include SPR (sold commercially as the BIACORE® system, GE Healthcare Life Sciences, Marlborough, Mass.) and reflectometric interference spectroscopy ("RifS") (See, e.g., Fagerstam et al., *Journal of Molecular Recognition,* 3:208-14 (1990); Nice et al., *J. Chromatogr.,* 646:159-168 (1993); Leipert et al., *Angew. Chem. Int. Ed.,* 37:3308-3311 (1998); Kroger et al., *Biosensors and Bioelectronics,* 17:937-944 (2002)).

[0380] The expressions "framework region" or "FR" refer to one or more of the framework regions within the variable regions of the light and heavy chains of an antibody (See Kabat et al., *Sequences of Proteins of Immunological Interest,* 4th edition, Bethesda, Md.: U.S. Dept. of Health and Human Services, Public Health Service, National Institutes of Health (1987)). These expressions include those amino acid sequence regions interposed between the CDRs within the variable regions of the light and heavy chains of an antibody.

[0381] The term "Fc region" is used to define a C-terminal region of an immunoglobulin heavy chain. The "Fc region" may be a native sequence Fc region or a variant Fc region. Although the boundaries of the Fc region of an immunoglobulin heavy chain might vary, the human IgG heavy chain Fc region is usually defined to stretch from an amino acid residue at position Cys226, or from Pro230, to the carboxyl-terminus thereof. The numbering of the residues in the Fc region is that of the EU index as in Kabat. Kabat et al., *Sequences of Proteins of Immunological Interest,* 5th edition, Bethesda, Md.: U.S. Dept. of Health and Human Services, Public Health Service, National Institutes of Health (1991). The Fc region of an immunoglobulin generally comprises two constant domains, CH2 and CH3.

[0382] The terms "Fc receptor" and "FcR" describe a receptor that binds to the Fc region of an antibody. The preferred FcR is a native sequence human FcR. Moreover, a preferred FcR is one that binds an IgG antibody (a gamma receptor) and includes receptors of the FcγRI, FcγRII, and FcγRIII subclasses, including allelic variants and alternatively spliced forms of these receptors. FcγRII receptors include FcγRIIA (an "activating receptor") and FcγRIIB (an "inhibiting receptor"), which have similar amino acid sequences that differ primarily in the cytoplasmic domains thereof. FcRs are reviewed in Ravetch and Kinet, *Ann. Rev. Immunol.,* 9:457-92 (1991); Capel et al., *Immunomethods,* 4:25-34 (1994); and de Haas et al., *J. Lab. Clin. Med.,* 126:330-41 (1995). "FcR" also includes the neonatal receptor, FcRn, which is responsible for the transfer of maternal IgGs to the fetus (Guyer et al., *J. Immunol.,* 117:587 (1976); and Kim et al., *J. Immunol.,* 24:249 (1994)), and which primarily functions to modulate and/or extend the half-life of antibodies in circulation. To the extent that the disclosed anti-PACAP antibodies are aglycosylated, as a result of the expression system and/or sequence, the subject antibodies are expected to bind FcRn receptors, but not to bind (or to minimally bind) Fcγ receptors.

[0383] A "functional Fc region" possesses at least one effector function of a native sequence Fc region. Exemplary "effector functions" include C1q binding; complement dependent cytotoxicity ("CDC"); Fc receptor binding; antibody-dependent cell-mediated cytotoxicity ("ADCC"); phagocytosis; down-regulation of cell surface receptors (e.g. B cell receptor ("BCR")), etc. Such effector functions generally require the Fc region to be combined with a binding domain (e.g. an antibody variable domain) and can be assessed using various assays known in the art for evaluating such antibody effector functions.

[0384] A "native sequence Fc region" comprises an amino acid sequence identical to the amino acid sequence of an Fc region found in nature. A "variant Fc region" comprises an amino acid sequence that differs from that of a native sequence Fc region by virtue of at least one amino acid modification, yet retains at least one effector function of the native sequence Fc region. Preferably, the variant Fc region has at least one amino acid substitution compared to a native sequence Fc region or to the Fc region of a parent polypeptide, e.g. from about one to about ten amino acid substitutions, and preferably from about one to about five amino acid substitutions in a native sequence Fc region or in the Fc region of the parent polypeptide. The variant Fc region herein will preferably possess at least about 80% sequence identity with a native sequence Fc region and/or with an Fc region of a parent polypeptide, and most preferably at least about 90% sequence identity therewith, more preferably at least about 95%, at least about 96%, at least about 97%, at least about 98%, or at least about 99% sequence identity therewith.

Anti-PA CAP Antibodies and Binding Fragments Thereof Having Binding Activity for PACAP

[0385] PACAP is a multifunctional vasodilatory peptide with expression throughout the central nervous system ("CNS") and periphery. PACAP is a member of the secretin/VIP/GRH family. PACAP exists in two α-amidated active forms, PACAP38 (SEQ ID NO: 1241) and PACAP27 (SEQ ID NO: 1242). Herein, the term "PACAP" includes either or both of PACAP38 and PACAP27 unless expressly indicated otherwise. PACAP is highly conserved between species.

[0386] In humans, PACAP is derived from a 176 amino acid precursor protein (preproPACAP) and the gene is located on chromosome 18p11, with PACAP38 encoded for by exon 5 (Vaudry et al., *Pharmacol. Rev.,* 61:283-357 (2009)). PreproPACAP contains an N-terminal 24 amino acid signal protein, a 29 amino acid PACAP-related peptide and PACAP in the C-terminal domain. The precursor is metabolized by prohormone convertase enzymes into biologically active PACAP38 and PACAP27.

[0387] VIP (SEQ ID NO: 1243) belongs to the same protein family as PACAP and shares high homology with PACAP, i.e., VIP and PACAP27 have 68% sequence homology at the amino acid level, as well as similar overall secondary structure, i.e. long alpha-helical structures at the C-terminus.

[0388] PACAP's actions are mediated via three different G-protein coupled receptors: PAC1-R, VPAC1-R, and VPAC2-R. VPAC1-R can associate with all of the receptor-associated membrane proteins ("RAMPs", Kaiser & Russo, *Neuropeptides* 47: 451-461 (2013)). PAC1-R is selective for

PACAP, whereas VPAC1-R and VPAC2-R bind to both VIP and PACAP with high affinity. PAC1-R binds to PACAP with 100-1000-fold higher affinity than VIP, i.e., K_D~0.5 nM for PACAP27/PACAP38 vs. K_D~500 nM for VIP. Conversely, VPAC1-R and VPAC2-R have equal affinities for PACAP and VIP (K_D~1 nM) (See Schytz et al. (2010)). All three receptors are widely expressed in both peripheral tissues and in the CNS, with PAC1-R predominantly expressed in the CNS, most abundantly in the olfactory bulb, thalamus, hypothalamus, the dentate gyrus of the hippocampus and in granule cells of the cerebellum (Hashimoto et al., *J. Comp. Neurol.,* 371:567-577 (1996); Shioda et al., *Neurosci. Res.,* 28:345-354 (1997)).

[0389] Activation of the PAC1-R, VPAC1-R, and/or VPAC2-R results in increased adenylate cyclase activity and, thus, increased cAMP production. However, PACAP receptors can also mediate their effects through PLC, leading to increased Ca^{2+} levels, and PLD.

[0390] PACAP has a wide range of biological effects, including a role in neurodevelopment, neuroprotection, neuromodulation, neurogenic inflammation, and nociception. PACAP is also reported to interact with glycosaminoglycans ("GAGs"). GAGs are long, unbranched polysaccharides composed of repeating disaccharide units, such as heparin, chondroitin, keratin, and hyaluronic acid. It has been shown that the cellular uptake of PACAP is dependent on the expression of GAG proteins and that PACAP bound to sulfated GAGs. Particularly, it was determined that PACAP38 binding to GAGs was capable of inducing receptor-independent cellular uptake of PACAP38. This study further demonstrated that a random coil-to-α-helix transition in PACAP38 was essential for GAG-dependent uptake of PACAP38, as a mutant PACAP38 that could not undergo the structural transition was not internalized by GAG-containing cell lines as efficiently as the wild-type form of PACAP38 (Neree et al., *FEBS Lett.,* 588(24):4590-4596, 2014). In a follow up study, it was determined that PACAP's ability to cluster GAGs, i.e., heparin, was directly related to its ability to function as a cell penetrating peptide ("CPP"). It is hypothesized that this activity is attributable to the heparin-binding, or Cardin-Weintraub, motif found in secretin/glucagon/GHRH family members, such as PACAP (Neree et al., *Int. J. Mol. Sci.,* 16:27391-27400, 2015). Interestingly, Neree et al. (2015) presented data demonstrating that PACAP38 was able to cluster sulfated GAGs in vitro. These data suggested that the observed clustering effect is important for the GAG-mediated cellular uptake of PACAP38, as other peptides, such as glucagon, displayed higher binding affinities for sulfated GAGs (heparin) but are not internalized by cells as efficiently as PACAP38. Further, it is reported that in in vitro studies in which cells are exposed to PACAP, cartilage formation is increased, including cartilage matrix that is rich in sulphated GAG proteins, consistent with its putative protective role expressed during various cellular stress responses (Juhász et al., *PLoS ONE,* 9(3):e91541, 2014). Using cell types that lack PACAP-specific receptors on their plasma membranes, such as CHO-K1 cells, Doan et al. presented data demonstrating the ability of such cells to engage in receptor-independent cellular uptake of various forms of fluorescently-labeled PACAP38 and PACAP27 (Doan et al., *Biochem. Biophys. Acta,* 1823:940-949, 2012).

[0391] The present invention provides exemplary antibodies or antigen binding fragments thereof that bind PACAP, including human PACAP. Other antibodies or antigen binding fragments thereof that bind PACAP, including those having different CDRs, and epitopic specificity may be obtained using the disclosure of the present specification, and using methods that are generally known in the art. Such antibodies and antigen binding fragments thereof antagonize the biological effects of PACAP in vivo and therefore are useful in treating or preventing PACAP-related conditions including, for example, headache, migraine, pain, photophobia, hot flush, PTSD, and anxiety disorders. In preferred embodiments, the antibody or antigen binding fragment thereof according to the invention comprises one or more CDRs, a V_L chain and/or V_H chain of the anti-PACAP antibodies and antigen binding fragments thereof described herein.

[0392] In some embodiments, an anti-PACAP antibody or antigen binding fragment thereof according to the invention will interfere with, block, reduce, or modulate the interaction between PACAP and its receptor(s) (e.g., PAC1-R, VPAC1-R, and VPAC2-R). In some instances an anti-PACAP antibody or antigen binding fragment thereof according to the invention is "neutralizing", e.g., it totally prevents the specific interaction of PACAP with PAC1-R, VPAC1-R, and/or VPAC2-R. In some embodiments, the antibody or antigen binding fragment thereof neutralizes PACAP, e.g., by remaining bound to PACAP in a location and/or manner that prevents PACAP from specifically binding to PAC1-R, VPAC1-R, and/or VPAC2-R.

[0393] In some embodiments, the antibody or antigen binding fragment thereof according to the invention is capable of inhibiting PACAP-mediated activity (including binding to PAC1-R-expressing cells). In some embodiments, the antibody or antigen binding fragment thereof according to the invention are humanized, such as humanized rabbit antibodies to PACAP.

[0394] As mentioned, the anti-PACAP antibodies or antigen binding fragments thereof according to the invention have a variety of uses. For example, the subject antibodies and fragments can be useful in therapeutic applications, as well as diagnostically in binding assays. The subject anti-PACAP antibodies or antigen binding fragments thereof are useful for affinity purification of PACAP, in particular human PACAP or its ligands and in screening assays to identify other antagonists of PACAP activity. Some of the antibodies or antigen binding fragments thereof are useful for inhibiting binding of PACAP to PAC1-R, VPAC1-R, and/or VPAC2-R, or inhibiting PACAP-mediated activities and/or biological effects.

[0395] As used herein, the term "one or more biological effects associated with PACAP refers to any biological effect mediated, induced, or otherwise attributable to PACAP, e.g., binding properties, functional properties, and other properties of biological significance. Non-limiting exemplary biological effects of PACAP include PACAP binding to PAC1-R, VPAC1-R, and/or VPAC2-R; PACAP activating PAC1-R, VPAC1-R, and/or VPAC2-R-mediated signaling; PACAP-mediated increase in cAMP production; PACAP-mediated increase in PLC activity; PACAP-mediated increase in PLD activity; PACAP-mediated increase in Ca^{2+} levels; and PACAP-mediated vasodilation, photophobia, mast cell degranulation, and/or neuronal activation. The subject anti-PACAP antibodies are capable of inhibiting one, a combination of, or all of these exemplary PACAP biological activities. For example, the anti-PACAP antibodies and

antigen binding fragments thereof provided herein are capable of inhibiting PACAP-induced vasodilation (see Example 7 and Example 8).

[0396] The antibody or antigen binding fragment thereof according to the invention can be used in a variety of therapeutic applications. For example, in some embodiments the anti-PACAP antibody or antigen binding fragment thereof are useful for treating conditions associated with PACAP, such as, but not limited to, migraine (with or without aura), hemiplegic migraines, cluster headaches, migrainous neuralgia, chronic headaches, tension headaches, general headaches, hot flush, photophobia, chronic paroxysmal hemicrania, secondary headaches due to an underlying structural problem in the head or neck, cranial neuralgia, sinus headaches (e.g., headache associated with sinusitis), allergy-induced headaches or migraines, pain, chronic pain, neuroinflammatory or inflammatory pain, post-operative incision pain, post-surgical pain, trauma-related pain, eye pain, tooth pain, complex regional pain syndrome, cancer pain (e.g., primary or metastatic bone cancer pain), fracture pain, osteoporotic fracture pain, pain resulting from burn, gout joint pain, pain associated with sickle cell crises, pain associated with temporomandibular disorders, cirrhosis, hepatitis, neurogenic pain, neuropathic pain, nociceptic pain, visceral pain, trigeminal neuralgia, post-herpetic neuralgia, phantom limb pain, fibromyalgia, menstrual pain, ovarialgia, reflex sympathetic dystrophy, osteoarthritis or rheumatoid arthritis pain, lower back pain, diabetic neuropathy, sciatica, dyspepsia, irritable bowel syndrome, inflammatory bowel disease, Crohn's disease, ileitis, ulcerative colitis, renal colic, dysmenorrhea, cystitis, interstitial cystitis, menstrual period, labor, menopause, pancreatitis, schizophrenia, depression, PTSD, anxiety disorders, diabetes, autoimmune diabetes, endothelial dysfunction, ischemia, Raynaud's syndrome, coronary heart disease ("CHD"), coronary artery disease ("CAD"), heart failure, peripheral arterial disease ("PAD"), pulmonary hypertension ("PH"), connective tissue disorders, stroke, Sjögren's syndrome, multiple sclerosis, bronchial hyperreactivity, asthma, bronchitis, bronchodilation, emphysema, chronic obstructive pulmonary disease ("COPD"), inflammatory dermatitis, adenocarcinoma in glandular tissue, blastoma in embryonic tissue of organs, carcinoma in epithelial tissue, leukemia in tissues that form blood cells, lymphoma in lymphatic tissue, myeloma in bone marrow, sarcoma in connective or supportive tissue, adrenal cancer, AIDS-related lymphoma, anemia, bladder cancer, bone cancer, brain cancer, breast cancer, carcinoid tumors, cervical cancer, chemotherapy, colon cancer, cytopenia, endometrial cancer, esophageal cancer, gastric cancer, head cancer, neck cancer, hepatobiliary cancer, kidney cancer, leukemia, liver cancer, lung cancer, lymphoma, Hodgkin's disease, non-Hodgkin's, nervous system tumors, oral cancer, ovarian cancer, pancreatic cancer, prostate cancer, rectal cancer, skin cancer, stomach cancer, testicular cancer, thyroid cancer, urethral cancer, cancer of bone marrow, multiple myeloma, tumors that metastasize to the bone, tumors infiltrating the nerve and hollow viscus, tumors near neural structures, acne vulgaris, atopic dermatitis, urticaria, keloids, hypertrophic scars and rosacea, allergic dermatitis, psoriasis, pruritus, neurogenic cutaneous redness, erythema, weight loss, anorexia, sarcoidosis, shock, sepsis, opiate withdrawal syndrome, morphine tolerance, epilepsy, LUT disorders such as urinary tract infection, abnormal voiding, urinary urgency, nocturia, urinary incontinence, overactive bladder, and for preventing or alleviating the pain associated with such LUT conditions.

[0397] Specific examples of visceral pain, i.e., pain associated with the viscera, or the internal organs of the body include pain that affects organs such as e.g., the heart, lungs, reproductive organs, bladder, ureters, the digestive organs, liver, pancreas, spleen, and kidneys. Conditions associated therewith include by way of example pancreatitis, labor, abdominal surgery associated with ileus, cystitis, menstrual period, or dysmenorrhea. Likewise, kidney pain, epigastric pain, pleural pain, and painful biliary colic, appendicitis pain may all be considered to be visceral pain. Substernal pain or pressure from early myocardial infarction is also visceral. Diseases of the stomach, duodenum or colon can cause visceral pain. Commonly encountered gastrointestinal ("GI") disorders that cause visceral pain include functional bowel disorder ("FBD") and inflammatory bowel disease ("IBD"). Such GI disorders may further include gastro-esophageal reflux, dyspepsia, irritable bowel syndrome ("IBS") and functional abdominal pain syndrome ("FAPS"), and, with respect to IBD, Crohn's disease, ileitis, and ulcerative colitis.

[0398] The subject anti-PACAP antibodies and antigen binding fragments thereof may be used alone or in association with other active agents or drugs, including other biologics, to treat any subject in which blocking, inhibiting, or neutralizing the in vivo effect of PACAP or blocking or inhibiting the interaction of PACAP and its receptors, PAC1-R, VPAC1-R, and VPAC2-R, is therapeutically desirable.

[0399] Exemplary anti-PACAP antibodies and antigen binding fragments thereof according to the invention, and the specific CDRs thereof are identified in this section. For convenience, each exemplified antibody or antigen binding fragment thereof, and corresponding sequences are separately identified by a specific nomenclature, i.e., Ab1, Ab1. H, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, and Ab19.

[0400] The anti-PACAP antibodies and antigen binding fragments thereof comprising the invention have binding affinity for PACAP, wherein the binding affinity comprises anti-PACAP antibodies or antigen binding fragments thereof specifically binding to PACAP38 and PACAP27, but not binding VIP, and/or antibodies or antigen binding fragments thereof specifically binding to PACAP38, but not binding to PACAP27 or VIP, and/or antibodies or antigen binding fragments thereof specifically binding to a linear and/or conformational epitope within PACAP38 and/or PACAP27. More specifically, the epitopes of PACAP38 and/or PACAP27 to which antagonistic anti-PACAP antibodies or antigen binding fragments thereof according to the invention bind will include those which are identified in Example 12 or residues thereof (as determined by use of alanine scanning) and/or other epitopic identification methods.

Exemplary Anti-PACAP Antibody Polypeptide Sequences

Antibody Ab1

[0401] In one embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that possess a heavy chain sequence comprising the sequence of SEQ ID NO: 1 which consists of the heavy chain variable region of SEQ ID NO: 2 linked to the heavy chain constant region of SEQ ID NO: 10.

[0402] In one embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a variable heavy chain sequence comprising the sequence set forth below:

(SEQ ID NO: 2)
QSVEESGGRLVTPGTPLTLTCTVSGFSLSSAVMNWVRQAPGKGLEWIGSI

VASGTTYYASWANGRFTISKTSSTTMDLKMTSPTTEDTATYFCARGGGEF

FIWGPGTLVTVSS.

[0403] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that bind the same epitope as Ab1, and that contain a constant heavy chain sequence comprising the polypeptide of SEQ ID NO: 1244, 1245, or 1246, or comprising the sequence set forth below:

(SEQ ID NO: 10)
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV

HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDARVEP

KSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS

HEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGK

EYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTC

LVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW

QQGNVFSCSVMHEALHNHYTQKSLSLSPGK.

[0404] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a light chain sequence comprising the sequence of SEQ ID NO: 21 which consists of the light chain variable region of SEQ ID NO: 22 linked to the light chain constant region of SEQ ID NO: 30.

[0405] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a variable light chain sequence comprising the sequence set forth below:

(SEQ ID NO: 22)
DPVMTQTPSSTSAAVGGTVTISCQSSESVYSNYLSWYQQKPGQPPNFLIY

QASNLASGVPSRFKGSGSGTQFTLTITDLECDDAATYYCAGGYSENIVGF

GGGTEVVVKR.

[0406] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP, that bind the same epitope as Ab1, and that contain a constant light chain sequence comprising the sequence set forth below:

(SEQ ID NO: 30)
TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGN

SQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKS

FNRGEC.

[0407] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 4; SEQ ID NO: 6; and SEQ ID NO: 8, which correspond to the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 1, or which contain the variable heavy chain sequence of SEQ ID NO: 2, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 24; SEQ ID NO: 26; and SEQ ID NO: 28, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 21, or which contain the variable light chain sequence of SEQ ID NO: 22, or antibodies or antigen-binding fragments containing combinations of sequences that are at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention and antigen-binding fragments comprise, or alternatively consist of, combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

[0408] The invention further contemplates anti-PACAP antibodies and antigen-binding fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 3; SEQ ID NO: 5; SEQ ID NO: 7; and SEQ ID NO: 9, which correspond to the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 1, or the variable heavy chain sequence of SEQ ID NO: 2, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 23; SEQ ID NO: 25; SEQ ID NO: 27; and SEQ ID NO: 29, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 21, or the variable light chain sequence of SEQ ID NO: 22, or combinations of these polypeptide sequences, or sequences that are at least 80%, 90%, 95%, 96%, 97%, 98%, or 99% identical therewith.

[0409] In another embodiment of the invention, the anti-PACAP antibodies and antigen-binding fragments of the invention or fragments comprise, or alternatively consist of, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them, or sequences that are at least 90% or 95% identical thereto.

[0410] In another embodiment of the invention, the anti-PACAP antibodies and antigen-binding fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 1, or SEQ ID NO: 2, or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, the antibodies and antigen-binding fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 21, or SEQ ID NO: 22, or polypeptides that are at least 90% or 95% identical thereto.

[0411] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, or three of the polypeptide sequences of SEQ ID NO: 4; SEQ ID NO: 6; and SEQ ID NO: 8, which correspond to the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 1, or the variable heavy chain sequence of SEQ ID NO: 2, or sequences that are at least 90% or 95% identical thereto.

[0412] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, or three of the polypeptide sequences of SEQ ID

NO: 24; SEQ ID NO: 26; and SEQ ID NO: 28, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 21, or the variable light chain sequence of SEQ ID NO: 22, or sequences that are at least 90% or 95% identical thereto.

[0413] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 3; SEQ ID NO: 5; SEQ ID NO: 7; and SEQ ID NO: 9, which correspond to the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 1, or the variable heavy chain sequence of SEQ ID NO: 2, or sequences that are at least 90% or 95% identical thereto.

[0414] In a further embodiment of the invention, the subject antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 23; SEQ ID NO: 25; SEQ ID NO: 27; and SEQ ID NO: 29, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 21, or the variable light chain sequence of SEQ ID NO: 22, or sequences that are at least 90% or 95% identical thereto.

[0415] The invention also contemplates anti-PACAP antibodies and antigen-binding fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 2; the variable light chain region of SEQ ID NO: 22; the complementarity determining regions (SEQ ID NO: 4; SEQ ID NO: 6; and SEQ ID NO: 8) of the variable heavy chain region of SEQ ID NO: 2; and the complementarity determining regions (SEQ ID NO: 24; SEQ ID NO: 26; and SEQ ID NO: 28) of the variable light chain region of SEQ ID NO: 22, or sequences that are at least 90% or 95% identical thereto. In another embodiment of the invention, fragments of the antibodies having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 2; the variable light chain region of SEQ ID NO: 22; the framework regions (SEQ ID NO: 3; SEQ ID NO: 5; SEQ ID NO: 7; and SEQ ID NO: 9) of the variable heavy chain region of SEQ ID NO: 2; and the framework regions (SEQ ID NO: 23; SEQ ID NO: 25; SEQ ID NO: 27; and SEQ ID NO: 29) of the variable light chain region of SEQ ID NO: 22, or sequences that are at least 90% or 95% identical thereto.

[0416] In another embodiment of the invention, the anti-PACAP antibody is Ab1, comprising, or alternatively consisting of, SEQ ID NO: 1 and SEQ ID NO: 21, or SEQ ID NO: 2 and SEQ ID NO: 22, or an antibody or antigen-binding fragment comprising the CDRs of Ab1 and having at least one of the biological activities set forth herein, or is an anti-PACAP antibody that competes with Ab1 in binding PACAP, preferably one containing sequences that are at least 90%, 95%, 96%, 97%, 98%, or 99% identical to that of Ab1, or an antibody that binds to the same or overlapping epitope (s) on PACAP as Ab1.

[0417] In a further embodiment of the invention, antigen-binding fragments comprise, or alternatively consist of, Fab fragments having binding specificity for PACAP. With respect to antibody Ab1, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 2 and the variable light chain sequence of SEQ ID NO: 22, or sequences that are at least 90%, 95%, 96%, 97%, 98%, or 99% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 2 and/or SEQ ID NO: 22 that retain the binding specificity for PACAP.

[0418] In one embodiment of the invention described herein, Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab1. In another embodiment of the invention, anti-PACAP antibodies such as Ab1 and Fab fragments may be produced via expression in mammalian cells, such as CHO, NSO, or HEK 293 cells, fungal, insect, or microbial systems, such as yeast cells (for example haploid or diploid yeast, such as haploid or diploid *Pichia*) and other yeast strains. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*.

[0419] In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to PACAP, including the heavy and/or light chains of Ab1, as well as fragments, variants, and combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them, or sequences that are at least 90% or 95% identical thereto.

Antibody Ab1.H

[0420] In one embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that possess a heavy chain sequence comprising the sequence of SEQ ID NO: 41 which consists of the heavy chain variable region of SEQ ID NO: 42 linked to the heavy chain constant region of SEQ ID NO: 50.

[0421] In one embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a variable heavy chain sequence comprising the sequence set forth below:

(SEQ ID NO: 42)

EVQLVESGGGLVQPGGSLRLSCAASGFTVSSAVMNWVRQAPGKGLEWIGS

IVASGTTYYASSANGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARGGG

EFFIWGQGTLVTVSS.

[0422] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that bind the same epitope as Ab1.H, and that contain a constant heavy chain sequence comprising the polypeptide of SEQ ID NO: 1244, 1245, or 1246, or comprising the sequence set forth below:

(SEQ ID NO: 50)

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV

HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEP

KSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS

HEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGK

-continued

EYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTC

LVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW

QQGNVFSCSVMHEALHNHYTQKSLSLSPGK.

[0423] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a light chain sequence comprising the sequence of SEQ ID NO: 61 which consists of the light chain variable region of SEQ ID NO: 62 linked to the light chain constant region of SEQ ID NO: 70.

[0424] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a variable light chain sequence comprising the sequence set forth below:

(SEQ ID NO: 62)

DIQMTQSPSTLSASVGDRVTITCQSSESVYSNYLSWYQQKPGKAPKFLIY

QASNLASGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCAGGYSENIVGF

GGGTKVEIKR.

[0425] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP, that bind the same epitope as Ab1.H, and that contain a constant light chain sequence comprising the sequence set forth below:

(SEQ ID NO: 70)

TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGN

SQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKS

FNRGEC.

[0426] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 44; SEQ ID NO: 46; and SEQ ID NO: 48, which correspond to the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 41, or which contain the variable heavy chain sequence of SEQ ID NO: 42, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 64; SEQ ID NO: 66; and SEQ ID NO: 68, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 61, or which contain the variable light chain sequence of SEQ ID NO: 62, or antibodies or antigen-binding fragments containing combinations of sequences that are at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention and antigen-binding fragments comprise, or alternatively consist of, combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

[0427] The invention further contemplates anti-PACAP antibodies and antigen-binding fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 43; SEQ ID NO: 45; SEQ ID NO: 47; and SEQ ID NO: 49, which correspond to the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 41, or the variable heavy chain sequence of SEQ ID NO: 42, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 63; SEQ ID NO: 65; SEQ ID NO: 67; and SEQ ID NO: 69, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 61, or the variable light chain sequence of SEQ ID NO: 62, or combinations of these polypeptide sequences, or sequences that are at least 80%, 90%, 95%, 96%, 97%, 98%, or 99% identical therewith.

[0428] In another embodiment of the invention, the anti-PACAP antibodies and antigen-binding fragments of the invention or fragments comprise, or alternatively consist of, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them, or sequences that are at least 90% or 95% identical thereto.

[0429] In another embodiment of the invention, the anti-PACAP antibodies and antigen-binding fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 41, or SEQ ID NO: 42, or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, the antibodies and antigen-binding fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 61, or SEQ ID NO: 62, or polypeptides that are at least 90% or 95% identical thereto.

[0430] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, or three of the polypeptide sequences of SEQ ID NO: 44; SEQ ID NO: 46; and SEQ ID NO: 48, which correspond to the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 41, or the variable heavy chain sequence of SEQ ID NO: 42, or sequences that are at least 90% or 95% identical thereto.

[0431] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, or three of the polypeptide sequences of SEQ ID NO: 64; SEQ ID NO: 66; and SEQ ID NO: 68, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 61, or the variable light chain sequence of SEQ ID NO: 62, or sequences that are at least 90% or 95% identical thereto.

[0432] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 43; SEQ ID NO: 45; SEQ ID NO: 47; and SEQ ID NO: 49, which correspond to the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 41, or the variable heavy chain sequence of SEQ ID NO: 42, or sequences that are at least 90% or 95% identical thereto.

[0433] In a further embodiment of the invention, the subject antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 63; SEQ ID NO: 65; SEQ ID NO: 67; and SEQ ID NO: 69, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 61, or the variable light chain sequence of SEQ ID NO: 62, or sequences that are at least 90% or 95% identical thereto.

[0434] The invention also contemplates anti-PACAP antibodies and antigen-binding fragments that include one or

more of the antibody fragments described herein. In one embodiment of the invention, antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 42; the variable light chain region of SEQ ID NO: 62; the complementarity determining regions (SEQ ID NO: 44; SEQ ID NO: 46; and SEQ ID NO: 48) of the variable heavy chain region of SEQ ID NO: 42; and the complementarity determining regions (SEQ ID NO: 64; SEQ ID NO: 66; and SEQ ID NO: 68) of the variable light chain region of SEQ ID NO: 62, or sequences that are at least 90% or 95% identical thereto. In another embodiment of the invention, fragments of the antibodies having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 42; the variable light chain region of SEQ ID NO: 62; the framework regions (SEQ ID NO: 43; SEQ ID NO: 45; SEQ ID NO: 47; and SEQ ID NO: 49) of the variable heavy chain region of SEQ ID NO: 42; and the framework regions (SEQ ID NO: 63; SEQ ID NO: 65; SEQ ID NO: 67; and SEQ ID NO: 69) of the variable light chain region of SEQ ID NO: 62, or sequences that are at least 90% or 95% identical thereto.

[0435] In another embodiment of the invention, the anti-PACAP antibody is Ab1.H, comprising, or alternatively consisting of, SEQ ID NO: 41 and SEQ ID NO: 61, or SEQ ID NO: 42 and SEQ ID NO: 62, or an antibody or antigen-binding fragment comprising the CDRs of Ab1.H and having at least one of the biological activities set forth herein, or is an anti-PACAP antibody that competes with Ab1.H in binding PACAP, preferably one containing sequences that are at least 90%, 95%, 96%, 97%, 98%, or 99% identical to that of Ab1.H, or an antibody that binds to the same or overlapping epitope(s) on PACAP as Ab1.H.

[0436] In a further embodiment of the invention, antigen-binding fragments comprise, or alternatively consist of, Fab fragments having binding specificity for PACAP. With respect to antibody Ab1.H, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 42 and the variable light chain sequence of SEQ ID NO: 62, or sequences that are at least 90%, 95%, 96%, 97%, 98%, or 99% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 42 and/or SEQ ID NO: 62 that retain the binding specificity for PACAP.

[0437] In one embodiment of the invention described herein, Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab1.H. In another embodiment of the invention, anti-PACAP antibodies such as Ab1.H and Fab fragments may be produced via expression in mammalian cells, such as CHO, NSO, or HEK 293 cells, fungal, insect, or microbial systems, such as yeast cells (for example haploid or diploid yeast, such as haploid or diploid *Pichia*) and other yeast strains. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*.

[0438] In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to PACAP, including the heavy and/or light chains of Ab1.H, as well as fragments, variants, and combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them, or sequences that are at least 90% or 95% identical thereto.

Antibody Ab2

[0439] In one embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that possess a heavy chain sequence comprising the sequence of SEQ ID NO: 81 which consists of the heavy chain variable region of SEQ ID NO: 82 linked to the heavy chain constant region of SEQ ID NO: 90.

[0440] In one embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a variable heavy chain sequence comprising the sequence set forth below:

(SEQ ID NO: 82)
QSVEESGGRLVTPGTPLTLTCTVSGFSLSGAAMNWVRQAPGKGLEWIGVI

GNSGSTYYASWAKGRFTISKTSSTTVDLKMTSPTTEDTATYFCARGGGEF

FIWGQGTLVTVSS.

[0441] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that bind the same epitope as Ab2, and that contain a constant heavy chain sequence comprising the polypeptide of SEQ ID NO: 1244, 1245, or 1246, or comprising the sequence set forth below:

(SEQ ID NO: 90)
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV

HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDARVEP

KSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS

HEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGK

EYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTC

LVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW

QQGNVFSCSVMHEALHNHYTQKSLSLSPGK.

[0442] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a light chain sequence comprising the sequence of SEQ ID NO: 101 which consists of the light chain variable region of SEQ ID NO: 102 linked to the light chain constant region of SEQ ID NO: 110.

[0443] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a variable light chain sequence comprising the sequence set forth below:

(SEQ ID NO: 102)
AQVLTQTPSPVSAAVGGTVTINCQSSESVYKNNYLSWYQQKPGQPPKFLI

YQASNLADGVPSRFKGSGSGTQFTLTISDLECDDAATYYCAGGYSTYMSG

FGGGTEVVVKR.

[0444] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP, that bind the same epitope as Ab2, and that contain a constant light chain sequence comprising the sequence set forth below:

(SEQ ID NO: 110)
TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGN

SQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKS

FNRGEC.

[0445] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 84; SEQ ID NO: 86; and SEQ ID NO: 88, which correspond to the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 81, or which contain the variable heavy chain sequence of SEQ ID NO: 82, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 104; SEQ ID NO: 106; and SEQ ID NO: 108, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 101, or which contain the variable light chain sequence of SEQ ID NO: 102, or antibodies or antigen-binding fragments containing combinations of sequences that are at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention and antigen-binding fragments comprise, or alternatively consist of, combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

[0446] The invention further contemplates anti-PACAP antibodies and antigen-binding fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 83; SEQ ID NO: 85; SEQ ID NO: 87; and SEQ ID NO: 89, which correspond to the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 81, or the variable heavy chain sequence of SEQ ID NO: 82, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 103; SEQ ID NO: 105; SEQ ID NO: 107; and SEQ ID NO: 109, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 101, or the variable light chain sequence of SEQ ID NO: 102, or combinations of these polypeptide sequences, or sequences that are at least 80%, 90%, 95%, 96%, 97%, 98%, or 99% identical therewith.

[0447] In another embodiment of the invention, the anti-PACAP antibodies and antigen-binding fragments of the invention or fragments comprise, or alternatively consist of, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them, or sequences that are at least 90% or 95% identical thereto.

[0448] In another embodiment of the invention, the anti-PACAP antibodies and antigen-binding fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 81, or SEQ ID NO: 82, or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, the antibodies and antigen-binding fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 101, or SEQ ID NO: 102, or polypeptides that are at least 90% or 95% identical thereto.

[0449] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, or three of the polypeptide sequences of SEQ ID NO: 84; SEQ ID NO: 86; and SEQ ID NO: 88, which correspond to the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 81, or the variable heavy chain sequence of SEQ ID NO: 82, or sequences that are at least 90% or 95% identical thereto.

[0450] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, or three of the polypeptide sequences of SEQ ID NO: 104; SEQ ID NO: 106; and SEQ ID NO: 108, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 101, or the variable light chain sequence of SEQ ID NO: 102, or sequences that are at least 90% or 95% identical thereto.

[0451] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 83; SEQ ID NO: 85; SEQ ID NO: 87; and SEQ ID NO: 89, which correspond to the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 81, or the variable heavy chain sequence of SEQ ID NO: 82, or sequences that are at least 90% or 95% identical thereto.

[0452] In a further embodiment of the invention, the subject antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 103; SEQ ID NO: 105; SEQ ID NO: 107; and SEQ ID NO: 109, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 101, or the variable light chain sequence of SEQ ID NO: 102, or sequences that are at least 90% or 95% identical thereto.

[0453] The invention also contemplates anti-PACAP antibodies and antigen-binding fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 82; the variable light chain region of SEQ ID NO: 102; the complementarity determining regions (SEQ ID NO: 84; SEQ ID NO: 86; and SEQ ID NO: 88) of the variable heavy chain region of SEQ ID NO: 82; and the complementarity determining regions (SEQ ID NO: 104; SEQ ID NO: 106; and SEQ ID NO: 108) of the variable light chain region of SEQ ID NO: 102, or sequences that are at least 90% or 95% identical thereto. In another embodiment of the invention, fragments of the antibodies having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 82; the variable light chain region of SEQ ID NO: 102; the framework regions (SEQ ID NO: 83; SEQ ID NO: 85; SEQ ID NO: 87; and SEQ ID NO: 89) of the variable heavy chain region of SEQ ID NO: 82; and the framework regions (SEQ ID NO: 103; SEQ ID NO: 105; SEQ ID NO: 107; and SEQ ID NO: 109) of the variable light chain region of SEQ ID NO: 102, or sequences that are at least 90% or 95% identical thereto.

[0454] In another embodiment of the invention, the anti-PACAP antibody is Ab2, comprising, or alternatively consisting of, SEQ ID NO: 81 and SEQ ID NO: 101, or SEQ ID

NO: 82 and SEQ ID NO: 102, or an antibody or antigen-binding fragment comprising the CDRs of Ab2 and having at least one of the biological activities set forth herein, or is an anti-PACAP antibody that competes with Ab2 in binding PACAP, preferably one containing sequences that are at least 90%, 95%, 96%, 97%, 98%, or 99% identical to that of Ab2, or an antibody that binds to the same or overlapping epitope (s) on PACAP as Ab2.

[0455] In a further embodiment of the invention, antigen-binding fragments comprise, or alternatively consist of, Fab fragments having binding specificity for PACAP. With respect to antibody Ab2, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 82 and the variable light chain sequence of SEQ ID NO: 102, or sequences that are at least 90%, 95%, 96%, 97%, 98%, or 99% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 82 and/or SEQ ID NO: 102 that retain the binding specificity for PACAP.

[0456] In one embodiment of the invention described herein, Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab2. In another embodiment of the invention, anti-PACAP antibodies such as Ab2 and Fab fragments may be produced via expression in mammalian cells, such as CHO, NSO, or HEK 293 cells, fungal, insect, or microbial systems, such as yeast cells (for example haploid or diploid yeast, such as haploid or diploid *Pichia*) and other yeast strains. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*.

[0457] In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to PACAP, including the heavy and/or light chains of Ab2, as well as fragments, variants, and combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them, or sequences that are at least 90% or 95% identical thereto.

Antibody Ab3

[0458] In one embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that possess a heavy chain sequence comprising the sequence of SEQ ID NO: 681 which consists of the heavy chain variable region of SEQ ID NO: 682 linked to the heavy chain constant region of SEQ ID NO: 690.

[0459] In one embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a variable heavy chain sequence comprising the sequence set forth below:

(SEQ ID NO: 682)
QEQLVESGGGLVQPEGSLTLTCTASGFSFSSSDYMCWVRQAPGKGLEWIG

CIDAGSSGDTYFASWAKGRFTISKTSSTTVTLQMTSLTAADTATYFCARH

LYGSITFAFGLWGQGTLVTVSS.

[0460] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that bind the same epitope as Ab3, and that contain a constant heavy chain sequence comprising the polypeptide of SEQ ID NO: 1244, 1245, or 1246, or comprising the sequence set forth below:

(SEQ ID NO: 690)
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV

HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDARVEP

KSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS

HEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGK

EYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTC

LVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW

QQGNVFSCSVMHEALHNHYTQKSLSLSPGK.

[0461] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a light chain sequence comprising the sequence of SEQ ID NO: 701 which consists of the light chain variable region of SEQ ID NO: 702 linked to the light chain constant region of SEQ ID NO: 710.

[0462] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a variable light chain sequence comprising the sequence set forth below:

(SEQ ID NO: 702)
AAVLTQTPSPVSAAVGGTVTINCQASQSIGSDLAWYQQKPGQPPKLLIYD

ASTLASGVPSRFSGSGSGTQFTLTISGVQCDDAATYYCQGTYYSSGWYTA

FGGGTEVVVKR.

[0463] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP, that bind the same epitope as Ab3, and that contain a constant light chain sequence comprising the sequence set forth below:

(SEQ ID NO: 710)
TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGN

SQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKS

FNRGEC.

[0464] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 684; SEQ ID NO: 686; and SEQ ID NO: 688, which correspond to the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 681, or which contain the variable heavy chain sequence of SEQ ID NO: 682, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 704; SEQ ID NO: 706; and SEQ ID NO: 708, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 701, or which contain the variable light chain sequence of SEQ ID NO: 702, or antibodies or antigen-binding fragments containing combinations of sequences that are at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention and antigen-binding fragments comprise, or alternatively consist of, combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or

the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

[0465] The invention further contemplates anti-PACAP antibodies and antigen-binding fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 683; SEQ ID NO: 685; SEQ ID NO: 687; and SEQ ID NO: 689, which correspond to the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 681, or the variable heavy chain sequence of SEQ ID NO: 682, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 703; SEQ ID NO: 705; SEQ ID NO: 707; and SEQ ID NO: 709, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 701, or the variable light chain sequence of SEQ ID NO: 702, or combinations of these polypeptide sequences, or sequences that are at least 80%, 90%, 95%, 96%, 97%, 98%, or 99% identical therewith.

[0466] In another embodiment of the invention, the anti-PACAP antibodies and antigen-binding fragments of the invention or fragments comprise, or alternatively consist of, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them, or sequences that are at least 90% or 95% identical thereto.

[0467] In another embodiment of the invention, the anti-PACAP antibodies and antigen-binding fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 681, or SEQ ID NO: 682, or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, the antibodies and antigen-binding fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 701, or SEQ ID NO: 702, or polypeptides that are at least 90% or 95% identical thereto.

[0468] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, or three of the polypeptide sequences of SEQ ID NO: 684; SEQ ID NO: 686; and SEQ ID NO: 688, which correspond to the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 681, or the variable heavy chain sequence of SEQ ID NO: 682, or sequences that are at least 90% or 95% identical thereto.

[0469] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, or three of the polypeptide sequences of SEQ ID NO: 704; SEQ ID NO: 706; and SEQ ID NO: 708, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 701, or the variable light chain sequence of SEQ ID NO: 702, or sequences that are at least 90% or 95% identical thereto.

[0470] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 683; SEQ ID NO: 685; SEQ ID NO: 687; and SEQ ID NO: 689, which correspond to the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 681, or the variable heavy chain sequence of SEQ ID NO: 682, or sequences that are at least 90% or 95% identical thereto.

[0471] In a further embodiment of the invention, the subject antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 703; SEQ ID NO: 705; SEQ ID NO: 707; and SEQ ID NO: 709, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 701, or the variable light chain sequence of SEQ ID NO: 702, or sequences that are at least 90% or 95% identical thereto.

[0472] The invention also contemplates anti-PACAP antibodies and antigen-binding fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 682; the variable light chain region of SEQ ID NO: 702; the complementarity determining regions (SEQ ID NO: 684; SEQ ID NO: 686; and SEQ ID NO: 688) of the variable heavy chain region of SEQ ID NO: 682; and the complementarity determining regions (SEQ ID NO: 704; SEQ ID NO: 706; and SEQ ID NO: 708) of the variable light chain region of SEQ ID NO: 702, or sequences that are at least 90% or 95% identical thereto. In another embodiment of the invention, fragments of the antibodies having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 682; the variable light chain region of SEQ ID NO: 702; the framework regions (SEQ ID NO: 683; SEQ ID NO: 685; SEQ ID NO: 687; and SEQ ID NO: 689) of the variable heavy chain region of SEQ ID NO: 682; and the framework regions (SEQ ID NO: 703; SEQ ID NO: 705; SEQ ID NO: 707; and SEQ ID NO: 709) of the variable light chain region of SEQ ID NO: 702, or sequences that are at least 90% or 95% identical thereto.

[0473] In another embodiment of the invention, the anti-PACAP antibody is Ab3, comprising, or alternatively consisting of, SEQ ID NO: 681 and SEQ ID NO: 701, or SEQ ID NO: 682 and SEQ ID NO: 702, or an antibody or antigen-binding fragment comprising the CDRs of Ab3 and having at least one of the biological activities set forth herein, or is an anti-PACAP antibody that competes with Ab3 in binding PACAP, preferably one containing sequences that are at least 90%, 95%, 96%, 97%, 98%, or 99% identical to that of Ab3, or an antibody that binds to the same or overlapping epitope(s) on PACAP as Ab3.

[0474] In a further embodiment of the invention, antigen-binding fragments comprise, or alternatively consist of, Fab fragments having binding specificity for PACAP. With respect to antibody Ab3, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 682 and the variable light chain sequence of SEQ ID NO: 702, or sequences that are at least 90%, 95%, 96%, 97%, 98%, or 99% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 682 and/or SEQ ID NO: 702 that retain the binding specificity for PACAP.

[0475] In one embodiment of the invention described herein, Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab3. In another embodiment of the invention, anti-PACAP antibodies such as Ab3 and Fab fragments may be produced via expression in mammalian cells, such as CHO, NSO, or HEK 293 cells, fungal, insect,

or microbial systems, such as yeast cells (for example haploid or diploid yeast, such as haploid or diploid *Pichia*) and other yeast strains. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*.

[0476] In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to PACAP, including the heavy and/or light chains of Ab3, as well as fragments, variants, and combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them, or sequences that are at least 90% or 95% identical thereto.

Antibody Ab4

[0477] In one embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that possess a heavy chain sequence comprising the sequence of SEQ ID NO: 641 which consists of the heavy chain variable region of SEQ ID NO: 642 linked to the heavy chain constant region of SEQ ID NO: 650.

[0478] In one embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a variable heavy chain sequence comprising the sequence set forth below:

(SEQ ID NO: 642)
QSVEESGGRLVTPGTPLTLTCTVSGFSLSSYDMSWVRQAPGKGLEYIGII

NTNDDTWYASWVKGRFTISKTSSTTVDLKMTSLTTEDTATYFCARISDAY

VFDYAYYFTLWGQGTLVTVSS.

[0479] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that bind the same epitope as Ab4, and that contain a constant heavy chain sequence comprising the polypeptide of SEQ ID NO: 1244, 1245, or 1246, or comprising the sequence set forth below:

(SEQ ID NO: 650)
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV

HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDARVEP

KSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS

HEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGK

EYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTC

LVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW

QQGNVFSCSVMHEALHNHYTQKSLSLSPGK.

[0480] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a light chain sequence comprising the sequence of SEQ ID NO: 661 which consists of the light chain variable region of SEQ ID NO: 662 linked to the light chain constant region of SEQ ID NO: 670.

[0481] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a variable light chain sequence comprising the sequence set forth below:

(SEQ ID NO: 662)
ALVMTQTPSSVSAAVGGTVTINCLASQNIYNSLAWYQQKPGQPPKLLIYR

ASTLASGVSSRFKGSGSGTQFTLTISGVECADAATYYCQQGAGADNIGNP

FGGGTEVVVKR.

[0482] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP, that bind the same epitope as Ab4, and that contain a constant light chain sequence comprising the sequence set forth below:

(SEQ ID NO: 670)
TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGN

SQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKS

FNRGEC.

[0483] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 644; SEQ ID NO: 646; and SEQ ID NO: 648, which correspond to the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 641, or which contain the variable heavy chain sequence of SEQ ID NO: 642, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 664; SEQ ID NO: 666; and SEQ ID NO: 668, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 661, or which contain the variable light chain sequence of SEQ ID NO: 662, or antibodies or antigen-binding fragments containing combinations of sequences that are at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention and antigen-binding fragments comprise, or alternatively consist of, combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

[0484] The invention further contemplates anti-PACAP antibodies and antigen-binding fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 643; SEQ ID NO: 645; SEQ ID NO: 647; and SEQ ID NO: 649, which correspond to the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 641, or the variable heavy chain sequence of SEQ ID NO: 642, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 663; SEQ ID NO: 665; SEQ ID NO: 667; and SEQ ID NO: 669, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 661, or the variable light chain sequence of SEQ ID NO: 662, or combinations of these polypeptide sequences, or sequences that are at least 80%, 90%, 95%, 96%, 97%, 98%, or 99% identical therewith.

[0485] In another embodiment of the invention, the anti-PACAP antibodies and antigen-binding fragments of the invention or fragments comprise, or alternatively consist of, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them, or sequences that are at least 90% or 95% identical thereto.

[0486] In another embodiment of the invention, the anti-PACAP antibodies and antigen-binding fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 641, or SEQ ID NO: 642, or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, the antibodies and antigen-binding fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 661, or SEQ ID NO: 662, or polypeptides that are at least 90% or 95% identical thereto.

[0487] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, or three of the polypeptide sequences of SEQ ID NO: 644; SEQ ID NO: 646; and SEQ ID NO: 648, which correspond to the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 641, or the variable heavy chain sequence of SEQ ID NO: 642, or sequences that are at least 90% or 95% identical thereto.

[0488] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, or three of the polypeptide sequences of SEQ ID NO: 664; SEQ ID NO: 666; and SEQ ID NO: 668, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 661, or the variable light chain sequence of SEQ ID NO: 662, or sequences that are at least 90% or 95% identical thereto.

[0489] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 643; SEQ ID NO: 645; SEQ ID NO: 647; and SEQ ID NO: 649, which correspond to the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 641, or the variable heavy chain sequence of SEQ ID NO: 642, or sequences that are at least 90% or 95% identical thereto.

[0490] In a further embodiment of the invention, the subject antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 663; SEQ ID NO: 665; SEQ ID NO: 667; and SEQ ID NO: 669, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 661, or the variable light chain sequence of SEQ ID NO: 662, or sequences that are at least 90% or 95% identical thereto.

[0491] The invention also contemplates anti-PACAP antibodies and antigen-binding fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 642; the variable light chain region of SEQ ID NO: 662; the complementarity determining regions (SEQ ID NO: 644; SEQ ID NO: 646; and SEQ ID NO: 648) of the variable heavy chain region of SEQ ID NO: 642; and the complementarity determining regions (SEQ ID NO: 664; SEQ ID NO: 666; and SEQ ID NO: 668) of the variable light chain region of SEQ ID NO: 662, or sequences that are at least 90% or 95% identical thereto. In another embodiment of the invention, fragments of the antibodies having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 642; the variable light chain region of SEQ ID NO: 662; the framework regions (SEQ ID NO: 643; SEQ ID NO: 645; SEQ ID NO: 647; and SEQ ID NO: 649) of the variable heavy chain region of SEQ ID NO: 642; and the framework regions (SEQ ID NO: 663; SEQ ID NO: 665; SEQ ID NO: 667; and SEQ ID NO: 669) of the variable light chain region of SEQ ID NO: 662, or sequences that are at least 90% or 95% identical thereto.

[0492] In another embodiment of the invention, the anti-PACAP antibody is Ab4, comprising, or alternatively consisting of, SEQ ID NO: 641 and SEQ ID NO: 661, or SEQ ID NO: 642 and SEQ ID NO: 662, or an antibody or antigen-binding fragment comprising the CDRs of Ab4 and having at least one of the biological activities set forth herein, or is an anti-PACAP antibody that competes with Ab4 in binding PACAP, preferably one containing sequences that are at least 90%, 95%, 96%, 97%, 98%, or 99% identical to that of Ab4, or an antibody that binds to the same or overlapping epitope(s) on PACAP as Ab4.

[0493] In a further embodiment of the invention, antigen-binding fragments comprise, or alternatively consist of, Fab fragments having binding specificity for PACAP. With respect to antibody Ab4, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 642 and the variable light chain sequence of SEQ ID NO: 662, or sequences that are at least 90%, 95%, 96%, 97%, 98%, or 99% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 642 and/or SEQ ID NO: 662 that retain the binding specificity for PACAP.

[0494] In one embodiment of the invention described herein, Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab4. In another embodiment of the invention, anti-PACAP antibodies such as Ab4 and Fab fragments may be produced via expression in mammalian cells, such as CHO, NSO, or HEK 293 cells, fungal, insect, or microbial systems, such as yeast cells (for example haploid or diploid yeast, such as haploid or diploid *Pichia*) and other yeast strains. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*.

[0495] In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to PACAP, including the heavy and/or light chains of Ab4, as well as fragments, variants, and combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them, or sequences that are at least 90% or 95% identical thereto.

Antibody Ab5

[0496] In one embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that possess a heavy chain sequence comprising the sequence of SEQ ID NO: 481 which consists of the heavy chain variable region of SEQ ID NO: 482 linked to the heavy chain constant region of SEQ ID NO: 490.

[0497] In one embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a variable heavy chain sequence comprising the sequence set forth below:

(SEQ ID NO: 482)
QSVEESGGRLVTPGTPLTLTCTVSGFSLSSYAMIWVRQAPGKGLEWIGII

YDNGDTYYASWAKGRFTISKTSTTVYLKIASPTTEDTATYFCAREPGSTT

QNDLWGQGTLVTVSS.

[0498] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that bind the same epitope as Ab5, and that contain a constant heavy chain sequence comprising the polypeptide of SEQ ID NO: 1244, 1245, or 1246, or comprising the sequence set forth below:

(SEQ ID NO: 490)
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV

HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDARVEP

KSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS

HEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGK

EYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTC

LVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW

QQGNVFSCSVMHEALHNHYTQKSLSLSPGK.

[0499] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a light chain sequence comprising the sequence of SEQ ID NO: 501 which consists of the light chain variable region of SEQ ID NO: 502 linked to the light chain constant region of SEQ ID NO: 510.

[0500] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a variable light chain sequence comprising the sequence set forth below:

(SEQ ID NO: 502)
DVVMTQTPASVSEPVGGTVTIKCQASENIYNSLLWYQQKPGQPPKLLIYR

ASTLASGVSSRFKGSGSGTEFTLTISDLECADAATYYCQNYYNIWTNGAA

FGGGTEVVVKR.

[0501] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP, that bind the same epitope as Ab5, and that contain a constant light chain sequence comprising the sequence set forth below:

(SEQ ID NO: 510)
TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGN

SQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKS

FNRGEC.

[0502] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 484; SEQ ID NO: 486; and SEQ ID NO: 488, which correspond to the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 481, or which contain the variable heavy chain sequence of SEQ ID NO: 482, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 504; SEQ ID NO: 506; and SEQ ID NO: 508, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 501, or which contain the variable light chain sequence of SEQ ID NO: 502, or antibodies or antigen-binding fragments containing combinations of sequences that are at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention and antigen-binding fragments comprise, or alternatively consist of, combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

[0503] The invention further contemplates anti-PACAP antibodies and antigen-binding fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 483; SEQ ID NO: 485; SEQ ID NO: 487; and SEQ ID NO: 489, which correspond to the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 481, or the variable heavy chain sequence of SEQ ID NO: 482, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 503; SEQ ID NO: 505; SEQ ID NO: 507; and SEQ ID NO: 509, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 501, or the variable light chain sequence of SEQ ID NO: 502, or combinations of these polypeptide sequences, or sequences that are at least 80%, 90%, 95%, 96%, 97%, 98%, or 99% identical therewith.

[0504] In another embodiment of the invention, the anti-PACAP antibodies and antigen-binding fragments of the invention or fragments comprise, or alternatively consist of, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them, or sequences that are at least 90% or 95% identical thereto.

[0505] In another embodiment of the invention, the anti-PACAP antibodies and antigen-binding fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 481, or SEQ ID NO: 482, or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, the antibodies and antigen-binding fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 501, or SEQ ID NO: 502, or polypeptides that are at least 90% or 95% identical thereto.

[0506] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, or three of the polypeptide sequences of SEQ ID NO: 484; SEQ ID NO: 486; and SEQ ID NO: 488, which correspond to the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 481, or the variable heavy chain sequence of SEQ ID NO: 482, or sequences that are at least 90% or 95% identical thereto.

[0507] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, or three of the polypeptide sequences of SEQ ID NO: 504; SEQ ID NO: 506; and SEQ ID NO: 508, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 501, or the variable light

chain sequence of SEQ ID NO: 502, or sequences that are at least 90% or 95% identical thereto.

[0508] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 483; SEQ ID NO: 485; SEQ ID NO: 487; and SEQ ID NO: 489, which correspond to the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 481, or the variable heavy chain sequence of SEQ ID NO: 482, or sequences that are at least 90% or 95% identical thereto.

[0509] In a further embodiment of the invention, the subject antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 503; SEQ ID NO: 505; SEQ ID NO: 507; and SEQ ID NO: 509, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 501, or the variable light chain sequence of SEQ ID NO: 502, or sequences that are at least 90% or 95% identical thereto.

[0510] The invention also contemplates anti-PACAP antibodies and antigen-binding fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 482; the variable light chain region of SEQ ID NO: 502; the complementarity determining regions (SEQ ID NO: 484; SEQ ID NO: 486; and SEQ ID NO: 488) of the variable heavy chain region of SEQ ID NO: 482; and the complementarity determining regions (SEQ ID NO: 504; SEQ ID NO: 506; and SEQ ID NO: 508) of the variable light chain region of SEQ ID NO: 502, or sequences that are at least 90% or 95% identical thereto. In another embodiment of the invention, fragments of the antibodies having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 482; the variable light chain region of SEQ ID NO: 502; the framework regions (SEQ ID NO: 483; SEQ ID NO: 485; SEQ ID NO: 487; and SEQ ID NO: 489) of the variable heavy chain region of SEQ ID NO: 482; and the framework regions (SEQ ID NO: 503; SEQ ID NO: 505; SEQ ID NO: 507; and SEQ ID NO: 509) of the variable light chain region of SEQ ID NO: 502, or sequences that are at least 90% or 95% identical thereto.

[0511] In another embodiment of the invention, the anti-PACAP antibody is Ab5, comprising, or alternatively consisting of, SEQ ID NO: 481 and SEQ ID NO: 501, or SEQ ID NO: 482 and SEQ ID NO: 502, or an antibody or antigen-binding fragment comprising the CDRs of Ab5 and having at least one of the biological activities set forth herein, or is an anti-PACAP antibody that competes with Ab5 in binding PACAP, preferably one containing sequences that are at least 90%, 95%, 96%, 97%, 98%, or 99% identical to that of Ab5, or an antibody that binds to the same or overlapping epitope(s) on PACAP as Ab5.

[0512] In a further embodiment of the invention, antigen-binding fragments comprise, or alternatively consist of, Fab fragments having binding specificity for PACAP. With respect to antibody Ab5, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 482 and the variable light chain sequence of SEQ ID NO: 502, or sequences that are at least 90%, 95%, 96%, 97%, 98%, or 99% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 482 and/or SEQ ID NO: 502 that retain the binding specificity for PACAP.

[0513] In one embodiment of the invention described herein, Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab5. In another embodiment of the invention, anti-PACAP antibodies such as Ab5 and Fab fragments may be produced via expression in mammalian cells, such as CHO, NSO, or HEK 293 cells, fungal, insect, or microbial systems, such as yeast cells (for example haploid or diploid yeast, such as haploid or diploid *Pichia*) and other yeast strains. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*.

[0514] In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to PACAP, including the heavy and/or light chains of Ab5, as well as fragments, variants, and combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them, or sequences that are at least 90% or 95% identical thereto.

Antibody Ab6

[0515] In one embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that possess a heavy chain sequence comprising the sequence of SEQ ID NO: 721 which consists of the heavy chain variable region of SEQ ID NO: 722 linked to the heavy chain constant region of SEQ ID NO: 730.

[0516] In one embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a variable heavy chain sequence comprising the sequence set forth below:

(SEQ ID NO: 722)
QQLEQSGGGAEGGLVKPGGSLELCCKASGFSLSSTYWMCWVRQAPGKGLE

WIGCIYTGSGSTDYASWVNGQFTLSRDIDQSTGCLQLNSLTVADTAMYYC

TKNFDLWGPGTLVTVSS.

[0517] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that bind the same epitope as Ab6, and that contain a constant heavy chain sequence comprising the polypeptide of SEQ ID NO: 1244, 1245, or 1246, or comprising the sequence set forth below:

(SEQ ID NO: 730)
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV

HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDARVEP

KSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS

HEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGK

EYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTC

-continued

LVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW

QQGNVFSCSVMHEALHNHYTQKSLSLSPGK.

[0518] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a light chain sequence comprising the sequence of SEQ ID NO: 741 which consists of the light chain variable region of SEQ ID NO: 742 linked to the light chain constant region of SEQ ID NO: 750.

[0519] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a variable light chain sequence comprising the sequence set forth below:

(SEQ ID NO: 742)

AQVLTQTPSSVSAAVGGTVTINCQSSPSVYSNNYLSWFQQKPGQPPKGLI

ADASTLASGVPSRFKGSGSGTQFTLTISGVQCDDAAAYYCLGYYDCGSTD

CHAFGGGTEVVVKR.

[0520] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP, that bind the same epitope as Ab6, and that contain a constant light chain sequence comprising the sequence set forth below:

(SEQ ID NO: 750)

TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGN

SQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKS

FNRGEC.

[0521] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 724; SEQ ID NO: 726; and SEQ ID NO: 728, which correspond to the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 721, or which contain the variable heavy chain sequence of SEQ ID NO: 722, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 744; SEQ ID NO: 746; and SEQ ID NO: 748, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 741, or which contain the variable light chain sequence of SEQ ID NO: 742, or antibodies or antigen-binding fragments containing combinations of sequences that are at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention and antigen-binding fragments comprise, or alternatively consist of, combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

[0522] The invention further contemplates anti-PACAP antibodies and antigen-binding fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 723; SEQ ID NO: 725; SEQ ID NO: 727; and SEQ ID NO: 729, which correspond to the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 721, or the variable heavy chain sequence of SEQ ID NO: 722, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 743; SEQ ID NO: 745; SEQ ID NO: 747; and SEQ ID NO: 749, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 741, or the variable light chain sequence of SEQ ID NO: 742, or combinations of these polypeptide sequences, or sequences that are at least 80%, 90%, 95%, 96%, 97%, 98%, or 99% identical therewith.

[0523] In another embodiment of the invention, the anti-PACAP antibodies and antigen-binding fragments of the invention or fragments comprise, or alternatively consist of, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them, or sequences that are at least 90% or 95% identical thereto.

[0524] In another embodiment of the invention, the anti-PACAP antibodies and antigen-binding fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 721, or SEQ ID NO: 722, or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, the antibodies and antigen-binding fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 741, or SEQ ID NO: 742, or polypeptides that are at least 90% or 95% identical thereto.

[0525] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, or three of the polypeptide sequences of SEQ ID NO: 724; SEQ ID NO: 726; and SEQ ID NO: 728, which correspond to the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 721, or the variable heavy chain sequence of SEQ ID NO: 722, or sequences that are at least 90% or 95% identical thereto.

[0526] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, or three of the polypeptide sequences of SEQ ID NO: 744; SEQ ID NO: 746; and SEQ ID NO: 748, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 741, or the variable light chain sequence of SEQ ID NO: 742, or sequences that are at least 90% or 95% identical thereto.

[0527] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 723; SEQ ID NO: 725; SEQ ID NO: 727; and SEQ ID NO: 729, which correspond to the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 721, or the variable heavy chain sequence of SEQ ID NO: 722, or sequences that are at least 90% or 95% identical thereto.

[0528] In a further embodiment of the invention, the subject antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 743; SEQ ID NO: 745; SEQ ID NO: 747; and SEQ ID NO: 749, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 741, or the variable light chain sequence of SEQ ID NO: 742, or sequences that are at least 90% or 95% identical thereto.

[0529] The invention also contemplates anti-PACAP antibodies and antigen-binding fragments that include one or

more of the antibody fragments described herein. In one embodiment of the invention, antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 722; the variable light chain region of SEQ ID NO: 742; the complementarity determining regions (SEQ ID NO: 724; SEQ ID NO: 726; and SEQ ID NO: 728) of the variable heavy chain region of SEQ ID NO: 722; and the complementarity determining regions (SEQ ID NO: 744; SEQ ID NO: 746; and SEQ ID NO: 748) of the variable light chain region of SEQ ID NO: 742, or sequences that are at least 90% or 95% identical thereto. In another embodiment of the invention, fragments of the antibodies having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 722; the variable light chain region of SEQ ID NO: 742; the framework regions (SEQ ID NO: 723; SEQ ID NO: 725; SEQ ID NO: 727; and SEQ ID NO: 729) of the variable heavy chain region of SEQ ID NO: 722; and the framework regions (SEQ ID NO: 743; SEQ ID NO: 745; SEQ ID NO: 747; and SEQ ID NO: 749) of the variable light chain region of SEQ ID NO: 742, or sequences that are at least 90% or 95% identical thereto.

[0530] In another embodiment of the invention, the anti-PACAP antibody is Ab6, comprising, or alternatively consisting of, SEQ ID NO: 721 and SEQ ID NO: 741, or SEQ ID NO: 722 and SEQ ID NO: 742, or an antibody or antigen-binding fragment comprising the CDRs of Ab6 and having at least one of the biological activities set forth herein, or is an anti-PACAP antibody that competes with Ab6 in binding PACAP, preferably one containing sequences that are at least 90%, 95%, 96%, 97%, 98%, or 99% identical to that of Ab6, or an antibody that binds to the same or overlapping epitope(s) on PACAP as Ab6.

[0531] In a further embodiment of the invention, antigen-binding fragments comprise, or alternatively consist of, Fab fragments having binding specificity for PACAP. With respect to antibody Ab6, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 722 and the variable light chain sequence of SEQ ID NO: 742, or sequences that are at least 90%, 95%, 96%, 97%, 98%, or 99% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 722 and/or SEQ ID NO: 742 that retain the binding specificity for PACAP.

[0532] In one embodiment of the invention described herein, Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab6. In another embodiment of the invention, anti-PACAP antibodies such as Ab6 and Fab fragments may be produced via expression in mammalian cells, such as CHO, NSO, or HEK 293 cells, fungal, insect, or microbial systems, such as yeast cells (for example haploid or diploid yeast, such as haploid or diploid *Pichia*) and other yeast strains. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*.

[0533] In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to PACAP, including the heavy and/or light chains of Ab6, as well as fragments, variants, and combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them, or sequences that are at least 90% or 95% identical thereto.

Antibody Ab7

[0534] In one embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that possess a heavy chain sequence comprising the sequence of SEQ ID NO: 521 which consists of the heavy chain variable region of SEQ ID NO: 522 linked to the heavy chain constant region of SEQ ID NO: 530.

[0535] In one embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a variable heavy chain sequence comprising the sequence set forth below:

(SEQ ID NO: 522)
QSVEESGGRLVTPGTPLTLTCTASGIDLSGYAMGWVRQAPGKGLEWIGDI

STYGTTDYASWVNGRFTISRTSTTVTLKMTSLTTEDTATYFCARDYWLSL

WGPGTLVTVSS.

[0536] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that bind the same epitope as Ab7, and that contain a constant heavy chain sequence comprising the polypeptide of SEQ ID NO: 1244, 1245, or 1246, or comprising the sequence set forth below:

(SEQ ID NO: 530)
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV

HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDARVEP

KSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS

HEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGK

EYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTC

LVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW

QQGNVFSCSVMHEALHNHYTQKSLSLSPGK.

[0537] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a light chain sequence comprising the sequence of SEQ ID NO: 541 which consists of the light chain variable region of SEQ ID NO: 542 linked to the light chain constant region of SEQ ID NO: 550.

[0538] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a variable light chain sequence comprising the sequence set forth below:

(SEQ ID NO: 542)
AAVLTQTPSPVSAAVGGTVTIKCQSSQSVYDNNALAWYQQKPGQPPKLLI

YAASTLASGVPSRFKGSGSGTQFTLTINGVQCDDAATYYCLGGYDDPADN

AFGGGTEVVVKR.

[0539] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding

specificity to PACAP, that bind the same epitope as Ab7, and that contain a constant light chain sequence comprising the sequence set forth below:

(SEQ ID NO: 550)
TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGN

SQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKS

FNRGEC.

[0540] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 524; SEQ ID NO: 526; and SEQ ID NO: 528, which correspond to the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 521, or which contain the variable heavy chain sequence of SEQ ID NO: 522, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 544; SEQ ID NO: 546; and SEQ ID NO: 548, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 541, or which contain the variable light chain sequence of SEQ ID NO: 542, or antibodies or antigen-binding fragments containing combinations of sequences that are at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention and antigen-binding fragments comprise, or alternatively consist of, combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

[0541] The invention further contemplates anti-PACAP antibodies and antigen-binding fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 523; SEQ ID NO: 525; SEQ ID NO: 527; and SEQ ID NO: 529, which correspond to the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 521, or the variable heavy chain sequence of SEQ ID NO: 522, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 543; SEQ ID NO: 545; SEQ ID NO: 547; and SEQ ID NO: 549, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 541, or the variable light chain sequence of SEQ ID NO: 542, or combinations of these polypeptide sequences, or sequences that are at least 80%, 90%, 95%, 96%, 97%, 98%, or 99% identical therewith.

[0542] In another embodiment of the invention, the anti-PACAP antibodies and antigen-binding fragments of the invention or fragments comprise, or alternatively consist of, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them, or sequences that are at least 90% or 95% identical thereto.

[0543] In another embodiment of the invention, the anti-PACAP antibodies and antigen-binding fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 521, or SEQ ID NO: 522, or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, the antibodies and antigen-binding fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 541, or SEQ ID NO: 542, or polypeptides that are at least 90% or 95% identical thereto.

[0544] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, or three of the polypeptide sequences of SEQ ID NO: 524; SEQ ID NO: 526; and SEQ ID NO: 528, which correspond to the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 521, or the variable heavy chain sequence of SEQ ID NO: 522, or sequences that are at least 90% or 95% identical thereto.

[0545] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, or three of the polypeptide sequences of SEQ ID NO: 544; SEQ ID NO: 546; and SEQ ID NO: 548, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 541, or the variable light chain sequence of SEQ ID NO: 542, or sequences that are at least 90% or 95% identical thereto.

[0546] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 523; SEQ ID NO: 525; SEQ ID NO: 527; and SEQ ID NO: 529, which correspond to the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 521, or the variable heavy chain sequence of SEQ ID NO: 522, or sequences that are at least 90% or 95% identical thereto.

[0547] In a further embodiment of the invention, the subject antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 543; SEQ ID NO: 545; SEQ ID NO: 547; and SEQ ID NO: 549, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 541, or the variable light chain sequence of SEQ ID NO: 542, or sequences that are at least 90% or 95% identical thereto.

[0548] The invention also contemplates anti-PACAP antibodies and antigen-binding fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 522; the variable light chain region of SEQ ID NO: 542; the complementarity determining regions (SEQ ID NO: 524; SEQ ID NO: 526; and SEQ ID NO: 528) of the variable heavy chain region of SEQ ID NO: 522; and the complementarity determining regions (SEQ ID NO: 544; SEQ ID NO: 546; and SEQ ID NO: 548) of the variable light chain region of SEQ ID NO: 542, or sequences that are at least 90% or 95% identical thereto. In another embodiment of the invention, fragments of the antibodies having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 522; the variable light chain region of SEQ ID NO: 542; the framework regions (SEQ ID NO: 523; SEQ ID NO: 525; SEQ ID NO: 527; and SEQ ID NO: 529) of the variable heavy chain region of SEQ ID NO: 522; and the framework regions (SEQ ID NO: 543; SEQ ID NO: 545; SEQ ID NO: 547; and

SEQ ID NO: 549) of the variable light chain region of SEQ ID NO: 542, or sequences that are at least 90% or 95% identical thereto.

[0549] In another embodiment of the invention, the anti-PACAP antibody is Ab7, comprising, or alternatively consisting of, SEQ ID NO: 521 and SEQ ID NO: 541, or SEQ ID NO: 522 and SEQ ID NO: 542, or an antibody or antigen-binding fragment comprising the CDRs of Ab7 and having at least one of the biological activities set forth herein, or is an anti-PACAP antibody that competes with Ab7 in binding PACAP, preferably one containing sequences that are at least 90%, 95%, 96%, 97%, 98%, or 99% identical to that of Ab7, or an antibody that binds to the same or overlapping epitope(s) on PACAP as Ab7.

[0550] In a further embodiment of the invention, antigen-binding fragments comprise, or alternatively consist of, Fab fragments having binding specificity for PACAP. With respect to antibody Ab7, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 522 and the variable light chain sequence of SEQ ID NO: 542, or sequences that are at least 90%, 95%, 96%, 97%, 98%, or 99% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 522 and/or SEQ ID NO: 542 that retain the binding specificity for PACAP.

[0551] In one embodiment of the invention described herein, Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab7. In another embodiment of the invention, anti-PACAP antibodies such as Ab7 and Fab fragments may be produced via expression in mammalian cells, such as CHO, NSO, or HEK 293 cells, fungal, insect, or microbial systems, such as yeast cells (for example haploid or diploid yeast, such as haploid or diploid *Pichia*) and other yeast strains. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*.

[0552] In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to PACAP, including the heavy and/or light chains of Ab7, as well as fragments, variants, and combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them, or sequences that are at least 90% or 95% identical thereto.

Antibody Ab8

[0553] In one embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that possess a heavy chain sequence comprising the sequence of SEQ ID NO: 761 which consists of the heavy chain variable region of SEQ ID NO: 762 linked to the heavy chain constant region of SEQ ID NO: 770.

[0554] In one embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a variable heavy chain sequence comprising the sequence set forth below:

(SEQ ID NO: 762)
QQLEQSGGGAEGGLVKPGGSLELCCKASGFSLTTSHWMCWVRQAPGKGLN

WIGCISAGSGDADYATWVDAQFTLSRDIDQNTGCLQLNSLTPADTAMYYC

TINFELWGQGTLVTVSS.

[0555] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that bind the same epitope as Ab8, and that contain a constant heavy chain sequence comprising the polypeptide of SEQ ID NO: 1244, 1245, or 1246, or comprising the sequence set forth below:

(SEQ ID NO: 770)
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV

HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDARVEP

KSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS

HEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGK

EYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTC

LVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW

QQGNVFSCSVMHEALHNHYTQKSLSLSPGK.

[0556] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a light chain sequence comprising the sequence of SEQ ID NO: 781 which consists of the light chain variable region of SEQ ID NO: 782 linked to the light chain constant region of SEQ ID NO: 790.

[0557] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a variable light chain sequence comprising the sequence set forth below:

(SEQ ID NO: 782)
AQVLTQTPSSVSAAVGGTVTINCQSSPSVYSSYLSWFQQKPGQPPKFLIY

EASKLASGVPSRFSGSGSGTQFTLTISGVQCSDAATYYCLGAYDCGRTDC

HAFGGGTEVVVKR.

[0558] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP, that bind the same epitope as Ab8, and that contain a constant light chain sequence comprising the sequence set forth below:

(SEQ ID NO: 790)
TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGN

SQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKS

FNRGEC.

[0559] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 764; SEQ ID NO: 766; and SEQ ID NO: 768, which correspond to the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 761, or which contain the variable heavy chain sequence of SEQ ID NO: 762, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 784; SEQ ID NO: 786; and SEQ ID NO: 788, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 781, or which contain the variable light chain sequence of SEQ ID NO: 782, or antibodies or antigen-binding fragments containing combinations of sequences that are at least 80%, 85%, 90%, 95%,

96%, 97%, 98%, or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention and antigen-binding fragments comprise, or alternatively consist of, combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

[0560] The invention further contemplates anti-PACAP antibodies and antigen-binding fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 763; SEQ ID NO: 765; SEQ ID NO: 767; and SEQ ID NO: 769, which correspond to the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 761, or the variable heavy chain sequence of SEQ ID NO: 762, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 783; SEQ ID NO: 785; SEQ ID NO: 787; and SEQ ID NO: 789, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 781, or the variable light chain sequence of SEQ ID NO: 782, or combinations of these polypeptide sequences, or sequences that are at least 80%, 90%, 95%, 96%, 97%, 98%, or 99% identical therewith.

[0561] In another embodiment of the invention, the anti-PACAP antibodies and antigen-binding fragments of the invention or fragments comprise, or alternatively consist of, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them, or sequences that are at least 90% or 95% identical thereto.

[0562] In another embodiment of the invention, the anti-PACAP antibodies and antigen-binding fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 761, or SEQ ID NO: 762, or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, the antibodies and antigen-binding fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 781, or SEQ ID NO: 782, or polypeptides that are at least 90% or 95% identical thereto.

[0563] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, or three of the polypeptide sequences of SEQ ID NO: 764; SEQ ID NO: 766; and SEQ ID NO: 768, which correspond to the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 761, or the variable heavy chain sequence of SEQ ID NO: 762, or sequences that are at least 90% or 95% identical thereto.

[0564] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, or three of the polypeptide sequences of SEQ ID NO: 784; SEQ ID NO: 786; and SEQ ID NO: 788, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 781, or the variable light chain sequence of SEQ ID NO: 782, or sequences that are at least 90% or 95% identical thereto.

[0565] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 763; SEQ ID NO: 765; SEQ ID NO: 767; and SEQ ID NO: 769, which correspond to the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 761, or the variable heavy chain sequence of SEQ ID NO: 762, or sequences that are at least 90% or 95% identical thereto.

[0566] In a further embodiment of the invention, the subject antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 783; SEQ ID NO: 785; SEQ ID NO: 787; and SEQ ID NO: 789, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 781, or the variable light chain sequence of SEQ ID NO: 782, or sequences that are at least 90% or 95% identical thereto.

[0567] The invention also contemplates anti-PACAP antibodies and antigen-binding fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 762; the variable light chain region of SEQ ID NO: 782; the complementarity determining regions (SEQ ID NO: 764; SEQ ID NO: 766; and SEQ ID NO: 768) of the variable heavy chain region of SEQ ID NO: 762; and the complementarity determining regions (SEQ ID NO: 784; SEQ ID NO: 786; and SEQ ID NO: 788) of the variable light chain region of SEQ ID NO: 782, or sequences that are at least 90% or 95% identical thereto. In another embodiment of the invention, fragments of the antibodies having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 762; the variable light chain region of SEQ ID NO: 782; the framework regions (SEQ ID NO: 763; SEQ ID NO: 765; SEQ ID NO: 767; and SEQ ID NO: 769) of the variable heavy chain region of SEQ ID NO: 762; and the framework regions (SEQ ID NO: 783; SEQ ID NO: 785; SEQ ID NO: 787; and SEQ ID NO: 789) of the variable light chain region of SEQ ID NO: 782, or sequences that are at least 90% or 95% identical thereto.

[0568] In another embodiment of the invention, the anti-PACAP antibody is Ab8, comprising, or alternatively consisting of, SEQ ID NO: 761 and SEQ ID NO: 781, or SEQ ID NO: 762 and SEQ ID NO: 782, or an antibody or antigen-binding fragment comprising the CDRs of Ab8 and having at least one of the biological activities set forth herein, or is an anti-PACAP antibody that competes with Ab8 in binding PACAP, preferably one containing sequences that are at least 90%, 95%, 96%, 97%, 98%, or 99% identical to that of Ab8, or an antibody that binds to the same or overlapping epitope(s) on PACAP as Ab8.

[0569] In a further embodiment of the invention, antigen-binding fragments comprise, or alternatively consist of, Fab fragments having binding specificity for PACAP. With respect to antibody Ab8, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 762 and the variable light chain sequence of SEQ ID NO: 782, or sequences that are at least 90%, 95%, 96%, 97%, 98%, or 99% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 762 and/or SEQ ID NO: 782 that retain the binding specificity for PACAP.

[0570] In one embodiment of the invention described herein, Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab8. In another embodiment of the invention, anti-PACAP antibodies such as Ab8 and Fab fragments may be produced via expression in mammalian cells, such as CHO, NSO, or HEK 293 cells, fungal, insect, or microbial systems, such as yeast cells (for example haploid or diploid yeast, such as haploid or diploid *Pichia*) and other yeast strains. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*.

[0571] In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to PACAP, including the heavy and/or light chains of Ab8, as well as fragments, variants, and combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them, or sequences that are at least 90% or 95% identical thereto.

Antibody Ab9

[0572] In one embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that possess a heavy chain sequence comprising the sequence of SEQ ID NO: 801 which consists of the heavy chain variable region of SEQ ID NO: 802 linked to the heavy chain constant region of SEQ ID NO: 810.

[0573] In one embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a variable heavy chain sequence comprising the sequence set forth below:

(SEQ ID NO: 802)
QQLEQSGGGAEGGLVKPGGSLKLSCKASGFTISRDYWICWVRQAPGKGLE

WIGCISAGGGSTDYANWVNGRFTLSRDIDQSTGCLQLNSLTDADTAMYYC

AGNLEIWGQGTLVTVSS.

[0574] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that bind the same epitope as Ab9, and that contain a constant heavy chain sequence comprising the polypeptide of SEQ ID NO: 1244, 1245, or 1246, or comprising the sequence set forth below:

(SEQ ID NO: 810)
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV

HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDARVEP

KSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS

HEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGK

EYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTC

LVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW

QQGNVFSCSVMHEALHNHYTQKSLSLSPGK.

[0575] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a light chain sequence comprising the sequence of SEQ ID NO: 821 which consists of the light chain variable region of SEQ ID NO: 822 linked to the light chain constant region of SEQ ID NO: 830.

[0576] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a variable light chain sequence comprising the sequence set forth below:

(SEQ ID NO: 822)
AQVLTQTPSSVSAAVGGTVTINCQSSPSIYSGAFLSWFQQKPGQPPKFLI

YEASKLASGVPSRFSGSGSGTQFTLTISDVQCDDAATYYCLGFYDCSSVD

CHAFGGGTEVVVKR.

[0577] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP, that bind the same epitope as Ab9, and that contain a constant light chain sequence comprising the sequence set forth below:

(SEQ ID NO: 830)
TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGN

SQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKS

FNRGEC.

[0578] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 804; SEQ ID NO: 806; and SEQ ID NO: 808, which correspond to the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 801, or which contain the variable heavy chain sequence of SEQ ID NO: 802, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 824; SEQ ID NO: 826; and SEQ ID NO: 828, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 821, or which contain the variable light chain sequence of SEQ ID NO: 822, or antibodies or antigen-binding fragments containing combinations of sequences that are at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention and antigen-binding fragments comprise, or alternatively consist of, combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

[0579] The invention further contemplates anti-PACAP antibodies and antigen-binding fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 803; SEQ ID NO: 805; SEQ ID NO: 807; and SEQ ID NO: 809, which correspond to the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 801, or the variable heavy chain sequence of SEQ ID NO: 802, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 823; SEQ ID NO: 825; SEQ ID NO: 827; and SEQ ID NO: 829, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 821, or the variable light chain sequence of SEQ ID NO: 822, or combinations of these polypeptide sequences, or sequences that are at least 80%, 90%, 95%, 96%, 97%, 98%, or 99% identical therewith.

[0580] In another embodiment of the invention, the anti-PACAP antibodies and antigen-binding fragments of the invention or fragments comprise, or alternatively consist of,

combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them, or sequences that are at least 90% or 95% identical thereto.

[0581] In another embodiment of the invention, the anti-PACAP antibodies and antigen-binding fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 801, or SEQ ID NO: 802, or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, the antibodies and antigen-binding fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 821, or SEQ ID NO: 822, or polypeptides that are at least 90% or 95% identical thereto.

[0582] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, or three of the polypeptide sequences of SEQ ID NO: 804; SEQ ID NO: 806; and SEQ ID NO: 808, which correspond to the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 801, or the variable heavy chain sequence of SEQ ID NO: 802, or sequences that are at least 90% or 95% identical thereto.

[0583] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, or three of the polypeptide sequences of SEQ ID NO: 824; SEQ ID NO: 826; and SEQ ID NO: 828, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 821, or the variable light chain sequence of SEQ ID NO: 822, or sequences that are at least 90% or 95% identical thereto.

[0584] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 803; SEQ ID NO: 805; SEQ ID NO: 807; and SEQ ID NO: 809, which correspond to the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 801, or the variable heavy chain sequence of SEQ ID NO: 802, or sequences that are at least 90% or 95% identical thereto.

[0585] In a further embodiment of the invention, the subject antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 823; SEQ ID NO: 825; SEQ ID NO: 827; and SEQ ID NO: 829, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 821, or the variable light chain sequence of SEQ ID NO: 822, or sequences that are at least 90% or 95% identical thereto.

[0586] The invention also contemplates anti-PACAP antibodies and antigen-binding fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 802; the variable light chain region of SEQ ID NO: 822; the complementarity determining regions (SEQ ID NO: 804; SEQ ID NO: 806; and SEQ ID NO: 808) of the variable heavy chain region of SEQ ID NO: 802; and the complementarity determining regions (SEQ ID NO: 824; SEQ ID NO: 826; and SEQ ID NO: 828) of the variable light chain region of SEQ ID NO: 822, or sequences that are at least 90% or 95% identical thereto. In another embodiment of the invention, fragments of the antibodies having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 802; the variable light chain region of SEQ ID NO: 822; the framework regions (SEQ ID NO: 803; SEQ ID NO: 805; SEQ ID NO: 807; and SEQ ID NO: 809) of the variable heavy chain region of SEQ ID NO: 802; and the framework regions (SEQ ID NO: 823; SEQ ID NO: 825; SEQ ID NO: 827; and SEQ ID NO: 829) of the variable light chain region of SEQ ID NO: 822, or sequences that are at least 90% or 95% identical thereto.

[0587] In another embodiment of the invention, the anti-PACAP antibody is Ab9, comprising, or alternatively consisting of, SEQ ID NO: 801 and SEQ ID NO: 821, or SEQ ID NO: 802 and SEQ ID NO: 822, or an antibody or antigen-binding fragment comprising the CDRs of Ab9 and having at least one of the biological activities set forth herein, or is an anti-PACAP antibody that competes with Ab9 in binding PACAP, preferably one containing sequences that are at least 90%, 95%, 96%, 97%, 98%, or 99% identical to that of Ab9, or an antibody that binds to the same or overlapping epitope(s) on PACAP as Ab9.

[0588] In a further embodiment of the invention, antigen-binding fragments comprise, or alternatively consist of, Fab fragments having binding specificity for PACAP. With respect to antibody Ab9, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 802 and the variable light chain sequence of SEQ ID NO: 822, or sequences that are at least 90%, 95%, 96%, 97%, 98%, or 99% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 802 and/or SEQ ID NO: 822 that retain the binding specificity for PACAP.

[0589] In one embodiment of the invention described herein, Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab9. In another embodiment of the invention, anti-PACAP antibodies such as Ab9 and Fab fragments may be produced via expression in mammalian cells, such as CHO, NSO, or HEK 293 cells, fungal, insect, or microbial systems, such as yeast cells (for example haploid or diploid yeast, such as haploid or diploid *Pichia*) and other yeast strains. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*.

[0590] In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to PACAP, including the heavy and/or light chains of Ab9, as well as fragments, variants, and combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them, or sequences that are at least 90% or 95% identical thereto.

Antibody Ab11

[0591] In one embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that possess a heavy chain sequence comprising the sequence of SEQ ID NO: 561 which consists of

the heavy chain variable region of SEQ ID NO: 562 linked to the heavy chain constant region of SEQ ID NO: 570.

[0592] In one embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a variable heavy chain sequence comprising the sequence set forth below:

(SEQ ID NO: 562)
QSVEESGGRLVTPGTPLTLTCTASGFSLSRYAMGWVRQAPGKGLEWIGDI

STYGTTDYASWVNGRFTISRTSTTVTLKMTSLTTEDTATYFCARDYWLSL

WGQGTLVTVSS.

[0593] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that bind the same epitope as Ab11, and that contain a constant heavy chain sequence comprising the polypeptide of SEQ ID NO: 1244, 1245, or 1246, or comprising the sequence set forth below:

(SEQ ID NO: 570)
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV

HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDARVEP

KSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS

HEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGK

EYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTC

LVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW

QQGNVFSCSVMHEALHNHYTQKSLSLSPGK.

[0594] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a light chain sequence comprising the sequence of SEQ ID NO: 581 which consists of the light chain variable region of SEQ ID NO: 582 linked to the light chain constant region of SEQ ID NO: 590.

[0595] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a variable light chain sequence comprising the sequence set forth below:

(SEQ ID NO: 582)
AAVLTQTPSPVSAAVGGTVTIKCQSSQSVYDNNALAWYQQKPGQPPKLLI

YAASNLASGVPDRFSGSGSGTQFTLTISGVQCDDAATYYCLGGYDDAADN

AFGGGTEVVVKR.

[0596] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP, that bind the same epitope as Ab11, and that contain a constant light chain sequence comprising the sequence set forth below:

(SEQ ID NO: 590)
TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGN

SQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKS

FNRGEC.

[0597] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 564; SEQ ID NO: 566; and SEQ ID NO: 568, which correspond to the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 561, or which contain the variable heavy chain sequence of SEQ ID NO: 562, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 584; SEQ ID NO: 586; and SEQ ID NO: 588, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 581, or which contain the variable light chain sequence of SEQ ID NO: 582, or antibodies or antigen-binding fragments containing combinations of sequences that are at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention and antigen-binding fragments comprise, or alternatively consist of, combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

[0598] The invention further contemplates anti-PACAP antibodies and antigen-binding fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 563; SEQ ID NO: 565; SEQ ID NO: 567; and SEQ ID NO: 569, which correspond to the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 561, or the variable heavy chain sequence of SEQ ID NO: 562, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 583; SEQ ID NO: 585; SEQ ID NO: 587; and SEQ ID NO: 589, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 581, or the variable light chain sequence of SEQ ID NO: 582, or combinations of these polypeptide sequences, or sequences that are at least 80%, 90%, 95%, 96%, 97%, 98%, or 99% identical therewith.

[0599] In another embodiment of the invention, the anti-PACAP antibodies and antigen-binding fragments of the invention or fragments comprise, or alternatively consist of, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them, or sequences that are at least 90% or 95% identical thereto.

[0600] In another embodiment of the invention, the anti-PACAP antibodies and antigen-binding fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 561, or SEQ ID NO: 562, or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, the antibodies and antigen-binding fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 581, or SEQ ID NO: 582, or polypeptides that are at least 90% or 95% identical thereto.

[0601] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, or three of the polypeptide sequences of SEQ ID NO: 564; SEQ ID NO: 566; and SEQ ID NO: 568, which correspond to the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 561, or the variable heavy chain sequence of SEQ ID NO: 562, or sequences that are at least 90% or 95% identical thereto.

[0602] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, or three of the polypeptide sequences of SEQ ID NO: 584; SEQ ID NO: 586; and SEQ ID NO: 588, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 581, or the variable light chain sequence of SEQ ID NO: 582, or sequences that are at least 90% or 95% identical thereto.

[0603] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 563; SEQ ID NO: 565; SEQ ID NO: 567; and SEQ ID NO: 569, which correspond to the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 561, or the variable heavy chain sequence of SEQ ID NO: 562, or sequences that are at least 90% or 95% identical thereto.

[0604] In a further embodiment of the invention, the subject antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 583; SEQ ID NO: 585; SEQ ID NO: 587; and SEQ ID NO: 589, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 581, or the variable light chain sequence of SEQ ID NO: 582, or sequences that are at least 90% or 95% identical thereto.

[0605] The invention also contemplates anti-PACAP antibodies and antigen-binding fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 562; the variable light chain region of SEQ ID NO: 582; the complementarity determining regions (SEQ ID NO: 564; SEQ ID NO: 566; and SEQ ID NO: 568) of the variable heavy chain region of SEQ ID NO: 562; and the complementarity determining regions (SEQ ID NO: 584; SEQ ID NO: 586; and SEQ ID NO: 588) of the variable light chain region of SEQ ID NO: 582, or sequences that are at least 90% or 95% identical thereto. In another embodiment of the invention, fragments of the antibodies having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 562; the variable light chain region of SEQ ID NO: 582; the framework regions (SEQ ID NO: 563; SEQ ID NO: 565; SEQ ID NO: 567; and SEQ ID NO: 569) of the variable heavy chain region of SEQ ID NO: 562; and the framework regions (SEQ ID NO: 583; SEQ ID NO: 585; SEQ ID NO: 587; and SEQ ID NO: 589) of the variable light chain region of SEQ ID NO: 582, or sequences that are at least 90% or 95% identical thereto.

[0606] In another embodiment of the invention, the anti-PACAP antibody is Ab11, comprising, or alternatively consisting of, SEQ ID NO: 561 and SEQ ID NO: 581, or SEQ ID NO: 562 and SEQ ID NO: 582, or an antibody or antigen-binding fragment comprising the CDRs of Ab11 and having at least one of the biological activities set forth herein, or is an anti-PACAP antibody that competes with Ab11 in binding PACAP, preferably one containing sequences that are at least 90%, 95%, 96%, 97%, 98%, or 99% identical to that of Ab11, or an antibody that binds to the same or overlapping epitope(s) on PACAP as Ab11.

[0607] In a further embodiment of the invention, antigen-binding fragments comprise, or alternatively consist of, Fab fragments having binding specificity for PACAP. With respect to antibody Ab11, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 562 and the variable light chain sequence of SEQ ID NO: 582, or sequences that are at least 90%, 95%, 96%, 97%, 98%, or 99% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 562 and/or SEQ ID NO: 582 that retain the binding specificity for PACAP.

[0608] In one embodiment of the invention described herein, Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab11. In another embodiment of the invention, anti-PACAP antibodies such as Ab11 and Fab fragments may be produced via expression in mammalian cells, such as CHO, NSO, or HEK 293 cells, fungal, insect, or microbial systems, such as yeast cells (for example haploid or diploid yeast, such as haploid or diploid *Pichia*) and other yeast strains. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*.

[0609] In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to PACAP, including the heavy and/or light chains of Ab11, as well as fragments, variants, and combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them, or sequences that are at least 90% or 95% identical thereto.

Antibody Ab12

[0610] In one embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that possess a heavy chain sequence comprising the sequence of SEQ ID NO: 601 which consists of the heavy chain variable region of SEQ ID NO: 602 linked to the heavy chain constant region of SEQ ID NO: 610.

[0611] In one embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a variable heavy chain sequence comprising the sequence set forth below:

(SEQ ID NO: 602)

QSVEESGGRLVTPGTPLTLTCTASGFSLSSYAMGWVRQAPGKGLEWIGDI

STYGTTDYASWVYGRFTISRTSTTVTLKMTSLTTEDTATYFCARDYWLSL

WGQGTLVTVSS.

[0612] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that bind the same epitope as Ab12, and that contain a constant heavy chain sequence comprising the polypeptide of SEQ ID NO: 1244, 1245, or 1246, or comprising the sequence set forth below:

(SEQ ID NO: 610)

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV

HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDARVEP

KSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS

-continued

HEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGK

EYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTC

LVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW

QQGNVFSCSVMHEALHNHYTQKSLSLSPGK.

[0613] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a light chain sequence comprising the sequence of SEQ ID NO: 621 which consists of the light chain variable region of SEQ ID NO: 622 linked to the light chain constant region of SEQ ID NO: 630.

[0614] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a variable light chain sequence comprising the sequence set forth below:

(SEQ ID NO: 622)

AAVLTQTPSPVSAAVGGTVTIKCQSSQSVYDNNALAWYQQKPGQPPKLLI

YAASTLASGVPSRFSGSGSGTEFTLTISGVQCDDAATYYCLGGYYDPADN

AFGGGTEVVVKR.

[0615] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP, that bind the same epitope as Ab12, and that contain a constant light chain sequence comprising the sequence set forth below:

(SEQ ID NO: 630)

TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGN

SQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKS

FNRGEC.

[0616] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 604; SEQ ID NO: 606; and SEQ ID NO: 608, which correspond to the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 601, or which contain the variable heavy chain sequence of SEQ ID NO: 602, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 624; SEQ ID NO: 626; and SEQ ID NO: 628, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 621, or which contain the variable light chain sequence of SEQ ID NO: 622, or antibodies or antigen-binding fragments containing combinations of sequences that are at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention and antigen-binding fragments comprise, or alternatively consist of, combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

[0617] The invention further contemplates anti-PACAP antibodies and antigen-binding fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 603; SEQ ID NO: 605; SEQ ID NO: 607; and SEQ ID NO: 609, which correspond to the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 601, or the variable heavy chain sequence of SEQ ID NO: 602, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 623; SEQ ID NO: 625; SEQ ID NO: 627; and SEQ ID NO: 629, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 621, or the variable light chain sequence of SEQ ID NO: 622, or combinations of these polypeptide sequences, or sequences that are at least 80%, 90%, 95%, 96%, 97%, 98%, or 99% identical therewith.

[0618] In another embodiment of the invention, the anti-PACAP antibodies and antigen-binding fragments of the invention or fragments comprise, or alternatively consist of, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them, or sequences that are at least 90% or 95% identical thereto.

[0619] In another embodiment of the invention, the anti-PACAP antibodies and antigen-binding fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 601, or SEQ ID NO: 602, or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, the antibodies and antigen-binding fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 621, or SEQ ID NO: 622, or polypeptides that are at least 90% or 95% identical thereto.

[0620] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, or three of the polypeptide sequences of SEQ ID NO: 604; SEQ ID NO: 606; and SEQ ID NO: 608, which correspond to the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 601, or the variable heavy chain sequence of SEQ ID NO: 602, or sequences that are at least 90% or 95% identical thereto.

[0621] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, or three of the polypeptide sequences of SEQ ID NO: 624; SEQ ID NO: 626; and SEQ ID NO: 628, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 621, or the variable light chain sequence of SEQ ID NO: 622, or sequences that are at least 90% or 95% identical thereto.

[0622] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 603; SEQ ID NO: 605; SEQ ID NO: 607; and SEQ ID NO: 609, which correspond to the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 601, or the variable heavy chain sequence of SEQ ID NO: 602, or sequences that are at least 90% or 95% identical thereto.

[0623] In a further embodiment of the invention, the subject antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 623; SEQ ID NO: 625; SEQ ID NO: 627; and SEQ ID NO: 629, which correspond to the FRs (constant regions) of the light chain sequence of SEQ

ID NO: 621, or the variable light chain sequence of SEQ ID NO: 622, or sequences that are at least 90% or 95% identical thereto.

[0624] The invention also contemplates anti-PACAP antibodies and antigen-binding fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 602; the variable light chain region of SEQ ID NO: 622; the complementarity determining regions (SEQ ID NO: 604; SEQ ID NO: 606; and SEQ ID NO: 608) of the variable heavy chain region of SEQ ID NO: 602; and the complementarity determining regions (SEQ ID NO: 624; SEQ ID NO: 626; and SEQ ID NO: 628) of the variable light chain region of SEQ ID NO: 622, or sequences that are at least 90% or 95% identical thereto. In another embodiment of the invention, fragments of the antibodies having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 602; the variable light chain region of SEQ ID NO: 622; the framework regions (SEQ ID NO: 603; SEQ ID NO: 605; SEQ ID NO: 607; and SEQ ID NO: 609) of the variable heavy chain region of SEQ ID NO: 602; and the framework regions (SEQ ID NO: 623; SEQ ID NO: 625; SEQ ID NO: 627; and SEQ ID NO: 629) of the variable light chain region of SEQ ID NO: 622, or sequences that are at least 90% or 95% identical thereto.

[0625] In another embodiment of the invention, the anti-PACAP antibody is Ab12, comprising, or alternatively consisting of, SEQ ID NO: 601 and SEQ ID NO: 621, or SEQ ID NO: 602 and SEQ ID NO: 622, or an antibody or antigen-binding fragment comprising the CDRs of Ab12 and having at least one of the biological activities set forth herein, or is an anti-PACAP antibody that competes with Ab12 in binding PACAP, preferably one containing sequences that are at least 90%, 95%, 96%, 97%, 98%, or 99% identical to that of Ab12, or an antibody that binds to the same or overlapping epitope(s) on PACAP as Ab12.

[0626] In a further embodiment of the invention, antigen-binding fragments comprise, or alternatively consist of, Fab fragments having binding specificity for PACAP. With respect to antibody Ab12, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 602 and the variable light chain sequence of SEQ ID NO: 622, or sequences that are at least 90%, 95%, 96%, 97%, 98%, or 99% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 602 and/or SEQ ID NO: 622 that retain the binding specificity for PACAP.

[0627] In one embodiment of the invention described herein, Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab12. In another embodiment of the invention, anti-PACAP antibodies such as Ab12 and Fab fragments may be produced via expression in mammalian cells, such as CHO, NSO, or HEK 293 cells, fungal, insect, or microbial systems, such as yeast cells (for example haploid or diploid yeast, such as haploid or diploid *Pichia*) and other yeast strains. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*.

[0628] In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to PACAP, including the heavy and/or light chains of Ab12, as well as fragments, variants, and combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them, or sequences that are at least 90% or 95% identical thereto.

Antibody Ab13

[0629] In one embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that possess a heavy chain sequence comprising the sequence of SEQ ID NO: 121 which consists of the heavy chain variable region of SEQ ID NO: 122 linked to the heavy chain constant region of SEQ ID NO: 130.

[0630] In one embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a variable heavy chain sequence comprising the sequence set forth below:

(SEQ ID NO: 122)
QSVEESGGRLVTPGTPLTLTCTVSGFSLSSAAMNWVRQAPGKGLEWIGII

DNTAGTYYAPWAKGRFTISKTSSTTVDLKMTSPTTEDTATYFCARGGGEF

FIWGPGTLVTVSS.

[0631] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that bind the same epitope as Ab13, and that contain a constant heavy chain sequence comprising the polypeptide of SEQ ID NO: 1244, 1245, or 1246, or comprising the sequence set forth below:

(SEQ ID NO: 130)
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV

HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEP

KSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS

HEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGK

EYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTC

LVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW

QQGNVFSCSVMHEALHNHYTQKSLSLSPGK.

[0632] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a light chain sequence comprising the sequence of SEQ ID NO: 141 which consists of the light chain variable region of SEQ ID NO: 142 linked to the light chain constant region of SEQ ID NO: 150.

[0633] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a variable light chain sequence comprising the sequence set forth below:

(SEQ ID NO: 142)
AQVLTQTPSSVSAAVGGTVTINCQSSQSVHDGSYLSWYQQKPGQPPNFLI

YQASNLASGVPSRFKGSGSGTQFTLTISDLECDDAATYYCAGGYSSNICG

FGGGTEVVVKR.

[0634] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding

specificity to PACAP, that bind the same epitope as Ab13, and that contain a constant light chain sequence comprising the sequence set forth below:

(SEQ ID NO: 150)
TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGN

SQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKS

FNRGEC.

[0635] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 124; SEQ ID NO: 126; and SEQ ID NO: 128, which correspond to the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 121, or which contain the variable heavy chain sequence of SEQ ID NO: 122, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 144; SEQ ID NO: 146; and SEQ ID NO: 148, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 141, or which contain the variable light chain sequence of SEQ ID NO: 142, or antibodies or antigen-binding fragments containing combinations of sequences that are at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention and antigen-binding fragments comprise, or alternatively consist of, combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

[0636] The invention further contemplates anti-PACAP antibodies and antigen-binding fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 123; SEQ ID NO: 125; SEQ ID NO: 127; and SEQ ID NO: 129, which correspond to the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 121, or the variable heavy chain sequence of SEQ ID NO: 122, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 143; SEQ ID NO: 145; SEQ ID NO: 147; and SEQ ID NO: 149, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 141, or the variable light chain sequence of SEQ ID NO: 142, or combinations of these polypeptide sequences, or sequences that are at least 80%, 90%, 95%, 96%, 97%, 98%, or 99% identical therewith.

[0637] In another embodiment of the invention, the anti-PACAP antibodies and antigen-binding fragments of the invention or fragments comprise, or alternatively consist of, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them, or sequences that are at least 90% or 95% identical thereto.

[0638] In another embodiment of the invention, the anti-PACAP antibodies and antigen-binding fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 121, or SEQ ID NO: 122, or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, the antibodies and antigen-binding fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 141, or SEQ ID NO: 142, or polypeptides that are at least 90% or 95% identical thereto.

[0639] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, or three of the polypeptide sequences of SEQ ID NO: 124; SEQ ID NO: 126; and SEQ ID NO: 128, which correspond to the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 121, or the variable heavy chain sequence of SEQ ID NO: 122, or sequences that are at least 90% or 95% identical thereto.

[0640] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, or three of the polypeptide sequences of SEQ ID NO: 144; SEQ ID NO: 146; and SEQ ID NO: 148, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 141, or the variable light chain sequence of SEQ ID NO: 142, or sequences that are at least 90% or 95% identical thereto.

[0641] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 123; SEQ ID NO: 125; SEQ ID NO: 127; and SEQ ID NO: 129, which correspond to the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 121, or the variable heavy chain sequence of SEQ ID NO: 122, or sequences that are at least 90% or 95% identical thereto.

[0642] In a further embodiment of the invention, the subject antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 143; SEQ ID NO: 145; SEQ ID NO: 147; and SEQ ID NO: 149, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 141, or the variable light chain sequence of SEQ ID NO: 142, or sequences that are at least 90% or 95% identical thereto.

[0643] The invention also contemplates anti-PACAP antibodies and antigen-binding fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 122; the variable light chain region of SEQ ID NO: 142; the complementarity determining regions (SEQ ID NO: 124; SEQ ID NO: 126; and SEQ ID NO: 128) of the variable heavy chain region of SEQ ID NO: 122; and the complementarity determining regions (SEQ ID NO: 144; SEQ ID NO: 146; and SEQ ID NO: 148) of the variable light chain region of SEQ ID NO: 142, or sequences that are at least 90% or 95% identical thereto. In another embodiment of the invention, fragments of the antibodies having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 122; the variable light chain region of SEQ ID NO: 142; the framework regions (SEQ ID NO: 123; SEQ ID NO: 125; SEQ ID NO: 127; and SEQ ID NO: 129) of the variable heavy chain region of SEQ ID NO: 122; and the framework regions (SEQ ID NO: 143; SEQ ID NO: 145; SEQ ID NO: 147; and

SEQ ID NO: 149) of the variable light chain region of SEQ ID NO: 142, or sequences that are at least 90% or 95% identical thereto.

[0644] In another embodiment of the invention, the anti-PACAP antibody is Ab13, comprising, or alternatively consisting of, SEQ ID NO: 121 and SEQ ID NO: 141, or SEQ ID NO: 122 and SEQ ID NO: 142, or an antibody or antigen-binding fragment comprising the CDRs of Ab13 and having at least one of the biological activities set forth herein, or is an anti-PACAP antibody that competes with Ab13 in binding PACAP, preferably one containing sequences that are at least 90%, 95%, 96%, 97%, 98%, or 99% identical to that of Ab13, or an antibody that binds to the same or overlapping epitope(s) on PACAP as Ab13.

[0645] In a further embodiment of the invention, antigen-binding fragments comprise, or alternatively consist of, Fab fragments having binding specificity for PACAP. With respect to antibody Ab13, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 122 and the variable light chain sequence of SEQ ID NO: 142, or sequences that are at least 90%, 95%, 96%, 97%, 98%, or 99% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 122 and/or SEQ ID NO: 142 that retain the binding specificity for PACAP.

[0646] In one embodiment of the invention described herein, Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab13. In another embodiment of the invention, anti-PACAP antibodies such as Ab13 and Fab fragments may be produced via expression in mammalian cells, such as CHO, NSO, or HEK 293 cells, fungal, insect, or microbial systems, such as yeast cells (for example haploid or diploid yeast, such as haploid or diploid *Pichia*) and other yeast strains. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*.

[0647] In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to PACAP, including the heavy and/or light chains of Ab13, as well as fragments, variants, and combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them, or sequences that are at least 90% or 95% identical thereto.

Antibody Ab14

[0648] In one embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that possess a heavy chain sequence comprising the sequence of SEQ ID NO: 161 which consists of the heavy chain variable region of SEQ ID NO: 162 linked to the heavy chain constant region of SEQ ID NO: 170.

[0649] In one embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a variable heavy chain sequence comprising the sequence set forth below:

(SEQ ID NO: 162)
QSVEASGGRLVTPGTPLTLTCTVSGFSLSSAAMNWVRQAPGKGLEWIGFI

EYSKNIVYASWAKGRFTISKVSSTTVDLKMTSPTTEDTATYFCARGGGEF

FIWGQGTLVTVSS.

[0650] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that bind the same epitope as Ab14, and that contain a constant heavy chain sequence comprising the polypeptide of SEQ ID NO: 1244, 1245, or 1246, or comprising the sequence set forth below:

(SEQ ID NO: 170)
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV

HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEP

KSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS

HEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGK

EYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTC

LVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW

QQGNVFSCSVMHEALHNHYTQKSLSLSPGK.

[0651] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a light chain sequence comprising the sequence of SEQ ID NO: 181 which consists of the light chain variable region of SEQ ID NO: 182 linked to the light chain constant region of SEQ ID NO: 190.

[0652] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a variable light chain sequence comprising the sequence set forth below:

(SEQ ID NO: 182)
AQVLTQTPSSVSAAVGGTVTINCQSSQSVYSNNRLSYYQQKPGQPPKLLI

YEASSLAYGVPSRFKGSGSGTQFTLTISDLECDDAATYYCAGAYSNSIYS

FGGGTEVVVKR.

[0653] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP, that bind the same epitope as Ab14, and that contain a constant light chain sequence comprising the sequence set forth below:

(SEQ ID NO: 190)
TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGN

SQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKS

FNRGEC.

[0654] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 164; SEQ ID NO: 166; and SEQ ID NO: 168, which correspond to the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 161, or which contain the variable heavy chain sequence of SEQ ID NO: 162, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 184; SEQ ID NO: 186; and SEQ ID NO: 188, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 181, or which contain the variable light chain sequence of SEQ ID NO: 182, or antibodies or antigen-binding fragments containing combinations of sequences that are at least 80%, 85%, 90%, 95%,

96%, 97%, 98%, or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention and antigen-binding fragments comprise, or alternatively consist of, combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

[0655] The invention further contemplates anti-PACAP antibodies and antigen-binding fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 163; SEQ ID NO: 165; SEQ ID NO: 167; and SEQ ID NO: 169, which correspond to the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 161, or the variable heavy chain sequence of SEQ ID NO: 162, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 183; SEQ ID NO: 185; SEQ ID NO: 187; and SEQ ID NO: 189, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 181, or the variable light chain sequence of SEQ ID NO: 182, or combinations of these polypeptide sequences, or sequences that are at least 80%, 90%, 95%, 96%, 97%, 98%, or 99% identical therewith.

[0656] In another embodiment of the invention, the anti-PACAP antibodies and antigen-binding fragments of the invention or fragments comprise, or alternatively consist of, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them, or sequences that are at least 90% or 95% identical thereto.

[0657] In another embodiment of the invention, the anti-PACAP antibodies and antigen-binding fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 161, or SEQ ID NO: 162, or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, the antibodies and antigen-binding fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 181, or SEQ ID NO: 182, or polypeptides that are at least 90% or 95% identical thereto.

[0658] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, or three of the polypeptide sequences of SEQ ID NO: 164; SEQ ID NO: 166; and SEQ ID NO: 168, which correspond to the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 161, or the variable heavy chain sequence of SEQ ID NO: 162, or sequences that are at least 90% or 95% identical thereto.

[0659] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, or three of the polypeptide sequences of SEQ ID NO: 184; SEQ ID NO: 186; and SEQ ID NO: 188, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 181, or the variable light chain sequence of SEQ ID NO: 182, or sequences that are at least 90% or 95% identical thereto.

[0660] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 163; SEQ ID NO: 165; SEQ ID NO: 167; and SEQ ID NO: 169, which correspond to the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 161, or the variable heavy chain sequence of SEQ ID NO: 162, or sequences that are at least 90% or 95% identical thereto.

[0661] In a further embodiment of the invention, the subject antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 183; SEQ ID NO: 185; SEQ ID NO: 187; and SEQ ID NO: 189, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 181, or the variable light chain sequence of SEQ ID NO: 182, or sequences that are at least 90% or 95% identical thereto.

[0662] The invention also contemplates anti-PACAP antibodies and antigen-binding fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 162; the variable light chain region of SEQ ID NO: 182; the complementarity determining regions (SEQ ID NO: 164; SEQ ID NO: 166; and SEQ ID NO: 168) of the variable heavy chain region of SEQ ID NO: 162; and the complementarity determining regions (SEQ ID NO: 184; SEQ ID NO: 186; and SEQ ID NO: 188) of the variable light chain region of SEQ ID NO: 182, or sequences that are at least 90% or 95% identical thereto. In another embodiment of the invention, fragments of the antibodies having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 162; the variable light chain region of SEQ ID NO: 182; the framework regions (SEQ ID NO: 163; SEQ ID NO: 165; SEQ ID NO: 167; and SEQ ID NO: 169) of the variable heavy chain region of SEQ ID NO: 162; and the framework regions (SEQ ID NO: 183; SEQ ID NO: 185; SEQ ID NO: 187; and SEQ ID NO: 189) of the variable light chain region of SEQ ID NO: 182, or sequences that are at least 90% or 95% identical thereto.

[0663] In another embodiment of the invention, the anti-PACAP antibody is Ab14, comprising, or alternatively consisting of, SEQ ID NO: 161 and SEQ ID NO: 181, or SEQ ID NO: 162 and SEQ ID NO: 182, or an antibody or antigen-binding fragment comprising the CDRs of Ab14 and having at least one of the biological activities set forth herein, or is an anti-PACAP antibody that competes with Ab14 in binding PACAP, preferably one containing sequences that are at least 90%, 95%, 96%, 97%, 98%, or 99% identical to that of Ab14, or an antibody that binds to the same or overlapping epitope(s) on PACAP as Ab14.

[0664] In a further embodiment of the invention, antigen-binding fragments comprise, or alternatively consist of, Fab fragments having binding specificity for PACAP. With respect to antibody Ab14, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 162 and the variable light chain sequence of SEQ ID NO: 182, or sequences that are at least 90%, 95%, 96%, 97%, 98%, or 99% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 162 and/or SEQ ID NO: 182 that retain the binding specificity for PACAP.

[0665] In one embodiment of the invention described herein, Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab14. In another embodiment of the invention, anti-PACAP antibodies such as Ab14 and Fab fragments may be produced via expression in mammalian cells, such as CHO, NSO, or HEK 293 cells, fungal, insect, or microbial systems, such as yeast cells (for example haploid or diploid yeast, such as haploid or diploid *Pichia*) and other yeast strains. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*.

[0666] In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to PACAP, including the heavy and/or light chains of Ab14, as well as fragments, variants, and combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them, or sequences that are at least 90% or 95% identical thereto.

Antibody Ab15

[0667] In one embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that possess a heavy chain sequence comprising the sequence of SEQ ID NO: 201 which consists of the heavy chain variable region of SEQ ID NO: 202 linked to the heavy chain constant region of SEQ ID NO: 210.

[0668] In one embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a variable heavy chain sequence comprising the sequence set forth below:

(SEQ ID NO: 202)
QSVEASGGHLVTPGTPLTLTCTVSGFSLSSAAMNWVRQAPGKGLEWIGSV

DERQNKYYASWAKGRFTISRTSSTTVNLKMTSPTTEDTATYFCARGGGEF

FIWGQGTLVTVSS.

[0669] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that bind the same epitope as Ab15, and that contain a constant heavy chain sequence comprising the polypeptide of SEQ ID NO: 1244, 1245, or 1246, or comprising the sequence set forth below:

(SEQ ID NO: 210)
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV

HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEP

KSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS

HEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGK

EYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTC

LVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW

QQGNVFSCSVMHEALHNHYTQKSLSLSPGK.

[0670] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a light chain sequence comprising the sequence of SEQ ID NO: 221 which consists of the light chain variable region of SEQ ID NO: 222 linked to the light chain constant region of SEQ ID NO: 230.

[0671] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a variable light chain sequence comprising the sequence set forth below:

(SEQ ID NO: 222)
AQVLTQTPSSVSAAVGGTVTINCQSSQSVYSNNRLSWYQQKPGQPPNLLI

YEASSLASGVPSRFSGSGSGTQFTLTISDLECDDAATYYCAGAYNTGIYG

FGGGTEVVVKR.

[0672] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP, that bind the same epitope as Ab15, and that contain a constant light chain sequence comprising the sequence set forth below:

(SEQ ID NO: 230)
TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGN

SQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKS

FNRGEC.

[0673] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 204; SEQ ID NO: 206; and SEQ ID NO: 208, which correspond to the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 201, or which contain the variable heavy chain sequence of SEQ ID NO: 202, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 224; SEQ ID NO: 226; and SEQ ID NO: 228, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 221, or which contain the variable light chain sequence of SEQ ID NO: 222, or antibodies or antigen-binding fragments containing combinations of sequences that are at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention and antigen-binding fragments comprise, or alternatively consist of, combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

[0674] The invention further contemplates anti-PACAP antibodies and antigen-binding fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 203; SEQ ID NO: 205; SEQ ID NO: 207; and SEQ ID NO: 209, which correspond to the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 201, or the variable heavy chain sequence of SEQ ID NO: 202, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 223; SEQ ID NO: 225; SEQ ID NO: 227; and SEQ ID NO: 229, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 221, or the variable light chain sequence of SEQ ID NO: 222, or combinations of these polypeptide sequences, or sequences that are at least 80%, 90%, 95%, 96%, 97%, 98%, or 99% identical therewith.

[0675] In another embodiment of the invention, the anti-PACAP antibodies and antigen-binding fragments of the invention or fragments comprise, or alternatively consist of,

combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them, or sequences that are at least 90% or 95% identical thereto.

[0676] In another embodiment of the invention, the anti-PACAP antibodies and antigen-binding fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 201, or SEQ ID NO: 202, or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, the antibodies and antigen-binding fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 221, or SEQ ID NO: 222, or polypeptides that are at least 90% or 95% identical thereto.

[0677] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, or three of the polypeptide sequences of SEQ ID NO: 204; SEQ ID NO: 206; and SEQ ID NO: 208, which correspond to the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 201, or the variable heavy chain sequence of SEQ ID NO: 202, or sequences that are at least 90% or 95% identical thereto.

[0678] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, or three of the polypeptide sequences of SEQ ID NO: 224; SEQ ID NO: 226; and SEQ ID NO: 228, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 221, or the variable light chain sequence of SEQ ID NO: 222, or sequences that are at least 90% or 95% identical thereto.

[0679] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 203; SEQ ID NO: 205; SEQ ID NO: 207; and SEQ ID NO: 209, which correspond to the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 201, or the variable heavy chain sequence of SEQ ID NO: 202, or sequences that are at least 90% or 95% identical thereto.

[0680] In a further embodiment of the invention, the subject antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 223; SEQ ID NO: 225; SEQ ID NO: 227; and SEQ ID NO: 229, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 221, or the variable light chain sequence of SEQ ID NO: 222, or sequences that are at least 90% or 95% identical thereto.

[0681] The invention also contemplates anti-PACAP antibodies and antigen-binding fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 202; the variable light chain region of SEQ ID NO: 222; the complementarity determining regions (SEQ ID NO: 204; SEQ ID NO: 206; and SEQ ID NO: 208) of the variable heavy chain region of SEQ ID NO: 202; and the complementarity determining regions (SEQ ID NO: 224; SEQ ID NO: 226; and SEQ ID NO: 228) of the variable light chain region of SEQ ID NO: 222, or sequences that are at least 90% or 95% identical thereto. In another embodiment of the invention, fragments of the antibodies having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 202; the variable light chain region of SEQ ID NO: 222; the framework regions (SEQ ID NO: 203; SEQ ID NO: 205; SEQ ID NO: 207; and SEQ ID NO: 209) of the variable heavy chain region of SEQ ID NO: 202; and the framework regions (SEQ ID NO: 223; SEQ ID NO: 225; SEQ ID NO: 227; and SEQ ID NO: 229) of the variable light chain region of SEQ ID NO: 222, or sequences that are at least 90% or 95% identical thereto.

[0682] In another embodiment of the invention, the anti-PACAP antibody is Ab15, comprising, or alternatively consisting of, SEQ ID NO: 201 and SEQ ID NO: 221, or SEQ ID NO: 202 and SEQ ID NO: 222, or an antibody or antigen-binding fragment comprising the CDRs of Ab15 and having at least one of the biological activities set forth herein, or is an anti-PACAP antibody that competes with Ab15 in binding PACAP, preferably one containing sequences that are at least 90%, 95%, 96%, 97%, 98%, or 99% identical to that of Ab15, or an antibody that binds to the same or overlapping epitope(s) on PACAP as Ab15.

[0683] In a further embodiment of the invention, antigen-binding fragments comprise, or alternatively consist of, Fab fragments having binding specificity for PACAP. With respect to antibody Ab15, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 202 and the variable light chain sequence of SEQ ID NO: 222, or sequences that are at least 90%, 95%, 96%, 97%, 98%, or 99% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 202 and/or SEQ ID NO: 222 that retain the binding specificity for PACAP.

[0684] In one embodiment of the invention described herein, Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab15. In another embodiment of the invention, anti-PACAP antibodies such as Ab15 and Fab fragments may be produced via expression in mammalian cells, such as CHO, NSO, or HEK 293 cells, fungal, insect, or microbial systems, such as yeast cells (for example haploid or diploid yeast, such as haploid or diploid *Pichia*) and other yeast strains. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*.

[0685] In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to PACAP, including the heavy and/or light chains of Ab15, as well as fragments, variants, and combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them, or sequences that are at least 90% or 95% identical thereto.

Antibody Ab16

[0686] In one embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that possess a heavy chain sequence comprising the sequence of SEQ ID NO: 241 which consists of

the heavy chain variable region of SEQ ID NO: 242 linked to the heavy chain constant region of SEQ ID NO: 250.

[0687] In one embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a variable heavy chain sequence comprising the sequence set forth below:

(SEQ ID NO: 242)
QSVEESGGRLVTPGTPLTLTCTVSGFSLSSAAMSWVRQAPGKGLEWIGII

DDSGNTYYASWAKARFTISKTSSTTVDLKMTSPTTEDTATYFCARGGGEF

FIWGPGTLVTVSS.

[0688] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that bind the same epitope as Ab16, and that contain a constant heavy chain sequence comprising the polypeptide of SEQ ID NO: 1244, 1245, or 1246, or comprising the sequence set forth below:

(SEQ ID NO: 250)
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV

HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEP

KSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS

HEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGK

EYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTC

LVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW

QQGNVFSCSVMHEALHNHYTQKSLSLSPGK.

[0689] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a light chain sequence comprising the sequence of SEQ ID NO: 261 which consists of the light chain variable region of SEQ ID NO: 262 linked to the light chain constant region of SEQ ID NO: 270.

[0690] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a variable light chain sequence comprising the sequence set forth below:

(SEQ ID NO: 262)
DPVLTQTPSSVSAAVGGTVTINCQSSQSVYNNKWLSWYQQKPGQSPKFLI

YQASNLASGVPSRFKGSGSGTQFTLTISDLECDDGATYYCAGGYRGNVCG

FGGGTEVVVKR.

[0691] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP, that bind the same epitope as Ab16, and that contain a constant light chain sequence comprising the sequence set forth below:

(SEQ ID NO: 270)
TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGN

SQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKS

FNRGEC.

[0692] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 244; SEQ ID NO: 246; and SEQ ID NO: 248, which correspond to the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 241, or which contain the variable heavy chain sequence of SEQ ID NO: 242, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 264; SEQ ID NO: 266; and SEQ ID NO: 268, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 261, or which contain the variable light chain sequence of SEQ ID NO: 262, or antibodies or antigen-binding fragments containing combinations of sequences that are at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention and antigen-binding fragments comprise, or alternatively consist of, combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

[0693] The invention further contemplates anti-PACAP antibodies and antigen-binding fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 243; SEQ ID NO: 245; SEQ ID NO: 247; and SEQ ID NO: 249, which correspond to the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 241, or the variable heavy chain sequence of SEQ ID NO: 242, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 263; SEQ ID NO: 265; SEQ ID NO: 267; and SEQ ID NO: 269, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 261, or the variable light chain sequence of SEQ ID NO: 262, or combinations of these polypeptide sequences, or sequences that are at least 80%, 90%, 95%, 96%, 97%, 98%, or 99% identical therewith.

[0694] In another embodiment of the invention, the anti-PACAP antibodies and antigen-binding fragments of the invention or fragments comprise, or alternatively consist of, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them, or sequences that are at least 90% or 95% identical thereto.

[0695] In another embodiment of the invention, the anti-PACAP antibodies and antigen-binding fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 241, or SEQ ID NO: 242, or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, the antibodies and antigen-binding fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 261, or SEQ ID NO: 262, or polypeptides that are at least 90% or 95% identical thereto.

[0696] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, or three of the polypeptide sequences of SEQ ID NO: 244; SEQ ID NO: 246; and SEQ ID NO: 248, which correspond to the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 241, or the variable heavy chain sequence of SEQ ID NO: 242, or sequences that are at least 90% or 95% identical thereto.

[0697] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, or three of the polypeptide sequences of SEQ ID NO: 264; SEQ ID NO: 266; and SEQ ID NO: 268, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 261, or the variable light chain sequence of SEQ ID NO: 262, or sequences that are at least 90% or 95% identical thereto.

[0698] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 243; SEQ ID NO: 245; SEQ ID NO: 247; and SEQ ID NO: 249, which correspond to the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 241, or the variable heavy chain sequence of SEQ ID NO: 242, or sequences that are at least 90% or 95% identical thereto.

[0699] In a further embodiment of the invention, the subject antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 263; SEQ ID NO: 265; SEQ ID NO: 267; and SEQ ID NO: 269, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 261, or the variable light chain sequence of SEQ ID NO: 262, or sequences that are at least 90% or 95% identical thereto.

[0700] The invention also contemplates anti-PACAP antibodies and antigen-binding fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 242; the variable light chain region of SEQ ID NO: 262; the complementarity determining regions (SEQ ID NO: 244; SEQ ID NO: 246; and SEQ ID NO: 248) of the variable heavy chain region of SEQ ID NO: 242; and the complementarity determining regions (SEQ ID NO: 264; SEQ ID NO: 266; and SEQ ID NO: 268) of the variable light chain region of SEQ ID NO: 262, or sequences that are at least 90% or 95% identical thereto. In another embodiment of the invention, fragments of the antibodies having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 242; the variable light chain region of SEQ ID NO: 262; the framework regions (SEQ ID NO: 243; SEQ ID NO: 245; SEQ ID NO: 247; and SEQ ID NO: 249) of the variable heavy chain region of SEQ ID NO: 242; and the framework regions (SEQ ID NO: 263; SEQ ID NO: 265; SEQ ID NO: 267; and SEQ ID NO: 269) of the variable light chain region of SEQ ID NO: 262, or sequences that are at least 90% or 95% identical thereto.

[0701] In another embodiment of the invention, the anti-PACAP antibody is Ab16, comprising, or alternatively consisting of, SEQ ID NO: 241 and SEQ ID NO: 261, or SEQ ID NO: 242 and SEQ ID NO: 262, or an antibody or antigen-binding fragment comprising the CDRs of Ab16 and having at least one of the biological activities set forth herein, or is an anti-PACAP antibody that competes with Ab16 in binding PACAP, preferably one containing sequences that are at least 90%, 95%, 96%, 97%, 98%, or 99% identical to that of Ab16, or an antibody that binds to the same or overlapping epitope(s) on PACAP as Ab16.

[0702] In a further embodiment of the invention, antigen-binding fragments comprise, or alternatively consist of, Fab fragments having binding specificity for PACAP. With respect to antibody Ab16, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 242 and the variable light chain sequence of SEQ ID NO: 262, or sequences that are at least 90%, 95%, 96%, 97%, 98%, or 99% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 242 and/or SEQ ID NO: 262 that retain the binding specificity for PACAP.

[0703] In one embodiment of the invention described herein, Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab16. In another embodiment of the invention, anti-PACAP antibodies such as Ab16 and Fab fragments may be produced via expression in mammalian cells, such as CHO, NSO, or HEK 293 cells, fungal, insect, or microbial systems, such as yeast cells (for example haploid or diploid yeast, such as haploid or diploid *Pichia*) and other yeast strains. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*.

[0704] In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to PACAP, including the heavy and/or light chains of Ab16, as well as fragments, variants, and combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them, or sequences that are at least 90% or 95% identical thereto.

Antibody Ab17

[0705] In one embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that possess a heavy chain sequence comprising the sequence of SEQ ID NO: 281 which consists of the heavy chain variable region of SEQ ID NO: 282 linked to the heavy chain constant region of SEQ ID NO: 290.

[0706] In one embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a variable heavy chain sequence comprising the sequence set forth below:

(SEQ ID NO: 282)
QSVEESGGRLVTPGTPLTLTCTVSGFSLSSAAMNWVRQAPGKGLEWIGIF

DPYSSTYYASWAKGRFTISKTSSTTVDLKMTSPTTEDTATYFCARGGGEF

FIWGPGTLVTVSS.

[0707] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that bind the same epitope as Ab17, and that contain a constant heavy chain sequence comprising the polypeptide of SEQ ID NO: 1244, 1245, or 1246, or comprising the sequence set forth below:

(SEQ ID NO: 290)
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV

HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEP

KSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS

-continued

HEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGK

EYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTC

LVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW

QQGNVFSCSVMHEALHNHYTQKSLSLSPGK.

[0708] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a light chain sequence comprising the sequence of SEQ ID NO: 301 which consists of the light chain variable region of SEQ ID NO: 302 linked to the light chain constant region of SEQ ID NO: 310.

[0709] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a variable light chain sequence comprising the sequence set forth below:

(SEQ ID NO: 302)

AQVLTQTPSSVSAAVGGTVTINCQSSQSVYKNKYLSWYQQKVGQPPKFLI

YQASNLASGVPSRFKGSGSGTQFTLTISDLECDDAATYYCAGGYSGNMVD

FGGGTEVVVKR.

[0710] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP, that bind the same epitope as Ab17, and that contain a constant light chain sequence comprising the sequence set forth below:

(SEQ ID NO: 310)

TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGN

SQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKS

FNRGEC.

[0711] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 284; SEQ ID NO: 286; and SEQ ID NO: 288, which correspond to the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 281, or which contain the variable heavy chain sequence of SEQ ID NO: 282, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 304; SEQ ID NO: 306; and SEQ ID NO: 308, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 301, or which contain the variable light chain sequence of SEQ ID NO: 302, or antibodies or antigen-binding fragments containing combinations of sequences that are at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention and antigen-binding fragments comprise, or alternatively consist of, combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

[0712] The invention further contemplates anti-PACAP antibodies and antigen-binding fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 283; SEQ ID NO: 285; SEQ ID NO: 287; and SEQ ID NO: 289, which correspond to the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 281, or the variable heavy chain sequence of SEQ ID NO: 282, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 303; SEQ ID NO: 305; SEQ ID NO: 307; and SEQ ID NO: 309, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 301, or the variable light chain sequence of SEQ ID NO: 302, or combinations of these polypeptide sequences, or sequences that are at least 80%, 90%, 95%, 96%, 97%, 98%, or 99% identical therewith.

[0713] In another embodiment of the invention, the anti-PACAP antibodies and antigen-binding fragments of the invention or fragments comprise, or alternatively consist of, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them, or sequences that are at least 90% or 95% identical thereto.

[0714] In another embodiment of the invention, the anti-PACAP antibodies and antigen-binding fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 281, or SEQ ID NO: 282, or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, the antibodies and antigen-binding fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 301, or SEQ ID NO: 302, or polypeptides that are at least 90% or 95% identical thereto.

[0715] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, or three of the polypeptide sequences of SEQ ID NO: 284; SEQ ID NO: 286; and SEQ ID NO: 288, which correspond to the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 281, or the variable heavy chain sequence of SEQ ID NO: 282, or sequences that are at least 90% or 95% identical thereto.

[0716] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, or three of the polypeptide sequences of SEQ ID NO: 304; SEQ ID NO: 306; and SEQ ID NO: 308, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 301, or the variable light chain sequence of SEQ ID NO: 302, or sequences that are at least 90% or 95% identical thereto.

[0717] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 283; SEQ ID NO: 285; SEQ ID NO: 287; and SEQ ID NO: 289, which correspond to the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 281, or the variable heavy chain sequence of SEQ ID NO: 282, or sequences that are at least 90% or 95% identical thereto.

[0718] In a further embodiment of the invention, the subject antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 303; SEQ ID NO: 305; SEQ ID NO: 307; and SEQ ID NO: 309, which correspond to the FRs (constant regions) of the light chain sequence of SEQ

ID NO: 301, or the variable light chain sequence of SEQ ID NO: 302, or sequences that are at least 90% or 95% identical thereto.

[0719] The invention also contemplates anti-PACAP antibodies and antigen-binding fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 282; the variable light chain region of SEQ ID NO: 302; the complementarity determining regions (SEQ ID NO: 284; SEQ ID NO: 286; and SEQ ID NO: 288) of the variable heavy chain region of SEQ ID NO: 282; and the complementarity determining regions (SEQ ID NO: 304; SEQ ID NO: 306; and SEQ ID NO: 308) of the variable light chain region of SEQ ID NO: 302, or sequences that are at least 90% or 95% identical thereto. In another embodiment of the invention, fragments of the antibodies having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 282; the variable light chain region of SEQ ID NO: 302; the framework regions (SEQ ID NO: 283; SEQ ID NO: 285; SEQ ID NO: 287; and SEQ ID NO: 289) of the variable heavy chain region of SEQ ID NO: 282; and the framework regions (SEQ ID NO: 303; SEQ ID NO: 305; SEQ ID NO: 307; and SEQ ID NO: 309) of the variable light chain region of SEQ ID NO: 302, or sequences that are at least 90% or 95% identical thereto.

[0720] In another embodiment of the invention, the anti-PACAP antibody is Ab17, comprising, or alternatively consisting of, SEQ ID NO: 281 and SEQ ID NO: 301, or SEQ ID NO: 282 and SEQ ID NO: 302, or an antibody or antigen-binding fragment comprising the CDRs of Ab17 and having at least one of the biological activities set forth herein, or is an anti-PACAP antibody that competes with Ab17 in binding PACAP, preferably one containing sequences that are at least 90%, 95%, 96%, 97%, 98%, or 99% identical to that of Ab17, or an antibody that binds to the same or overlapping epitope(s) on PACAP as Ab17.

[0721] In a further embodiment of the invention, antigen-binding fragments comprise, or alternatively consist of, Fab fragments having binding specificity for PACAP. With respect to antibody Ab17, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 282 and the variable light chain sequence of SEQ ID NO: 302, or sequences that are at least 90%, 95%, 96%, 97%, 98%, or 99% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 282 and/or SEQ ID NO: 302 that retain the binding specificity for PACAP.

[0722] In one embodiment of the invention described herein, Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab17. In another embodiment of the invention, anti-PACAP antibodies such as Ab17 and Fab fragments may be produced via expression in mammalian cells, such as CHO, NSO, or HEK 293 cells, fungal, insect, or microbial systems, such as yeast cells (for example haploid or diploid yeast, such as haploid or diploid *Pichia*) and other yeast strains. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*.

[0723] In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to PACAP, including the heavy and/or light chains of Ab17, as well as fragments, variants, and combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them, or sequences that are at least 90% or 95% identical thereto.

Antibody Ab18

[0724] In one embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that possess a heavy chain sequence comprising the sequence of SEQ ID NO: 321 which consists of the heavy chain variable region of SEQ ID NO: 322 linked to the heavy chain constant region of SEQ ID NO: 330.

[0725] In one embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a variable heavy chain sequence comprising the sequence set forth below:

(SEQ ID NO: 322)
QSVEESGGRLVTPGTPLTLTCTVSGFSLSSAALSWVRQAPGKGLEWIGII

DKGVMSYYASWAKGRFTISKTSSTTVDLKVTSPTTEDTATYFCARGGGEF

FIWGQGTLVTVSS.

[0726] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that bind the same epitope as Ab18, and that contain a constant heavy chain sequence comprising the polypeptide of SEQ ID NO: 1244, 1245, or 1246, or comprising the sequence set forth below:

(SEQ ID NO: 330)
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV

HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEP

KSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS

HEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGK

EYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTC

LVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW

QQGNVFSCSVMHEALHNHYTQKSLSLSPGK.

[0727] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a light chain sequence comprising the sequence of SEQ ID NO: 341 which consists of the light chain variable region of SEQ ID NO: 342 linked to the light chain constant region of SEQ ID NO: 350.

[0728] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a variable light chain sequence comprising the sequence set forth below:

(SEQ ID NO: 342)
AQVLTQTPSSVSAAVGGTVTINCQSSKSVYNNNWLSWYQQKPGQPPKFLI

YQASNLASGVPSRFKGSGSGTQFTLTISDLECDDAATYYCAGGYSGNIVG

FGGGTEVVVKR.

[0729] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding

specificity to PACAP, that bind the same epitope as Ab18, and that contain a constant light chain sequence comprising the sequence set forth below:

(SEQ ID NO: 350)
TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGN

SQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKS

FNRGEC.

[0730] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 324; SEQ ID NO: 326; and SEQ ID NO: 328, which correspond to the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 321, or which contain the variable heavy chain sequence of SEQ ID NO: 322, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 344; SEQ ID NO: 346; and SEQ ID NO: 348, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 341, or which contain the variable light chain sequence of SEQ ID NO: 342, or antibodies or antigen-binding fragments containing combinations of sequences that are at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention and antigen-binding fragments comprise, or alternatively consist of, combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

[0731] The invention further contemplates anti-PACAP antibodies and antigen-binding fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 323; SEQ ID NO: 325; SEQ ID NO: 327; and SEQ ID NO: 329, which correspond to the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 321, or the variable heavy chain sequence of SEQ ID NO: 322, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 343; SEQ ID NO: 345; SEQ ID NO: 347; and SEQ ID NO: 349, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 341, or the variable light chain sequence of SEQ ID NO: 342, or combinations of these polypeptide sequences, or sequences that are at least 80%, 90%, 95%, 96%, 97%, 98%, or 99% identical therewith.

[0732] In another embodiment of the invention, the anti-PACAP antibodies and antigen-binding fragments of the invention or fragments comprise, or alternatively consist of, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them, or sequences that are at least 90% or 95% identical thereto.

[0733] In another embodiment of the invention, the anti-PACAP antibodies and antigen-binding fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 321, or SEQ ID NO: 322, or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, the antibodies and antigen-binding fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 341, or SEQ ID NO: 342, or polypeptides that are at least 90% or 95% identical thereto.

[0734] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, or three of the polypeptide sequences of SEQ ID NO: 324; SEQ ID NO: 326; and SEQ ID NO: 328, which correspond to the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 321, or the variable heavy chain sequence of SEQ ID NO: 322, or sequences that are at least 90% or 95% identical thereto.

[0735] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, or three of the polypeptide sequences of SEQ ID NO: 344; SEQ ID NO: 346; and SEQ ID NO: 348, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 341, or the variable light chain sequence of SEQ ID NO: 342, or sequences that are at least 90% or 95% identical thereto.

[0736] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 323; SEQ ID NO: 325; SEQ ID NO: 327; and SEQ ID NO: 329, which correspond to the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 321, or the variable heavy chain sequence of SEQ ID NO: 322, or sequences that are at least 90% or 95% identical thereto.

[0737] In a further embodiment of the invention, the subject antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 343; SEQ ID NO: 345; SEQ ID NO: 347; and SEQ ID NO: 349, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 341, or the variable light chain sequence of SEQ ID NO: 342, or sequences that are at least 90% or 95% identical thereto.

[0738] The invention also contemplates anti-PACAP antibodies and antigen-binding fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 322; the variable light chain region of SEQ ID NO: 342; the complementarity determining regions (SEQ ID NO: 324; SEQ ID NO: 326; and SEQ ID NO: 328) of the variable heavy chain region of SEQ ID NO: 322; and the complementarity determining regions (SEQ ID NO: 344; SEQ ID NO: 346; and SEQ ID NO: 348) of the variable light chain region of SEQ ID NO: 342, or sequences that are at least 90% or 95% identical thereto. In another embodiment of the invention, fragments of the antibodies having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 322; the variable light chain region of SEQ ID NO: 342; the framework regions (SEQ ID NO: 323; SEQ ID NO: 325; SEQ ID NO: 327; and SEQ ID NO: 329) of the variable heavy chain region of SEQ ID NO: 322; and the framework regions (SEQ ID NO: 343; SEQ ID NO: 345; SEQ ID NO: 347; and

SEQ ID NO: 349) of the variable light chain region of SEQ ID NO: 342, or sequences that are at least 90% or 95% identical thereto.

[0739] In another embodiment of the invention, the anti-PACAP antibody is Ab18, comprising, or alternatively consisting of, SEQ ID NO: 321 and SEQ ID NO: 341, or SEQ ID NO: 322 and SEQ ID NO: 342, or an antibody or antigen-binding fragment comprising the CDRs of Ab18 and having at least one of the biological activities set forth herein, or is an anti-PACAP antibody that competes with Ab18 in binding PACAP, preferably one containing sequences that are at least 90%, 95%, 96%, 97%, 98%, or 99% identical to that of Ab18, or an antibody that binds to the same or overlapping epitope(s) on PACAP as Ab18.

[0740] In a further embodiment of the invention, antigen-binding fragments comprise, or alternatively consist of, Fab fragments having binding specificity for PACAP. With respect to antibody Ab18, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 322 and the variable light chain sequence of SEQ ID NO: 342, or sequences that are at least 90%, 95%, 96%, 97%, 98%, or 99% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 322 and/or SEQ ID NO: 342 that retain the binding specificity for PACAP.

[0741] In one embodiment of the invention described herein, Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab18. In another embodiment of the invention, anti-PACAP antibodies such as Ab18 and Fab fragments may be produced via expression in mammalian cells, such as CHO, NSO, or HEK 293 cells, fungal, insect, or microbial systems, such as yeast cells (for example haploid or diploid yeast, such as haploid or diploid *Pichia*) and other yeast strains. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*.

[0742] In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to PACAP, including the heavy and/or light chains of Ab18, as well as fragments, variants, and combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them, or sequences that are at least 90% or 95% identical thereto.

Antibody Ab19

[0743] In one embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that possess a heavy chain sequence comprising the sequence of SEQ ID NO: 361 which consists of the heavy chain variable region of SEQ ID NO: 362 linked to the heavy chain constant region of SEQ ID NO: 370.

[0744] In one embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a variable heavy chain sequence comprising the sequence set forth below:

(SEQ ID NO: 362)
QSVEASGGRLVTPGTPLTLTCTVSGFSLSSATMNWVRQAPGKGLEWIGLI

GGNDERYYASWAKGRFTISKTSSTTVDLKMTSPTTEDTATYFCARGGGEF

FIWGPGTLVTVSS.

[0745] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that bind the same epitope as Ab19, and that contain a constant heavy chain sequence comprising the polypeptide of SEQ ID NO: 1244, 1245, or 1246, or comprising the sequence set forth below:

(SEQ ID NO: 370)
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV

HTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEP

KSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS

HEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGK

EYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTC

LVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW

QQGNVFSCSVMHEALHNHYTQKSLSLSPGK.

[0746] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a light chain sequence comprising the sequence of SEQ ID NO: 381 which consists of the light chain variable region of SEQ ID NO: 382 linked to the light chain constant region of SEQ ID NO: 390.

[0747] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain a variable light chain sequence comprising the sequence set forth below:

(SEQ ID NO: 382)
AQVLTQTPSSVSAAVGGTVTINCQSSESVYTNDRLSWYQQKPGQPPKLLI

YEASKLASGVPPRFSGSGSGTQFTLTISDLECDDAATYYCAGAYSTSIHG

FGGGTEVVVKR.

[0748] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP, that bind the same epitope as Ab19, and that contain a constant light chain sequence comprising the sequence set forth below:

(SEQ ID NO: 390)
TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGN

SQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKS

FNRGEC.

[0749] In another embodiment, the invention includes antibodies and antigen-binding fragments having binding specificity to PACAP that contain one, two, or three of the polypeptide sequences of SEQ ID NO: 364; SEQ ID NO: 366; and SEQ ID NO: 368, which correspond to the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 361, or which contain the variable heavy chain sequence of SEQ ID NO: 362, and/or which further contain one, two, or three of the polypeptide sequences of SEQ ID NO: 384; SEQ ID NO: 386; and SEQ ID NO: 388, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 381, or which contain the variable light chain sequence of SEQ ID NO: 382, or antibodies or antigen-binding fragments containing combinations of sequences that are at least 80%, 85%, 90%, 95%,

96%, 97%, 98%, or 99% identical thereto. In another embodiment of the invention, the antibodies of the invention and antigen-binding fragments comprise, or alternatively consist of, combinations of one or more of the exemplified variable heavy chain and variable light chain sequences, or the heavy chain and light chain sequences set forth above, or sequences that are at least 90% or 95% identical thereto.

[0750] The invention further contemplates anti-PACAP antibodies and antigen-binding fragments comprising one, two, three, or four of the polypeptide sequences of SEQ ID NO: 363; SEQ ID NO: 365; SEQ ID NO: 367; and SEQ ID NO: 369, which correspond to the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 361, or the variable heavy chain sequence of SEQ ID NO: 362, and/or one, two, three, or four of the polypeptide sequences of SEQ ID NO: 383; SEQ ID NO: 385; SEQ ID NO: 387; and SEQ ID NO: 389, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 381, or the variable light chain sequence of SEQ ID NO: 382, or combinations of these polypeptide sequences, or sequences that are at least 80%, 90%, 95%, 96%, 97%, 98%, or 99% identical therewith.

[0751] In another embodiment of the invention, the anti-PACAP antibodies and antigen-binding fragments of the invention or fragments comprise, or alternatively consist of, combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them, or sequences that are at least 90% or 95% identical thereto.

[0752] In another embodiment of the invention, the anti-PACAP antibodies and antigen-binding fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 361, or SEQ ID NO: 362, or polypeptides that are at least 90% or 95% identical thereto. In another embodiment of the invention, the antibodies and antigen-binding fragments of the invention comprise, or alternatively consist of, the polypeptide sequence of SEQ ID NO: 381, or SEQ ID NO: 382, or polypeptides that are at least 90% or 95% identical thereto.

[0753] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, or three of the polypeptide sequences of SEQ ID NO: 364; SEQ ID NO: 366; and SEQ ID NO: 368, which correspond to the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 361, or the variable heavy chain sequence of SEQ ID NO: 362, or sequences that are at least 90% or 95% identical thereto.

[0754] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, or three of the polypeptide sequences of SEQ ID NO: 384; SEQ ID NO: 386; and SEQ ID NO: 388, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 381, or the variable light chain sequence of SEQ ID NO: 382, or sequences that are at least 90% or 95% identical thereto.

[0755] In a further embodiment of the invention, the antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 363; SEQ ID NO: 365; SEQ ID NO: 367; and SEQ ID NO: 369, which correspond to the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 361, or the variable heavy chain sequence of SEQ ID NO: 362, or sequences that are at least 90% or 95% identical thereto.

[0756] In a further embodiment of the invention, the subject antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or four of the polypeptide sequences of SEQ ID NO: 383; SEQ ID NO: 385; SEQ ID NO: 387; and SEQ ID NO: 389, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 381, or the variable light chain sequence of SEQ ID NO: 382, or sequences that are at least 90% or 95% identical thereto.

[0757] The invention also contemplates anti-PACAP antibodies and antigen-binding fragments that include one or more of the antibody fragments described herein. In one embodiment of the invention, antibodies and antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 362; the variable light chain region of SEQ ID NO: 382; the complementarity determining regions (SEQ ID NO: 364; SEQ ID NO: 366; and SEQ ID NO: 368) of the variable heavy chain region of SEQ ID NO: 362; and the complementarity determining regions (SEQ ID NO: 384; SEQ ID NO: 386; and SEQ ID NO: 388) of the variable light chain region of SEQ ID NO: 382, or sequences that are at least 90% or 95% identical thereto. In another embodiment of the invention, fragments of the antibodies having binding specificity to PACAP comprise, or alternatively consist of, one, two, three, or more, including all of the following antibody fragments: the variable heavy chain region of SEQ ID NO: 362; the variable light chain region of SEQ ID NO: 382; the framework regions (SEQ ID NO: 363; SEQ ID NO: 365; SEQ ID NO: 367; and SEQ ID NO: 369) of the variable heavy chain region of SEQ ID NO: 362; and the framework regions (SEQ ID NO: 383; SEQ ID NO: 385; SEQ ID NO: 387; and SEQ ID NO: 389) of the variable light chain region of SEQ ID NO: 382, or sequences that are at least 90% or 95% identical thereto.

[0758] In another embodiment of the invention, the anti-PACAP antibody is Ab19, comprising, or alternatively consisting of, SEQ ID NO: 361 and SEQ ID NO: 381, or SEQ ID NO: 362 and SEQ ID NO: 382, or an antibody or antigen-binding fragment comprising the CDRs of Ab19 and having at least one of the biological activities set forth herein, or is an anti-PACAP antibody that competes with Ab19 in binding PACAP, preferably one containing sequences that are at least 90%, 95%, 96%, 97%, 98%, or 99% identical to that of Ab19, or an antibody that binds to the same or overlapping epitope(s) on PACAP as Ab19.

[0759] In a further embodiment of the invention, antigen-binding fragments comprise, or alternatively consist of, Fab fragments having binding specificity for PACAP. With respect to antibody Ab19, the Fab fragment preferably includes the variable heavy chain sequence of SEQ ID NO: 362 and the variable light chain sequence of SEQ ID NO: 382, or sequences that are at least 90%, 95%, 96%, 97%, 98%, or 99% identical thereto. This embodiment of the invention further includes Fabs containing additions, deletions, and variants of SEQ ID NO: 362 and/or SEQ ID NO: 382 that retain the binding specificity for PACAP.

[0760] In one embodiment of the invention described herein, Fab fragments may be produced by enzymatic digestion (e.g., papain) of Ab19. In another embodiment of the invention, anti-PACAP antibodies such as Ab19 and Fab fragments may be produced via expression in mammalian cells, such as CHO, NSO, or HEK 293 cells, fungal, insect, or microbial systems, such as yeast cells (for example haploid or diploid yeast, such as haploid or diploid *Pichia*) and other yeast strains. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*.

[0761] In an additional embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to PACAP, including the heavy and/or light chains of Ab19, as well as fragments, variants, and combinations of one or more of the FRs, CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them, or sequences that are at least 90% or 95% identical thereto.

[0762] In another embodiment, the invention contemplates an isolated anti-PACAP antibody comprising a V_H polypeptide sequence selected from: SEQ ID NO: 2, SEQ ID NO: 42, SEQ ID NO: 82, SEQ ID NO: 122, SEQ ID NO: 162, SEQ ID NO: 202, SEQ ID NO: 242, SEQ ID NO: 282, SEQ ID NO: 322, SEQ ID NO: 362, SEQ ID NO: 482; SEQ ID NO: 522; SEQ ID NO: 562; SEQ ID NO: 602; SEQ ID NO: 642; SEQ ID NO: 682; SEQ ID NO: 722; SEQ ID NO: 762; SEQ ID NO: 802, or a variant thereof; and further comprising a V_L polypeptide sequence selected from: SEQ ID NO: 22, SEQ ID NO: 62, SEQ ID NO: 102, SEQ ID NO: 142, SEQ ID NO: 182, SEQ ID NO: 222, SEQ ID NO: 262, SEQ ID NO: 302, SEQ ID NO: 342, SEQ ID NO: 382, SEQ ID NO: 502; SEQ ID NO: 542; SEQ ID NO: 582; SEQ ID NO: 622; SEQ ID NO: 662; SEQ ID NO: 702; SEQ ID NO: 742; SEQ ID NO: 782; SEQ ID NO: 822, or a variant thereof, wherein one or more of the framework region residues ("FR residues") and/or CDR residues in said V_H or V_L polypeptide has been substituted with another amino acid residue resulting in an anti-PACAP antibody that specifically binds PACAP. The invention also includes humanized and chimeric forms of these antibodies. The chimeric and humanized antibodies may include an Fc derived from IgG1, IgG2, IgG3, or IgG4 constant regions.

[0763] In one embodiment of the invention, the chimeric or humanized antibodies or fragments or V_H or V_L polypeptides originate or are derived from one or more rabbit antibodies, e.g., a rabbit antibody isolated from a clonal rabbit B cell population.

[0764] In some aspects, the invention provides a vector comprising a nucleic acid molecule encoding an anti-PACAP antibody or fragment thereof as disclosed herein. In some embodiments, the invention provides a host cell comprising a nucleic acid molecule encoding an anti-PACAP antibody or fragment thereof as disclosed herein.

[0765] In some aspects, the invention provides an isolated antibody or antigen binding fragment thereof that competes for binding to PACAP with an antibody or antigen binding fragment thereof disclosed herein.

[0766] In some aspects, the invention provides a nucleic acid molecule encoding an antibody or antigen binding fragment thereof as disclosed herein.

[0767] In some aspects, the invention provides a pharmaceutical or diagnostic composition comprising at least one antibody or antigen binding fragment thereof as disclosed herein.

[0768] In some aspects, the invention provides a method for treating or preventing a condition associated with elevated PACAP levels in a subject, comprising administering to a subject in need thereof an effective amount of at least one isolated antibody or antigen binding fragment thereof as disclosed herein.

[0769] In some aspects, the invention provides a method of inhibiting binding of PACAP to PAC1-R, VPAC1-R, and/or VPAC2-R in a subject comprising administering an effective amount of at least one antibody or antigen binding fragment thereof as disclosed herein.

[0770] In some aspects, the invention provides an antibody or antigen binding fragment thereof that selectively binds to PACAP, wherein the antibody or antigen binding fragment thereof binds to PACAP with a K_D of less than or equal to 5×10^{-5} M, 10^{-5} M, 5×10^{-6} M, 10^{-6} M, 5×10^{-7} M, 10^{-7} M, 5×10^{-8} M, 10^{-8} M, 5×10^{-9} M, 10^{-9} M, 5×10^{-10} M, 10^{-10} M, 5×10^{-11} M, 10^{-11} M, 5×10^{-12} M, 10^{-12} M, 5×10^{-13} M, or 10^{-13} M; preferably, with a K_D of less than or equal to 5×10^{-10} M, 10^{-10} M, 5×10^{-11} M, 10^{-11} M, 5×10^{-12} M, or 10^{-12} M; more preferably, with a K_D that is less than about 100 pM, less than about 50 pM, less than about 40 pM, less than about 25 pM, less than about 1 pM, between about 10 pM and about 100 pM, between about 1 pM and about 100 pM, or between about 1 pM and about 10 pM. Preferably, the anti-PACAP antibody or antigen binding fragment thereof has no cross-reactivity or minimal cross-reactivity with VIP.

[0771] The inventive antibodies and antigen binding fragments thereof may be modified post-translationally to add effector moieties such as chemical linkers, detectable moieties such as for example fluorescent dyes, enzymes, substrates, bioluminescent materials, radioactive materials, and chemiluminescent moieties, or functional moieties such as for example streptavidin, avidin, biotin, a cytotoxin, a cytotoxic agent, and radioactive materials.

[0772] Antibodies and antigen binding fragments thereof may also be chemically modified to provide additional advantages such as increased solubility, stability and circulating time (in vivo half-life) of the polypeptide, or decreased immunogenicity (See U.S. Pat. No. 4,179,337). The chemical moieties for derivatization may be selected from water soluble polymers such as polyethylene glycol, ethylene glycol/propylene glycol copolymers, carboxymethylcellulose, dextran, polyvinyl alcohol, and the like. The antibodies and fragments thereof may be modified at random positions within the molecule, or at predetermined positions within the molecule and may include one, two, three, or more attached chemical moieties.

[0773] The polymer may be of any molecular weight, and may be branched or unbranched. For polyethylene glycol, the preferred molecular weight is between about 1 kDa and about 100 kDa (the term "about" indicating that in preparations of polyethylene glycol, some molecules will weigh more, some less, than the stated molecular weight) for ease in handling and manufacturing. Other sizes may be used, depending on the desired therapeutic profile (e.g., the duration of sustained release desired, the effects, if any on biological activity, the ease in handling, the degree or lack of antigenicity and other known effects of the polyethylene glycol to a therapeutic protein or analog). For example, the

polyethylene glycol may have an average molecular weight of about 200, 500, 1000, 1500, 2000, 2500, 3000, 3500, 4000, 4500, 5000, 5500, 6000, 6500, 7000, 7500, 8000, 8500, 9000, 9500, 10,000, 10,500, 11,000, 11,500, 12,000, 12,500, 13,000, 13,500, 14,000, 14,500, 15,000, 15,500, 16,000, 16,500, 17,000, 17,500, 18,000, 18,500, 19,000, 19,500, 20,000, 25,000, 30,000, 35,000, 40,000, 50,000, 55,000, 60,000, 65,000, 70,000, 75,000, 80,000, 85,000, 90,000, 95,000, or 100,000 kDa. Branched polyethylene glycols are described, for example, in U.S. Pat. No. 5,643,575; Morpurgo et al., *Appl. Biochem. Biotechnol.,* 56:59-72 (1996); Vorobjev et al., *Nucleosides and Nucleotides,* 18:2745-2750 (1999); and Caliceti et al., *Bioconjug. Chem.,* 10:638-646 (1999), the disclosures of each of which are incorporated herein by reference.

[0774] There are a number of attachment methods available to those skilled in the art (See e.g., EP 0 401 384, herein incorporated by reference, disclosing a method of coupling PEG to G-CSF; and Malik et al., *Exp. Hematol.,* 20:1028-1035 (1992) (reporting pegylation of GM-CSF using tresyl chloride)). For example, polyethylene glycol may be covalently bound through amino acid residues via a reactive group, such as, a free amino or carboxyl group. Reactive groups are those to which an activated polyethylene glycol molecule may be bound. The amino acid residues having a free amino group may include lysine residues and the N-terminal amino acid residues; those having a free carboxyl group may include aspartic acid residues glutamic acid residues and the C-terminal amino acid residue. Sulfhydryl groups may also be used as a reactive group for attaching the polyethylene glycol molecules. Preferred for therapeutic purposes is attachment at an amino group, such as attachment at the N-terminus or lysine group.

[0775] As suggested above, polyethylene glycol may be attached to proteins via linkage to any of a number of amino acid residues. For example, polyethylene glycol can be linked to polypeptides via covalent bonds to lysine, histidine, aspartic acid, glutamic acid, or cysteine residues. One or more reaction chemistries may be employed to attach polyethylene glycol to specific amino acid residues (e.g., lysine, histidine, aspartic acid, glutamic acid, or cysteine) or to more than one type of amino acid residue (e.g., lysine, histidine, aspartic acid, glutamic acid, cysteine and combinations thereof).

[0776] Alternatively, antibodies or antigen binding fragments thereof may have increased in vivo half-lives via fusion with albumin (including but not limited to recombinant human serum albumin or fragments or variants thereof (See, e.g., U.S. Pat. No. 5,876,969, EP 0 413 622, and U.S. Pat. No. 5,766,883, herein incorporated by reference in their entirety)), or other circulating blood proteins such as transferrin or ferritin. In a preferred embodiment, polypeptides and/or antibodies of the present invention (including fragments or variants thereof) are fused with the mature form of human serum albumin (i.e., amino acids 1-585 of human serum albumin as shown in FIGS. 1 and 2 of EP 0 322 094) which is herein incorporated by reference in its entirety. Polynucleotides encoding fusion proteins of the invention are also encompassed by the invention.

[0777] Regarding detectable moieties, further exemplary enzymes include, but are not limited to, horseradish peroxidase, acetylcholinesterase, alkaline phosphatase, beta-galactosidase, and luciferase. Further exemplary fluorescent materials include, but are not limited to, rhodamine, fluorescein, fluorescein isothiocyanate, umbelliferone, dichlorotriazinylamine, phycoerythrin, and dansyl chloride. Further exemplary chemiluminescent moieties include, but are not limited to, luminol. Further exemplary bioluminescent materials include, but are not limited to, luciferin and aequorin. Further exemplary radioactive materials include, but are not limited to, Iodine 125 (^{125}I), Carbon 14 (^{14}C), Sulfur 35 (^{35}S), Tritium (^{3}H) and Phosphorus 32 (^{32}P).

[0778] Methods are known in the art for conjugating an antibody or antigen binding fragment thereof to a detectable moiety and the like, such as for example those methods described by Hunter et al., *Nature,* 144:945 (1962); David et al., *Biochemistry,* 13:1014 (1974); Pain et al., *J. Immunol. Meth.,* 40:219 (1981); and Nygren, *J., Histochem. and Cytochem.,* 30:407 (1982).

[0779] Embodiments described herein further include variants and equivalents that are substantially homologous to the antibodies, antibody fragments, diabodies, SMIPs, camelbodies, nanobodies, IgNAR, polypeptides, variable regions, and CDRs set forth herein. These may contain, e.g., conservative substitution mutations, (i.e., the substitution of one or more amino acids by similar amino acids). For example, conservative substitution refers to the substitution of an amino acid with another within the same general class, e.g., one acidic amino acid with another acidic amino acid, one basic amino acid with another basic amino acid, or one neutral amino acid by another neutral amino acid. What is intended by a conservative amino acid substitution is well known in the art.

[0780] In another embodiment, the invention contemplates polypeptide sequences having at least 90% or greater sequence homology to any one or more of the polypeptide sequences of antigen binding fragments, variable regions and CDRs set forth herein. More preferably, the invention contemplates polypeptide sequences having at least 95% or greater sequence homology, even more preferably at least 98% or greater sequence homology, and still more preferably at least 99% or greater sequence homology to any one or more of the polypeptide sequences of antigen binding fragments, variable regions, and CDRs set forth herein.

[0781] Methods for determining homology between nucleic acid and amino acid sequences are well known to those of ordinary skill in the art.

[0782] In another embodiment, the invention further contemplates the above-recited polypeptide homologs of the antigen binding fragments, variable regions and CDRs set forth herein further having anti-PACAP activity. Non-limiting examples of anti-PACAP activity are set forth herein, e.g., ability to inhibit PACAP binding to PAC1-R, VPAC1-R, and/or VPAC2-R, thereby resulting in the reduced production of cAMP.

[0783] In another embodiment, the invention further contemplates the generation and use of antibodies that bind any of the foregoing sequences, including, but not limited to, anti-idiotypic antibodies. In an exemplary embodiment, such an anti-idiotypic antibody could be administered to a subject who has received an anti-PACAP antibody to modulate, reduce, or neutralize, the effect of the anti-PACAP antibody. Such antibodies could also be useful for treatment of an autoimmune disease characterized by the presence of anti-PACAP antibodies. A further exemplary use of such antibodies, e.g., anti-idiotypic antibodies, is for detection of the anti-PACAP antibodies of the present invention, for example to monitor the levels of the anti-PACAP antibodies

present in a subject's blood or other bodily fluids. For example, in one embodiment, the invention provides a method of using the anti-idiotypic antibody to monitor the in vivo levels of said anti-PACAP antibody or antigen binding fragment thereof in a subject or to neutralize said anti-PACAP antibody in a subject being administered said anti-PACAP antibody or antigen binding fragment thereof.

[0784] The present invention also contemplates anti-PACAP antibodies comprising any of the polypeptide or polynucleotide sequences described herein substituted for any of the other polynucleotide sequences described herein. For example, without limitation thereto, the present invention contemplates antibodies comprising the combination of any of the variable light chain and variable heavy chain sequences described herein, and further contemplates antibodies resulting from substitution of any of the CDR sequences described herein for any of the other CDR sequences described herein.

Exemplary Polynucleotides Encoding Anti-PACAP Antibody Polypeptides

[0785] The invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to PACAP.

Antibody Ab1

[0786] In one embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to PACAP. In one embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the polynucleotide sequence of SEQ ID NO: 11 which encodes the heavy chain sequence of SEQ ID NO: 1 and which consists of the heavy chain variable region coding sequence of SEQ ID NO: 12 and the heavy chain constant region coding sequence of SEQ ID NO: 20.

[0787] In another embodiment of the invention, the polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the variable heavy chain polypeptide sequence of SEQ ID NO: 2:

(SEQ ID NO: 12)

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cagtcggtggaggagtccgggggtcgcctggtcacgcctgggacacccct

gacactcacctgcaccgtctctggattctccctcagtagcgctgtaatga

attgggtccgccaggctccagggaaggggctggaatggatcggaagtatt

gttgctagtggtaccacatactacgcgagctgggcgaacggccgattcac

catctccaaaacctcgtcgaccacgatggatctgaaaatgaccagtccga

caaccgaggacacggccacctatttctgtgccagagggggagggaatttt

ttcatctggggcccggggaccctcgtcaccgtctcgagc.
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[0788] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the constant heavy chain polypeptide sequence of SEQ ID NO: 10:

(SEQ ID NO: 20)

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gcctccaccaagggcccatcggtcttcccctggcaccctcctccaagag

cacctctgggggcacagcggccctgggctgcctggtcaaggactacttcc

-continued

ccgaaccggtgacggtgtcgtggaactcaggcgccctgaccagcggcgtg

cacaccttcccggctgtcctacagtcctcaggactctactccctcagcag

cgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgca

acgtgaatcacaagcccagcaacaccaaggtggacgcgagagttgagccc

aaatcttgtgacaaaactcacacatgcccaccgtgcccagcacctgaact

cctgggggggaccgtcagtcttcctcttcccccaaaacccaaggacaccc

tcatgatctcccggaccctgaggtcacatgcgtggtggtggacgtgagc

cacgaagaccctgaggtcaagttcaactggtacgtggacggcgtggaggt

gcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtacc

gtgtggtcagcgtcctcaccgtcctgcaccaggactggctgaatggcaag

gagtacaagtgcaaggtctccaacaaagccctcccagccccatcgagaa

aaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccc

tgcccccatcccgggaggagatgaccaagaaccaggtcagcctgacctgc

ctggtcaaaggcttctatcccagcgacatcgccgtggagtgggagagcaa

tgggcagccggagaacaactacaagaccacgcctcccgtgctggactccg

acggctccttcttcctctacagcaagctcaccgtggacaagagcaggtgg

cagcaggggaacgtcttctcatgctccgtgatgcatgaggctctgcacaa

ccactacacgcagaagagcctctccctgtctccgggtaaa.
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[0789] In another embodiment of the invention, polynucleotides comprise, or alternatively consist of, the polynucleotide sequence of SEQ ID NO: 31 which encodes the light chain polypeptide sequence of SEQ ID NO: 21 and which consists of the light chain variable region coding sequence of SEQ ID NO: 32 and the light chain constant region coding sequence of SEQ ID NO: 40.

[0790] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the variable light chain polypeptide sequence of SEQ ID NO: 22:

(SEQ ID NO: 32)

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gaccctgtgatgacccagactccatcttccacgtctgcggctgtgggagg

cacagtcaccatcagttgccagtccagtgagagtgtttatagtaactact

tatcctggtatcagcagaaaccagggcagcctcccaacttcctgatctac

caggcatccaatttggcatctggggtcccatcgcggttcaaaggcagtgg

atctgggacacagttcactctcaccatcaccgacctggagtgtgacgatg

ccgccacttattactgtgcaggcggttatagtgaaaacattgttggtttc

ggcggagggaccgaggtggtggtcaaacgt.
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[0791] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the constant light chain polypeptide sequence of SEQ ID NO: 30:

(SEQ ID NO: 40)
acggtagcggccccatctgtcttcatcttcccgccatctgatgagcagtt

gaaatctggaactgcctctgttgtgtgcctgctgaataacttctatccca

gagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaac

tcccaggagagtgtcacagagcaggacagcaaggacagcacctacagcct

cagcagcaccctgacgctgagcaaagcagactacgagaaacacaaagtct

acgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagc

ttcaacaggggagagtgt.

[0792] In a further embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one or more of the polynucleotide sequences of SEQ ID NO: 14; SEQ ID NO: 16; and SEQ ID NO: 18, which correspond to polynucleotides encoding the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 1, or the variable heavy chain sequence of SEQ ID NO: 2, and/or one or more of the polynucleotide sequences of SEQ ID NO: 34; SEQ ID NO: 36; and SEQ ID NO: 38, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 21, or the variable light chain sequence of SEQ ID NO: 22, or combinations of these polynucleotide sequences. In another embodiment of the invention, the polynucleotides encoding the antibodies of the invention or antigen-binding fragments thereof comprise, or alternatively consist of, combinations of polynucleotides encoding one or more of the CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them.

[0793] In a further embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one or more of the polynucleotide sequences of SEQ ID NO: 13; SEQ ID NO: 15; SEQ ID NO: 17; and SEQ ID NO: 19, which correspond to polynucleotides encoding the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 1, or the variable heavy chain sequence of SEQ ID NO: 2, and/or one or more of the polynucleotide sequences of SEQ ID NO: 33; SEQ ID NO: 35; SEQ ID NO: 37; and SEQ ID NO: 39, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 21, or the variable light chain sequence of SEQ ID NO: 22, or combinations of these polynucleotide sequences. In another embodiment of the invention, the polynucleotides encoding the antibodies of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them.

[0794] The invention also contemplates polynucleotide sequences including one or more of the polynucleotide sequences encoding antigen-binding fragments described herein. In one embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three or more, including all of the following polynucleotides encoding antigen-binding fragments: the polynucleotide SEQ ID NO: 11 encoding the heavy chain sequence of SEQ ID NO: 1; the polynucleotide SEQ ID NO: 12 encoding the variable heavy chain sequence of SEQ ID NO: 2; the polynucleotide SEQ ID NO: 31 encoding the light chain sequence of SEQ ID NO: 21; the polynucleotide SEQ ID NO: 32 encoding the variable light chain sequence of SEQ ID NO: 22; polynucleotides encoding the CDRs (SEQ ID NO: 14; SEQ ID NO: 16; and SEQ ID NO: 18) of the heavy chain sequence of SEQ ID NO: 1, or the variable heavy chain sequence of SEQ ID NO: 2; polynucleotides encoding the CDRs (SEQ ID NO: 34; SEQ ID NO: 36; and SEQ ID NO: 38) of the light chain sequence of SEQ ID NO: 21, or the variable light chain sequence of SEQ ID NO: 22; polynucleotides encoding the FRs (SEQ ID NO: 13; SEQ ID NO: 15; SEQ ID NO: 17; and SEQ ID NO: 19) of the heavy chain sequence of SEQ ID NO: 1, or the variable heavy chain sequence of SEQ ID NO: 2; and polynucleotides encoding the FRs (SEQ ID NO: 33; SEQ ID NO: 35; SEQ ID NO: 37; and SEQ ID NO: 39) of the light chain sequence of SEQ ID NO: 21, or the variable light chain sequence of SEQ ID NO: 22.

[0795] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, polynucleotides encoding Fab fragments having binding specificity for PACAP. With respect to antibody Ab1, the polynucleotides encoding the full length Ab1 antibody comprise, or alternatively consist of, the polynucleotide SEQ ID NO: 11 encoding the heavy chain sequence of SEQ ID NO: 1, and the polynucleotide SEQ ID NO: 31 encoding the light chain sequence of SEQ ID NO: 21.

[0796] Another embodiment of the invention contemplates these polynucleotides incorporated into an expression vector for expression in mammalian cells such as CHO, NSO, or HEK-293 cells, or in fungal, insect, or microbial systems such as yeast cells such as the yeast *Pichia*. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*. In one embodiment of the invention described herein, Fab fragments can be produced by enzymatic digestion (e.g., papain) of Ab1 following expression of the full-length polynucleotides in a suitable host. In another embodiment of the invention, anti-PACAP antibodies, such as Ab1 or Fab fragments thereof, can be produced via expression of Ab1 polynucleotides in mammalian cells such as CHO, NSO, or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example diploid yeast such as diploid *Pichia*) and other yeast strains. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*.

Antibody Ab1.H

[0797] In one embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to PACAP. In one embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the polynucleotide sequence of SEQ ID NO: 51 which encodes the heavy chain sequence of SEQ ID NO: 41 and which consists of the heavy chain variable region coding sequence of SEQ ID NO: 52 and the heavy chain constant region coding sequence of SEQ ID NO: 60.

[0798] In another embodiment of the invention, the polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the variable heavy chain polypeptide sequence of SEQ ID NO: 42:

(SEQ ID NO: 52)

gaggtgcagcttgtggagtctgggggaggcttggtccagcctgggggtc

cctgagactctcctgtgcagcctctggattcaccgtcagtagcgctgtaa

tgaattgggtccgtcaggctccagggaaggggctggagtggatcggaagt

attgttgctagtggtaccacatactacgctagctctgctaacggccgatt

caccatctccagagacaattccaagaacaccctgtatcttcaaatgaaca

gcctgagagctgaggacactgctgtgtattactgtgctagaggggaggg

gaatttttcatctggggccaagggaccctcgtcaccgtctcgagc.

[0799] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the constant heavy chain polypeptide sequence of SEQ ID NO: 50:

(SEQ ID NO: 60)

gcctccaccaagggcccatcggtcttccccctggcaccctcctccaagag

cacctctgggggcacagcggccctgggctgcctggtcaaggactacttcc

ccgaaccggtgacggtgtcgtggaactcaggcgccctgaccagcggcgtg

cacaccttcccggctgtcctacagtcctcaggactctactccctcagcag

cgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgca

acgtgaatcacaagcccagcaacaccaaggtggacaagaaagttgagccc

aaatcttgtgacaaaactcacacatgcccaccgtgcccagcacctgaact

cctgggggggaccgtcagtcttcctcttcccccaaaacccaaggacaccc

tcatgatctcccggacccctgaggtcacatgcgtggtggtggacgtgagc

cacgaagaccctgaggtcaagttcaactggtacgtggacggcgtggaggt

gcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtacc

gtgtggtcagcgtcctcaccgtcctgcaccaggactggctgaatggcaag

gagtacaagtgcaaggtctccaacaaagccctcccagcccccatcgagaa

aaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccc

tgcccccatcccgggaggagatgaccaagaaccaggtcagcctgacctgc

ctggtcaaaggcttctatcccagcgacatcgccgtggagtgggagagcaa

tgggcagccggagaacaactacaagaccacgcctcccgtgctggactccg

acggctccttcttcctctacagcaagctcaccgtggacaagagcaggtgg

cagcaggggaacgtcttctcatgctccgtgatgcatgaggctctgcacaa

ccactacacgcagaagagcctctccctgtctccgggtaaa.

[0800] In another embodiment of the invention, polynucleotides comprise, or alternatively consist of, the polynucleotide sequence of SEQ ID NO: 71 which encodes the light chain polypeptide sequence of SEQ ID NO: 61 and which consists of the light chain variable region coding sequence of SEQ ID NO: 72 and the light chain constant region coding sequence of SEQ ID NO: 80.

[0801] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the variable light chain polypeptide sequence of SEQ ID NO: 62:

(SEQ ID NO: 72)

gacatccagatgacccagtctccttccaccctgtctgcatctgtaggaga

cagagtcaccatcacttgtcagtccagtgagagtgtttatagtaactact

tatcctggtatcagcagaaaccaggaaaagcccctaagttcctgatctat

caggcatccaatttggcatctggagtcccatcaaggttcagcggcagtgg

atctggaacagaattcactctcaccatcagcagcctgcagcctgatgatt

ttgcaacttactactgtgcaggcggttatagtgaaaacattgttggtttc

ggcggaggaaccaaggtggaaatcaaacgt.

[0802] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the constant light chain polypeptide sequence of SEQ ID NO: 70:

(SEQ ID NO: 80)

acggtagcggccccatctgtcttcatcttcccgccatctgatgagcagtt

gaaatctggaactgcctctgttgtgtgcctgctgaataacttctatccca

gagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaac

tcccaggagagtgtcacagagcaggacagcaaggacagcacctacagcct

cagcagcaccctgacgctgagcaaagcagactacgagaaacacaaagtct

acgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagc

ttcaacaggggagagtgt.

[0803] In a further embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one or more of the polynucleotide sequences of SEQ ID NO: 54; SEQ ID NO: 56; and SEQ ID NO: 58, which correspond to polynucleotides encoding the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 41, or the variable heavy chain sequence of SEQ ID NO: 42, and/or one or more of the polynucleotide sequences of SEQ ID NO: 74; SEQ ID NO: 76; and SEQ ID NO: 78, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 61, or the variable light chain sequence of SEQ ID NO: 62, or combinations of these polynucleotide sequences. In another embodiment of the invention, the polynucleotides encoding the antibodies of the invention or antigen-binding fragments thereof comprise, or alternatively consist of, combinations of polynucleotides encoding one or more of the CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them.

[0804] In a further embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one or more of the polynucleotide sequences of SEQ ID NO: 53; SEQ ID NO: 55; SEQ ID NO: 57; and SEQ ID NO: 59, which correspond to polynucleotides encoding the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 41, or the variable heavy chain sequence of SEQ ID NO: 42, and/or one or more of the polynucleotide sequences of SEQ ID NO: 73; SEQ ID NO: 75; SEQ ID NO: 77; and SEQ ID NO: 79, which correspond to the FRs

(constant regions) of the light chain sequence of SEQ ID NO: 61, or the variable light chain sequence of SEQ ID NO: 62, or combinations of these polynucleotide sequences. In another embodiment of the invention, the polynucleotides encoding the antibodies of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them.

[0805] The invention also contemplates polynucleotide sequences including one or more of the polynucleotide sequences encoding antigen-binding fragments described herein. In one embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three or more, including all of the following polynucleotides encoding antigen-binding fragments: the polynucleotide SEQ ID NO: 51 encoding the heavy chain sequence of SEQ ID NO: 41; the polynucleotide SEQ ID NO: 52 encoding the variable heavy chain sequence of SEQ ID NO: 42; the polynucleotide SEQ ID NO: 71 encoding the light chain sequence of SEQ ID NO: 61; the polynucleotide SEQ ID NO: 72 encoding the variable light chain sequence of SEQ ID NO: 62; polynucleotides encoding the CDRs (SEQ ID NO: 54; SEQ ID NO: 56; and SEQ ID NO: 58) of the heavy chain sequence of SEQ ID NO: 41, or the variable heavy chain sequence of SEQ ID NO: 42; polynucleotides encoding the CDRs (SEQ ID NO: 74; SEQ ID NO: 76; and SEQ ID NO: 78) of the light chain sequence of SEQ ID NO: 61, or the variable light chain sequence of SEQ ID NO: 62; polynucleotides encoding the FRs (SEQ ID NO: 53; SEQ ID NO: 55; SEQ ID NO: 57; and SEQ ID NO: 59) of the heavy chain sequence of SEQ ID NO: 41, or the variable heavy chain sequence of SEQ ID NO: 42; and polynucleotides encoding the FRs (SEQ ID NO: 73; SEQ ID NO: 75; SEQ ID NO: 77; and SEQ ID NO: 79) of the light chain sequence of SEQ ID NO: 61, or the variable light chain sequence of SEQ ID NO: 62.

[0806] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, polynucleotides encoding Fab fragments having binding specificity for PACAP. With respect to antibody Ab1.H, the polynucleotides encoding the full length Ab1.H antibody comprise, or alternatively consist of, the polynucleotide SEQ ID NO: 51 encoding the heavy chain sequence of SEQ ID NO: 41, and the polynucleotide SEQ ID NO: 71 encoding the light chain sequence of SEQ ID NO: 61.

[0807] Another embodiment of the invention contemplates these polynucleotides incorporated into an expression vector for expression in mammalian cells such as CHO, NSO, or HEK-293 cells, or in fungal, insect, or microbial systems such as yeast cells such as the yeast *Pichia*. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*. In one embodiment of the invention described herein, Fab fragments can be produced by enzymatic digestion (e.g., papain) of Ab1.H following expression of the full-length polynucleotides in a suitable host. In another embodiment of the invention, anti-PACAP antibodies, such as Ab1.H or Fab fragments thereof, can be produced via expression of Ab1.H polynucleotides in mammalian cells such as CHO, NSO, or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example diploid yeast such as diploid *Pichia*) and other yeast strains. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*.

Antibody Ab2

[0808] In one embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to PACAP. In one embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the polynucleotide sequence of SEQ ID NO: 91 which encodes the heavy chain sequence of SEQ ID NO: 81 and which consists of the heavy chain variable region coding sequence of SEQ ID NO: 92 and the heavy chain constant region coding sequence of SEQ ID NO: 100.

[0809] In another embodiment of the invention, the polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the variable heavy chain polypeptide sequence of SEQ ID NO: 82:

(SEQ ID NO: 92)

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cagtcggtggaggagtccgggggtcgcctggtcacgcctgggacacccct

gacactcacctgcaccgtctctggattctccctcagtggcgctgcgatga

actgggtccgccaggctccagggaaggggctggaatggatcggagttatt

ggtaatagtggtagcacatactacgcgtcctgggcgaaaggccgattcac

catctccaaaacctcgtcgaccacggtggatctgaaaatgaccagtccga

caaccgaggacacggccacctatttctgtgccagagggggaggggaattt

ttcatctggggccaagggaccctggtcaccgtctcgagc.
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[0810] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the constant heavy chain polypeptide sequence of SEQ ID NO: 90:

(SEQ ID NO: 100)

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gcctccaccaagggcccatcggtcttcccctggcaccctcctccaagag

cacctctgggggcacagcggccctgggctgcctggtcaaggactacttcc

ccgaaccggtgacggtgtcgtggaactcaggcgccctgaccagcggcgtg

cacaccttcccggctgtcctacagtcctcaggactctactccctcagcag

cgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgca

acgtgaatcacaagcccagcaacaccaaggtggacgcgagagttgagccc

aaatcttgtgacaaaactcacacatgcccaccgtgcccagcacctgaact

cctgggggggaccgtcagtcttcctcttcccccaaaacccaaggacaccc

tcatgatctcccggaccctgaggtcacatgcgtggtggtggacgtgagc

cacgaagaccctgaggtcaagttcaactggtacgtggacggcgtggaggt

gcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtacc

gtgtggtcagcgtcctcaccgtcctgcaccaggactggctgaatggcaag

gagtacaagtgcaaggtctccaacaaagccctcccagcccccatcgagaa

aaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccc

tgcccccatcccgggaggagatgaccaagaaccaggtcagcctgacctgc

ctggtcaaaggcttctatcccagcgacatcgccgtggagtgggagagcaa

tgggcagccggagaacaactacaagaccacgcctcccgtgctggactccg
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acggctccttcttcctctacagcaagctcaccgtggacaagagcaggtgg

cagcaggggaacgtcttctcatgctccgtgatgcatgaggctctgcacaa

ccactacacgcagaagagcctctccctgtctccgggtaaa.

[0811] In another embodiment of the invention, polynucleotides comprise, or alternatively consist of, the polynucleotide sequence of SEQ ID NO: 111 which encodes the light chain polypeptide sequence of SEQ ID NO: 101 and which consists of the light chain variable region coding sequence of SEQ ID NO: 112 and the light chain constant region coding sequence of SEQ ID NO: 120.

[0812] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the variable light chain polypeptide sequence of SEQ ID NO: 102:

(SEQ ID NO: 112)

gcccaagtgctgacccagactccatccccagtgtctgcagctgtgggagg

caccgtcaccatcaattgccagtccagtgagagtgtttataagaacaact

acttatcctggtatcagcagaaaccagggcagcctcccaagttcctgatc

taccaggcatccaatttggcagatggggtcccatcgcggttcaaaggcag

tggatctgggacacagttcactctcaccatcagcgacctggagtgtgacg

atgccgccacttattactgtgcaggcggttatagtacttatatgtctggt

ttcggcggagggaccgaggtggtggtcaaacgt.

[0813] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the constant light chain polypeptide sequence of SEQ ID NO: 110:

(SEQ ID NO: 120)

acggtagcggccccatctgtcttcatcttcccgccatctgatgagcagtt

gaaatctggaactgcctctgttgtgtgcctgctgaataacttctatccca

gagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaac

tcccaggagagtgtcacagagcaggacagcaaggacagcacctacagcct

cagcagcaccctgacgctgagcaaagcagactacgagaaacacaaagtct

acgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagc

ttcaacaggggagagtgt.

[0814] In a further embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one or more of the polynucleotide sequences of SEQ ID NO: 94; SEQ ID NO: 96; and SEQ ID NO: 98, which correspond to polynucleotides encoding the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 81, or the variable heavy chain sequence of SEQ ID NO: 82, and/or one or more of the polynucleotide sequences of SEQ ID NO: 114; SEQ ID NO: 116; and SEQ ID NO: 118, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 101, or the variable light chain sequence of SEQ ID NO: 102, or combinations of these polynucleotide sequences. In another embodiment of the invention, the polynucleotides encoding the antibodies of the invention or antigen-binding fragments thereof comprise, or alternatively consist of, combinations of polynucleotides encoding one or more of the CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them.

[0815] In a further embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one or more of the polynucleotide sequences of SEQ ID NO: 93; SEQ ID NO: 95; SEQ ID NO: 97; and SEQ ID NO: 99, which correspond to polynucleotides encoding the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 81, or the variable heavy chain sequence of SEQ ID NO: 82, and/or one or more of the polynucleotide sequences of SEQ ID NO: 113; SEQ ID NO: 115; SEQ ID NO: 117; and SEQ ID NO: 119, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 101, or the variable light chain sequence of SEQ ID NO: 102, or combinations of these polynucleotide sequences. In another embodiment of the invention, the polynucleotides encoding the antibodies of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them.

[0816] The invention also contemplates polynucleotide sequences including one or more of the polynucleotide sequences encoding antigen-binding fragments described herein. In one embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three or more, including all of the following polynucleotides encoding antigen-binding fragments: the polynucleotide SEQ ID NO: 91 encoding the heavy chain sequence of SEQ ID NO: 81; the polynucleotide SEQ ID NO: 92 encoding the variable heavy chain sequence of SEQ ID NO: 82; the polynucleotide SEQ ID NO: 111 encoding the light chain sequence of SEQ ID NO: 101; the polynucleotide SEQ ID NO: 112 encoding the variable light chain sequence of SEQ ID NO: 102; polynucleotides encoding the CDRs (SEQ ID NO: 94; SEQ ID NO: 96; and SEQ ID NO: 98) of the heavy chain sequence of SEQ ID NO: 81, or the variable heavy chain sequence of SEQ ID NO: 82; polynucleotides encoding the CDRs (SEQ ID NO: 114; SEQ ID NO: 116; and SEQ ID NO: 118) of the light chain sequence of SEQ ID NO: 101, or the variable light chain sequence of SEQ ID NO: 102; polynucleotides encoding the FRs (SEQ ID NO: 93; SEQ ID NO: 95; SEQ ID NO: 97; and SEQ ID NO: 99) of the heavy chain sequence of SEQ ID NO: 81, or the variable heavy chain sequence of SEQ ID NO: 82; and polynucleotides encoding the FRs (SEQ ID NO: 113; SEQ ID NO: 115; SEQ ID NO: 117; and SEQ ID NO: 119) of the light chain sequence of SEQ ID NO: 101, or the variable light chain sequence of SEQ ID NO: 102.

[0817] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, polynucleotides encoding Fab fragments having binding specificity for PACAP. With respect to antibody Ab2, the polynucleotides encoding the full length Ab2 antibody comprise, or alternatively consist of, the polynucle-

otide SEQ ID NO: 91 encoding the heavy chain sequence of SEQ ID NO: 81, and the polynucleotide SEQ ID NO: 111 encoding the light chain sequence of SEQ ID NO: 101.

[0818] Another embodiment of the invention contemplates these polynucleotides incorporated into an expression vector for expression in mammalian cells such as CHO, NSO, or HEK-293 cells, or in fungal, insect, or microbial systems such as yeast cells such as the yeast *Pichia. Suitable Pichia* species include, but are not limited to, *Pichia pastoris*. In one embodiment of the invention described herein, Fab fragments can be produced by enzymatic digestion (e.g., papain) of Ab2 following expression of the full-length polynucleotides in a suitable host. In another embodiment of the invention, anti-PACAP antibodies, such as Ab2 or Fab fragments thereof, can be produced via expression of Ab2 polynucleotides in mammalian cells such as CHO, NSO, or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example diploid yeast such as diploid *Pichia*) and other yeast strains. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris.*

Antibody Ab3

[0819] In one embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to PACAP. In one embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the polynucleotide sequence of SEQ ID NO: 691 which encodes the heavy chain sequence of SEQ ID NO: 681 and which consists of the heavy chain variable region coding sequence of SEQ ID NO: 692 and the heavy chain constant region coding sequence of SEQ ID NO: 700.

[0820] In another embodiment of the invention, the polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the variable heavy chain polypeptide sequence of SEQ ID NO: 682:

(SEQ ID NO: 692)

caggagcagctggtggagtccgggggaggcctggtccagcctgagggatc

cctgacactcacctgcacagcctctggattctccttcagtagcagcgact

acatgtgctgggtccgccaggctccagggaaggggctggagtggatcgga

tgcattgatgctggtagtagtggtgacacttacttcgcgagctgggcgaa

aggccgattcaccatctccaaaacctcgtcgaccacggtgactctgcaaa

tgaccagtctgacagccgcggacacggccacctatttctgtgcgagacat

ctttatggtagtattactttcgcctttggcttgtggggccagggcaccct

ggtcaccgtctcgagc.

[0821] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the constant heavy chain polypeptide sequence of SEQ ID NO: 690:

(SEQ ID NO: 700)

gcctccaccaagggcccatcggtcttccccctggcaccctcctccaagag

cacctctgggggcacagcggccctgggctgcctggtcaaggactacttcc

-continued

ccgaaccggtgacggtgtcgtggaactcaggcgccctgaccagcggcgtg

cacaccttcccggctgtcctacagtcctcaggactctactccctcagcag

cgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgca

acgtgaatcacaagcccagcaacaccaaggtggacgcgagagttgagccc

aaatcttgtgacaaaactcacacatgcccaccgtgcccagcacctgaact

cctgggggggaccgtcagtcttcctcttcccccaaaacccaaggacaccc

tcatgatctcccggaccctgaggtcacatgcgtggtggtggacgtgagc

cacgaagaccctgaggtcaagttcaactggtacgtggacggcgtggaggt

gcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtacc

gtgtggtcagcgtcctcaccgtcctgcaccaggactggctgaatggcaag

gagtacaagtgcaaggtctccaacaaagccctcccagcccccatcgagaa

aaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccc

tgcccccatcccgggaggagatgaccaagaaccaggtcagcctgacctgc

ctggtcaaaggcttctatcccagcgacatcgccgtggagtgggagagcaa

tgggcagccggagaacaactacaagaccacgcctcccgtgctggactccg

acggctccttcttcctctacagcaagctcaccgtggacaagagcaggtgg

cagcaggggaacgtcttctcatgctccgtgatgcatgaggctctgcacaa

ccactacacgcagaagagcctctccctgtctccgggtaaa.

[0822] In another embodiment of the invention, polynucleotides comprise, or alternatively consist of, the polynucleotide sequence of SEQ ID NO: 711 which encodes the light chain polypeptide sequence of SEQ ID NO: 701 and which consists of the light chain variable region coding sequence of SEQ ID NO: 712 and the light chain constant region coding sequence of SEQ ID NO: 720.

[0823] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the variable light chain polypeptide sequence of SEQ ID NO: 702:

(SEQ ID NO: 712)

gcagccgtgctgacccagacaccatcgcccgtgtctgcagctgtgggagg

cacagtcaccatcaattgccaggccagtcagagcattggtagcgacttag

cctggtatcagcagaaaccagggcagcctcccaagctcctgatctatgat

gcatccactctggcatctggggtcccatcgcggttcagcggcagtggatc

tgggacacagttcactctcaccatcagcggcgtgcagtgtgacgatgctg

ccacttactactgtcaaggcacttattatagtagtggttggtacactgct

ttcggcggagggaccgaggtggtggtcaaacgt.

[0824] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the constant light chain polypeptide sequence of SEQ ID NO: 710:

(SEQ ID NO: 720)
acggtagcggccccatctgtcttcatcttcccgccatctgatgagcagtt

gaaatctggaactgcctctgttgtgtgcctgctgaataacttctatccca

gagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaac

tcccaggagagtgtcacagagcaggacagcaaggacagcacctacagcct

cagcagcaccctgacgctgagcaaagcagactacgagaaacacaaagtct

acgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagc

ttcaacaggggagagtgt.

[0825] In a further embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one or more of the polynucleotide sequences of SEQ ID NO: 694; SEQ ID NO: 696; and SEQ ID NO: 698, which correspond to polynucleotides encoding the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 681, or the variable heavy chain sequence of SEQ ID NO: 682, and/or one or more of the polynucleotide sequences of SEQ ID NO: 714; SEQ ID NO: 716; and SEQ ID NO: 718, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 701, or the variable light chain sequence of SEQ ID NO: 702, or combinations of these polynucleotide sequences. In another embodiment of the invention, the polynucleotides encoding the antibodies of the invention or antigen-binding fragments thereof comprise, or alternatively consist of, combinations of polynucleotides encoding one or more of the CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them.

[0826] In a further embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one or more of the polynucleotide sequences of SEQ ID NO: 693; SEQ ID NO: 695; SEQ ID NO: 697; and SEQ ID NO: 699, which correspond to polynucleotides encoding the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 681, or the variable heavy chain sequence of SEQ ID NO: 682, and/or one or more of the polynucleotide sequences of SEQ ID NO: 713; SEQ ID NO: 715; SEQ ID NO: 717; and SEQ ID NO: 719, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 701, or the variable light chain sequence of SEQ ID NO: 702, or combinations of these polynucleotide sequences. In another embodiment of the invention, the polynucleotides encoding the antibodies of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them.

[0827] The invention also contemplates polynucleotide sequences including one or more of the polynucleotide sequences encoding antigen-binding fragments described herein. In one embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three or more, including all of the following polynucleotides encoding antigen-binding fragments: the polynucleotide SEQ ID NO: 691 encoding the heavy chain sequence of SEQ ID NO: 681; the polynucleotide SEQ ID NO: 692 encoding the variable heavy chain sequence of SEQ ID NO: 682; the polynucleotide SEQ ID NO: 711 encoding the light chain sequence of SEQ ID NO: 701; the polynucleotide SEQ ID NO: 712 encoding the variable light chain sequence of SEQ ID NO: 702; polynucleotides encoding the CDRs (SEQ ID NO: 694; SEQ ID NO: 696; and SEQ ID NO: 698) of the heavy chain sequence of SEQ ID NO: 681, or the variable heavy chain sequence of SEQ ID NO: 682; polynucleotides encoding the CDRs (SEQ ID NO: 714; SEQ ID NO: 716; and SEQ ID NO: 718) of the light chain sequence of SEQ ID NO: 701, or the variable light chain sequence of SEQ ID NO: 702; polynucleotides encoding the FRs (SEQ ID NO: 693; SEQ ID NO: 695; SEQ ID NO: 697; and SEQ ID NO: 699) of the heavy chain sequence of SEQ ID NO: 681, or the variable heavy chain sequence of SEQ ID NO: 682; and polynucleotides encoding the FRs (SEQ ID NO: 713; SEQ ID NO: 715; SEQ ID NO: 717; and SEQ ID NO: 719) of the light chain sequence of SEQ ID NO: 701, or the variable light chain sequence of SEQ ID NO: 702.

[0828] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, polynucleotides encoding Fab fragments having binding specificity for PACAP. With respect to antibody Ab3, the polynucleotides encoding the full length Ab3 antibody comprise, or alternatively consist of, the polynucleotide SEQ ID NO: 691 encoding the heavy chain sequence of SEQ ID NO: 681, and the polynucleotide SEQ ID NO: 711 encoding the light chain sequence of SEQ ID NO: 701.

[0829] Another embodiment of the invention contemplates these polynucleotides incorporated into an expression vector for expression in mammalian cells such as CHO, NSO, or HEK-293 cells, or in fungal, insect, or microbial systems such as yeast cells such as the yeast *Pichia*. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*. In one embodiment of the invention described herein, Fab fragments can be produced by enzymatic digestion (e.g., papain) of Ab3 following expression of the full-length polynucleotides in a suitable host. In another embodiment of the invention, anti-PACAP antibodies, such as Ab3 or Fab fragments thereof, can be produced via expression of Ab3 polynucleotides in mammalian cells such as CHO, NSO, or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example diploid yeast such as diploid *Pichia*) and other yeast strains. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*.

Antibody Ab4

[0830] In one embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to PACAP. In one embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the polynucleotide sequence of SEQ ID NO: 651 which encodes the heavy chain sequence of SEQ ID NO: 641 and which consists of the heavy chain variable region coding sequence of SEQ ID NO: 652 and the heavy chain constant region coding sequence of SEQ ID NO: 660.

[0831] In another embodiment of the invention, the polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the variable heavy chain polypeptide sequence of SEQ ID NO: 642:

(SEQ ID NO: 652)

cagtcggtggaggagtccgggggtcgcctggtcacgcctgggacacccct

gacactcacctgcaccgtctctggattctccctcagcagctacgacatga

gctgggtccgccaggctccaggaaaggggctggaatacatcggcatcatt

aatactaatgatgacacatggtacgcgagctgggtgaaaggccgattcac

catctccaaaacctcgtcgaccacggtggatctgaaaatgaccagtctga

caaccgaggacacggccacctatttctgtgccagaatatccgatgcttat

gtttttgattatgcgtattactttactttgtggggccaggggaccctggt

caccgtctcgagc.

[0832] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the constant heavy chain polypeptide sequence of SEQ ID NO: 650:

(SEQ ID NO: 660)

gcctccaccaagggcccatcggtcttcccccctggcaccctcctccaagag

cacctctgggggcacagcggccctgggctgcctggtcaaggactacttcc

ccgaaccggtgacggtgtcgtggaactcaggcgccctgaccagcggcgtg

cacaccttcccggctgtcctacagtcctcaggactctactccctcagcag

cgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgca

acgtgaatcacaagcccagcaacaccaaggtggacgcgagagttgagccc

aaatcttgtgacaaaactcacacatgcccaccgtgcccagcacctgaact

cctgggggggaccgtcagtcttcctcttcccccaaaacccaaggacaccc

tcatgatctcccggaccccctgaggtcacatgcgtggtggtggacgtgagc

cacgaagaccctgaggtcaagttcaactggtacgtggacggcgtggaggt

gcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtacc

gtgtggtcagcgtcctcaccgtcctgcaccaggactggctgaatggcaag

gagtacaagtgcaaggtctccaacaaagccctcccagcccccatcgagaa

aaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccc

tgcccccatcccgggaggagatgaccaagaaccaggtcagcctgacctgc

ctggtcaaaggcttctatcccagcgacatcgccgtggagtgggagagcaa

tgggcagccggagaacaactacaagaccacgcctcccgtgctggactccg

acggctccttcttcctctacagcaagctcaccgtggacaagagcaggtgg

cagcaggggaacgtcttctcatgctccgtgatgcatgaggctctgcacaa

ccactacacgcagaagagcctctccctgtctccgggtaaa.

[0833] In another embodiment of the invention, polynucleotides comprise, or alternatively consist of, the polynucleotide sequence of SEQ ID NO: 671 which encodes the light chain polypeptide sequence of SEQ ID NO: 661 and which consists of the light chain variable region coding sequence of SEQ ID NO: 672 and the light chain constant region coding sequence of SEQ ID NO: 680.

[0834] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the variable light chain polypeptide sequence of SEQ ID NO: 662:

(SEQ ID NO: 672)

gcccttgtgatgacccagactccatcctccgtgtctgcagctgtgggagg

cacagtcaccatcaattgcctggccagtcagaacatttacaattctttag

cctggtatcagcagaaaccagggcagcctcccaagctcctgatctacagg

gcatccactctggcatctggggtctcatcgcggttcaaaggcagtggatc

tgggacacagttcactctcaccatcagcggcgtggagtgtgccgatgctg

ccacttactactgtcaacagggtgctggtgctgataatattggtaatcct

ttcggcggagggaccgaggtggtggtcaaacgt.

[0835] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the constant light chain polypeptide sequence of SEQ ID NO: 670:

(SEQ ID NO: 680)

acggtagcggccccatctgtcttcatcttcccgccatctgatgagcagtt

gaaatctggaactgcctctgttgtgtgcctgctgaataacttctatccca

gagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaac

tcccaggagagtgtcacagagcaggacagcaaggacagcacctacagcct

cagcagcaccctgacgctgagcaaagcagactacgagaaacacaaagtct

acgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagc

ttcaacaggggagagtgt.

[0836] In a further embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one or more of the polynucleotide sequences of SEQ ID NO: 654; SEQ ID NO: 656; and SEQ ID NO: 658, which correspond to polynucleotides encoding the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 641, or the variable heavy chain sequence of SEQ ID NO: 642, and/or one or more of the polynucleotide sequences of SEQ ID NO: 674; SEQ ID NO: 676; and SEQ ID NO: 678, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 661, or the variable light chain sequence of SEQ ID NO: 662, or combinations of these polynucleotide sequences. In another embodiment of the invention, the polynucleotides encoding the antibodies of the invention or antigen-binding fragments thereof comprise, or alternatively consist of, combinations of polynucleotides encoding one or more of the CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them.

[0837] In a further embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one or more of the polynucleotide sequences of SEQ ID NO: 653; SEQ ID NO: 655; SEQ ID NO: 657; and SEQ ID NO: 659, which correspond to polynucleotides encoding the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 641, or the variable heavy chain

sequence of SEQ ID NO: 642, and/or one or more of the polynucleotide sequences of SEQ ID NO: 673; SEQ ID NO: 675; SEQ ID NO: 677; and SEQ ID NO: 679, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 661, or the variable light chain sequence of SEQ ID NO: 662, or combinations of these polynucleotide sequences. In another embodiment of the invention, the polynucleotides encoding the antibodies of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them.

[0838] The invention also contemplates polynucleotide sequences including one or more of the polynucleotide sequences encoding antigen-binding fragments described herein. In one embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three or more, including all of the following polynucleotides encoding antigen-binding fragments: the polynucleotide SEQ ID NO: 651 encoding the heavy chain sequence of SEQ ID NO: 641; the polynucleotide SEQ ID NO: 652 encoding the variable heavy chain sequence of SEQ ID NO: 642; the polynucleotide SEQ ID NO: 671 encoding the light chain sequence of SEQ ID NO: 661; the polynucleotide SEQ ID NO: 672 encoding the variable light chain sequence of SEQ ID NO: 662; polynucleotides encoding the CDRs (SEQ ID NO: 654; SEQ ID NO: 656; and SEQ ID NO: 658) of the heavy chain sequence of SEQ ID NO: 641, or the variable heavy chain sequence of SEQ ID NO: 642; polynucleotides encoding the CDRs (SEQ ID NO: 674; SEQ ID NO: 676; and SEQ ID NO: 678) of the light chain sequence of SEQ ID NO: 661, or the variable light chain sequence of SEQ ID NO: 662; polynucleotides encoding the FRs (SEQ ID NO: 653; SEQ ID NO: 655; SEQ ID NO: 657; and SEQ ID NO: 659) of the heavy chain sequence of SEQ ID NO: 641, or the variable heavy chain sequence of SEQ ID NO: 642; and polynucleotides encoding the FRs (SEQ ID NO: 673; SEQ ID NO: 675; SEQ ID NO: 677; and SEQ ID NO: 679) of the light chain sequence of SEQ ID NO: 661, or the variable light chain sequence of SEQ ID NO: 662.

[0839] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, polynucleotides encoding Fab fragments having binding specificity for PACAP. With respect to antibody Ab4, the polynucleotides encoding the full length Ab4 antibody comprise, or alternatively consist of, the polynucleotide SEQ ID NO: 651 encoding the heavy chain sequence of SEQ ID NO: 641, and the polynucleotide SEQ ID NO: 671 encoding the light chain sequence of SEQ ID NO: 661.

[0840] Another embodiment of the invention contemplates these polynucleotides incorporated into an expression vector for expression in mammalian cells such as CHO, NSO, or HEK-293 cells, or in fungal, insect, or microbial systems such as yeast cells such as the yeast *Pichia*. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*. In one embodiment of the invention described herein, Fab fragments can be produced by enzymatic digestion (e.g., papain) of Ab4 following expression of the full-length polynucleotides in a suitable host. In another embodiment of the invention, anti-PACAP antibodies, such as Ab4 or Fab fragments thereof, can be produced via expression of Ab4 polynucleotides in mammalian cells such as CHO, NSO, or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example diploid yeast such as diploid *Pichia*) and other yeast strains. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*.

Antibody Ab5

[0841] In one embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to PACAP. In one embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the polynucleotide sequence of SEQ ID NO: 491 which encodes the heavy chain sequence of SEQ ID NO: 481 and which consists of the heavy chain variable region coding sequence of SEQ ID NO: 492 and the heavy chain constant region coding sequence of SEQ ID NO: 500.

[0842] In another embodiment of the invention, the polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the variable heavy chain polypeptide sequence of SEQ ID NO: 482:

(SEQ ID NO: 492)

```
cagtcggtggaggagtccgggggtcgcctggtcacgcctgggacacccct

gacactcacctgcacagtctctggattctccctcagtagctatgcgatga

tctgggtccgccaggctccagggaaggggctggaatggatcggaatcatt

tatgataatggtgacacatactacgcgagctgggcgaaaggccggttcac

catctccaaaacctcgaccacggtgtatctgaagatcgccagtccgacaa

ccgaggacacggccacctacttctgtgccagagagcctggtagtactact

cagaatgacttgtggggccaagggaccctggtcaccgtctcgagc.
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[0843] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the constant heavy chain polypeptide sequence of SEQ ID NO: 490:

(SEQ ID NO: 500)

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gcctccaccaagggcccatcggtcttcccctggcaccctcctccaagag

cacctctgggggcacagcggccctgggctgcctggtcaaggactacttcc

ccgaaccggtgacggtgtcgtggaactcaggcgccctgaccagcggcgtg

cacaccttcccggctgtcctacagtcctcaggactctactccctcagcag

cgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgca

acgtgaatcacaagcccagcaacaccaaggtggacgcgagagttgagccc

aaatcttgtgacaaaactcacacatgcccaccgtgcccagcacctgaact

cctgggggggaccgtcagtcttcctcttcccccaaaacccaaggacaccc

tcatgatctcccggaccctgaggtcacatgcgtggtggtggacgtgagc

cacgaagaccctgaggtcaagttcaactggtacgtggacggcgtggaggt

gcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtacc

gtgtggtcagcgtcctcaccgtcctgcaccaggactggctgaatggcaag

gagtacaagtgcaaggtctccaacaaagccctcccagcccccatcgagaa
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aaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccc

tgccccatcccgggaggagatgaccaagaaccaggtcagcctgacctgc

ctggtcaaaggcttctatcccagcgacatcgccgtggagtgggagagcaa

tgggcagccggagaacaactacaagaccacgcctcccgtgctggactccg

acggctccttcttcctctacagcaagctcaccgtggacaagagcaggtgg

cagcaggggaacgtcttctcatgctccgtgatgcatgaggctctgcacaa

ccactacacgcagaagagcctctccctgtctccgggtaaa.

[0844] In another embodiment of the invention, polynucleotides comprise, or alternatively consist of, the polynucleotide sequence of SEQ ID NO: 511 which encodes the light chain polypeptide sequence of SEQ ID NO: 501 and which consists of the light chain variable region coding sequence of SEQ ID NO: 512 and the light chain constant region coding sequence of SEQ ID NO: 520.

[0845] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the variable light chain polypeptide sequence of SEQ ID NO: 502:

(SEQ ID NO: 512)

gatgttgtgatgacccagactccagcctccgtgtctgaacctgtgggagg

cacagtcaccatcaagtgccaggccagtgagaacatttacaactctttac

tctggtatcagcagaaaccagggcagcctcccaagctcctgatctatagg

gcatccactctggcatctggggtctcatcgcggttcaaaggcagtggatc

tgggacagagttcactctcaccatcagcgacctggagtgtgccgatgctg

ccacttactactgtcaaaactattataatatatggactaatggtgctgct

ttcggcggagggaccgaggtggtggtcaaacgt.

[0846] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the constant light chain polypeptide sequence of SEQ ID NO: 510:

(SEQ ID NO: 520)

acggtagcggccccatctgtcttcatcttcccgccatctgatgagcagtt

gaaatctggaactgcctctgttgtgtgcctgctgaataacttctatccca

gagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaac

tcccaggagagtgtcacagagcaggacagcaaggacagcacctacagcct

cagcagcaccctgacgctgagcaaagcagactacgagaaacacaaagtct

acgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagc

ttcaacaggggagagtgt.

[0847] In a further embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one or more of the polynucleotide sequences of SEQ ID NO: 494; SEQ ID NO: 496; and SEQ ID NO: 498, which correspond to polynucleotides encoding the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 481, or the variable heavy chain sequence of SEQ ID NO: 482, and/or one or more of the polynucleotide sequences of SEQ ID NO: 514; SEQ ID NO: 516; and SEQ ID NO: 518, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 501, or the variable light chain sequence of SEQ ID NO: 502, or combinations of these polynucleotide sequences. In another embodiment of the invention, the polynucleotides encoding the antibodies of the invention or antigen-binding fragments thereof comprise, or alternatively consist of, combinations of polynucleotides encoding one or more of the CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them.

[0848] In a further embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one or more of the polynucleotide sequences of SEQ ID NO: 493; SEQ ID NO: 495; SEQ ID NO: 497; and SEQ ID NO: 499, which correspond to polynucleotides encoding the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 481, or the variable heavy chain sequence of SEQ ID NO: 482, and/or one or more of the polynucleotide sequences of SEQ ID NO: 513; SEQ ID NO: 515; SEQ ID NO: 517; and SEQ ID NO: 519, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 501, or the variable light chain sequence of SEQ ID NO: 502, or combinations of these polynucleotide sequences. In another embodiment of the invention, the polynucleotides encoding the antibodies of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them.

[0849] The invention also contemplates polynucleotide sequences including one or more of the polynucleotide sequences encoding antigen-binding fragments described herein. In one embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three or more, including all of the following polynucleotides encoding antigen-binding fragments: the polynucleotide SEQ ID NO: 491 encoding the heavy chain sequence of SEQ ID NO: 481; the polynucleotide SEQ ID NO: 492 encoding the variable heavy chain sequence of SEQ ID NO: 482; the polynucleotide SEQ ID NO: 511 encoding the light chain sequence of SEQ ID NO: 501; the polynucleotide SEQ ID NO: 512 encoding the variable light chain sequence of SEQ ID NO: 502; polynucleotides encoding the CDRs (SEQ ID NO: 494; SEQ ID NO: 496; and SEQ ID NO: 498) of the heavy chain sequence of SEQ ID NO: 481, or the variable heavy chain sequence of SEQ ID NO: 482; polynucleotides encoding the CDRs (SEQ ID NO: 514; SEQ ID NO: 516; and SEQ ID NO: 518) of the light chain sequence of SEQ ID NO: 501, or the variable light chain sequence of SEQ ID NO: 502; polynucleotides encoding the FRs (SEQ ID NO: 493; SEQ ID NO: 495; SEQ ID NO: 497; and SEQ ID NO: 499) of the heavy chain sequence of SEQ ID NO: 481, or the variable heavy chain sequence of SEQ ID NO: 482; and polynucleotides encoding the FRs (SEQ ID NO: 513; SEQ ID NO: 515; SEQ ID NO: 517; and SEQ ID NO: 519) of the light chain sequence of SEQ ID NO: 501, or the variable light chain sequence of SEQ ID NO: 502.

[0850] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, polynucleotides encoding Fab fragments having binding specificity for PACAP. With respect to antibody Ab5, the polynucleotides encoding the full length Ab5 antibody comprise, or alternatively consist of, the polynucleotide SEQ ID NO: 491 encoding the heavy chain sequence of SEQ ID NO: 481, and the polynucleotide SEQ ID NO: 511 encoding the light chain sequence of SEQ ID NO: 501.

[0851] Another embodiment of the invention contemplates these polynucleotides incorporated into an expression vector for expression in mammalian cells such as CHO, NSO, or HEK-293 cells, or in fungal, insect, or microbial systems such as yeast cells such as the yeast *Pichia*. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*. In one embodiment of the invention described herein, Fab fragments can be produced by enzymatic digestion (e.g., papain) of Ab5 following expression of the full-length polynucleotides in a suitable host. In another embodiment of the invention, anti-PACAP antibodies, such as Ab5 or Fab fragments thereof, can be produced via expression of Ab5 polynucleotides in mammalian cells such as CHO, NSO, or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example diploid yeast such as diploid *Pichia*) and other yeast strains. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*.

Antibody Ab6

[0852] In one embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to PACAP. In one embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the polynucleotide sequence of SEQ ID NO: 731 which encodes the heavy chain sequence of SEQ ID NO: 721 and which consists of the heavy chain variable region coding sequence of SEQ ID NO: 732 and the heavy chain constant region coding sequence of SEQ ID NO: 740.

[0853] In another embodiment of the invention, the polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the variable heavy chain polypeptide sequence of SEQ ID NO: 722:

(SEQ ID NO: 732)

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cagcagctggagcagtccggaggaggagccgaaggaggcctggtcaagcc

tgggggatccctggaactctgctgcaaggcctctggattctccctcagta

gcacctactggatgtgctgggtccgccaggctccagggaaggggctggag

tggattggatgcatttatactggtagtggtagcacagactacgcgagctg

ggtgaatggccaattcactctctccagagacatcgaccagagcacaggtt

gcctacaactgaacagtctgacagtcgcggacacggccatgtattactgt

acgaaaaattttgacttgtggggcccgggcaccctggtcaccgtctcgag

c.
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[0854] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the constant heavy chain polypeptide sequence of SEQ ID NO: 730:

(SEQ ID NO: 740)

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gcctccaccaagggcccatcggtcttcccctggcaccctcctccaagag

cacctctgggggcacagcggccctgggctgcctggtcaaggactacttcc

ccgaaccggtgacggtgtcgtggaactcaggcgccctgaccagcggcgtg

cacaccttcccggctgtcctacagtcctcaggactctactccctcagcag

cgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgca

acgtgaatcacaagcccagcaacaccaaggtggacgcgagagttgagccc

aaatcttgtgacaaaactcacacatgcccaccgtgcccagcacctgaact

cctgggggggaccgtcagtcttcctcttcccccaaaacccaaggacaccc

tcatgatctcccggaccctgaggtcacatgcgtggtggtggacgtgagc

cacgaagaccctgaggtcaagttcaactggtacgtggacggcgtggaggt

gcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtacc

gtgtggtcagcgtcctcaccgtcctgcaccaggactggctgaatggcaag

gagtacaagtgcaaggtctccaacaaagccctcccagcccccatcgagaa

aaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccc

tgcccccatcccgggaggagatgaccaagaaccaggtcagcctgacctgc

ctggtcaaaggcttctatcccagcgacatcgccgtggagtgggagagcaa

tgggcagccggagaacaactacaagaccacgcctcccgtgctggactccg

acggctccttcttcctctacagcaagctcaccgtggacaagagcaggtgg

cagcaggggaacgtcttctcatgctccgtgatgcatgaggctctgcacaa

ccactacacgcagaagagcctctccctgtctccgggtaaa.
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[0855] In another embodiment of the invention, polynucleotides comprise, or alternatively consist of, the polynucleotide sequence of SEQ ID NO: 751 which encodes the light chain polypeptide sequence of SEQ ID NO: 741 and which consists of the light chain variable region coding sequence of SEQ ID NO: 752 and the light chain constant region coding sequence of SEQ ID NO: 760.

[0856] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the variable light chain polypeptide sequence of SEQ ID NO: 742:

(SEQ ID NO: 752)

```
gcccaagtgctgacccagactccatcctccgtgtctgcagctgtgggagg

cacagtcaccatcaattgccagtccagtccgagtgtttatagtaacaact

acttatcctggtttcagcagaaaccagggcagcctcccaaaggcctgatc

gctgatgcatccactctggcatctggggtcccatcgcggttcaaaggcag

tggatctgggacacagttcactctcaccatcagcggcgtgcagtgtgacg

atgctgccgcttactactgtctaggctattatgattgtggtagtactgat

tgtcatgctttcggcggagggaccgaggtggtggtcaaacgt.
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[0857] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the constant light chain polypeptide sequence of SEQ ID NO: 750:

(SEQ ID NO: 760)
acggtagcggccccatctgtcttcatcttcccgccatctgatgagcagtt

gaaatctggaactgcctctgttgtgtgcctgctgaataacttctatccca

gagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaac

tcccaggagagtgtcacagagcaggacagcaaggacagcacctacagcct

cagcagcaccctgacgctgagcaaagcagactacgagaaacacaaagtct

acgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagc

ttcaacaggggagagtgt.

[0858] In a further embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one or more of the polynucleotide sequences of SEQ ID NO: 734; SEQ ID NO: 736; and SEQ ID NO: 738, which correspond to polynucleotides encoding the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 721, or the variable heavy chain sequence of SEQ ID NO: 722, and/or one or more of the polynucleotide sequences of SEQ ID NO: 754; SEQ ID NO: 756; and SEQ ID NO: 758, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 741, or the variable light chain sequence of SEQ ID NO: 742, or combinations of these polynucleotide sequences. In another embodiment of the invention, the polynucleotides encoding the antibodies of the invention or antigen-binding fragments thereof comprise, or alternatively consist of, combinations of polynucleotides encoding one or more of the CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them.

[0859] In a further embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one or more of the polynucleotide sequences of SEQ ID NO: 733; SEQ ID NO: 735; SEQ ID NO: 737; and SEQ ID NO: 739, which correspond to polynucleotides encoding the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 721, or the variable heavy chain sequence of SEQ ID NO: 722, and/or one or more of the polynucleotide sequences of SEQ ID NO: 753; SEQ ID NO: 755; SEQ ID NO: 757; and SEQ ID NO: 759, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 741, or the variable light chain sequence of SEQ ID NO: 742, or combinations of these polynucleotide sequences. In another embodiment of the invention, the polynucleotides encoding the antibodies of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them.

[0860] The invention also contemplates polynucleotide sequences including one or more of the polynucleotide sequences encoding antigen-binding fragments described herein. In one embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three or more, including all of the following polynucleotides encoding antigen-binding fragments: the polynucleotide SEQ ID NO: 731 encoding the heavy chain sequence of SEQ ID NO: 721; the polynucleotide SEQ ID NO: 732 encoding the variable heavy chain sequence of SEQ ID NO: 722; the polynucleotide SEQ ID NO: 751 encoding the light chain sequence of SEQ ID NO: 741; the polynucleotide SEQ ID NO: 752 encoding the variable light chain sequence of SEQ ID NO: 742; polynucleotides encoding the CDRs (SEQ ID NO: 734; SEQ ID NO: 736; and SEQ ID NO: 738) of the heavy chain sequence of SEQ ID NO: 721, or the variable heavy chain sequence of SEQ ID NO: 722; polynucleotides encoding the CDRs (SEQ ID NO: 754; SEQ ID NO: 756; and SEQ ID NO: 758) of the light chain sequence of SEQ ID NO: 741, or the variable light chain sequence of SEQ ID NO: 742; polynucleotides encoding the FRs (SEQ ID NO: 733; SEQ ID NO: 735; SEQ ID NO: 737; and SEQ ID NO: 739) of the heavy chain sequence of SEQ ID NO: 721, or the variable heavy chain sequence of SEQ ID NO: 722; and polynucleotides encoding the FRs (SEQ ID NO: 753; SEQ ID NO: 755; SEQ ID NO: 757; and SEQ ID NO: 759) of the light chain sequence of SEQ ID NO: 741, or the variable light chain sequence of SEQ ID NO: 742.

[0861] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, polynucleotides encoding Fab fragments having binding specificity for PACAP. With respect to antibody Ab6, the polynucleotides encoding the full length Ab6 antibody comprise, or alternatively consist of, the polynucleotide SEQ ID NO: 731 encoding the heavy chain sequence of SEQ ID NO: 721, and the polynucleotide SEQ ID NO: 751 encoding the light chain sequence of SEQ ID NO: 741.

[0862] Another embodiment of the invention contemplates these polynucleotides incorporated into an expression vector for expression in mammalian cells such as CHO, NSO, or HEK-293 cells, or in fungal, insect, or microbial systems such as yeast cells such as the yeast *Pichia. Suitable Pichia* species include, but are not limited to, *Pichia pastoris*. In one embodiment of the invention described herein, Fab fragments can be produced by enzymatic digestion (e.g., papain) of Ab6 following expression of the full-length polynucleotides in a suitable host. In another embodiment of the invention, anti-PACAP antibodies, such as Ab6 or Fab fragments thereof, can be produced via expression of Ab6 polynucleotides in mammalian cells such as CHO, NSO, or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example diploid yeast such as diploid *Pichia*) and other yeast strains. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris.*

Antibody Ab7

[0863] In one embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to PACAP. In one embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the polynucleotide sequence of SEQ ID NO: 531 which encodes the heavy chain sequence of SEQ ID NO: 521 and which consists of the heavy chain variable region coding sequence of SEQ ID NO: 532 and the heavy chain constant region coding sequence of SEQ ID NO: 540.

[0864] In another embodiment of the invention, the polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the variable heavy chain polypeptide sequence of SEQ ID NO: 522:

(SEQ ID NO: 532)

cagtcggtggaggagtccgggggtcgcctggtaacgcctgggacacccct

gacactcacctgcacagcctctggaatcgacctcagtggctatgcaatgg

gctgggtccgccaggctccagggaaggggctggaatggatcggagacatt

agtacctatggtaccacagactacgcgagctgggtgaatggccgattcac

catctccagaacctcgaccacggtgactctgaaaatgaccagtctgacaa

ccgaggacacggccacctatttctgtgccagagactattggttgagcttg

tggggcccgggcaccctcgtcaccgtctcgagc.

[0865] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the constant heavy chain polypeptide sequence of SEQ ID NO: 530:

(SEQ ID NO: 540)

gcctccaccaagggcccatcggtcttcccctggcaccctcctccaagag

cacctctgggggcacagcggccctgggctgcctggtcaaggactacttcc

ccgaaccggtgacggtgtcgtggaactcaggcgccctgaccagcggcgtg

cacaccttcccggctgtcctacagtcctcaggactctactccctcagcag

cgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgca

acgtgaatcacaagcccagcaacaccaaggtggacgcgagagttgagccc

aaatcttgtgacaaaactcacacatgcccaccgtgcccagcacctgaact

cctgggggggaccgtcagtcttcctcttcccccaaaacccaaggacaccc

tcatgatctcccggaccctgaggtcacatgcgtggtggtggacgtgagc

cacgaagaccctgaggtcaagttcaactggtacgtggacggcgtggaggt

gcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtacc

gtgtggtcagcgtcctcaccgtcctgcaccaggactggctgaatggcaag

gagtacaagtgcaaggtctccaacaaagccctcccagcccccatcgagaa

aaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccc

tgcccccatcccgggaggagatgaccaagaaccaggtcagcctgacctgc

ctggtcaaaggcttctatcccagcgacatcgccgtggagtgggagagcaa

tgggcagccggagaacaactacaagaccacgcctcccgtgctggactccg

acggctccttcttcctctacagcaagctcaccgtggacaagagcaggtgg

cagcaggggaacgtcttctcatgctccgtgatgcatgaggctctgcacaa

ccactacacgcagaagagcctctccctgtctccgggtaaa.

[0866] In another embodiment of the invention, polynucleotides comprise, or alternatively consist of, the polynucleotide sequence of SEQ ID NO: 551 which encodes the light chain polypeptide sequence of SEQ ID NO: 541 and which consists of the light chain variable region coding sequence of SEQ ID NO: 552 and the light chain constant region coding sequence of SEQ ID NO: 560.

[0867] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the variable light chain polypeptide sequence of SEQ ID NO: 542:

(SEQ ID NO: 552)

gcagccgtgctgacccagacaccatcgcccgtgtctgcagctgtgggagg

cacagtcaccatcaagtgccagtccagtcagagtgtttatgataacaatg

ctttagcctggtatcagcagaaaccagggcagcctcccaagctcctgatc

tatgctgcatccactctggcatctggggtcccatcgcggttcaaaggcag

tggatctgggacacagttcactctcaccatcaacggcgtgcagtgtgacg

atgctgccacttactactgtctaggcggttatgatgatcctgctgataat

gctttcggcggagggaccgaggtggtggtcaaacgt.

[0868] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the constant light chain polypeptide sequence of SEQ ID NO: 550:

(SEQ ID NO: 560)

acggtagcggccccatctgtcttcatcttcccgccatctgatgagcagtt

gaaatctggaactgcctctgttgtgtgcctgctgaataacttctatccca

gagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaac

tcccaggagagtgtcacagagcaggacagcaaggacagcacctacagcct

cagcagcaccctgacgctgagcaaagcagactacgagaaacacaaagtct

acgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagc

ttcaacaggggagagtgt.

[0869] In a further embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one or more of the polynucleotide sequences of SEQ ID NO: 534; SEQ ID NO: 536; and SEQ ID NO: 538, which correspond to polynucleotides encoding the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 521, or the variable heavy chain sequence of SEQ ID NO: 522, and/or one or more of the polynucleotide sequences of SEQ ID NO: 554; SEQ ID NO: 556; and SEQ ID NO: 558, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 541, or the variable light chain sequence of SEQ ID NO: 542, or combinations of these polynucleotide sequences. In another embodiment of the invention, the polynucleotides encoding the antibodies of the invention or antigen-binding fragments thereof comprise, or alternatively consist of, combinations of polynucleotides encoding one or more of the CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them.

[0870] In a further embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one or more of the polynucleotide sequences of SEQ ID NO: 533; SEQ ID NO: 535; SEQ ID NO: 537; and SEQ ID NO: 539, which correspond to polynucleotides encoding the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 521, or the variable heavy chain sequence of SEQ ID NO: 522, and/or one or more of the polynucleotide sequences of SEQ ID NO: 553; SEQ ID NO: 555; SEQ ID NO: 557; and SEQ ID NO: 559, which

correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 541, or the variable light chain sequence of SEQ ID NO: 542, or combinations of these polynucleotide sequences. In another embodiment of the invention, the polynucleotides encoding the antibodies of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them.

[0871] The invention also contemplates polynucleotide sequences including one or more of the polynucleotide sequences encoding antigen-binding fragments described herein. In one embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three or more, including all of the following polynucleotides encoding antigen-binding fragments: the polynucleotide SEQ ID NO: 531 encoding the heavy chain sequence of SEQ ID NO: 521; the polynucleotide SEQ ID NO: 532 encoding the variable heavy chain sequence of SEQ ID NO: 522; the polynucleotide SEQ ID NO: 551 encoding the light chain sequence of SEQ ID NO: 541; the polynucleotide SEQ ID NO: 552 encoding the variable light chain sequence of SEQ ID NO: 542; polynucleotides encoding the CDRs (SEQ ID NO: 534; SEQ ID NO: 536; and SEQ ID NO: 538) of the heavy chain sequence of SEQ ID NO: 521, or the variable heavy chain sequence of SEQ ID NO: 522; polynucleotides encoding the CDRs (SEQ ID NO: 554; SEQ ID NO: 556; and SEQ ID NO: 558) of the light chain sequence of SEQ ID NO: 541, or the variable light chain sequence of SEQ ID NO: 542; polynucleotides encoding the FRs (SEQ ID NO: 533; SEQ ID NO: 535; SEQ ID NO: 537; and SEQ ID NO: 539) of the heavy chain sequence of SEQ ID NO: 521, or the variable heavy chain sequence of SEQ ID NO: 522; and polynucleotides encoding the FRs (SEQ ID NO: 553; SEQ ID NO: 555; SEQ ID NO: 557; and SEQ ID NO: 559) of the light chain sequence of SEQ ID NO: 541, or the variable light chain sequence of SEQ ID NO: 542.

[0872] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, polynucleotides encoding Fab fragments having binding specificity for PACAP. With respect to antibody Ab7, the polynucleotides encoding the full length Ab7 antibody comprise, or alternatively consist of, the polynucleotide SEQ ID NO: 531 encoding the heavy chain sequence of SEQ ID NO: 521, and the polynucleotide SEQ ID NO: 551 encoding the light chain sequence of SEQ ID NO: 541.

[0873] Another embodiment of the invention contemplates these polynucleotides incorporated into an expression vector for expression in mammalian cells such as CHO, NSO, or HEK-293 cells, or in fungal, insect, or microbial systems such as yeast cells such as the yeast *Pichia*. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*. In one embodiment of the invention described herein, Fab fragments can be produced by enzymatic digestion (e.g., papain) of Ab7 following expression of the full-length polynucleotides in a suitable host. In another embodiment of the invention, anti-PACAP antibodies, such as Ab7 or Fab fragments thereof, can be produced via expression of Ab7 polynucleotides in mammalian cells such as CHO, NSO, or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example diploid yeast such as diploid *Pichia*) and other yeast strains. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*.

Antibody Ab8

[0874] In one embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to PACAP. In one embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the polynucleotide sequence of SEQ ID NO: 771 which encodes the heavy chain sequence of SEQ ID NO: 761 and which consists of the heavy chain variable region coding sequence of SEQ ID NO: 772 and the heavy chain constant region coding sequence of SEQ ID NO: 780.

[0875] In another embodiment of the invention, the polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the variable heavy chain polypeptide sequence of SEQ ID NO: 762:

(SEQ ID NO: 772)

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cagcagctggagcagtccggaggaggagccgaaggaggcctggtcaagcc

tgggggatccctggaactctgctgcaaagcctctggattctccctcacta

cgagccactggatgtgttgggtccgccaggctccagggaaggggctgaat

tggattggatgcattagtgccggtagtggtgacgcagactacgcgacctg

ggtggatgcccaattcactctctccagagacatcgaccagaacacaggtt

gcctacaattgaacagtctgacacccgcggacacggccatgtattactgt

acgataaattttgagttgtggggccaaggcaccctggtcaccgtctcgag

c.
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[0876] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the constant heavy chain polypeptide sequence of SEQ ID NO: 770:

(SEQ ID NO: 780)

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gcctccaccaagggcccatcggtcttcccctggcaccctcctccaagag

cacctctgggggcacagcggccctgggctgcctggtcaaggactacttcc

ccgaaccggtgacggtgtcgtggaactcaggcgccctgaccagcggcgtg

cacaccttcccggctgtcctacagtcctcaggactctactccctcagcag

cgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgca

acgtgaatcacaagcccagcaacaccaaggtggacgcgagagttgagccc

aaatcttgtgacaaaactcacacatgcccaccgtgcccagcacctgaact

cctgggggggaccgtcagtcttcctcttcccccaaaacccaaggacaccc

tcatgatctcccggacccctgaggtcacatgcgtggtggtggacgtgagc

cacgaagaccctgaggtcaagttcaactggtacgtggacggcgtggaggt

gcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtacc

gtgtggtcagcgtcctcaccgtcctgcaccaggactggctgaatggcaag

gagtacaagtgcaaggtctccaacaaagccctcccagccccatcgagaa
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aaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccc

tgcccccatcccgggaggagatgaccaagaaccaggtcagcctgacctgc

ctggtcaaaggcttctatcccagcgacatcgccgtggagtgggagagcaa

tgggcagccggagaacaactacaagaccacgcctcccgtgctggactccg

acggctccttcttcctctacagcaagctcaccgtggacaagagcaggtgg

cagcaggggaacgtcttctcatgctccgtgatgcatgaggctctgcacaa

ccactacacgcagaagagcctctccctgtctccgggtaaa.

[0877] In another embodiment of the invention, polynucleotides comprise, or alternatively consist of, the polynucleotide sequence of SEQ ID NO: 791 which encodes the light chain polypeptide sequence of SEQ ID NO: 781 and which consists of the light chain variable region coding sequence of SEQ ID NO: 792 and the light chain constant region coding sequence of SEQ ID NO: 800.

[0878] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the variable light chain polypeptide sequence of SEQ ID NO: 782:

(SEQ ID NO: 792)

gcccaagtgctgacccagactccatcctccgtgtctgcagctgtgggagg

cacagtcaccatcaattgccagtccagtccgagtgtttatagtagctact

tatcctggtttcagcagaaaccagggcagcctcccaagttcctgatctac

gaagcatccaaactggcatctggggtcccatcgcggttcagcggcagtgg

atctgggacacagttcactctcaccatcagcggcgtgcagtgtagcgatg

ctgccacttactactgtcttggcgcgtatgattgtggtcgtactgattgt

catgctttcggcggagggaccgaggtggtggtcaaacgt.

[0879] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the constant light chain polypeptide sequence of SEQ ID NO: 790:

(SEQ ID NO: 800)

acggtagcggccccatctgtcttcatcttcccgccatctgatgagcagtt

gaaatctggaactgcctctgttgtgtgcctgctgaataacttctatccca

gagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaac

tcccaggagagtgtcacagagcaggacagcaaggacagcacctacagcct

cagcagcaccctgacgctgagcaaagcagactacgagaaacacaaagtct

acgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagc

ttcaacaggggagagtgt.

[0880] In a further embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one or more of the polynucleotide sequences of SEQ ID NO: 774; SEQ ID NO: 776; and SEQ ID NO: 778, which correspond to polynucleotides encoding the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 761, or the variable heavy chain sequence of SEQ ID NO: 762, and/or one or more of the polynucleotide sequences of SEQ ID NO: 794; SEQ ID NO: 796; and SEQ ID NO: 798, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 781, or the variable light chain sequence of SEQ ID NO: 782, or combinations of these polynucleotide sequences. In another embodiment of the invention, the polynucleotides encoding the antibodies of the invention or antigen-binding fragments thereof comprise, or alternatively consist of, combinations of polynucleotides encoding one or more of the CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them.

[0881] In a further embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one or more of the polynucleotide sequences of SEQ ID NO: 773; SEQ ID NO: 775; SEQ ID NO: 777; and SEQ ID NO: 779, which correspond to polynucleotides encoding the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 761, or the variable heavy chain sequence of SEQ ID NO: 762, and/or one or more of the polynucleotide sequences of SEQ ID NO: 793; SEQ ID NO: 795; SEQ ID NO: 797; and SEQ ID NO: 799, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 781, or the variable light chain sequence of SEQ ID NO: 782, or combinations of these polynucleotide sequences. In another embodiment of the invention, the polynucleotides encoding the antibodies of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them.

[0882] The invention also contemplates polynucleotide sequences including one or more of the polynucleotide sequences encoding antigen-binding fragments described herein. In one embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three or more, including all of the following polynucleotides encoding antigen-binding fragments: the polynucleotide SEQ ID NO: 771 encoding the heavy chain sequence of SEQ ID NO: 761; the polynucleotide SEQ ID NO: 772 encoding the variable heavy chain sequence of SEQ ID NO: 762; the polynucleotide SEQ ID NO: 791 encoding the light chain sequence of SEQ ID NO: 781; the polynucleotide SEQ ID NO: 792 encoding the variable light chain sequence of SEQ ID NO: 782; polynucleotides encoding the CDRs (SEQ ID NO: 774; SEQ ID NO: 776; and SEQ ID NO: 778) of the heavy chain sequence of SEQ ID NO: 761, or the variable heavy chain sequence of SEQ ID NO: 762; polynucleotides encoding the CDRs (SEQ ID NO: 794; SEQ ID NO: 796; and SEQ ID NO: 798) of the light chain sequence of SEQ ID NO: 781, or the variable light chain sequence of SEQ ID NO: 782; polynucleotides encoding the FRs (SEQ ID NO: 773; SEQ ID NO: 775; SEQ ID NO: 777; and SEQ ID NO: 779) of the heavy chain sequence of SEQ ID NO: 761, or the variable heavy chain sequence of SEQ ID NO: 762; and polynucleotides encoding the FRs (SEQ ID NO: 793; SEQ ID NO: 795; SEQ ID NO: 797; and SEQ ID NO: 799) of the light chain sequence of SEQ ID NO: 781, or the variable light chain sequence of SEQ ID NO: 782.

[0883] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, polynucleotides encoding Fab fragments having binding specificity for PACAP. With respect to antibody Ab8, the polynucleotides encoding the full length Ab8 antibody comprise, or alternatively consist of, the polynucleotide SEQ ID NO: 771 encoding the heavy chain sequence of SEQ ID NO: 761, and the polynucleotide SEQ ID NO: 791 encoding the light chain sequence of SEQ ID NO: 781.

[0884] Another embodiment of the invention contemplates these polynucleotides incorporated into an expression vector for expression in mammalian cells such as CHO, NSO, or HEK-293 cells, or in fungal, insect, or microbial systems such as yeast cells such as the yeast *Pichia*. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*. In one embodiment of the invention described herein, Fab fragments can be produced by enzymatic digestion (e.g., papain) of Ab8 following expression of the full-length polynucleotides in a suitable host. In another embodiment of the invention, anti-PACAP antibodies, such as Ab8 or Fab fragments thereof, can be produced via expression of Ab8 polynucleotides in mammalian cells such as CHO, NSO, or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example diploid yeast such as diploid *Pichia*) and other yeast strains. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*.

Antibody Ab9

[0885] In one embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to PACAP. In one embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the polynucleotide sequence of SEQ ID NO: 811 which encodes the heavy chain sequence of SEQ ID NO: 801 and which consists of the heavy chain variable region coding sequence of SEQ ID NO: 812 and the heavy chain constant region coding sequence of SEQ ID NO: 820.

[0886] In another embodiment of the invention, the polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the variable heavy chain polypeptide sequence of SEQ ID NO: 802:

(SEQ ID NO: 812)

cagcagctggagcagtccggaggaggagccgaaggaggcctggtcaagcc

tgggggatccctgaaactctcctgcaaagcctctggattcaccatcagta

gggactactggatatgttgggtccgccaggctccagggaaggggctggag

tggattggatgcattagtgctggtggtggtagcacagactacgcgaactg

ggtgaatggccgattcactctctccagagacatcgaccagagcacaggtt

gccttcaactgaacagtctgacagacgcggacacggccatgtattactgt

gcgggaaatctagagatctggggccaagggaccctggtcaccgtctcgag

c.

[0887] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the constant heavy chain polypeptide sequence of SEQ ID NO: 810:

(SEQ ID NO: 820)

gcctccaccaagggcccatcggtcttcccctggcaccctcctccaagag

cacctctgggggcacagcggccctgggctgcctggtcaaggactacttcc

ccgaaccggtgacggtgtcgtggaactcaggcgccctgaccagcggcgtg

cacaccttcccggctgtcctacagtcctcaggactctactccctcagcag

cgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgca

acgtgaatcacaagcccagcaacaccaaggtggacgcgagagttgagccc

aaatcttgtgacaaaactcacacatgcccaccgtgcccagcacctgaact

cctgggggggaccgtcagtcttcctcttcccccaaaacccaaggacaccc

tcatgatctcccggaccctgaggtcacatgcgtggtggtggacgtgagc

cacgaagaccctgaggtcaagttcaactggtacgtggacggcgtggaggt

gcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtacc

gtgtggtcagcgtcctcaccgtcctgcaccaggactggctgaatggcaag

gagtacaagtgcaaggtctccaacaaagccctcccagcccccatcgagaa

aaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccc

tgcccccatcccgggaggagatgaccaagaaccaggtcagcctgacctgc

ctggtcaaaggcttctatcccagcgacatcgccgtggagtgggagagcaa

tgggcagccggagaacaactacaagaccacgcctcccgtgctggactccg

acggctccttcttcctctacagcaagctcaccgtggacaagagcaggtgg

cagcaggggaacgtcttctcatgctccgtgatgcatgaggctctgcacaa

ccactacacgcagaagagcctctccctgtctccgggtaaa.

[0888] In another embodiment of the invention, polynucleotides comprise, or alternatively consist of, the polynucleotide sequence of SEQ ID NO: 831 which encodes the light chain polypeptide sequence of SEQ ID NO: 821 and which consists of the light chain variable region coding sequence of SEQ ID NO: 832 and the light chain constant region coding sequence of SEQ ID NO: 840.

[0889] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the variable light chain polypeptide sequence of SEQ ID NO: 822:

(SEQ ID NO: 832)

gcccaagtgctgacccagactccatcctccgtgtctgcagctgtgggagg

cacagtcaccatcaattgccagtccagtccgagtatttatagtggcgcct

ttttatcctggtttcagcagaaaccagggcagcctcccaagttcctgatc

tacgaagcctccaaactggcatctggggtcccatcgcggttcagtggcag

tggatctgggacacagttcactctcaccatcagcgacgtacagtgtgacg

atgctgccacttactactgtctaggcttttatgattgtagcagtgttgat

tgccatgctttcggcggagggaccgaggtggtggtcaaacgt.

[0890] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the constant light chain polypeptide sequence of SEQ ID NO: 830:

(SEQ ID NO: 840)
acggtagcggccccatctgtcttcatcttcccgccatctgatgagcagtt

gaaatctggaactgcctctgttgtgtgcctgctgaataacttctatccca

gagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaac

tcccaggagagtgtcacagagcaggacagcaaggacagcacctacagcct

cagcagcaccctgacgctgagcaaagcagactacgagaaacacaaagtct

acgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagc

ttcaacaggggagagtgt.

[0891] In a further embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one or more of the polynucleotide sequences of SEQ ID NO: 814; SEQ ID NO: 816; and SEQ ID NO: 818, which correspond to polynucleotides encoding the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 801, or the variable heavy chain sequence of SEQ ID NO: 802, and/or one or more of the polynucleotide sequences of SEQ ID NO: 834; SEQ ID NO: 836; and SEQ ID NO: 838, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 821, or the variable light chain sequence of SEQ ID NO: 822, or combinations of these polynucleotide sequences. In another embodiment of the invention, the polynucleotides encoding the antibodies of the invention or antigen-binding fragments thereof comprise, or alternatively consist of, combinations of polynucleotides encoding one or more of the CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them.

[0892] In a further embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one or more of the polynucleotide sequences of SEQ ID NO: 813; SEQ ID NO: 815; SEQ ID NO: 817; and SEQ ID NO: 819, which correspond to polynucleotides encoding the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 801, or the variable heavy chain sequence of SEQ ID NO: 802, and/or one or more of the polynucleotide sequences of SEQ ID NO: 833; SEQ ID NO: 835; SEQ ID NO: 837; and SEQ ID NO: 839, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 821, or the variable light chain sequence of SEQ ID NO: 822, or combinations of these polynucleotide sequences. In another embodiment of the invention, the polynucleotides encoding the antibodies of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them.

[0893] The invention also contemplates polynucleotide sequences including one or more of the polynucleotide sequences encoding antigen-binding fragments described herein. In one embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three or more, including all of the following polynucleotides encoding antigen-binding fragments: the polynucleotide SEQ ID NO: 811 encoding the heavy chain sequence of SEQ ID NO: 801; the polynucleotide SEQ ID NO: 812 encoding the variable heavy chain sequence of SEQ ID NO: 802; the polynucleotide SEQ ID NO: 831 encoding the light chain sequence of SEQ ID NO: 821; the polynucleotide SEQ ID NO: 832 encoding the variable light chain sequence of SEQ ID NO: 822; polynucleotides encoding the CDRs (SEQ ID NO: 814; SEQ ID NO: 816; and SEQ ID NO: 818) of the heavy chain sequence of SEQ ID NO: 801, or the variable heavy chain sequence of SEQ ID NO: 802; polynucleotides encoding the CDRs (SEQ ID NO: 834; SEQ ID NO: 836; and SEQ ID NO: 838) of the light chain sequence of SEQ ID NO: 821, or the variable light chain sequence of SEQ ID NO: 822; polynucleotides encoding the FRs (SEQ ID NO: 813; SEQ ID NO: 815; SEQ ID NO: 817; and SEQ ID NO: 819) of the heavy chain sequence of SEQ ID NO: 801, or the variable heavy chain sequence of SEQ ID NO: 802; and polynucleotides encoding the FRs (SEQ ID NO: 833; SEQ ID NO: 835; SEQ ID NO: 837; and SEQ ID NO: 839) of the light chain sequence of SEQ ID NO: 821, or the variable light chain sequence of SEQ ID NO: 822.

[0894] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, polynucleotides encoding Fab fragments having binding specificity for PACAP. With respect to antibody Ab9, the polynucleotides encoding the full length Ab9 antibody comprise, or alternatively consist of, the polynucleotide SEQ ID NO: 811 encoding the heavy chain sequence of SEQ ID NO: 801, and the polynucleotide SEQ ID NO: 831 encoding the light chain sequence of SEQ ID NO: 821.

[0895] Another embodiment of the invention contemplates these polynucleotides incorporated into an expression vector for expression in mammalian cells such as CHO, NSO, or HEK-293 cells, or in fungal, insect, or microbial systems such as yeast cells such as the yeast *Pichia*. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*. In one embodiment of the invention described herein, Fab fragments can be produced by enzymatic digestion (e.g., papain) of Ab9 following expression of the full-length polynucleotides in a suitable host. In another embodiment of the invention, anti-PACAP antibodies, such as Ab9 or Fab fragments thereof, can be produced via expression of Ab9 polynucleotides in mammalian cells such as CHO, NSO, or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example diploid yeast such as diploid *Pichia*) and other yeast strains. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*.

Antibody Ab11

[0896] In one embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to PACAP. In one embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the polynucleotide sequence of SEQ ID NO: 571 which encodes the heavy chain sequence of SEQ ID NO: 561 and which consists of the heavy chain variable region coding sequence of SEQ ID NO: 572 and the heavy chain constant region coding sequence of SEQ ID NO: 580.

[0897] In another embodiment of the invention, the polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the variable heavy chain polypeptide sequence of SEQ ID NO: 562:

(SEQ ID NO: 572)

cagtcggtggaggagtctgggggtcgcctggtcacgcctgggacacccct

gacactcacctgcacagcctctggattctccctcagtagatatgcaatgg

gctgggtccgccaggctccagggaaggggctggaatggatcggagacatt

agtacttatggtaccacagactacgcgagctgggtgaatggccgattcac

catctccagaacctcgaccacggtgactctgaaaatgaccagtctgacaa

ccgaggacacggccacctatttctgtgccagagactattggttgagcttg

tggggccaaggcaccctcgtcaccgtctcgagc.

[0898] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the constant heavy chain polypeptide sequence of SEQ ID NO: 570:

(SEQ ID NO: 580)

gcctccaccaagggcccatcggtcttccccctggcaccctcctccaagag

cacctctgggggcacagcggccctgggctgcctggtcaaggactacttcc

ccgaaccggtgacggtgtcgtggaactcaggcgccctgaccagcggcgtg

cacaccttcccggctgtcctacagtcctcaggactctactccctcagcag

cgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgca

acgtgaatcacaagcccagcaacaccaaggtggacgcgagagttgagccc

aaatcttgtgacaaaactcacacatgcccaccgtgcccagcacctgaact

cctgggggggaccgtcagtcttcctcttcccccaaaacccaaggacaccc

tcatgatctcccggaccctgaggtcacatgcgtggtggtggacgtgagc

cacgaagaccctgaggtcaagttcaactggtacgtggacggcgtggaggt

gcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtacc

gtgtggtcagcgtcctcaccgtcctgcaccaggactggctgaatggcaag

gagtacaagtgcaaggtctccaacaaagccctcccagcccccatcgagaa

aaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccc

tgcccccatcccgggaggagatgaccaagaaccaggtcagcctgacctgc

ctggtcaaaggcttctatcccagcgacatcgccgtggagtgggagagcaa

tgggcagccggagaacaactacaagaccacgcctcccgtgctggactccg

acggctccttcttcctctacagcaagctcaccgtggacaagagcaggtgg

cagcaggggaacgtcttctcatgctccgtgatgcatgaggctctgcacaa

ccactacacgcagaagagcctctccctgtctccgggtaaa.

[0899] In another embodiment of the invention, polynucleotides comprise, or alternatively consist of, the polynucleotide sequence of SEQ ID NO: 591 which encodes the light chain polypeptide sequence of SEQ ID NO: 581 and which consists of the light chain variable region coding sequence of SEQ ID NO: 592 and the light chain constant region coding sequence of SEQ ID NO: 600.

[0900] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the variable light chain polypeptide sequence of SEQ ID NO: 582:

(SEQ ID NO: 592)

gcagccgtgctgacccagacaccatcgcccgtgtctgcagctgtgggagg

cacagtcaccatcaagtgccagtccagtcagagtgtttatgataacaatg

ctttagcctggtatcagcagaaaccaggacagcctcccaagctcctgatc

tatgctgcatccaatctggcatctggggtcccagataggttcagcggcag

tggatctgggacacagttcactctcaccatcagcggcgtgcagtgtgacg

atgctgccacttactactgtctaggcggttatgatgatgctgctgataat

gctttcggcggagggaccgaggtggtggtcaaacgt.

[0901] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the constant light chain polypeptide sequence of SEQ ID NO: 590:

(SEQ ID NO: 600)

acggtagcggccccatctgtcttcatcttcccgccatctgatgagcagtt

gaaatctggaactgcctctgttgtgtgcctgctgaataacttctatccca

gagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaac

tcccaggagagtgtcacagagcaggacagcaaggacagcacctacagcct

cagcagcaccctgacgctgagcaaagcagactacgagaaacacaaagtct

acgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagc

ttcaacaggggagagtgt.

[0902] In a further embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one or more of the polynucleotide sequences of SEQ ID NO: 574; SEQ ID NO: 576; and SEQ ID NO: 578, which correspond to polynucleotides encoding the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 561, or the variable heavy chain sequence of SEQ ID NO: 562, and/or one or more of the polynucleotide sequences of SEQ ID NO: 594; SEQ ID NO: 596; and SEQ ID NO: 598, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 581, or the variable light chain sequence of SEQ ID NO: 582, or combinations of these polynucleotide sequences. In another embodiment of the invention, the polynucleotides encoding the antibodies of the invention or antigen-binding fragments thereof comprise, or alternatively consist of, combinations of polynucleotides encoding one or more of the CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them.

[0903] In a further embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one or more of the polynucleotide sequences of SEQ ID NO: 573; SEQ ID NO: 575; SEQ ID NO: 577; and SEQ ID NO: 579, which correspond to polynucleotides encoding the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 561, or the variable heavy chain sequence of SEQ ID NO: 562, and/or one or more of the polynucleotide sequences of SEQ ID NO: 593; SEQ ID NO: 595; SEQ ID NO: 597; and SEQ ID NO: 599, which

correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 581, or the variable light chain sequence of SEQ ID NO: 582, or combinations of these polynucleotide sequences. In another embodiment of the invention, the polynucleotides encoding the antibodies of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them.

[0904] The invention also contemplates polynucleotide sequences including one or more of the polynucleotide sequences encoding antigen-binding fragments described herein. In one embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three or more, including all of the following polynucleotides encoding antigen-binding fragments: the polynucleotide SEQ ID NO: 571 encoding the heavy chain sequence of SEQ ID NO: 561; the polynucleotide SEQ ID NO: 572 encoding the variable heavy chain sequence of SEQ ID NO: 562; the polynucleotide SEQ ID NO: 591 encoding the light chain sequence of SEQ ID NO: 581; the polynucleotide SEQ ID NO: 592 encoding the variable light chain sequence of SEQ ID NO: 582; polynucleotides encoding the CDRs (SEQ ID NO: 574; SEQ ID NO: 576; and SEQ ID NO: 578) of the heavy chain sequence of SEQ ID NO: 561, or the variable heavy chain sequence of SEQ ID NO: 562; polynucleotides encoding the CDRs (SEQ ID NO: 594; SEQ ID NO: 596; and SEQ ID NO: 598) of the light chain sequence of SEQ ID NO: 581, or the variable light chain sequence of SEQ ID NO: 582; polynucleotides encoding the FRs (SEQ ID NO: 573; SEQ ID NO: 575; SEQ ID NO: 577; and SEQ ID NO: 579) of the heavy chain sequence of SEQ ID NO: 561, or the variable heavy chain sequence of SEQ ID NO: 562; and polynucleotides encoding the FRs (SEQ ID NO: 593; SEQ ID NO: 595; SEQ ID NO: 597; and SEQ ID NO: 599) of the light chain sequence of SEQ ID NO: 581, or the variable light chain sequence of SEQ ID NO: 582.

[0905] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, polynucleotides encoding Fab fragments having binding specificity for PACAP. With respect to antibody Ab11, the polynucleotides encoding the full length Ab11 antibody comprise, or alternatively consist of, the polynucleotide SEQ ID NO: 571 encoding the heavy chain sequence of SEQ ID NO: 561, and the polynucleotide SEQ ID NO: 591 encoding the light chain sequence of SEQ ID NO: 581.

[0906] Another embodiment of the invention contemplates these polynucleotides incorporated into an expression vector for expression in mammalian cells such as CHO, NSO, or HEK-293 cells, or in fungal, insect, or microbial systems such as yeast cells such as the yeast *Pichia*. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*. In one embodiment of the invention described herein, Fab fragments can be produced by enzymatic digestion (e.g., papain) of Ab11 following expression of the full-length polynucleotides in a suitable host. In another embodiment of the invention, anti-PACAP antibodies, such as Ab11 or Fab fragments thereof, can be produced via expression of Ab11 polynucleotides in mammalian cells such as CHO, NSO, or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example diploid yeast such as diploid *Pichia*) and other yeast strains. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*.

Antibody Ab12

[0907] In one embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to PACAP. In one embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the polynucleotide sequence of SEQ ID NO: 611 which encodes the heavy chain sequence of SEQ ID NO: 601 and which consists of the heavy chain variable region coding sequence of SEQ ID NO: 612 and the heavy chain constant region coding sequence of SEQ ID NO: 620.

[0908] In another embodiment of the invention, the polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the variable heavy chain polypeptide sequence of SEQ ID NO: 602:

(SEQ ID NO: 612)

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cagtcggtggaggagtccgggggtcgcctggtcacgcctgggacacccct

gacactcacctgcacagcctctggattctccctcagtagctatgcaatgg

gctgggtccgccaggctccagggaaggggctggaatggatcggagacatt

agtacttatggtaccacagactacgcgagctgggtgtatggccgattcac

catctccagaacctcgaccacggtgactctgaaaatgaccagtctgacaa

ccgaggacacggccacctatttctgtgccagagactattggttgagcttg

tggggccaaggcaccctggtcaccgtctcgagc.
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[0909] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the constant heavy chain polypeptide sequence of SEQ ID NO: 610:

(SEQ ID NO: 620)

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gcctccaccaagggcccatcggtcttcccccctggcaccctcctccaagag

cacctctgggggcacagcggccctgggctgcctggtcaaggactacttcc

ccgaaccggtgacggtgtcgtggaactcaggcgccctgaccagcggcgtg

cacaccttcccggctgtcctacagtcctcaggactctactccctcagcag

cgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgca

acgtgaatcacaagcccagcaacaccaaggtggacgcgagagttgagccc

aaatcttgtgacaaaactcacacatgcccaccgtgcccagcacctgaact

cctgggggggaccgtcagtcttcctcttcccccaaaacccaaggacaccc

tcatgatctcccggacccctgaggtcacatgcgtggtggtggacgtgagc

cacgaagaccctgaggtcaagttcaactggtacgtggacggcgtggaggt

gcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtacc

gtgtggtcagcgtcctcaccgtcctgcaccaggactggctgaatggcaag

gagtacaagtgcaaggtctccaacaaagccctcccagcccccatcgagaa

aaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccc
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tgcccccatcccgggaggagatgaccaagaaccaggtcagcctgacctgc

ctggtcaaaggcttctatcccagcgacatcgccgtggagtgggagagcaa

tgggcagccggagaacaactacaagaccacgcctcccgtgctggactccg

acggctccttcttcctctacagcaagctcaccgtggacaagagcaggtgg

cagcaggggaacgtcttctcatgctccgtgatgcatgaggctctgcacaa

ccactacacgcagaagagcctctccctgtctccgggtaaa.

[0910] In another embodiment of the invention, polynucleotides comprise, or alternatively consist of, the polynucleotide sequence of SEQ ID NO: 631 which encodes the light chain polypeptide sequence of SEQ ID NO: 621 and which consists of the light chain variable region coding sequence of SEQ ID NO: 632 and the light chain constant region coding sequence of SEQ ID NO: 640.

[0911] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the variable light chain polypeptide sequence of SEQ ID NO: 622:

(SEQ ID NO: 632)

gcagccgtgctgacccagacaccatcgcccgtgtctgcagctgtgggagg

cacagtcaccatcaagtgccagtccagtcagagtgtttatgataacaatg

ctttagcctggtatcagcagaaaccagggcagcctcccaagctcctgatc

tatgctgcatccactctggcatctggggtcccatcgcggttcagtggcag

tggatctgggacagagttcactctcaccatcagcggcgtgcagtgtgacg

atgctgccacttactactgtctaggcggttattatgatcctgctgataat

gctttcggcggagggaccgaggtggtggtcaaacgt.

[0912] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the constant light chain polypeptide sequence of SEQ ID NO: 630:

(SEQ ID NO: 640)

acggtagcggccccatctgtcttcatcttcccgccatctgatgagcagtt

gaaatctggaactgcctctgttgtgtgcctgctgaataacttctatccca

gagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaac

tcccaggagagtgtcacagagcaggacagcaaggacagcacctacagcct

cagcagcaccctgacgctgagcaaagcagactacgagaaacacaaagtct

acgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagc

ttcaacaggggagagtgt.

[0913] In a further embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one or more of the polynucleotide sequences of SEQ ID NO: 614; SEQ ID NO: 616; and SEQ ID NO: 618, which correspond to polynucleotides encoding the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 601, or the variable heavy chain sequence of SEQ ID NO: 602, and/or one or more of the polynucleotide sequences of SEQ ID NO: 634; SEQ ID NO: 636; and SEQ ID NO: 638, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 621, or the variable light chain sequence of SEQ ID NO: 622, or combinations of these polynucleotide sequences. In another embodiment of the invention, the polynucleotides encoding the antibodies of the invention or antigen-binding fragments thereof comprise, or alternatively consist of, combinations of polynucleotides encoding one or more of the CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them.

[0914] In a further embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one or more of the polynucleotide sequences of SEQ ID NO: 613; SEQ ID NO: 615; SEQ ID NO: 617; and SEQ ID NO: 619, which correspond to polynucleotides encoding the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 601, or the variable heavy chain sequence of SEQ ID NO: 602, and/or one or more of the polynucleotide sequences of SEQ ID NO: 633; SEQ ID NO: 635; SEQ ID NO: 637; and SEQ ID NO: 639, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 621, or the variable light chain sequence of SEQ ID NO: 622, or combinations of these polynucleotide sequences. In another embodiment of the invention, the polynucleotides encoding the antibodies of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them.

[0915] The invention also contemplates polynucleotide sequences including one or more of the polynucleotide sequences encoding antigen-binding fragments described herein. In one embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three or more, including all of the following polynucleotides encoding antigen-binding fragments: the polynucleotide SEQ ID NO: 611 encoding the heavy chain sequence of SEQ ID NO: 601; the polynucleotide SEQ ID NO: 612 encoding the variable heavy chain sequence of SEQ ID NO: 602; the polynucleotide SEQ ID NO: 631 encoding the light chain sequence of SEQ ID NO: 621; the polynucleotide SEQ ID NO: 632 encoding the variable light chain sequence of SEQ ID NO: 622; polynucleotides encoding the CDRs (SEQ ID NO: 614; SEQ ID NO: 616; and SEQ ID NO: 618) of the heavy chain sequence of SEQ ID NO: 601, or the variable heavy chain sequence of SEQ ID NO: 602; polynucleotides encoding the CDRs (SEQ ID NO: 634; SEQ ID NO: 636; and SEQ ID NO: 638) of the light chain sequence of SEQ ID NO: 621, or the variable light chain sequence of SEQ ID NO: 622; polynucleotides encoding the FRs (SEQ ID NO: 613; SEQ ID NO: 615; SEQ ID NO: 617; and SEQ ID NO: 619) of the heavy chain sequence of SEQ ID NO: 601, or the variable heavy chain sequence of SEQ ID NO: 602; and polynucleotides encoding the FRs (SEQ ID NO: 633; SEQ ID NO: 635; SEQ ID NO: 637; and SEQ ID NO: 639) of the light chain sequence of SEQ ID NO: 621, or the variable light chain sequence of SEQ ID NO: 622.

[0916] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, polynucleotides encoding Fab fragments having

binding specificity for PACAP. With respect to antibody Ab12, the polynucleotides encoding the full length Ab12 antibody comprise, or alternatively consist of, the polynucleotide SEQ ID NO: 611 encoding the heavy chain sequence of SEQ ID NO: 601, and the polynucleotide SEQ ID NO: 631 encoding the light chain sequence of SEQ ID NO: 621.

[0917] Another embodiment of the invention contemplates these polynucleotides incorporated into an expression vector for expression in mammalian cells such as CHO, NSO, or HEK-293 cells, or in fungal, insect, or microbial systems such as yeast cells such as the yeast *Pichia*. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*. In one embodiment of the invention described herein, Fab fragments can be produced by enzymatic digestion (e.g., papain) of Ab12 following expression of the full-length polynucleotides in a suitable host. In another embodiment of the invention, anti-PACAP antibodies, such as Ab12 or Fab fragments thereof, can be produced via expression of Ab12 polynucleotides in mammalian cells such as CHO, NSO, or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example diploid yeast such as diploid *Pichia*) and other yeast strains. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*.

Antibody Ab13

[0918] In one embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to PACAP. In one embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the polynucleotide sequence of SEQ ID NO: 131 which encodes the heavy chain sequence of SEQ ID NO: 121 and which consists of the heavy chain variable region coding sequence of SEQ ID NO: 132 and the heavy chain constant region coding sequence of SEQ ID NO: 140.

[0919] In another embodiment of the invention, the polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the variable heavy chain polypeptide sequence of SEQ ID NO: 122:

(SEQ ID NO: 132)

cagtcggtggaggagtccgggggtcgcctggtcacgcctgggacacccct

gacactcacctgcaccgtctctggattctccctcagtagcgctgcaatga

actgggtccgccaggctccagggaaggggctggaatggatcggaattatt

gataatactgctggcacatattacgcgccctgggcgaaaggccgattcac

catctccaaaacctcgtcgaccacggtggatctgaaaatgaccagtccga

caaccgaggacacggccacctatttctgtgccagaggggagggaatttt

ttcatctggggcccgggcaccctcgtcaccgtctcgagc.

[0920] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the constant heavy chain polypeptide sequence of SEQ ID NO: 130:

(SEQ ID NO: 140)

gcctccaccaagggcccatcggtcttcccccctggcaccctcctccaagag

cacctctgggggcacagcggccctgggctgcctggtcaaggactacttcc

-continued

ccgaaccggtgacggtgtcgtggaactcaggcgccctgaccagcggcgtg

cacaccttcccggctgtcctacagtcctcaggactctactccctcagcag

cgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgca

acgtgaatcacaagcccagcaacaccaaggtggacaagaaagttgagccc

aaatcttgtgacaaaactcacacatgcccaccgtgcccagcacctgaact

cctgggggggaccgtcagtcttcctcttcccccaaaacccaaggacaccc

tcatgatctcccggaccctgaggtcacatgcgtggtggtggacgtgagc

cacgaagaccctgaggtcaagttcaactggtacgtggacggcgtggaggt

gcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtacc

gtgtggtcagcgtcctcaccgtcctgcaccaggactggctgaatggcaag

gagtacaagtgcaaggtctccaacaaagccctcccagccccatcgagaa

aaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccc

tgcccccatcccgggaggagatgaccaagaaccaggtcagcctgacctgc

ctggtcaaaggcttctatcccagcgacatcgccgtggagtgggagagcaa

tgggcagccggagaacaactacaagaccacgcctcccgtgctggactccg

acggctccttcttcctctacagcaagctcaccgtggacaagagcaggtgg

cagcaggggaacgtcttctcatgctccgtgatgcatgaggctctgcacaa

ccactacacgcagaagagcctctccctgtctccgggtaaa.

[0921] In another embodiment of the invention, polynucleotides comprise, or alternatively consist of, the polynucleotide sequence of SEQ ID NO: 151 which encodes the light chain polypeptide sequence of SEQ ID NO: 141 and which consists of the light chain variable region coding sequence of SEQ ID NO: 152 and the light chain constant region coding sequence of SEQ ID NO: 160.

[0922] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the variable light chain polypeptide sequence of SEQ ID NO: 142:

(SEQ ID NO: 152)

gcgcaagtgctgacccagactccatcgtccgtgtctgcagctgtgggagg

cacagtcaccatcaattgccagtccagtcagagtgttcatgatggcagct

acttatcctggtatcagcagaaaccagggcagcctcccaacttcctgatc

taccaggcatccaatttggcatctggggtcccatcgcggttcaaaggcag

tggatctgggacacagttcactctcaccatcagcgacctggagtgtgacg

atgccgccacttattactgtgcaggcggttatagtagtaatatttgtggt

ttcggcggagggaccgaggtggtggtcaaacgt.

[0923] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the constant light chain polypeptide sequence of SEQ ID NO: 150:

(SEQ ID NO: 160)

acggtagcggccccatctgtcttcatcttcccgccatctgatgagcagtt

gaaatctggaactgcctctgttgtgtgcctgctgaataacttctatccca

gagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaac

tcccaggagagtgtcacagagcaggacagcaaggacagcacctacagcct

cagcagcaccctgacgctgagcaaagcagactacgagaaacacaaagtct

acgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagc

ttcaacaggggagagtgt.

[0924] In a further embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one or more of the polynucleotide sequences of SEQ ID NO: 134; SEQ ID NO: 136; and SEQ ID NO: 138, which correspond to polynucleotides encoding the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 121, or the variable heavy chain sequence of SEQ ID NO: 122, and/or one or more of the polynucleotide sequences of SEQ ID NO: 154; SEQ ID NO: 156; and SEQ ID NO: 158, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 141, or the variable light chain sequence of SEQ ID NO: 142, or combinations of these polynucleotide sequences. In another embodiment of the invention, the polynucleotides encoding the antibodies of the invention or antigen-binding fragments thereof comprise, or alternatively consist of, combinations of polynucleotides encoding one or more of the CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them.

[0925] In a further embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one or more of the polynucleotide sequences of SEQ ID NO: 133; SEQ ID NO: 135; SEQ ID NO: 137; and SEQ ID NO: 139, which correspond to polynucleotides encoding the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 121, or the variable heavy chain sequence of SEQ ID NO: 122, and/or one or more of the polynucleotide sequences of SEQ ID NO: 153; SEQ ID NO: 155; SEQ ID NO: 157; and SEQ ID NO: 159, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 141, or the variable light chain sequence of SEQ ID NO: 142, or combinations of these polynucleotide sequences. In another embodiment of the invention, the polynucleotides encoding the antibodies of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them.

[0926] The invention also contemplates polynucleotide sequences including one or more of the polynucleotide sequences encoding antigen-binding fragments described herein. In one embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three or more, including all of the following polynucleotides encoding antigen-binding fragments: the polynucleotide SEQ ID NO: 131 encoding the heavy chain sequence of SEQ ID NO: 121; the polynucleotide SEQ ID NO: 132 encoding the variable heavy chain sequence of SEQ ID NO: 122; the polynucleotide SEQ ID NO: 151 encoding the light chain sequence of SEQ ID NO: 141; the polynucleotide SEQ ID NO: 152 encoding the variable light chain sequence of SEQ ID NO: 142; polynucleotides encoding the CDRs (SEQ ID NO: 134; SEQ ID NO: 136; and SEQ ID NO: 138) of the heavy chain sequence of SEQ ID NO: 121, or the variable heavy chain sequence of SEQ ID NO: 122; polynucleotides encoding the CDRs (SEQ ID NO: 154; SEQ ID NO: 156; and SEQ ID NO: 158) of the light chain sequence of SEQ ID NO: 141, or the variable light chain sequence of SEQ ID NO: 142; polynucleotides encoding the FRs (SEQ ID NO: 133; SEQ ID NO: 135; SEQ ID NO: 137; and SEQ ID NO: 139) of the heavy chain sequence of SEQ ID NO: 121, or the variable heavy chain sequence of SEQ ID NO: 122; and polynucleotides encoding the FRs (SEQ ID NO: 153; SEQ ID NO: 155; SEQ ID NO: 157; and SEQ ID NO: 159) of the light chain sequence of SEQ ID NO: 141, or the variable light chain sequence of SEQ ID NO: 142.

[0927] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, polynucleotides encoding Fab fragments having binding specificity for PACAP. With respect to antibody Ab13, the polynucleotides encoding the full length Ab13 antibody comprise, or alternatively consist of, the polynucleotide SEQ ID NO: 131 encoding the heavy chain sequence of SEQ ID NO: 121, and the polynucleotide SEQ ID NO: 151 encoding the light chain sequence of SEQ ID NO: 141.

[0928] Another embodiment of the invention contemplates these polynucleotides incorporated into an expression vector for expression in mammalian cells such as CHO, NSO, or HEK-293 cells, or in fungal, insect, or microbial systems such as yeast cells such as the yeast *Pichia*. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*. In one embodiment of the invention described herein, Fab fragments can be produced by enzymatic digestion (e.g., papain) of Ab13 following expression of the full-length polynucleotides in a suitable host. In another embodiment of the invention, anti-PACAP antibodies, such as Ab13 or Fab fragments thereof, can be produced via expression of Ab13 polynucleotides in mammalian cells such as CHO, NSO, or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example diploid yeast such as diploid *Pichia*) and other yeast strains. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*.

Antibody Ab14

[0929] In one embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to PACAP. In one embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the polynucleotide sequence of SEQ ID NO: 171 which encodes the heavy chain sequence of SEQ ID NO: 161 and which consists of the heavy chain variable region coding sequence of SEQ ID NO: 172 and the heavy chain constant region coding sequence of SEQ ID NO: 180.

[0930] In another embodiment of the invention, the polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the variable heavy chain polypeptide sequence of SEQ ID NO: 162:

(SEQ ID NO: 172)

cagtcggtggaggcgtccgggggtcgcctggtcacgcctgggacacccct

gacactcacctgcaccgtctctggattctccctcagtagcgctgcaatga

actgggtccgccaggctccagggaaggggctggaatggatcggatttatt

gagtatagtaagaatatagtttacgcgtcctgggcgaaaggccgattcac

catctccaaagtctcgtcgaccacggtggatctgaaaatgaccagtccga

caaccgaggacacggccacctatttctgtgccaggggggggaggggaattt

ttcatctggggccaaggcaccctggtcaccgtctcgagc.

[0931] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the constant heavy chain polypeptide sequence of SEQ ID NO: 170:

(SEQ ID NO: 180)

gcctccaccaagggcccatcggtcttcccctggcaccctcctccaagag

cacctctgggggcacagcggccctgggctgcctggtcaaggactacttcc

ccgaaccggtgacggtgtcgtggaactcaggcgccctgaccagcggcgtg

cacaccttcccggctgtcctacagtcctcaggactctactccctcagcag

cgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgca

acgtgaatcacaagcccagcaacaccaaggtggacaagaaagttgagccc

aaatcttgtgacaaaactcacacatgcccaccgtgcccagcacctgaact

cctgggggggaccgtcagtcttcctcttcccccaaaacccaaggacaccc

tcatgatctcccggaccccctgaggtcacatgcgtggtggtggacgtgagc

cacgaagaccctgaggtcaagttcaactggtacgtggacggcgtggaggt

gcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtacc

gtgtggtcagcgtcctcaccgtcctgcaccaggactggctgaatggcaag

gagtacaagtgcaaggtctccaacaaagccctcccagcccccatcgagaa

aaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccc

tgcccccatcccgggaggagatgaccaagaaccaggtcagcctgacctgc

ctggtcaaaggcttctatcccagcgacatcgccgtggagtgggagagcaa

tgggcagccggagaacaactacaagaccacgcctcccgtgctggactccg

acggctccttcttcctctacagcaagctcaccgtggacaagagcaggtgg

cagcaggggaacgtcttctcatgctccgtgatgcatgaggctctgcacaa

ccactacacgcagaagagcctctccctgtctccgggtaaa.

[0932] In another embodiment of the invention, polynucleotides comprise, or alternatively consist of, the polynucleotide sequence of SEQ ID NO: 191 which encodes the light chain polypeptide sequence of SEQ ID NO: 181 and which consists of the light chain variable region coding sequence of SEQ ID NO: 192 and the light chain constant region coding sequence of SEQ ID NO: 200.

[0933] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the variable light chain polypeptide sequence of SEQ ID NO: 182:

(SEQ ID NO: 192)

gcgcaagtgctgacccagactccatcgtccgtgtctgcagctgtgggagg

cacagtcaccatcaattgccagtccagtcagagtgtttatagtaacaacc

ggttatcgtactatcagcagaaaccagggcagcctcccaagctcctgatc

tacgaagcatccagtctggcatatggggtcccatcgcggttcaaaggcag

tggatctgggacacagttcactctcaccatcagcgacctggagtgtgacg

atgccgccacttattactgtgcaggtgcctatagtaatagtatttatagt

ttcggcggagggaccgaggtggtggtcaaacgt.

[0934] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the constant light chain polypeptide sequence of SEQ ID NO: 190:

(SEQ ID NO: 200)

acggtagcggccccatctgtcttcatcttcccgccatctgatgagcagtt

gaaatctggaactgcctctgttgtgtgcctgctgaataacttctatccca

gagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaac

tcccaggagagtgtcacagagcaggacagcaaggacagcacctacagcct

cagcagcaccctgacgctgagcaaagcagactacgagaaacacaaagtct

acgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagc

ttcaacaggggagagtgt.

[0935] In a further embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one or more of the polynucleotide sequences of SEQ ID NO: 174; SEQ ID NO: 176; and SEQ ID NO: 178, which correspond to polynucleotides encoding the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 161, or the variable heavy chain sequence of SEQ ID NO: 162, and/or one or more of the polynucleotide sequences of SEQ ID NO: 194; SEQ ID NO: 196; and SEQ ID NO: 198, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 181, or the variable light chain sequence of SEQ ID NO: 182, or combinations of these polynucleotide sequences. In another embodiment of the invention, the polynucleotides encoding the antibodies of the invention or antigen-binding fragments thereof comprise, or alternatively consist of, combinations of polynucleotides encoding one or more of the CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them.

[0936] In a further embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one or more of the polynucleotide sequences of SEQ ID NO: 173; SEQ ID NO: 175; SEQ ID NO: 177; and SEQ ID NO: 179, which correspond to polynucleotides encoding the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 161, or the variable heavy chain sequence of SEQ ID NO: 162, and/or one or more of the polynucleotide sequences of SEQ ID NO: 193; SEQ ID NO: 195; SEQ ID NO: 197; and SEQ ID NO: 199, which

correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 181, or the variable light chain sequence of SEQ ID NO: 182, or combinations of these polynucleotide sequences. In another embodiment of the invention, the polynucleotides encoding the antibodies of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them.

[0937] The invention also contemplates polynucleotide sequences including one or more of the polynucleotide sequences encoding antigen-binding fragments described herein. In one embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three or more, including all of the following polynucleotides encoding antigen-binding fragments: the polynucleotide SEQ ID NO: 171 encoding the heavy chain sequence of SEQ ID NO: 161; the polynucleotide SEQ ID NO: 172 encoding the variable heavy chain sequence of SEQ ID NO: 162; the polynucleotide SEQ ID NO: 191 encoding the light chain sequence of SEQ ID NO: 181; the polynucleotide SEQ ID NO: 192 encoding the variable light chain sequence of SEQ ID NO: 182; polynucleotides encoding the CDRs (SEQ ID NO: 174; SEQ ID NO: 176; and SEQ ID NO: 178) of the heavy chain sequence of SEQ ID NO: 161, or the variable heavy chain sequence of SEQ ID NO: 162; polynucleotides encoding the CDRs (SEQ ID NO: 194; SEQ ID NO: 196; and SEQ ID NO: 198) of the light chain sequence of SEQ ID NO: 181, or the variable light chain sequence of SEQ ID NO: 182; polynucleotides encoding the FRs (SEQ ID NO: 173; SEQ ID NO: 175; SEQ ID NO: 177; and SEQ ID NO: 179) of the heavy chain sequence of SEQ ID NO: 161, or the variable heavy chain sequence of SEQ ID NO: 162; and polynucleotides encoding the FRs (SEQ ID NO: 193; SEQ ID NO: 195; SEQ ID NO: 197; and SEQ ID NO: 199) of the light chain sequence of SEQ ID NO: 181, or the variable light chain sequence of SEQ ID NO: 182.

[0938] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, polynucleotides encoding Fab fragments having binding specificity for PACAP. With respect to antibody Ab14, the polynucleotides encoding the full length Ab14 antibody comprise, or alternatively consist of, the polynucleotide SEQ ID NO: 171 encoding the heavy chain sequence of SEQ ID NO: 161, and the polynucleotide SEQ ID NO: 191 encoding the light chain sequence of SEQ ID NO: 181.

[0939] Another embodiment of the invention contemplates these polynucleotides incorporated into an expression vector for expression in mammalian cells such as CHO, NSO, or HEK-293 cells, or in fungal, insect, or microbial systems such as yeast cells such as the yeast *Pichia*. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*. In one embodiment of the invention described herein, Fab fragments can be produced by enzymatic digestion (e.g., papain) of Ab14 following expression of the full-length polynucleotides in a suitable host. In another embodiment of the invention, anti-PACAP antibodies, such as Ab14 or Fab fragments thereof, can be produced via expression of Ab14 polynucleotides in mammalian cells such as CHO, NSO, or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example diploid yeast such as diploid *Pichia*) and other yeast strains. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*.

Antibody Ab15

[0940] In one embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to PACAP. In one embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the polynucleotide sequence of SEQ ID NO: 211 which encodes the heavy chain sequence of SEQ ID NO: 201 and which consists of the heavy chain variable region coding sequence of SEQ ID NO: 212 and the heavy chain constant region coding sequence of SEQ ID NO: 220.

[0941] In another embodiment of the invention, the polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the variable heavy chain polypeptide sequence of SEQ ID NO: 202:

(SEQ ID NO: 212)

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cagtcggtggaggcgtccgggggtcacctagtcacgcctgggacacccct

gacactcacctgcaccgtctctggattctccctcagtagcgctgcaatga

actgggtccgccaggctccagggaaggggctggaatggatcggatcggtt

gatgagcgtcagaataaatattacgcgtcctgggcgaaaggccgattcac

catctccagaacctcgtcgaccacggtgaatctgaaaatgaccagtccga

caaccgaggacacggccacctatttctgtgccagaggggagggaatttt

ttcatctggggccagggcaccctcgtcaccgtctcgagc.
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[0942] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the constant heavy chain polypeptide sequence of SEQ ID NO: 210:

(SEQ ID NO: 220)

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gcctccaccaagggcccatcggtcttcccccctggcaccctcctccaagag

cacctctgggggcacagcggccctgggctgcctggtcaaggactacttcc

ccgaaccggtgacggtgtcgtggaactcaggcgccctgaccagcggcgtg

cacaccttcccggctgtcctacagtcctcaggactctactccctcagcag

cgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgca

acgtgaatcacaagcccagcaacaccaaggtggacaagaaagttgagccc

aaatcttgtgacaaaactcacacatgcccaccgtgcccagcacctgaact

cctgggggggaccgtcagtcttcctcttcccccaaaacccaaggacaccc

tcatgatctcccggacccctgaggtcacatgcgtggtggtggacgtgagc

cacgaagaccctgaggtcaagttcaactggtacgtggacggcgtggaggt

gcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtacc

gtgtggtcagcgtcctcaccgtcctgcaccaggactggctgaatggcaag

gagtacaagtgcaaggtctccaacaaagccctcccagcccccatcgagaa

aaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccc
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tgcccccatcccgggaggagatgaccaagaaccaggtcagcctgacctgc

ctggtcaaaggcttctatcccagcgacatcgccgtggagtgggagagcaa

tgggcagccggagaacaactacaagaccacgcctcccgtgctggactccg

acggctccttcttcctctacagcaagctcaccgtggacaagagcaggtgg

cagcaggggaacgtcttctcatgctccgtgatgcatgaggctctgcacaa

ccactacacgcagaagagcctctccctgtctccgggtaaa.

[0943] In another embodiment of the invention, polynucleotides comprise, or alternatively consist of, the polynucleotide sequence of SEQ ID NO: 231 which encodes the light chain polypeptide sequence of SEQ ID NO: 221 and which consists of the light chain variable region coding sequence of SEQ ID NO: 232 and the light chain constant region coding sequence of SEQ ID NO: 240.

[0944] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the variable light chain polypeptide sequence of SEQ ID NO: 222:

(SEQ ID NO: 232)

gcgcaagtgctgacccagactccatcgtccgtgtctgcagctgtgggagg

cacagtcaccatcaattgccagtccagtcagagtgtttatagtaacaacc

gcttatcctggtatcagcagaaaccagggcagcctcccaatctcctgatc

tacgaagcatccagtctggcatctggggtcccatcgcggttcagcggcag

tggatctgggacacagttcactctcaccatcagcgacctggagtgtgacg

atgccgccacttattactgtgcaggcgcttataatactgggatttatggt

ttcggcggagggaccgaggtggtggtcaaacgt.

[0945] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the constant light chain polypeptide sequence of SEQ ID NO: 230:

(SEQ ID NO: 240)

acggtagcggccccatctgtcttcatcttcccgccatctgatgagcagtt

gaaatctggaactgcctctgttgtgtgcctgctgaataacttctatccca

gagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaac

tcccaggagagtgtcacagagcaggacagcaaggacagcacctacagcct

cagcagcaccctgacgctgagcaaagcagactacgagaaacacaaagtct

acgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagc

ttcaacaggggagagtgt.

[0946] In a further embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one or more of the polynucleotide sequences of SEQ ID NO: 214; SEQ ID NO: 216; and SEQ ID NO: 218, which correspond to polynucleotides encoding the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 201, or the variable heavy chain sequence of SEQ ID NO: 202, and/or one or more of the polynucleotide sequences of SEQ ID NO: 234; SEQ ID NO: 236; and SEQ ID NO: 238, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 221, or the variable light chain sequence of SEQ ID NO: 222, or combinations of these polynucleotide sequences. In another embodiment of the invention, the polynucleotides encoding the antibodies of the invention or antigen-binding fragments thereof comprise, or alternatively consist of, combinations of polynucleotides encoding one or more of the CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them.

[0947] In a further embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one or more of the polynucleotide sequences of SEQ ID NO: 213; SEQ ID NO: 215; SEQ ID NO: 217; and SEQ ID NO: 219, which correspond to polynucleotides encoding the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 201, or the variable heavy chain sequence of SEQ ID NO: 202, and/or one or more of the polynucleotide sequences of SEQ ID NO: 233; SEQ ID NO: 235; SEQ ID NO: 237; and SEQ ID NO: 239, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 221, or the variable light chain sequence of SEQ ID NO: 222, or combinations of these polynucleotide sequences. In another embodiment of the invention, the polynucleotides encoding the antibodies of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them.

[0948] The invention also contemplates polynucleotide sequences including one or more of the polynucleotide sequences encoding antigen-binding fragments described herein. In one embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three or more, including all of the following polynucleotides encoding antigen-binding fragments: the polynucleotide SEQ ID NO: 211 encoding the heavy chain sequence of SEQ ID NO: 201; the polynucleotide SEQ ID NO: 212 encoding the variable heavy chain sequence of SEQ ID NO: 202; the polynucleotide SEQ ID NO: 231 encoding the light chain sequence of SEQ ID NO: 221; the polynucleotide SEQ ID NO: 232 encoding the variable light chain sequence of SEQ ID NO: 222; polynucleotides encoding the CDRs (SEQ ID NO: 214; SEQ ID NO: 216; and SEQ ID NO: 218) of the heavy chain sequence of SEQ ID NO: 201, or the variable heavy chain sequence of SEQ ID NO: 202; polynucleotides encoding the CDRs (SEQ ID NO: 234; SEQ ID NO: 236; and SEQ ID NO: 238) of the light chain sequence of SEQ ID NO: 221, or the variable light chain sequence of SEQ ID NO: 222; polynucleotides encoding the FRs (SEQ ID NO: 213; SEQ ID NO: 215; SEQ ID NO: 217; and SEQ ID NO: 219) of the heavy chain sequence of SEQ ID NO: 201, or the variable heavy chain sequence of SEQ ID NO: 202; and polynucleotides encoding the FRs (SEQ ID NO: 233; SEQ ID NO: 235; SEQ ID NO: 237; and SEQ ID NO: 239) of the light chain sequence of SEQ ID NO: 221, or the variable light chain sequence of SEQ ID NO: 222.

[0949] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively con-

sist of, polynucleotides encoding Fab fragments having binding specificity for PACAP. With respect to antibody Ab15, the polynucleotides encoding the full length Ab15 antibody comprise, or alternatively consist of, the polynucleotide SEQ ID NO: 211 encoding the heavy chain sequence of SEQ ID NO: 201, and the polynucleotide SEQ ID NO: 231 encoding the light chain sequence of SEQ ID NO: 221.

[0950] Another embodiment of the invention contemplates these polynucleotides incorporated into an expression vector for expression in mammalian cells such as CHO, NSO, or HEK-293 cells, or in fungal, insect, or microbial systems such as yeast cells such as the yeast *Pichia*. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*. In one embodiment of the invention described herein, Fab fragments can be produced by enzymatic digestion (e.g., papain) of Ab15 following expression of the full-length polynucleotides in a suitable host. In another embodiment of the invention, anti-PACAP antibodies, such as Ab15 or Fab fragments thereof, can be produced via expression of Ab15 polynucleotides in mammalian cells such as CHO, NSO, or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example diploid yeast such as diploid *Pichia*) and other yeast strains. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*.

Antibody Ab16

[0951] In one embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to PACAP. In one embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the polynucleotide sequence of SEQ ID NO: 251 which encodes the heavy chain sequence of SEQ ID NO: 241 and which consists of the heavy chain variable region coding sequence of SEQ ID NO: 252 and the heavy chain constant region coding sequence of SEQ ID NO: 260.

[0952] In another embodiment of the invention, the polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the variable heavy chain polypeptide sequence of SEQ ID NO: 242:

(SEQ ID NO: 252)

cagtcggtggaggagtccgggggtcgcctggtcacgcctgggacacccct

gacactcacctgcaccgtctctggattctccctcagtagcgctgcaatga

gctgggtccgccaggctccagggaaggggctggaatggatcggaattatt

gatgatagtggtaacacatactacgcgtcctgggcgaaagcccgattcac

catctccaaaacctcgtcgaccacggtggatctgaaaatgaccagtccga

caaccgaggacacggccacctatttctgtgccagaggggagggagtttt

ttcatctggggcccgggcaccctcgtcaccgtctcgagc.

[0953] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the constant heavy chain polypeptide sequence of SEQ ID NO: 250:

(SEQ ID NO: 260)

gcctccaccaagggcccatcggtcttcccctggcaccctcctccaagag

cacctctgggggcacagcggccctgggctgcctggtcaaggactacttcc

ccgaaccggtgacggtgtcgtggaactcaggcgccctgaccagcggcgtg

cacaccttcccggctgtcctacagtcctcaggactctactccctcagcag

cgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgca

acgtgaatcacaagcccagcaacaccaaggtggacaagaaagttgagccc

aaatcttgtgacaaaactcacacatgcccaccgtgcccagcacctgaact

cctgggggggaccgtcagtcttcctcttcccccaaaacccaaggacaccc

tcatgatctcccggaccctgaggtcacatgcgtggtggtggacgtgagc

cacgaagaccctgaggtcaagttcaactggtacgtggacggcgtggaggt

gcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtacc

gtgtggtcagcgtcctcaccgtcctgcaccaggactggctgaatggcaag

gagtacaagtgcaaggtctccaacaaagccctcccagcccccatcgagaa

aaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccc

tgcccccatcccgggaggagatgaccaagaaccaggtcagcctgacctgc

ctggtcaaaggcttctatcccagcgacatcgccgtggagtgggagagcaa

tgggcagccggagaacaactacaagaccacgcctcccgtgctggactccg

acggctccttcttcctctacagcaagctcaccgtggacaagagcaggtgg

cagcaggggaacgtcttctcatgctccgtgatgcatgaggctctgcacaa

ccactacacgcagaagagcctctccctgtctccgggtaaa.

[0954] In another embodiment of the invention, polynucleotides comprise, or alternatively consist of, the polynucleotide sequence of SEQ ID NO: 271 which encodes the light chain polypeptide sequence of SEQ ID NO: 261 and which consists of the light chain variable region coding sequence of SEQ ID NO: 272 and the light chain constant region coding sequence of SEQ ID NO: 280.

[0955] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the variable light chain polypeptide sequence of SEQ ID NO: 262:

(SEQ ID NO: 272)

gaccctgtgctgacccagactccatcgtccgtgtctgcagctgtgggagg

cacagtcaccatcaattgccagtccagtcagagtgtttataataacaagt

ggttatcctggtatcagcagaaaccaggacagtctcccaagttcctgatt

taccaggcatccaatttggcatctggggtcccatcgcggttcaaaggcag

tggatctgggacacagttcactctcaccatcagcgacctggagtgtgacg

atggcgccacttattactgtgcaggcggctaccgtggtaatgtttgtggt

ttcggcggagggaccgaggtggtggtcaaacgt.

[0956] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the constant light chain polypeptide sequence of SEQ ID NO: 270:

(SEQ ID NO: 280)
acggtagcggccccatctgtcttcatcttcccgccatctgatgagcagtt

gaaatctggaactgcctctgttgtgtgcctgctgaataacttctatccca

gagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaac

tcccaggagagtgtcacagagcaggacagcaaggacagcacctacagcct

cagcagcaccctgacgctgagcaaagcagactacgagaaacacaaagtct

acgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagc

ttcaacaggggagagtgt.

[0957] In a further embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one or more of the polynucleotide sequences of SEQ ID NO: 254; SEQ ID NO: 256; and SEQ ID NO: 258, which correspond to polynucleotides encoding the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 241, or the variable heavy chain sequence of SEQ ID NO: 242, and/or one or more of the polynucleotide sequences of SEQ ID NO: 274; SEQ ID NO: 276; and SEQ ID NO: 278, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 261, or the variable light chain sequence of SEQ ID NO: 262, or combinations of these polynucleotide sequences. In another embodiment of the invention, the polynucleotides encoding the antibodies of the invention or antigen-binding fragments thereof comprise, or alternatively consist of, combinations of polynucleotides encoding one or more of the CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them.

[0958] In a further embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one or more of the polynucleotide sequences of SEQ ID NO: 253; SEQ ID NO: 255; SEQ ID NO: 257; and SEQ ID NO: 259, which correspond to polynucleotides encoding the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 241, or the variable heavy chain sequence of SEQ ID NO: 242, and/or one or more of the polynucleotide sequences of SEQ ID NO: 273; SEQ ID NO: 275; SEQ ID NO: 277; and SEQ ID NO: 279, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 261, or the variable light chain sequence of SEQ ID NO: 262, or combinations of these polynucleotide sequences. In another embodiment of the invention, the polynucleotides encoding the antibodies of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them.

[0959] The invention also contemplates polynucleotide sequences including one or more of the polynucleotide sequences encoding antigen-binding fragments described herein. In one embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three or more, including all of the following polynucleotides encoding antigen-binding fragments: the polynucleotide SEQ ID NO: 251 encoding the heavy chain sequence of SEQ ID NO: 241; the polynucleotide SEQ ID NO: 252 encoding the variable heavy chain sequence of SEQ ID NO: 242; the polynucleotide SEQ ID NO: 271 encoding the light chain sequence of SEQ ID NO: 261; the polynucleotide SEQ ID NO: 272 encoding the variable light chain sequence of SEQ ID NO: 262; polynucleotides encoding the CDRs (SEQ ID NO: 254; SEQ ID NO: 256; and SEQ ID NO: 258) of the heavy chain sequence of SEQ ID NO: 241, or the variable heavy chain sequence of SEQ ID NO: 242; polynucleotides encoding the CDRs (SEQ ID NO: 274; SEQ ID NO: 276; and SEQ ID NO: 278) of the light chain sequence of SEQ ID NO: 261, or the variable light chain sequence of SEQ ID NO: 262; polynucleotides encoding the FRs (SEQ ID NO: 253; SEQ ID NO: 255; SEQ ID NO: 257; and SEQ ID NO: 259) of the heavy chain sequence of SEQ ID NO: 241, or the variable heavy chain sequence of SEQ ID NO: 242; and polynucleotides encoding the FRs (SEQ ID NO: 273; SEQ ID NO: 275; SEQ ID NO: 277; and SEQ ID NO: 279) of the light chain sequence of SEQ ID NO: 261, or the variable light chain sequence of SEQ ID NO: 262.

[0960] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, polynucleotides encoding Fab fragments having binding specificity for PACAP. With respect to antibody Ab16, the polynucleotides encoding the full length Ab16 antibody comprise, or alternatively consist of, the polynucleotide SEQ ID NO: 251 encoding the heavy chain sequence of SEQ ID NO: 241, and the polynucleotide SEQ ID NO: 271 encoding the light chain sequence of SEQ ID NO: 261.

[0961] Another embodiment of the invention contemplates these polynucleotides incorporated into an expression vector for expression in mammalian cells such as CHO, NSO, or HEK-293 cells, or in fungal, insect, or microbial systems such as yeast cells such as the yeast *Pichia*. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*. In one embodiment of the invention described herein, Fab fragments can be produced by enzymatic digestion (e.g., papain) of Ab16 following expression of the full-length polynucleotides in a suitable host. In another embodiment of the invention, anti-PACAP antibodies, such as Ab16 or Fab fragments thereof, can be produced via expression of Ab16 polynucleotides in mammalian cells such as CHO, NSO, or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example diploid yeast such as diploid *Pichia*) and other yeast strains. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*.

Antibody Ab17

[0962] In one embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to PACAP. In one embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the polynucleotide sequence of SEQ ID NO: 291 which encodes the heavy chain sequence of SEQ ID NO: 281 and which consists of the heavy chain variable region coding sequence of SEQ ID NO: 292 and the heavy chain constant region coding sequence of SEQ ID NO: 300.

[0963] In another embodiment of the invention, the polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the variable heavy chain polypeptide sequence of SEQ ID NO: 282:

(SEQ ID NO: 292)

cagtcagtggaggagtccgggggtcgcctggtcacgcctgggacacccct

aacactcacctgcaccgtctctggattctccctcagtagcgctgcaatga

actgggtccgccaggctccagggaaggggctggaatggatcggtatttttt

gatccttatagtagtacatactacgcgtcctgggcgaaaggccgattcac

catctccaaaacctcgtcgaccacggtggatctgaaaatgaccagtccga

caaccgaggacacggccacctatttctgtgccagagggggaggggaattt

ttcatctggggcccaggcaccctcgtcaccgtctcgagc.

[0964] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the constant heavy chain polypeptide sequence of SEQ ID NO: 290:

(SEQ ID NO: 300)

gcctccaccaagggcccatcggtcttcccctggcaccctcctccaagag

cacctctgggggcacagcggccctgggctgcctggtcaaggactacttcc

ccgaaccggtgacggtgtcgtggaactcaggcgccctgaccagcggcgtg

cacaccttcccggctgtcctacagtcctcaggactctactccctcagcag

cgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgca

acgtgaatcacaagcccagcaacaccaaggtggacaagaaagttgagccc

aaatcttgtgacaaaactcacacatgcccaccgtgcccagcacctgaact

cctgggggggaccgtcagtcttcctcttcccccaaaacccaaggacaccc

tcatgatctcccggaccctgaggtcacatgcgtggtggtggacgtgagc

cacgaagaccctgaggtcaagttcaactggtacgtggacggcgtggaggt

gcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtacc

gtgtggtcagcgtcctcaccgtcctgcaccaggactggctgaatggcaag

gagtacaagtgcaaggtctccaacaaagccctcccagcccccatcgagaa

aaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccc

tgcccccatcccgggaggagatgaccaagaaccaggtcagcctgacctgc

ctggtcaaaggcttctatcccagcgacatcgccgtggagtgggagagcaa

tgggcagccggagaacaactacaagaccacgcctcccgtgctggactccg

acggctccttcttcctctacagcaagctcaccgtggacaagagcaggtgg

cagcaggggaacgtcttctcatgctccgtgatgcatgaggctctgcacaa

ccactacacgcagaagagcctctccctgtctccgggtaaa.

[0965] In another embodiment of the invention, polynucleotides comprise, or alternatively consist of, the polynucleotide sequence of SEQ ID NO: 311 which encodes the light chain polypeptide sequence of SEQ ID NO: 301 and which consists of the light chain variable region coding sequence of SEQ ID NO: 312 and the light chain constant region coding sequence of SEQ ID NO: 320.

[0966] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the variable light chain polypeptide sequence of SEQ ID NO: 302:

(SEQ ID NO: 312)

gcccaagtgctgacccagactccatcgtccgtgtctgcagctgtgggagg

cacagtcaccatcaattgccagtccagtcagagtgtttataagaataagt

acttatcctggtatcagcagaaagtagggcagcctcccaagttcctgatc

taccaggcatccaatttggcatctggggtcccatcgcggttcaaaggcag

tggatctgggacacagttcactctcaccatcagcgacctggagtgtgacg

atgccgccacttattactgtgcaggcggttatagtggtaatatggttgat

ttcggcggagggaccgaggtggtggtcaaacgt.

[0967] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the constant light chain polypeptide sequence of SEQ ID NO: 310:

(SEQ ID NO: 320)

acggtagcggccccatctgtcttcatcttcccgccatctgatgagcagtt

gaaatctggaactgcctctgttgtgtgcctgctgaataacttctatccca

gagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaac

tcccaggagagtgtcacagagcaggacagcaaggacagcacctacagcct

cagcagcaccctgacgctgagcaaagcagactacgagaaacacaaagtct

acgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagc

ttcaacaggggagagtgt.

[0968] In a further embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one or more of the polynucleotide sequences of SEQ ID NO: 294; SEQ ID NO: 296; and SEQ ID NO: 298, which correspond to polynucleotides encoding the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 281, or the variable heavy chain sequence of SEQ ID NO: 282, and/or one or more of the polynucleotide sequences of SEQ ID NO: 314; SEQ ID NO: 316; and SEQ ID NO: 318, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 301, or the variable light chain sequence of SEQ ID NO: 302, or combinations of these polynucleotide sequences. In another embodiment of the invention, the polynucleotides encoding the antibodies of the invention or antigen-binding fragments thereof comprise, or alternatively consist of, combinations of polynucleotides encoding one or more of the CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them.

[0969] In a further embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one or more of the polynucleotide sequences of SEQ ID NO: 293; SEQ ID NO: 295; SEQ ID NO: 297; and SEQ ID NO: 299, which correspond to polynucleotides encoding the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 281, or the variable heavy chain sequence of SEQ ID NO: 282, and/or one or more of the polynucleotide sequences of SEQ ID NO: 313; SEQ ID NO: 315; SEQ ID NO: 317; and SEQ ID NO: 319, which

correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 301, or the variable light chain sequence of SEQ ID NO: 302, or combinations of these polynucleotide sequences. In another embodiment of the invention, the polynucleotides encoding the antibodies of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them.

[0970] The invention also contemplates polynucleotide sequences including one or more of the polynucleotide sequences encoding antigen-binding fragments described herein. In one embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three or more, including all of the following polynucleotides encoding antigen-binding fragments: the polynucleotide SEQ ID NO: 291 encoding the heavy chain sequence of SEQ ID NO: 281; the polynucleotide SEQ ID NO: 292 encoding the variable heavy chain sequence of SEQ ID NO: 282; the polynucleotide SEQ ID NO: 311 encoding the light chain sequence of SEQ ID NO: 301; the polynucleotide SEQ ID NO: 312 encoding the variable light chain sequence of SEQ ID NO: 302; polynucleotides encoding the CDRs (SEQ ID NO: 294; SEQ ID NO: 296; and SEQ ID NO: 298) of the heavy chain sequence of SEQ ID NO: 281, or the variable heavy chain sequence of SEQ ID NO: 282; polynucleotides encoding the CDRs (SEQ ID NO: 314; SEQ ID NO: 316; and SEQ ID NO: 318) of the light chain sequence of SEQ ID NO: 301, or the variable light chain sequence of SEQ ID NO: 302; polynucleotides encoding the FRs (SEQ ID NO: 293; SEQ ID NO: 295; SEQ ID NO: 297; and SEQ ID NO: 299) of the heavy chain sequence of SEQ ID NO: 281, or the variable heavy chain sequence of SEQ ID NO: 282; and polynucleotides encoding the FRs (SEQ ID NO: 313; SEQ ID NO: 315; SEQ ID NO: 317; and SEQ ID NO: 319) of the light chain sequence of SEQ ID NO: 301, or the variable light chain sequence of SEQ ID NO: 302.

[0971] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, polynucleotides encoding Fab fragments having binding specificity for PACAP. With respect to antibody Ab17, the polynucleotides encoding the full length Ab17 antibody comprise, or alternatively consist of, the polynucleotide SEQ ID NO: 291 encoding the heavy chain sequence of SEQ ID NO: 281, and the polynucleotide SEQ ID NO: 311 encoding the light chain sequence of SEQ ID NO: 301.

[0972] Another embodiment of the invention contemplates these polynucleotides incorporated into an expression vector for expression in mammalian cells such as CHO, NSO, or HEK-293 cells, or in fungal, insect, or microbial systems such as yeast cells such as the yeast *Pichia*. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*. In one embodiment of the invention described herein, Fab fragments can be produced by enzymatic digestion (e.g., papain) of Ab17 following expression of the full-length polynucleotides in a suitable host. In another embodiment of the invention, anti-PACAP antibodies, such as Ab17 or Fab fragments thereof, can be produced via expression of Ab17 polynucleotides in mammalian cells such as CHO, NSO, or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example diploid yeast such as diploid *Pichia*) and other yeast strains. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*.

Antibody Ab18

[0973] In one embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to PACAP. In one embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the polynucleotide sequence of SEQ ID NO: 331 which encodes the heavy chain sequence of SEQ ID NO: 321 and which consists of the heavy chain variable region coding sequence of SEQ ID NO: 332 and the heavy chain constant region coding sequence of SEQ ID NO: 340.

[0974] In another embodiment of the invention, the polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the variable heavy chain polypeptide sequence of SEQ ID NO: 322:

(SEQ ID NO: 332)

```
cagtcggtggaggagtccgggggtcgcctggtcacgcctgggacacccct

gacactcacctgcaccgtctctggattctccctcagtagcgctgcattga

gctgggtccgccaggctccagggaaggggctggaatggatcggaattatt

gataagggtgttatgtcttactacgcgtcctgggcgaaaggccgattcac

catctccaaaacctcgtcgaccacggtggatctaaaagtgaccagtccga

caaccgaggacacggccacctatttctgtgccagagggggggggaatttt

ttcatctggggccagggcaccctcgtcaccgtctcgagc.
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[0975] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the constant heavy chain polypeptide sequence of SEQ ID NO: 330:

(SEQ ID NO: 340)

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gcctccaccaagggcccatcggtcttcccccctggcaccctcctccaagag

cacctctgggggcacagcggccctgggctgcctggtcaaggactacttcc

ccgaaccggtgacggtgtcgtggaactcaggcgccctgaccagcggcgtg

cacaccttcccggctgtcctacagtcctcaggactctactccctcagcag

cgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgca

acgtgaatcacaagcccagcaacaccaaggtggacaagaaagttgagccc

aaatcttgtgacaaaactcacacatgcccaccgtgcccagcacctgaact

cctgggggggaccgtcagtcttcctcttcccccaaaacccaaggacaccc

tcatgatctcccggacccctgaggtcacatgcgtggtggtggacgtgagc

cacgaagaccctgaggtcaagttcaactggtacgtggacggcgtggaggt

gcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtacc

gtgtggtcagcgtcctcaccgtcctgcaccaggactggctgaatggcaag

gagtacaagtgcaaggtctccaacaaagccctcccagcccccatcgagaa

aaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccc
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tgcccccatcccgggaggagatgaccaagaaccaggtcagcctgacctgc

ctggtcaaaggcttctatcccagcgacatcgccgtggagtgggagagcaa

tgggcagccggagaacaactacaagaccacgcctcccgtgctggactccg

acggctccttcttcctctacagcaagctcaccgtggacaagagcaggtgg

cagcaggggaacgtcttctcatgctccgtgatgcatgaggctctgcacaa

ccactacacgcagaagagcctctccctgtctccgggtaaa.

[0976] In another embodiment of the invention, polynucleotides comprise, or alternatively consist of, the polynucleotide sequence of SEQ ID NO: 351 which encodes the light chain polypeptide sequence of SEQ ID NO: 341 and which consists of the light chain variable region coding sequence of SEQ ID NO: 352 and the light chain constant region coding sequence of SEQ ID NO: 360.

[0977] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the variable light chain polypeptide sequence of SEQ ID NO: 342:

(SEQ ID NO: 352)

gcgcaagtgctgacccagactccatcgtccgtgtctgcagctgtgggagg

cacagtcaccatcaattgccagtccagtaagagtgtttataacaacaatt

ggttatcctggtatcaacagaaaccagggcagcctcccaagttcctgatc

taccaggcatccaatttggcatctggggtcccgtcgcggttcaaaggcag

tggatctgggacacagttcactctcaccatcagcgacctcgagtgtgacg

atgccgccacttattactgtgcaggcggttatagtggtaatattgttggt

ttcggcggagggaccgaggtggtggtcaaacgt.

[0978] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the constant light chain polypeptide sequence of SEQ ID NO: 350:

(SEQ ID NO: 360)

acggtagcggccccatctgtcttcatcttcccgccatctgatgagcagtt

gaaatctggaactgcctctgttgtgtgcctgctgaataacttctatccca

gagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaac

tcccaggagagtgtcacagagcaggacagcaaggacagcacctacagcct

cagcagcaccctgacgctgagcaaagcagactacgagaaacacaaagtct

acgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagc

ttcaacaggggagagtgt.

[0979] In a further embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one or more of the polynucleotide sequences of SEQ ID NO: 334; SEQ ID NO: 336; and SEQ ID NO: 338, which correspond to polynucleotides encoding the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 321, or the variable heavy chain sequence of SEQ ID NO: 322, and/or one or more of the polynucleotide sequences of SEQ ID NO: 354; SEQ ID NO: 356; and SEQ ID NO: 358, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 341, or the variable light chain sequence of SEQ ID NO: 342, or combinations of these polynucleotide sequences. In another embodiment of the invention, the polynucleotides encoding the antibodies of the invention or antigen-binding fragments thereof comprise, or alternatively consist of, combinations of polynucleotides encoding one or more of the CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them.

[0980] In a further embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one or more of the polynucleotide sequences of SEQ ID NO: 333; SEQ ID NO: 335; SEQ ID NO: 337; and SEQ ID NO: 339, which correspond to polynucleotides encoding the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 321, or the variable heavy chain sequence of SEQ ID NO: 322, and/or one or more of the polynucleotide sequences of SEQ ID NO: 353; SEQ ID NO: 355; SEQ ID NO: 357; and SEQ ID NO: 359, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 341, or the variable light chain sequence of SEQ ID NO: 342, or combinations of these polynucleotide sequences. In another embodiment of the invention, the polynucleotides encoding the antibodies of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them.

[0981] The invention also contemplates polynucleotide sequences including one or more of the polynucleotide sequences encoding antigen-binding fragments described herein. In one embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three or more, including all of the following polynucleotides encoding antigen-binding fragments: the polynucleotide SEQ ID NO: 331 encoding the heavy chain sequence of SEQ ID NO: 321; the polynucleotide SEQ ID NO: 332 encoding the variable heavy chain sequence of SEQ ID NO: 322; the polynucleotide SEQ ID NO: 351 encoding the light chain sequence of SEQ ID NO: 341; the polynucleotide SEQ ID NO: 352 encoding the variable light chain sequence of SEQ ID NO: 342; polynucleotides encoding the CDRs (SEQ ID NO: 334; SEQ ID NO: 336; and SEQ ID NO: 338) of the heavy chain sequence of SEQ ID NO: 321, or the variable heavy chain sequence of SEQ ID NO: 322; polynucleotides encoding the CDRs (SEQ ID NO: 354; SEQ ID NO: 356; and SEQ ID NO: 358) of the light chain sequence of SEQ ID NO: 341, or the variable light chain sequence of SEQ ID NO: 342; polynucleotides encoding the FRs (SEQ ID NO: 333; SEQ ID NO: 335; SEQ ID NO: 337; and SEQ ID NO: 339) of the heavy chain sequence of SEQ ID NO: 321, or the variable heavy chain sequence of SEQ ID NO: 322; and polynucleotides encoding the FRs (SEQ ID NO: 353; SEQ ID NO: 355; SEQ ID NO: 357; and SEQ ID NO: 359) of the light chain sequence of SEQ ID NO: 341, or the variable light chain sequence of SEQ ID NO: 342.

[0982] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively con-

sist of, polynucleotides encoding Fab fragments having binding specificity for PACAP. With respect to antibody Ab18, the polynucleotides encoding the full length Ab18 antibody comprise, or alternatively consist of, the polynucleotide SEQ ID NO: 331 encoding the heavy chain sequence of SEQ ID NO: 321, and the polynucleotide SEQ ID NO: 351 encoding the light chain sequence of SEQ ID NO: 341.

[0983] Another embodiment of the invention contemplates these polynucleotides incorporated into an expression vector for expression in mammalian cells such as CHO, NSO, or HEK-293 cells, or in fungal, insect, or microbial systems such as yeast cells such as the yeast *Pichia*. *Suitable Pichia* species include, but are not limited to, *Pichia pastoris*. In one embodiment of the invention described herein, Fab fragments can be produced by enzymatic digestion (e.g., papain) of Ab18 following expression of the full-length polynucleotides in a suitable host. In another embodiment of the invention, anti-PACAP antibodies, such as Ab18 or Fab fragments thereof, can be produced via expression of Ab18 polynucleotides in mammalian cells such as CHO, NSO, or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example diploid yeast such as diploid *Pichia*) and other yeast strains. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*.

Antibody Ab19

[0984] In one embodiment, the invention is further directed to polynucleotides encoding antibody polypeptides having binding specificity to PACAP. In one embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the polynucleotide sequence of SEQ ID NO: 371 which encodes the heavy chain sequence of SEQ ID NO: 361 and which consists of the heavy chain variable region coding sequence of SEQ ID NO: 372 and the heavy chain constant region coding sequence of SEQ ID NO: 380.

[0985] In another embodiment of the invention, the polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the variable heavy chain polypeptide sequence of SEQ ID NO: 362:

(SEQ ID NO: 372)

```
cagtcggtggaggcgtccgggggtcgcctggtcacgcctgggacacccct

gacactcacctgcaccgtctctggattctccctcagtagcgctacaatga

actgggtccgccaggctccagggaaggggctggaatggatcgggcttatt

ggcggtaatgacgaaagatactacgcgtcctgggcgaaaggccgattcac

catctccaaaacctcgtcgaccacggtggatctgaaaatgaccagtccga

caaccgaggacacggccacctatttctgtgccagagggggggggaatttt

ttcatctggggcccgggcaccctggtcaccgtctcgagc.
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[0986] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the constant heavy chain polypeptide sequence of SEQ ID NO: 370:

(SEQ ID NO: 380)

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gcctccaccaagggcccatcggtcttcccctggcaccctcctccaagag

cacctctgggggcacagcggccctgggctgcctggtcaaggactacttcc

ccgaaccggtgacggtgtcgtggaactcaggcgccctgaccagcggcgtg

cacaccttcccggctgtcctacagtcctcaggactctactccctcagcag

cgtggtgaccgtgccctccagcagcttgggcacccagacctacatctgca

acgtgaatcacaagcccagcaacaccaaggtggacaagaaagttgagccc

aaatcttgtgacaaaactcacacatgcccaccgtgcccagcacctgaact

cctgggggggaccgtcagtcttcctcttcccccaaaacccaaggacaccc

tcatgatctcccggaccctgaggtcacatgcgtggtggtggacgtgagc

cacgaagaccctgaggtcaagttcaactggtacgtggacggcgtggaggt

gcataatgccaagacaaagccgcgggaggagcagtacgccagcacgtacc

gtgtggtcagcgtcctcaccgtcctgcaccaggactggctgaatggcaag

gagtacaagtgcaaggtctccaacaaagccctcccagccccatcgagaa

aaccatctccaaagccaaagggcagccccgagaaccacaggtgtacaccc

tgccccatcccgggaggagatgaccaagaaccaggtcagcctgacctgc

ctggtcaaaggcttctatcccagcgacatcgccgtggagtgggagagcaa

tgggcagccggagaacaactacaagaccacgcctcccgtgctggactccg

acggctccttcttcctctacagcaagctcaccgtggacaagagcaggtgg

cagcaggggaacgtcttctcatgctccgtgatgcatgaggctctgcacaa

ccactacacgcagaagagcctctccctgtctccgggtaaa.
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[0987] In another embodiment of the invention, polynucleotides comprise, or alternatively consist of, the polynucleotide sequence of SEQ ID NO: 391 which encodes the light chain polypeptide sequence of SEQ ID NO: 381 and which consists of the light chain variable region coding sequence of SEQ ID NO: 392 and the light chain constant region coding sequence of SEQ ID NO: 400.

[0988] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the variable light chain polypeptide sequence of SEQ ID NO: 382:

(SEQ ID NO: 392)

```
gcgcaagtgctgacccagactccatcgtccgtgtctgcagctgtgggagg

cacagtcaccatcaattgccagtccagtgagagtgtttatactaacgacc

gcttatcctggtatcagcagaaaccagggcagcctcccaagctcctgatc

tacgaagcatccaagctggcatctggggtcccaccgcggttcagcggcag

tggatctgggacacagttcactctcaccatcagcgacctggagtgtgacg

atgccgccacttattactgtgcaggcgcttatagtactagtatccatggt

ttcggcggagggaccgaggtggtggtcaaacgt.
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[0989] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, the following polynucleotide sequence encoding the constant light chain polypeptide sequence of SEQ ID NO: 390:

(SEQ ID NO: 400)
acggtagcggccccatctgtcttcatcttcccgccatctgatgagcagtt

gaaatctggaactgcctctgttgtgtgcctgctgaataacttctatccca

gagaggccaaagtacagtggaaggtggataacgccctccaatcgggtaac

tcccaggagagtgtcacagagcaggacagcaaggacagcacctacagcct

cagcagcaccctgacgctgagcaaagcagactacgagaaacacaaagtct

acgcctgcgaagtcacccatcagggcctgagctcgcccgtcacaaagagc

ttcaacaggggagagtgt.

[0990] In a further embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one or more of the polynucleotide sequences of SEQ ID NO: 374; SEQ ID NO: 376; and SEQ ID NO: 378, which correspond to polynucleotides encoding the CDRs (hypervariable regions) of the heavy chain sequence of SEQ ID NO: 361, or the variable heavy chain sequence of SEQ ID NO: 362, and/or one or more of the polynucleotide sequences of SEQ ID NO: 394; SEQ ID NO: 396; and SEQ ID NO: 398, which correspond to the CDRs (hypervariable regions) of the light chain sequence of SEQ ID NO: 381, or the variable light chain sequence of SEQ ID NO: 382, or combinations of these polynucleotide sequences. In another embodiment of the invention, the polynucleotides encoding the antibodies of the invention or antigen-binding fragments thereof comprise, or alternatively consist of, combinations of polynucleotides encoding one or more of the CDRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them.

[0991] In a further embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one or more of the polynucleotide sequences of SEQ ID NO: 373; SEQ ID NO: 375; SEQ ID NO: 377; and SEQ ID NO: 379, which correspond to polynucleotides encoding the FRs (constant regions) of the heavy chain sequence of SEQ ID NO: 361, or the variable heavy chain sequence of SEQ ID NO: 362, and/or one or more of the polynucleotide sequences of SEQ ID NO: 393; SEQ ID NO: 395; SEQ ID NO: 397; and SEQ ID NO: 399, which correspond to the FRs (constant regions) of the light chain sequence of SEQ ID NO: 381, or the variable light chain sequence of SEQ ID NO: 382, or combinations of these polynucleotide sequences. In another embodiment of the invention, the polynucleotides encoding the antibodies of the invention or fragments thereof comprise, or alternatively consist of, combinations of one or more of the FRs, the variable heavy chain and variable light chain sequences, and the heavy chain and light chain sequences set forth above, including all of them.

[0992] The invention also contemplates polynucleotide sequences including one or more of the polynucleotide sequences encoding antigen-binding fragments described herein. In one embodiment of the invention, polynucleotides encoding antigen-binding fragments having binding specificity to PACAP comprise, or alternatively consist of, one, two, three or more, including all of the following polynucleotides encoding antigen-binding fragments: the polynucleotide SEQ ID NO: 371 encoding the heavy chain sequence of SEQ ID NO: 361; the polynucleotide SEQ ID NO: 372 encoding the variable heavy chain sequence of SEQ ID NO: 362; the polynucleotide SEQ ID NO: 391 encoding the light chain sequence of SEQ ID NO: 381; the polynucleotide SEQ ID NO: 392 encoding the variable light chain sequence of SEQ ID NO: 382; polynucleotides encoding the CDRs (SEQ ID NO: 374; SEQ ID NO: 376; and SEQ ID NO: 378) of the heavy chain sequence of SEQ ID NO: 361, or the variable heavy chain sequence of SEQ ID NO: 362; polynucleotides encoding the CDRs (SEQ ID NO: 394; SEQ ID NO: 396; and SEQ ID NO: 398) of the light chain sequence of SEQ ID NO: 381, or the variable light chain sequence of SEQ ID NO: 382; polynucleotides encoding the FRs (SEQ ID NO: 373; SEQ ID NO: 375; SEQ ID NO: 377; and SEQ ID NO: 379) of the heavy chain sequence of SEQ ID NO: 361, or the variable heavy chain sequence of SEQ ID NO: 362; and polynucleotides encoding the FRs (SEQ ID NO: 393; SEQ ID NO: 395; SEQ ID NO: 397; and SEQ ID NO: 399) of the light chain sequence of SEQ ID NO: 381, or the variable light chain sequence of SEQ ID NO: 382.

[0993] In another embodiment of the invention, polynucleotides of the invention comprise, or alternatively consist of, polynucleotides encoding Fab fragments having binding specificity for PACAP. With respect to antibody Ab19, the polynucleotides encoding the full length Ab19 antibody comprise, or alternatively consist of, the polynucleotide SEQ ID NO: 371 encoding the heavy chain sequence of SEQ ID NO: 361, and the polynucleotide SEQ ID NO: 391 encoding the light chain sequence of SEQ ID NO: 381.

[0994] Another embodiment of the invention contemplates these polynucleotides incorporated into an expression vector for expression in mammalian cells such as CHO, NSO, or HEK-293 cells, or in fungal, insect, or microbial systems such as yeast cells such as the yeast *Pichia*. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*. In one embodiment of the invention described herein, Fab fragments can be produced by enzymatic digestion (e.g., papain) of Ab19 following expression of the full-length polynucleotides in a suitable host. In another embodiment of the invention, anti-PACAP antibodies, such as Ab19 or Fab fragments thereof, can be produced via expression of Ab19 polynucleotides in mammalian cells such as CHO, NSO, or HEK 293 cells, fungal, insect, or microbial systems such as yeast cells (for example diploid yeast such as diploid *Pichia*) and other yeast strains. Suitable *Pichia* species include, but are not limited to, *Pichia pastoris*.

[0995] Host cells and vectors comprising said polynucleotides are also contemplated.

[0996] The invention further contemplates vectors comprising the polynucleotide sequences encoding the variable heavy and light chain polypeptide sequences, as well as the individual CDRs (hypervariable regions), as set forth herein, as well as host cells comprising said vector sequences. In embodiments of the invention, the host cells are mammalian cells, such as CHO cells. In embodiments of the invention, the host cells are yeast cells, such as yeast cells of the genus *Pichia*.

B-Cell Screening and Isolation

[0997] In one embodiment, the present invention contemplates the preparation and isolation of a clonal population of antigen-specific B-cells that may be used for isolating at least one PACAP antigen-specific cell, which can be used to produce a monoclonal antibody against PACAP, which is

specific to a desired PACAP antigen, or a nucleic acid sequence corresponding to such an antibody. Methods of preparing and isolating said clonal population of antigen-specific B-cells are taught, for example, in U.S. Patent Publication No. US2007/0269868 to Carvalho-Jensen et al., the disclosure of which is herein incorporated by reference in its entirety. Methods of preparing and isolating said clonal population of antigen-specific B-cells are also taught herein in the examples. Methods of "enriching" a cell population by size or density are known in the art. See, e.g., U.S. Pat. No. 5,627,052. These steps can be used in addition to enriching the cell population by antigen-specificity.

Methods of Humanizing Antibodies

[0998] In another embodiment, the present invention contemplates methods for humanizing antibody heavy and light chains. Methods for humanizing antibody heavy and light chains that may be applied to anti-PACAP antibodies are taught, for example, in U.S. Patent Publication No. US2009/0022659 to Olson et al., and in U.S. Pat. No. 7,935,340 to Garcia-Martinez et al., the disclosures of each of which are herein incorporated by reference in their entireties.

Methods of Producing Antibodies and Fragments Thereof

[0999] In another embodiment, the present invention contemplates methods for producing anti-PACAP antibodies and fragments thereof. Methods for producing anti-PACAP antibodies and fragments thereof secreted from polyploidal, preferably diploid or tetraploid strains of mating competent yeast are taught, for example, in U.S. Patent Publication No. US2009/0022659 to Olson et al., and in U.S. Pat. No. 7,935,340 to Garcia-Martinez et al., the disclosures of each of which are herein incorporated by reference in their entireties.

[1000] Other methods of producing antibodies are well known to those of ordinary skill in the art. For example, methods of producing chimeric antibodies are now well known in the art (See, for example, U.S. Pat. No. 4,816,567 to Cabilly et al.; Morrison et al., *Proc. Natl. Acad. Sci. U.S.A.,* 81:8651-55 (1984); Neuberger et al., *Nature,* 314: 268-270 (1985); Boulianne, G. L. et al., *Nature,* 312:643-46 (1984), the disclosures of each of which are herein incorporated by reference in their entireties).

[1001] Likewise, other methods of producing humanized antibodies are now well known in the art (See, for example, U.S. Pat. Nos. 5,530,101, 5,585,089, 5,693,762, and 6,180, 370 to Queen et al; U.S. Pat. Nos. 5,225,539 and 6,548,640 to Winter; U.S. Pat. Nos. 6,054,297, 6,407,213 and 6,639, 055 to Carter et al; U.S. Pat. No. 6,632,927 to Adair; Jones, P. T. et al., *Nature,* 321:522-525 (1986); Reichmann, L. et al., *Nature,* 332:323-327 (1988); Verhoeyen, M. et al., *Science,* 239:1534-36 (1988), the disclosures of each of which are herein incorporated by reference in their entireties).

[1002] Antibody polypeptides of the invention having PACAP binding specificity may also be produced by constructing, using conventional techniques well known to those of ordinary skill in the art, an expression vector containing a promoter (optionally as a component of a eukaryotic or prokaryotic operon) and a DNA sequence encoding an antibody heavy chain in which the DNA sequence encoding the CDRs required for antibody specificity is derived from a non-human cell source, preferably a rabbit B-cell source, while the DNA sequence encoding the remaining parts of the antibody chain is derived from a human cell source.

[1003] A second expression vector is produced using the same conventional means well known to those of ordinary skill in the art, said expression vector containing a promoter (optionally as a component of a eukaryotic or prokaryotic operon) and a DNA sequence encoding an antibody light chain in which the DNA sequence encoding the CDRs required for antibody specificity is derived from a non-human cell source, preferably a rabbit B-cell source, while the DNA sequence encoding the remaining parts of the antibody chain is derived from a human cell source.

[1004] The expression vectors are transfected into a host cell by convention techniques well known to those of ordinary skill in the art to produce a transfected host cell, said transfected host cell cultured by conventional techniques well known to those of ordinary skill in the art to produce said antibody polypeptides.

[1005] The host cell may be co-transfected with the two expression vectors described above, the first expression vector containing DNA encoding a promoter (optionally as a component of a eukaryotic or prokaryotic operon) and a light chain-derived polypeptide and the second vector containing DNA encoding a promoter (optionally as a component of a eukaryotic or prokaryotic operon) and a heavy chain-derived polypeptide. The two vectors contain different selectable markers, but preferably achieve substantially equal expression of the heavy and light chain polypeptides. Alternatively, a single vector may be used, the vector including DNA encoding both the heavy and light chain polypeptides. The coding sequences for the heavy and light chains may comprise cDNA, genomic DNA, or both.

[1006] The host cells used to express the antibody polypeptides may be either a bacterial cell such as *E. coli*, or a eukaryotic cell such as *P. pastoris*. In one embodiment of the invention, a mammalian cell of a well-defined type for this purpose, such as a myeloma cell, a CHO cell line, a NSO cell line, or a HEK293 cell line may be used.

[1007] The general methods by which the vectors may be constructed, transfection methods required to produce the host cell and culturing methods required to produce the antibody polypeptides from said host cells all include conventional techniques. Although preferably the cell line used to produce the antibody is a mammalian cell line, any other suitable cell line, such as a bacterial cell line such as an *E. coli*-derived bacterial strain, or a yeast cell line, may alternatively be used.

[1008] Similarly, once produced the antibody polypeptides may be purified according to standard procedures in the art, such as for example cross-flow filtration, ammonium sulphate precipitation, affinity column chromatography, hydrophobic interaction chromatography ("HIC"), and the like.

[1009] The antibody polypeptides described herein may also be used for the design and synthesis of either peptide or non-peptide mimetics that would be useful for the same therapeutic applications as the antibody polypeptides of the invention (See, for example, Saragobi et al., *Science,* 253: 792-795 (1991), the contents of which are herein incorporated by reference in its entirety).

Screening Assays

[1010] The screening assays described here are designed to identify high affinity anti-PACAP Abs which may be useful in the treatment of diseases and disorders associated with PACAP in subjects exhibiting symptoms of a PACAP associated disease or disorder.

[1011] In some embodiments, the antibody is used as a diagnostic tool. The antibody can be used to assay the amount of PACAP present in a sample and/or subject. As will be appreciated by one of skill in the art, such antibodies need not be neutralizing antibodies. In some embodiments, the diagnostic antibody is not a neutralizing antibody. In some embodiments, the diagnostic antibody binds to a different epitope than the neutralizing antibody binds to. In some embodiments, the two antibodies do not compete with one another.

[1012] In some embodiments, the antibodies disclosed herein are used or provided in an assay kit and/or method for the detection of PACAP in mammalian tissues or cells in order to screen/diagnose for a disease or disorder associated with changes in levels of PACAP. The kit comprises an antibody that binds PACAP and means for indicating the binding of the antibody with PACAP, if present, and optionally PACAP protein levels. Various means for indicating the presence of an antibody can be used. For example, fluorophores, other molecular probes, or enzymes can be linked to the antibody and the presence of the antibody can be observed in a variety of ways. The method for screening for such disorders can involve the use of the kit, or simply the use of one of the disclosed antibodies and the determination of whether the antibody binds to PACAP in a sample. As will be appreciated by one of skill in the art, high or elevated levels of PACAP will result in larger amounts of the antibody binding to PACAP in the sample. Thus, degree of antibody binding can be used to determine how much PACAP is in a sample. Subjects or samples with an amount of PACAP that is greater than a predetermined amount (e.g., an amount or range that a person without a PACAP-related disorder would have) can be characterized as having a PACAP-mediated disorder, e.g., migraine, headache, pain, or other condition.

[1013] The present invention further provides for a kit for detecting binding of an anti-PACAP antibody of the invention to PACAP. In particular, the kit may be used to detect the presence of PACAP specifically reactive with an anti-PACAP antibody of the invention or an immunoreactive fragment thereof. The kit may also include an antibody bound to a substrate, a secondary antibody reactive with the antigen and a reagent for detecting a reaction of the secondary antibody with the antigen. Such a kit may be an ELISA kit and can comprise the substrate, primary and secondary antibodies when appropriate, and any other necessary reagents such as detectable moieties, enzyme substrates, and color reagents, for example as described herein. The diagnostic kit may also be in the form of an immunoblot kit. The diagnostic kit may also be in the form of a chemiluminescent kit (Meso Scale Discovery, Gaithersburg, Md.). The diagnostic kit may also be a lanthanide-based detection kit (PerkinElmer, San Jose, Calif.).

[1014] A skilled clinician would understand that a biological sample includes, but is not limited to, sera, plasma, urine, saliva, mucous, pleural fluid, synovial fluid, and spinal fluid.

Methods of Ameliorating or Reducing Symptoms of or Treating, or Preventing, Diseases and Disorders Associated with PACAP

[1015] In another embodiment of the invention, anti-PACAP antibodies described herein, or antigen binding fragments thereof, are useful for ameliorating or reducing the symptoms of, or treating, or preventing, diseases and disorders associated with PACAP. Anti-PACAP antibodies described herein, or antigen binding fragments thereof, as well as combinations, can also be administered in a therapeutically effective amount to patients in need of treatment of diseases and disorders associated with PACAP in the form of a pharmaceutical composition as described in greater detail below.

[1016] In another embodiment of the invention, anti-PACAP antibodies described herein, or antigen binding fragments thereof, are useful (either alone or in combination with another agent) for ameliorating or reducing the symptoms of, or treating, or preventing a disease or condition associated with PACAP.

[1017] In another embodiment of the invention, anti-PACAP antibodies described herein, or antigen binding fragments thereof, with or without a second agent, are useful for ameliorating or reducing the symptoms of, or treating, or preventing, the following non-limiting listing of diseases and disorders: migraine (with or without aura), hemiplegic migraines, cluster headaches, migrainous neuralgia, chronic headaches, tension headaches, general headaches, hot flush, photophobia, chronic paroxysmal hemicrania, secondary headaches due to an underlying structural problem in the head or neck, cranial neuralgia, sinus headaches (e.g., headache associated with sinusitis), allergy-induced headaches or migraines, pain, chronic pain, neuroinflammatory or inflammatory pain, post-operative incision pain, post-surgical pain, trauma-related pain, eye pain, tooth pain, complex regional pain syndrome, cancer pain (e.g., primary or metastatic bone cancer pain), fracture pain, osteoporotic fracture pain, pain resulting from burn, gout joint pain, pain associated with sickle cell crises, pain associated with temporomandibular disorders, cirrhosis, hepatitis, neurogenic pain, neuropathic pain, nociceptic pain, visceral pain, trigeminal neuralgia, post-herpetic neuralgia, phantom limb pain, fibromyalgia, menstrual pain, ovarialgia, reflex sympathetic dystrophy, osteoarthritis or rheumatoid arthritis pain, lower back pain, diabetic neuropathy, sciatica, dyspepsia, irritable bowel syndrome, inflammatory bowel disease, Crohn's disease, ileitis, ulcerative colitis, renal colic, dysmenorrhea, cystitis, interstitial cystitis, menstrual period, labor, menopause, pancreatitis, schizophrenia, depression, post-traumatic stress disorder, anxiety disorders, diabetes, autoimmune diabetes, endothelial dysfunction, ischemia, Raynaud's syndrome, coronary heart disease ("CHD"), coronary artery disease ("CAD"), heart failure, peripheral arterial disease ("PAD"), pulmonary hypertension ("PH"), connective tissue disorders, stroke, Sjögren's syndrome, multiple sclerosis, bronchial hyperreactivity, asthma, bronchitis, bronchodilation, emphysema, chronic obstructive pulmonary disease ("COPD"), inflammatory dermatitis, adenocarcinoma in glandular tissue, blastoma in embryonic tissue of organs, carcinoma in epithelial tissue, leukemia in tissues that form blood cells, lymphoma in lymphatic tissue, myeloma in bone marrow, sarcoma in connective or supportive tissue, adrenal cancer, AIDS-related lymphoma, anemia, bladder cancer, bone cancer, brain cancer, breast cancer, carcinoid tumors,

cervical cancer, chemotherapy, colon cancer, cytopenia, endometrial cancer, esophageal cancer, gastric cancer, head cancer, neck cancer, hepatobiliary cancer, kidney cancer, leukemia, liver cancer, lung cancer, lymphoma, Hodgkin's disease, non-Hodgkin's, nervous system tumors, oral cancer, ovarian cancer, pancreatic cancer, prostate cancer, rectal cancer, skin cancer, stomach cancer, testicular cancer, thyroid cancer, urethral cancer, cancer of bone marrow, multiple myeloma, tumors that metastasize to the bone, tumors infiltrating the nerve and hollow viscus, tumors near neural structures. Further preferably the cancer pain comprises visceral pain, preferably visceral pain which arises from pancreatic cancer and/or metastases in the abdomen. Further preferably the cancer pain comprises somatic pain, preferably somatic pain due to one or more of metastasis in the bone, postsurgical pain, sarcomas cancer of the connective tissue, cancer of bone tissue, cancer of blood-forming cells of the bone marrow, multiple myeloma, leukemia, primary or secondary bone cancer, acne vulgaris, atopic dermatitis, urticaria, keloids, hypertrophic scars and rosacea, allergic dermatitis, psoriasis, pruritus, neurogenic cutaneous redness, erythema, weight loss, anorexia, sarcoidosis, shock, sepsis, opiate withdrawal syndrome, morphine tolerance, epilepsy, lower urinary tract ("LUT") disorders such as urinary tract infection, abnormal voiding, urinary urgency, nocturia, urinary incontinence, overactive bladder and for preventing or alleviating the pain associated with such LUT conditions. Preferably, the subject anti-PACAP antibodies and antigen binding fragments described herein are useful for ameliorating or reducing the symptoms of, treating, or preventing migraine, headache and a pain associated disease or condition.

[1018] In particular, the subject anti-PACAP antibodies and antigen binding fragments can also be useful for ameliorating or reducing the symptoms of, treating, or preventing photophobia, occurring with a headache and/or migraine as well as occurring independent of a headache and/or a migraine.

[1019] Migraineurs typically develop worsening pain and migraine symptoms when exposed to light, a phenomenon known as photophobia. Photophobia is also common in ocular disorders, such as iritis and uveitis, and intracranial disorders, such as meningitis. In the classic visual pathway, light activates rods and cones in the retina, which activate retinal ganglion cells that project via the optic nerve, to the lateral geniculate nucleus, superior colliculus, and then the visual cortex. This pathway includes image-forming and non-image-forming data. A new pathway (non-image-forming information) allows maintenance of normal circadian rhythms via the suprachiasmatic nucleus and is regulated by intrinsically photosensitive retinal ganglion cells (ipRGCs). These ipRGCs are independent of the rods and cones and contain melanopsin, a photopigment.

[1020] Noseda, R. et al., *Nat. Neurosci.,* 13:239-245 (2010) studied blind individuals who had migraine and correlated these findings with rat models involving tracing of ipRGC projections to areas in perception of pain from the dura. Of the blind patients with migraine, 6 had no light perception due to severe optic nerve damage or bilateral enucleation. These subjects experienced abnormal sleep patterns and poor pupillary light responses. Their migraines did not worsen with light exposure. In contrast, 14 blind subjects who were able to detect light despite minimal perception of images had normal sleep patterns and a normal pupillary light reflex. Despite widespread rod and cone degeneration, these patients had worsening migraine symptoms with light exposure during migraine attacks, suggesting that ipRGCs, and not rods and cones, are important in photophobia.

[1021] These retinal projections of non-image-forming brain areas project to the contralateral dorsocaudal region of the posterior thalamus, as demonstrated by anterograde tracing in the rat. ipRGC input to this area modulates dura-sensitive pain neurons, which also project to this region. Thalamic neurons, dually sensitive to dural pain and light input, project widely to multiple cortical regions, including the primary somatosensory cortex, the primary and secondary motor cortices, the parietal association cortex, and the primary and secondary visual cortices. These cortical projections may help explain other common migraine symptoms, in addition to photophobia, such as motor weakness or incoordination, visual disturbances, and poor concentration.

[1022] Photophobia also accompanies other less frequent but likewise disabling conditions, such as cluster headache and other trigeminal autonomic cephalalgias and blepharospasm. The mechanisms underlying photophobia involve the trigeminal system. Photophobia in blind patients suggests contributions from a nonvisual pathway. In addition, trigeminal autonomic cephalalgias, a less common group of primary headache disorders, are characterized by unilateral trigeminal-mediated pain frequently associated with ipsilateral photophobia.

[1023] Common causes of photophobia include migraine headaches, cataracts, or severe ophthalmologic diseases such as uveitis or corneal abrasion. A more extensive list of disorders associated with photophobia includes eye related causes such as achromatopsia, aniridia, anticholinergic drugs may cause photophobia by paralyzing the iris sphincter muscle, aphakia (absence of the lens of the eye), buphthalmos (abnormally narrow angle between the cornea and iris), cataracts, cone dystrophy, congenital abnormalities of the eye, viral conjunctivitis ("pink eye"), corneal abrasion, corneal dystrophy, corneal ulcer, disruption of the corneal epithelium, such as that caused by a corneal foreign body or keratitis, ectopia lentis, endophthalmitis, eye trauma caused by disease, injury, or infection such as chalazion, episcleritis, glaucoma, keratoconus, or optic nerve hypoplasia, hydrophthalmos, or congenital glaucoma iritis, optic neuritis, pigment dispersion syndrome, pupillary dilation (naturally or chemically induced), retinal detachment, scarring of the cornea or sclera and uveitis.

[1024] In addition, photophobia has nervous-system-related or neurological causes including: autism spectrum disorders, Chiari malformation, dyslexia, encephalitis including myalgic encephalomyelitis aka chronic fatigue syndrome, meningitis, subarachnoid hemorrhage, tumor of the posterior cranial fossa, as well as other causes such as ankylosing spondylitis, albinism, ariboflavinosis, benzodiazepines (long term use of or withdrawal from benzodiazepines), chemotherapy, chikungunya, cystinosis, Ehlers-Danlos syndrome, hangover, influenza, infectious mononucleosis, magnesium deficiency, mercury poisoning, migraine, rabies, and tyrosinemia type II, also known as "Richner-Hanhart syndrome".

[1025] Additionally, it is known that photophobia is elevated in depression, bipolar disorder and agoraphobia.

[1026] The subject anti-PACAP antibodies and antigen binding fragments described herein can be effective for treating or preventing photophobia in any of these conditions, preferably, in a subject with post-traumatic stress disorder ("PTSD") or in a subject with traumatic brain injury.

[1027] Headaches may be classified by cause, as discussed below.

[1028] Primary Headaches.

[1029] A primary headache is caused by problems with or overactivity of pain-sensitive structures in the head. A primary headache is generally not considered to be a symptom of an underlying disease. Instead, chemical activity in the brain, the nerves or blood vessels of the head outside the skull, or muscles of the head and neck, or some combination of these factors, may play a role in primary headaches. Some people may carry genes that make them more likely to develop such headaches. Exemplary common primary headaches include, but are not limited to, cluster headache; tension headache (or tension-type headache); and trigeminal autonomic cephalalgia ("TAC"), including paroxysmal hemicrania. There are other headache patterns that may be considered types of primary headache, e.g., chronic daily headaches, cough headaches, exercise headaches, and sex headaches. These headaches are less common and have distinct features, such as an unusual duration or pain associated with a certain activity. Although these headaches are generally considered primary, each of them could be a symptom of an underlying disease. Additionally, some primary headaches can be triggered by lifestyle factors, including: alcohol; certain foods (e.g., processed meats that contain nitrates); changes in sleep or lack of sleep; poor posture; skipped meals; and stress.

[1030] Secondary Headaches.

[1031] A secondary headache is a symptom of a disease that can activate the pain-sensitive nerves of the head. Any number of conditions, which can vary greatly in severity, may cause secondary headaches. Exemplary sources of secondary headaches include, but are not limited to, acute sinusitis; arterial tears (carotid or vertebral dissections); venous thrombosis in the brain; brain aneurysm; brain arteriovenous malformation; carbon monoxide poisoning; Chiari malformation; concussion; dehydration; dental problems; ear infection (middle ear); encephalitis; giant cell arteritis; glaucoma; hangovers; influenza (flu); intracranial hematoma; medications to treat other disorders; meningitis; monosodium glutamate ("MSG"); overuse of pain medication; panic attacks; post-concussion syndrome; pressure from tight-fitting headgear, e.g., helmet or goggles; pseudotumor cerebri; toxoplasmosis; and trigeminal neuralgia. Specific types of secondary headaches include, but are not limited to, external compression headaches (a result of pressure-causing headgear); ice cream headaches (commonly called "brain freeze"); rebound headaches (caused by overuse of pain medication); sinus headaches (caused by inflammation and congestion in sinus cavities); spinal headaches (caused by low levels of cerebrospinal fluid, possibly the result of trauma, spinal tap or spinal anesthesia); and thunderclap headaches (a group of disorders that involves sudden, severe headaches).

[1032] Exemplary, non-limiting pain associated diseases and disorders that can be treated and/or prevented by the administration of the anti-PACAP antibodies of the present invention include, pain resulting from any condition associated with neurogenic, neuropathic, inflammatory, or nociceptic pain. Preferably, the pain-associated disorder will be associated with increased PACAP at the pain site.

[1033] In certain embodiments, the pain associated disorder to be treated is cancer pain arising from malignancy or from cancer selected from one or more of: adenocarcinoma in glandular tissue, blastoma in embryonic tissue of organs, carcinoma in epithelial tissue, leukemia in tissues that form blood cells, lymphoma in lymphatic tissue, myeloma in bone marrow, sarcoma in connective or supportive tissue, adrenal cancer, AIDS-related lymphoma, anemia, bladder cancer, bone cancer, brain cancer, breast cancer, carcinoid tumors, cervical cancer, chemotherapy, colon cancer, cytopenia, endometrial cancer, esophageal cancer, gastric cancer, head cancer, neck cancer, hepatobiliary cancer, kidney cancer, leukemia, liver cancer, lung cancer, lymphoma, Hodgkin's disease, non-Hodgkin's, nervous system tumors, oral cancer, ovarian cancer, pancreatic cancer, prostate cancer, rectal cancer, skin cancer, stomach cancer, testicular cancer, thyroid cancer, urethral cancer, cancer of bone marrow, multiple myeloma, tumors that metastasize to the bone, tumors infiltrating the nerve and hollow viscus, tumors near neural structures. Further preferably the cancer pain comprises visceral pain, preferably visceral pain which arises from pancreatic cancer and/or metastases in the abdomen. Further preferably the cancer pain comprises somatic pain, preferably somatic pain due to one or more of metastasis in the bone, postsurgical pain, sarcomas cancer of the connective tissue, cancer of bone tissue, cancer of blood-forming cells of the bone marrow, multiple myeloma, leukemia, primary or secondary bone cancer.

[1034] In other embodiments, the pain associated condition to be treated is associated with neuropathic pain and included, by way of example, trigeminal neuralgia, post-herpetic neuralgia, phantom limb pain, fibromyalgia, and reflex sympathetic dystrophy are preferably treated.

[1035] Further exemplary pain associated diseases or conditions, include but are not limited to, general pain, chronic pain, inflammatory pain, post-operative incision pain, post-surgical pain, trauma-related pain, lower back pain, eye pain, tooth pain, complex regional pain syndrome, cancer pain (e.g., primary or metastatic bone cancer pain), fracture pain, osteoporotic fracture pain, pain resulting from burn, gout joint pain, pain associated with sickle cell crises, pain associated with temporomandibular disorders, cirrhosis, hepatitis, neurogenic pain, neuropathic pain, nociceptic pain, visceral pain, trigeminal neuralgia, post-herpetic neuralgia, phantom limb pain, fibromyalgia, menstrual pain, ovarialgia, reflex sympathetic dystrophy, osteoarthritis or rheumatoid arthritis pain, lower back pain, diabetic neuropathy, sciatica, dyspepsia, irritable bowel syndrome, inflammatory bowel disease, Crohn's disease, ileitis, ulcerative colitis, renal colic, dysmenorrhea, cystitis, interstitial cystitis, menstrual period, labor, menopause, pancreatitis, schizophrenia, depression, post-traumatic stress disorder, anxiety disorders, diabetes, autoimmune diabetes, endothelial dysfunction, ischemia, Raynaud's syndrome, coronary heart disease ("CHD"), coronary artery disease ("CAD"), heart failure, peripheral arterial disease ("PAD"), pulmonary hypertension ("PH"), connective tissue disorders, stroke, Sjögren's syndrome, multiple sclerosis, overactive bladder, bronchial hyperreactivity, asthma, bronchitis, bronchodilation, emphysema, chronic obstructive pulmonary disease ("COPD"), inflammatory dermatitis, acne vulgaris, atopic

dermatitis, urticaria, keloids, hypertrophic scars and rosacea, allergic dermatitis, psoriasis, puritus, neurogenic cutaneous redness, erythema, sarcoidosis, shock, sepsis, and opiate withdrawal syndrome.

[1036] Thus, the present invention includes methods of treating, preventing, and/or ameliorating any disease or disorder associated with PACAP activity or PACAP upregulation (including any of the above mentioned exemplary pain associated diseases, disorders and conditions) through use of the antibodies and antigen binding fragments of the invention.

[1037] Also, the subject PACAP antibodies and antigen binding fragments may be used alone or in conjunction with other active agents, e.g., opioids and non-opioid analgesics such as NSAIDs to elicit analgesia or to potentiate the efficacy of another analgesic.

[1038] The subject antibodies potentially may be combined with any opioid analgesic or NSAID or other analgesic, potentially another antibody or another biologic such as, e.g., an anti-NGF or anti-CGRP or anti-CGRP-R antibody or antibody fragment or NGF, CGRP or CGRP-R polypeptide fragment or conjugate, in order to increase or enhance pain management. This may allow for such analgesic compounds to be administered for longer duration or at reduced dosages thereby potentially alleviating adverse side effects associated therewith.

[1039] Of particular interest is the co-administration of the subject anti-PACAP antibodies and antibody fragments with an anti-CGRP antibody (e.g., ALD403) or anti-CGRP-R antibody or antibody fragment and, moreover, the use of the subject anti-PACAP antibodies and antibody fragments to treat subjects that previously received an anti-CGRP or anti-CGRP-R antibody or antibody fragment. For example, the previously treated subject (who previously received at least one anti-CGRP or anti-CGRP-R antibody or antibody fragment administration) may be a migraineur who did not adequately respond to anti-CGRP or anti-CGRP-R antibody treatment ("poor responder") and/or has elicited an immune response to the anti-CGRP or anti-CGRP-R antibody or antibody fragment.

[1040] Likewise, the co-administration of the subject anti-PACAP antibodies and antigen binding fragments with BOTOX® (Botulinum toxin) is also of particular interest, e.g., in treating a migraineur. In some instances, the migraineur may not have adequately responded to previous treatments ("poor responder") and/or has elicited an immune response to the previous treatment.

[1041] In some embodiments, aspirin and/or acetaminophen may be taken in conjunction with the subject anti-PACAP antibody or antigen binding fragment. Aspirin is another type of non-steroidal anti-inflammatory compound.

[1042] The subject to which the pharmaceutical formulation is administered can be, e.g., any human or non-human animal that is in need of such treatment, prevention and/or amelioration, or who would otherwise benefit from the inhibition or attenuation of PACAP-mediated activity. For example, the subject can be an individual that is diagnosed with, or who is deemed to be at risk of being afflicted by any of the aforementioned diseases or disorders. The present invention further includes the use of any of the pharmaceutical formulations disclosed herein in the manufacture of a medicament for the treatment, prevention and/or amelioration of any disease or disorder associated with PACAP activity (including any of the above mentioned exemplary diseases, disorders and conditions).

Administration

[1043] In one embodiment of the invention, the anti-PACAP antibodies described herein, or PACAP binding fragments thereof, as well as combinations of said antibodies or antigen binding fragments thereof, are administered to a subject at a concentration of between 0.1 mg/ml and about any one of 0.5, 1, 5, 10, 15 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, or 200 mg/ml, +/−10% error.

[1044] In another embodiment of the invention, the anti-PACAP antibodies and fragments thereof described herein are administered to a subject at a dose of between about 0.01 and 100.0 or 200.0 mg/kg of body weight of the recipient subject. In certain embodiments, depending on the type and severity of the PACAP-related disease, about 1 μg/kg to 50 mg/kg (e.g., 0.1-20 mg/kg) of antibody is an initial candidate dosage for administration to the patient, whether, for example, by one or more separate administrations, or by continuous infusion. In another embodiment, about 1 μg/kg to 15 mg/kg (e.g., 0.1 mg/kg-10 mg/kg) of antibody is an initial candidate dosage for administration to the patient. A typical daily dosage might range from about 1 μg/kg to 100 mg/kg or more, depending on several factors, e.g., the particular mammal being treated, the clinical condition of the individual patient, the cause of the disorder, the site of delivery of the agent, the method of administration, the scheduling of administration, and other factors known to medical practitioners. However, other dosage regimens may be useful.

[1045] For example, in addition to the relative dosages (mg/kg) discussed herein, the subject anti-PACAP antibodies and antigen binding fragments thereof can be administered to a subject at an absolute dose (mg). Accordingly, in one embodiment of the invention, the anti-PACAP antibodies and antigen binding fragments thereof described herein are administered to a subject at a dose of between about 1 microgram and about 1000 milligrams regardless of the route of administration.

[1046] In a preferred embodiment of the invention, the anti-PACAP antibodies described herein, or anti-PACAP antigen binding fragments thereof, as well as combinations of said antibodies or antigen binding fragments thereof, are administered to a recipient subject with a frequency of once every twenty-six weeks or less, such as once every sixteen weeks or less, once every eight weeks or less, once every four weeks or less, once every two weeks or less, once every week or less, or once daily or less.

[1047] According to preferred embodiments, the antibody containing medicament or pharmaceutical composition is peripherally administered to a subject via a route selected from one or more of: orally, sublingually, buccally, topically, rectally, via inhalation, transdermally, subcutaneously, intravenously, intra-arterially, or intramuscularly, via intracardiac administration, intraosseously, intradermally, intraperitoneally, transmucosally, vaginally, intravitreally, epicutaneously, intra-articularly, peri-articularly, or locally.

[1048] Fab fragments may be administered every two weeks or less, every week or less, once daily or less, multiple times per day, and/or every few hours. In one embodiment of the invention, a patient receives Fab fragments of 0.1

mg/kg to 40 mg/kg per day given in divided doses of 1 to 6 times a day, or in a continuous perfusion form, effective to obtain desired results.

[1049] It is to be understood that the concentration of the antibody or Fab administered to a given patient may be greater or lower than the exemplary administration concentrations set forth above.

[1050] A person of skill in the art would be able to determine an effective dosage and frequency of administration through routine experimentation, for example guided by the disclosure herein and the teachings in, *Goodman & Gilman's The Pharmacological Basis of Therapeutics*, Brunton, L. L. et al. editors, 11th edition, New York, New York: McGraw-Hill (2006); Howland, R. D. et al., *Pharmacology, Volume* 864, *Lippincott's illustrated reviews*., Philadelphia, Pa.: Lippincott Williams & Wilkins (2006); and Golan, D. E., *Principles of pharmacology: the pathophysiologic basis of drug therapy*, Philadelphia, Pa.: Lippincott Williams & Wilkins (2007).

[1051] In another embodiment of the invention, the anti-PACAP antibodies described herein, or PACAP binding fragments thereof, as well as combinations of said antibodies or antigen binding fragments thereof, are administered to a subject in a pharmaceutical formulation. In a preferred embodiment, the subject is a human.

[1052] A "pharmaceutical composition" or "medicament" refers to a chemical or biological composition suitable for administration to a subject, preferably a mammal, more preferably a human. Such compositions may be specifically formulated for administration via one or more of a number of routes, including but not limited to buccal, epicutaneous, epidural, inhalation, intraarterial, intracardial, intracerebroventricular, intradermal, intramuscular, intranasal, intraocular, intraperitoneal, intraspinal, intrathecal, intravenous, oral, parenteral, rectally via an enema or suppository, subcutaneous, subdermal, sublingual, transdermal, and transmucosal. In addition, administration can occur by means of injection, powder, liquid, gel, drops, or other means of administration.

[1053] In one embodiment of the invention, the anti-PACAP antibodies described herein, or PACAP binding fragments thereof, as well as combinations of said antibodies or antigen binding fragments thereof, may be optionally administered in combination with one or more active agents. Such active agents include analgesic, anti-histamine, antipyretic, anti-inflammatory, antibiotic, antiviral, and anti-cytokine agents. Active agents include agonists, antagonists, and modulators of TNF-α, IL-2, IL-4, IL-6, IL-10, IL-12, IL-13, IL-18, IFN-α, IFN-γ, BAFF, CXCL13, IP-10, VEGF, EPO, EGF, HRG, Hepatocyte Growth Factor ("HGF"), Hepcidin, NGF, CGRP including antibodies reactive against any of the foregoing, and antibodies reactive against any of their receptors. Active agents also include but are not limited to 2-arylpropionic acids, aceclofenac, acemetacin, acetylsalicylic acid (aspirin), alclofenac, alminoprofen, amoxiprin, ampyrone, arylalkanoic acids, azapropazone, benorylate/benorilate, benoxaprofen, bromfenac, carprofen, celecoxib, choline magnesium salicylate, clofezone, COX-2 inhibitors, dexibuprofen, dexketoprofen, diclofenac, diflunisal, droxicam, ethenzamide, etodolac, etoricoxib, faislamine, fenamic acids, fenbufen, fenoprofen, flufenamic acid, flunoxaprofen, flurbiprofen, ibuprofen, ibuproxam, indomethacin, indoprofen, kebuzone, ketoprofen, ketorolac, lornoxicam, loxoprofen, lumiracoxib, magnesium salicylate, meclofenamic acid, mefenamic acid, meloxicam, metamizole, methyl salicylate, mofebutazone, nabumetone, naproxen, N-arylanthranilic acids, NGF, oxametacin, oxaprozin, oxicams, oxyphenbutazone, oxytocin, parecoxib, phenazone, phenylbutazone, phenylbutazone, piroxicam, pirprofen, profens, proglumetacin, pyrazolidine derivatives, rofecoxib, salicyl salicylate, salicylamide, salicylates, substance P, sulfinpyrazone, sulindac, suprofen, tenoxicam, tiaprofenic acid, tolfenamic acid, tolmetin, and valdecoxib. For instance, the selected anti-PACAP antibodies, or PACAP-binding fragments thereof, as well as combinations of these antibodies or antigen binding fragments, can be optionally administered in combination with oxytocin, for instance administered in a nasal formulation, for intranasal delivery.

[1054] An anti-histamine can be any compound that opposes the action of histamine or its release from cells (e.g., mast cells). Anti-histamines include but are not limited to acrivastine, astemizole, azatadine, azelastine, betatastine, brompheniramine, buclizine, cetirizine, cetirizine analogues, chlorpheniramine, clemastine, CS 560, cyproheptadine, desloratadine, dexchlorpheniramine, ebastine, epinastine, fexofenadine, HSR 609, hydroxyzine, levocabastine, loratadine, methscopolamine, mizolastine, norastemizole, phenindamine, promethazine, pyrilamine, terfenadine, and tranilast.

[1055] Antibiotics include but are not limited to amikacin, aminoglycosides, amoxicillin, ampicillin, ansamycins, arsphenamine, azithromycin, azlocillin, aztreonam, bacitracin, carbacephem, carbapenems, carbenicillin, cefaclor, cefadroxil, cefalexin, cefalothin, cefalotin, cefamandole, cefazolin, cefdinir, cefditoren, cefepime, cefixime, cefoperazone, cefotaxime, cefoxitin, cefpodoxime, cefprozil, ceftazidime, ceftibuten, ceftizoxime, ceftobiprole, ceftriaxone, cefuroxime, cephalosporins, chloramphenicol, cilastatin, ciprofloxacin, clarithromycin, clindamycin, cloxacillin, colistin, co-trimoxazole, dalfopristin, demeclocycline, dicloxacillin, dirithromycin, doripenem, doxycycline, enoxacin, ertapenem, erythromycin, ethambutol, flucloxacillin, fosfomycin, furazolidone, fusidic acid, gatifloxacin, geldanamycin, gentamicin, glycopeptides, herbimycin, imipenem, isoniazid, kanamycin, levofloxacin, lincomycin, linezolid, lomefloxacin, loracarbef, macrolides, mafenide, meropenem, methicillin, metronidazole, mezlocillin, minocycline, monobactams, moxifloxacin, mupirocin, nafcillin, neomycin, netilmicin, nitrofurantoin, norfloxacin, ofloxacin, oxacillin, oxytetracycline, paromomycin, penicillin, penicillins, piperacillin, platensimycin, polymyxin B, polypeptides, prontosil, pyrazinamide, quinolones, quinupristin, rifampicin, rifampin, roxithromycin, spectinomycin, streptomycin, sulfacetamide, sulfamethizole, sulfanilamide, sulfasalazine, sulfisoxazole, sulfonamides, teicoplanin, telithromycin, tetracycline, tetracyclines, ticarcillin, tinidazole, tobramycin, trimethoprim, trimethoprim-sulfamethoxazole, troleandomycin, trovafloxacin, and vancomycin.

[1056] Active agents also include aldosterone, beclomethasone, betamethasone, corticosteroids, cortisol, cortisone acetate, deoxycorticosterone acetate, dexamethasone, fludrocortisone acetate, glucocorticoids, hydrocortisone, methylprednisolone, prednisolone, prednisone, steroids, and triamcinolone. Any suitable combination of these active agents is also contemplated.

[1057] A "pharmaceutical excipient" or a "pharmaceutically acceptable excipient" is a carrier, usually a liquid, in which an active therapeutic agent is formulated. In one

embodiment of the invention, the active therapeutic agent is a humanized antibody described herein, or one or more fragments thereof. The excipient generally does not provide any pharmacological activity to the formulation, though it may provide chemical and/or biological stability, and release characteristics. Exemplary formulations can be found, for example, in *Remington's Pharmaceutical Sciences*, Gennaro, A. editor, 19th edition, Philadelphia, Pa.: Williams and Wilkins (1995), which is incorporated by reference.

[1058] As used herein "pharmaceutically acceptable carrier" or "excipient" includes any and all solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic, and absorption delaying agents that are physiologically compatible. In one embodiment, the carrier is suitable for parenteral administration. Alternatively, the carrier can be suitable for intravenous, intraperitoneal, intramuscular, or sublingual administration. Pharmaceutically acceptable carriers include sterile aqueous solutions or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersions. The use of such media and agents for pharmaceutically active substances is well known in the art. Except insofar as any conventional media or agent is incompatible with the active compound, use thereof in the pharmaceutical compositions of the invention is contemplated. Supplementary active compounds can also be incorporated into the compositions.

[1059] Pharmaceutical compositions typically must be sterile and stable under the conditions of manufacture and storage. The invention contemplates that the pharmaceutical composition is present in lyophilized form. The composition can be formulated as a solution, microemulsion, liposome, or other ordered structure suitable to high drug concentration. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (for example, glycerol, propylene glycol, and liquid polyethylene glycol), and suitable mixtures thereof. The invention further contemplates the inclusion of a stabilizer in the pharmaceutical composition. The proper fluidity can be maintained, for example, by the maintenance of the required particle size in the case of dispersion and by the use of surfactants.

[1060] In many cases, it will be preferable to include isotonic agents, for example, sugars, polyalcohols such as mannitol and sorbitol, or sodium chloride in the composition. Absorption of the injectable compositions can be prolonged by including an agent that delays absorption, for example, monostearate salts and gelatin. Moreover, the alkaline polypeptide can be formulated in a time-release formulation, for example in a composition that includes a slow release polymer. The active compounds can be prepared with carriers that will protect the compound against rapid release, such as a controlled release formulation, including implants and microencapsulated delivery systems. Biodegradable, biocompatible polymers can be used, such as ethylene vinyl acetate, polyanhydrides, polyglycolic acid, collagen, polyorthoesters, polylactic acid, polylactic and polyglycolic copolymers ("PLG"). Many methods for the preparation of such formulations are known to those skilled in the art.

[1061] For each of the recited embodiments, the compounds can be administered by a variety of dosage forms. Any biologically acceptable dosage form known to persons of ordinary skill in the art, and combinations thereof, are contemplated. Examples of such dosage forms include, without limitation, reconstitutable powders, elixirs, liquids, solutions, suspensions, emulsions, powders, granules, particles, microparticles, dispersible granules, cachets, inhalants, aerosol inhalants, patches, particle inhalants, implants, depot implants, injectables (including subcutaneous, intramuscular, intravenous, and intradermal), infusions, and combinations thereof.

[1062] The above description of various illustrated embodiments of the invention is not intended to be exhaustive or to limit the invention to the precise form disclosed. While specific embodiments of, and examples for, the invention are described herein for illustrative purposes, various equivalent modifications are possible within the scope of the invention, as those skilled in the relevant art will recognize. The teachings provided herein of the invention can be applied to other purposes, other than the examples described above.

[1063] These and other changes can be made to the invention in light of the above detailed description. In general, in the following claims, the terms used should not be construed to limit the invention to the specific embodiments disclosed in the specification and the claims. Accordingly, the invention is not limited by the disclosure, but instead the scope of the invention is to be determined entirely by the following claims.

[1064] The invention may be practiced in ways other than those particularly described in the foregoing description and examples. Numerous modifications and variations of the invention are possible in light of the above teachings and, therefore, are within the scope of the appended claims.

[1065] Certain teachings related to methods for obtaining a clonal population of antigen-specific B-cells were disclosed in U.S. Patent Publication No. US2013/0316353, the disclosure of which is herein incorporated by reference in its entirety.

[1066] Certain teachings related to humanization of rabbit-derived monoclonal antibodies and preferred sequence modifications to maintain antigen-binding affinity were disclosed in International Publication No. WO 2008/144757, entitled *Novel Rabbit Antibody Humanization Methods and Humanized Rabbit Antibodies*, filed May 21, 2008, the disclosure of which is herein incorporated by reference in its entirety.

[1067] Certain teachings related to producing antibodies or fragments thereof using mating competent yeast and corresponding methods were disclosed in U.S. Patent Publication No. US2006/0270045, the disclosure of which is herein incorporated by reference in its entirety.

[1068] Certain teachings related to producing antibodies or fragments thereof in *Pichia* and preferred methods for obtaining and purifying antibodies are also disclosed in U.S. Patent Publication Nos. 2014/0288272; 2014/0287952; 2013/0055888; and 2012/0277408, the disclosures of each of which are herein incorporated by reference in their entirety.

[1069] Certain teachings related to producing antibodies or fragments thereof in CHO cells and exemplary methods for obtaining and purifying antibodies are also disclosed in U.S. patent and Publication Nos. 7,932,087; 2009/0285795; 9,090,672; and 2010/0221781; the disclosures of each of which are herein incorporated by reference in their entirety.

[1070] Certain anti-PACAP antibody polynucleotides and polypeptides are disclosed in the sequence listing accompa-

nying this patent application filing, and the disclosure of said sequence listing is herein incorporated by reference in its entirety.

[1071] The entire disclosure of each document cited (including patents, patent applications, journal articles, abstracts, manuals, books, or other disclosures) in the Background of the Invention, Detailed Description, and Examples is herein incorporated by reference in their entireties.

[1072] The following examples are put forth so as to provide those of ordinary skill in the art with a complete disclosure and description of how to make and use the subject invention, and are not intended to limit the scope of what is regarded as the invention. Efforts have been made to ensure accuracy with respect to the numbers used (e.g. amounts, temperature, concentrations, etc.), but some experimental errors and deviations should be allowed for. Unless otherwise indicated, parts are parts by weight, molecular weight is average molecular weight, temperature is in degrees centigrade; and pressure is at or near atmospheric.

EXAMPLES

Example 1

Preparation of Antibodies that Selectively Bind PACAP

[1073] By using an antibody selection protocol substantially as described herein, a panel of antibodies specific to PACAP38 and PACAP27, and a panel of antibodies specific to PACAP38 only, were produced.

Immunization Strategy

[1074] Rabbits were immunized with PACAP38 (American Peptide, Vista, Calif.) (SEQ ID NO: 1241). Peptides were prepared for immunization as follows. A 0.15 ml volume of 10 mg/ml keyhole limpet hemocyanin ("KLH") dissolved in Dulbecco's phosphate buffered saline ("DPBS") supplemented to 1M NaCl was combined with 1.0 ml of 1 mg/ml peptide (dissolved in deionized water). Then 1.0 ml of 40 mM carbodiimide was added prior to a 12-hour incubation at room temperature with gentle mixing. Excess carbodiimide and unconjugated peptide were removed by dialysis to DPBS prior to sterile filtration. Next unconjugated peptide equal to the initial mass of KLH was added prior to preparation for injection into rabbits. Alternatively, equal masses of sterile KLH and peptide were mixed without carbodiimide chemistry.

[1075] Immunizations were performed by diluting 200 μg of antigen to 0.5 ml with DPBS and mixing with an equal volume of complete Freund's adjuvant for subcutaneous 1 ml injection at Day 1.

[1076] Boost injections of 100 μg were performed with incomplete Freund's adjuvant at Days 21 and 42.

Antibody Selection Functional Titer Assessment

[1077] To identify antibodies that neutralize PACAP38 (SEQ ID NO: 1241) induced signaling via PAC1-R, polyclonal antibody solutions were first purified via Protein A and dialyzed into a neutral buffer. Briefly, antibody solutions were incubated with PACAP38 (SEQ ID NO: 1241) at 4× the final concentration (100 pM) for 1 hr. While the antibody/antigen complexes were incubated, PAC1-R expressing PC-12 cells (Japanese Collection of Research Bioresources Cell Bank) were washed and re-suspended at 2×10^6 cells per ml in cell culture media. Cells (10 μl) and antigen/antibody complex (40 μl) were transferred to a homogenous time resolved fluorescence ("HTRF") plate and shaken at room temperature for 30 min. Following the incubation, 20 μl of (1:20 diluted) Eu^{3+} cryptate-labeled mAb anti-cAMP and 20 μl of (1:20 diluted) d2-labeled cAMP in lysis buffer were added, and the plate was incubated for 1 hr while shaking. Following incubation, plates were read (excitation 330 nm, emission 620/665 nm), and a ratio of 620:665 signal was determined.

Tissue Harvesting

[1078] Once acceptable titers were established, the rabbit (s) were sacrificed. Spleen, lymph nodes, and whole blood were harvested and processed as follows:

[1079] Spleen and lymph nodes were processed into a single cell suspension by disassociating the tissue and pushing through sterile wire mesh at 70 μm (Thermo Fisher Scientific, Waltham, Mass.) with a plunger of a 20 cc syringe. Cells were collected in phosphate buffered saline ("PBS"). Cells were then washed twice by centrifugation. After the last wash, cell density was determined by trypan blue. Cells were centrifuged at 1500 RPM for 10 minutes; the supernatant was then discarded. Cells were resuspended in the appropriate volume of 10% dimethyl sulfoxide ("DMSO", Sigma-Aldrich Co., St. Louis, Mo.) in fetal bovine serum ("FBS" HYCLONE™, GE Healthcare Life Sciences, Marlborough, Mass.) and dispensed at 1 ml/vial. Vials were stored at −70° C. in a slow freezing chamber for 24 hours and stored in liquid nitrogen.

[1080] Peripheral blood mononuclear cells ("PBMCs") were isolated by mixing whole blood with equal parts of PBS. 35 ml of the whole blood mixture was carefully layered onto 8 ml of LYMPHOLYTE® Rabbit (Cedarlane Laboratories, Burlington, Ontario) into a 45 ml conical tube (Corning, Corning, N.Y.) and centrifuged for 30 minutes at 2500 RPM at room temperature without brakes. After centrifugation, the PBMC layers were carefully removed using a glass Pasteur pipette (VWR International, Radnor, Pa.), combined, and placed into a clean 50 ml vial. Cells were washed twice with PBS by centrifugation at 1500 RPM for 10 minutes at room temperature, and cell density was determined by trypan blue staining. After the last wash, cells were resuspended in an appropriate volume of 10% DMSO/FBS medium and frozen as described above.

B-Cell Selection, Enrichment, and Culture Conditions

[1081] On the day of setting up B-cell culture, PBMC, splenocyte, or lymph node vials were thawed for use. Vials were removed from liquid nitrogen tank and placed in a 37° C. water bath until thawed. Contents of vials were transferred into 15 ml conical centrifuge tube (Corning, Inc., Corning, N.Y.) and 10 ml of modified RPMI was slowly added to the tube. Cells were centrifuged for 5 minutes at 2000 RPM, and the supernatant was discarded. Cells were resuspended in 10 ml of fresh media. Cell density and viability was determined by trypan blue.

[1082] For positive selection of anti-PACAP38 producing B-cells, biotinylated PACAP38 (SEQ ID NO: 1241) was pre-loaded onto the streptavidin beads as follows. 75 μl of

streptavidin beads (Miltenyi Biotec, Auburn, Calif.) were mixed with N-terminally biotinylated PACAP38 (10 μg/ml final concentration) and 300 μl of PBS supplemented with 0.5% biotin free bovine serum albumin ("BSA") and 2 mM EDTA ("PBF"). This mixture was incubated at 4° C. for 30 minutes, and unbound biotinylated PACAP38 (AnaSpec, Fremont, Calif.) was removed using a MACS® separation column (Miltenyi Biotec, Auburn, Calif.) with a 1 ml rinse to remove unbound material. The bound material was plunged out by detachment from the magnet and used to resuspend cells from above in 100 μl per 1×10^7 cells. The mixture was then incubated at 4° C. for 30 minutes and washed once with 10 ml of PBF. After washing, the cells were resuspended in 500 μl of PBF and set aside. A MACS® MS column (Miltenyi Biotec, Auburn, Calif.) was pre-rinsed with 500 μl of PBF on a magnetic stand (Miltenyi Biotec, Auburn, Calif.). Cell suspension was applied to the column through a pre-filter, and unbound fraction was collected. The column was washed with 2.5 ml of PBF buffer. The column was removed from the magnet stand and placed onto a clean, sterile 1.5 ml EPPENDORF™ tube. 1 ml of PBF buffer was added to the top of the column, and positive selected cells were collected. The yield and viability of positive cell fraction was determined by trypan blue staining. Positive selection yielded an average of 1% of the starting cell concentration.

[1083] A pilot cell screen was established to provide information on seeding levels for the culture. Plates were seeded at 5, 10, 25, 50, 100, or 200 enriched B-cells/well. In addition, each well contained 25-50K cells/well of irradiated EL-4.B5 cells (5,000 Rads) and an appropriate level of activated rabbit T-cell supernatant (See U.S. Patent Application Publication No. 20070269868) (ranging from 1-5% depending on preparation) in high glucose modified RPMI medium at a final volume of 250 μl/well. Cultures were incubated for 5 to 7 days at 37° C. in 4% CO_2.

B-Cell Culture Screening by Antigen-Recognition (ELISA)

[1084] To identify wells producing anti-PACAP38 antibodies, B-cell supernatants were tested by antigen-recognition (ELISA). Briefly, NEUTRAVIDIN™-coated plates (Thermo Fisher Scientific, Waltham, Mass.), were coated with either N-term or C-term biotinylated PACAP38 (AnaSpec Inc., Fremont, Calif.) (50 μl per well; 1 μg/ml) diluted in ELISA buffer (0.5% fish skin gelatin in PBS pH 7.4) either for approximately 1 hour at room temperature or alternatively overnight at 4° C. The plates were then further blocked with ELISA buffer for one hour at room temperature and washed using PBS with 0.05% Tween 20 ("wash buffer"). B-cell supernatant samples (50 μl) were transferred onto the wells and incubated for one hour at room temperature. After this incubation, the plate was washed with wash buffer. For development, an anti-rabbit specific Fc-Horse Radish Peroxidase ("Fc-HRP") (1:5000 dilution in ELISA buffer) was added onto the wells and incubated for 45 minutes at room temperature. After a 3× wash step with wash solution, the plate was developed using 3,3',5,5'-Tetramethylbenzidine ("TMB") substrate for two minutes at room temperature, and the reaction was quenched using 0.5M HCl. The well absorbance was read at 450 nm.

[1085] To identify wells producing anti-PACAP38 antibodies that do not recognize VIP (SEQ ID NO: 1243), supernatant from wells positive for PACAP38 binding by ELISA were tested by ELISA for binding to VIP. Briefly, biotinylated VIP (AnaSpec Inc., Fremont, Calif.) was bound onto NEUTRAVIDIN™ coated plates (50 μg per well, 1 μg/μl each peptide). B-cell supernatant samples (50 μl) were tested without prior dilution. Recognition in this assay may indicate cross reactivity with a closely related peptide, VIP.

Identification of Functional Activity in B-Cell Supernatants Using One or More Assays

[1086] To identify wells producing anti-PACAP38 antibodies that block signaling of PACAP38 via PAC1-R, supernatant from positive wells for PACAP38 binding by ELISA were tested in a cAMP HTRF assay (Cisbio US, Bedford, Mass.). Supernatants (78 μl) were pre-incubated with 2 μl 5 nM PACAP38 (American Peptide Company, Sunnyvale, Calif.) for 1 hour at 37° C. During the incubation, PC-12 cells were prepared as described for titer assessment. Cells (10 μl) and antigen/antibody complex (40 μl) were transferred to an HTRF plate and shaken at room temperature for 30 minutes. Following the incubation, 20 μl of (1:20 diluted) Eu^{3+} cryptate-labeled mAb anti-cAMP and 20 μl of (1:20 diluted) d2-labeled cAMP in lysis buffer were added, and the plate was incubated for 1 hour while shaking. Following incubation plates were read (excitation 330 nm, emission 620/665 nm), and a ratio of 620:665 signal was determined.

Isolation of Antigen-Specific B-Cells

[1087] Antigen-specific B-cells were isolated (for general methods see co-owned publication no. WO 2014/146074, which is hereby incorporated by reference in its entirety). Plates containing wells of interest were removed from −70° C., and the cells from each well were recovered using five washes of 200 μl of medium (10% RPMI complete, 55 μM β-mercaptoethanol ("BME")) per well. The recovered cells were pelleted by centrifugation and the supernatant was carefully removed. Cells from each well were then re-suspended in 100 μl of medium and transferred to a 96 well plate. Cells were incubated for 90 minutes at 37° C. Following incubation, cells were pelleted by centrifugation, stained with a fluorescein isothiocyanate-labeled ("FITC-labeled") anti-rabbit IgG (final concentration 6.25 μg/ml) (Creative Diagnostics, Shirley, N.Y.), and washed with up to 2 ml fluorescence-activated cell sorting buffer ("FACS buffer") (Dulbecco's PBS w/2% FBS) and re-suspended in 250 μl of FACS buffer.

[1088] Control wells from the same culture sets that were similar in composition to pooled wells of interest were thawed and stained alongside target wells. These samples were initially run on FACS (BD INFLUX™, Becton, Dickinson and Company, Franklin Lakes, N.J.), and gates were established for IgG, viability, and physical parameters (Forward scatter ("FSC")/side scatter ("SSC")) that differentiate B-cells from the murine EL4 cells. Once gates were established, the sample of interest was run, and IgG positive, viable cells that were of a consistent physical (FSC/SSC) population were sorted individually into wells of a 96 well plate pre-loaded with RT-PCR master mix. Upwards of 8 cells per well were sorted. Sorted plates were removed from the sorter and transferred directly to thermocyclers for PCR.

Amplification and Sequence Determination of Antibody Sequences from FACS-Sorted B-Cells

[1089] Antibody sequences were recovered using a combined RT-PCR based method from a single cell sorted B-cell. Primers containing restriction enzymes were designed to

anneal in conserved and constant regions of the target immunoglobulin genes (heavy and light), such as rabbit immunoglobulin sequences, and a two-step nested PCR recovery was used to amplify the antibody sequence. Amplicons from each well were sequenced and analyzed. Representative antibodies from the resulting sequence clusters were selected for recombinant protein expression. The original heavy and light variable regions amplified from rabbit cells were cloned into human heavy and light chain constant region expression vectors via restriction enzyme digestion and ligation, and via Gibson method. Vectors containing subcloned DNA fragments were amplified and purified. The sequences of the subcloned heavy and light chains were verified prior to expression.

Recombinant Production of Monoclonal Antibody of Desired Antigen Specificity and/or Functional Properties

[1090] To determine antigen specificity and functional properties of recovered antibodies from specific B-cells, the heavy and light chain plasmids were co-transfected to generate rabbit/human chimeric antibodies for testing. Briefly, heavy and light chimeric plasmids were transiently transfected into HEK-293 cells. Transfections were allowed to incubate for 5-7 days, and upon harvest, cells were pelleted by centrifugation. Supernatants were submitted for purification via Protein A. Resulting purified chimeric antibodies were then evaluated in a variety of assays to confirm specificity and potency.

[1091] Using the above-described methods, numerous functional (antagonistic) antibodies that bind PACAP38 and PACAP27, or that bind PACAP38 only, but which do not, or do not appreciably, bind to VIP were identified. Polypeptide and exemplary coding sequences of exemplary antagonistic anti-PACAP antibodies are contained in the included biological sequence listing.

[1092] The full-length antibodies Ab1, Ab1.H, Ab2, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab5, Ab7, Ab11, Ab12, Ab4, Ab3, Ab6, Ab8, Ab9, Ab22, and Ab23 used in these examples were expressed as the heavy chain polypeptides having the sequences of SEQ ID NOS: 1; 41; 81; 121; 161; 201; 241; 281; 321; 361; 481; 521; 561; 601; 641; 681; 721; 761; 801; 881; and 921, respectively, and the light chain polypeptides of SEQ ID NOS: 21; 61; 101; 141; 181; 221; 261; 301; 341; 381; 501; 541; 581; 621; 661; 701; 741; 781; 821; 901; and 941, respectively. The heavy chain polypeptides of antibodies Ab1, Ab1.H, Ab2, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab5, Ab7, Ab11, Ab12, Ab4, Ab3, Ab6, Ab8, Ab9, Ab22, and Ab23 were expressed from the polynucleotides of SEQ ID NOS: 11; 51; 91; 131; 171; 211; 251; 291; 331; 371; 491; 531; 571; 611; 651; 691; 731; 771; 811; 891; and 931, respectively. The light chain polypeptides of antibodies Ab1, Ab1.H, Ab2, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab5, Ab7, Ab11, Ab12, Ab4, Ab3, Ab6, Ab8, Ab9, Ab22, and Ab23 were expressed from the polynucleotides of SEQ ID NOS: 31; 71; 111; 151; 191; 231; 271; 311; 351 391; 511; 551; 591; 631; 671; 711; 751; 791; 831; 911; and 951, respectively. Additional features of said antibodies are identified by SEQ ID NOS in FIGS. **1-12**.

Antigen Binding Specificity of Antibodies by Competitive HTRF Binding Assay

[1093] The binding and functional properties of exemplary anti-PACAP38 and anti-PACAP27 antibodies produced according to the invention are further described below.

[1094] To identify antibodies that preferentially bind PACAP38 (SEQ ID NO: 1241) and PACAP27 (SEQ ID NO: 1242), but do not bind VIP (SEQ ID NO: 1243), or to identify antibodies that specifically bind PACAP38, but do not bind appreciably PACAP27, or do not appreciably bind VIP, etc., a competition HTRF binding assay was performed.

[1095] In parallel, 10 μl of an antibody dilution series (highest final concentration of 100 nM) were incubated with 10 μl of N-terminal or C-terminal biotinylated PACAP38 (35 nM final) alone, or in combination with either PACAP27 (350 nM final) or VIP (350 nM final), i.e., 10× PACAP27 or 10×VIP, respectively, in a HTRF plate. 20 μl of Eu^{3+} cryptate labeled anti-hu Fc donor and 20 μl of d2-labeled streptavidin acceptor were added to each well and incubated for 1 hour at room temperature. Fluorescence was measured at 620 and 665 nm with a delay of 300 μsec.

[1096] FIG. **13**A-T provide representative binding data for Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab10, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, and Ab1.H to PACAP38 and to PACAP27, and the inability of VIP to compete with binding of PACAP38. FIG. **13**U and FIG. **13**V provide representative binding data for the anti-PACAP antibodies Ab22 and Ab23 to PACAP38 and the inability of PACAP27 or VIP to compete with binding of PACAP38. The lack of effect of VIP on binding to PACAP38 indicated its inability to compete with binding of PACAP38. These results demonstrated that Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab10, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, and Ab1.H bind to PACAP38 and PACAP27, but do not bind (or do not appreciably bind) VIP. These results also demonstrated that Ab22 and Ab23 bind to PACAP38, but do not bind (or do not appreciably bind) PACAP27 or VIP.

[1097] EC_{50} values, i.e. the concentration of an antibody that yields a response halfway between the baseline and the maximum value within a specified time period, were computed for each antibody based upon their binding curves and are shown in Table 1 below. The results demonstrated that Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab10, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab22, Ab23, and Ab1.H bound to and recognized human PACAP38 with high affinity. A humanized form of antibody Ab1 was produced and is identified by an appended ".H", i.e., Ab1.H also bound PACAP38 with high affinity.

TABLE 1

Binding (EC_{50}) of PACAP38 by anti-PACAP antibodies

ANTIBODY	PACAP38-binding EC_{50} (nM)
Ab1	0.43
Ab2	0.35
Ab3	0.45
Ab4	0.66
Ab5	0.60
Ab6	0.50
Ab7	0.45
Ab8	0.48
Ab9	0.23
Ab10	0.36
Ab11	0.53
Ab12	0.51
Ab13	0.48
Ab14	0.57
Ab15	0.62

TABLE 1-continued

Binding (EC_{50}) of PACAP38 by anti-PACAP antibodies

ANTIBODY	PACAP38-binding EC_{50} (nM)
Ab16	0.68
Ab17	0.46
Ab18	0.48
Ab19	0.43
Ab1.H	0.46
Ab22	0.57
Ab23	0.56

Ability of Anti-PACAP Antibodies to Neutralize PACAP38-Induced and PACAP27-Induced cAMP Production

[1098] The ability of anti-PACAP antibodies to neutralize PACAP38-induced and PACAP27-induced PAC1-R signaling was tested in a cell-based assay.

[1099] For Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab10, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab22, Ab23, Ab1.H, Ab10.H, Ab3.H, Ab4.H, Ab5.H, Ab9.H and Ab12.H, to identify antibodies that neutralized PACAP38-induced and PACAP27-induced signaling via PAC1-R, antibody solutions were incubated with either PACAP38 or with PACAP27 at 4× the final concentration (100 pM) for 1 hour. While the antibody/antigen complexes were incubated, PAC1-R expressing PC-12 cells (Japanese Collection of Research Bioresources Cell Bank) were washed and re-suspended at 2×10^6 cells per ml in cell culture media. Cells (10 μl) and antigen/antibody complex (40 μl) were transferred to an HTRF plate and shaken at room temperature for 30 minutes. Following the incubation, 20 μl of (1:20 diluted) Eu^{3+} cryptate-labeled mAb anti-cAMP and 20 μl of (1:20 diluted) d2-labeled cAMP in lysis buffer were added, and the plate was incubated for 1 hour while shaking. Following incubation, plates were read (excitation 330 nm, emission 620/665 nm), and a ratio of 620:665 signal was determined. The final concentration of PACAP38 and PACAP27 in each well was 0.1 nM.

[1100] FIG. **16**A-BB (PACAP38) and FIG. **17**A-BB (PACAP27) show inhibition curves (for Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab10, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab1.H, Ab10.H, Ab22, Ab23, Ab3.H, Ab4.H, Ab5.H, Ab9.H, and Ab12.H) that are representative of the inhibition curves that were obtained with the tested antibodies. The inhibition results were quantified for each antibody to yield an IC_{50} value, which are summarized in Table 2 below. These results demonstrated that anti-PACAP antibodies Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab10, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab22, Ab23, Ab1.H, Ab10.H, Ab3.H, Ab4.H, Ab5.H, Ab9.H, and Ab12.H inhibited PACAP38-induced cAMP increase in cells expressing PAC1-R (see FIG. **16**A-BB). Additionally, these results demonstrated that anti-PACAP antibodies Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab10, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab1.H, Ab10.H, Ab3.H, Ab4.H, Ab5.H, Ab9.H, and Ab12.H, but not Ab22 or Ab23, inhibited PACAP27-induced cAMP increase in cells expressing PAC1-R (see FIG. **17**A-BB).

TABLE 2

Inhibition (IC_{50}) of PACAP38-induced and PACAP27-induced cAMP increase in cells expressing PAC1-R by anti-PACAP antibodies

ANTIBODY	Inhibition of 0.1 nM PACAP38-induced PAC1-R mediated cAMP increase IC_{50} (pM)	Inhibition of 0.1 nM PACAP27-induced PAC1-R mediated cAMP increase IC_{50} (pM)
Ab1	292.9	72.9
Ab2	236.6	63.0
Ab3	227.3	90.0
Ab4	340.4	76.9
Ab5	326.9	353.3
Ab6	51.2	380.0
Ab7	111.3	45.8
Ab8	39.3	49.0
Ab9	987.0	2840.0
Ab10	180.3	227.0
Ab11	56.7	109.3
Ab12	51.1	60.4
Ab13	82.4	74.1
Ab14	154.4	95.7
Ab15	162.0	155.5
Ab16	211.8	192.4
Ab17	97.7	77.6
Ab18	117.7	91.6
Ab19	100.8	87.4
Ab1.H	259.6	57.7
Ab10.H	163.4	84.0
Ab22	101.4	n/a *
Ab23	114.9	n/a *
Ab3.H	1320.0	1207.0
Ab4.H	307.0	293.6
Ab5.H	378.4	216.8
Ab9.H	278.0	270.5
Ab12.H	113.9	86.3

* n/a: not active because these Abs are PACAP38 specific

Example 2

Binding Affinities of Anti-PA CAP Antibodies

[1101] Binding affinities of monoclonal antibodies for human PACAP were estimated using SPR on the PROTEON™ XPR36 (Bio-Rad, Hercules, Calif.). Antibody was immobilized to the surface of general amine coupling ("GLC" or "GLM") Chips (Bio-Rad, Hercules, Calif.). A dilution series of human PACAP38 (SEQ ID NO: 1241) prepared in 1×PBST Buffer (4.3 mM Na Phosphate, 1.4 mM K Phosphate, 135 mM NaCl, 2.7 mM KCl 0.05% Polysorbate-20) purchased from Teknova (Cat# P1192, Teknova, Hollister, Calif.) and supplemented with 0.25 M arginine (from J.T. BAKER®), 0.2 mg/ml BSA (Jackson Immuno Research Labs, West Grove, Pa.), and 0.005% sodium azide (VWR International, Radnor, Pa.) with the pH adjusted to 7 was used to query the antibodies. Antigen (ranging from 1.23 nM to 100 nM) was typically run sequentially with association times of 2-4 minutes and dissociation times of 3-120 minutes grouped with the PROTEON™ Manager Software (v3.1.0.6 (Bio-Rad, Hercules, Calif.)) and fitted using a 1:1 Langmuir binding model. Surfaces were regenerated between analyte queries using 0.85% Phosphoric Acid. A single K_D was calculated for each antibody with association times limited near the rate of diffusion (1.0×10^6) and dissociation times limited to 1.5×10^{-5} where no discernible dissociation was observed.

[1102] The same procedure was used to determine binding affinities of antibodies for human VIP (SEQ ID NO: 1243)

and PACAP27 (SEQ ID NO: 1242) though peptide concentrations ranged from 1.23 nM to 1000 nM with association times of 200 seconds and dissociation times of 3-120 minutes.

[1103] The measured antibody affinities for PACAP38 are listed in Table 3.

TABLE 3

Antibody affinity constants for PACAP38

Antibody	ka (1/Ms)	kd (1/s)	K_D (M)
Ab1	3.7E+05	1.0E−05	2.7E−11
Ab2	2.3E+05	1.0E−05	4.4E−11
Ab3	2.6E+05	4.2E−05	1.6E−10
Ab4	3.3E+05	7.2E−05	2.2E−10
Ab5	2.4E+05	1.0E−05	4.1E−11
Ab6	3.0E+05	4.1E−05	1.4E−10
Ab7	1.8E+05	1.0E−05	5.6E−11
Ab8	3.5E+05	1.0E−05	2.9E−11
Ab9	8.2E+05	1.1E−04	1.4E−10
Ab10	2.6E+05	2.0E−05	7.5E−11
Ab11	2.7E+05	3.1E−05	1.1E−10
Ab12	3.1E+05	1.0E−05	3.2E−11
Ab13	4.2E+05	2.7E−05	6.4E−11
Ab14	3.2E+05	1.0E−05	3.1E−11
Ab15	5.3E+05	2.7E−05	5.0E−11
Ab16	9.1E+05	1.0E−05	1.1E−11
Ab17	5.0E+05	1.0E−05	2.0E−11
Ab18	4.3E+05	1.0E−05	2.3E−11
Ab19	2.7E+05	2.5E−05	9.3E−11
Ab22	3.7E+05	1.0E−05	2.7E−11
Ab23	5.1E+05	3.6E−05	7.1E−11
Ab1.H	4.7E+05	1.0E−05	2.1E−11
Ab3.H	4.9E+05	1.4E−04	2.9E−10
Ab4.H	3.1E+05	3.2E−05	1.0E−10
Ab5.H	5.5E+05	1.7E−05	3.1E−11
Ab9.H	1.0E+06	6.1E−05	6.1E−11
Ab10.H	3.4E+05	1.0E−05	2.9E−11
Ab12.H	3.8E+05	1.0E−05	2.6E−11

[1104] Examples of antibody affinity constants for VIP are listed in Table 4.

TABLE 4

Antibody affinity constants for VIP

Antibody	ka (1/Ms)	kd (1/s)	K_D (M)
Ab1	2.5E+05	2.5E−02	9.9E−08
Ab2	5.8E+05	8.4E−02	1.4E−07
Ab3	1.0E+00	1.0E−01	1.0E−01
Ab4	1.7E+05	2.1E−02	1.2E−07
Ab5	1.2E+05	8.6E−01	7.2E−06
Ab6	3.1E+03	1.4E−04	4.4E−08
Ab7	2.6E+05	8.8E−03	3.4E−08
Ab8	4.8E+05	1.0E−01	2.1E−07
Ab9	1.0E+00	1.0E−01	1.0E−01
Ab10	3.7E+04	1.0E−02	2.8E−07
Ab11	2.0E+05	4.7E−02	2.3E−07
Ab12	2.9E+05	2.4E−03	8.2E−09
Ab13	3.2E+05	4.6E−02	1.4E−07
Ab14	2.7E+05	6.7E−02	2.5E−07
Ab15	1.6E+05	1.3E−01	8.2E−07
Ab16	3.6E+05	9.6E−02	2.6E−07
Ab17	3.1E+05	1.7E−02	5.5E−08
Ab18	3.1E+05	1.2E−01	4.0E−07
Ab19	2.8E+05	2.8E−01	1.0E−06
Ab22	2.7E+05	1.8E−01	6.9E−07
Ab23	4.3E+05	3.2E−01	7.3E−07
Ab1.H	3.8E+04	1.8E−01	4.8E−06
Ab3.H	1.0E+00	1.0E−01	1.0E−01
Ab4.H	3.3E+05	2.4E−02	7.2E−08

TABLE 4-continued

Antibody affinity constants for VIP

Antibody	ka (1/Ms)	kd (1/s)	K_D (M)
Ab5.H	1.0E+00	1.0E−01	1.0E−01
Ab9.H	9.3E+04	1.4E−01	1.5E−06
Ab10.H	3.8E+05	3.9E−02	1.0E−07
Ab12.H	2.8E+05	1.4E−02	5.1E−08

[1105] Examples of antibody affinity constants for PACAP27 are listed in Table 5.

TABLE 5

Antibody affinity constants for PACAP27

Antibody	ka (1/Ms)	kd (1/s)	K_D (M)
Ab1	1.0E+06	1.0E−05	1.0E−11
Ab2	8.3E+05	1.0E−05	1.2E−11
Ab3	3.7E+05	1.4E−04	3.7E−10
Ab4	3.9E+05	2.0E−04	5.1E−10
Ab5	2.5E+05	2.4E−05	9.6E−11
Ab6	3.9E+05	8.2E−05	2.1E−10
Ab7	2.3E+05	4.5E−05	2.0E−10
Ab8	4.4E+05	6.0E−05	1.4E−10
Ab9	9.6E+05	3.2E−04	3.4E−10
Ab10	1.0E+06	1.0E−05	1.0E−11
Ab11	2.6E+05	1.1E−04	4.2E−10
Ab12	2.9E+05	2.1E−05	7.0E−11
Ab13	5.4E+05	6.6E−05	1.2E−10
Ab14	2.7E+05	2.0E−05	7.4E−11
Ab15	4.7E+05	7.8E−05	1.7E−10
Ab16	8.2E+05	2.9E−05	3.5E−11
Ab17	3.7E+05	1.0E−05	2.7E−11
Ab18	4.4E+05	1.0E−05	2.3E−11
Ab19	4.2E+05	1.3E−04	3.1E−10
Ab22	1.0E+00	1.0E−01	1.0E−01
Ab23	8.9E+05	3.1E−02	3.5E−08
Ab1.H	7.6E+05	1.0E−05	1.3E−11
Ab3.H	3.3E+05	3.4E−04	1.0E−09
Ab4.H	3.3E+05	1.0E−05	3.1E−11
Ab5.H	2.7E+05	1.3E−04	4.8E−10
Ab9.H	6.2E+05	7.7E−05	1.2E−10
Ab10.H	5.3E+05	1.8E−05	3.3E−11
Ab12.H	2.6E+05	7.9E−05	3.0E−10

[1106] The binding affinity results of Tables 3 and 5 present data demonstrating that Ab23 weakly bound to PACAP27 as compared to its binding affinity for PACAP38. Tables 3 and 5 additionally present data demonstrating that Ab22 did not specifically recognize PACAP27, but that Ab22 specifically bound to PACAP38.

Example 3

Inhibition of PACAP38-Induced Signaling Via VPAC1-R

[1107] To identify antibodies that neutralize PACAP38-induced signaling via human VPAC1-R, CHO-K1 cells expressing human VPAC1-R were used in a cAMP HTRF cell-based assay. Antibody dilutions were incubated with PACAP38 at 4× the final concentration (5 nM) for 1 hour. While the antibody/antigen complexes were incubated for 1 hour, VPAC1-R expressing CHO-K1 cells (generated at Alder Biopharmaceuticals, by stable transfection of CHO-K1 cells (ATCC, catalog # CCL-61) with human VPAC1-R cDNA; selected clone 1 was used for in vitro cell based assays) were detached with 0.25% trypsin for 4 minutes. The

cells were washed and re-suspended at 1×10^6 cells per ml culture media. 20 µl of Ab/antigen mixture was mixed with 20 µl of cells in HTRF plates and incubated with shaking for 30 minutes. 20 µl of Eu^{3+} cryptate labeled anti-cAMP mAb (1:20 diluted) and 20 µl of (1:20 diluted) d2-labeled cAMP in lysis buffer were added to each well and incubated for 1 hour with shaking. The final concentration of PACAP38 in each well was 5 nM. Following incubation, plates were read (excitation 330 nm, emission 620/665 nm), and a ratio of 620:665 signal was determined.

[1108] FIG. **18**A-BB are representative of the inhibition curves obtained by this method (results are shown for Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab10, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab1.H, Ab10.H, Ab22, Ab23, Ab3.H, Ab4.H, Ab5.H, Ab9.H, and Ab12.H, respectively). The computed IC_{50} values for each antibody, which are shown below in Table 6, demonstrated that Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab10, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab1.H, Ab10.H, Ab22, Ab23, Ab3.H, Ab4.H, Ab5.H, Ab9.H, and Ab12.H inhibited PACAP38-induced cAMP increase in cells expressing human VPAC1-R.

TABLE 6

Inhibition (IC_{50}) of PACAP38-induced cAMP increase in cells expressing human VPAC1-R by anti-PACAP antibodies

ANTIBODY	Inhibition of 5 nM PACAP38-induced human VPAC1-R mediated cAMP increase IC_{50} (pM)
Ab1	664.7
Ab2	688.3
Ab3	1736.0
Ab4	942.8
Ab5	720.7
Ab6	797.1
Ab7	687.3
Ab8	481.2
Ab9	4059.0
Ab10	649.1
Ab11	541.0
Ab12	292.2
Ab13	2183.0
Ab14	2626.0
Ab15	3715.0
Ab16	3533.0
Ab17	780.1
Ab18	911.2
Ab19	826.8
Ab1.H	1021.1
Ab10.H	1336.0
Ab22	1300.0
Ab23	2667.0
Ab3.H	7332.0
Ab4.H	2600.0
Ab5.H	2772.0
Ab9.H	2465.0
Ab12.H	1284.0

Example 4

Inhibition of PACAP38-Induced Signaling Via VPAC2-R

[1109] To identify antibodies that neutralize PACAP38-induced signaling via human VPAC2-R, CHO-K1 cells expressing human VPAC2-R were used in a cAMP HTRF cell based assay. Antibody dilutions were incubated with PACAP38 at 4× the final concentration (1 nM) for 1 hr. While the antibody/antigen complexes were incubated for 1 hour, VPAC2-R expressing CHO-K1 cells (generated at Alder Biopharmaceuticals, by stable transfection of CHO-K1 cells (ATCC, catalog # CCL-61) with human VPAC2-R cDNA; selected clone 8 was used for in vitro cell based assays) were detached with 0.25% trypsin for 4 minutes. The cells were washed and re-suspended at 1×10^6 cells per ml culture media. 20 µl of Ab/antigen mixture was mixed with 20 µl of cells in HTRF plates and incubated with shaking for 30 minutes. 20 µl of Eu^{3+} cryptate labeled anti-cAMP mAb (1:20 diluted) and 20 µl of (1:20 diluted) d2-labeled cAMP in lysis buffer were added to each well and incubated for 1 hour with shaking. The final concentration of PACAP38 in the wells was 1 nM. Following incubation, plates were read (excitation 330 nm, emission 620/665 nm) and, a ratio of 620:665 signal was determined.

[1110] FIG. **19**A-BB are representative of the inhibition curves obtained by this method (results are shown for Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab10, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab1.H, Ab10.H, Ab22, Ab23, Ab3.H, Ab4.H, Ab5.H, Ab9.H, and Ab12.H, respectively). The computed IC_{50} values for each antibody, which are shown below in Table 7, demonstrated that Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab10, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab1.H, Ab10.H, Ab22, Ab23, Ab3.H, Ab4.H, Ab5.H, Ab9.H, and Ab12.H inhibited PACAP38-induced cAMP increase in cells expressing human VPAC2-R.

TABLE 7

Inhibition (IC_{50}) of PACAP38-induced cAMP increase in cells expressing human VPAC2-R by anti-PACAP antibodies

ANTIBODY	Inhibition of 1 nM PACAP38-induced human VPAC2-R mediated cAMP increase IC_{50} (pM)
Ab1	146.7
Ab2	174.1
Ab3	667.4
Ab4	217.9
Ab5	239.3
Ab6	216.9
Ab7	162.4
Ab8	146.9
Ab9	6965.0
Ab10	188.5
Ab11	265.2
Ab12	179.0
Ab13	652.2
Ab14	840.4
Ab15	22850.0
Ab16	1146.0
Ab17	205.0
Ab18	285.4
Ab19	953.5
Ab1.H	983.0
Ab10.H	988.0
Ab22	515.0
Ab23	1789.0
Ab3.H	64240.0
Ab4.H	4487.0
Ab5.H	7466.0

TABLE 7-continued

Inhibition (IC_{50}) of PACAP38-induced cAMP increase in cells expressing human VPAC2-R by anti-PACAP antibodies

ANTIBODY	Inhibition of 1 nM PACAP38-induced human VPAC2-R mediated cAMP increase IC_{50} (pM)
Ab9.H	2649.0
Ab12.H	653.0

Example 5

Inhibition of PACAP38 Binding to PAC1-R-Expressing Cells

[1111] To identify antibodies that block PACAP38 binding to PAC1-R-expressing cells, adherent PC-12 cells (ATCC, Manassas, Va.) expressing PAC1-R were used in a Europium-based PAC1-R-expressing cells binding assay.

[1112] Antibody solutions were incubated with N-terminal biotinylated PACAP38 at 10× the final concentration (100 nM or 30 nM) for 1 hr, then added to PC-12 cells that were plated 24 hrs prior in black clear bottom 96 well plates (COSTAR™, Corning Incorporated, Corning, N.Y.) and further incubated for 1 hr at room temperature. After three washes, the cells were incubated with 20 μl Europium-labeled streptavidin (PerkinElmer, Waltham, Mass.) for 1 hr at room temperature. Cells were washed three times, then 20 μl DELFIA® Enhancement solution (PerkinElmer, Waltham, Mass.) was added to each well and incubated for 15 minutes with gentle shaking. Plates were read (Time Resolved Fluorescence ("TRF")) on SPECTRAMAX® (Molecular Devices, Sunnyvale, Calif.) plate reader.

[1113] FIG. **14**A-BB are representative of the inhibition curves obtained by this method (results are shown for Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab10, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab1.H, Ab10.H, Ab22, Ab23, Ab3.H, Ab4.H, Ab5.H, Ab9.H, and Ab12.H, respectively) wherein the PAC1-R expressing cells were PC-12 cells. The computed IC_{50} values for each antibody, which are shown below in Table 8, demonstrated that Ab1, Ab2, Ab3, Ab4, Ab5, Ab6, Ab7, Ab8, Ab9, Ab10, Ab11, Ab12, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab1.H, Ab10.H, Ab22, Ab23, Ab3.H, Ab4.H, Ab5.H, Ab9.H, and Ab12.H inhibited PACAP38 binding to PAC1-R expressing cells.

TABLE 8

Inhibition (IC_{50}) of PACAP38 binding to PAC1-R-expressing PC-12 cells by anti-PACAP antibodies.

ANTIBODY	Inhibition of 100 nM biotinylated PACAP38 binding to PAC1-R-expressing PC-12 cells IC_{50} (nM)
Ab1	12.7
Ab2	26.6
Ab3	17.2
Ab4	28.6

TABLE 8-continued

Inhibition (IC_{50}) of PACAP38 binding to PAC1-R-expressing PC-12 cells by anti-PACAP antibodies.

Ab5	16.3
Ab6	7.8
Ab7	22.0
Ab8	20.3
Ab9	33.3
Ab10	17.8
Ab11	24.6
Ab12	22.6
Ab13	53.1
Ab14	17.9
Ab15	36.7
Ab16	27.3
Ab17	33.1
Ab18	30.6
Ab19	162

ANTIBODY	Inhibition of 30 nM Biotinylated PACAP38 binding to PAC1-R-expressing PC-12 cells IC_{50} (nM)
Ab1.H	56.3
Ab10.H	14.5
Ab22	13.8
Ab23	14.9
Ab3.H	88.3
Ab4.H	98.0
Ab5.H	34.9
Ab9.H	22.5
Ab12.H	68.1

Example 6

PACAP38-Mediated Binding of Anti-PACAP Antibodies to the Cell Surface of PAC1-R Expressing Cells

[1114] To identify anti-PACAP antibodies that bind, via PACAP38, to the cell surface of PAC1-R expressing cells, adherent PC-12 cells (Japanese Collection of Research Bioresources Cell Bank) expressing PAC1-R were used in a cell surface binding-based assay. To perform the binding experiment, PAC1-R expressing PC-12 cells were first seeded into Corning 96 well white solid bottom plates (Corning, Corning, N.Y.). Cells were initially seeded at 1×10^5 cells/well in a solution of complete RPMI ("cRPMI": RPMI medium supplemented with 10% sterile heat-inactivated FBS and 1% sterile antibiotic/antimycotic)+10% FBS, and the plates were allowed to incubate overnight at 37° C. On the day of the binding assay, antibodies at an initial concentration of 15 μg/ml were diluted at a 1:3 ratio in DELFIA® binding buffer (50 mM Tris, 150 mM NaCl, 0.1% azide, 2% horse serum) (Perkin-Elmer, Waltham, Mass.) to a total volume of 60 μL in a separate 96 well round bottom plate. PACAP38 was prepared for the binding assay by diluting it in DELFIA® binding buffer to a concentration of 200 nM, and then 60 μl of the diluted PACAP38 was added to each of the antibody-containing wells to form antibody:antigen complexes. Following addition of PACAP38, the antibody:antigen complexes were incubated at room temperature on a shaker for 1 hour. Separately, the PC-12 cells were prepared for addition of antibody:antigen complexes by washing the cells two times with DELFIA® wash buffer (50 mM Tris, 150 mM NaCl, 0.1% Azide) (Perkin-Elmer,

Waltham, Mass.). After washing the cells two times and following the 1 hour room temperature incubation of the antibody:antigen complexes, 50 μl of the antibody:antigen complex was added to each well containing cells. The mixtures of cells and antibody:antigen complexes were then incubated for 30 minutes at room temperature. Following this 30 minute incubation, each mixture was washed two times with DELFIA® wash buffer (Perkin-Elmer, Waltham, Mass.).

[1115] DELFIA® Europium labeled anti-human IgG detection reagent (Cat #1244-330, Perkin-Elmer, Waltham, Mass.) was diluted to a concentration of 300 ng/ml in DELFIA® Binding Buffer. Following dilution, 50 μl of the anti-human IgG detection reagent was added to each well containing cells, and a 30 minute incubation at room temperature followed this addition of IgG detection reagent. After completion of the 30 minute room temperature incubation, the cells were then washed two times with DELFIA® wash buffer. Next, 50 μl of DELFIA® Enhancement Solution (Cat #1244-105, Perkin-Elmer, Waltham, Mass.) was added to each well containing cells for a final 15 minute room temperature incubation with shaking. The plates were then read (TRF, excitation 330 nm, emission 620 nm) on a SPECTRAMAX® (Molecular Devices, Sunnyvale, Calif.) plate reader.

[1116] FIGS. **15**A-J are representative of the binding curves obtained by this method (results are shown for Ab1.H, Ab3.H, Ab4.H, Ab5.H, Ab9.H, Ab12.H, Ab10, Ab10.H, Ab22, and Ab23, respectively) wherein the PAC1-R expressing cells were PC-12 cells. Ab1.H, Ab3.H, Ab4.H, Ab5.H, Ab9.H, and Ab12.H demonstrated binding to the surface of PAC1-R expressing cells in the presence of PACAP38, while Ab10, Ab10.H, Ab22, and Ab23 did not appear to appreciably bind to the surface of PAC1-R expressing cells using this assay. The binding of Ab1.H, Ab3.H, Ab4.H, Ab5.H, Ab9.H, and Ab12.H to the cell surface of PAC1-R cells was only observed in the presence of PACAP38. Without intent to be bound by theory, it is hypothesized that the binding of the antibodies to the cell surface was mediated by binding of PACAP38 to GAGs that were present on the cell surface, since binding of PACAP38 by GAGs has been previously demonstrated as a PAC1-R receptor independent mechanism of PACAP38 binding and internalization by PC-12 cells (see Doan et al. (2012), Juhász et al. (2014), and Neree et al. (2015)).

Example 7

Inhibition of PACAP38-Induced Dermal Vasodilation in Rabbits by Anti-PACAP Antibody Ab1.H

[1117] Intradermal injection of PACAP38 has been shown to elicit a localized vasodilation in rabbits and humans (Warren et al., *J. Cardio. Pharmacol.,* 29(1): 83-87 (1992); Seelinger et al., *Am. J. Path.,* 177(5):2563-2575 (2010)). An in vivo efficacy study was conducted to determine the activity of Ab1.H to inhibit a localized dermal vasodilation induced by an intradermal injection of PACAP38 in male New Zealand White rabbits.

[1118] Groups of 4 rabbits were dosed with either 90 mg/kg of Ab1.H or with negative control vehicle (25 mM histidine, 250 mM sorbitol, pH 6.0). Injections were performed by IV (ear vein) bolus administration on day 0. Prior to each rabbit PACAP38 challenge, the scapular region of each animal was clipped free of hair and wiped with 20% (v/v) alcohol in water. On day 2, the animals were pre-anesthetized with ketamine hydrochloride and maintained under deep anesthesia with isoflurane gas. Four sites (Region of Interest ("ROI")) for injection were identified on the back of each animal using a SHARPIE® permanent marker. Dermal vasodilation and blood perfusion were monitored using the PeriCam PSI NR system for Laser Speckle Contrast Analysis ("LASCA") imaging (Perimed, Jäffälla, Sweden), before (baseline) and for 35 minutes after intradermal PACAP38 challenge. Intradermal PACAP38 challenge was performed as follows: each animal received single intradermal administrations (100 μl/site) of vehicle (one site or ROI) and PACAP38 at 30 pmoles/site (3 sites or 3 ROIs). The blood perfusion rates for each ROI were reported by the PeriCam PSI NR system in Perfusion units ("PU") and analyzed using PIMSoft (Ver. 1.5 (Perimed, Jarfällä, Sweden)).

[1119] For each treatment group, the relative % PU change following Ab1.H or negative control administration compared to baseline was calculated for each ROI (% PU change for each PACAP38 challenge site—% PU change for the vehicle site). The relative % PU change in the Ab1.H group was compared to the relative % PU change in the Negative control group by performing a two-tailed unpaired t-test statistical evaluation using GraphPad Prism (version 5.0d, GraphPad Software, La Jolla, Calif.) software.

[1120] FIG. **20** demonstrates that Ab1.H inhibited PACAP38-induced dermal vasodilation in rabbits, indicating effectiveness of the antibody at neutralizing PACAP38 activity in vivo.

Example 8

Inhibition of PACAP38-Induced Dermal Vasodilation in Rabbits by Anti-PACAP Antibody Ab10

[1121] Intradermal injection of PACAP38 has been shown to elicit a localized vasodilation in rabbits and humans (Warren et al. (1992); Seelinger et al. (2010)). An in vivo efficacy study was conducted to determine the activity of Ab10 to inhibit a localized dermal vasodilation induced by an intradermal injection of PACAP38 in male New Zealand White rabbits.

[1122] Groups of 4 rabbits were dosed with either 72 mg/kg of Ab10 or with isotype antibody control. Injections were by (ear vein) bolus intravenous administration on day 0. Prior to each rabbit PACAP38 challenge, the scapular region of each animal was clipped free of hair and wiped with 20% (v/v) alcohol in water. On day 2, the animals were pre-anesthetized with ketamine hydrochloride and maintained under deep anesthesia with isoflurane gas. Four sites (ROIs) for injection were identified on the back of each animal using a SHARPIE® permanent marker. Dermal vasodilation and blood perfusion were monitored using the PeriCam PSI NR system for LASCA imaging (Perimed, Jäfälla, Sweden), before (baseline) and for 35 minutes after intradermal PACAP38 challenge. Intradermal PACAP38 challenge was performed as follows: each animal received single intradermal administrations (100 μl/site) of vehicle (one site or ROI) and PACAP38 at 30 pmoles/site (3 sites or 3 ROIs). The blood perfusion rates for each ROI were reported by the PeriCam PSI NR system in PU and analyzed using PIMSoft (Ver. 1.5 (Perimed, Järfälla, Sweden)).

[1123] For each treatment group, the relative % PU change following Ab10 or Isotype Ab control administration compared to baseline was calculated for each ROI (% PU change for each PACAP38 challenge site—% PU change for the vehicle site). The relative % PU change in the Ab10 group was compared to the relative % PU change in the Isotype Ab control group by performing a two-tailed unpaired t-test statistical evaluation using GraphPad Prism (version 5.0d, GraphPad Software, La Jolla, Calif.) software.

[1124] FIG. **21** demonstrates that Ab10 inhibited PACAP38-induced dermal vasodilation in rabbits, indicating effectiveness of the antibody at neutralizing PACAP38 activity in vivo.

Example 9

Epitope Binning of Anti-PACAP Antibodies, Ab1 and Ab10

[1125] Ab1 was biotinylated at a 10:1 molar ratio with biotin (Thermo Fisher Scientific, Waltham, Mass.) per manufacturer guidelines. A 5 step biolayer interferometry experiment was performed as follows: In step 1, streptavidin biosensors (Pall ForteBio LLC, Menlo Park, Calif.) were equilibrated for 50 seconds in 1× kinetics buffer (a 1:10 dilution in DBS of Pall ForteBio LLC, Menlo Park, Calif., cat#18-5032). In step 2, a 2 μg/ml dilution of biotinylated antibody Ab1 in 1× kinetics buffer was immobilized for 500 seconds onto Streptavidin biosensors. In step 3, the antibody-functionalized biosensors were incubated in a solution of 2 μM unlabeled PACAP peptide (American Peptide Company, Sunnyvale, Calif., catalog #34-0-20) in 1× kinetics buffer for 200 seconds. In step 4, the sensors were placed into 67 nM solutions of either unlabeled antibody Ab10 (FIG. **22**A) or unlabeled antibody Ab1 as control (FIG. **22**B) in 1× kinetics buffer for a 1000 second association step. Stability of binding was monitored during step 5 for a 1000 second dissociation in 1× kinetics buffer. In FIG. **22**A, the "sandwich-style" capture of Ab10 via Ab1-captured PACAP indicates simultaneous and non-competitive binding of these two antibodies to PACAP. The control experiment in FIG. **22**B shows minimal "sandwich-style" capture of Ab1 via Ab1-captured PACAP. The experiment was conducted on a ForteBio OCTET® QK instrument (Pall ForteBio LLC, Menlo Park, Calif.) at 30° C. and 1000 RPM.

Example 10

Inhibition of PACAP27 Binding to Human PAC1-R by Anti-PA CAP Antibodies

[1126] To identify antibodies that block PACAP27 binding to PAC1-R, antibodies at an initial concentration of 30 nM were diluted in incubation buffer (50 mM Hepes pH 7.4, 1 mM $CaCl_2$, 5 mM $MgCl_2$, 0.2% BSA) and serial 1:3 dilutions were performed. Antibody dilutions (30 nM, 10 nM, 3 nM, 1 nM, 0.3 nM, 0.1 nM, 0.03 nM, 0.01 nM, 0.003 nM and 0.001 nM) were then mixed and pre-incubated at 25° C. for 30 minutes with 0.1 nM of ^{125}I-labelled PACAP27 in incubation buffer. The antibody: ^{125}I-labelled PACAP27 mixture was then added to 0.5 μg aliquots of cell membranes derived from Chem-1 cells expressing human recombinant PAC1-R long isoform in incubation buffer. The mixture was then incubated for 1 hour at 25° C. Following incubation, the samples were filtered and washed. Afterward, the filters were counted to quantitate ^{125}I-labelled PACAP27. As an experimental control, non-specific binding to the cell membranes was estimated using 0.1 μM of labeled PACAP27. The results indicated that Ab1.H, Ab10.H, and Ab12.H were capable of blocking PACAP27 binding to PAC1-R, thereby demonstrating inhibition of ligand-receptor binding by the tested antibodies presented in Table 9.

TABLE 9

Inhibition (IC_{50}) of 0.1 nM ^{125}I-PACAP27 binding to PAC1-R by anti-PACAP antibodies

ANTIBODY	IC_{50} (nM)
Ab1.H	0.70
Ab10.H	0.22
Ab12.H	0.16

Example 11

Effect of Anti-PACAP Antibody on Light Aversion

[1127] To examine the effect of anti-PACAP antibodies on photophobia, a mouse model was employed in which mice were administered PACAP to trigger photophobia. Photophobia was detected using a light aversion assay using a light-dark box as described in Kaiser et al., *J. Neurosci.*, 32(44):15439-15449, 2012. Mice were then administered anti-PACAP antibodies Ab1.H or Ab10.H or an unrelated control antibody and their aversion to light quantitated. Results are reflected in FIGS. **23-25**.

Light Aversion Assay

[1128] As described in Kaiser et al., the testing chambers were a plexiglass open field (27 cm wide×27 cm deep×20.3 cm high) containing three sets of 16 beam infrared arrays (two sets of perpendicular beams cross at a height of 1.0 cm to detect mouse location and locomotion, and the third beam crosses the width of the chamber at a height of 7.3 cm to detect vertical activity). The field was divided in two equal sized zones by a dark insert, which is a five-sided, black-colored plexiglass box with a top, but no floor. The use of infrared light beams allowed tracking in both zones. An opening (5.2 cm×6.8 cm) in the dark insert allowed free movement between zones. While the dark insert blocked direct light, some light could still enter through the opening. Each testing chamber was located inside a sound-attenuating cubicle (56 cm wide×38 cm deep×36 cm high) with a fan for ventilation (Med Associates, Inc.®, St. Albans, Vt.). A computer using Activity Monitor v6.02 (Med Associated Inc.) was used for recording data from the six chambers.

[1129] For each chamber, a LED panel was attached to the ceiling of the sound-attenuating cubicle. The LED panel contains 36 collimated 1 watt LEDs (5500 k Daylight White) (LEDwholesalers.com, Burlingame, Calif.). To control light intensity, each LED panel was connected to a dimmable LED driver (LINEARdrive®; eldoLED America Inc., San Jose, Calif.) leading to a potential range of light intensity from 3.0×10^2 to 2.7×10^4 1×. Levels were further attenuated to 5.5×10^1 1× using wax paper placed on a clear plexiglass tray below the LEDs. Light intensity was measured with Traceable Dual-Display Light Meter (Control Company, Friendswood, Tex.) placed on the floor of the testing cham-

ber. At 2.7×10^4 1×, LED lights generated some heat in the sound attenuating chamber with the dark zone at ~25° C. and light zone at ~27° C.

[1130] On the day of the experiment, mice were transported from animal housing and allowed to acclimate to the testing room (~22° C.) for at least 30 to 60 minutes with standard overhead fluorescent lighting (~200 1× inside the housing cage). Room lights remained on, unless noted otherwise. In addition, all sound-generating equipment were turned on during acclimation and remained on until testing was complete. There was minimal human presence in the room during acclimation. Behavioral testing was performed between 0800 CST and 1400 CST. Any abnormal physical conditions (e.g. missing eye) were noted.

[1131] Ten week old male and female CD1 mice were used in the study (strain #022, Charles River, Wilmington, Mass., US). Mice were allowed to recover from shipping for one to two weeks prior to testing.

Acclimation

[1132] All mice were acclimated in the testing room at least 30 to 60 minutes prior to being placed in the light/dark chamber. The light intensity in the chamber was initially set to 2.7×10^3 1×. The mice were tested for thirty minutes in the chamber every day they were exposed to the light/dark chamber. Baseline time in light for each mouse was obtained by exposing the mice to the light/dark chamber twice, with a period of rest of three days between baseline measurements (FIGS. **23** and **25**, "Baseline1" and "Baseline2," or "Baseline", respectively).

Treatment

[1133] The mice were administered 30 mg/kg of either anti-PACAP antibody or control IgG antibody (negative control antibody having the same framework as the tested antibodies and that recognizes digoxigenin) by i.p. injection. The mice were then returned to their home cage to rest for one day (24 hours) prior to testing. The mice were then administered 0.6 mg/kg PACAP or vehicle by i.p. injection and rested for 30 minutes. The mice were then placed in the light/dark chamber for 30 minutes (FIG. **23** and FIG. **25**, "Treatment"). After each mouse was exposed to the light/dark chamber, the light/dark chamber and components were cleaned with germicidal wipes and dried. About 5 to 7 minutes after a mouse was placed in the light/dark chamber, the next mouse to be tested was injected with PACAP or vehicle, as described above. This interval was approximately the amount of time required to clean the light/dark chamber between experiments.

Motility Measurements

[1134] Motility was measured at 5 minute intervals over the 30 minute testing period as described in Kaiser et al., *J. Neurosci.,* 2012. Briefly, the number of vertical movements, such as rearing, ambulatory distance (cm, the total distance traveled during ambulatory movement status), transitions, and resting (percentage of time spent breaking no new beams), were measured by light beam. All motility parameters were normalized to the time spent in each zone to account for different amount of time spent in that zone; thus, the raw value for each parameter was divided by the time spent in that zone during the 5 min interval. Time spent in each chamber was analyzed using GraphPad Prism software (GraphPad Software, San Diego, Calif.), and reported as mean±standard error of the mean ("SEM"). Comparison was calculated by two-way repeated measure ANOVA, with Bonferroni's multiple-comparison test for post-hoc analysis.

[1135] Mice were excluded based on three criteria: (1) after the first two exposures to the box the baseline time in light was analyzed and any mouse that spent+/−one standard deviation of mean time in light at baseline was removed from the experiment and not given drug treatment, (2) mice were excluded from analysis if they were identified as statistical outliers (box plot, 10-90%), and (3) mice were excluded if they moved less than 10% of the time (combined light and dark).

[1136] In two experiments comparing the response of mice administered either antibody Ab1.H or Ab10.H to control IgG, the results indicate that mice administered either PACAP antibody Ab1.H or Ab10.H spent more time in light as compared to IgG control mice. FIG. **23** shows that mice behaved normally and similarly in both baseline measurements. On the other hand, the data provided in FIG. **23** show that mice treated with control IgG antibody and then PACAP spent statistically less time in light (squares) than mice administered anti-PACAP antibody Ab1.H and then PACAP (circles). (See, FIG. **23**, "Treatment"). The data provided in FIG. **25** also show that mice behaved normally and similarly in baseline measurements. On the other hand, the data provided in FIG. **25** show that mice treated with control IgG antibody and then PACAP spent statistically less time in light (triangles) than mice administered anti-PACAP antibody Ab10.H and then PACAP (inverted triangles). (See, FIG. **25**, "Treatment"). Time between each measurement was three days. The mean±SEM is provided for each 5-minute interval. Mice administered vehicle only behaved as normal controls. Data provided in FIG. **24** shows that administration of either anti-PACAP antibody Ab1.H, or control IgG, and vehicle ("Veh+PAC Ab" and "Veh+Con Ab," respectively) did not markedly alter mouse behavior. FIG. **24** also shows that the average time of the mouse in light decreased when PACAP and control IgG were administered ("PACAP+Con Ab"), whereas mice administered anti-PACAP antibody Ab1.H and PACAP exhibited normal, non-light-sensitive behavior ("PACAP+PAC Ab").

Example 12

Epitope Mapping of Anti-PACAP Antibodies

[1137] In order to determine the epitopes contained within PACAP to which the anti-PACAP antibodies and antigen binding fragments thereof of the invention bind, alanine scanning experiments were used. To perform these experiments, PACAP peptides were synthesized with a single point mutation in each position replacing the native amino acid with an Alanine ("Ala"), and the consequences of a single point mutation as it relates to binding affinity of PACAP and an antibody were measured.

[1138] Since an alanine residue already occupies positions 18, 24, and 25 of wild-type PACAP, according to convention, these Ala residues were replaced with Valine ("Val") to determine the possible effects of the removal of the alanine at these positions on the binding of the subject anti-PACAP antibodies to PACAP. Per the usual convention these Ala mutants were labeled according to the position in PACAP 1-38 followed by the letter code for the substituted amino acid, e.g., 10A indicates PACAP 1-38 substituted with

alanine at amino acid position 10. Binding of monoclonal antibodies for human PACAP and each mutant peptide was detected using SPR on the PROTEON™ XRP36 (Bio-Rad Laboratories, Hercules, Calif.). Samples and sample controls were immobilized onto a PROTEON™ GLC sensor chip (Bio-Rad Laboratories, Hercules, Calif.) at a single density using standard amine coupling. The running buffer used for immobilization was DPBS/modified (HYCLONE™, GE Healthcare Life Sciences, Marlborough, Mass.) and immobilization was conducted at 25° C. The PROTEON™ GLC sensor chip (Bio-Rad Laboratories, Hercules, Calif.) was initialized and pre-conditioned per the manufacturer's protocol (bi-directional injections of 0.5% SDS, 50 mM NaOH, 100 mM HCl).

[1139] The immobilization process was performed stepwise to ensure a unique antibody on the spots of the PROTEON™ Chip (Bio-Rad Laboratories, Hercules, Calif.). The surface of the chip was activated with a 1:1 mixture of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide/N-hydroxysuccinimide ("EDAC/NHS") and flow rate of 30 μL/min×5 minutes. Antibody samples were previously dialyzed or exchanged to 10 mM HEPES 150 mM NaCl pH 7.2, and the antibody concentration was quantified using a NANODROP™2000 spectrophotometer (Thermo Fisher Scientific, Waltham, Mass.). The immobilization targeted 2000-3000 response units ("RU"). Antibody samples (5 μg/ml) in 10 mM sodium acetate, pH 5.5, were flowed at 30×4 minutes. Deactivation was achieved at a flow rate of 30 μL/min for 5 minutes using 0.3 M ethanolamine concomitantly with the next activation.

[1140] Following immobilization, the running buffer was changed to 1×PBST (4.3 mM sodium phosphate, 1.4 mM potassium phosphate, 135 mM NaCl, 2.7 mM KCl, 0.05% TWEEN®) with 0.2 M arginine HCl (to reduce non-specific binding), BSA (0.2 mg/ml, as a carrier) and PROCLIN300® (0.005% as a preservative, Sigma Aldrich, St. Louis, Mo.) and the chip surface was allowed to re-equilibrate with an injection of new running buffer. Stock solutions of human PACAP peptide (1-38) and alanine/valine mutant peptides (Molecular Weight(s): 4.5 kD) at a concentration of 1 mg/ml were added to the running buffer to final concentrations of 0.45 μg/ml (100 nM). These mixtures were then used to query individual spots on the chip surface with flow rates of 100 μL/min×2 minutes and allowed to dissociate for 600 seconds. Chip surfaces were regenerated between analytes by the addition of 0.85% phosphoric acid.

[1141] Each of antibodies Ab1, Ab2, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab5, Ab7, Ab11, Ab12, Ab4, Ab3, Ab6, Ab8, Ab9, Ab22, and Ab23 were examined under the same conditions as herein described

[1142] Sensorgrams representing affinity data of mutant peptide binding to a panel of antibodies were assessed using multiple parameters. A visual inspection was first performed for each sensorgram to assess apparent maximal response ("R_{max}") relative to the wild-type PACAP peptide (1-38). Second, a visual inspection of the dissociation phase was performed with an emphasis on the curve shape relative to the wild-type PACAP peptide. Off-rates (dissociation rates) were calculated for wild-type PACAP peptide and the binding of each mutant peptide to the panel of antibodies. Finally, as a control experiment to confirm the integrity of each peptide variant (wild-type or mutant), the binding affinity of each member of the peptide library was individually determined for each member of a panel of antibodies that were known to bind wild-type PACAP, to ensure that each Ala mutant PACAP peptide exhibited binding affinity that was similar to the binding affinity of wild-type PACAP peptide. Collective assessment of all described parameters identified PACAP amino acid residues important for PACAP/antibody binding.

[1143] Binding and dissociation data are shown in FIGS. **26**A-**45**B for binding of antibodies Ab1, Ab2, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab5, Ab7, Ab11, Ab12, Ab4, Ab3, Ab6, Ab8, Ab9, Ab22, and Ab23 to wild-type PACAP and PACAP mutants. The upper panel in each figure contains the binding data for residues in PACAP that appeared to be important for antibody binding (labeled at the right end of the graph, e.g., "10A" indicates the binding data for the mutant containing alanine at position 10 of PACAP). The lower panel provides data points representing the degree of binding of the remaining PACAP alanine mutants, i.e., PACAP alanine mutants that bound to the tested antibody similar to wild-type PACAP. Based thereon, the residue was determined to likely not be important for antibody binding. As a positive control, both the upper and lower panels for each Figure also disclose the binding data obtained using wild-type PACAP (labeled huPACAP(1-38)).

[1144] FIGS. **46**A-**47**B summarizes the PACAP residue positions determined to contribute to antibody binding affinity based on data obtained in these alanine scanning studies. The positions listed in each column identify the PACAP alanine scanning mutants whose mutation led to a decrease in PACAP/antibody binding affinity. The residue positions are listed in column 3 of FIGS. **46**A-**47**B according to the spatial arrangement of the residues along the PACAP primary sequence (from amino acid residue 1-38). The PACAP residue positions contributing most to antibody binding were interpreted to jointly comprise the epitopes bound by each antibody. Based on data obtained in these alanine scanning studies, the epitopes bound by each antibody were concluded to comprise the following residues:

[1145] (i) Ab1: residues 5, 6, 8, 10, and 13 of human PACAP;

[1146] (ii) Ab2: residues 5, 6, 8, 9, 10, 13, and 14 of human PACAP;

[1147] (iii) Ab13: residues 6, 8, 9, 10, and 13 of human PACAP;

[1148] (iv) Ab14: residues 5, 6, 8, 9, 10, and 13 of human PACAP;

[1149] (v) Ab15: residues 5, 6, 8, 9, 10, 12, 13, and 14 of human PACAP;

[1150] (vi) Ab16: residues 5, 6, 8, 10, and 13 of human PACAP;

[1151] (vii) Ab17: residues 5, 6, 8, 10, and 13 of human PACAP;

[1152] (viii) Ab18: residues 5, 6, 8, 9, 10, 12, and 13 of human PACAP;

[1153] (ix) Ab19: residues 4, 5, 6, 8, 9, 10, 12, 13, 14, and 17 of human PACAP;

[1154] (x) Ab5: residues 3, 4, 5, 6, 7, 10, 13, and 14 of human PACAP;

[1155] (xi) Ab7: residues 6, 8, 10, 11, 13, 14, and 18 of human PACAP;

[1156] (xii) Ab11: residues 6, 8, 10, 11, 13, 14, 18, and 22 of human PACAP;

[1157] (xiii) Ab12: residues 6, 8, 10, 11, 13, 14, and 18 of human PACAP;

[1158] (xiv) Ab4: residues 8, 9, 10, 13, 14, 17, and 18 of human PACAP;

[1159] (xv) Ab3: residues 8, 9, 10, 11, 12, 13, 14, 17, and 21 of human PACAP;

[1160] (xvi) Ab6: residues 5, 6, 9, 10, 12, 13, 14, and 17 of human PACAP;

[1161] (xvii) Ab8: residues 7, 10, 13, and 14 of human PACAP;

[1162] (xviii) Ab9: residues 7, 10, 12, 13, 14, and 17 of human PACAP;

[1163] (xix) Ab22: residues 22, 23, 27, 28, and 31 of human PACAP; and

[1164] (xx) Ab23: residues 12, 20, 23, 24, 26, 27, and 28 of human PACAP.

[1165] It was further noted based on the alanine scanning experimental results that the affinity of each of antibodies Ab1, Ab2, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab5, Ab7, Ab11, Ab12, Ab4, Ab3, Ab6, Ab8, and Ab9 for PACAP involves or depends on residues 10 and/or 13 of human PACAP, and in some instances involves or further depends on residues 8 and/or 14.

[1166] Additionally, it was observed that the affinity of each of antibodies Ab22 and Ab23 to PACAP involves or requires specific amino acid residues that are present in human wild-type PACAP38, but which are not present in human wild-type PACAP27, e.g., residues 28 or 31 of PACAP38.

[1167] With respect to the foregoing alanine scanning results humanized variants of the subject anti-PACAP antibodies should interact with the identical or substantially identical residues of human PACAP as humanization should not appreciably impact the specificity of the binding of the humanized anti-PACAP antibody to human PACAP compared to the parent (unhumanized) antibody. Particularly, Ab3.H should interact with the same residues on human PACAP as Ab3, Ab4.H should interact with the same residues on human PACAP as Ab4, Ab5.H should interact with the same residues on human PACAP as Ab5, Ab9.H should interact with the same residues on human PACAP Ab9, and Ab12.H should interact with the same residues on human PACAP as Ab12.

[1168] Antibodies which bind to the same or overlapping epitopes on human PACAP as the subject antibodies may be produced and identified using method described herein. It is reasonable to anticipate that antibodies which bind to the same or overlapping epitope as any of the antibodies identified herein will likely possess similar biological activity absent a meaningful difference in binding kinetics. Particularly, such antibodies should antagonize one or more of the biological effects elicited by PACAP analogously to the exemplified anti-PACAP antibodies which bind these epitopes. Additionally, antibodies that bind to these same or overlapping epitopes, or a subset of residues thereof, are anticipated to mimic the binding characteristics of the subject antibodies. For example such antibodies are expected to selectively bind to PACAP and not bind or bind with much less affinity (weaker) to VIP or other peptides within this family of neuropeptides.

[1169] Having fully described and enabled the invention, the invention is further described by the claims that follow.

SEQUENCE LISTING

<160> NUMBER OF SEQ ID NOS: 1246

<210> SEQ ID NO 1
<211> LENGTH: 443
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 1

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Gln Ser Val Glu Glu Ser Gly Gly Arg Leu Val Thr Pro Gly Thr Pro
1               5                  10                  15

Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Ser Ser Ala Val
            20                  25                  30

Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
        35                  40                  45

Ser Ile Val Ala Ser Gly Thr Thr Tyr Tyr Ala Ser Trp Ala Asn Gly
    50                  55                  60

Arg Phe Thr Ile Ser Lys Thr Ser Ser Thr Thr Met Asp Leu Lys Met
65                  70                  75                  80

Thr Ser Pro Thr Thr Glu Asp Thr Ala Thr Tyr Phe Cys Ala Arg Gly
                85                  90                  95

Gly Gly Glu Phe Phe Ile Trp Gly Pro Gly Thr Leu Val Thr Val Ser
            100                 105                 110

Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser
        115                 120                 125

Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp
    130                 135                 140
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Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
145                 150                 155                 160

Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr
                165                 170                 175

Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln
            180                 185                 190

Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp
        195                 200                 205

Ala Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro
    210                 215                 220

Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro
225                 230                 235                 240

Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr
                245                 250                 255

Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn
            260                 265                 270

Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
        275                 280                 285

Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
    290                 295                 300

Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
305                 310                 315                 320

Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys
                325                 330                 335

Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu
            340                 345                 350

Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
        355                 360                 365

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
    370                 375                 380

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
385                 390                 395                 400

Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
                405                 410                 415

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
            420                 425                 430

Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
        435                 440


<210> SEQ ID NO 2
<211> LENGTH: 113
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 2

Gln Ser Val Glu Glu Ser Gly Gly Arg Leu Val Thr Pro Gly Thr Pro
1               5                   10                  15

Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Ser Ser Ala Val
            20                  25                  30

Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
        35                  40                  45
```

-continued

Ser Ile Val Ala Ser Gly Thr Thr Tyr Tyr Ala Ser Trp Ala Asn Gly
50 55 60

Arg Phe Thr Ile Ser Lys Thr Ser Ser Thr Thr Met Asp Leu Lys Met
65 70 75 80

Thr Ser Pro Thr Thr Glu Asp Thr Ala Thr Tyr Phe Cys Ala Arg Gly
85 90 95

Gly Gly Glu Phe Phe Ile Trp Gly Pro Gly Thr Leu Val Thr Val Ser
100 105 110

Ser

<210> SEQ ID NO 3
<211> LENGTH: 29
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 3

Gln Ser Val Glu Glu Ser Gly Gly Arg Leu Val Thr Pro Gly Thr Pro
1 5 10 15

Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Ser
20 25

<210> SEQ ID NO 4
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 4

Ser Ala Val Met Asn
1 5

<210> SEQ ID NO 5
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 5

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
1 5 10

<210> SEQ ID NO 6
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 6

Ser Ile Val Ala Ser Gly Thr Thr Tyr Tyr Ala Ser Trp Ala Asn Gly
1 5 10 15

<210> SEQ ID NO 7
<211> LENGTH: 31
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 7

Arg Phe Thr Ile Ser Lys Thr Ser Ser Thr Thr Met Asp Leu Lys Met
1 5 10 15

Thr Ser Pro Thr Thr Glu Asp Thr Ala Thr Tyr Phe Cys Ala Arg
20 25 30

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<210> SEQ ID NO 8
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 8

Gly Gly Gly Glu Phe Phe Ile
1 5

<210> SEQ ID NO 9
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 9

Trp Gly Pro Gly Thr Leu Val Thr Val Ser Ser
1 5 10

<210> SEQ ID NO 10
<211> LENGTH: 330
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 10

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65 70 75 80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Ala
85 90 95

Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
100 105 110

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
115 120 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
130 135 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145 150 155 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
165 170 175

Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
180 185 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
195 200 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
210 215 220

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Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
225                 230                 235                 240

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
                245                 250                 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
            260                 265                 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
        275                 280                 285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
    290                 295                 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305                 310                 315                 320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
                325                 330


<210> SEQ ID NO 11
<211> LENGTH: 1329
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 11

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tgcaccgtct ctggattctc cctcagtagc gctgtaatga attgggtccg ccaggctcca    120

gggaaggggc tggaatggat cggaagtatt gttgctagtg gtaccacata ctacgcgagc    180

tgggcgaacg gccgattcac catctccaaa acctcgtcga ccacgatgga tctgaaaatg    240

accagtccga caaccgagga cacggccacc tatttctgtg ccagaggggg aggggaattt    300

ttcatctggg gcccggggac cctcgtcacc gtctcgagcg cctccaccaa gggcccatcg    360

gtcttccccc tggcaccctc ctccaagagc acctctgggg gcacagcggc cctgggctgc    420

ctggtcaagg actacttccc cgaaccggtg acggtgtcgt ggaactcagg cgccctgacc    480

agcggcgtgc acaccttccc ggctgtccta cagtcctcag gactctactc cctcagcagc    540

gtggtgaccg tgccctccag cagcttgggc acccagacct acatctgcaa cgtgaatcac    600

aagcccagca acaccaaggt ggacgcgaga gttgagccca aatcttgtga caaaactcac    660

acatgcccac cgtgcccagc acctgaactc ctgggggggac cgtcagtctt cctcttcccc    720

ccaaaaccca aggacaccct catgatctcc cggacccctg aggtcacatg cgtggtggtg    780

gacgtgagcc acgaagaccc tgaggtcaag ttcaactggt acgtggacgg cgtggaggtg    840

cataatgcca agacaaagcc gcgggaggag cagtacgcca gcacgtaccg tgtggtcagc    900

gtcctcaccg tcctgcacca ggactggctg aatggcaagg agtacaagtg caaggtctcc    960

aacaaagccc tcccagcccc catcgagaaa accatctcca aagccaaagg gcagccccga   1020

gaaccacagg tgtacaccct gcccccatcc cgggaggaga tgaccaagaa ccaggtcagc   1080

ctgacctgcc tggtcaaagg cttctatccc agcgacatcg ccgtggagtg ggagagcaat   1140

gggcagccgg agaacaacta caagaccacg cctcccgtgc tggactccga cggctccttc   1200

ttcctctaca gcaagctcac cgtggacaag agcaggtggc agcaggggaa cgtcttctca   1260

tgctccgtga tgcatgaggc tctgcacaac cactacacgc agaagagcct ctccctgtct   1320

ccgggtaaa                                                          1329
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<210> SEQ ID NO 12
<211> LENGTH: 339
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 12

cagtcggtgg aggagtccgg gggtcgcctg gtcacgcctg ggacacccct gacactcacc 60

tgcaccgtct ctggattctc cctcagtagc gctgtaatga attgggtccg ccaggctcca 120

gggaaggggc tggaatggat cggaagtatt gttgctagtg gtaccacata ctacgcgagc 180

tgggcgaacg gccgattcac catctccaaa acctcgtcga ccacgatgga tctgaaaatg 240

accagtccga caaccgagga cacggccacc tatttctgtg ccagaggggg aggggaattt 300

ttcatctggg gcccggggac cctcgtcacc gtctcgagc 339

<210> SEQ ID NO 13
<211> LENGTH: 87
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 13

cagtcggtgg aggagtccgg gggtcgcctg gtcacgcctg ggacacccct gacactcacc 60

tgcaccgtct ctggattctc cctcagt 87

<210> SEQ ID NO 14
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 14

agcgctgtaa tgaat 15

<210> SEQ ID NO 15
<211> LENGTH: 42
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 15

tgggtccgcc aggctccagg gaaggggctg gaatggatcg ga 42

<210> SEQ ID NO 16
<211> LENGTH: 48
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 16

agtattgttg ctagtggtac cacatactac gcgagctggg cgaacggc 48

<210> SEQ ID NO 17
<211> LENGTH: 93
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 17

cgattcacca tctccaaaac ctcgtcgacc acgatggatc tgaaaatgac cagtccgaca 60

accgaggaca cggccaccta tttctgtgcc aga 93

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<210> SEQ ID NO 18
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 18

gggggagggg aatttttcat c 21

<210> SEQ ID NO 19
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 19

tggggcccgg ggaccctcgt caccgtctcg agc 33

<210> SEQ ID NO 20
<211> LENGTH: 990
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 20

gcctccacca agggcccatc ggtcttcccc ctggcaccct cctccaagag cacctctggg 60

ggcacagcgg ccctgggctg cctggtcaag gactacttcc ccgaaccggt gacggtgtcg 120

tggaactcag gcgccctgac cagcggcgtg cacaccttcc cggctgtcct acagtcctca 180

ggactctact ccctcagcag cgtggtgacc gtgccctcca gcagcttggg cacccagacc 240

tacatctgca acgtgaatca caagcccagc aacaccaagg tggacgcgag agttgagccc 300

aaatcttgtg acaaaactca cacatgccca ccgtgcccag cacctgaact cctgggggga 360

ccgtcagtct tcctcttccc cccaaaaccc aaggacaccc tcatgatctc ccggaccccct 420

gaggtcacat gcgtggtggt ggacgtgagc cacgaagacc ctgaggtcaa gttcaactgg 480

tacgtggacg gcgtggaggt gcataatgcc aagacaaagc cgcgggagga gcagtacgcc 540

agcacgtacc gtgtggtcag cgtcctcacc gtcctgcacc aggactggct gaatggcaag 600

gagtacaagt gcaaggtctc caacaaagcc ctcccagccc ccatcgagaa aaccatctcc 660

aaagccaaag ggcagccccg agaaccacag gtgtacaccc tgcccccatc ccgggaggag 720

atgaccaaga accaggtcag cctgacctgc ctggtcaaag gcttctatcc cagcgacatc 780

gccgtggagt gggagagcaa tgggcagccg gagaacaact acaagaccac gcctcccgtg 840

ctggactccg acggctcctt cttcctctac agcaagctca ccgtggacaa gagcaggtgg 900

cagcagggga acgtcttctc atgctccgtg atgcatgagg ctctgcacaa ccactacacg 960

cagaagagcc tctccctgtc tccgggtaaa 990

<210> SEQ ID NO 21
<211> LENGTH: 216
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 21

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Asp Pro Val Met Thr Gln Thr Pro Ser Ser Thr Ser Ala Ala Val Gly
1               5                   10                  15

Gly Thr Val Thr Ile Ser Cys Gln Ser Ser Glu Ser Val Tyr Ser Asn
            20                  25                  30

Tyr Leu Ser Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Asn Phe Leu
        35                  40                  45

Ile Tyr Gln Ala Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Lys
    50                  55                  60

Gly Ser Gly Ser Gly Thr Gln Phe Thr Leu Thr Ile Thr Asp Leu Glu
65                  70                  75                  80

Cys Asp Asp Ala Ala Thr Tyr Tyr Cys Ala Gly Gly Tyr Ser Glu Asn
                85                  90                  95

Ile Val Gly Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg Thr Val
            100                 105                 110

Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys
        115                 120                 125

Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg
    130                 135                 140

Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn
145                 150                 155                 160

Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser
                165                 170                 175

Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys
            180                 185                 190

Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr
        195                 200                 205

Lys Ser Phe Asn Arg Gly Glu Cys
    210                 215


<210> SEQ ID NO 22
<211> LENGTH: 110
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 22

Asp Pro Val Met Thr Gln Thr Pro Ser Ser Thr Ser Ala Ala Val Gly
1               5                   10                  15

Gly Thr Val Thr Ile Ser Cys Gln Ser Ser Glu Ser Val Tyr Ser Asn
            20                  25                  30

Tyr Leu Ser Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Asn Phe Leu
        35                  40                  45

Ile Tyr Gln Ala Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Lys
    50                  55                  60

Gly Ser Gly Ser Gly Thr Gln Phe Thr Leu Thr Ile Thr Asp Leu Glu
65                  70                  75                  80

Cys Asp Asp Ala Ala Thr Tyr Tyr Cys Ala Gly Gly Tyr Ser Glu Asn
                85                  90                  95

Ile Val Gly Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg
            100                 105                 110


<210> SEQ ID NO 23
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<211> LENGTH: 23
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 23

Asp Pro Val Met Thr Gln Thr Pro Ser Ser Thr Ser Ala Ala Val Gly
1 5 10 15

Gly Thr Val Thr Ile Ser Cys
20

<210> SEQ ID NO 24
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 24

Gln Ser Ser Glu Ser Val Tyr Ser Asn Tyr Leu Ser
1 5 10

<210> SEQ ID NO 25
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 25

Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Asn Phe Leu Ile Tyr
1 5 10 15

<210> SEQ ID NO 26
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 26

Gln Ala Ser Asn Leu Ala Ser
1 5

<210> SEQ ID NO 27
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 27

Gly Val Pro Ser Arg Phe Lys Gly Ser Gly Ser Gly Thr Gln Phe Thr
1 5 10 15

Leu Thr Ile Thr Asp Leu Glu Cys Asp Asp Ala Ala Thr Tyr Tyr Cys
20 25 30

<210> SEQ ID NO 28
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 28

Ala Gly Gly Tyr Ser Glu Asn Ile Val Gly
1 5 10

<210> SEQ ID NO 29
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:

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<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 29

Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg
1 5 10

<210> SEQ ID NO 30
<211> LENGTH: 106
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 30

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
1 5 10 15

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
20 25 30

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
35 40 45

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
50 55 60

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
65 70 75 80

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
85 90 95

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
100 105

<210> SEQ ID NO 31
<211> LENGTH: 648
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 31

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atcagttgcc agtccagtga gagtgtttat agtaactact tatcctggta tcagcagaaa 120

ccagggcagc ctcccaactt cctgatctac caggcatcca atttggcatc tggggtccca 180

tcgcggttca aaggcagtgg atctgggaca cagttcactc tcaccatcac cgacctggag 240

tgtgacgatg ccgccactta ttactgtgca ggcggttata gtgaaaacat tgttggtttc 300

ggcggaggga ccgaggtggt ggtcaaacgt acggtagcgg ccccatctgt cttcatcttc 360

ccgccatctg atgagcagtt gaaatctgga actgcctctg ttgtgtgcct gctgaataac 420

ttctatccca gagaggccaa agtacagtgg aaggtggata acgccctcca atcgggtaac 480

tcccaggaga gtgtcacaga gcaggacagc aaggacagca cctacagcct cagcagcacc 540

ctgacgctga gcaaagcaga ctacgagaaa cacaaagtct acgcctgcga agtcacccat 600

cagggcctga gctcgcccgt cacaaagagc ttcaacaggg gagagtgt 648

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<211> LENGTH: 330
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:

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<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 32

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atcagttgcc agtccagtga gagtgtttat agtaactact tatcctggta tcagcagaaa 120

ccagggcagc ctcccaactt cctgatctac caggcatcca atttggcatc tggggtccca 180

tcgcggttca aaggcagtgg atctgggaca cagttcactc tcaccatcac cgacctggag 240

tgtgacgatg ccgccactta ttactgtgca ggcggttata gtgaaaacat tgttggtttc 300

ggcggaggga ccgaggtggt ggtcaaacgt 330

<210> SEQ ID NO 33
<211> LENGTH: 69
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 33

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atcagttgc 69

<210> SEQ ID NO 34
<211> LENGTH: 36
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 34

cagtccagtg agagtgttta tagtaactac ttatcc 36

<210> SEQ ID NO 35
<211> LENGTH: 45
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 35

tggtatcagc agaaaccagg gcagcctccc aacttcctga tctac 45

<210> SEQ ID NO 36
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 36

caggcatcca atttggcatc t 21

<210> SEQ ID NO 37
<211> LENGTH: 96
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 37

ggggtcccat cgcggttcaa aggcagtgga tctgggacac agttcactct caccatcacc 60

gacctggagt gtgacgatgc cgccacttat tactgt 96

<210> SEQ ID NO 38
<211> LENGTH: 30
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

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<400> SEQUENCE: 38

gcaggcggtt atagtgaaaa cattgttggt 30

<210> SEQ ID NO 39
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 39

ttcggcggag ggaccgaggt ggtggtcaaa cgt 33

<210> SEQ ID NO 40
<211> LENGTH: 318
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 40

acggtagcgg ccccatctgt cttcatcttc ccgccatctg atgagcagtt gaaatctgga 60

actgcctctg ttgtgtgcct gctgaataac ttctatccca gagaggccaa agtacagtgg 120

aaggtggata acgccctcca atcgggtaac tcccaggaga gtgtcacaga gcaggacagc 180

aaggacagca cctacagcct cagcagcacc ctgacgctga gcaaagcaga ctacgagaaa 240

cacaaagtct acgcctgcga agtcacccat cagggcctga gctcgcccgt cacaaagagc 300

ttcaacaggg gagagtgt 318

<210> SEQ ID NO 41
<211> LENGTH: 445
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 41

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Val Ser Ser Ala
20 25 30

Val Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Ser Ile Val Ala Ser Gly Thr Thr Tyr Tyr Ala Ser Ser Ala Asn
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Arg Gly Gly Gly Glu Phe Phe Ile Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
115 120 125

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
130 135 140

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala

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145                 150                 155                 160

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
                165                 170                 175

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
            180                 185                 190

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
        195                 200                 205

Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
    210                 215                 220

Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu
225                 230                 235                 240

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
                245                 250                 255

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
            260                 265                 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
        275                 280                 285

Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu
    290                 295                 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305                 310                 315                 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
                325                 330                 335

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
            340                 345                 350

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
        355                 360                 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
    370                 375                 380

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
385                 390                 395                 400

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
                405                 410                 415

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
            420                 425                 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
        435                 440                 445


<210> SEQ ID NO 42
<211> LENGTH: 115
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 42

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Val Ser Ser Ala
            20                  25                  30

Val Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile
        35                  40                  45

Gly Ser Ile Val Ala Ser Gly Thr Thr Tyr Tyr Ala Ser Ser Ala Asn
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    50                  55                  60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu
65                  70                  75                  80

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95

Arg Gly Gly Gly Glu Phe Phe Ile Trp Gly Gln Gly Thr Leu Val Thr
            100                 105                 110

Val Ser Ser
        115


<210> SEQ ID NO 43
<211> LENGTH: 30
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 43

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Val Ser
            20                  25                  30


<210> SEQ ID NO 44
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 44

Ser Ala Val Met Asn
1               5


<210> SEQ ID NO 45
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 45

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
1               5                   10


<210> SEQ ID NO 46
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 46

Ser Ile Val Ala Ser Gly Thr Thr Tyr Tyr Ala Ser Ser Ala Asn Gly
1               5                   10                  15


<210> SEQ ID NO 47
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 47
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Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln
1               5                   10                  15

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
            20                  25                  30


<210> SEQ ID NO 48
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 48

Gly Gly Gly Glu Phe Phe Ile
1               5


<210> SEQ ID NO 49
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 49

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
1               5                   10


<210> SEQ ID NO 50
<211> LENGTH: 330
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 50

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1               5                   10                  15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
            20                  25                  30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
        35                  40                  45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
    50                  55                  60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65                  70                  75                  80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
                85                  90                  95

Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
            100                 105                 110

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
        115                 120                 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
    130                 135                 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145                 150                 155                 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
                165                 170                 175

Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
            180                 185                 190
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His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
        195                 200                 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
    210                 215                 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
225                 230                 235                 240

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
                245                 250                 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
            260                 265                 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
        275                 280                 285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
    290                 295                 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305                 310                 315                 320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
                325                 330


<210> SEQ ID NO 51
<211> LENGTH: 1335
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 51

gaggtgcagc ttgtggagtc tgggggaggc ttggtccagc ctgggggtc cctgagactc     60

tcctgtgcag cctctggatt caccgtcagt agcgctgtaa tgaattgggt ccgtcaggct    120

ccagggaagg ggctggagtg gatcggaagt attgttgcta gtggtaccac atactacgct    180

agctctgcta acggccgatt caccatctcc agagacaatt ccaagaacac cctgtatctt    240

caaatgaaca gcctgagagc tgaggacact gctgtgtatt actgtgctag agggggaggg    300

gaatttttca tctggggcca agggaccctc gtcaccgtct cgagcgcctc caccaagggc    360

ccatcggtct tccccctggc accctcctcc aagagcacct ctgggggcac agcggccctg    420

ggctgcctgg tcaaggacta cttccccgaa ccggtgacgg tgtcgtggaa ctcaggcgcc    480

ctgaccagcg gcgtgcacac cttcccggct gtcctacagt cctcaggact ctactccctc    540

agcagcgtgg tgaccgtgcc ctccagcagc ttgggcaccc agacctacat ctgcaacgtg    600

aatcacaagc ccagcaacac caaggtggac aagaaagttg agcccaaatc ttgtgacaaa    660

actcacacat gcccaccgtg cccagcacct gaactcctgg ggggaccgtc agtcttcctc    720

ttccccccaa aacccaagga caccctcatg atctcccgga cccctgaggt cacatgcgtg    780

gtggtggacg tgagccacga agaccctgag gtcaagttca actggtacgt ggacggcgtg    840

gaggtgcata atgccaagac aaagccgcgg gaggagcagt acgccagcac gtaccgtgtg    900

gtcagcgtcc tcaccgtcct gcaccaggac tggctgaatg gcaaggagta caagtgcaag    960

gtctccaaca aagccctccc agcccccatc gagaaaacca tctccaaagc caaagggcag   1020

ccccgagaac cacaggtgta caccctgccc ccatcccggg aggagatgac caagaaccag   1080

gtcagcctga cctgcctggt caaaggcttc tatcccagcg acatcgccgt ggagtgggag   1140
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agcaatgggc agccggagaa caactacaag accacgcctc ccgtgctgga ctccgacggc 1200

tccttcttcc tctacagcaa gctcaccgtg gacaagagca ggtggcagca ggggaacgtc 1260

ttctcatgct ccgtgatgca tgaggctctg cacaaccact acacgcagaa gagcctctcc 1320

ctgtctccgg gtaaa 1335

<210> SEQ ID NO 52
<211> LENGTH: 345
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 52

gaggtgcagc ttgtggagtc tgggggaggc ttggtccagc ctgggggtc cctgagactc 60

tcctgtgcag cctctggatt caccgtcagt agcgctgtaa tgaattgggt ccgtcaggct 120

ccagggaagg ggctggagtg gatcggaagt attgttgcta gtggtaccac atactacgct 180

agctctgcta acggccgatt caccatctcc agagacaatt ccaagaacac cctgtatctt 240

caaatgaaca gcctgagagc tgaggacact gctgtgtatt actgtgctag agggggaggg 300

gaatttttca tctggggcca agggaccctc gtcaccgtct cgagc 345

<210> SEQ ID NO 53
<211> LENGTH: 90
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 53

gaggtgcagc ttgtggagtc tgggggaggc ttggtccagc ctgggggtc cctgagactc 60

tcctgtgcag cctctggatt caccgtcagt 90

<210> SEQ ID NO 54
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 54

agcgctgtaa tgaat 15

<210> SEQ ID NO 55
<211> LENGTH: 42
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 55

tgggtccgtc aggctccagg gaaggggctg gagtggatcg ga 42

<210> SEQ ID NO 56
<211> LENGTH: 48
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 56

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agtattgttg ctagtggtac cacatactac gctagctctg ctaacggc 48

<210> SEQ ID NO 57
<211> LENGTH: 96
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 57

cgattcacca tctccagaga caattccaag aacaccctgt atcttcaaat gaacagcctg 60

agagctgagg acactgctgt gtattactgt gctaga 96

<210> SEQ ID NO 58
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 58

gggggagggg aatttttcat c 21

<210> SEQ ID NO 59
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 59

tggggccaag ggaccctcgt caccgtctcg agc 33

<210> SEQ ID NO 60
<211> LENGTH: 990
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 60

gcctccacca agggcccatc ggtcttcccc ctggcaccct cctccaagag cacctctggg 60

ggcacagcgg ccctgggctg cctggtcaag gactacttcc ccgaaccggt gacggtgtcg 120

tggaactcag gcgccctgac cagcggcgtg cacaccttcc cggctgtcct acagtcctca 180

ggactctact ccctcagcag cgtggtgacc gtgccctcca gcagcttggg cacccagacc 240

tacatctgca acgtgaatca caagcccagc aacaccaagg tggacaagaa agttgagccc 300

aaatcttgtg acaaaactca cacatgccca ccgtgcccag cacctgaact cctgggggga 360

ccgtcagtct tcctcttccc cccaaaaccc aaggacaccc tcatgatctc ccggacccct 420

gaggtcacat gcgtggtggt ggacgtgagc cacgaagacc ctgaggtcaa gttcaactgg 480

tacgtggacg gcgtggaggt gcataatgcc aagacaaagc cgcgggagga gcagtacgcc 540

agcacgtacc gtgtggtcag cgtcctcacc gtcctgcacc aggactggct gaatggcaag 600

gagtacaagt gcaaggtctc caacaaagcc ctcccagccc ccatcgagaa aaccatctcc 660

aaagccaaag ggcagccccg agaaccacag gtgtacaccc tgcccccatc ccgggaggag 720

atgaccaaga accaggtcag cctgacctgc ctggtcaaag gcttctatcc cagcgacatc 780

gccgtggagt gggagagcaa tgggcagccg gagaacaact acaagaccac gcctcccgtg 840

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ctggactccg acggctcctt cttcctctac agcaagctca ccgtggacaa gagcaggtgg 900

cagcagggga acgtcttctc atgctccgtg atgcatgagg ctctgcacaa ccactacacg 960

cagaagagcc tctccctgtc tccgggtaaa 990

<210> SEQ ID NO 61
<211> LENGTH: 216
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 61

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Gln Ser Ser Glu Ser Val Tyr Ser Asn
20 25 30

Tyr Leu Ser Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Phe Leu
35 40 45

Ile Tyr Gln Ala Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln
65 70 75 80

Pro Asp Asp Phe Ala Thr Tyr Tyr Cys Ala Gly Gly Tyr Ser Glu Asn
85 90 95

Ile Val Gly Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val
100 105 110

Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys
115 120 125

Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg
130 135 140

Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn
145 150 155 160

Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser
165 170 175

Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys
180 185 190

Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr
195 200 205

Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> SEQ ID NO 62
<211> LENGTH: 110
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 62

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Gln Ser Ser Glu Ser Val Tyr Ser Asn
20 25 30

Tyr Leu Ser Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Phe Leu
35 40 45

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Ile Tyr Gln Ala Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln
65 70 75 80

Pro Asp Asp Phe Ala Thr Tyr Tyr Cys Ala Gly Gly Tyr Ser Glu Asn
85 90 95

Ile Val Gly Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg
100 105 110

<210> SEQ ID NO 63
<211> LENGTH: 23
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 63

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys
20

<210> SEQ ID NO 64
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 64

Gln Ser Ser Glu Ser Val Tyr Ser Asn Tyr Leu Ser
1 5 10

<210> SEQ ID NO 65
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 65

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Phe Leu Ile Tyr
1 5 10 15

<210> SEQ ID NO 66
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 66

Gln Ala Ser Asn Leu Ala Ser
1 5

<210> SEQ ID NO 67
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 67

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr
1 5 10 15

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Leu Thr Ile Ser Ser Leu Gln Pro Asp Asp Phe Ala Thr Tyr Tyr Cys
20 25 30

<210> SEQ ID NO 68
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 68

Ala Gly Gly Tyr Ser Glu Asn Ile Val Gly
1 5 10

<210> SEQ ID NO 69
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 69

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg
1 5 10

<210> SEQ ID NO 70
<211> LENGTH: 106
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 70

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
1 5 10 15

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
20 25 30

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
35 40 45

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
50 55 60

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
65 70 75 80

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
85 90 95

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
100 105

<210> SEQ ID NO 71
<211> LENGTH: 648
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 71

gacatccaga tgacccagtc tccttccacc ctgtctgcat ctgtaggaga cagagtcacc 60

atcacttgtc agtccagtga gagtgtttat agtaactact tatcctggta tcagcagaaa 120

ccaggaaaag cccctaagtt cctgatctat caggcatcca atttggcatc tggagtccca 180

tcaaggttca gcggcagtgg atctggaaca gaattcactc tcaccatcag cagcctgcag 240

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cctgatgatt ttgcaactta ctactgtgca ggcggttata gtgaaaacat tgttggtttc 300

ggcggaggaa ccaaggtgga aatcaaacgt acggtagcgg ccccatctgt cttcatcttc 360

ccgccatctg atgagcagtt gaaatctgga actgcctctg ttgtgtgcct gctgaataac 420

ttctatccca gagaggccaa agtacagtgg aaggtggata acgccctcca atcgggtaac 480

tcccaggaga gtgtcacaga gcaggacagc aaggacagca cctacagcct cagcagcacc 540

ctgacgctga gcaaagcaga ctacgagaaa cacaaagtct acgcctgcga agtcacccat 600

cagggcctga gctcgcccgt cacaaagagc ttcaacaggg gagagtgt 648

<210> SEQ ID NO 72
<211> LENGTH: 330
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 72

gacatccaga tgacccagtc tccttccacc ctgtctgcat ctgtaggaga cagagtcacc 60

atcacttgtc agtccagtga gagtgtttat agtaactact tatcctggta tcagcagaaa 120

ccaggaaaag cccctaagtt cctgatctat caggcatcca atttggcatc tggagtccca 180

tcaaggttca gcggcagtgg atctggaaca gaattcactc tcaccatcag cagcctgcag 240

cctgatgatt ttgcaactta ctactgtgca ggcggttata gtgaaaacat tgttggtttc 300

ggcggaggaa ccaaggtgga aatcaaacgt 330

<210> SEQ ID NO 73
<211> LENGTH: 69
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 73

gacatccaga tgacccagtc tccttccacc ctgtctgcat ctgtaggaga cagagtcacc 60

atcacttgt 69

<210> SEQ ID NO 74
<211> LENGTH: 36
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 74

cagtccagtg agagtgttta tagtaactac ttatcc 36

<210> SEQ ID NO 75
<211> LENGTH: 45
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 75

tggtatcagc agaaaccagg aaaagcccct aagttcctga tctat 45

<210> SEQ ID NO 76
<211> LENGTH: 21

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<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 76

caggcatcca atttggcatc t 21

<210> SEQ ID NO 77
<211> LENGTH: 96
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 77

ggagtcccat caaggttcag cggcagtgga tctggaacag aattcactct caccatcagc 60

agcctgcagc ctgatgattt tgcaacttac tactgt 96

<210> SEQ ID NO 78
<211> LENGTH: 30
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 78

gcaggcggtt atagtgaaaa cattgttggt 30

<210> SEQ ID NO 79
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 79

ttcggcggag gaaccaaggt ggaaatcaaa cgt 33

<210> SEQ ID NO 80
<211> LENGTH: 318
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 80

acggtagcgg ccccatctgt cttcatcttc ccgccatctg atgagcagtt gaaatctgga 60

actgcctctg ttgtgtgcct gctgaataac ttctatccca gagaggccaa agtacagtgg 120

aaggtggata acgccctcca atcgggtaac tcccaggaga gtgtcacaga gcaggacagc 180

aaggacagca cctacagcct cagcagcacc ctgacgctga gcaaagcaga ctacgagaaa 240

cacaaagtct acgcctgcga agtcacccat cagggcctga gctcgcccgt cacaaagagc 300

ttcaacaggg gagagtgt 318

<210> SEQ ID NO 81
<211> LENGTH: 443
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 81

Gln Ser Val Glu Glu Ser Gly Gly Arg Leu Val Thr Pro Gly Thr Pro

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1               5                   10                  15

Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Ser Gly Ala Ala
            20                  25                  30

Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
        35                  40                  45

Val Ile Gly Asn Ser Gly Ser Thr Tyr Tyr Ala Ser Trp Ala Lys Gly
    50                  55                  60

Arg Phe Thr Ile Ser Lys Thr Ser Ser Thr Thr Val Asp Leu Lys Met
65                  70                  75                  80

Thr Ser Pro Thr Thr Glu Asp Thr Ala Thr Tyr Phe Cys Ala Arg Gly
                85                  90                  95

Gly Gly Glu Phe Phe Ile Trp Gly Gln Gly Thr Leu Val Thr Val Ser
            100                 105                 110

Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser
        115                 120                 125

Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp
    130                 135                 140

Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
145                 150                 155                 160

Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr
                165                 170                 175

Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln
            180                 185                 190

Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp
        195                 200                 205

Ala Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro
    210                 215                 220

Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro
225                 230                 235                 240

Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr
                245                 250                 255

Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn
            260                 265                 270

Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
        275                 280                 285

Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
    290                 295                 300

Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
305                 310                 315                 320

Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys
                325                 330                 335

Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu
            340                 345                 350

Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
        355                 360                 365

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
    370                 375                 380

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
385                 390                 395                 400

Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
                405                 410                 415
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Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
420 425 430

Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440

<210> SEQ ID NO 82
<211> LENGTH: 113
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 82

Gln Ser Val Glu Glu Ser Gly Gly Arg Leu Val Thr Pro Gly Thr Pro
1 5 10 15

Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Ser Gly Ala Ala
20 25 30

Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
35 40 45

Val Ile Gly Asn Ser Gly Ser Thr Tyr Tyr Ala Ser Trp Ala Lys Gly
50 55 60

Arg Phe Thr Ile Ser Lys Thr Ser Ser Thr Thr Val Asp Leu Lys Met
65 70 75 80

Thr Ser Pro Thr Thr Glu Asp Thr Ala Thr Tyr Phe Cys Ala Arg Gly
85 90 95

Gly Gly Glu Phe Phe Ile Trp Gly Gln Gly Thr Leu Val Thr Val Ser
100 105 110

Ser

<210> SEQ ID NO 83
<211> LENGTH: 29
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 83

Gln Ser Val Glu Glu Ser Gly Gly Arg Leu Val Thr Pro Gly Thr Pro
1 5 10 15

Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Ser
20 25

<210> SEQ ID NO 84
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 84

Gly Ala Ala Met Asn
1 5

<210> SEQ ID NO 85
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 85

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
1 5 10

-continued

<210> SEQ ID NO 86
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 86

Val Ile Gly Asn Ser Gly Ser Thr Tyr Tyr Ala Ser Trp Ala Lys Gly
1 5 10 15

<210> SEQ ID NO 87
<211> LENGTH: 31
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 87

Arg Phe Thr Ile Ser Lys Thr Ser Ser Thr Thr Val Asp Leu Lys Met
1 5 10 15

Thr Ser Pro Thr Thr Glu Asp Thr Ala Thr Tyr Phe Cys Ala Arg
20 25 30

<210> SEQ ID NO 88
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 88

Gly Gly Gly Glu Phe Phe Ile
1 5

<210> SEQ ID NO 89
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 89

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
1 5 10

<210> SEQ ID NO 90
<211> LENGTH: 330
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 90

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65 70 75 80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Ala
85 90 95

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Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
            100                 105                 110

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
        115                 120                 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
    130                 135                 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145                 150                 155                 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
                165                 170                 175

Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
            180                 185                 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
        195                 200                 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
    210                 215                 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
225                 230                 235                 240

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
                245                 250                 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
            260                 265                 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
        275                 280                 285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
    290                 295                 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305                 310                 315                 320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
                325                 330


<210> SEQ ID NO 91
<211> LENGTH: 1329
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 91

cagtcggtgg aggagtccgg gggtcgcctg gtcacgcctg ggacacccct gacactcacc     60

tgcaccgtct ctggattctc cctcagtggc gctgcgatga actgggtccg ccaggctcca    120

gggaaggggc tggaatggat cggagttatt ggtaatagtg gtagcacata ctacgcgtcc    180

tgggcgaaag gccgattcac catctccaaa acctcgtcga ccacggtgga tctgaaaatg    240

accagtccga caaccgagga cacggccacc tatttctgtg ccagaggggg aggggaattt    300

ttcatctggg gccaagggac cctggtcacc gtctcgagcg cctccaccaa gggcccatcg    360

gtcttccccc tggcaccctc ctccaagagc acctctgggg gcacagcggc cctgggctgc    420

ctggtcaagg actacttccc cgaaccggtg acggtgtcgt ggaactcagg cgccctgacc    480

agcggcgtgc acaccttccc ggctgtccta cagtcctcag gactctactc cctcagcagc    540

gtggtgaccg tgccctccag cagcttgggc acccagacct acatctgcaa cgtgaatcac    600
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aagcccagca acaccaaggt ggacgcgaga gttgagccca aatcttgtga caaaactcac 660

acatgcccac cgtgcccagc acctgaactc ctgggggggac cgtcagtctt cctcttcccc 720

ccaaaaccca aggacaccct catgatctcc cggacccctg aggtcacatg cgtggtggtg 780

gacgtgagcc acgaagaccc tgaggtcaag ttcaactggt acgtggacgg cgtggaggtg 840

cataatgcca agacaaagcc gcgggaggag cagtacgcca gcacgtaccg tgtggtcagc 900

gtcctcaccg tcctgcacca ggactggctg aatggcaagg agtacaagtg caaggtctcc 960

aacaaagccc tcccagcccc catcgagaaa accatctcca aagccaaagg gcagccccga 1020

gaaccacagg tgtacaccct gcccccatcc cgggaggaga tgaccaagaa ccaggtcagc 1080

ctgacctgcc tggtcaaagg cttctatccc agcgacatcg ccgtggagtg ggagagcaat 1140

gggcagccgg agaacaacta caagaccacg cctcccgtgc tggactccga cggctccttc 1200

ttcctctaca gcaagctcac cgtggacaag agcaggtggc agcaggggaa cgtcttctca 1260

tgctccgtga tgcatgaggc tctgcacaac cactacacgc agaagagcct ctccctgtct 1320

ccgggtaaa 1329

<210> SEQ ID NO 92
<211> LENGTH: 339
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 92

cagtcggtgg aggagtccgg gggtcgcctg gtcacgcctg ggacacccct gacactcacc 60

tgcaccgtct ctggattctc cctcagtggc gctgcgatga actgggtccg ccaggctcca 120

gggaaggggc tggaatggat cggagttatt ggtaatagtg gtagcacata ctacgcgtcc 180

tgggcgaaag gccgattcac catctccaaa acctcgtcga ccacggtgga tctgaaaatg 240

accagtccga caaccgagga cacggccacc tatttctgtg ccagaggggg aggggaattt 300

ttcatctggg gccaagggac cctggtcacc gtctcgagc 339

<210> SEQ ID NO 93
<211> LENGTH: 87
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 93

cagtcggtgg aggagtccgg gggtcgcctg gtcacgcctg ggacacccct gacactcacc 60

tgcaccgtct ctggattctc cctcagt 87

<210> SEQ ID NO 94
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 94

ggcgctgcga tgaac 15

<210> SEQ ID NO 95
<211> LENGTH: 42
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

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<400> SEQUENCE: 95

tgggtccgcc aggctccagg gaaggggctg gaatggatcg ga 42

<210> SEQ ID NO 96
<211> LENGTH: 48
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 96

gttattggta atagtggtag cacatactac gcgtcctggg cgaaaggc 48

<210> SEQ ID NO 97
<211> LENGTH: 93
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 97

cgattcacca tctccaaaac ctcgtcgacc acggtggatc tgaaaatgac cagtccgaca 60

accgaggaca cggccaccta tttctgtgcc aga 93

<210> SEQ ID NO 98
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 98

gggggagggg aatttttcat c 21

<210> SEQ ID NO 99
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 99

tggggccaag ggaccctggt caccgtctcg agc 33

<210> SEQ ID NO 100
<211> LENGTH: 990
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 100

gcctccacca agggcccatc ggtcttcccc ctggcaccct cctccaagag cacctctggg 60

ggcacagcgg ccctgggctg cctggtcaag gactacttcc ccgaaccggt gacggtgtcg 120

tggaactcag gcgccctgac cagcggcgtg cacaccttcc cggctgtcct acagtcctca 180

ggactctact ccctcagcag cgtggtgacc gtgccctcca gcagcttggg cacccagacc 240

tacatctgca acgtgaatca caagcccagc aacaccaagg tggacgcgag agttgagccc 300

aaatcttgtg acaaaactca cacatgccca ccgtgcccag cacctgaact cctgggggga 360

ccgtcagtct tcctcttccc cccaaaaccc aaggacaccc tcatgatctc ccggacccct 420

gaggtcacat gcgtggtggt ggacgtgagc cacgaagacc ctgaggtcaa gttcaactgg 480

tacgtggacg gcgtggaggt gcataatgcc aagacaaagc cgcgggagga gcagtacgcc 540

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agcacgtacc gtgtggtcag cgtcctcacc gtcctgcacc aggactggct gaatggcaag 600

gagtacaagt gcaaggtctc caacaaagcc ctcccagccc ccatcgagaa aaccatctcc 660

aaagccaaag ggcagccccg agaaccacag gtgtacaccc tgcccccatc ccgggaggag 720

atgaccaaga accaggtcag cctgacctgc ctggtcaaag gcttctatcc cagcgacatc 780

gccgtggagt gggagagcaa tgggcagccg gagaacaact acaagaccac gcctcccgtg 840

ctggactccg acggctcctt cttcctctac agcaagctca ccgtggacaa gagcaggtgg 900

cagcagggga acgtcttctc atgctccgtg atgcatgagg ctctgcacaa ccactacacg 960

cagaagagcc tctccctgtc tccgggtaaa 990

<210> SEQ ID NO 101
<211> LENGTH: 217
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 101

Ala Gln Val Leu Thr Gln Thr Pro Ser Pro Val Ser Ala Ala Val Gly
1 5 10 15

Gly Thr Val Thr Ile Asn Cys Gln Ser Ser Glu Ser Val Tyr Lys Asn
20 25 30

Asn Tyr Leu Ser Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Phe
35 40 45

Leu Ile Tyr Gln Ala Ser Asn Leu Ala Asp Gly Val Pro Ser Arg Phe
50 55 60

Lys Gly Ser Gly Ser Gly Thr Gln Phe Thr Leu Thr Ile Ser Asp Leu
65 70 75 80

Glu Cys Asp Asp Ala Ala Thr Tyr Tyr Cys Ala Gly Gly Tyr Ser Thr
85 90 95

Tyr Met Ser Gly Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg Thr
100 105 110

Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu
115 120 125

Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro
130 135 140

Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly
145 150 155 160

Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr
165 170 175

Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His
180 185 190

Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val
195 200 205

Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> SEQ ID NO 102
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

-continued

<400> SEQUENCE: 102

Ala Gln Val Leu Thr Gln Thr Pro Ser Pro Val Ser Ala Ala Val Gly
1 5 10 15

Gly Thr Val Thr Ile Asn Cys Gln Ser Ser Glu Ser Val Tyr Lys Asn
20 25 30

Asn Tyr Leu Ser Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Phe
35 40 45

Leu Ile Tyr Gln Ala Ser Asn Leu Ala Asp Gly Val Pro Ser Arg Phe
50 55 60

Lys Gly Ser Gly Ser Gly Thr Gln Phe Thr Leu Thr Ile Ser Asp Leu
65 70 75 80

Glu Cys Asp Asp Ala Ala Thr Tyr Tyr Cys Ala Gly Gly Tyr Ser Thr
85 90 95

Tyr Met Ser Gly Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg
100 105 110

<210> SEQ ID NO 103
<211> LENGTH: 23
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 103

Ala Gln Val Leu Thr Gln Thr Pro Ser Pro Val Ser Ala Ala Val Gly
1 5 10 15

Gly Thr Val Thr Ile Asn Cys
20

<210> SEQ ID NO 104
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 104

Gln Ser Ser Glu Ser Val Tyr Lys Asn Asn Tyr Leu Ser
1 5 10

<210> SEQ ID NO 105
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 105

Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Phe Leu Ile Tyr
1 5 10 15

<210> SEQ ID NO 106
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 106

Gln Ala Ser Asn Leu Ala Asp
1 5

<210> SEQ ID NO 107
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

-continued

<400> SEQUENCE: 107

Gly Val Pro Ser Arg Phe Lys Gly Ser Gly Ser Gly Thr Gln Phe Thr
1 5 10 15

Leu Thr Ile Ser Asp Leu Glu Cys Asp Asp Ala Ala Thr Tyr Tyr Cys
20 25 30

<210> SEQ ID NO 108
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 108

Ala Gly Gly Tyr Ser Thr Tyr Met Ser Gly
1 5 10

<210> SEQ ID NO 109
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 109

Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg
1 5 10

<210> SEQ ID NO 110
<211> LENGTH: 106
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 110

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
1 5 10 15

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
20 25 30

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
35 40 45

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
50 55 60

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
65 70 75 80

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
85 90 95

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
100 105

<210> SEQ ID NO 111
<211> LENGTH: 651
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 111

gcccaagtgc tgacccagac tccatcccca gtgtctgcag ctgtgggagg caccgtcacc 60

atcaattgcc agtccagtga gagtgtttat aagaacaact acttatcctg gtatcagcag 120

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aaaccagggc agcctcccaa gttcctgatc taccaggcat ccaatttggc agatggggtc 180

ccatcgcggt tcaaaggcag tggatctggg acacagttca ctctcaccat cagcgacctg 240

gagtgtgacg atgccgccac ttattactgt gcaggcggtt atagtactta tatgtctggt 300

ttcggcggag ggaccgaggt ggtggtcaaa cgtacggtag cggccccatc tgtcttcatc 360

ttcccgccat ctgatgagca gttgaaatct ggaactgcct ctgttgtgtg cctgctgaat 420

aacttctatc ccagagaggc caaagtacag tggaaggtgg ataacgccct ccaatcgggt 480

aactcccagg agagtgtcac agagcaggac agcaaggaca gcacctacag cctcagcagc 540

accctgacgc tgagcaaagc agactacgag aaacacaaag tctacgcctg cgaagtcacc 600

catcagggcc tgagctcgcc cgtcacaaag agcttcaaca ggggagagtg t 651

<210> SEQ ID NO 112
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 112

gcccaagtgc tgacccagac tccatcccca gtgtctgcag ctgtgggagg caccgtcacc 60

atcaattgcc agtccagtga gagtgtttat aagaacaact acttatcctg gtatcagcag 120

aaaccagggc agcctcccaa gttcctgatc taccaggcat ccaatttggc agatggggtc 180

ccatcgcggt tcaaaggcag tggatctggg acacagttca ctctcaccat cagcgacctg 240

gagtgtgacg atgccgccac ttattactgt gcaggcggtt atagtactta tatgtctggt 300

ttcggcggag ggaccgaggt ggtggtcaaa cgt 333

<210> SEQ ID NO 113
<211> LENGTH: 69
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 113

gcccaagtgc tgacccagac tccatcccca gtgtctgcag ctgtgggagg caccgtcacc 60

atcaattgc 69

<210> SEQ ID NO 114
<211> LENGTH: 39
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 114

cagtccagtg agagtgttta taagaacaac tacttatcc 39

<210> SEQ ID NO 115
<211> LENGTH: 45
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 115

tggtatcagc agaaaccagg gcagcctccc aagttcctga tctac 45

<210> SEQ ID NO 116
<211> LENGTH: 21

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<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 116

caggcatcca atttggcaga t 21

<210> SEQ ID NO 117
<211> LENGTH: 96
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 117

ggggtcccat cgcggttcaa aggcagtgga tctgggacac agttcactct caccatcagc 60

gacctggagt gtgacgatgc cgccacttat tactgt 96

<210> SEQ ID NO 118
<211> LENGTH: 30
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 118

gcaggcggtt atagtactta tatgtctggt 30

<210> SEQ ID NO 119
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 119

ttcggcggag ggaccgaggt ggtggtcaaa cgt 33

<210> SEQ ID NO 120
<211> LENGTH: 318
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 120

acggtagcgg ccccatctgt cttcatcttc ccgccatctg atgagcagtt gaaatctgga 60

actgcctctg ttgtgtgcct gctgaataac ttctatccca gagaggccaa agtacagtgg 120

aaggtggata acgccctcca atcgggtaac tcccaggaga gtgtcacaga gcaggacagc 180

aaggacagca cctacagcct cagcagcacc ctgacgctga gcaaagcaga ctacgagaaa 240

cacaaagtct acgcctgcga agtcacccat cagggcctga gctcgcccgt cacaaagagc 300

ttcaacaggg gagagtgt 318

<210> SEQ ID NO 121
<211> LENGTH: 443
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 121

Gln Ser Val Glu Glu Ser Gly Gly Arg Leu Val Thr Pro Gly Thr Pro
1 5 10 15

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Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Ser Ser Ala Ala
            20                  25                  30

Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
        35                  40                  45

Ile Ile Asp Asn Thr Ala Gly Thr Tyr Tyr Ala Pro Trp Ala Lys Gly
    50                  55                  60

Arg Phe Thr Ile Ser Lys Thr Ser Ser Thr Thr Val Asp Leu Lys Met
65                  70                  75                  80

Thr Ser Pro Thr Thr Glu Asp Thr Ala Thr Tyr Phe Cys Ala Arg Gly
                85                  90                  95

Gly Gly Glu Phe Phe Ile Trp Gly Pro Gly Thr Leu Val Thr Val Ser
            100                 105                 110

Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser
        115                 120                 125

Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp
    130                 135                 140

Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
145                 150                 155                 160

Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr
                165                 170                 175

Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln
            180                 185                 190

Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp
        195                 200                 205

Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro
    210                 215                 220

Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro
225                 230                 235                 240

Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr
                245                 250                 255

Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn
            260                 265                 270

Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
        275                 280                 285

Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
    290                 295                 300

Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
305                 310                 315                 320

Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys
                325                 330                 335

Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu
            340                 345                 350

Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
        355                 360                 365

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
    370                 375                 380

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
385                 390                 395                 400

Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
                405                 410                 415

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
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            420                 425                 430

Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
        435                 440


<210> SEQ ID NO 122
<211> LENGTH: 113
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 122

Gln Ser Val Glu Glu Ser Gly Gly Arg Leu Val Thr Pro Gly Thr Pro
1               5                   10                  15

Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Ser Ser Ala Ala
            20                  25                  30

Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
        35                  40                  45

Ile Ile Asp Asn Thr Ala Gly Thr Tyr Tyr Ala Pro Trp Ala Lys Gly
    50                  55                  60

Arg Phe Thr Ile Ser Lys Thr Ser Ser Thr Thr Val Asp Leu Lys Met
65                  70                  75                  80

Thr Ser Pro Thr Thr Glu Asp Thr Ala Thr Tyr Phe Cys Ala Arg Gly
                85                  90                  95

Gly Gly Glu Phe Phe Ile Trp Gly Pro Gly Thr Leu Val Thr Val Ser
            100                 105                 110

Ser


<210> SEQ ID NO 123
<211> LENGTH: 29
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 123

Gln Ser Val Glu Glu Ser Gly Gly Arg Leu Val Thr Pro Gly Thr Pro
1               5                   10                  15

Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Ser
            20                  25


<210> SEQ ID NO 124
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 124

Ser Ala Ala Met Asn
1               5


<210> SEQ ID NO 125
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 125

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
1               5                   10


<210> SEQ ID NO 126
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<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 126

Ile Ile Asp Asn Thr Ala Gly Thr Tyr Tyr Ala Pro Trp Ala Lys Gly
1 5 10 15

<210> SEQ ID NO 127
<211> LENGTH: 31
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 127

Arg Phe Thr Ile Ser Lys Thr Ser Ser Thr Thr Val Asp Leu Lys Met
1 5 10 15

Thr Ser Pro Thr Thr Glu Asp Thr Ala Thr Tyr Phe Cys Ala Arg
20 25 30

<210> SEQ ID NO 128
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 128

Gly Gly Gly Glu Phe Phe Ile
1 5

<210> SEQ ID NO 129
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 129

Trp Gly Pro Gly Thr Leu Val Thr Val Ser Ser
1 5 10

<210> SEQ ID NO 130
<211> LENGTH: 330
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 130

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65 70 75 80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95

Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys

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            100                 105                 110

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
        115                 120                 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
    130                 135                 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145                 150                 155                 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
                165                 170                 175

Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
            180                 185                 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
        195                 200                 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
    210                 215                 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
225                 230                 235                 240

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
                245                 250                 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
            260                 265                 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
        275                 280                 285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
    290                 295                 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305                 310                 315                 320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
                325                 330


<210> SEQ ID NO 131
<211> LENGTH: 1329
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 131

cagtcggtgg aggagtccgg gggtcgcctg gtcacgcctg ggacacccct gacactcacc     60

tgcaccgtct ctggattctc cctcagtagc gctgcaatga actgggtccg ccaggctcca    120

gggaaggggc tggaatggat cggaattatt gataatactg ctggcacata ttacgcgccc    180

tgggcgaaag gccgattcac catctccaaa acctcgtcga ccacggtgga tctgaaaatg    240

accagtccga caaccgagga cacggccacc tatttctgtg ccagaggggg aggggaattt    300

ttcatctggg gcccgggcac cctcgtcacc gtctcgagcg cctccaccaa gggcccatcg    360

gtcttccccc tggcaccctc ctccaagagc acctctgggg gcacagcggc cctgggctgc    420

ctggtcaagg actacttccc cgaaccggtg acggtgtcgt ggaactcagg cgccctgacc    480

agcggcgtgc acaccttccc ggctgtccta cagtcctcag gactctactc cctcagcagc    540

gtggtgaccg tgccctccag cagcttgggc acccagacct acatctgcaa cgtgaatcac    600

aagcccagca acaccaaggt ggacaagaaa gttgagccca aatcttgtga caaaactcac    660
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acatgcccac cgtgcccagc acctgaactc ctggggggac cgtcagtctt cctcttcccc 720

ccaaaaccca aggacaccct catgatctcc cggacccctg aggtcacatg cgtggtggtg 780

gacgtgagcc acgaagaccc tgaggtcaag ttcaactggt acgtggacgg cgtggaggtg 840

cataatgcca agacaaagcc gcgggaggag cagtacgcca gcacgtaccg tgtggtcagc 900

gtcctcaccg tcctgcacca ggactggctg aatggcaagg agtacaagtg caaggtctcc 960

aacaaagccc tcccagcccc catcgagaaa accatctcca aagccaaagg gcagccccga 1020

gaaccacagg tgtacaccct gcccccatcc cgggaggaga tgaccaagaa ccaggtcagc 1080

ctgacctgcc tggtcaaagg cttctatccc agcgacatcg ccgtggagtg ggagagcaat 1140

gggcagccgg agaacaacta caagaccacg cctcccgtgc tggactccga cggctccttc 1200

ttcctctaca gcaagctcac cgtggacaag agcaggtggc agcaggggaa cgtcttctca 1260

tgctccgtga tgcatgaggc tctgcacaac cactacacgc agaagagcct ctccctgtct 1320

ccgggtaaa 1329

<210> SEQ ID NO 132
<211> LENGTH: 339
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 132

cagtcggtgg aggagtccgg gggtcgcctg gtcacgcctg ggacacccct gacactcacc 60

tgcaccgtct ctggattctc cctcagtagc gctgcaatga actgggtccg ccaggctcca 120

gggaaggggc tggaatggat cggaattatt gataatactg ctggcacata ttacgcgccc 180

tgggcgaaag gccgattcac catctccaaa acctcgtcga ccacggtgga tctgaaaatg 240

accagtccga caaccgagga cacggccacc tatttctgtg ccagaggggg aggggaattt 300

ttcatctggg gcccgggcac cctcgtcacc gtctcgagc 339

<210> SEQ ID NO 133
<211> LENGTH: 87
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 133

cagtcggtgg aggagtccgg gggtcgcctg gtcacgcctg ggacacccct gacactcacc 60

tgcaccgtct ctggattctc cctcagt 87

<210> SEQ ID NO 134
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 134

agcgctgcaa tgaac 15

<210> SEQ ID NO 135
<211> LENGTH: 42
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 135

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tgggtccgcc aggctccagg gaaggggctg gaatggatcg ga 42

<210> SEQ ID NO 136
<211> LENGTH: 48
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 136

attattgata atactgctgg cacatattac gcgccctggg cgaaaggc 48

<210> SEQ ID NO 137
<211> LENGTH: 93
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 137

cgattcacca tctccaaaac ctcgtcgacc acggtggatc tgaaaatgac cagtccgaca 60

accgaggaca cggccaccta tttctgtgcc aga 93

<210> SEQ ID NO 138
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 138

gggggagggg aatttttcat c 21

<210> SEQ ID NO 139
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 139

tggggcccgg gcaccctcgt caccgtctcg agc 33

<210> SEQ ID NO 140
<211> LENGTH: 990
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 140

gcctccacca agggcccatc ggtcttcccc ctggcaccct cctccaagag cacctctggg 60

ggcacagcgg ccctgggctg cctggtcaag gactacttcc ccgaaccggt gacggtgtcg 120

tggaactcag gcgccctgac cagcggcgtg cacaccttcc cggctgtcct acagtcctca 180

ggactctact ccctcagcag cgtggtgacc gtgccctcca gcagcttggg cacccagacc 240

tacatctgca acgtgaatca caagcccagc aacaccaagg tggacaagaa agttgagccc 300

aaatcttgtg acaaaactca cacatgccca ccgtgcccag cacctgaact cctgggggga 360

ccgtcagtct tcctcttccc cccaaaaccc aaggacaccc tcatgatctc ccggaccccc 420

gaggtcacat gcgtggtggt ggacgtgagc cacgaagacc ctgaggtcaa gttcaactgg 480

tacgtggacg gcgtggaggt gcataatgcc aagacaaagc cgcgggagga gcagtacgcc 540

agcacgtacc gtgtggtcag cgtcctcacc gtcctgcacc aggactggct gaatggcaag 600

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gagtacaagt gcaaggtctc caacaaagcc ctcccagccc ccatcgagaa aaccatctcc 660

aaagccaaag ggcagccccg agaaccacag gtgtacaccc tgcccccatc ccgggaggag 720

atgaccaaga accaggtcag cctgacctgc ctggtcaaag gcttctatcc cagcgacatc 780

gccgtggagt gggagagcaa tgggcagccg gagaacaact acaagaccac gcctcccgtg 840

ctggactccg acggctcctt cttcctctac agcaagctca ccgtggacaa gagcaggtgg 900

cagcagggga acgtcttctc atgctccgtg atgcatgagg ctctgcacaa ccactacacg 960

cagaagagcc tctccctgtc tccgggtaaa 990

<210> SEQ ID NO 141
<211> LENGTH: 217
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 141

Ala Gln Val Leu Thr Gln Thr Pro Ser Ser Val Ser Ala Ala Val Gly
1 5 10 15

Gly Thr Val Thr Ile Asn Cys Gln Ser Ser Gln Ser Val His Asp Gly
20 25 30

Ser Tyr Leu Ser Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Asn Phe
35 40 45

Leu Ile Tyr Gln Ala Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe
50 55 60

Lys Gly Ser Gly Ser Gly Thr Gln Phe Thr Leu Thr Ile Ser Asp Leu
65 70 75 80

Glu Cys Asp Asp Ala Ala Thr Tyr Tyr Cys Ala Gly Gly Tyr Ser Ser
85 90 95

Asn Ile Cys Gly Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg Thr
100 105 110

Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu
115 120 125

Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro
130 135 140

Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly
145 150 155 160

Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr
165 170 175

Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His
180 185 190

Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val
195 200 205

Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> SEQ ID NO 142
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 142

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Ala Gln Val Leu Thr Gln Thr Pro Ser Ser Val Ser Ala Ala Val Gly
1 5 10 15

Gly Thr Val Thr Ile Asn Cys Gln Ser Ser Gln Ser Val His Asp Gly
20 25 30

Ser Tyr Leu Ser Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Asn Phe
35 40 45

Leu Ile Tyr Gln Ala Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe
50 55 60

Lys Gly Ser Gly Ser Gly Thr Gln Phe Thr Leu Thr Ile Ser Asp Leu
65 70 75 80

Glu Cys Asp Asp Ala Ala Thr Tyr Tyr Cys Ala Gly Gly Tyr Ser Ser
85 90 95

Asn Ile Cys Gly Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg
100 105 110

<210> SEQ ID NO 143
<211> LENGTH: 23
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 143

Ala Gln Val Leu Thr Gln Thr Pro Ser Ser Val Ser Ala Ala Val Gly
1 5 10 15

Gly Thr Val Thr Ile Asn Cys
20

<210> SEQ ID NO 144
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 144

Gln Ser Ser Gln Ser Val His Asp Gly Ser Tyr Leu Ser
1 5 10

<210> SEQ ID NO 145
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 145

Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Asn Phe Leu Ile Tyr
1 5 10 15

<210> SEQ ID NO 146
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 146

Gln Ala Ser Asn Leu Ala Ser
1 5

<210> SEQ ID NO 147
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 147

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```
Gly Val Pro Ser Arg Phe Lys Gly Ser Gly Ser Gly Thr Gln Phe Thr
1               5                   10                  15

Leu Thr Ile Ser Asp Leu Glu Cys Asp Asp Ala Ala Thr Tyr Tyr Cys
            20                  25                  30


<210> SEQ ID NO 148
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 148

Ala Gly Gly Tyr Ser Ser Asn Ile Cys Gly
1               5                   10


<210> SEQ ID NO 149
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 149

Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg
1               5                   10


<210> SEQ ID NO 150
<211> LENGTH: 106
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 150

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
1               5                   10                  15

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
            20                  25                  30

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
        35                  40                  45

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
    50                  55                  60

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
65                  70                  75                  80

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
                85                  90                  95

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
            100                 105


<210> SEQ ID NO 151
<211> LENGTH: 651
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 151

gcgcaagtgc tgacccagac tccatcgtcc gtgtctgcag ctgtgggagg cacagtcacc     60

atcaattgcc agtccagtca gagtgttcat gatggcagct acttatcctg gtatcagcag    120

aaaccagggc agcctcccaa cttcctgatc taccaggcat ccaatttggc atctggggtc    180
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ccatcgcggt tcaaaggcag tggatctggg acacagttca ctctcaccat cagcgacctg 240

gagtgtgacg atgccgccac ttattactgt gcaggcggtt atagtagtaa tatttgtggt 300

ttcggcggag ggaccgaggt ggtggtcaaa cgtacggtag cggccccatc tgtcttcatc 360

ttcccgccat ctgatgagca gttgaaatct ggaactgcct ctgttgtgtg cctgctgaat 420

aacttctatc ccagagaggc caaagtacag tggaaggtgg ataacgccct ccaatcgggt 480

aactcccagg agagtgtcac agagcaggac agcaaggaca gcacctacag cctcagcagc 540

accctgacgc tgagcaaagc agactacgag aaacacaaag tctacgcctg cgaagtcacc 600

catcagggcc tgagctcgcc cgtcacaaag agcttcaaca ggggagagtg t 651

<210> SEQ ID NO 152
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 152

gcgcaagtgc tgacccagac tccatcgtcc gtgtctgcag ctgtgggagg cacagtcacc 60

atcaattgcc agtccagtca gagtgttcat gatggcagct acttatcctg gtatcagcag 120

aaaccagggc agcctcccaa cttcctgatc taccaggcat ccaatttggc atctggggtc 180

ccatcgcggt tcaaaggcag tggatctggg acacagttca ctctcaccat cagcgacctg 240

gagtgtgacg atgccgccac ttattactgt gcaggcggtt atagtagtaa tatttgtggt 300

ttcggcggag ggaccgaggt ggtggtcaaa cgt 333

<210> SEQ ID NO 153
<211> LENGTH: 69
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 153

gcgcaagtgc tgacccagac tccatcgtcc gtgtctgcag ctgtgggagg cacagtcacc 60

atcaattgc 69

<210> SEQ ID NO 154
<211> LENGTH: 39
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 154

cagtccagtc agagtgttca tgatggcagc tacttatcc 39

<210> SEQ ID NO 155
<211> LENGTH: 45
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 155

tggtatcagc agaaaccagg gcagcctccc aacttcctga tctac 45

<210> SEQ ID NO 156
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

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<400> SEQUENCE: 156

caggcatcca atttggcatc t 21

<210> SEQ ID NO 157
<211> LENGTH: 96
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 157

ggggtcccat cgcggttcaa aggcagtgga tctgggacac agttcactct caccatcagc 60

gacctggagt gtgacgatgc cgccacttat tactgt 96

<210> SEQ ID NO 158
<211> LENGTH: 30
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 158

gcaggcggtt atagtagtaa tatttgtggt 30

<210> SEQ ID NO 159
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 159

ttcggcggag ggaccgaggt ggtggtcaaa cgt 33

<210> SEQ ID NO 160
<211> LENGTH: 318
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 160

acggtagcgg ccccatctgt cttcatcttc ccgccatctg atgagcagtt gaaatctgga 60

actgcctctg ttgtgtgcct gctgaataac ttctatccca gagaggccaa agtacagtgg 120

aaggtggata acgccctcca atcgggtaac tcccaggaga gtgtcacaga gcaggacagc 180

aaggacagca cctacagcct cagcagcacc ctgacgctga gcaaagcaga ctacgagaaa 240

cacaaagtct acgcctgcga agtcacccat cagggcctga gctcgcccgt cacaaagagc 300

ttcaacaggg gagagtgt 318

<210> SEQ ID NO 161
<211> LENGTH: 443
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 161

Gln Ser Val Glu Ala Ser Gly Gly Arg Leu Val Thr Pro Gly Thr Pro
1 5 10 15

Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Ser Ser Ala Ala
20 25 30

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Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
        35                  40                  45

Phe Ile Glu Tyr Ser Lys Asn Ile Val Tyr Ala Ser Trp Ala Lys Gly
    50                  55                  60

Arg Phe Thr Ile Ser Lys Val Ser Ser Thr Thr Val Asp Leu Lys Met
65                  70                  75                  80

Thr Ser Pro Thr Thr Glu Asp Thr Ala Thr Tyr Phe Cys Ala Arg Gly
                85                  90                  95

Gly Gly Glu Phe Phe Ile Trp Gly Gln Gly Thr Leu Val Thr Val Ser
            100                 105                 110

Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser
        115                 120                 125

Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp
    130                 135                 140

Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
145                 150                 155                 160

Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr
                165                 170                 175

Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln
            180                 185                 190

Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp
        195                 200                 205

Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro
    210                 215                 220

Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro
225                 230                 235                 240

Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr
                245                 250                 255

Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn
            260                 265                 270

Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
        275                 280                 285

Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
    290                 295                 300

Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
305                 310                 315                 320

Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys
                325                 330                 335

Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu
            340                 345                 350

Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
        355                 360                 365

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
    370                 375                 380

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
385                 390                 395                 400

Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
                405                 410                 415

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
            420                 425                 430
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Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440

<210> SEQ ID NO 162
<211> LENGTH: 113
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 162

Gln Ser Val Glu Ala Ser Gly Gly Arg Leu Val Thr Pro Gly Thr Pro
1 5 10 15

Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Ser Ser Ala Ala
20 25 30

Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
35 40 45

Phe Ile Glu Tyr Ser Lys Asn Ile Val Tyr Ala Ser Trp Ala Lys Gly
50 55 60

Arg Phe Thr Ile Ser Lys Val Ser Ser Thr Thr Val Asp Leu Lys Met
65 70 75 80

Thr Ser Pro Thr Thr Glu Asp Thr Ala Thr Tyr Phe Cys Ala Arg Gly
85 90 95

Gly Gly Glu Phe Phe Ile Trp Gly Gln Gly Thr Leu Val Thr Val Ser
100 105 110

Ser

<210> SEQ ID NO 163
<211> LENGTH: 29
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 163

Gln Ser Val Glu Ala Ser Gly Gly Arg Leu Val Thr Pro Gly Thr Pro
1 5 10 15

Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Ser
20 25

<210> SEQ ID NO 164
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 164

Ser Ala Ala Met Asn
1 5

<210> SEQ ID NO 165
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 165

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
1 5 10

<210> SEQ ID NO 166
<211> LENGTH: 16
<212> TYPE: PRT

-continued

<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 166

Phe Ile Glu Tyr Ser Lys Asn Ile Val Tyr Ala Ser Trp Ala Lys Gly
1 5 10 15

<210> SEQ ID NO 167
<211> LENGTH: 31
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 167

Arg Phe Thr Ile Ser Lys Val Ser Ser Thr Thr Val Asp Leu Lys Met
1 5 10 15

Thr Ser Pro Thr Thr Glu Asp Thr Ala Thr Tyr Phe Cys Ala Arg
20 25 30

<210> SEQ ID NO 168
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 168

Gly Gly Gly Glu Phe Phe Ile
1 5

<210> SEQ ID NO 169
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 169

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
1 5 10

<210> SEQ ID NO 170
<211> LENGTH: 330
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 170

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65 70 75 80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95

Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
100 105 110

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Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
        115                 120                 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
    130                 135                 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145                 150                 155                 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
                165                 170                 175

Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
            180                 185                 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
        195                 200                 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
    210                 215                 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
225                 230                 235                 240

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
                245                 250                 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
            260                 265                 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
        275                 280                 285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
    290                 295                 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305                 310                 315                 320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
                325                 330


<210> SEQ ID NO 171
<211> LENGTH: 1329
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 171

cagtcggtgg aggcgtccgg gggtcgcctg gtcacgcctg ggacacccct gacactcacc     60

tgcaccgtct ctggattctc cctcagtagc gctgcaatga actgggtccg ccaggctcca    120

gggaaggggc tggaatggat cggatttatt gagtatagta agaatatagt ttacgcgtcc    180

tgggcgaaag gccgattcac catctccaaa gtctcgtcga ccacggtgga tctgaaaatg    240

accagtccga caaccgagga cacggccacc tatttctgtg ccaggggggg aggggaattt    300

ttcatctggg gccaaggcac cctggtcacc gtctcgagcg cctccaccaa gggcccatcg    360

gtcttccccc tggcaccctc ctccaagagc acctctgggg gcacagcggc cctgggctgc    420

ctggtcaagg actacttccc cgaaccggtg acggtgtcgt ggaactcagg cgccctgacc    480

agcggcgtgc acaccttccc ggctgtccta cagtcctcag gactctactc cctcagcagc    540

gtggtgaccg tgccctccag cagcttgggc acccagacct acatctgcaa cgtgaatcac    600

aagcccagca acaccaaggt ggacaagaaa gttgagccca aatcttgtga caaaactcac    660

acatgcccac cgtgcccagc acctgaactc ctgggggggac cgtcagtctt cctcttcccc    720
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ccaaaaccca aggacaccct catgatctcc cggacccctg aggtcacatg cgtggtggtg 780

gacgtgagcc acgaagaccc tgaggtcaag ttcaactggt acgtggacgg cgtggaggtg 840

cataatgcca agacaaagcc gcgggaggag cagtacgcca gcacgtaccg tgtggtcagc 900

gtcctcaccg tcctgcacca ggactggctg aatggcaagg agtacaagtg caaggtctcc 960

aacaaagccc tcccagcccc catcgagaaa accatctcca aagccaaagg gcagccccga 1020

gaaccacagg tgtacaccct gccccccatcc cgggaggaga tgaccaagaa ccaggtcagc 1080

ctgacctgcc tggtcaaagg cttctatccc agcgacatcg ccgtggagtg ggagagcaat 1140

gggcagccgg agaacaacta caagaccacg cctcccgtgc tggactccga cggctccttc 1200

ttcctctaca gcaagctcac cgtggacaag agcaggtggc agcaggggaa cgtcttctca 1260

tgctccgtga tgcatgaggc tctgcacaac cactacacgc agaagagcct ctccctgtct 1320

ccgggtaaa 1329

<210> SEQ ID NO 172
<211> LENGTH: 339
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 172

cagtcggtgg aggcgtccgg gggtcgcctg gtcacgcctg ggacacccct gacactcacc 60

tgcaccgtct ctggattctc cctcagtagc gctgcaatga actgggtccg ccaggctcca 120

gggaaggggc tggaatggat cggatttatt gagtatagta agaatatagt ttacgcgtcc 180

tgggcgaaag gccgattcac catctccaaa gtctcgtcga ccacggtgga tctgaaaatg 240

accagtccga caaccgagga cacggccacc tatttctgtg ccaggggggg aggggaattt 300

ttcatctggg gccaaggcac cctggtcacc gtctcgagc 339

<210> SEQ ID NO 173
<211> LENGTH: 87
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 173

cagtcggtgg aggcgtccgg gggtcgcctg gtcacgcctg ggacacccct gacactcacc 60

tgcaccgtct ctggattctc cctcagt 87

<210> SEQ ID NO 174
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 174

agcgctgcaa tgaac 15

<210> SEQ ID NO 175
<211> LENGTH: 42
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 175

tgggtccgcc aggctccagg gaaggggctg gaatggatcg ga 42

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<210> SEQ ID NO 176
<211> LENGTH: 48
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 176

tttattgagt atagtaagaa tatagtttac gcgtcctggg cgaaaggc 48

<210> SEQ ID NO 177
<211> LENGTH: 93
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 177

cgattcacca tctccaaagt ctcgtcgacc acggtggatc tgaaaatgac cagtccgaca 60

accgaggaca cggccaccta tttctgtgcc agg 93

<210> SEQ ID NO 178
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 178

gggggagggg aatttttcat c 21

<210> SEQ ID NO 179
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 179

tggggccaag gcaccctggt caccgtctcg agc 33

<210> SEQ ID NO 180
<211> LENGTH: 990
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 180

gcctccacca agggcccatc ggtcttcccc ctggcaccct cctccaagag cacctctggg 60

ggcacagcgg ccctgggctg cctggtcaag gactacttcc ccgaaccggt gacggtgtcg 120

tggaactcag gcgccctgac cagcggcgtg cacaccttcc cggctgtcct acagtcctca 180

ggactctact ccctcagcag cgtggtgacc gtgccctcca gcagcttggg cacccagacc 240

tacatctgca acgtgaatca caagcccagc aacaccaagg tggacaagaa agttgagccc 300

aaatcttgtg acaaaactca cacatgccca ccgtgcccag cacctgaact cctgggggga 360

ccgtcagtct tcctcttccc cccaaaaccc aaggacaccc tcatgatctc ccggacccct 420

gaggtcacat gcgtggtggt ggacgtgagc cacgaagacc ctgaggtcaa gttcaactgg 480

tacgtggacg gcgtggaggt gcataatgcc aagacaaagc cgcgggagga gcagtacgcc 540

agcacgtacc gtgtggtcag cgtcctcacc gtcctgcacc aggactggct gaatggcaag 600

gagtacaagt gcaaggtctc caacaaagcc ctcccagccc ccatcgagaa aaccatctcc 660

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aaagccaaag ggcagccccg agaaccacag gtgtacaccc tgcccccatc ccgggaggag 720

atgaccaaga accaggtcag cctgacctgc ctggtcaaag gcttctatcc cagcgacatc 780

gccgtggagt gggagagcaa tgggcagccg gagaacaact acaagaccac gcctcccgtg 840

ctggactccg acggctcctt cttcctctac agcaagctca ccgtggacaa gagcaggtgg 900

cagcaggggа acgtcttctc atgctccgtg atgcatgagg ctctgcacaa ccactacacg 960

cagaagagcc tctccctgtc tccgggtaaa 990

<210> SEQ ID NO 181
<211> LENGTH: 217
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 181

Ala Gln Val Leu Thr Gln Thr Pro Ser Ser Val Ser Ala Ala Val Gly
1 5 10 15

Gly Thr Val Thr Ile Asn Cys Gln Ser Ser Gln Ser Val Tyr Ser Asn
20 25 30

Asn Arg Leu Ser Tyr Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu
35 40 45

Leu Ile Tyr Glu Ala Ser Ser Leu Ala Tyr Gly Val Pro Ser Arg Phe
50 55 60

Lys Gly Ser Gly Ser Gly Thr Gln Phe Thr Leu Thr Ile Ser Asp Leu
65 70 75 80

Glu Cys Asp Asp Ala Ala Thr Tyr Tyr Cys Ala Gly Ala Tyr Ser Asn
85 90 95

Ser Ile Tyr Ser Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg Thr
100 105 110

Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu
115 120 125

Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro
130 135 140

Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly
145 150 155 160

Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr
165 170 175

Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His
180 185 190

Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val
195 200 205

Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> SEQ ID NO 182
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 182

Ala Gln Val Leu Thr Gln Thr Pro Ser Ser Val Ser Ala Ala Val Gly
1 5 10 15

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Gly Thr Val Thr Ile Asn Cys Gln Ser Ser Gln Ser Val Tyr Ser Asn
            20                  25                  30

Asn Arg Leu Ser Tyr Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu
        35                  40                  45

Leu Ile Tyr Glu Ala Ser Ser Leu Ala Tyr Gly Val Pro Ser Arg Phe
    50                  55                  60

Lys Gly Ser Gly Ser Gly Thr Gln Phe Thr Leu Thr Ile Ser Asp Leu
65                  70                  75                  80

Glu Cys Asp Asp Ala Ala Thr Tyr Tyr Cys Ala Gly Ala Tyr Ser Asn
                85                  90                  95

Ser Ile Tyr Ser Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg
            100                 105                 110


<210> SEQ ID NO 183
<211> LENGTH: 23
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 183

Ala Gln Val Leu Thr Gln Thr Pro Ser Ser Val Ser Ala Ala Val Gly
1               5                   10                  15

Gly Thr Val Thr Ile Asn Cys
            20


<210> SEQ ID NO 184
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 184

Gln Ser Ser Gln Ser Val Tyr Ser Asn Asn Arg Leu Ser
1               5                   10


<210> SEQ ID NO 185
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 185

Tyr Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr
1               5                   10                  15


<210> SEQ ID NO 186
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 186

Glu Ala Ser Ser Leu Ala Tyr
1               5


<210> SEQ ID NO 187
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 187

Gly Val Pro Ser Arg Phe Lys Gly Ser Gly Ser Gly Thr Gln Phe Thr
1               5                   10                  15
```

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Leu Thr Ile Ser Asp Leu Glu Cys Asp Asp Ala Ala Thr Tyr Tyr Cys
20 25 30

<210> SEQ ID NO 188
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 188

Ala Gly Ala Tyr Ser Asn Ser Ile Tyr Ser
1 5 10

<210> SEQ ID NO 189
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 189

Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg
1 5 10

<210> SEQ ID NO 190
<211> LENGTH: 106
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 190

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
1 5 10 15

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
20 25 30

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
35 40 45

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
50 55 60

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
65 70 75 80

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
85 90 95

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
100 105

<210> SEQ ID NO 191
<211> LENGTH: 651
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 191

gcgcaagtgc tgacccagac tccatcgtcc gtgtctgcag ctgtgggagg cacagtcacc 60

atcaattgcc agtccagtca gagtgtttat agtaacaacc ggttatcgta ctatcagcag 120

aaaccagggc agcctcccaa gctcctgatc tacgaagcat ccagtctggc atatggggtc 180

ccatcgcggt tcaaaggcag tggatctggg acacagttca ctctcaccat cagcgacctg 240

-continued

gagtgtgacg atgccgccac ttattactgt gcaggtgcct atagtaatag tatttatagt 300

ttcggcggag ggaccgaggt ggtggtcaaa cgtacggtag cggccccatc tgtcttcatc 360

ttcccgccat ctgatgagca gttgaaatct ggaactgcct ctgttgtgtg cctgctgaat 420

aacttctatc ccagagaggc caaagtacag tggaaggtgg ataacgccct ccaatcgggt 480

aactcccagg agagtgtcac agagcaggac agcaaggaca gcacctacag cctcagcagc 540

accctgacgc tgagcaaagc agactacgag aaacacaaag tctacgcctg cgaagtcacc 600

catcagggcc tgagctcgcc cgtcacaaag agcttcaaca ggggagagtg t 651

<210> SEQ ID NO 192
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 192

gcgcaagtgc tgacccagac tccatcgtcc gtgtctgcag ctgtgggagg cacagtcacc 60

atcaattgcc agtccagtca gagtgtttat agtaacaacc ggttatcgta ctatcagcag 120

aaaccagggc agcctcccaa gctcctgatc tacgaagcat ccagtctggc atatggggtc 180

ccatcgcggt tcaaaggcag tggatctggg acacagttca ctctcaccat cagcgacctg 240

gagtgtgacg atgccgccac ttattactgt gcaggtgcct atagtaatag tatttatagt 300

ttcggcggag ggaccgaggt ggtggtcaaa cgt 333

<210> SEQ ID NO 193
<211> LENGTH: 69
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 193

gcgcaagtgc tgacccagac tccatcgtcc gtgtctgcag ctgtgggagg cacagtcacc 60

atcaattgc 69

<210> SEQ ID NO 194
<211> LENGTH: 39
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 194

cagtccagtc agagtgttta tagtaacaac cggttatcg 39

<210> SEQ ID NO 195
<211> LENGTH: 45
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 195

tactatcagc agaaaccagg gcagcctccc aagctcctga tctac 45

<210> SEQ ID NO 196
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 196

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gaagcatcca gtctggcata t 21

<210> SEQ ID NO 197
<211> LENGTH: 96
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 197

ggggtcccat cgcggttcaa aggcagtgga tctgggacac agttcactct caccatcagc 60

gacctggagt gtgacgatgc cgccacttat tactgt 96

<210> SEQ ID NO 198
<211> LENGTH: 30
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 198

gcaggtgcct atagtaatag tatttatagt 30

<210> SEQ ID NO 199
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 199

ttcggcggag ggaccgaggt ggtggtcaaa cgt 33

<210> SEQ ID NO 200
<211> LENGTH: 318
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 200

acggtagcgg ccccatctgt cttcatcttc ccgccatctg atgagcagtt gaaatctgga 60

actgcctctg ttgtgtgcct gctgaataac ttctatccca gagaggccaa agtacagtgg 120

aaggtggata acgccctcca atcgggtaac tcccaggaga gtgtcacaga gcaggacagc 180

aaggacagca cctacagcct cagcagcacc ctgacgctga gcaaagcaga ctacgagaaa 240

cacaaagtct acgcctgcga agtcacccat cagggcctga gctcgcccgt cacaaagagc 300

ttcaacaggg gagagtgt 318

<210> SEQ ID NO 201
<211> LENGTH: 443
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 201

Gln Ser Val Glu Ala Ser Gly Gly His Leu Val Thr Pro Gly Thr Pro
1 5 10 15

Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Ser Ser Ala Ala
20 25 30

Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly

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        35                  40                  45

Ser Val Asp Glu Arg Gln Asn Lys Tyr Tyr Ala Ser Trp Ala Lys Gly
    50                  55                  60

Arg Phe Thr Ile Ser Arg Thr Ser Ser Thr Thr Val Asn Leu Lys Met
65                  70                  75                  80

Thr Ser Pro Thr Thr Glu Asp Thr Ala Thr Tyr Phe Cys Ala Arg Gly
                85                  90                  95

Gly Gly Glu Phe Phe Ile Trp Gly Gln Gly Thr Leu Val Thr Val Ser
            100                 105                 110

Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser
        115                 120                 125

Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp
    130                 135                 140

Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
145                 150                 155                 160

Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr
                165                 170                 175

Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln
            180                 185                 190

Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp
        195                 200                 205

Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro
    210                 215                 220

Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro
225                 230                 235                 240

Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr
                245                 250                 255

Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn
            260                 265                 270

Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
        275                 280                 285

Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
    290                 295                 300

Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
305                 310                 315                 320

Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys
                325                 330                 335

Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu
            340                 345                 350

Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
        355                 360                 365

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
    370                 375                 380

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
385                 390                 395                 400

Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
                405                 410                 415

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
            420                 425                 430

Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
        435                 440
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<210> SEQ ID NO 202
<211> LENGTH: 113
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 202

Gln Ser Val Glu Ala Ser Gly Gly His Leu Val Thr Pro Gly Thr Pro
1 5 10 15

Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Ser Ser Ala Ala
20 25 30

Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
35 40 45

Ser Val Asp Glu Arg Gln Asn Lys Tyr Tyr Ala Ser Trp Ala Lys Gly
50 55 60

Arg Phe Thr Ile Ser Arg Thr Ser Ser Thr Thr Val Asn Leu Lys Met
65 70 75 80

Thr Ser Pro Thr Thr Glu Asp Thr Ala Thr Tyr Phe Cys Ala Arg Gly
85 90 95

Gly Gly Glu Phe Phe Ile Trp Gly Gln Gly Thr Leu Val Thr Val Ser
100 105 110

Ser

<210> SEQ ID NO 203
<211> LENGTH: 29
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 203

Gln Ser Val Glu Ala Ser Gly Gly His Leu Val Thr Pro Gly Thr Pro
1 5 10 15

Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Ser
20 25

<210> SEQ ID NO 204
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 204

Ser Ala Ala Met Asn
1 5

<210> SEQ ID NO 205
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 205

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
1 5 10

<210> SEQ ID NO 206
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

-continued

<400> SEQUENCE: 206

Ser Val Asp Glu Arg Gln Asn Lys Tyr Tyr Ala Ser Trp Ala Lys Gly
1 5 10 15

<210> SEQ ID NO 207
<211> LENGTH: 31
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 207

Arg Phe Thr Ile Ser Arg Thr Ser Ser Thr Thr Val Asn Leu Lys Met
1 5 10 15

Thr Ser Pro Thr Thr Glu Asp Thr Ala Thr Tyr Phe Cys Ala Arg
20 25 30

<210> SEQ ID NO 208
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 208

Gly Gly Gly Glu Phe Phe Ile
1 5

<210> SEQ ID NO 209
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 209

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
1 5 10

<210> SEQ ID NO 210
<211> LENGTH: 330
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 210

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65 70 75 80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95

Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
100 105 110

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
115 120 125

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Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
    130                 135                 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145                 150                 155                 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
                165                 170                 175

Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
            180                 185                 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
        195                 200                 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
    210                 215                 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
225                 230                 235                 240

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
                245                 250                 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
            260                 265                 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
        275                 280                 285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
    290                 295                 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305                 310                 315                 320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
                325                 330
```

<210> SEQ ID NO 211
<211> LENGTH: 1329
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 211

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cagtcggtgg aggcgtccgg gggtcaccta gtcacgcctg ggacacccct gacactcacc     60

tgcaccgtct ctggattctc cctcagtagc gctgcaatga actgggtccg ccaggctcca    120

gggaaggggc tggaatggat cggatcggtt gatgagcgtc agaataaata ttacgcgtcc    180

tgggcgaaag gccgattcac catctccaga acctcgtcga ccacggtgaa tctgaaaatg    240

accagtccga caaccgagga cacggccacc tatttctgtg ccagaggggg aggggaattt    300

ttcatctggg gccagggcac cctcgtcacc gtctcgagcg cctccaccaa gggcccatcg    360

gtcttccccc tggcaccctc ctccaagagc acctctgggg gcacagcggc cctgggctgc    420

ctggtcaagg actacttccc cgaaccggtg acggtgtcgt ggaactcagg cgccctgacc    480

agcggcgtgc acaccttccc ggctgtccta cagtcctcag gactctactc cctcagcagc    540

gtggtgaccg tgccctccag cagcttgggc acccagacct acatctgcaa cgtgaatcac    600

aagcccagca acaccaaggt ggacaagaaa gttgagccca aatcttgtga caaaactcac    660

acatgcccac cgtgcccagc acctgaactc ctgggggggac cgtcagtctt cctcttcccc    720

ccaaaaccca aggacaccct catgatctcc cggacccctg aggtcacatg cgtggtggtg    780
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gacgtgagcc acgaagaccc tgaggtcaag ttcaactggt acgtggacgg cgtggaggtg 840

cataatgcca agacaaagcc gcgggaggag cagtacgcca gcacgtaccg tgtggtcagc 900

gtcctcaccg tcctgcacca ggactggctg aatggcaagg agtacaagtg caaggtctcc 960

aacaaagccc tcccagcccc catcgagaaa accatctcca aagccaaagg gcagccccga 1020

gaaccacagg tgtacaccct gcccccatcc cgggaggaga tgaccaagaa ccaggtcagc 1080

ctgacctgcc tggtcaaagg cttctatccc agcgacatcg ccgtggagtg ggagagcaat 1140

gggcagccgg agaacaacta caagaccacg cctcccgtgc tggactccga cggctccttc 1200

ttcctctaca gcaagctcac cgtggacaag agcaggtggc agcaggggaa cgtcttctca 1260

tgctccgtga tgcatgaggc tctgcacaac cactacacgc agaagagcct ctccctgtct 1320

ccgggtaaa 1329

<210> SEQ ID NO 212
<211> LENGTH: 339
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 212

cagtcggtgg aggcgtccgg gggtcaccta gtcacgcctg ggacacccct gacactcacc 60

tgcaccgtct ctggattctc cctcagtagc gctgcaatga actgggtccg ccaggctcca 120

gggaaggggc tggaatggat cggatcggtt gatgagcgtc agaataaata ttacgcgtcc 180

tgggcgaaag gccgattcac catctccaga acctcgtcga ccacggtgaa tctgaaaatg 240

accagtccga caaccgagga cacggccacc tatttctgtg ccagaggggg aggggaattt 300

ttcatctggg gccagggcac cctcgtcacc gtctcgagc 339

<210> SEQ ID NO 213
<211> LENGTH: 87
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 213

cagtcggtgg aggcgtccgg gggtcaccta gtcacgcctg ggacacccct gacactcacc 60

tgcaccgtct ctggattctc cctcagt 87

<210> SEQ ID NO 214
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 214

agcgctgcaa tgaac 15

<210> SEQ ID NO 215
<211> LENGTH: 42
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 215

tgggtccgcc aggctccagg gaaggggctg gaatggatcg ga 42

<210> SEQ ID NO 216

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<211> LENGTH: 48
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 216

tcggttgatg agcgtcagaa taaatattac gcgtcctggg cgaaaggc 48

<210> SEQ ID NO 217
<211> LENGTH: 93
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 217

cgattcacca tctccagaac ctcgtcgacc acggtgaatc tgaaaatgac cagtccgaca 60

accgaggaca cggccaccta tttctgtgcc aga 93

<210> SEQ ID NO 218
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 218

gggggagggg aatttttcat c 21

<210> SEQ ID NO 219
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 219

tggggccagg gcaccctcgt caccgtctcg agc 33

<210> SEQ ID NO 220
<211> LENGTH: 990
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 220

gcctccacca agggcccatc ggtcttcccc ctggcaccct cctccaagag cacctctggg 60

ggcacagcgg ccctgggctg cctggtcaag gactacttcc ccgaaccggt gacggtgtcg 120

tggaactcag gcgccctgac cagcggcgtg cacaccttcc cggctgtcct acagtcctca 180

ggactctact ccctcagcag cgtggtgacc gtgccctcca gcagcttggg cacccagacc 240

tacatctgca acgtgaatca caagcccagc aacaccaagg tggacaagaa agttgagccc 300

aaatcttgtg acaaaactca cacatgccca ccgtgcccag cacctgaact cctgggggga 360

ccgtcagtct tcctcttccc cccaaaaccc aaggacaccc tcatgatctc ccggacccct 420

gaggtcacat gcgtggtggt ggacgtgagc cacgaagacc ctgaggtcaa gttcaactgg 480

tacgtggacg gcgtggaggt gcataatgcc aagacaaagc cgcgggagga gcagtacgcc 540

agcacgtacc gtgtggtcag cgtcctcacc gtcctgcacc aggactggct gaatggcaag 600

gagtacaagt gcaaggtctc caacaaagcc ctcccagccc ccatcgagaa aaccatctcc 660

aaagccaaag ggcagccccg agaaccacag gtgtacaccc tgcccccatc ccgggaggag 720

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atgaccaaga accaggtcag cctgacctgc ctggtcaaag gcttctatcc cagcgacatc 780

gccgtggagt gggagagcaa tgggcagccg gagaacaact acaagaccac gcctcccgtg 840

ctggactccg acggctcctt cttcctctac agcaagctca ccgtggacaa gagcaggtgg 900

cagcagggga acgtcttctc atgctccgtg atgcatgagg ctctgcacaa ccactacacg 960

cagaagagcc tctccctgtc tccgggtaaa 990

<210> SEQ ID NO 221
<211> LENGTH: 217
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 221

Ala Gln Val Leu Thr Gln Thr Pro Ser Ser Val Ser Ala Ala Val Gly
1 5 10 15

Gly Thr Val Thr Ile Asn Cys Gln Ser Ser Gln Ser Val Tyr Ser Asn
20 25 30

Asn Arg Leu Ser Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Asn Leu
35 40 45

Leu Ile Tyr Glu Ala Ser Ser Leu Ala Ser Gly Val Pro Ser Arg Phe
50 55 60

Ser Gly Ser Gly Ser Gly Thr Gln Phe Thr Leu Thr Ile Ser Asp Leu
65 70 75 80

Glu Cys Asp Asp Ala Ala Thr Tyr Tyr Cys Ala Gly Ala Tyr Asn Thr
85 90 95

Gly Ile Tyr Gly Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg Thr
100 105 110

Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu
115 120 125

Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro
130 135 140

Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly
145 150 155 160

Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr
165 170 175

Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His
180 185 190

Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val
195 200 205

Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> SEQ ID NO 222
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 222

Ala Gln Val Leu Thr Gln Thr Pro Ser Ser Val Ser Ala Ala Val Gly
1 5 10 15

Gly Thr Val Thr Ile Asn Cys Gln Ser Ser Gln Ser Val Tyr Ser Asn

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            20                  25                  30

Asn Arg Leu Ser Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Asn Leu
        35                  40                  45

Leu Ile Tyr Glu Ala Ser Ser Leu Ala Ser Gly Val Pro Ser Arg Phe
    50                  55                  60

Ser Gly Ser Gly Ser Gly Thr Gln Phe Thr Leu Thr Ile Ser Asp Leu
65                  70                  75                  80

Glu Cys Asp Asp Ala Ala Thr Tyr Tyr Cys Ala Gly Ala Tyr Asn Thr
                85                  90                  95

Gly Ile Tyr Gly Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg
            100                 105                 110


<210> SEQ ID NO 223
<211> LENGTH: 23
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 223

Ala Gln Val Leu Thr Gln Thr Pro Ser Ser Val Ser Ala Ala Val Gly
1               5                   10                  15

Gly Thr Val Thr Ile Asn Cys
            20


<210> SEQ ID NO 224
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 224

Gln Ser Ser Gln Ser Val Tyr Ser Asn Asn Arg Leu Ser
1               5                   10


<210> SEQ ID NO 225
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 225

Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Asn Leu Leu Ile Tyr
1               5                   10                  15


<210> SEQ ID NO 226
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 226

Glu Ala Ser Ser Leu Ala Ser
1               5


<210> SEQ ID NO 227
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 227

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Gln Phe Thr
1               5                   10                  15

Leu Thr Ile Ser Asp Leu Glu Cys Asp Asp Ala Ala Thr Tyr Tyr Cys
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            20                  25                  30

<210> SEQ ID NO 228
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 228

Ala Gly Ala Tyr Asn Thr Gly Ile Tyr Gly
1               5                   10


<210> SEQ ID NO 229
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 229

Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg
1               5                   10


<210> SEQ ID NO 230
<211> LENGTH: 106
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 230

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
1               5                   10                  15

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
            20                  25                  30

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
        35                  40                  45

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
    50                  55                  60

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
65                  70                  75                  80

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
                85                  90                  95

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
            100                 105


<210> SEQ ID NO 231
<211> LENGTH: 651
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 231

gcgcaagtgc tgacccagac tccatcgtcc gtgtctgcag ctgtgggagg cacagtcacc     60

atcaattgcc agtccagtca gagtgtttat agtaacaacc gcttatcctg gtatcagcag    120

aaaccagggc agcctcccaa tctcctgatc tacgaagcat ccagtctggc atctggggtc    180

ccatcgcggt tcagcggcag tggatctggg acacagttca ctctcaccat cagcgacctg    240

gagtgtgacg atgccgccac ttattactgt gcaggcgctt ataatactgg gatttatggt    300
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ttcggcggag ggaccgaggt ggtggtcaaa cgtacggtag cggccccatc tgtcttcatc 360

ttcccgccat ctgatgagca gttgaaatct ggaactgcct ctgttgtgtg cctgctgaat 420

aacttctatc ccagagaggc caaagtacag tggaaggtgg ataacgccct ccaatcgggt 480

aactcccagg agagtgtcac agagcaggac agcaaggaca gcacctacag cctcagcagc 540

accctgacgc tgagcaaagc agactacgag aaacacaaag tctacgcctg cgaagtcacc 600

catcagggcc tgagctcgcc cgtcacaaag agcttcaaca ggggagagtg t 651

<210> SEQ ID NO 232
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 232

gcgcaagtgc tgacccagac tccatcgtcc gtgtctgcag ctgtgggagg cacagtcacc 60

atcaattgcc agtccagtca gagtgtttat agtaacaacc gcttatcctg gtatcagcag 120

aaaccagggc agcctcccaa tctcctgatc tacgaagcat ccagtctggc atctggggtc 180

ccatcgcggt tcagcggcag tggatctggg acacagttca ctctcaccat cagcgacctg 240

gagtgtgacg atgccgccac ttattactgt gcaggcgctt ataatactgg gatttatggt 300

ttcggcggag ggaccgaggt ggtggtcaaa cgt 333

<210> SEQ ID NO 233
<211> LENGTH: 69
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 233

gcgcaagtgc tgacccagac tccatcgtcc gtgtctgcag ctgtgggagg cacagtcacc 60

atcaattgc 69

<210> SEQ ID NO 234
<211> LENGTH: 39
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 234

cagtccagtc agagtgttta tagtaacaac cgcttatcc 39

<210> SEQ ID NO 235
<211> LENGTH: 45
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 235

tggtatcagc agaaaccagg gcagcctccc aatctcctga tctac 45

<210> SEQ ID NO 236
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 236

gaagcatcca gtctggcatc t 21

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<210> SEQ ID NO 237
<211> LENGTH: 96
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 237

ggggtcccat cgcggttcag cggcagtgga tctgggacac agttcactct caccatcagc 60

gacctggagt gtgacgatgc cgccacttat tactgt 96

<210> SEQ ID NO 238
<211> LENGTH: 30
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 238

gcaggcgctt ataatactgg gatttatggt 30

<210> SEQ ID NO 239
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 239

ttcggcggag ggaccgaggt ggtggtcaaa cgt 33

<210> SEQ ID NO 240
<211> LENGTH: 318
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 240

acggtagcgg ccccatctgt cttcatcttc ccgccatctg atgagcagtt gaaatctgga 60

actgcctctg ttgtgtgcct gctgaataac ttctatccca gagaggccaa agtacagtgg 120

aaggtggata acgccctcca atcgggtaac tcccaggaga gtgtcacaga gcaggacagc 180

aaggacagca cctacagcct cagcagcacc ctgacgctga gcaaagcaga ctacgagaaa 240

cacaaagtct acgcctgcga agtcacccat cagggcctga gctcgcccgt cacaaagagc 300

ttcaacaggg gagagtgt 318

<210> SEQ ID NO 241
<211> LENGTH: 443
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 241

Gln Ser Val Glu Glu Ser Gly Gly Arg Leu Val Thr Pro Gly Thr Pro
1 5 10 15

Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Ser Ser Ala Ala
20 25 30

Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
35 40 45

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Ile Ile Asp Asp Ser Gly Asn Thr Tyr Tyr Ala Ser Trp Ala Lys Ala
    50                  55                  60

Arg Phe Thr Ile Ser Lys Thr Ser Ser Thr Thr Val Asp Leu Lys Met
65                  70                  75                  80

Thr Ser Pro Thr Thr Glu Asp Thr Ala Thr Tyr Phe Cys Ala Arg Gly
                85                  90                  95

Gly Gly Glu Phe Phe Ile Trp Gly Pro Gly Thr Leu Val Thr Val Ser
            100                 105                 110

Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser
        115                 120                 125

Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp
    130                 135                 140

Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
145                 150                 155                 160

Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr
                165                 170                 175

Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln
            180                 185                 190

Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp
        195                 200                 205

Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro
    210                 215                 220

Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro
225                 230                 235                 240

Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr
                245                 250                 255

Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn
            260                 265                 270

Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
        275                 280                 285

Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
    290                 295                 300

Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
305                 310                 315                 320

Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys
                325                 330                 335

Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu
            340                 345                 350

Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
        355                 360                 365

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
    370                 375                 380

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
385                 390                 395                 400

Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
                405                 410                 415

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
            420                 425                 430

Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
        435                 440
```

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<210> SEQ ID NO 242
<211> LENGTH: 113
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 242

Gln Ser Val Glu Glu Ser Gly Gly Arg Leu Val Thr Pro Gly Thr Pro
1 5 10 15

Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Ser Ser Ala Ala
20 25 30

Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
35 40 45

Ile Ile Asp Asp Ser Gly Asn Thr Tyr Tyr Ala Ser Trp Ala Lys Ala
50 55 60

Arg Phe Thr Ile Ser Lys Thr Ser Ser Thr Thr Val Asp Leu Lys Met
65 70 75 80

Thr Ser Pro Thr Thr Glu Asp Thr Ala Thr Tyr Phe Cys Ala Arg Gly
85 90 95

Gly Gly Glu Phe Phe Ile Trp Gly Pro Gly Thr Leu Val Thr Val Ser
100 105 110

Ser

<210> SEQ ID NO 243
<211> LENGTH: 29
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 243

Gln Ser Val Glu Glu Ser Gly Gly Arg Leu Val Thr Pro Gly Thr Pro
1 5 10 15

Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Ser
20 25

<210> SEQ ID NO 244
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 244

Ser Ala Ala Met Ser
1 5

<210> SEQ ID NO 245
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 245

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
1 5 10

<210> SEQ ID NO 246
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 246

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Ile Ile Asp Asp Ser Gly Asn Thr Tyr Tyr Ala Ser Trp Ala Lys Ala
1               5                   10                  15


<210> SEQ ID NO 247
<211> LENGTH: 31
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 247

Arg Phe Thr Ile Ser Lys Thr Ser Ser Thr Thr Val Asp Leu Lys Met
1               5                   10                  15

Thr Ser Pro Thr Thr Glu Asp Thr Ala Thr Tyr Phe Cys Ala Arg
            20                  25                  30


<210> SEQ ID NO 248
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 248

Gly Gly Gly Glu Phe Phe Ile
1               5


<210> SEQ ID NO 249
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 249

Trp Gly Pro Gly Thr Leu Val Thr Val Ser Ser
1               5                   10


<210> SEQ ID NO 250
<211> LENGTH: 330
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 250

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1               5                   10                  15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
            20                  25                  30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
        35                  40                  45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
    50                  55                  60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65                  70                  75                  80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
                85                  90                  95

Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
            100                 105                 110

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
        115                 120                 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
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    130                 135                 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145                 150                 155                 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
                165                 170                 175

Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
            180                 185                 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
        195                 200                 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
    210                 215                 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
225                 230                 235                 240

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
                245                 250                 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
            260                 265                 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
        275                 280                 285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
    290                 295                 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305                 310                 315                 320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
                325                 330


<210> SEQ ID NO 251
<211> LENGTH: 1329
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 251

cagtcggtgg aggagtccgg gggtcgcctg gtcacgcctg ggacacccct gacactcacc     60

tgcaccgtct ctggattctc cctcagtagc gctgcaatga gctgggtccg ccaggctcca    120

gggaaggggc tggaatggat cggaattatt gatgatagtg gtaacacata ctacgcgtcc    180

tgggcgaaag cccgattcac catctccaaa acctcgtcga ccacggtgga tctgaaaatg    240

accagtccga caaccgagga cacggccacc tatttctgtg ccagaggggg aggggagttt    300

ttcatctggg gcccgggcac cctcgtcacc gtctcgagcg cctccaccaa gggcccatcg    360

gtcttccccc tggcaccctc ctccaagagc acctctgggg gcacagcggc cctgggctgc    420

ctggtcaagg actacttccc cgaaccggtg acggtgtcgt ggaactcagg cgccctgacc    480

agcggcgtgc acaccttccc ggctgtccta cagtcctcag gactctactc cctcagcagc    540

gtggtgaccg tgccctccag cagcttgggc acccagacct acatctgcaa cgtgaatcac    600

aagcccagca acaccaaggt ggacaagaaa gttgagccca aatcttgtga caaaactcac    660

acatgcccac cgtgcccagc acctgaactc ctgggggggac cgtcagtctt cctcttcccc    720

ccaaaaccca aggacaccct catgatctcc cggacccctg aggtcacatg cgtggtggtg    780

gacgtgagcc acgaagaccc tgaggtcaag ttcaactggt acgtggacgg cgtggaggtg    840
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cataatgcca agacaaagcc gcgggaggag cagtacgcca gcacgtaccg tgtggtcagc 900

gtcctcaccg tcctgcacca ggactggctg aatggcaagg agtacaagtg caaggtctcc 960

aacaaagccc tcccagcccc catcgagaaa accatctcca aagccaaagg gcagccccga 1020

gaaccacagg tgtacaccct gccccccatcc cgggaggaga tgaccaagaa ccaggtcagc 1080

ctgacctgcc tggtcaaagg cttctatccc agcgacatcg ccgtggagtg ggagagcaat 1140

gggcagccgg agaacaacta caagaccacg cctcccgtgc tggactccga cggctccttc 1200

ttcctctaca gcaagctcac cgtggacaag agcaggtggc agcaggggaa cgtcttctca 1260

tgctccgtga tgcatgaggc tctgcacaac cactacacgc agaagagcct ctccctgtct 1320

ccgggtaaa 1329

<210> SEQ ID NO 252
<211> LENGTH: 339
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 252

cagtcggtgg aggagtccgg gggtcgcctg gtcacgcctg ggacacccct gacactcacc 60

tgcaccgtct ctggattctc cctcagtagc gctgcaatga gctgggtccg ccaggctcca 120

gggaaggggc tggaatggat cggaattatt gatgatagtg gtaacacata ctacgcgtcc 180

tgggcgaaag cccgattcac catctccaaa acctcgtcga ccacggtgga tctgaaaatg 240

accagtccga caaccgagga cacggccacc tatttctgtg ccagaggggg aggggagttt 300

ttcatctggg gcccgggcac cctcgtcacc gtctcgagc 339

<210> SEQ ID NO 253
<211> LENGTH: 87
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 253

cagtcggtgg aggagtccgg gggtcgcctg gtcacgcctg ggacacccct gacactcacc 60

tgcaccgtct ctggattctc cctcagt 87

<210> SEQ ID NO 254
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 254

agcgctgcaa tgagc 15

<210> SEQ ID NO 255
<211> LENGTH: 42
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 255

tgggtccgcc aggctccagg gaaggggctg gaatggatcg ga 42

<210> SEQ ID NO 256
<211> LENGTH: 48
<212> TYPE: DNA

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<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 256

attattgatg atagtggtaa cacatactac gcgtcctggg cgaaagcc 48

<210> SEQ ID NO 257
<211> LENGTH: 93
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 257

cgattcacca tctccaaaac ctcgtcgacc acggtggatc tgaaaatgac cagtccgaca 60

accgaggaca cggccaccta tttctgtgcc aga 93

<210> SEQ ID NO 258
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 258

gggggagggg agtttttcat c 21

<210> SEQ ID NO 259
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 259

tggggcccgg gcaccctcgt caccgtctcg agc 33

<210> SEQ ID NO 260
<211> LENGTH: 990
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 260

gcctccacca agggcccatc ggtcttcccc ctggcaccct cctccaagag cacctctggg 60

ggcacagcgg ccctgggctg cctggtcaag gactacttcc ccgaaccggt gacggtgtcg 120

tggaactcag gcgccctgac cagcggcgtg cacaccttcc cggctgtcct acagtcctca 180

ggactctact ccctcagcag cgtggtgacc gtgccctcca gcagcttggg cacccagacc 240

tacatctgca acgtgaatca caagcccagc aacaccaagg tggacaagaa agttgagccc 300

aaatcttgtg acaaaactca cacatgccca ccgtgcccag cacctgaact cctgggggga 360

ccgtcagtct tcctcttccc cccaaaaccc aaggacaccc tcatgatctc ccggacccct 420

gaggtcacat gcgtggtggt ggacgtgagc cacgaagacc ctgaggtcaa gttcaactgg 480

tacgtggacg gcgtggaggt gcataatgcc aagacaaagc cgcgggagga gcagtacgcc 540

agcacgtacc gtgtggtcag cgtcctcacc gtcctgcacc aggactggct gaatggcaag 600

gagtacaagt gcaaggtctc caacaaagcc ctcccagccc ccatcgagaa aaccatctcc 660

aaagccaaag ggcagccccg agaaccacag gtgtacaccc tgcccccatc ccgggaggag 720

atgaccaaga accaggtcag cctgacctgc ctggtcaaag gcttctatcc cagcgacatc 780

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gccgtggagt gggagagcaa tgggcagccg gagaacaact acaagaccac gcctcccgtg 840

ctggactccg acggctcctt cttcctctac agcaagctca ccgtggacaa gagcaggtgg 900

cagcagggga acgtcttctc atgctccgtg atgcatgagg ctctgcacaa ccactacacg 960

cagaagagcc tctccctgtc tccgggtaaa 990

<210> SEQ ID NO 261
<211> LENGTH: 217
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 261

Asp Pro Val Leu Thr Gln Thr Pro Ser Ser Val Ser Ala Ala Val Gly
1 5 10 15

Gly Thr Val Thr Ile Asn Cys Gln Ser Ser Gln Ser Val Tyr Asn Asn
20 25 30

Lys Trp Leu Ser Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Phe
35 40 45

Leu Ile Tyr Gln Ala Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe
50 55 60

Lys Gly Ser Gly Ser Gly Thr Gln Phe Thr Leu Thr Ile Ser Asp Leu
65 70 75 80

Glu Cys Asp Asp Gly Ala Thr Tyr Tyr Cys Ala Gly Gly Tyr Arg Gly
85 90 95

Asn Val Cys Gly Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg Thr
100 105 110

Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu
115 120 125

Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro
130 135 140

Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly
145 150 155 160

Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr
165 170 175

Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His
180 185 190

Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val
195 200 205

Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> SEQ ID NO 262
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 262

Asp Pro Val Leu Thr Gln Thr Pro Ser Ser Val Ser Ala Ala Val Gly
1 5 10 15

Gly Thr Val Thr Ile Asn Cys Gln Ser Ser Gln Ser Val Tyr Asn Asn
20 25 30

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Lys Trp Leu Ser Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Phe
        35                  40                  45

Leu Ile Tyr Gln Ala Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe
    50                  55                  60

Lys Gly Ser Gly Ser Gly Thr Gln Phe Thr Leu Thr Ile Ser Asp Leu
65                  70                  75                  80

Glu Cys Asp Asp Gly Ala Thr Tyr Tyr Cys Ala Gly Gly Tyr Arg Gly
                85                  90                  95

Asn Val Cys Gly Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg
            100                 105                 110


<210> SEQ ID NO 263
<211> LENGTH: 23
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 263

Asp Pro Val Leu Thr Gln Thr Pro Ser Ser Val Ser Ala Ala Val Gly
1               5                   10                  15

Gly Thr Val Thr Ile Asn Cys
            20


<210> SEQ ID NO 264
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 264

Gln Ser Ser Gln Ser Val Tyr Asn Asn Lys Trp Leu Ser
1               5                   10


<210> SEQ ID NO 265
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 265

Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Phe Leu Ile Tyr
1               5                   10                  15


<210> SEQ ID NO 266
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 266

Gln Ala Ser Asn Leu Ala Ser
1               5


<210> SEQ ID NO 267
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 267

Gly Val Pro Ser Arg Phe Lys Gly Ser Gly Ser Gly Thr Gln Phe Thr
1               5                   10                  15

Leu Thr Ile Ser Asp Leu Glu Cys Asp Asp Gly Ala Thr Tyr Tyr Cys
            20                  25                  30
```

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<210> SEQ ID NO 268
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 268

Ala Gly Gly Tyr Arg Gly Asn Val Cys Gly
1 5 10

<210> SEQ ID NO 269
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 269

Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg
1 5 10

<210> SEQ ID NO 270
<211> LENGTH: 106
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 270

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
1 5 10 15

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
20 25 30

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
35 40 45

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
50 55 60

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
65 70 75 80

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
85 90 95

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
100 105

<210> SEQ ID NO 271
<211> LENGTH: 651
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 271

gaccctgtgc tgacccagac tccatcgtcc gtgtctgcag ctgtgggagg cacagtcacc 60

atcaattgcc agtccagtca gagtgtttat aataacaagt ggttatcctg gtatcagcag 120

aaaccaggac agtctcccaa gttcctgatt taccaggcat ccaatttggc atctggggtc 180

ccatcgcggt tcaaaggcag tggatctggg acacagttca ctctcaccat cagcgacctg 240

gagtgtgacg atggcgccac ttattactgt gcaggcggct accgtggtaa tgtttgtggt 300

ttcggcggag ggaccgaggt ggtggtcaaa cgtacggtag cggccccatc tgtcttcatc 360

-continued

ttcccgccat ctgatgagca gttgaaatct ggaactgcct ctgttgtgtg cctgctgaat 420

aacttctatc ccagagaggc caaagtacag tggaaggtgg ataacgccct ccaatcgggt 480

aactcccagg agagtgtcac agagcaggac agcaaggaca gcacctacag cctcagcagc 540

accctgacgc tgagcaaagc agactacgag aaacacaaag tctacgcctg cgaagtcacc 600

catcagggcc tgagctcgcc cgtcacaaag agcttcaaca ggggagagtg t 651

<210> SEQ ID NO 272
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 272

gaccctgtgc tgacccagac tccatcgtcc gtgtctgcag ctgtgggagg cacagtcacc 60

atcaattgcc agtccagtca gagtgtttat aataacaagt ggttatcctg gtatcagcag 120

aaaccaggac agtctcccaa gttcctgatt taccaggcat ccaatttggc atctggggtc 180

ccatcgcggt tcaaaggcag tggatctggg acacagttca ctctcaccat cagcgacctg 240

gagtgtgacg atggcgccac ttattactgt gcaggcggct accgtggtaa tgtttgtggt 300

ttcggcggag ggaccgaggt ggtggtcaaa cgt 333

<210> SEQ ID NO 273
<211> LENGTH: 69
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 273

gaccctgtgc tgacccagac tccatcgtcc gtgtctgcag ctgtgggagg cacagtcacc 60

atcaattgc 69

<210> SEQ ID NO 274
<211> LENGTH: 39
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 274

cagtccagtc agagtgttta taataacaag tggttatcc 39

<210> SEQ ID NO 275
<211> LENGTH: 45
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 275

tggtatcagc agaaaccagg acagtctccc aagttcctga tttac 45

<210> SEQ ID NO 276
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 276

caggcatcca atttggcatc t 21

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<210> SEQ ID NO 277
<211> LENGTH: 96
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 277

ggggtcccat cgcggttcaa aggcagtgga tctgggacac agttcactct caccatcagc 60

gacctggagt gtgacgatgg cgccacttat tactgt 96

<210> SEQ ID NO 278
<211> LENGTH: 30
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 278

gcaggcggct accgtggtaa tgtttgtggt 30

<210> SEQ ID NO 279
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 279

ttcggcggag ggaccgaggt ggtggtcaaa cgt 33

<210> SEQ ID NO 280
<211> LENGTH: 318
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 280

acggtagcgg ccccatctgt cttcatcttc ccgccatctg atgagcagtt gaaatctgga 60

actgcctctg ttgtgtgcct gctgaataac ttctatccca gagaggccaa agtacagtgg 120

aaggtggata acgccctcca atcgggtaac tcccaggaga gtgtcacaga gcaggacagc 180

aaggacagca cctacagcct cagcagcacc ctgacgctga gcaaagcaga ctacgagaaa 240

cacaaagtct acgcctgcga agtcacccat cagggcctga gctcgcccgt cacaaagagc 300

ttcaacaggg gagagtgt 318

<210> SEQ ID NO 281
<211> LENGTH: 443
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 281

Gln Ser Val Glu Glu Ser Gly Gly Arg Leu Val Thr Pro Gly Thr Pro
1 5 10 15

Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Ser Ser Ala Ala
20 25 30

Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
35 40 45

Ile Phe Asp Pro Tyr Ser Ser Thr Tyr Tyr Ala Ser Trp Ala Lys Gly
50 55 60

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Arg Phe Thr Ile Ser Lys Thr Ser Ser Thr Thr Val Asp Leu Lys Met
65                  70                  75                  80

Thr Ser Pro Thr Thr Glu Asp Thr Ala Thr Tyr Phe Cys Ala Arg Gly
                85                  90                  95

Gly Gly Glu Phe Phe Ile Trp Gly Pro Gly Thr Leu Val Thr Val Ser
            100                 105                 110

Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser
        115                 120                 125

Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp
    130                 135                 140

Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
145                 150                 155                 160

Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr
                165                 170                 175

Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln
            180                 185                 190

Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp
        195                 200                 205

Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro
    210                 215                 220

Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro
225                 230                 235                 240

Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr
                245                 250                 255

Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn
            260                 265                 270

Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
        275                 280                 285

Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
    290                 295                 300

Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
305                 310                 315                 320

Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys
                325                 330                 335

Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu
            340                 345                 350

Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
        355                 360                 365

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
    370                 375                 380

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
385                 390                 395                 400

Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
                405                 410                 415

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
            420                 425                 430

Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
        435                 440


<210> SEQ ID NO 282
<211> LENGTH: 113
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<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 282

Gln Ser Val Glu Glu Ser Gly Gly Arg Leu Val Thr Pro Gly Thr Pro
1 5 10 15

Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Ser Ser Ala Ala
20 25 30

Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
35 40 45

Ile Phe Asp Pro Tyr Ser Ser Thr Tyr Tyr Ala Ser Trp Ala Lys Gly
50 55 60

Arg Phe Thr Ile Ser Lys Thr Ser Ser Thr Thr Val Asp Leu Lys Met
65 70 75 80

Thr Ser Pro Thr Thr Glu Asp Thr Ala Thr Tyr Phe Cys Ala Arg Gly
85 90 95

Gly Gly Glu Phe Phe Ile Trp Gly Pro Gly Thr Leu Val Thr Val Ser
100 105 110

Ser

<210> SEQ ID NO 283
<211> LENGTH: 29
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 283

Gln Ser Val Glu Glu Ser Gly Gly Arg Leu Val Thr Pro Gly Thr Pro
1 5 10 15

Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Ser
20 25

<210> SEQ ID NO 284
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 284

Ser Ala Ala Met Asn
1 5

<210> SEQ ID NO 285
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 285

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
1 5 10

<210> SEQ ID NO 286
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 286

Ile Phe Asp Pro Tyr Ser Ser Thr Tyr Tyr Ala Ser Trp Ala Lys Gly
1 5 10 15

-continued

<210> SEQ ID NO 287
<211> LENGTH: 31
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 287

Arg Phe Thr Ile Ser Lys Thr Ser Ser Thr Thr Val Asp Leu Lys Met
1 5 10 15

Thr Ser Pro Thr Thr Glu Asp Thr Ala Thr Tyr Phe Cys Ala Arg
20 25 30

<210> SEQ ID NO 288
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 288

Gly Gly Gly Glu Phe Phe Ile
1 5

<210> SEQ ID NO 289
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 289

Trp Gly Pro Gly Thr Leu Val Thr Val Ser Ser
1 5 10

<210> SEQ ID NO 290
<211> LENGTH: 330
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 290

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65 70 75 80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95

Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
100 105 110

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
115 120 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
130 135 140

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Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145                 150                 155                 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
                165                 170                 175

Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
            180                 185                 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
        195                 200                 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
    210                 215                 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
225                 230                 235                 240

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
                245                 250                 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
            260                 265                 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
        275                 280                 285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
    290                 295                 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305                 310                 315                 320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
                325                 330


<210> SEQ ID NO 291
<211> LENGTH: 1329
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 291

cagtcagtgg aggagtccgg gggtcgcctg gtcacgcctg ggacacccct aacactcacc     60

tgcaccgtct ctggattctc cctcagtagc gctgcaatga actgggtccg ccaggctcca    120

gggaaggggc tggaatggat cggtattttt gatccttata gtagtacata ctacgcgtcc    180

tgggcgaaag gccgattcac catctccaaa acctcgtcga ccacggtgga tctgaaaatg    240

accagtccga caaccgagga cacggccacc tatttctgtg ccagaggggg aggggaattt    300

ttcatctggg gcccaggcac cctcgtcacc gtctcgagcg cctccaccaa gggcccatcg    360

gtcttccccc tggcaccctc ctccaagagc acctctgggg gcacagcggc cctgggctgc    420

ctggtcaagg actacttccc cgaaccggtg acggtgtcgt ggaactcagg cgccctgacc    480

agcggcgtgc acaccttccc ggctgtccta cagtcctcag gactctactc cctcagcagc    540

gtggtgaccg tgccctccag cagcttgggc acccagacct acatctgcaa cgtgaatcac    600

aagcccagca acaccaaggt ggacaagaaa gttgagccca aatcttgtga caaaactcac    660

acatgcccac cgtgcccagc acctgaactc ctgggggggac cgtcagtctt cctcttcccc    720

ccaaaaccca aggacaccct catgatctcc cggacccctg aggtcacatg cgtggtggtg    780

gacgtgagcc acgaagaccc tgaggtcaag ttcaactggt acgtggacgg cgtggaggtg    840

cataatgcca agacaaagcc gcgggaggag cagtacgcca gcacgtaccg tgtggtcagc    900
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gtcctcaccg tcctgcacca ggactggctg aatggcaagg agtacaagtg caaggtctcc 960

aacaaagccc tcccagcccc catcgagaaa accatctcca aagccaaagg gcagccccga 1020

gaaccacagg tgtacaccct gcccccatcc cgggaggaga tgaccaagaa ccaggtcagc 1080

ctgacctgcc tggtcaaagg cttctatccc agcgacatcg ccgtggagtg ggagagcaat 1140

gggcagccgg agaacaacta caagaccacg cctcccgtgc tggactccga cggctccttc 1200

ttcctctaca gcaagctcac cgtggacaag agcaggtggc agcaggggaa cgtcttctca 1260

tgctccgtga tgcatgaggc tctgcacaac cactacacgc agaagagcct ctccctgtct 1320

ccgggtaaa 1329

<210> SEQ ID NO 292
<211> LENGTH: 339
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 292

cagtcagtgg aggagtccgg gggtcgcctg gtcacgcctg ggacacccct aacactcacc 60

tgcaccgtct ctggattctc cctcagtagc gctgcaatga actgggtccg ccaggctcca 120

gggaaggggc tggaatggat cggtatttttt gatccttata gtagtacata ctacgcgtcc 180

tgggcgaaag gccgattcac catctccaaa acctcgtcga ccacggtgga tctgaaaatg 240

accagtccga caaccgagga cacggccacc tatttctgtg ccagaggggg aggggaattt 300

ttcatctggg gcccaggcac cctcgtcacc gtctcgagc 339

<210> SEQ ID NO 293
<211> LENGTH: 87
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 293

cagtcagtgg aggagtccgg gggtcgcctg gtcacgcctg ggacacccct aacactcacc 60

tgcaccgtct ctggattctc cctcagt 87

<210> SEQ ID NO 294
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 294

agcgctgcaa tgaac 15

<210> SEQ ID NO 295
<211> LENGTH: 42
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 295

tgggtccgcc aggctccagg gaaggggctg gaatggatcg gt 42

<210> SEQ ID NO 296
<211> LENGTH: 48
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

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<400> SEQUENCE: 296

atttttgatc cttatagtag tacatactac gcgtcctggg cgaaaggc 48

<210> SEQ ID NO 297
<211> LENGTH: 93
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 297

cgattcacca tctccaaaac ctcgtcgacc acggtggatc tgaaaatgac cagtccgaca 60

accgaggaca cggccaccta tttctgtgcc aga 93

<210> SEQ ID NO 298
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 298

gggggagggg aatttttcat c 21

<210> SEQ ID NO 299
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 299

tggggcccag gcaccctcgt caccgtctcg agc 33

<210> SEQ ID NO 300
<211> LENGTH: 990
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 300

gcctccacca agggcccatc ggtcttcccc ctggcaccct cctccaagag cacctctggg 60

ggcacagcgg ccctgggctg cctggtcaag gactacttcc ccgaaccggt gacggtgtcg 120

tggaactcag gcgccctgac cagcggcgtg cacaccttcc cggctgtcct acagtcctca 180

ggactctact ccctcagcag cgtggtgacc gtgccctcca gcagcttggg cacccagacc 240

tacatctgca acgtgaatca caagcccagc aacaccaagg tggacaagaa agttgagccc 300

aaatcttgtg acaaaactca cacatgccca ccgtgcccag cacctgaact cctgggggga 360

ccgtcagtct tcctcttccc cccaaaaccc aaggacaccc tcatgatctc ccggacccct 420

gaggtcacat gcgtggtggt ggacgtgagc cacgaagacc ctgaggtcaa gttcaactgg 480

tacgtggacg gcgtggaggt gcataatgcc aagacaaagc cgcgggagga gcagtacgcc 540

agcacgtacc gtgtggtcag cgtcctcacc gtcctgcacc aggactggct gaatggcaag 600

gagtacaagt gcaaggtctc caacaaagcc ctcccagccc ccatcgagaa aaccatctcc 660

aaagccaaag ggcagccccg agaaccacag gtgtacaccc tgcccccatc ccgggaggag 720

atgaccaaga accaggtcag cctgacctgc ctggtcaaag gcttctatcc cagcgacatc 780

gccgtggagt gggagagcaa tgggcagccg gagaacaact acaagaccac gcctcccgtg 840

-continued

ctggactccg acggctcctt cttcctctac agcaagctca ccgtggacaa gagcaggtgg 900

cagcagggga acgtcttctc atgctccgtg atgcatgagg ctctgcacaa ccactacacg 960

cagaagagcc tctccctgtc tccgggtaaa 990

<210> SEQ ID NO 301
<211> LENGTH: 217
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 301

Ala Gln Val Leu Thr Gln Thr Pro Ser Ser Val Ser Ala Ala Val Gly
1 5 10 15

Gly Thr Val Thr Ile Asn Cys Gln Ser Ser Gln Ser Val Tyr Lys Asn
20 25 30

Lys Tyr Leu Ser Trp Tyr Gln Gln Lys Val Gly Gln Pro Pro Lys Phe
35 40 45

Leu Ile Tyr Gln Ala Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe
50 55 60

Lys Gly Ser Gly Ser Gly Thr Gln Phe Thr Leu Thr Ile Ser Asp Leu
65 70 75 80

Glu Cys Asp Asp Ala Ala Thr Tyr Tyr Cys Ala Gly Gly Tyr Ser Gly
85 90 95

Asn Met Val Asp Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg Thr
100 105 110

Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu
115 120 125

Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro
130 135 140

Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly
145 150 155 160

Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr
165 170 175

Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His
180 185 190

Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val
195 200 205

Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> SEQ ID NO 302
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 302

Ala Gln Val Leu Thr Gln Thr Pro Ser Ser Val Ser Ala Ala Val Gly
1 5 10 15

Gly Thr Val Thr Ile Asn Cys Gln Ser Ser Gln Ser Val Tyr Lys Asn
20 25 30

Lys Tyr Leu Ser Trp Tyr Gln Gln Lys Val Gly Gln Pro Pro Lys Phe
35 40 45

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Leu Ile Tyr Gln Ala Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe
50 55 60

Lys Gly Ser Gly Ser Gly Thr Gln Phe Thr Leu Thr Ile Ser Asp Leu
65 70 75 80

Glu Cys Asp Asp Ala Ala Thr Tyr Tyr Cys Ala Gly Gly Tyr Ser Gly
85 90 95

Asn Met Val Asp Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg
100 105 110

<210> SEQ ID NO 303
<211> LENGTH: 23
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 303

Ala Gln Val Leu Thr Gln Thr Pro Ser Ser Val Ser Ala Ala Val Gly
1 5 10 15

Gly Thr Val Thr Ile Asn Cys
20

<210> SEQ ID NO 304
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 304

Gln Ser Ser Gln Ser Val Tyr Lys Asn Lys Tyr Leu Ser
1 5 10

<210> SEQ ID NO 305
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 305

Trp Tyr Gln Gln Lys Val Gly Gln Pro Pro Lys Phe Leu Ile Tyr
1 5 10 15

<210> SEQ ID NO 306
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 306

Gln Ala Ser Asn Leu Ala Ser
1 5

<210> SEQ ID NO 307
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 307

Gly Val Pro Ser Arg Phe Lys Gly Ser Gly Ser Gly Thr Gln Phe Thr
1 5 10 15

Leu Thr Ile Ser Asp Leu Glu Cys Asp Asp Ala Ala Thr Tyr Tyr Cys
20 25 30

<210> SEQ ID NO 308

-continued

<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 308

Ala Gly Gly Tyr Ser Gly Asn Met Val Asp
1 5 10

<210> SEQ ID NO 309
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 309

Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg
1 5 10

<210> SEQ ID NO 310
<211> LENGTH: 106
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 310

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
1 5 10 15

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
20 25 30

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
35 40 45

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
50 55 60

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
65 70 75 80

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
85 90 95

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
100 105

<210> SEQ ID NO 311
<211> LENGTH: 651
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 311

gcccaagtgc tgacccagac tccatcgtcc gtgtctgcag ctgtgggagg cacagtcacc 60

atcaattgcc agtccagtca gagtgtttat aagaataagt acttatcctg gtatcagcag 120

aaagtagggc agcctcccaa gttcctgatc taccaggcat ccaatttggc atctggggtc 180

ccatcgcggt tcaaaggcag tggatctggg acacagttca ctctcaccat cagcgacctg 240

gagtgtgacg atgccgccac ttattactgt gcaggcggtt atagtggtaa tatggttgat 300

ttcggcggag ggaccgaggt ggtggtcaaa cgtacggtag cggccccatc tgtcttcatc 360

ttcccgccat ctgatgagca gttgaaatct ggaactgcct ctgttgtgtg cctgctgaat 420

-continued

aacttctatc ccagagaggc caaagtacag tggaaggtgg ataacgccct ccaatcgggt 480

aactcccagg agagtgtcac agagcaggac agcaaggaca gcacctacag cctcagcagc 540

accctgacgc tgagcaaagc agactacgag aaacacaaag tctacgcctg cgaagtcacc 600

catcagggcc tgagctcgcc cgtcacaaag agcttcaaca ggggagagtg t 651

<210> SEQ ID NO 312
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 312

gcccaagtgc tgacccagac tccatcgtcc gtgtctgcag ctgtgggagg cacagtcacc 60

atcaattgcc agtccagtca gagtgtttat aagaataagt acttatcctg gtatcagcag 120

aaagtagggc agcctcccaa gttcctgatc taccaggcat ccaatttggc atctggggtc 180

ccatcgcggt tcaaaggcag tggatctggg acacagttca ctctcaccat cagcgacctg 240

gagtgtgacg atgccgccac ttattactgt gcaggcggtt atagtggtaa tatggttgat 300

ttcggcggag ggaccgaggt ggtggtcaaa cgt 333

<210> SEQ ID NO 313
<211> LENGTH: 69
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 313

gcccaagtgc tgacccagac tccatcgtcc gtgtctgcag ctgtgggagg cacagtcacc 60

atcaattgc 69

<210> SEQ ID NO 314
<211> LENGTH: 39
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 314

cagtccagtc agagtgttta taagaataag tacttatcc 39

<210> SEQ ID NO 315
<211> LENGTH: 45
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 315

tggtatcagc agaaagtagg gcagcctccc aagttcctga tctac 45

<210> SEQ ID NO 316
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 316

caggcatcca atttggcatc t 21

<210> SEQ ID NO 317
<211> LENGTH: 96

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<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 317

ggggtcccat cgcggttcaa aggcagtgga tctgggacac agttcactct caccatcagc 60

gacctggagt gtgacgatgc cgccacttat tactgt 96

<210> SEQ ID NO 318
<211> LENGTH: 30
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 318

gcaggcggtt atagtggtaa tatggttgat 30

<210> SEQ ID NO 319
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 319

ttcggcggag ggaccgaggt ggtggtcaaa cgt 33

<210> SEQ ID NO 320
<211> LENGTH: 318
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 320

acggtagcgg ccccatctgt cttcatcttc ccgccatctg atgagcagtt gaaatctgga 60

actgcctctg ttgtgtgcct gctgaataac ttctatccca gagaggccaa agtacagtgg 120

aaggtggata acgccctcca atcgggtaac tcccaggaga gtgtcacaga gcaggacagc 180

aaggacagca cctacagcct cagcagcacc ctgacgctga gcaaagcaga ctacgagaaa 240

cacaaagtct acgcctgcga agtcacccat cagggcctga gctcgcccgt cacaaagagc 300

ttcaacaggg gagagtgt 318

<210> SEQ ID NO 321
<211> LENGTH: 443
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 321

Gln Ser Val Glu Glu Ser Gly Gly Arg Leu Val Thr Pro Gly Thr Pro
1 5 10 15

Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Ser Ser Ala Ala
20 25 30

Leu Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
35 40 45

Ile Ile Asp Lys Gly Val Met Ser Tyr Tyr Ala Ser Trp Ala Lys Gly
50 55 60

Arg Phe Thr Ile Ser Lys Thr Ser Ser Thr Thr Val Asp Leu Lys Val

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65                  70                  75                  80

Thr Ser Pro Thr Thr Glu Asp Thr Ala Thr Tyr Phe Cys Ala Arg Gly
                85                  90                  95

Gly Gly Glu Phe Phe Ile Trp Gly Gln Gly Thr Leu Val Thr Val Ser
            100                 105                 110

Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser
        115                 120                 125

Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp
    130                 135                 140

Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
145                 150                 155                 160

Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr
                165                 170                 175

Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln
            180                 185                 190

Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp
        195                 200                 205

Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro
    210                 215                 220

Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro
225                 230                 235                 240

Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr
                245                 250                 255

Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn
            260                 265                 270

Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
        275                 280                 285

Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
    290                 295                 300

Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
305                 310                 315                 320

Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys
                325                 330                 335

Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu
            340                 345                 350

Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
        355                 360                 365

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
    370                 375                 380

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
385                 390                 395                 400

Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
                405                 410                 415

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
            420                 425                 430

Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
        435                 440


<210> SEQ ID NO 322
<211> LENGTH: 113
<212> TYPE: PRT
<213> ORGANISM: Artificial
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<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 322

Gln Ser Val Glu Glu Ser Gly Gly Arg Leu Val Thr Pro Gly Thr Pro
1 5 10 15

Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Ser Ser Ala Ala
20 25 30

Leu Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
35 40 45

Ile Ile Asp Lys Gly Val Met Ser Tyr Tyr Ala Ser Trp Ala Lys Gly
50 55 60

Arg Phe Thr Ile Ser Lys Thr Ser Ser Thr Thr Val Asp Leu Lys Val
65 70 75 80

Thr Ser Pro Thr Thr Glu Asp Thr Ala Thr Tyr Phe Cys Ala Arg Gly
85 90 95

Gly Gly Glu Phe Phe Ile Trp Gly Gln Gly Thr Leu Val Thr Val Ser
100 105 110

Ser

<210> SEQ ID NO 323
<211> LENGTH: 29
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 323

Gln Ser Val Glu Glu Ser Gly Gly Arg Leu Val Thr Pro Gly Thr Pro
1 5 10 15

Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Ser
20 25

<210> SEQ ID NO 324
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 324

Ser Ala Ala Leu Ser
1 5

<210> SEQ ID NO 325
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 325

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
1 5 10

<210> SEQ ID NO 326
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 326

Ile Ile Asp Lys Gly Val Met Ser Tyr Tyr Ala Ser Trp Ala Lys Gly
1 5 10 15

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<210> SEQ ID NO 327
<211> LENGTH: 31
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 327

Arg Phe Thr Ile Ser Lys Thr Ser Ser Thr Thr Val Asp Leu Lys Val
1 5 10 15

Thr Ser Pro Thr Thr Glu Asp Thr Ala Thr Tyr Phe Cys Ala Arg
20 25 30

<210> SEQ ID NO 328
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 328

Gly Gly Gly Glu Phe Phe Ile
1 5

<210> SEQ ID NO 329
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 329

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
1 5 10

<210> SEQ ID NO 330
<211> LENGTH: 330
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 330

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65 70 75 80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95

Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
100 105 110

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
115 120 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
130 135 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145 150 155 160

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Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
                165                 170                 175

Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
            180                 185                 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
        195                 200                 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
    210                 215                 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
225                 230                 235                 240

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
                245                 250                 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
            260                 265                 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
        275                 280                 285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
    290                 295                 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305                 310                 315                 320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
                325                 330


<210> SEQ ID NO 331
<211> LENGTH: 1329
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 331

cagtcggtgg aggagtccgg gggtcgcctg gtcacgcctg ggacacccct gacactcacc     60

tgcaccgtct ctggattctc cctcagtagc gctgcattga gctgggtccg ccaggctcca    120

gggaaggggc tggaatggat cggaattatt gataagggtg ttatgtctta ctacgcgtcc    180

tgggcgaaag gccgattcac catctccaaa acctcgtcga ccacggtgga tctaaaagtg    240

accagtccga caaccgagga cacggccacc tatttctgtg ccagaggggg gggggaattt    300

ttcatctggg gccagggcac cctcgtcacc gtctcgagcg cctccaccaa gggcccatcg    360

gtcttccccc tggcaccctc ctccaagagc acctctgggg gcacagcggc cctgggctgc    420

ctggtcaagg actacttccc cgaaccggtg acggtgtcgt ggaactcagg cgccctgacc    480

agcggcgtgc acaccttccc ggctgtccta cagtcctcag gactctactc cctcagcagc    540

gtggtgaccg tgccctccag cagcttgggc acccagacct acatctgcaa cgtgaatcac    600

aagcccagca acaccaaggt ggacaagaaa gttgagccca aatcttgtga caaaactcac    660

acatgcccac cgtgcccagc acctgaactc ctgggggggac cgtcagtctt cctcttcccc    720

ccaaaaccca aggacaccct catgatctcc cggacccctg aggtcacatg cgtggtggtg    780

gacgtgagcc acgaagaccc tgaggtcaag ttcaactggt acgtggacgg cgtggaggtg    840

cataatgcca agacaaagcc gcgggaggag cagtacgcca gcacgtaccg tgtggtcagc    900

gtcctcaccg tcctgcacca ggactggctg aatggcaagg agtacaagtg caaggtctcc    960
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aacaaagccc tcccagcccc catcgagaaa accatctcca aagccaaagg gcagccccga 1020

gaaccacagg tgtacaccct gcccccatcc cgggaggaga tgaccaagaa ccaggtcagc 1080

ctgacctgcc tggtcaaagg cttctatccc agcgacatcg ccgtggagtg ggagagcaat 1140

gggcagccgg agaacaacta caagaccacg cctcccgtgc tggactccga cggctccttc 1200

ttcctctaca gcaagctcac cgtggacaag agcaggtggc agcaggggaa cgtcttctca 1260

tgctccgtga tgcatgaggc tctgcacaac cactacacgc agaagagcct ctccctgtct 1320

ccgggtaaa 1329

<210> SEQ ID NO 332
<211> LENGTH: 339
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 332

cagtcggtgg aggagtccgg gggtcgcctg gtcacgcctg ggacacccct gacactcacc 60

tgcaccgtct ctggattctc cctcagtagc gctgcattga gctgggtccg ccaggctcca 120

gggaaggggc tggaatggat cggaattatt gataagggtg ttatgtctta ctacgcgtcc 180

tgggcgaaag gccgattcac catctccaaa acctcgtcga ccacggtgga tctaaaagtg 240

accagtccga caaccgagga cacggccacc tatttctgtg ccagaggggg gggggaattt 300

ttcatctggg gccagggcac cctcgtcacc gtctcgagc 339

<210> SEQ ID NO 333
<211> LENGTH: 87
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 333

cagtcggtgg aggagtccgg gggtcgcctg gtcacgcctg ggacacccct gacactcacc 60

tgcaccgtct ctggattctc cctcagt 87

<210> SEQ ID NO 334
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 334

agcgctgcat tgagc 15

<210> SEQ ID NO 335
<211> LENGTH: 42
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 335

tgggtccgcc aggctccagg gaaggggctg gaatggatcg ga 42

<210> SEQ ID NO 336
<211> LENGTH: 48
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 336

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attattgata agggtgttat gtcttactac gcgtcctggg cgaaaggc 48

<210> SEQ ID NO 337
<211> LENGTH: 93
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 337

cgattcacca tctccaaaac ctcgtcgacc acggtggatc taaaagtgac cagtccgaca 60

accgaggaca cggccaccta tttctgtgcc aga 93

<210> SEQ ID NO 338
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 338

ggggggggag aatttttcat c 21

<210> SEQ ID NO 339
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 339

tggggccagg gcaccctcgt caccgtctcg agc 33

<210> SEQ ID NO 340
<211> LENGTH: 990
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 340

gcctccacca agggcccatc ggtcttcccc ctggcaccct cctccaagag cacctctggg 60

ggcacagcgg ccctgggctg cctggtcaag gactacttcc ccgaaccggt gacggtgtcg 120

tggaactcag gcgccctgac cagcggcgtg cacaccttcc cggctgtcct acagtcctca 180

ggactctact ccctcagcag cgtggtgacc gtgccctcca gcagcttggg cacccagacc 240

tacatctgca acgtgaatca caagcccagc aacaccaagg tggacaagaa agttgagccc 300

aaatcttgtg acaaaactca cacatgccca ccgtgcccag cacctgaact cctgggggga 360

ccgtcagtct tcctcttccc cccaaaaccc aaggacaccc tcatgatctc ccggacccct 420

gaggtcacat gcgtggtggt ggacgtgagc cacgaagacc ctgaggtcaa gttcaactgg 480

tacgtggacg gcgtggaggt gcataatgcc aagacaaagc cgcgggagga gcagtacgcc 540

agcacgtacc gtgtggtcag cgtcctcacc gtcctgcacc aggactggct gaatggcaag 600

gagtacaagt gcaaggtctc caacaaagcc ctcccagccc ccatcgagaa aaccatctcc 660

aaagccaaag ggcagccccg agaaccacag gtgtacaccc tgcccccatc ccgggaggag 720

atgaccaaga accaggtcag cctgacctgc ctggtcaaag gcttctatcc cagcgacatc 780

gccgtggagt gggagagcaa tgggcagccg gagaacaact acaagaccac gcctcccgtg 840

ctggactccg acggctcctt cttcctctac agcaagctca ccgtggacaa gagcaggtgg 900

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cagcagggga acgtcttctc atgctccgtg atgcatgagg ctctgcacaa ccactacacg 960

cagaagagcc tctccctgtc tccgggtaaa 990

<210> SEQ ID NO 341
<211> LENGTH: 217
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 341

Ala Gln Val Leu Thr Gln Thr Pro Ser Ser Val Ser Ala Ala Val Gly
1 5 10 15

Gly Thr Val Thr Ile Asn Cys Gln Ser Ser Lys Ser Val Tyr Asn Asn
20 25 30

Asn Trp Leu Ser Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Phe
35 40 45

Leu Ile Tyr Gln Ala Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe
50 55 60

Lys Gly Ser Gly Ser Gly Thr Gln Phe Thr Leu Thr Ile Ser Asp Leu
65 70 75 80

Glu Cys Asp Asp Ala Ala Thr Tyr Tyr Cys Ala Gly Gly Tyr Ser Gly
85 90 95

Asn Ile Val Gly Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg Thr
100 105 110

Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu
115 120 125

Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro
130 135 140

Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly
145 150 155 160

Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr
165 170 175

Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His
180 185 190

Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val
195 200 205

Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> SEQ ID NO 342
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 342

Ala Gln Val Leu Thr Gln Thr Pro Ser Ser Val Ser Ala Ala Val Gly
1 5 10 15

Gly Thr Val Thr Ile Asn Cys Gln Ser Ser Lys Ser Val Tyr Asn Asn
20 25 30

Asn Trp Leu Ser Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Phe
35 40 45

Leu Ile Tyr Gln Ala Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe

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    50                  55                  60

Lys Gly Ser Gly Ser Gly Thr Gln Phe Thr Leu Thr Ile Ser Asp Leu
65                  70                  75                  80

Glu Cys Asp Asp Ala Ala Thr Tyr Tyr Cys Ala Gly Gly Tyr Ser Gly
                85                  90                  95

Asn Ile Val Gly Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg
            100                 105                 110


<210> SEQ ID NO 343
<211> LENGTH: 23
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 343

Ala Gln Val Leu Thr Gln Thr Pro Ser Ser Val Ser Ala Ala Val Gly
1               5                   10                  15

Gly Thr Val Thr Ile Asn Cys
            20


<210> SEQ ID NO 344
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 344

Gln Ser Ser Lys Ser Val Tyr Asn Asn Asn Trp Leu Ser
1               5                   10


<210> SEQ ID NO 345
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 345

Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Phe Leu Ile Tyr
1               5                   10                  15


<210> SEQ ID NO 346
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 346

Gln Ala Ser Asn Leu Ala Ser
1               5


<210> SEQ ID NO 347
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 347

Gly Val Pro Ser Arg Phe Lys Gly Ser Gly Ser Gly Thr Gln Phe Thr
1               5                   10                  15

Leu Thr Ile Ser Asp Leu Glu Cys Asp Asp Ala Ala Thr Tyr Tyr Cys
            20                  25                  30


<210> SEQ ID NO 348
<211> LENGTH: 10
<212> TYPE: PRT
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<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 348

Ala Gly Gly Tyr Ser Gly Asn Ile Val Gly
1 5 10

<210> SEQ ID NO 349
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 349

Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg
1 5 10

<210> SEQ ID NO 350
<211> LENGTH: 106
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 350

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
1 5 10 15

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
20 25 30

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
35 40 45

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
50 55 60

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
65 70 75 80

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
85 90 95

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
100 105

<210> SEQ ID NO 351
<211> LENGTH: 651
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 351

gcgcaagtgc tgacccagac tccatcgtcc gtgtctgcag ctgtgggagg cacagtcacc 60

atcaattgcc agtccagtaa gagtgtttat aacaacaatt ggttatcctg gtatcaacag 120

aaaccagggc agcctcccaa gttcctgatc taccaggcat ccaatttggc atctggggtc 180

ccgtcgcggt tcaaaggcag tggatctggg acacagttca ctctcaccat cagcgacctc 240

gagtgtgacg atgccgccac ttattactgt gcaggcggtt atagtggtaa tattgttggt 300

ttcggcggag ggaccgaggt ggtggtcaaa cgtacggtag cggccccatc tgtcttcatc 360

ttcccgccat ctgatgagca gttgaaatct ggaactgcct ctgttgtgtg cctgctgaat 420

aacttctatc ccagagaggc caaagtacag tggaaggtgg ataacgccct ccaatcgggt 480

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aactcccagg agagtgtcac agagcaggac agcaaggaca gcacctacag cctcagcagc 540

accctgacgc tgagcaaagc agactacgag aaacacaaag tctacgcctg cgaagtcacc 600

catcagggcc tgagctcgcc cgtcacaaag agcttcaaca ggggagagtg t 651

<210> SEQ ID NO 352
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 352

gcgcaagtgc tgacccagac tccatcgtcc gtgtctgcag ctgtgggagg cacagtcacc 60

atcaattgcc agtccagtaa gagtgtttat aacaacaatt ggttatcctg gtatcaacag 120

aaaccagggc agcctcccaa gttcctgatc taccaggcat ccaatttggc atctggggtc 180

ccgtcgcggt tcaaaggcag tggatctggg acacagttca ctctcaccat cagcgacctc 240

gagtgtgacg atgccgccac ttattactgt gcaggcggtt atagtggtaa tattgttggt 300

ttcggcggag ggaccgaggt ggtggtcaaa cgt 333

<210> SEQ ID NO 353
<211> LENGTH: 69
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 353

gcgcaagtgc tgacccagac tccatcgtcc gtgtctgcag ctgtgggagg cacagtcacc 60

atcaattgc 69

<210> SEQ ID NO 354
<211> LENGTH: 39
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 354

cagtccagta agagtgttta taacaacaat tggttatcc 39

<210> SEQ ID NO 355
<211> LENGTH: 45
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 355

tggtatcaac agaaaccagg gcagcctccc aagttcctga tctac 45

<210> SEQ ID NO 356
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 356

caggcatcca atttggcatc t 21

<210> SEQ ID NO 357
<211> LENGTH: 96
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

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<400> SEQUENCE: 357

ggggtcccgt cgcggttcaa aggcagtgga tctgggacac agttcactct caccatcagc 60

gacctcgagt gtgacgatgc cgccacttat tactgt 96

<210> SEQ ID NO 358
<211> LENGTH: 30
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 358

gcaggcggtt atagtggtaa tattgttggt 30

<210> SEQ ID NO 359
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 359

ttcggcggag ggaccgaggt ggtggtcaaa cgt 33

<210> SEQ ID NO 360
<211> LENGTH: 318
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 360

acggtagcgg ccccatctgt cttcatcttc ccgccatctg atgagcagtt gaaatctgga 60

actgcctctg ttgtgtgcct gctgaataac ttctatccca gagaggccaa agtacagtgg 120

aaggtggata acgccctcca atcgggtaac tcccaggaga gtgtcacaga gcaggacagc 180

aaggacagca cctacagcct cagcagcacc ctgacgctga gcaaagcaga ctacgagaaa 240

cacaaagtct acgcctgcga agtcacccat cagggcctga gctcgcccgt cacaaagagc 300

ttcaacaggg gagagtgt 318

<210> SEQ ID NO 361
<211> LENGTH: 443
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 361

Gln Ser Val Glu Ala Ser Gly Gly Arg Leu Val Thr Pro Gly Thr Pro
1 5 10 15

Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Ser Ser Ala Thr
20 25 30

Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
35 40 45

Leu Ile Gly Gly Asn Asp Glu Arg Tyr Tyr Ala Ser Trp Ala Lys Gly
50 55 60

Arg Phe Thr Ile Ser Lys Thr Ser Ser Thr Thr Val Asp Leu Lys Met
65 70 75 80

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Thr Ser Pro Thr Thr Glu Asp Thr Ala Thr Tyr Phe Cys Ala Arg Gly
                85                  90                  95

Gly Gly Glu Phe Phe Ile Trp Gly Pro Gly Thr Leu Val Thr Val Ser
            100                 105                 110

Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser
        115                 120                 125

Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp
    130                 135                 140

Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
145                 150                 155                 160

Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr
                165                 170                 175

Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln
            180                 185                 190

Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp
        195                 200                 205

Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro
    210                 215                 220

Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro
225                 230                 235                 240

Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr
                245                 250                 255

Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn
            260                 265                 270

Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
        275                 280                 285

Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
    290                 295                 300

Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
305                 310                 315                 320

Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys
                325                 330                 335

Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu
            340                 345                 350

Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
        355                 360                 365

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
    370                 375                 380

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
385                 390                 395                 400

Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
                405                 410                 415

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
            420                 425                 430

Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
        435                 440
```

<210> SEQ ID NO 362
<211> LENGTH: 113
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

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<400> SEQUENCE: 362

Gln Ser Val Glu Ala Ser Gly Gly Arg Leu Val Thr Pro Gly Thr Pro
1 5 10 15

Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Ser Ser Ala Thr
20 25 30

Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
35 40 45

Leu Ile Gly Gly Asn Asp Glu Arg Tyr Tyr Ala Ser Trp Ala Lys Gly
50 55 60

Arg Phe Thr Ile Ser Lys Thr Ser Ser Thr Thr Val Asp Leu Lys Met
65 70 75 80

Thr Ser Pro Thr Thr Glu Asp Thr Ala Thr Tyr Phe Cys Ala Arg Gly
85 90 95

Gly Gly Glu Phe Phe Ile Trp Gly Pro Gly Thr Leu Val Thr Val Ser
100 105 110

Ser

<210> SEQ ID NO 363
<211> LENGTH: 29
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 363

Gln Ser Val Glu Ala Ser Gly Gly Arg Leu Val Thr Pro Gly Thr Pro
1 5 10 15

Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Ser
20 25

<210> SEQ ID NO 364
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 364

Ser Ala Thr Met Asn
1 5

<210> SEQ ID NO 365
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 365

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
1 5 10

<210> SEQ ID NO 366
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 366

Leu Ile Gly Gly Asn Asp Glu Arg Tyr Tyr Ala Ser Trp Ala Lys Gly
1 5 10 15

<210> SEQ ID NO 367
<211> LENGTH: 31

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<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 367

Arg Phe Thr Ile Ser Lys Thr Ser Ser Thr Thr Val Asp Leu Lys Met
1 5 10 15

Thr Ser Pro Thr Thr Glu Asp Thr Ala Thr Tyr Phe Cys Ala Arg
20 25 30

<210> SEQ ID NO 368
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 368

Gly Gly Gly Glu Phe Phe Ile
1 5

<210> SEQ ID NO 369
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 369

Trp Gly Pro Gly Thr Leu Val Thr Val Ser Ser
1 5 10

<210> SEQ ID NO 370
<211> LENGTH: 330
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 370

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65 70 75 80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95

Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
100 105 110

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
115 120 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
130 135 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145 150 155 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu

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                165                 170                 175

Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
            180                 185                 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
        195                 200                 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
    210                 215                 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
225                 230                 235                 240

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
                245                 250                 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
            260                 265                 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
        275                 280                 285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
    290                 295                 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305                 310                 315                 320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
                325                 330


<210> SEQ ID NO 371
<211> LENGTH: 1329
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 371

cagtcggtgg aggcgtccgg gggtcgcctg gtcacgcctg ggacacccct gacactcacc     60

tgcaccgtct ctggattctc cctcagtagc gctacaatga actgggtccg ccaggctcca    120

gggaaggggc tggaatggat cgggcttatt ggcggtaatg acgaaagata ctacgcgtcc    180

tgggcgaaag gccgattcac catctccaaa acctcgtcga ccacggtgga tctgaaaatg    240

accagtccga caaccgagga cacggccacc tatttctgtg ccagaggggg gggggaattt    300

ttcatctggg gcccgggcac cctggtcacc gtctcgagcg cctccaccaa gggcccatcg    360

gtcttccccc tggcaccctc ctccaagagc acctctgggg gcacagcggc cctgggctgc    420

ctggtcaagg actacttccc cgaaccggtg acggtgtcgt ggaactcagg cgccctgacc    480

agcggcgtgc acaccttccc ggctgtccta cagtcctcag gactctactc cctcagcagc    540

gtggtgaccg tgccctccag cagcttgggc acccagacct acatctgcaa cgtgaatcac    600

aagcccagca acaccaaggt ggacaagaaa gttgagccca aatcttgtga caaaactcac    660

acatgcccac cgtgcccagc acctgaactc ctgggggggac cgtcagtctt cctcttcccc    720

ccaaaaccca aggacaccct catgatctcc cggacccctg aggtcacatg cgtggtggtg    780

gacgtgagcc acgaagaccc tgaggtcaag ttcaactggt acgtggacgg cgtggaggtg    840

cataatgcca agacaaagcc gcgggaggag cagtacgcca gcacgtaccg tgtggtcagc    900

gtcctcaccg tcctgcacca ggactggctg aatggcaagg agtacaagtg caaggtctcc    960

aacaaagccc tcccagcccc catcgagaaa accatctcca aagccaaagg gcagccccga   1020
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gaaccacagg tgtacaccct gcccccatcc cgggaggaga tgaccaagaa ccaggtcagc 1080

ctgacctgcc tggtcaaagg cttctatccc agcgacatcg ccgtggagtg ggagagcaat 1140

gggcagccgg agaacaacta caagaccacg cctcccgtgc tggactccga cggctccttc 1200

ttcctctaca gcaagctcac cgtggacaag agcaggtggc agcaggggaa cgtcttctca 1260

tgctccgtga tgcatgaggc tctgcacaac cactacacgc agaagagcct ctccctgtct 1320

ccgggtaaa 1329

<210> SEQ ID NO 372
<211> LENGTH: 339
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 372

cagtcggtgg aggcgtccgg gggtcgcctg gtcacgcctg ggacacccct gacactcacc 60

tgcaccgtct ctggattctc cctcagtagc gctacaatga actgggtccg ccaggctcca 120

gggaaggggc tggaatggat cgggcttatt ggcggtaatg acgaaagata ctacgcgtcc 180

tgggcgaaag gccgattcac catctccaaa acctcgtcga ccacggtgga tctgaaaatg 240

accagtccga caaccgagga cacggccacc tatttctgtg ccagaggggg gggggaattt 300

ttcatctggg gcccgggcac cctggtcacc gtctcgagc 339

<210> SEQ ID NO 373
<211> LENGTH: 87
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 373

cagtcggtgg aggcgtccgg gggtcgcctg gtcacgcctg ggacacccct gacactcacc 60

tgcaccgtct ctggattctc cctcagt 87

<210> SEQ ID NO 374
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 374

agcgctacaa tgaac 15

<210> SEQ ID NO 375
<211> LENGTH: 42
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 375

tgggtccgcc aggctccagg gaaggggctg gaatggatcg gg 42

<210> SEQ ID NO 376
<211> LENGTH: 48
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 376

cttattggcg gtaatgacga aagatactac gcgtcctggg cgaaaggc 48

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<210> SEQ ID NO 377
<211> LENGTH: 93
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 377

cgattcacca tctccaaaac ctcgtcgacc acggtggatc tgaaaatgac cagtccgaca 60

accgaggaca cggccaccta tttctgtgcc aga 93

<210> SEQ ID NO 378
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 378

ggggggggggg aatttttcat c 21

<210> SEQ ID NO 379
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 379

tggggcccgg gcaccctggt caccgtctcg agc 33

<210> SEQ ID NO 380
<211> LENGTH: 990
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 380

gcctccacca agggcccatc ggtcttcccc ctggcaccct cctccaagag cacctctggg 60

ggcacagcgg ccctgggctg cctggtcaag gactacttcc ccgaaccggt gacggtgtcg 120

tggaactcag gcgccctgac cagcggcgtg cacaccttcc cggctgtcct acagtcctca 180

ggactctact ccctcagcag cgtggtgacc gtgccctcca gcagcttggg cacccagacc 240

tacatctgca acgtgaatca caagcccagc aacaccaagg tggacaagaa agttgagccc 300

aaatcttgtg acaaaactca cacatgccca ccgtgcccag cacctgaact cctgggggga 360

ccgtcagtct tcctcttccc cccaaaaccc aaggacaccc tcatgatctc ccggacccct 420

gaggtcacat gcgtggtggt ggacgtgagc cacgaagacc ctgaggtcaa gttcaactgg 480

tacgtggacg gcgtggaggt gcataatgcc aagacaaagc cgcgggagga gcagtacgcc 540

agcacgtacc gtgtggtcag cgtcctcacc gtcctgcacc aggactggct gaatggcaag 600

gagtacaagt gcaaggtctc caacaaagcc ctcccagccc ccatcgagaa aaccatctcc 660

aaagccaaag ggcagccccg agaaccacag gtgtacaccc tgcccccatc ccgggaggag 720

atgaccaaga accaggtcag cctgacctgc ctggtcaaag gcttctatcc cagcgacatc 780

gccgtggagt gggagagcaa tgggcagccg gagaacaact acaagaccac gcctcccgtg 840

ctggactccg acggctcctt cttcctctac agcaagctca ccgtggacaa gagcaggtgg 900

cagcagggga acgtcttctc atgctccgtg atgcatgagg ctctgcacaa ccactacacg 960

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cagaagagcc tctccctgtc tccgggtaaa 990

<210> SEQ ID NO 381
<211> LENGTH: 217
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 381

Ala Gln Val Leu Thr Gln Thr Pro Ser Ser Val Ser Ala Ala Val Gly
1 5 10 15

Gly Thr Val Thr Ile Asn Cys Gln Ser Ser Glu Ser Val Tyr Thr Asn
20 25 30

Asp Arg Leu Ser Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu
35 40 45

Leu Ile Tyr Glu Ala Ser Lys Leu Ala Ser Gly Val Pro Pro Arg Phe
50 55 60

Ser Gly Ser Gly Ser Gly Thr Gln Phe Thr Leu Thr Ile Ser Asp Leu
65 70 75 80

Glu Cys Asp Asp Ala Ala Thr Tyr Tyr Cys Ala Gly Ala Tyr Ser Thr
85 90 95

Ser Ile His Gly Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg Thr
100 105 110

Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu
115 120 125

Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro
130 135 140

Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly
145 150 155 160

Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr
165 170 175

Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His
180 185 190

Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val
195 200 205

Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> SEQ ID NO 382
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 382

Ala Gln Val Leu Thr Gln Thr Pro Ser Ser Val Ser Ala Ala Val Gly
1 5 10 15

Gly Thr Val Thr Ile Asn Cys Gln Ser Ser Glu Ser Val Tyr Thr Asn
20 25 30

Asp Arg Leu Ser Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu
35 40 45

Leu Ile Tyr Glu Ala Ser Lys Leu Ala Ser Gly Val Pro Pro Arg Phe
50 55 60

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Ser Gly Ser Gly Ser Gly Thr Gln Phe Thr Leu Thr Ile Ser Asp Leu
65 70 75 80

Glu Cys Asp Asp Ala Ala Thr Tyr Tyr Cys Ala Gly Ala Tyr Ser Thr
85 90 95

Ser Ile His Gly Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg
100 105 110

<210> SEQ ID NO 383
<211> LENGTH: 23
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 383

Ala Gln Val Leu Thr Gln Thr Pro Ser Ser Val Ser Ala Ala Val Gly
1 5 10 15

Gly Thr Val Thr Ile Asn Cys
20

<210> SEQ ID NO 384
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 384

Gln Ser Ser Glu Ser Val Tyr Thr Asn Asp Arg Leu Ser
1 5 10

<210> SEQ ID NO 385
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 385

Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr
1 5 10 15

<210> SEQ ID NO 386
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 386

Glu Ala Ser Lys Leu Ala Ser
1 5

<210> SEQ ID NO 387
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 387

Gly Val Pro Pro Arg Phe Ser Gly Ser Gly Ser Gly Thr Gln Phe Thr
1 5 10 15

Leu Thr Ile Ser Asp Leu Glu Cys Asp Asp Ala Ala Thr Tyr Tyr Cys
20 25 30

<210> SEQ ID NO 388
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

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<400> SEQUENCE: 388

Ala Gly Ala Tyr Ser Thr Ser Ile His Gly
1 5 10

<210> SEQ ID NO 389
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 389

Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg
1 5 10

<210> SEQ ID NO 390
<211> LENGTH: 106
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 390

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
1 5 10 15

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
20 25 30

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
35 40 45

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
50 55 60

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
65 70 75 80

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
85 90 95

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
100 105

<210> SEQ ID NO 391
<211> LENGTH: 651
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 391

gcgcaagtgc tgacccagac tccatcgtcc gtgtctgcag ctgtgggagg cacagtcacc 60

atcaattgcc agtccagtga gagtgtttat actaacgacc gcttatcctg gtatcagcag 120

aaaccagggc agcctcccaa gctcctgatc tacgaagcat ccaagctggc atctggggtc 180

ccaccgcggt tcagcggcag tggatctggg acacagttca ctctcaccat cagcgacctg 240

gagtgtgacg atgccgccac ttattactgt gcaggcgctt atagtactag tatccatggt 300

ttcggcggag ggaccgaggt ggtggtcaaa cgtacggtag cggccccatc tgtcttcatc 360

ttcccgccat ctgatgagca gttgaaatct ggaactgcct ctgttgtgtg cctgctgaat 420

aacttctatc ccagagaggc caaagtacag tggaaggtgg ataacgccct ccaatcgggt 480

aactcccagg agagtgtcac agagcaggac agcaaggaca gcacctacag cctcagcagc 540

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accctgacgc tgagcaaagc agactacgag aaacacaaag tctacgcctg cgaagtcacc 600

catcagggcc tgagctcgcc cgtcacaaag agcttcaaca ggggagagtg t 651

<210> SEQ ID NO 392
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 392

gcgcaagtgc tgacccagac tccatcgtcc gtgtctgcag ctgtgggagg cacagtcacc 60

atcaattgcc agtccagtga gagtgtttat actaacgacc gcttatcctg gtatcagcag 120

aaaccagggc agcctcccaa gctcctgatc tacgaagcat ccaagctggc atctggggtc 180

ccaccgcggt tcagcggcag tggatctggg acacagttca ctctcaccat cagcgacctg 240

gagtgtgacg atgccgccac ttattactgt gcaggcgctt atagtactag tatccatggt 300

ttcggcggag ggaccgaggt ggtggtcaaa cgt 333

<210> SEQ ID NO 393
<211> LENGTH: 69
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 393

gcgcaagtgc tgacccagac tccatcgtcc gtgtctgcag ctgtgggagg cacagtcacc 60

atcaattgc 69

<210> SEQ ID NO 394
<211> LENGTH: 39
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 394

cagtccagtg agagtgttta tactaacgac cgcttatcc 39

<210> SEQ ID NO 395
<211> LENGTH: 45
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 395

tggtatcagc agaaaccagg gcagcctccc aagctcctga tctac 45

<210> SEQ ID NO 396
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 396

gaagcatcca agctggcatc t 21

<210> SEQ ID NO 397
<211> LENGTH: 96
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 397

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ggggtcccac cgcggttcag cggcagtgga tctgggacac agttcactct caccatcagc 60

gacctggagt gtgacgatgc cgccacttat tactgt 96

<210> SEQ ID NO 398
<211> LENGTH: 30
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 398

gcaggcgctt atagtactag tatccatggt 30

<210> SEQ ID NO 399
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 399

ttcggcggag ggaccgaggt ggtggtcaaa cgt 33

<210> SEQ ID NO 400
<211> LENGTH: 318
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 400

acggtagcgg ccccatctgt cttcatcttc ccgccatctg atgagcagtt gaaatctgga 60

actgcctctg ttgtgtgcct gctgaataac ttctatccca gagaggccaa agtacagtgg 120

aaggtggata acgccctcca atcgggtaac tcccaggaga gtgtcacaga gcaggacagc 180

aaggacagca cctacagcct cagcagcacc ctgacgctga gcaaagcaga ctacgagaaa 240

cacaaagtct acgcctgcga agtcacccat cagggcctga gctcgcccgt cacaaagagc 300

ttcaacaggg gagagtgt 318

<210> SEQ ID NO 401

<400> SEQUENCE: 401

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<210> SEQ ID NO 402

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<210> SEQ ID NO 403

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<210> SEQ ID NO 404

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<210> SEQ ID NO 405

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<210> SEQ ID NO 406

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<210> SEQ ID NO 407

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<210> SEQ ID NO 408

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<210> SEQ ID NO 409

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<210> SEQ ID NO 410

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<210> SEQ ID NO 411

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<210> SEQ ID NO 412

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<210> SEQ ID NO 414

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<210> SEQ ID NO 416

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<210> SEQ ID NO 417

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<210> SEQ ID NO 418

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<210> SEQ ID NO 419

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<210> SEQ ID NO 420

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<210> SEQ ID NO 421

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<210> SEQ ID NO 422

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<210> SEQ ID NO 423

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<210> SEQ ID NO 428

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<210> SEQ ID NO 429

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<210> SEQ ID NO 430

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<210> SEQ ID NO 437

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<210> SEQ ID NO 445

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<210> SEQ ID NO 446

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<210> SEQ ID NO 447

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<210> SEQ ID NO 448

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<210> SEQ ID NO 449

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<210> SEQ ID NO 451

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<210> SEQ ID NO 452

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<210> SEQ ID NO 453

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<210> SEQ ID NO 454

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<210> SEQ ID NO 455

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<210> SEQ ID NO 471

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<210> SEQ ID NO 472

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<210> SEQ ID NO 474

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<210> SEQ ID NO 475

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<210> SEQ ID NO 476

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<210> SEQ ID NO 478

<400> SEQUENCE: 478

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<210> SEQ ID NO 479

<400> SEQUENCE: 479

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<210> SEQ ID NO 480

<400> SEQUENCE: 480

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<210> SEQ ID NO 481
<211> LENGTH: 445
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 481

```
Gln Ser Val Glu Glu Ser Gly Gly Arg Leu Val Thr Pro Gly Thr Pro
1               5                  10                  15

Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Ser Ser Tyr Ala
            20                  25                  30

Met Ile Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
        35                  40                  45

Ile Ile Tyr Asp Asn Gly Asp Thr Tyr Tyr Ala Ser Trp Ala Lys Gly
    50                  55                  60

Arg Phe Thr Ile Ser Lys Thr Ser Thr Thr Val Tyr Leu Lys Ile Ala
65                  70                  75                  80

Ser Pro Thr Thr Glu Asp Thr Ala Thr Tyr Phe Cys Ala Arg Glu Pro
                85                  90                  95

Gly Ser Thr Thr Gln Asn Asp Leu Trp Gly Gln Gly Thr Leu Val Thr
            100                 105                 110

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
        115                 120                 125

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
    130                 135                 140

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
145                 150                 155                 160

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
                165                 170                 175

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
            180                 185                 190

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
        195                 200                 205

Val Asp Ala Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
    210                 215                 220

Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu
225                 230                 235                 240

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
                245                 250                 255

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
            260                 265                 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
        275                 280                 285

Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu
    290                 295                 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305                 310                 315                 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
                325                 330                 335

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
            340                 345                 350
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```
Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
        355                 360                 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
    370                 375                 380

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
385                 390                 395                 400

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
                405                 410                 415

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
            420                 425                 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
        435                 440                 445


<210> SEQ ID NO 482
<211> LENGTH: 115
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 482

Gln Ser Val Glu Glu Ser Gly Gly Arg Leu Val Thr Pro Gly Thr Pro
1               5                   10                  15

Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Ser Ser Tyr Ala
            20                  25                  30

Met Ile Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
        35                  40                  45

Ile Ile Tyr Asp Asn Gly Asp Thr Tyr Tyr Ala Ser Trp Ala Lys Gly
    50                  55                  60

Arg Phe Thr Ile Ser Lys Thr Ser Thr Thr Val Tyr Leu Lys Ile Ala
65                  70                  75                  80

Ser Pro Thr Thr Glu Asp Thr Ala Thr Tyr Phe Cys Ala Arg Glu Pro
                85                  90                  95

Gly Ser Thr Thr Gln Asn Asp Leu Trp Gly Gln Gly Thr Leu Val Thr
            100                 105                 110

Val Ser Ser
        115


<210> SEQ ID NO 483
<211> LENGTH: 29
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 483

Gln Ser Val Glu Glu Ser Gly Gly Arg Leu Val Thr Pro Gly Thr Pro
1               5                   10                  15

Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Ser
            20                  25


<210> SEQ ID NO 484
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 484

Ser Tyr Ala Met Ile
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1               5


<210> SEQ ID NO 485
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 485

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
1               5                   10


<210> SEQ ID NO 486
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 486

Ile Ile Tyr Asp Asn Gly Asp Thr Tyr Tyr Ala Ser Trp Ala Lys Gly
1               5                   10                  15


<210> SEQ ID NO 487
<211> LENGTH: 30
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 487

Arg Phe Thr Ile Ser Lys Thr Ser Thr Thr Val Tyr Leu Lys Ile Ala
1               5                   10                  15

Ser Pro Thr Thr Glu Asp Thr Ala Thr Tyr Phe Cys Ala Arg
            20                  25                  30


<210> SEQ ID NO 488
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 488

Glu Pro Gly Ser Thr Thr Gln Asn Asp Leu
1               5                   10


<210> SEQ ID NO 489
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 489

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
1               5                   10


<210> SEQ ID NO 490
<211> LENGTH: 330
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 490

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1               5                   10                  15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
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            20                  25                  30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
        35                  40                  45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
    50                  55                  60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65                  70                  75                  80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Ala
                85                  90                  95

Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
            100                 105                 110

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
        115                 120                 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
    130                 135                 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145                 150                 155                 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
                165                 170                 175

Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
            180                 185                 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
        195                 200                 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
    210                 215                 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
225                 230                 235                 240

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
                245                 250                 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
            260                 265                 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
        275                 280                 285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
    290                 295                 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305                 310                 315                 320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
                325                 330


<210> SEQ ID NO 491
<211> LENGTH: 1335
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 491

cagtcggtgg aggagtccgg gggtcgcctg gtcacgcctg ggacacccct gacactcacc     60

tgcacagtct ctggattctc cctcagtagc tatgcgatga tctgggtccg ccaggctcca    120

gggaaggggc tggaatggat cggaatcatt tatgataatg gtgacacata ctacgcgagc    180

tgggcgaaag gccggttcac catctccaaa acctcgacca cggtgtatct gaagatcgcc    240
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agtccgacaa ccgaggacac ggccacctac ttctgtgcca gagagcctgg tagtactact 300

cagaatgact tgtggggcca agggaccctg gtcaccgtct cgagcgcctc caccaagggc 360

ccatcggtct tcccccctggc accctcctcc aagagcacct ctgggggcac agcggccctg 420

ggctgcctgg tcaaggacta cttccccgaa ccggtgacgg tgtcgtggaa ctcaggcgcc 480

ctgaccagcg gcgtgcacac cttcccggct gtcctacagt cctcaggact ctactccctc 540

agcagcgtgg tgaccgtgcc ctccagcagc ttgggcaccc agacctacat ctgcaacgtg 600

aatcacaagc ccagcaacac caaggtggac gcgagagttg agcccaaatc ttgtgacaaa 660

actcacacat gcccaccgtg cccagcacct gaactcctgg ggggaccgtc agtcttcctc 720

ttccccccaa aacccaagga caccctcatg atctcccgga cccctgaggt cacatgcgtg 780

gtggtggacg tgagccacga agaccctgag gtcaagttca actggtacgt ggacggcgtg 840

gaggtgcata atgccaagac aaagccgcgg gaggagcagt acgccagcac gtaccgtgtg 900

gtcagcgtcc tcaccgtcct gcaccaggac tggctgaatg gcaaggagta caagtgcaag 960

gtctccaaca aagccctccc agcccccatc gagaaaacca tctccaaagc caaagggcag 1020

ccccgagaac cacaggtgta caccctgccc ccatcccggg aggagatgac caagaaccag 1080

gtcagcctga cctgcctggt caaaggcttc tatcccagcg acatcgccgt ggagtgggag 1140

agcaatgggc agccggagaa caactacaag accacgcctc ccgtgctgga ctccgacggc 1200

tccttcttcc tctacagcaa gctcaccgtg gacaagagca ggtggcagca ggggaacgtc 1260

ttctcatgct ccgtgatgca tgaggctctg cacaaccact acacgcagaa gagcctctcc 1320

ctgtctccgg gtaaa 1335

<210> SEQ ID NO 492
<211> LENGTH: 345
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 492

cagtcggtgg aggagtccgg gggtcgcctg gtcacgcctg ggacacccct gacactcacc 60

tgcacagtct ctggattctc cctcagtagc tatgcgatga tctgggtccg ccaggctcca 120

gggaaggggc tggaatggat cggaatcatt tatgataatg gtgacacata ctacgcgagc 180

tgggcgaaag gccggttcac catctccaaa acctcgacca cggtgtatct gaagatcgcc 240

agtccgacaa ccgaggacac ggccacctac ttctgtgcca gagagcctgg tagtactact 300

cagaatgact tgtggggcca agggaccctg gtcaccgtct cgagc 345

<210> SEQ ID NO 493
<211> LENGTH: 87
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 493

cagtcggtgg aggagtccgg gggtcgcctg gtcacgcctg ggacacccct gacactcacc 60

tgcacagtct ctggattctc cctcagt 87

<210> SEQ ID NO 494
<211> LENGTH: 15

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<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 494

agctatgcga tgatc 15

<210> SEQ ID NO 495
<211> LENGTH: 42
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 495

tgggtccgcc aggctccagg gaaggggctg gaatggatcg ga 42

<210> SEQ ID NO 496
<211> LENGTH: 48
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 496

atcatttatg ataatggtga cacatactac gcgagctggg cgaaaggc 48

<210> SEQ ID NO 497
<211> LENGTH: 90
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 497

cggttcacca tctccaaaac ctcgaccacg gtgtatctga agatcgccag tccgacaacc 60

gaggacacgg ccacctactt ctgtgccaga 90

<210> SEQ ID NO 498
<211> LENGTH: 30
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 498

gagcctggta gtactactca gaatgacttg 30

<210> SEQ ID NO 499
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 499

tggggccaag ggaccctggt caccgtctcg agc 33

<210> SEQ ID NO 500
<211> LENGTH: 990
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 500

gcctccacca agggcccatc ggtcttcccc ctggcaccct cctccaagag cacctctggg 60

ggcacagcgg ccctgggctg cctggtcaag gactacttcc ccgaaccggt gacggtgtcg 120

tggaactcag gcgccctgac cagcggcgtg cacaccttcc cggctgtcct acagtcctca 180

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ggactctact ccctcagcag cgtggtgacc gtgccctcca gcagcttggg cacccagacc    240

tacatctgca acgtgaatca caagcccagc aacaccaagg tggacgcgag agttgagccc    300

aaatcttgtg acaaaactca cacatgccca ccgtgcccag cacctgaact cctgggggga    360

ccgtcagtct tcctcttccc cccaaaaccc aaggacaccc tcatgatctc ccggacccct    420

gaggtcacat gcgtggtggt ggacgtgagc cacgaagacc ctgaggtcaa gttcaactgg    480

tacgtggacg gcgtggaggt gcataatgcc aagacaaagc cgcgggagga gcagtacgcc    540

agcacgtacc gtgtggtcag cgtcctcacc gtcctgcacc aggactggct gaatggcaag    600

gagtacaagt gcaaggtctc caacaaagcc ctcccagccc ccatcgagaa aaccatctcc    660

aaagccaaag ggcagccccg agaaccacag gtgtacaccc tgcccccatc ccgggaggag    720

atgaccaaga accaggtcag cctgacctgc ctggtcaaag gcttctatcc cagcgacatc    780

gccgtggagt gggagagcaa tgggcagccg gagaacaact acaagaccac gcctcccgtg    840

ctggactccg acggctcctt cttcctctac agcaagctca ccgtggacaa gagcaggtgg    900

cagcagggga acgtcttctc atgctccgtg atgcatgagg ctctgcacaa ccactacacg    960

cagaagagcc tctccctgtc tccgggtaaa                                     990
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<210> SEQ ID NO 501
<211> LENGTH: 217
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 501

```
Asp Val Val Met Thr Gln Thr Pro Ala Ser Val Ser Glu Pro Val Gly
1               5                   10                  15

Gly Thr Val Thr Ile Lys Cys Gln Ala Ser Glu Asn Ile Tyr Asn Ser
            20                  25                  30

Leu Leu Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Arg Ala Ser Thr Leu Ala Ser Gly Val Ser Ser Arg Phe Lys Gly
    50                  55                  60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Asp Leu Glu Cys
65                  70                  75                  80

Ala Asp Ala Ala Thr Tyr Tyr Cys Gln Asn Tyr Tyr Asn Ile Trp Thr
                85                  90                  95

Asn Gly Ala Ala Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg Thr
            100                 105                 110

Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu
        115                 120                 125

Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro
    130                 135                 140

Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly
145                 150                 155                 160

Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr
                165                 170                 175

Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His
            180                 185                 190

Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val
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        195                 200                 205

Thr Lys Ser Phe Asn Arg Gly Glu Cys
    210                 215


<210> SEQ ID NO 502
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 502

Asp Val Val Met Thr Gln Thr Pro Ala Ser Val Ser Glu Pro Val Gly
1               5                   10                  15

Gly Thr Val Thr Ile Lys Cys Gln Ala Ser Glu Asn Ile Tyr Asn Ser
            20                  25                  30

Leu Leu Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Arg Ala Ser Thr Leu Ala Ser Gly Val Ser Ser Arg Phe Lys Gly
    50                  55                  60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Asp Leu Glu Cys
65                  70                  75                  80

Ala Asp Ala Ala Thr Tyr Tyr Cys Gln Asn Tyr Tyr Asn Ile Trp Thr
                85                  90                  95

Asn Gly Ala Ala Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg
            100                 105                 110


<210> SEQ ID NO 503
<211> LENGTH: 23
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 503

Asp Val Val Met Thr Gln Thr Pro Ala Ser Val Ser Glu Pro Val Gly
1               5                   10                  15

Gly Thr Val Thr Ile Lys Cys
            20


<210> SEQ ID NO 504
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 504

Gln Ala Ser Glu Asn Ile Tyr Asn Ser Leu Leu
1               5                   10


<210> SEQ ID NO 505
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 505

Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr
1               5                   10                  15


<210> SEQ ID NO 506
<211> LENGTH: 7
<212> TYPE: PRT
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<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 506

Arg Ala Ser Thr Leu Ala Ser
1 5

<210> SEQ ID NO 507
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 507

Gly Val Ser Ser Arg Phe Lys Gly Ser Gly Ser Gly Thr Glu Phe Thr
1 5 10 15

Leu Thr Ile Ser Asp Leu Glu Cys Ala Asp Ala Ala Thr Tyr Tyr Cys
20 25 30

<210> SEQ ID NO 508
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 508

Gln Asn Tyr Tyr Asn Ile Trp Thr Asn Gly Ala Ala
1 5 10

<210> SEQ ID NO 509
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 509

Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg
1 5 10

<210> SEQ ID NO 510
<211> LENGTH: 106
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 510

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
1 5 10 15

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
20 25 30

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
35 40 45

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
50 55 60

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
65 70 75 80

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
85 90 95

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
100 105

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<210> SEQ ID NO 511
<211> LENGTH: 651
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 511

gatgttgtga tgacccagac tccagcctcc gtgtctgaac ctgtgggagg cacagtcacc 60

atcaagtgcc aggccagtga gaacatttac aactctttac tctggtatca gcagaaacca 120

gggcagcctc ccaagctcct gatctatagg gcatccactc tggcatctgg ggtctcatcg 180

cggttcaaag gcagtggatc tgggacagag ttcactctca ccatcagcga cctggagtgt 240

gccgatgctg ccacttacta ctgtcaaaac tattataata tatggactaa tggtgctgct 300

ttcggcggag ggaccgaggt ggtggtcaaa cgtacggtag cggccccatc tgtcttcatc 360

ttcccgccat ctgatgagca gttgaaatct ggaactgcct ctgttgtgtg cctgctgaat 420

aacttctatc ccagagaggc caaagtacag tggaaggtgg ataacgccct ccaatcgggt 480

aactcccagg agagtgtcac agagcaggac agcaaggaca gcacctacag cctcagcagc 540

accctgacgc tgagcaaagc agactacgag aaacacaaag tctacgcctg cgaagtcacc 600

catcagggcc tgagctcgcc cgtcacaaag agcttcaaca ggggagagtg t 651

<210> SEQ ID NO 512
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 512

gatgttgtga tgacccagac tccagcctcc gtgtctgaac ctgtgggagg cacagtcacc 60

atcaagtgcc aggccagtga gaacatttac aactctttac tctggtatca gcagaaacca 120

gggcagcctc ccaagctcct gatctatagg gcatccactc tggcatctgg ggtctcatcg 180

cggttcaaag gcagtggatc tgggacagag ttcactctca ccatcagcga cctggagtgt 240

gccgatgctg ccacttacta ctgtcaaaac tattataata tatggactaa tggtgctgct 300

ttcggcggag ggaccgaggt ggtggtcaaa cgt 333

<210> SEQ ID NO 513
<211> LENGTH: 69
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 513

gatgttgtga tgacccagac tccagcctcc gtgtctgaac ctgtgggagg cacagtcacc 60

atcaagtgc 69

<210> SEQ ID NO 514
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 514

caggccagtg agaacattta caactcttta ctc 33

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<210> SEQ ID NO 515
<211> LENGTH: 45
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 515

tggtatcagc agaaaccagg gcagcctccc aagctcctga tctat 45

<210> SEQ ID NO 516
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 516

agggcatcca ctctggcatc t 21

<210> SEQ ID NO 517
<211> LENGTH: 96
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 517

ggggtctcat cgcggttcaa aggcagtgga tctgggacag agttcactct caccatcagc 60

gacctggagt gtgccgatgc tgccacttac tactgt 96

<210> SEQ ID NO 518
<211> LENGTH: 36
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 518

caaaactatt ataatatatg gactaatggt gctgct 36

<210> SEQ ID NO 519
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 519

ttcggcggag ggaccgaggt ggtggtcaaa cgt 33

<210> SEQ ID NO 520
<211> LENGTH: 318
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 520

acggtagcgg ccccatctgt cttcatcttc ccgccatctg atgagcagtt gaaatctgga 60

actgcctctg ttgtgtgcct gctgaataac ttctatccca gagaggccaa agtacagtgg 120

aaggtggata acgccctcca atcgggtaac tcccaggaga gtgtcacaga gcaggacagc 180

aaggacagca cctacagcct cagcagcacc ctgacgctga gcaaagcaga ctacgagaaa 240

cacaaagtct acgcctgcga agtcacccat cagggcctga gctcgcccgt cacaaagagc 300

ttcaacaggg gagagtgt 318

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<210> SEQ ID NO 521
<211> LENGTH: 441
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 521

```
Gln Ser Val Glu Glu Ser Gly Gly Arg Leu Val Thr Pro Gly Thr Pro
1               5                  10                  15

Leu Thr Leu Thr Cys Thr Ala Ser Gly Ile Asp Leu Ser Gly Tyr Ala
            20                  25                  30

Met Gly Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
        35                  40                  45

Asp Ile Ser Thr Tyr Gly Thr Thr Asp Tyr Ala Ser Trp Val Asn Gly
    50                  55                  60

Arg Phe Thr Ile Ser Arg Thr Ser Thr Thr Val Thr Leu Lys Met Thr
65                  70                  75                  80

Ser Leu Thr Thr Glu Asp Thr Ala Thr Tyr Phe Cys Ala Arg Asp Tyr
                85                  90                  95

Trp Leu Ser Leu Trp Gly Pro Gly Thr Leu Val Thr Val Ser Ser Ala
            100                 105                 110

Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser
        115                 120                 125

Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe
    130                 135                 140

Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly
145                 150                 155                 160

Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu
                165                 170                 175

Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr
            180                 185                 190

Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Ala Arg
        195                 200                 205

Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro
    210                 215                 220

Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
225                 230                 235                 240

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
                245                 250                 255

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
            260                 265                 270

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
        275                 280                 285

Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
    290                 295                 300

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
305                 310                 315                 320

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
                325                 330                 335

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met
            340                 345                 350
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Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
        355                 360                 365

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
    370                 375                 380

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
385                 390                 395                 400

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
                405                 410                 415

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
            420                 425                 430

Lys Ser Leu Ser Leu Ser Pro Gly Lys
        435                 440


<210> SEQ ID NO 522
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 522

Gln Ser Val Glu Glu Ser Gly Gly Arg Leu Val Thr Pro Gly Thr Pro
1               5                   10                  15

Leu Thr Leu Thr Cys Thr Ala Ser Gly Ile Asp Leu Ser Gly Tyr Ala
            20                  25                  30

Met Gly Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
        35                  40                  45

Asp Ile Ser Thr Tyr Gly Thr Thr Asp Tyr Ala Ser Trp Val Asn Gly
    50                  55                  60

Arg Phe Thr Ile Ser Arg Thr Ser Thr Thr Val Thr Leu Lys Met Thr
65                  70                  75                  80

Ser Leu Thr Thr Glu Asp Thr Ala Thr Tyr Phe Cys Ala Arg Asp Tyr
                85                  90                  95

Trp Leu Ser Leu Trp Gly Pro Gly Thr Leu Val Thr Val Ser Ser
            100                 105                 110


<210> SEQ ID NO 523
<211> LENGTH: 29
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 523

Gln Ser Val Glu Glu Ser Gly Gly Arg Leu Val Thr Pro Gly Thr Pro
1               5                   10                  15

Leu Thr Leu Thr Cys Thr Ala Ser Gly Ile Asp Leu Ser
            20                  25


<210> SEQ ID NO 524
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 524

Gly Tyr Ala Met Gly
1               5


<210> SEQ ID NO 525
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<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 525

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
1 5 10

<210> SEQ ID NO 526
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 526

Asp Ile Ser Thr Tyr Gly Thr Thr Asp Tyr Ala Ser Trp Val Asn Gly
1 5 10 15

<210> SEQ ID NO 527
<211> LENGTH: 30
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 527

Arg Phe Thr Ile Ser Arg Thr Ser Thr Thr Val Thr Leu Lys Met Thr
1 5 10 15

Ser Leu Thr Thr Glu Asp Thr Ala Thr Tyr Phe Cys Ala Arg
20 25 30

<210> SEQ ID NO 528
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 528

Asp Tyr Trp Leu Ser Leu
1 5

<210> SEQ ID NO 529
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 529

Trp Gly Pro Gly Thr Leu Val Thr Val Ser Ser
1 5 10

<210> SEQ ID NO 530
<211> LENGTH: 330
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 530

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

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Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
    50                  55                  60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65                  70                  75                  80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Ala
                85                  90                  95

Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
            100                 105                 110

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
        115                 120                 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
    130                 135                 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145                 150                 155                 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
                165                 170                 175

Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
            180                 185                 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
        195                 200                 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
    210                 215                 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
225                 230                 235                 240

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
                245                 250                 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
            260                 265                 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
        275                 280                 285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
    290                 295                 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305                 310                 315                 320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
                325                 330


<210> SEQ ID NO 531
<211> LENGTH: 1323
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 531

cagtcggtgg aggagtccgg gggtcgcctg gtaacgcctg ggacacccct gacactcacc     60

tgcacagcct ctggaatcga cctcagtggc tatgcaatgg gctgggtccg ccaggctcca    120

gggaaggggc tggaatggat cggagacatt agtacctatg gtaccacaga ctacgcgagc    180

tgggtgaatg gccgattcac catctccaga acctcgacca cggtgactct gaaaatgacc    240

agtctgacaa ccgaggacac ggccacctat ttctgtgcca gagactattg gttgagcttg    300

tggggcccgg gcaccctcgt caccgtctcg agcgcctcca ccaagggccc atcggtcttc    360
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ccctggcac cctcctccaa gagcacctct gggggcacag cggccctggg ctgcctggtc 420

aaggactact tccccgaacc ggtgacggtg tcgtggaact caggcgccct gaccagcggc 480

gtgcacacct tcccggctgt cctacagtcc tcaggactct actccctcag cagcgtggtg 540

accgtgccct ccagcagctt gggcacccag acctacatct gcaacgtgaa tcacaagccc 600

agcaacacca aggtggacgc gagagttgag cccaaatctt gtgacaaaac tcacacatgc 660

ccaccgtgcc cagcacctga actcctgggg ggaccgtcag tcttcctctt cccccaaaa 720

cccaaggaca ccctcatgat ctcccggacc cctgaggtca catgcgtggt ggtggacgtg 780

agccacgaag accctgaggt caagttcaac tggtacgtgg acggcgtgga ggtgcataat 840

gccaagacaa agccgcggga ggagcagtac gccagcacgt accgtgtggt cagcgtcctc 900

accgtcctgc accaggactg gctgaatggc aaggagtaca agtgcaaggt ctccaacaaa 960

gccctcccag cccccatcga gaaaaccatc tccaaagcca aagggcagcc ccgagaacca 1020

caggtgtaca ccctgccccc atcccgggag gagatgacca agaaccaggt cagcctgacc 1080

tgcctggtca aaggcttcta tcccagcgac atcgccgtgg agtgggagag caatgggcag 1140

ccggagaaca actacaagac cacgcctccc gtgctggact ccgacggctc cttcttcctc 1200

tacagcaagc tcaccgtgga caagagcagg tggcagcagg ggaacgtctt ctcatgctcc 1260

gtgatgcatg aggctctgca caaccactac acgcagaaga gcctctccct gtctccgggt 1320

aaa 1323

<210> SEQ ID NO 532
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 532

cagtcggtgg aggagtccgg gggtcgcctg gtaacgcctg ggacacccct gacactcacc 60

tgcacagcct ctggaatcga cctcagtggc tatgcaatgg gctgggtccg ccaggctcca 120

gggaaggggc tggaatggat cggagacatt agtacctatg gtaccacaga ctacgcgagc 180

tgggtgaatg gccgattcac catctccaga acctcgacca cggtgactct gaaaatgacc 240

agtctgacaa ccgaggacac ggccacctat ttctgtgcca gagactattg gttgagcttg 300

tggggcccgg gcaccctcgt caccgtctcg agc 333

<210> SEQ ID NO 533
<211> LENGTH: 87
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 533

cagtcggtgg aggagtccgg gggtcgcctg gtaacgcctg ggacacccct gacactcacc 60

tgcacagcct ctggaatcga cctcagt 87

<210> SEQ ID NO 534
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 534

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ggctatgcaa tgggc 15

<210> SEQ ID NO 535
<211> LENGTH: 42
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 535

tgggtccgcc aggctccagg gaaggggctg gaatggatcg ga 42

<210> SEQ ID NO 536
<211> LENGTH: 48
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 536

gacattagta cctatggtac cacagactac gcgagctggg tgaatggc 48

<210> SEQ ID NO 537
<211> LENGTH: 90
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 537

cgattcacca tctccagaac ctcgaccacg gtgactctga aaatgaccag tctgacaacc 60

gaggacacgg ccacctattt ctgtgccaga 90

<210> SEQ ID NO 538
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 538

gactattggt tgagcttg 18

<210> SEQ ID NO 539
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 539

tggggcccgg gcaccctcgt caccgtctcg agc 33

<210> SEQ ID NO 540
<211> LENGTH: 990
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 540

gcctccacca agggcccatc ggtcttcccc ctggcaccct cctccaagag cacctctggg 60

ggcacagcgg ccctgggctg cctggtcaag gactacttcc ccgaaccggt gacggtgtcg 120

tggaactcag gcgccctgac cagcggcgtg cacaccttcc cggctgtcct acagtcctca 180

ggactctact ccctcagcag cgtggtgacc gtgccctcca gcagcttggg cacccagacc 240

tacatctgca acgtgaatca caagcccagc aacaccaagg tggacgcgag agttgagccc 300

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aaatcttgtg acaaaactca cacatgccca ccgtgcccag cacctgaact cctgggggga    360

ccgtcagtct tcctcttccc cccaaaaccc aaggacaccc tcatgatctc ccggacccct    420

gaggtcacat gcgtggtggt ggacgtgagc cacgaagacc ctgaggtcaa gttcaactgg    480

tacgtggacg gcgtggaggt gcataatgcc aagacaaagc cgcgggagga gcagtacgcc    540

agcacgtacc gtgtggtcag cgtcctcacc gtcctgcacc aggactggct gaatggcaag    600

gagtacaagt gcaaggtctc caacaaagcc ctcccagccc ccatcgagaa aaccatctcc    660

aaagccaaag ggcagccccg agaaccacag gtgtacaccc tgcccccatc ccgggaggag    720

atgaccaaga accaggtcag cctgacctgc ctggtcaaag gcttctatcc cagcgacatc    780

gccgtggagt gggagagcaa tgggcagccg gagaacaact acaagaccac gcctcccgtg    840

ctggactccg acggctcctt cttcctctac agcaagctca ccgtggacaa gagcaggtgg    900

cagcagggga acgtcttctc atgctccgtg atgcatgagg ctctgcacaa ccactacacg    960

cagaagagcc tctccctgtc tccgggtaaa                                     990


<210> SEQ ID NO 541
<211> LENGTH: 218
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 541

Ala Ala Val Leu Thr Gln Thr Pro Ser Pro Val Ser Ala Ala Val Gly
1               5                   10                  15

Gly Thr Val Thr Ile Lys Cys Gln Ser Ser Gln Ser Val Tyr Asp Asn
            20                  25                  30

Asn Ala Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu
        35                  40                  45

Leu Ile Tyr Ala Ala Ser Thr Leu Ala Ser Gly Val Pro Ser Arg Phe
    50                  55                  60

Lys Gly Ser Gly Ser Gly Thr Gln Phe Thr Leu Thr Ile Asn Gly Val
65                  70                  75                  80

Gln Cys Asp Asp Ala Ala Thr Tyr Tyr Cys Leu Gly Gly Tyr Asp Asp
                85                  90                  95

Pro Ala Asp Asn Ala Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg
            100                 105                 110

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
        115                 120                 125

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
    130                 135                 140

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
145                 150                 155                 160

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
                165                 170                 175

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
            180                 185                 190

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
        195                 200                 205

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
    210                 215
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<210> SEQ ID NO 542
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 542

Ala Ala Val Leu Thr Gln Thr Pro Ser Pro Val Ser Ala Ala Val Gly
1 5 10 15

Gly Thr Val Thr Ile Lys Cys Gln Ser Ser Gln Ser Val Tyr Asp Asn
20 25 30

Asn Ala Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu
35 40 45

Leu Ile Tyr Ala Ala Ser Thr Leu Ala Ser Gly Val Pro Ser Arg Phe
50 55 60

Lys Gly Ser Gly Ser Gly Thr Gln Phe Thr Leu Thr Ile Asn Gly Val
65 70 75 80

Gln Cys Asp Asp Ala Ala Thr Tyr Tyr Cys Leu Gly Gly Tyr Asp Asp
85 90 95

Pro Ala Asp Asn Ala Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg
100 105 110

<210> SEQ ID NO 543
<211> LENGTH: 23
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 543

Ala Ala Val Leu Thr Gln Thr Pro Ser Pro Val Ser Ala Ala Val Gly
1 5 10 15

Gly Thr Val Thr Ile Lys Cys
20

<210> SEQ ID NO 544
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 544

Gln Ser Ser Gln Ser Val Tyr Asp Asn Asn Ala Leu Ala
1 5 10

<210> SEQ ID NO 545
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 545

Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr
1 5 10 15

<210> SEQ ID NO 546
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 546

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Ala Ala Ser Thr Leu Ala Ser
1 5

<210> SEQ ID NO 547
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 547

Gly Val Pro Ser Arg Phe Lys Gly Ser Gly Ser Gly Thr Gln Phe Thr
1 5 10 15

Leu Thr Ile Asn Gly Val Gln Cys Asp Asp Ala Ala Thr Tyr Tyr Cys
20 25 30

<210> SEQ ID NO 548
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 548

Leu Gly Gly Tyr Asp Asp Pro Ala Asp Asn Ala
1 5 10

<210> SEQ ID NO 549
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 549

Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg
1 5 10

<210> SEQ ID NO 550
<211> LENGTH: 106
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 550

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
1 5 10 15

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
20 25 30

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
35 40 45

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
50 55 60

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
65 70 75 80

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
85 90 95

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
100 105

<210> SEQ ID NO 551
<211> LENGTH: 654
<212> TYPE: DNA

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<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 551

gcagccgtgc tgacccagac accatcgccc gtgtctgcag ctgtgggagg cacagtcacc 60

atcaagtgcc agtccagtca gagtgtttat gataacaatg ctttagcctg gtatcagcag 120

aaaccagggc agcctcccaa gctcctgatc tatgctgcat ccactctggc atctggggtc 180

ccatcgcggt tcaaaggcag tggatctggg acacagttca ctctcaccat caacggcgtg 240

cagtgtgacg atgctgccac ttactactgt ctaggcggtt atgatgatcc tgctgataat 300

gctttcggcg gagggaccga ggtggtggtc aaacgtacgg tagcggcccc atctgtcttc 360

atcttcccgc catctgatga gcagttgaaa tctggaactg cctctgttgt gtgcctgctg 420

aataacttct atcccagaga ggccaaagta cagtggaagg tggataacgc cctccaatcg 480

ggtaactccc aggagagtgt cacagagcag gacagcaagg acagcaccta cagcctcagc 540

agcaccctga cgctgagcaa agcagactac gagaaacaca aagtctacgc ctgcgaagtc 600

acccatcagg gcctgagctc gcccgtcaca aagagcttca acaggggaga gtgt 654

<210> SEQ ID NO 552
<211> LENGTH: 336
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 552

gcagccgtgc tgacccagac accatcgccc gtgtctgcag ctgtgggagg cacagtcacc 60

atcaagtgcc agtccagtca gagtgtttat gataacaatg ctttagcctg gtatcagcag 120

aaaccagggc agcctcccaa gctcctgatc tatgctgcat ccactctggc atctggggtc 180

ccatcgcggt tcaaaggcag tggatctggg acacagttca ctctcaccat caacggcgtg 240

cagtgtgacg atgctgccac ttactactgt ctaggcggtt atgatgatcc tgctgataat 300

gctttcggcg gagggaccga ggtggtggtc aaacgt 336

<210> SEQ ID NO 553
<211> LENGTH: 69
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 553

gcagccgtgc tgacccagac accatcgccc gtgtctgcag ctgtgggagg cacagtcacc 60

atcaagtgc 69

<210> SEQ ID NO 554
<211> LENGTH: 39
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 554

cagtccagtc agagtgttta tgataacaat gctttagcc 39

<210> SEQ ID NO 555
<211> LENGTH: 45
<212> TYPE: DNA

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<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 555

tggtatcagc agaaaccagg gcagcctccc aagctcctga tctat 45

<210> SEQ ID NO 556
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 556

gctgcatcca ctctggcatc t 21

<210> SEQ ID NO 557
<211> LENGTH: 96
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 557

ggggtcccat cgcggttcaa aggcagtgga tctgggacac agttcactct caccatcaac 60

ggcgtgcagt gtgacgatgc tgccacttac tactgt 96

<210> SEQ ID NO 558
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 558

ctaggcggtt atgatgatcc tgctgataat gct 33

<210> SEQ ID NO 559
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 559

ttcggcggag ggaccgaggt ggtggtcaaa cgt 33

<210> SEQ ID NO 560
<211> LENGTH: 318
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 560

acggtagcgg ccccatctgt cttcatcttc ccgccatctg atgagcagtt gaaatctgga 60

actgcctctg ttgtgtgcct gctgaataac ttctatccca gagaggccaa agtacagtgg 120

aaggtggata acgccctcca atcgggtaac tcccaggaga gtgtcacaga gcaggacagc 180

aaggacagca cctacagcct cagcagcacc ctgacgctga gcaaagcaga ctacgagaaa 240

cacaaagtct acgcctgcga agtcacccat cagggcctga gctcgcccgt cacaaagagc 300

ttcaacaggg gagagtgt 318

<210> SEQ ID NO 561
<211> LENGTH: 441
<212> TYPE: PRT

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<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 561

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Gln Ser Val Glu Glu Ser Gly Gly Arg Leu Val Thr Pro Gly Thr Pro
1               5                   10                  15

Leu Thr Leu Thr Cys Thr Ala Ser Gly Phe Ser Leu Ser Arg Tyr Ala
            20                  25                  30

Met Gly Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
        35                  40                  45

Asp Ile Ser Thr Tyr Gly Thr Thr Asp Tyr Ala Ser Trp Val Asn Gly
    50                  55                  60

Arg Phe Thr Ile Ser Arg Thr Ser Thr Thr Val Thr Leu Lys Met Thr
65                  70                  75                  80

Ser Leu Thr Thr Glu Asp Thr Ala Thr Tyr Phe Cys Ala Arg Asp Tyr
                85                  90                  95

Trp Leu Ser Leu Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala
            100                 105                 110

Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser
        115                 120                 125

Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe
    130                 135                 140

Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly
145                 150                 155                 160

Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu
                165                 170                 175

Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr
            180                 185                 190

Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Ala Arg
        195                 200                 205

Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro
    210                 215                 220

Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
225                 230                 235                 240

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
                245                 250                 255

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
            260                 265                 270

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
        275                 280                 285

Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
    290                 295                 300

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
305                 310                 315                 320

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
                325                 330                 335

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met
            340                 345                 350

Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
        355                 360                 365

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
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    370                 375                 380

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
385                 390                 395                 400

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
                405                 410                 415

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
            420                 425                 430

Lys Ser Leu Ser Leu Ser Pro Gly Lys
        435                 440


<210> SEQ ID NO 562
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 562

Gln Ser Val Glu Glu Ser Gly Gly Arg Leu Val Thr Pro Gly Thr Pro
1               5                   10                  15

Leu Thr Leu Thr Cys Thr Ala Ser Gly Phe Ser Leu Ser Arg Tyr Ala
            20                  25                  30

Met Gly Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
        35                  40                  45

Asp Ile Ser Thr Tyr Gly Thr Thr Asp Tyr Ala Ser Trp Val Asn Gly
    50                  55                  60

Arg Phe Thr Ile Ser Arg Thr Ser Thr Thr Val Thr Leu Lys Met Thr
65                  70                  75                  80

Ser Leu Thr Thr Glu Asp Thr Ala Thr Tyr Phe Cys Ala Arg Asp Tyr
                85                  90                  95

Trp Leu Ser Leu Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
            100                 105                 110


<210> SEQ ID NO 563
<211> LENGTH: 29
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 563

Gln Ser Val Glu Glu Ser Gly Gly Arg Leu Val Thr Pro Gly Thr Pro
1               5                   10                  15

Leu Thr Leu Thr Cys Thr Ala Ser Gly Phe Ser Leu Ser
            20                  25


<210> SEQ ID NO 564
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 564

Arg Tyr Ala Met Gly
1               5


<210> SEQ ID NO 565
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus
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<400> SEQUENCE: 565

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
1 5 10

<210> SEQ ID NO 566
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 566

Asp Ile Ser Thr Tyr Gly Thr Thr Asp Tyr Ala Ser Trp Val Asn Gly
1 5 10 15

<210> SEQ ID NO 567
<211> LENGTH: 30
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 567

Arg Phe Thr Ile Ser Arg Thr Ser Thr Thr Val Thr Leu Lys Met Thr
1 5 10 15

Ser Leu Thr Thr Glu Asp Thr Ala Thr Tyr Phe Cys Ala Arg
20 25 30

<210> SEQ ID NO 568
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 568

Asp Tyr Trp Leu Ser Leu
1 5

<210> SEQ ID NO 569
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 569

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
1 5 10

<210> SEQ ID NO 570
<211> LENGTH: 330
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 570

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60

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Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65                  70                  75                  80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Ala
                85                  90                  95

Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
            100                 105                 110

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
        115                 120                 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
    130                 135                 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145                 150                 155                 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
                165                 170                 175

Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
            180                 185                 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
        195                 200                 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
    210                 215                 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
225                 230                 235                 240

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
                245                 250                 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
            260                 265                 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
        275                 280                 285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
    290                 295                 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305                 310                 315                 320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
                325                 330


<210> SEQ ID NO 571
<211> LENGTH: 1323
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 571

cagtcggtgg aggagtctgg gggtcgcctg gtcacgcctg ggacacccct gacactcacc     60

tgcacagcct ctggattctc cctcagtaga tatgcaatgg gctgggtccg ccaggctcca    120

gggaaggggc tggaatggat cggagacatt agtacttatg gtaccacaga ctacgcgagc    180

tgggtgaatg gccgattcac catctccaga acctcgacca cggtgactct gaaaatgacc    240

agtctgacaa ccgaggacac ggccacctat ttctgtgcca gagactattg gttgagcttg    300

tggggccaag gcaccctcgt caccgtctcg agcgcctcca ccaagggccc atcggtcttc    360

cccctggcac cctcctccaa gagcacctct gggggcacag cggccctggg ctgcctggtc    420

aaggactact tccccgaacc ggtgacggtg tcgtggaact caggcgccct gaccagcggc    480
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gtgcacacct tcccggctgt cctacagtcc tcaggactct actccctcag cagcgtggtg 540

accgtgccct ccagcagctt gggcacccag acctacatct gcaacgtgaa tcacaagccc 600

agcaacacca aggtggacgc gagagttgag cccaaatctt gtgacaaaac tcacacatgc 660

ccaccgtgcc cagcacctga actcctgggg ggaccgtcag tcttcctctt cccccaaaa 720

cccaaggaca ccctcatgat ctcccggacc cctgaggtca catgcgtggt ggtggacgtg 780

agccacgaag accctgaggt caagttcaac tggtacgtgg acggcgtgga ggtgcataat 840

gccaagacaa agccgcggga ggagcagtac gccagcacgt accgtgtggt cagcgtcctc 900

accgtcctgc accaggactg gctgaatggc aaggagtaca agtgcaaggt ctccaacaaa 960

gccctcccag cccccatcga gaaaaccatc tccaaagcca aagggcagcc ccgagaacca 1020

caggtgtaca ccctgccccc atcccgggag gagatgacca agaaccaggt cagcctgacc 1080

tgcctggtca aaggcttcta tcccagcgac atcgccgtgg agtgggagag caatgggcag 1140

ccggagaaca actacaagac cacgcctccc gtgctggact ccgacggctc cttcttcctc 1200

tacagcaagc tcaccgtgga caagagcagg tggcagcagg ggaacgtctt ctcatgctcc 1260

gtgatgcatg aggctctgca caaccactac acgcagaaga gcctctccct gtctccgggt 1320

aaa 1323

<210> SEQ ID NO 572
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 572

cagtcggtgg aggagtctgg gggtcgcctg gtcacgcctg ggacacccct gacactcacc 60

tgcacagcct ctggattctc cctcagtaga tatgcaatgg gctgggtccg ccaggctcca 120

gggaaggggc tggaatggat cggagacatt agtacttatg gtaccacaga ctacgcgagc 180

tgggtgaatg gccgattcac catctccaga acctcgacca cggtgactct gaaaatgacc 240

agtctgacaa ccgaggacac ggccacctat ttctgtgcca gagactattg gttgagcttg 300

tggggccaag gcaccctcgt caccgtctcg agc 333

<210> SEQ ID NO 573
<211> LENGTH: 87
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 573

cagtcggtgg aggagtctgg gggtcgcctg gtcacgcctg ggacacccct gacactcacc 60

tgcacagcct ctggattctc cctcagt 87

<210> SEQ ID NO 574
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 574

agatatgcaa tgggc 15

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<210> SEQ ID NO 575
<211> LENGTH: 42
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 575

tgggtccgcc aggctccagg gaaggggctg gaatggatcg ga 42

<210> SEQ ID NO 576
<211> LENGTH: 48
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 576

gacattagta cttatggtac cacagactac gcgagctggg tgaatggc 48

<210> SEQ ID NO 577
<211> LENGTH: 90
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 577

cgattcacca tctccagaac ctcgaccacg gtgactctga aaatgaccag tctgacaacc 60

gaggacacgg ccacctattt ctgtgccaga 90

<210> SEQ ID NO 578
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 578

gactattggt tgagcttg 18

<210> SEQ ID NO 579
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 579

tggggccaag gcaccctcgt caccgtctcg agc 33

<210> SEQ ID NO 580
<211> LENGTH: 990
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 580

gcctccacca agggcccatc ggtcttcccc ctggcaccct cctccaagag cacctctggg 60

ggcacagcgg ccctgggctg cctggtcaag gactacttcc ccgaaccggt gacggtgtcg 120

tggaactcag gcgccctgac cagcggcgtg cacaccttcc cggctgtcct acagtcctca 180

ggactctact ccctcagcag cgtggtgacc gtgccctcca gcagcttggg cacccagacc 240

tacatctgca acgtgaatca caagcccagc aacaccaagg tggacgcgag agttgagccc 300

aaatcttgtg acaaaactca cacatgccca ccgtgcccag cacctgaact cctgggggga 360

ccgtcagtct tcctcttccc cccaaaaccc aaggacaccc tcatgatctc ccggacccct 420

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gaggtcacat gcgtggtggt ggacgtgagc cacgaagacc ctgaggtcaa gttcaactgg 480

tacgtggacg gcgtggaggt gcataatgcc aagacaaagc cgcgggagga gcagtacgcc 540

agcacgtacc gtgtggtcag cgtcctcacc gtcctgcacc aggactggct gaatggcaag 600

gagtacaagt gcaaggtctc caacaaagcc ctcccagccc ccatcgagaa aaccatctcc 660

aaagccaaag ggcagccccg agaaccacag gtgtacaccc tgcccccatc ccgggaggag 720

atgaccaaga accaggtcag cctgacctgc ctggtcaaag gcttctatcc cagcgacatc 780

gccgtggagt gggagagcaa tgggcagccg gagaacaact acaagaccac gcctcccgtg 840

ctggactccg acggctcctt cttcctctac agcaagctca ccgtggacaa gagcaggtgg 900

cagcagggga acgtcttctc atgctccgtg atgcatgagg ctctgcacaa ccactacacg 960

cagaagagcc tctccctgtc tccgggtaaa 990

<210> SEQ ID NO 581
<211> LENGTH: 218
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 581

Ala Ala Val Leu Thr Gln Thr Pro Ser Pro Val Ser Ala Ala Val Gly
1 5 10 15

Gly Thr Val Thr Ile Lys Cys Gln Ser Ser Gln Ser Val Tyr Asp Asn
20 25 30

Asn Ala Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu
35 40 45

Leu Ile Tyr Ala Ala Ser Asn Leu Ala Ser Gly Val Pro Asp Arg Phe
50 55 60

Ser Gly Ser Gly Ser Gly Thr Gln Phe Thr Leu Thr Ile Ser Gly Val
65 70 75 80

Gln Cys Asp Asp Ala Ala Thr Tyr Tyr Cys Leu Gly Gly Tyr Asp Asp
85 90 95

Ala Ala Asp Asn Ala Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg
100 105 110

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
115 120 125

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
130 135 140

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
145 150 155 160

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
165 170 175

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
180 185 190

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
195 200 205

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> SEQ ID NO 582
<211> LENGTH: 112

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<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 582

Ala Ala Val Leu Thr Gln Thr Pro Ser Pro Val Ser Ala Ala Val Gly
1 5 10 15

Gly Thr Val Thr Ile Lys Cys Gln Ser Ser Gln Ser Val Tyr Asp Asn
20 25 30

Asn Ala Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu
35 40 45

Leu Ile Tyr Ala Ala Ser Asn Leu Ala Ser Gly Val Pro Asp Arg Phe
50 55 60

Ser Gly Ser Gly Ser Gly Thr Gln Phe Thr Leu Thr Ile Ser Gly Val
65 70 75 80

Gln Cys Asp Asp Ala Ala Thr Tyr Tyr Cys Leu Gly Gly Tyr Asp Asp
85 90 95

Ala Ala Asp Asn Ala Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg
100 105 110

<210> SEQ ID NO 583
<211> LENGTH: 23
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 583

Ala Ala Val Leu Thr Gln Thr Pro Ser Pro Val Ser Ala Ala Val Gly
1 5 10 15

Gly Thr Val Thr Ile Lys Cys
20

<210> SEQ ID NO 584
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 584

Gln Ser Ser Gln Ser Val Tyr Asp Asn Asn Ala Leu Ala
1 5 10

<210> SEQ ID NO 585
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 585

Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr
1 5 10 15

<210> SEQ ID NO 586
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 586

Ala Ala Ser Asn Leu Ala Ser
1 5

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<210> SEQ ID NO 587
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 587

Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Gln Phe Thr
1 5 10 15

Leu Thr Ile Ser Gly Val Gln Cys Asp Asp Ala Ala Thr Tyr Tyr Cys
20 25 30

<210> SEQ ID NO 588
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 588

Leu Gly Gly Tyr Asp Asp Ala Ala Asp Asn Ala
1 5 10

<210> SEQ ID NO 589
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 589

Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg
1 5 10

<210> SEQ ID NO 590
<211> LENGTH: 106
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 590

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
1 5 10 15

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
20 25 30

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
35 40 45

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
50 55 60

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
65 70 75 80

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
85 90 95

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
100 105

<210> SEQ ID NO 591
<211> LENGTH: 654
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

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<400> SEQUENCE: 591

gcagccgtgc tgacccagac accatcgccc gtgtctgcag ctgtgggagg cacagtcacc 60

atcaagtgcc agtccagtca gagtgtttat gataacaatg ctttagcctg gtatcagcag 120

aaaccaggac agcctcccaa gctcctgatc tatgctgcat ccaatctggc atctggggtc 180

ccagataggt tcagcggcag tggatctggg acacagttca ctctcaccat cagcggcgtg 240

cagtgtgacg atgctgccac ttactactgt ctaggcggtt atgatgatgc tgctgataat 300

gctttcggcg gagggaccga ggtggtggtc aaacgtacgg tagcggcccc atctgtcttc 360

atcttcccgc catctgatga gcagttgaaa tctggaactg cctctgttgt gtgcctgctg 420

aataacttct atcccagaga ggccaaagta cagtggaagg tggataacgc cctccaatcg 480

ggtaactccc aggagagtgt cacagagcag gacagcaagg acagcaccta cagcctcagc 540

agcaccctga cgctgagcaa agcagactac gagaaacaca aagtctacgc ctgcgaagtc 600

acccatcagg gcctgagctc gcccgtcaca aagagcttca acaggggaga gtgt 654

<210> SEQ ID NO 592
<211> LENGTH: 336
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 592

gcagccgtgc tgacccagac accatcgccc gtgtctgcag ctgtgggagg cacagtcacc 60

atcaagtgcc agtccagtca gagtgtttat gataacaatg ctttagcctg gtatcagcag 120

aaaccaggac agcctcccaa gctcctgatc tatgctgcat ccaatctggc atctggggtc 180

ccagataggt tcagcggcag tggatctggg acacagttca ctctcaccat cagcggcgtg 240

cagtgtgacg atgctgccac ttactactgt ctaggcggtt atgatgatgc tgctgataat 300

gctttcggcg gagggaccga ggtggtggtc aaacgt 336

<210> SEQ ID NO 593
<211> LENGTH: 69
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 593

gcagccgtgc tgacccagac accatcgccc gtgtctgcag ctgtgggagg cacagtcacc 60

atcaagtgc 69

<210> SEQ ID NO 594
<211> LENGTH: 39
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 594

cagtccagtc agagtgttta tgataacaat gctttagcc 39

<210> SEQ ID NO 595
<211> LENGTH: 45
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 595

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tggtatcagc agaaaccagg acagcctccc aagctcctga tctat 45

<210> SEQ ID NO 596
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 596

gctgcatcca atctggcatc t 21

<210> SEQ ID NO 597
<211> LENGTH: 96
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 597

ggggtcccag ataggttcag cggcagtgga tctgggacac agttcactct caccatcagc 60

ggcgtgcagt gtgacgatgc tgccacttac tactgt 96

<210> SEQ ID NO 598
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 598

ctaggcggtt atgatgatgc tgctgataat gct 33

<210> SEQ ID NO 599
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 599

ttcggcggag ggaccgaggt ggtggtcaaa cgt 33

<210> SEQ ID NO 600
<211> LENGTH: 318
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 600

acggtagcgg ccccatctgt cttcatcttc ccgccatctg atgagcagtt gaaatctgga 60

actgcctctg ttgtgtgcct gctgaataac ttctatccca gagaggccaa agtacagtgg 120

aaggtggata acgccctcca atcgggtaac tcccaggaga gtgtcacaga gcaggacagc 180

aaggacagca cctacagcct cagcagcacc ctgacgctga gcaaagcaga ctacgagaaa 240

cacaaagtct acgcctgcga agtcacccat cagggcctga gctcgcccgt cacaaagagc 300

ttcaacaggg gagagtgt 318

<210> SEQ ID NO 601
<211> LENGTH: 441
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

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<400> SEQUENCE: 601

```
Gln Ser Val Glu Glu Ser Gly Gly Arg Leu Val Thr Pro Gly Thr Pro
1               5                   10                  15

Leu Thr Leu Thr Cys Thr Ala Ser Gly Phe Ser Leu Ser Ser Tyr Ala
            20                  25                  30

Met Gly Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
        35                  40                  45

Asp Ile Ser Thr Tyr Gly Thr Thr Asp Tyr Ala Ser Trp Val Tyr Gly
    50                  55                  60

Arg Phe Thr Ile Ser Arg Thr Ser Thr Thr Val Thr Leu Lys Met Thr
65                  70                  75                  80

Ser Leu Thr Thr Glu Asp Thr Ala Thr Tyr Phe Cys Ala Arg Asp Tyr
                85                  90                  95

Trp Leu Ser Leu Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala
            100                 105                 110

Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser
        115                 120                 125

Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe
    130                 135                 140

Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly
145                 150                 155                 160

Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu
                165                 170                 175

Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr
            180                 185                 190

Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Ala Arg
        195                 200                 205

Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro
    210                 215                 220

Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
225                 230                 235                 240

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
                245                 250                 255

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
            260                 265                 270

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
        275                 280                 285

Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
    290                 295                 300

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
305                 310                 315                 320

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
                325                 330                 335

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met
            340                 345                 350

Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
        355                 360                 365

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
    370                 375                 380

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
385                 390                 395                 400
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Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
405 410 415

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
420 425 430

Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440

<210> SEQ ID NO 602
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 602

Gln Ser Val Glu Glu Ser Gly Gly Arg Leu Val Thr Pro Gly Thr Pro
1 5 10 15

Leu Thr Leu Thr Cys Thr Ala Ser Gly Phe Ser Leu Ser Ser Tyr Ala
20 25 30

Met Gly Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
35 40 45

Asp Ile Ser Thr Tyr Gly Thr Thr Asp Tyr Ala Ser Trp Val Tyr Gly
50 55 60

Arg Phe Thr Ile Ser Arg Thr Ser Thr Thr Val Thr Leu Lys Met Thr
65 70 75 80

Ser Leu Thr Thr Glu Asp Thr Ala Thr Tyr Phe Cys Ala Arg Asp Tyr
85 90 95

Trp Leu Ser Leu Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
100 105 110

<210> SEQ ID NO 603
<211> LENGTH: 29
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 603

Gln Ser Val Glu Glu Ser Gly Gly Arg Leu Val Thr Pro Gly Thr Pro
1 5 10 15

Leu Thr Leu Thr Cys Thr Ala Ser Gly Phe Ser Leu Ser
20 25

<210> SEQ ID NO 604
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 604

Ser Tyr Ala Met Gly
1 5

<210> SEQ ID NO 605
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 605

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
1 5 10

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<210> SEQ ID NO 606
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 606

Asp Ile Ser Thr Tyr Gly Thr Thr Asp Tyr Ala Ser Trp Val Tyr Gly
1 5 10 15

<210> SEQ ID NO 607
<211> LENGTH: 30
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 607

Arg Phe Thr Ile Ser Arg Thr Ser Thr Thr Val Thr Leu Lys Met Thr
1 5 10 15

Ser Leu Thr Thr Glu Asp Thr Ala Thr Tyr Phe Cys Ala Arg
20 25 30

<210> SEQ ID NO 608
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 608

Asp Tyr Trp Leu Ser Leu
1 5

<210> SEQ ID NO 609
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 609

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
1 5 10

<210> SEQ ID NO 610
<211> LENGTH: 330
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 610

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65 70 75 80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Ala

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               85                  90                  95

Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
            100                 105                 110

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
        115                 120                 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
    130                 135                 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145                 150                 155                 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
                165                 170                 175

Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
            180                 185                 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
        195                 200                 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
    210                 215                 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
225                 230                 235                 240

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
                245                 250                 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
            260                 265                 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
        275                 280                 285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
    290                 295                 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305                 310                 315                 320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
                325                 330


<210> SEQ ID NO 611
<211> LENGTH: 1323
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 611

cagtcggtgg aggagtccgg gggtcgcctg gtcacgcctg ggacacccct gacactcacc     60

tgcacagcct ctggattctc cctcagtagc tatgcaatgg gctgggtccg ccaggctcca    120

gggaaggggc tggaatggat cggagacatt agtacttatg gtaccacaga ctacgcgagc    180

tgggtgtatg gccgattcac catctccaga acctcgacca cggtgactct gaaaatgacc    240

agtctgacaa ccgaggacac ggccacctat ttctgtgcca gagactattg gttgagcttg    300

tggggccaag gcaccctggt caccgtctcg agcgcctcca ccaagggccc atcggtcttc    360

cccctggcac cctcctccaa gagcacctct gggggcacag cggccctggg ctgcctggtc    420

aaggactact tccccgaacc ggtgacggtg tcgtggaact caggcgccct gaccagcggc    480

gtgcacacct tcccggctgt cctacagtcc tcaggactct actccctcag cagcgtggtg    540

accgtgccct ccagcagctt gggcacccag acctacatct gcaacgtgaa tcacaagccc    600
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agcaacacca aggtggacgc gagagttgag cccaaatctt gtgacaaaac tcacacatgc 660

ccaccgtgcc cagcacctga actcctgggg ggaccgtcag tcttcctctt cccccaaaa 720

cccaaggaca ccctcatgat ctcccggacc cctgaggtca catgcgtggt ggtggacgtg 780

agccacgaag accctgaggt caagttcaac tggtacgtgg acggcgtgga ggtgcataat 840

gccaagacaa agccgcggga ggagcagtac gccagcacgt accgtgtggt cagcgtcctc 900

accgtcctgc accaggactg gctgaatggc aaggagtaca agtgcaaggt ctccaacaaa 960

gccctcccag cccccatcga gaaaaccatc tccaaagcca aagggcagcc ccgagaacca 1020

caggtgtaca ccctgccccc atcccgggag gagatgacca agaaccaggt cagcctgacc 1080

tgcctggtca aaggcttcta tcccagcgac atcgccgtgg agtgggagag caatgggcag 1140

ccggagaaca actacaagac cacgcctccc gtgctggact ccgacggctc cttcttcctc 1200

tacagcaagc tcaccgtgga caagagcagg tggcagcagg ggaacgtctt ctcatgctcc 1260

gtgatgcatg aggctctgca caaccactac acgcagaaga gcctctccct gtctccgggt 1320

aaa 1323

<210> SEQ ID NO 612
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 612

cagtcggtgg aggagtccgg gggtcgcctg gtcacgcctg ggacacccct gacactcacc 60

tgcacagcct ctggattctc cctcagtagc tatgcaatgg gctgggtccg ccaggctcca 120

gggaaggggc tggaatggat cggagacatt agtacttatg gtaccacaga ctacgcgagc 180

tgggtgtatg gccgattcac catctccaga acctcgacca cggtgactct gaaaatgacc 240

agtctgacaa ccgaggacac ggccacctat ttctgtgcca gagactattg gttgagcttg 300

tggggccaag gcaccctggt caccgtctcg agc 333

<210> SEQ ID NO 613
<211> LENGTH: 87
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 613

cagtcggtgg aggagtccgg gggtcgcctg gtcacgcctg ggacacccct gacactcacc 60

tgcacagcct ctggattctc cctcagt 87

<210> SEQ ID NO 614
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 614

agctatgcaa tgggc 15

<210> SEQ ID NO 615
<211> LENGTH: 42
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

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<400> SEQUENCE: 615

tgggtccgcc aggctccagg gaaggggctg gaatggatcg ga 42

<210> SEQ ID NO 616
<211> LENGTH: 48
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 616

gacattagta cttatggtac cacagactac gcgagctggg tgtatggc 48

<210> SEQ ID NO 617
<211> LENGTH: 90
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 617

cgattcacca tctccagaac ctcgaccacg gtgactctga aaatgaccag tctgacaacc 60

gaggacacgg ccacctattt ctgtgccaga 90

<210> SEQ ID NO 618
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 618

gactattggt tgagcttg 18

<210> SEQ ID NO 619
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 619

tggggccaag gcaccctggt caccgtctcg agc 33

<210> SEQ ID NO 620
<211> LENGTH: 990
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 620

gcctccacca agggcccatc ggtcttcccc ctggcaccct cctccaagag cacctctggg 60

ggcacagcgg ccctgggctg cctggtcaag gactacttcc ccgaaccggt gacggtgtcg 120

tggaactcag gcgccctgac cagcggcgtg cacaccttcc cggctgtcct acagtcctca 180

ggactctact ccctcagcag cgtggtgacc gtgccctcca gcagcttggg cacccagacc 240

tacatctgca acgtgaatca caagcccagc aacaccaagg tggacgcgag agttgagccc 300

aaatcttgtg acaaaactca cacatgccca ccgtgcccag cacctgaact cctgggggga 360

ccgtcagtct tcctcttccc cccaaaaccc aaggacaccc tcatgatctc ccggaccccct 420

gaggtcacat gcgtggtggt ggacgtgagc cacgaagacc ctgaggtcaa gttcaactgg 480

tacgtggacg gcgtggaggt gcataatgcc aagacaaagc cgcgggagga gcagtacgcc 540

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agcacgtacc gtgtggtcag cgtcctcacc gtcctgcacc aggactggct gaatggcaag 600

gagtacaagt gcaaggtctc caacaaagcc ctcccagccc ccatcgagaa aaccatctcc 660

aaagccaaag ggcagccccg agaaccacag gtgtacaccc tgcccccatc ccgggaggag 720

atgaccaaga accaggtcag cctgacctgc ctggtcaaag gcttctatcc cagcgacatc 780

gccgtggagt gggagagcaa tgggcagccg gagaacaact acaagaccac gcctcccgtg 840

ctggactccg acggctcctt cttcctctac agcaagctca ccgtggacaa gagcaggtgg 900

cagcagggga acgtcttctc atgctccgtg atgcatgagg ctctgcacaa ccactacacg 960

cagaagagcc tctccctgtc tccgggtaaa 990

<210> SEQ ID NO 621
<211> LENGTH: 218
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 621

Ala Ala Val Leu Thr Gln Thr Pro Ser Pro Val Ser Ala Ala Val Gly
1 5 10 15

Gly Thr Val Thr Ile Lys Cys Gln Ser Ser Gln Ser Val Tyr Asp Asn
20 25 30

Asn Ala Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu
35 40 45

Leu Ile Tyr Ala Ala Ser Thr Leu Ala Ser Gly Val Pro Ser Arg Phe
50 55 60

Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Gly Val
65 70 75 80

Gln Cys Asp Asp Ala Ala Thr Tyr Tyr Cys Leu Gly Gly Tyr Tyr Asp
85 90 95

Pro Ala Asp Asn Ala Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg
100 105 110

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
115 120 125

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
130 135 140

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
145 150 155 160

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
165 170 175

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
180 185 190

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
195 200 205

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> SEQ ID NO 622
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

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<400> SEQUENCE: 622

Ala Ala Val Leu Thr Gln Thr Pro Ser Pro Val Ser Ala Ala Val Gly
1 5 10 15

Gly Thr Val Thr Ile Lys Cys Gln Ser Ser Gln Ser Val Tyr Asp Asn
20 25 30

Asn Ala Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu
35 40 45

Leu Ile Tyr Ala Ala Ser Thr Leu Ala Ser Gly Val Pro Ser Arg Phe
50 55 60

Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Gly Val
65 70 75 80

Gln Cys Asp Asp Ala Ala Thr Tyr Tyr Cys Leu Gly Gly Tyr Tyr Asp
85 90 95

Pro Ala Asp Asn Ala Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg
100 105 110

<210> SEQ ID NO 623
<211> LENGTH: 23
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 623

Ala Ala Val Leu Thr Gln Thr Pro Ser Pro Val Ser Ala Ala Val Gly
1 5 10 15

Gly Thr Val Thr Ile Lys Cys
20

<210> SEQ ID NO 624
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 624

Gln Ser Ser Gln Ser Val Tyr Asp Asn Asn Ala Leu Ala
1 5 10

<210> SEQ ID NO 625
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 625

Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr
1 5 10 15

<210> SEQ ID NO 626
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 626

Ala Ala Ser Thr Leu Ala Ser
1 5

<210> SEQ ID NO 627
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

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<400> SEQUENCE: 627

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr
1 5 10 15

Leu Thr Ile Ser Gly Val Gln Cys Asp Asp Ala Ala Thr Tyr Tyr Cys
20 25 30

<210> SEQ ID NO 628
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 628

Leu Gly Gly Tyr Tyr Asp Pro Ala Asp Asn Ala
1 5 10

<210> SEQ ID NO 629
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 629

Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg
1 5 10

<210> SEQ ID NO 630
<211> LENGTH: 106
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 630

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
1 5 10 15

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
20 25 30

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
35 40 45

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
50 55 60

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
65 70 75 80

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
85 90 95

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
100 105

<210> SEQ ID NO 631
<211> LENGTH: 654
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 631

gcagccgtgc tgacccagac accatcgccc gtgtctgcag ctgtgggagg cacagtcacc 60

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atcaagtgcc agtccagtca gagtgtttat gataacaatg ctttagcctg gtatcagcag 120

aaaccagggc agcctcccaa gctcctgatc tatgctgcat ccactctggc atctggggtc 180

ccatcgcggt tcagtggcag tggatctggg acagagttca ctctcaccat cagcggcgtg 240

cagtgtgacg atgctgccac ttactactgt ctaggcggtt attatgatcc tgctgataat 300

gctttcggcg gagggaccga ggtggtggtc aaacgtacgg tagcggcccc atctgtcttc 360

atcttcccgc catctgatga gcagttgaaa tctggaactg cctctgttgt gtgcctgctg 420

aataacttct atcccagaga ggccaaagta cagtggaagg tggataacgc cctccaatcg 480

ggtaactccc aggagagtgt cacagagcag gacagcaagg acagcaccta cagcctcagc 540

agcaccctga cgctgagcaa agcagactac gagaaacaca aagtctacgc ctgcgaagtc 600

acccatcagg gcctgagctc gcccgtcaca aagagcttca acaggggaga gtgt 654

<210> SEQ ID NO 632
<211> LENGTH: 336
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 632

gcagccgtgc tgacccagac accatcgccc gtgtctgcag ctgtgggagg cacagtcacc 60

atcaagtgcc agtccagtca gagtgtttat gataacaatg ctttagcctg gtatcagcag 120

aaaccagggc agcctcccaa gctcctgatc tatgctgcat ccactctggc atctggggtc 180

ccatcgcggt tcagtggcag tggatctggg acagagttca ctctcaccat cagcggcgtg 240

cagtgtgacg atgctgccac ttactactgt ctaggcggtt attatgatcc tgctgataat 300

gctttcggcg gagggaccga ggtggtggtc aaacgt 336

<210> SEQ ID NO 633
<211> LENGTH: 69
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 633

gcagccgtgc tgacccagac accatcgccc gtgtctgcag ctgtgggagg cacagtcacc 60

atcaagtgc 69

<210> SEQ ID NO 634
<211> LENGTH: 39
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 634

cagtccagtc agagtgttta tgataacaat gctttagcc 39

<210> SEQ ID NO 635
<211> LENGTH: 45
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 635

tggtatcagc agaaaccagg gcagcctccc aagctcctga tctat 45

<210> SEQ ID NO 636

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<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 636

gctgcatcca ctctggcatc t 21

<210> SEQ ID NO 637
<211> LENGTH: 96
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 637

ggggtcccat cgcggttcag tggcagtgga tctgggacag agttcactct caccatcagc 60

ggcgtgcagt gtgacgatgc tgccacttac tactgt 96

<210> SEQ ID NO 638
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 638

ctaggcggtt attatgatcc tgctgataat gct 33

<210> SEQ ID NO 639
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 639

ttcggcggag ggaccgaggt ggtggtcaaa cgt 33

<210> SEQ ID NO 640
<211> LENGTH: 318
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 640

acggtagcgg ccccatctgt cttcatcttc ccgccatctg atgagcagtt gaaatctgga 60

actgcctctg ttgtgtgcct gctgaataac ttctatccca gagaggccaa agtacagtgg 120

aaggtggata acgccctcca atcgggtaac tcccaggaga gtgtcacaga gcaggacagc 180

aaggacagca cctacagcct cagcagcacc ctgacgctga gcaaagcaga ctacgagaaa 240

cacaaagtct acgcctgcga agtcacccat cagggcctga gctcgcccgt cacaaagagc 300

ttcaacaggg gagagtgt 318

<210> SEQ ID NO 641
<211> LENGTH: 451
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 641

Gln Ser Val Glu Glu Ser Gly Gly Arg Leu Val Thr Pro Gly Thr Pro
1 5 10 15

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Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Ser Ser Tyr Asp
            20                  25                  30

Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Tyr Ile Gly
        35                  40                  45

Ile Ile Asn Thr Asn Asp Asp Thr Trp Tyr Ala Ser Trp Val Lys Gly
    50                  55                  60

Arg Phe Thr Ile Ser Lys Thr Ser Ser Thr Thr Val Asp Leu Lys Met
65                  70                  75                  80

Thr Ser Leu Thr Thr Glu Asp Thr Ala Thr Tyr Phe Cys Ala Arg Ile
                85                  90                  95

Ser Asp Ala Tyr Val Phe Asp Tyr Ala Tyr Tyr Phe Thr Leu Trp Gly
            100                 105                 110

Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
        115                 120                 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
    130                 135                 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145                 150                 155                 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
                165                 170                 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
            180                 185                 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
        195                 200                 205

Lys Pro Ser Asn Thr Lys Val Asp Ala Arg Val Glu Pro Lys Ser Cys
    210                 215                 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
225                 230                 235                 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
                245                 250                 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
            260                 265                 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
        275                 280                 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr
    290                 295                 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305                 310                 315                 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
                325                 330                 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
            340                 345                 350

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
        355                 360                 365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
    370                 375                 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385                 390                 395                 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
                405                 410                 415
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Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
            420                 425                 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
        435                 440                 445

Pro Gly Lys
    450


<210> SEQ ID NO 642
<211> LENGTH: 121
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 642

Gln Ser Val Glu Glu Ser Gly Gly Arg Leu Val Thr Pro Gly Thr Pro
1               5                   10                  15

Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Ser Ser Tyr Asp
            20                  25                  30

Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Tyr Ile Gly
        35                  40                  45

Ile Ile Asn Thr Asn Asp Asp Thr Trp Tyr Ala Ser Trp Val Lys Gly
    50                  55                  60

Arg Phe Thr Ile Ser Lys Thr Ser Ser Thr Thr Val Asp Leu Lys Met
65                  70                  75                  80

Thr Ser Leu Thr Thr Glu Asp Thr Ala Thr Tyr Phe Cys Ala Arg Ile
                85                  90                  95

Ser Asp Ala Tyr Val Phe Asp Tyr Ala Tyr Tyr Phe Thr Leu Trp Gly
            100                 105                 110

Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> SEQ ID NO 643
<211> LENGTH: 29
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 643

Gln Ser Val Glu Glu Ser Gly Gly Arg Leu Val Thr Pro Gly Thr Pro
1               5                   10                  15

Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Ser
            20                  25


<210> SEQ ID NO 644
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 644

Ser Tyr Asp Met Ser
1               5


<210> SEQ ID NO 645
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 645
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Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Tyr Ile Gly
1 5 10

<210> SEQ ID NO 646
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 646

Ile Ile Asn Thr Asn Asp Asp Thr Trp Tyr Ala Ser Trp Val Lys Gly
1 5 10 15

<210> SEQ ID NO 647
<211> LENGTH: 31
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 647

Arg Phe Thr Ile Ser Lys Thr Ser Ser Thr Thr Val Asp Leu Lys Met
1 5 10 15

Thr Ser Leu Thr Thr Glu Asp Thr Ala Thr Tyr Phe Cys Ala Arg
20 25 30

<210> SEQ ID NO 648
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 648

Ile Ser Asp Ala Tyr Val Phe Asp Tyr Ala Tyr Tyr Phe Thr Leu
1 5 10 15

<210> SEQ ID NO 649
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 649

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
1 5 10

<210> SEQ ID NO 650
<211> LENGTH: 330
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 650

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65 70 75 80

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Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Ala
85 90 95

Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
100 105 110

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
115 120 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
130 135 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145 150 155 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
165 170 175

Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
180 185 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
195 200 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
210 215 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
225 230 235 240

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
245 250 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
260 265 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
275 280 285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
290 295 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305 310 315 320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
325 330

<210> SEQ ID NO 651
<211> LENGTH: 1353
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 651

cagtcggtgg aggagtccgg gggtcgcctg gtcacgcctg ggacacccct gacactcacc 60

tgcaccgtct ctggattctc cctcagcagc tacgacatga gctgggtccg ccaggctcca 120

ggaaaggggc tggaatacat cggcatcatt aatactaatg atgacacatg gtacgcgagc 180

tgggtgaaag gccgattcac catctccaaa acctcgtcga ccacggtgga tctgaaaatg 240

accagtctga caaccgagga cacggccacc tatttctgtg ccagaatatc cgatgcttat 300

gtttttgatt atgcgtatta ctttactttg tggggccagg ggaccctggt caccgtctcg 360

agcgcctcca ccaagggccc atcggtcttc cccctggcac cctcctccaa gagcacctct 420

gggggcacag cggccctggg ctgcctggtc aaggactact tccccgaacc ggtgacggtg 480

tcgtggaact caggcgccct gaccagcggc gtgcacacct tcccggctgt cctacagtcc 540

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tcaggactct actccctcag cagcgtggtg accgtgccct ccagcagctt gggcacccag 600

acctacatct gcaacgtgaa tcacaagccc agcaacacca aggtggacgc gagagttgag 660

cccaaatctt gtgacaaaac tcacacatgc ccaccgtgcc cagcacctga actcctgggg 720

ggaccgtcag tcttcctctt cccccaaaa cccaaggaca ccctcatgat ctcccggacc 780

cctgaggtca catgcgtggt ggtggacgtg agccacgaag accctgaggt caagttcaac 840

tggtacgtgg acggcgtgga ggtgcataat gccaagacaa agccgcggga ggagcagtac 900

gccagcacgt accgtgtggt cagcgtcctc accgtcctgc accaggactg gctgaatggc 960

aaggagtaca agtgcaaggt ctccaacaaa gccctcccag cccccatcga gaaaaccatc 1020

tccaaagcca aagggcagcc ccgagaacca caggtgtaca ccctgccccc atcccgggag 1080

gagatgacca agaaccaggt cagcctgacc tgcctggtca aaggcttcta tcccagcgac 1140

atcgccgtgg agtgggagag caatgggcag ccggagaaca actacaagac cacgcctccc 1200

gtgctggact ccgacggctc cttcttcctc tacagcaagc tcaccgtgga caagagcagg 1260

tggcagcagg ggaacgtctt ctcatgctcc gtgatgcatg aggctctgca caaccactac 1320

acgcagaaga gcctctccct gtctccgggt aaa 1353

<210> SEQ ID NO 652
<211> LENGTH: 363
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 652

cagtcggtgg aggagtccgg gggtcgcctg gtcacgcctg ggacacccct gacactcacc 60

tgcaccgtct ctggattctc cctcagcagc tacgacatga gctgggtccg ccaggctcca 120

ggaaaggggc tggaatacat cggcatcatt aatactaatg atgacacatg gtacgcgagc 180

tgggtgaaag gccgattcac catctccaaa acctcgtcga ccacggtgga tctgaaaatg 240

accagtctga caaccgagga cacggccacc tatttctgtg ccagaatatc cgatgcttat 300

gtttttgatt atgcgtatta ctttactttg tggggccagg ggaccctggt caccgtctcg 360

agc 363

<210> SEQ ID NO 653
<211> LENGTH: 87
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 653

cagtcggtgg aggagtccgg gggtcgcctg gtcacgcctg ggacacccct gacactcacc 60

tgcaccgtct ctggattctc cctcagc 87

<210> SEQ ID NO 654
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 654

agctacgaca tgagc 15

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<210> SEQ ID NO 655
<211> LENGTH: 42
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 655

tgggtccgcc aggctccagg aaaggggctg gaatacatcg gc 42

<210> SEQ ID NO 656
<211> LENGTH: 48
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 656

atcattaata ctaatgatga cacatggtac gcgagctggg tgaaaggc 48

<210> SEQ ID NO 657
<211> LENGTH: 93
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 657

cgattcacca tctccaaaac ctcgtcgacc acggtggatc tgaaaatgac cagtctgaca 60

accgaggaca cggccaccta tttctgtgcc aga 93

<210> SEQ ID NO 658
<211> LENGTH: 45
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 658

atatccgatg cttatgtttt tgattatgcg tattacttta ctttg 45

<210> SEQ ID NO 659
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 659

tggggccagg ggaccctggt caccgtctcg agc 33

<210> SEQ ID NO 660
<211> LENGTH: 990
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 660

gcctccacca agggcccatc ggtcttcccc ctggcaccct cctccaagag cacctctggg 60

ggcacagcgg ccctgggctg cctggtcaag gactacttcc ccgaaccggt gacggtgtcg 120

tggaactcag gcgccctgac cagcggcgtg cacaccttcc cggctgtcct acagtcctca 180

ggactctact ccctcagcag cgtggtgacc gtgccctcca gcagcttggg cacccagacc 240

tacatctgca acgtgaatca caagcccagc aacaccaagg tggacgcgag agttgagccc 300

aaatcttgtg acaaaactca cacatgccca ccgtgcccag cacctgaact cctgggggga 360

ccgtcagtct tcctcttccc cccaaaaccc aaggacaccc tcatgatctc ccggaccccct 420

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gaggtcacat gcgtggtggt ggacgtgagc cacgaagacc ctgaggtcaa gttcaactgg 480

tacgtggacg gcgtggaggt gcataatgcc aagacaaagc cgcgggagga gcagtacgcc 540

agcacgtacc gtgtggtcag cgtcctcacc gtcctgcacc aggactggct gaatggcaag 600

gagtacaagt gcaaggtctc caacaaagcc ctcccagccc ccatcgagaa aaccatctcc 660

aaagccaaag ggcagccccg agaaccacag gtgtacaccc tgcccccatc ccgggaggag 720

atgaccaaga accaggtcag cctgacctgc ctggtcaaag gcttctatcc cagcgacatc 780

gccgtggagt gggagagcaa tgggcagccg gagaacaact acaagaccac gcctcccgtg 840

ctggactccg acggctcctt cttcctctac agcaagctca ccgtggacaa gagcaggtgg 900

cagcagggga acgtcttctc atgctccgtg atgcatgagg ctctgcacaa ccactacacg 960

cagaagagcc tctccctgtc tccgggtaaa 990

<210> SEQ ID NO 661
<211> LENGTH: 217
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 661

Ala Leu Val Met Thr Gln Thr Pro Ser Ser Val Ser Ala Ala Val Gly
1 5 10 15

Gly Thr Val Thr Ile Asn Cys Leu Ala Ser Gln Asn Ile Tyr Asn Ser
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile
35 40 45

Tyr Arg Ala Ser Thr Leu Ala Ser Gly Val Ser Ser Arg Phe Lys Gly
50 55 60

Ser Gly Ser Gly Thr Gln Phe Thr Leu Thr Ile Ser Gly Val Glu Cys
65 70 75 80

Ala Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Gly Ala Gly Ala Asp Asn
85 90 95

Ile Gly Asn Pro Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg Thr
100 105 110

Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu
115 120 125

Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro
130 135 140

Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly
145 150 155 160

Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr
165 170 175

Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His
180 185 190

Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val
195 200 205

Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> SEQ ID NO 662
<211> LENGTH: 111

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<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 662

Ala Leu Val Met Thr Gln Thr Pro Ser Ser Val Ser Ala Ala Val Gly
1 5 10 15

Gly Thr Val Thr Ile Asn Cys Leu Ala Ser Gln Asn Ile Tyr Asn Ser
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile
35 40 45

Tyr Arg Ala Ser Thr Leu Ala Ser Gly Val Ser Ser Arg Phe Lys Gly
50 55 60

Ser Gly Ser Gly Thr Gln Phe Thr Leu Thr Ile Ser Gly Val Glu Cys
65 70 75 80

Ala Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Gly Ala Gly Ala Asp Asn
85 90 95

Ile Gly Asn Pro Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg
100 105 110

<210> SEQ ID NO 663
<211> LENGTH: 23
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 663

Ala Leu Val Met Thr Gln Thr Pro Ser Ser Val Ser Ala Ala Val Gly
1 5 10 15

Gly Thr Val Thr Ile Asn Cys
20

<210> SEQ ID NO 664
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 664

Leu Ala Ser Gln Asn Ile Tyr Asn Ser Leu Ala
1 5 10

<210> SEQ ID NO 665
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 665

Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr
1 5 10 15

<210> SEQ ID NO 666
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 666

Arg Ala Ser Thr Leu Ala Ser
1 5

-continued

<210> SEQ ID NO 667
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 667

Gly Val Ser Ser Arg Phe Lys Gly Ser Gly Ser Gly Thr Gln Phe Thr
1 5 10 15

Leu Thr Ile Ser Gly Val Glu Cys Ala Asp Ala Ala Thr Tyr Tyr Cys
20 25 30

<210> SEQ ID NO 668
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 668

Gln Gln Gly Ala Gly Ala Asp Asn Ile Gly Asn Pro
1 5 10

<210> SEQ ID NO 669
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 669

Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg
1 5 10

<210> SEQ ID NO 670
<211> LENGTH: 106
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 670

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
1 5 10 15

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
20 25 30

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
35 40 45

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
50 55 60

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
65 70 75 80

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
85 90 95

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
100 105

<210> SEQ ID NO 671
<211> LENGTH: 651
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

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<400> SEQUENCE: 671

gcccttgtga tgacccagac tccatcctcc gtgtctgcag ctgtgggagg cacagtcacc 60

atcaattgcc tggccagtca gaacatttac aattctttag cctggtatca gcagaaacca 120

gggcagcctc ccaagctcct gatctacagg gcatccactc tggcatctgg ggtctcatcg 180

cggttcaaag gcagtggatc tgggacacag ttcactctca ccatcagcgg cgtggagtgt 240

gccgatgctg ccacttacta ctgtcaacag ggtgctggtg ctgataatat tggtaatcct 300

ttcggcggag ggaccgaggt ggtggtcaaa cgtacggtag cggccccatc tgtcttcatc 360

ttcccgccat ctgatgagca gttgaaatct ggaactgcct ctgttgtgtg cctgctgaat 420

aacttctatc ccagagaggc caaagtacag tggaaggtgg ataacgccct ccaatcgggt 480

aactcccagg agagtgtcac agagcaggac agcaaggaca gcacctacag cctcagcagc 540

accctgacgc tgagcaaagc agactacgag aaacacaaag tctacgcctg cgaagtcacc 600

catcagggcc tgagctcgcc cgtcacaaag agcttcaaca ggggagagtg t 651

<210> SEQ ID NO 672
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 672

gcccttgtga tgacccagac tccatcctcc gtgtctgcag ctgtgggagg cacagtcacc 60

atcaattgcc tggccagtca gaacatttac aattctttag cctggtatca gcagaaacca 120

gggcagcctc ccaagctcct gatctacagg gcatccactc tggcatctgg ggtctcatcg 180

cggttcaaag gcagtggatc tgggacacag ttcactctca ccatcagcgg cgtggagtgt 240

gccgatgctg ccacttacta ctgtcaacag ggtgctggtg ctgataatat tggtaatcct 300

ttcggcggag ggaccgaggt ggtggtcaaa cgt 333

<210> SEQ ID NO 673
<211> LENGTH: 69
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 673

gcccttgtga tgacccagac tccatcctcc gtgtctgcag ctgtgggagg cacagtcacc 60

atcaattgc 69

<210> SEQ ID NO 674
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 674

ctggccagtc agaacattta caattcttta gcc 33

<210> SEQ ID NO 675
<211> LENGTH: 45
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 675

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tggtatcagc agaaaccagg gcagcctccc aagctcctga tctac 45

<210> SEQ ID NO 676
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 676

agggcatcca ctctggcatc t 21

<210> SEQ ID NO 677
<211> LENGTH: 96
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 677

ggggtctcat cgcggttcaa aggcagtgga tctgggacac agttcactct caccatcagc 60

ggcgtggagt gtgccgatgc tgccacttac tactgt 96

<210> SEQ ID NO 678
<211> LENGTH: 36
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 678

caacagggtg ctggtgctga taatattggt aatcct 36

<210> SEQ ID NO 679
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 679

ttcggcggag ggaccgaggt ggtggtcaaa cgt 33

<210> SEQ ID NO 680
<211> LENGTH: 318
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 680

acggtagcgg ccccatctgt cttcatcttc ccgccatctg atgagcagtt gaaatctgga 60

actgcctctg ttgtgtgcct gctgaataac ttctatccca gagaggccaa agtacagtgg 120

aaggtggata acgccctcca atcgggtaac tcccaggaga gtgtcacaga gcaggacagc 180

aaggacagca cctacagcct cagcagcacc ctgacgctga gcaaagcaga ctacgagaaa 240

cacaaagtct acgcctgcga agtcacccat cagggcctga gctcgcccgt cacaaagagc 300

ttcaacaggg gagagtgt 318

<210> SEQ ID NO 681
<211> LENGTH: 452
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

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<400> SEQUENCE: 681

```
Gln Glu Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Glu Gly
1               5                   10                  15

Ser Leu Thr Leu Thr Cys Thr Ala Ser Gly Phe Ser Phe Ser Ser Ser
            20                  25                  30

Asp Tyr Met Cys Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
        35                  40                  45

Ile Gly Cys Ile Asp Ala Gly Ser Ser Gly Asp Thr Tyr Phe Ala Ser
    50                  55                  60

Trp Ala Lys Gly Arg Phe Thr Ile Ser Lys Thr Ser Ser Thr Thr Val
65                  70                  75                  80

Thr Leu Gln Met Thr Ser Leu Thr Ala Ala Asp Thr Ala Thr Tyr Phe
                85                  90                  95

Cys Ala Arg His Leu Tyr Gly Ser Ile Thr Phe Ala Phe Gly Leu Trp
            100                 105                 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
        115                 120                 125

Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr
    130                 135                 140

Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
145                 150                 155                 160

Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
                165                 170                 175

Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
            180                 185                 190

Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn
        195                 200                 205

His Lys Pro Ser Asn Thr Lys Val Asp Ala Arg Val Glu Pro Lys Ser
    210                 215                 220

Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
225                 230                 235                 240

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
                245                 250                 255

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
            260                 265                 270

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
        275                 280                 285

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr
    290                 295                 300

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
305                 310                 315                 320

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
                325                 330                 335

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
            340                 345                 350

Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val
        355                 360                 365

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
    370                 375                 380

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
385                 390                 395                 400
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Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
                405                 410                 415

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
            420                 425                 430

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
        435                 440                 445

Ser Pro Gly Lys
    450


<210> SEQ ID NO 682
<211> LENGTH: 122
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 682

Gln Glu Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Glu Gly
1               5                   10                  15

Ser Leu Thr Leu Thr Cys Thr Ala Ser Gly Phe Ser Phe Ser Ser Ser
            20                  25                  30

Asp Tyr Met Cys Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp
        35                  40                  45

Ile Gly Cys Ile Asp Ala Gly Ser Ser Gly Asp Thr Tyr Phe Ala Ser
    50                  55                  60

Trp Ala Lys Gly Arg Phe Thr Ile Ser Lys Thr Ser Ser Thr Thr Val
65                  70                  75                  80

Thr Leu Gln Met Thr Ser Leu Thr Ala Ala Asp Thr Ala Thr Tyr Phe
                85                  90                  95

Cys Ala Arg His Leu Tyr Gly Ser Ile Thr Phe Ala Phe Gly Leu Trp
            100                 105                 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> SEQ ID NO 683
<211> LENGTH: 30
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 683

Gln Glu Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Glu Gly
1               5                   10                  15

Ser Leu Thr Leu Thr Cys Thr Ala Ser Gly Phe Ser Phe Ser
            20                  25                  30


<210> SEQ ID NO 684
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 684

Ser Ser Asp Tyr Met Cys
1               5


<210> SEQ ID NO 685
<211> LENGTH: 14
<212> TYPE: PRT
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<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 685

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
1 5 10

<210> SEQ ID NO 686
<211> LENGTH: 18
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 686

Cys Ile Asp Ala Gly Ser Ser Gly Asp Thr Tyr Phe Ala Ser Trp Ala
1 5 10 15

Lys Gly

<210> SEQ ID NO 687
<211> LENGTH: 31
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 687

Arg Phe Thr Ile Ser Lys Thr Ser Ser Thr Thr Val Thr Leu Gln Met
1 5 10 15

Thr Ser Leu Thr Ala Ala Asp Thr Ala Thr Tyr Phe Cys Ala Arg
20 25 30

<210> SEQ ID NO 688
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 688

His Leu Tyr Gly Ser Ile Thr Phe Ala Phe Gly Leu
1 5 10

<210> SEQ ID NO 689
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 689

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
1 5 10

<210> SEQ ID NO 690
<211> LENGTH: 330
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 690

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

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```
Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
    50                  55                  60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65                  70                  75                  80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Ala
                85                  90                  95

Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
            100                 105                 110

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
        115                 120                 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
    130                 135                 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145                 150                 155                 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
                165                 170                 175

Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
            180                 185                 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
        195                 200                 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
    210                 215                 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
225                 230                 235                 240

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
                245                 250                 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
            260                 265                 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
        275                 280                 285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
    290                 295                 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305                 310                 315                 320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
                325                 330


<210> SEQ ID NO 691
<211> LENGTH: 1356
<212> TYPE: DNA
        <213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 691

caggagcagc tggtggagtc cgggggaggc ctggtccagc ctgagggatc cctgacactc     60

acctgcacag cctctggatt ctccttcagt agcagcgact acatgtgctg ggtccgccag    120

gctccaggga aggggctgga gtggatcgga tgcattgatg ctggtagtag tggtgacact    180

tacttcgcga gctgggcgaa aggccgattc accatctcca aaacctcgtc gaccacggtg    240

actctgcaaa tgaccagtct gacagccgcg gacacggcca cctatttctg tgcgagacat    300

ctttatggta gtattacttt cgcctttggc ttgtggggcc agggcaccct ggtcaccgtc    360
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tcgagcgcct ccaccaaggg cccatcggtc ttcccctgg caccctcctc caagagcacc 420

tctgggggca cagcggccct gggctgcctg gtcaaggact acttccccga accggtgacg 480

gtgtcgtgga actcaggcgc cctgaccagc ggcgtgcaca ccttcccggc tgtcctacag 540

tcctcaggac tctactccct cagcagcgtg gtgaccgtgc cctccagcag cttgggcacc 600

cagacctaca tctgcaacgt gaatcacaag cccagcaaca ccaaggtgga cgcgagagtt 660

gagcccaaat cttgtgacaa aactcacaca tgcccaccgt gcccagcacc tgaactcctg 720

gggggaccgt cagtcttcct cttccccca aaacccaagg acaccctcat gatctcccgg 780

acccctgagg tcacatgcgt ggtggtggac gtgagccacg aagaccctga ggtcaagttc 840

aactggtacg tggacggcgt ggaggtgcat aatgccaaga caaagccgcg ggaggagcag 900

tacgccagca cgtaccgtgt ggtcagcgtc ctcaccgtcc tgcaccagga ctggctgaat 960

ggcaaggagt acaagtgcaa ggtctccaac aaagccctcc cagccccat cgagaaaacc 1020

atctccaaag ccaaagggca gccccgagaa ccacaggtgt acaccctgcc cccatcccgg 1080

gaggagatga ccaagaacca ggtcagcctg acctgcctgg tcaaaggctt ctatcccagc 1140

gacatcgccg tggagtggga gagcaatggg cagccggaga acaactacaa gaccacgcct 1200

cccgtgctgg actccgacgg ctccttcttc ctctacagca agctcaccgt ggacaagagc 1260

aggtggcagc aggggaacgt cttctcatgc tccgtgatgc atgaggctct gcacaaccac 1320

tacacgcaga agagcctctc cctgtctccg ggtaaa 1356

<210> SEQ ID NO 692
<211> LENGTH: 366
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 692

caggagcagc tggtggagtc cgggggaggc ctggtccagc ctgagggatc cctgacactc 60

acctgcacag cctctggatt ctccttcagt agcagcgact acatgtgctg ggtccgccag 120

gctccaggga aggggctgga gtggatcgga tgcattgatg ctggtagtag tggtgacact 180

tacttcgcga gctgggcgaa aggccgattc accatctcca aaacctcgtc gaccacggtg 240

actctgcaaa tgaccagtct gacagccgcg gacacggcca cctatttctg tgcgagacat 300

ctttatggta gtattacttt cgcctttggc ttgtggggcc agggcaccct ggtcaccgtc 360

tcgagc 366

<210> SEQ ID NO 693
<211> LENGTH: 90
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 693

caggagcagc tggtggagtc cgggggaggc ctggtccagc ctgagggatc cctgacactc 60

acctgcacag cctctggatt ctccttcagt 90

<210> SEQ ID NO 694
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

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<400> SEQUENCE: 694

agcagcgact acatgtgc 18

<210> SEQ ID NO 695
<211> LENGTH: 42
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 695

tgggtccgcc aggctccagg gaaggggctg gagtggatcg ga 42

<210> SEQ ID NO 696
<211> LENGTH: 54
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 696

tgcattgatg ctggtagtag tggtgacact tacttcgcga gctgggcgaa aggc 54

<210> SEQ ID NO 697
<211> LENGTH: 93
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 697

cgattcacca tctccaaaac ctcgtcgacc acggtgactc tgcaaatgac cagtctgaca 60

gccgcggaca cggccaccta tttctgtgcg aga 93

<210> SEQ ID NO 698
<211> LENGTH: 36
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 698

catctttatg gtagtattac tttcgccttt ggcttg 36

<210> SEQ ID NO 699
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 699

tggggccagg gcaccctggt caccgtctcg agc 33

<210> SEQ ID NO 700
<211> LENGTH: 990
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 700

gcctccacca agggcccatc ggtcttcccc ctggcaccct cctccaagag cacctctggg 60

ggcacagcgg ccctgggctg cctggtcaag gactacttcc ccgaaccggt gacggtgtcg 120

tggaactcag gcgccctgac cagcggcgtg cacaccttcc cggctgtcct acagtcctca 180

ggactctact ccctcagcag cgtggtgacc gtgccctcca gcagcttggg cacccagacc 240

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tacatctgca acgtgaatca caagcccagc aacaccaagg tggacgcgag agttgagccc    300

aaatcttgtg acaaaactca cacatgccca ccgtgcccag cacctgaact cctgggggga    360

ccgtcagtct tcctcttccc cccaaaaccc aaggacaccc tcatgatctc ccggacccct    420

gaggtcacat gcgtggtggt ggacgtgagc cacgaagacc ctgaggtcaa gttcaactgg    480

tacgtggacg gcgtggaggt gcataatgcc aagacaaagc cgcgggagga gcagtacgcc    540

agcacgtacc gtgtggtcag cgtcctcacc gtcctgcacc aggactggct gaatggcaag    600

gagtacaagt gcaaggtctc caacaaagcc ctcccagccc ccatcgagaa aaccatctcc    660

aaagccaaag ggcagccccg agaaccacag gtgtacaccc tgcccccatc ccgggaggag    720

atgaccaaga accaggtcag cctgacctgc ctggtcaaag gcttctatcc cagcgacatc    780

gccgtggagt gggagagcaa tgggcagccg gagaacaact acaagaccac gcctcccgtg    840

ctggactccg acggctcctt cttcctctac agcaagctca ccgtggacaa gagcaggtgg    900

cagcagggga acgtcttctc atgctccgtg atgcatgagg ctctgcacaa ccactacacg    960

cagaagagcc tctccctgtc tccgggtaaa                                     990
```

<210> SEQ ID NO 701
<211> LENGTH: 217
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 701

```
Ala Ala Val Leu Thr Gln Thr Pro Ser Pro Val Ser Ala Ala Val Gly
1               5                   10                  15

Gly Thr Val Thr Ile Asn Cys Gln Ala Ser Gln Ser Ile Gly Ser Asp
            20                  25                  30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Asp Ala Ser Thr Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Gln Phe Thr Leu Thr Ile Ser Gly Val Gln Cys
65                  70                  75                  80

Asp Asp Ala Ala Thr Tyr Tyr Cys Gln Gly Thr Tyr Tyr Ser Ser Gly
                85                  90                  95

Trp Tyr Thr Ala Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg Thr
            100                 105                 110

Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu
        115                 120                 125

Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro
    130                 135                 140

Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly
145                 150                 155                 160

Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr
                165                 170                 175

Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His
            180                 185                 190

Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val
        195                 200                 205
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Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> SEQ ID NO 702
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 702

Ala Ala Val Leu Thr Gln Thr Pro Ser Pro Val Ser Ala Ala Val Gly
1 5 10 15

Gly Thr Val Thr Ile Asn Cys Gln Ala Ser Gln Ser Ile Gly Ser Asp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile
35 40 45

Tyr Asp Ala Ser Thr Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Gln Phe Thr Leu Thr Ile Ser Gly Val Gln Cys
65 70 75 80

Asp Asp Ala Ala Thr Tyr Tyr Cys Gln Gly Thr Tyr Tyr Ser Ser Gly
85 90 95

Trp Tyr Thr Ala Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg
100 105 110

<210> SEQ ID NO 703
<211> LENGTH: 23
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 703

Ala Ala Val Leu Thr Gln Thr Pro Ser Pro Val Ser Ala Ala Val Gly
1 5 10 15

Gly Thr Val Thr Ile Asn Cys
20

<210> SEQ ID NO 704
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 704

Gln Ala Ser Gln Ser Ile Gly Ser Asp Leu Ala
1 5 10

<210> SEQ ID NO 705
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 705

Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr
1 5 10 15

<210> SEQ ID NO 706
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

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<400> SEQUENCE: 706

Asp Ala Ser Thr Leu Ala Ser
1 5

<210> SEQ ID NO 707
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 707

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Gln Phe Thr
1 5 10 15

Leu Thr Ile Ser Gly Val Gln Cys Asp Asp Ala Ala Thr Tyr Tyr Cys
20 25 30

<210> SEQ ID NO 708
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 708

Gln Gly Thr Tyr Tyr Ser Ser Gly Trp Tyr Thr Ala
1 5 10

<210> SEQ ID NO 709
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 709

Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg
1 5 10

<210> SEQ ID NO 710
<211> LENGTH: 106
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 710

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
1 5 10 15

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
20 25 30

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
35 40 45

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
50 55 60

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
65 70 75 80

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
85 90 95

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
100 105

<210> SEQ ID NO 711

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<211> LENGTH: 651
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 711

gcagccgtgc tgacccagac accatcgccc gtgtctgcag ctgtgggagg cacagtcacc 60

atcaattgcc aggccagtca gagcattggt agcgacttag cctggtatca gcagaaacca 120

gggcagcctc ccaagctcct gatctatgat gcatccactc tggcatctgg ggtcccatcg 180

cggttcagcg gcagtggatc tgggacacag ttcactctca ccatcagcgg cgtgcagtgt 240

gacgatgctg ccacttacta ctgtcaaggc acttattata gtagtggttg gtacactgct 300

ttcggcggag ggaccgaggt ggtggtcaaa cgtacggtag cggccccatc tgtcttcatc 360

ttcccgccat ctgatgagca gttgaaatct ggaactgcct ctgttgtgtg cctgctgaat 420

aacttctatc ccagagaggc caaagtacag tggaaggtgg ataacgccct ccaatcgggt 480

aactcccagg agagtgtcac agagcaggac agcaaggaca gcacctacag cctcagcagc 540

accctgacgc tgagcaaagc agactacgag aaacacaaag tctacgcctg cgaagtcacc 600

catcagggcc tgagctcgcc cgtcacaaag agcttcaaca ggggagagtg t 651

<210> SEQ ID NO 712
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 712

gcagccgtgc tgacccagac accatcgccc gtgtctgcag ctgtgggagg cacagtcacc 60

atcaattgcc aggccagtca gagcattggt agcgacttag cctggtatca gcagaaacca 120

gggcagcctc ccaagctcct gatctatgat gcatccactc tggcatctgg ggtcccatcg 180

cggttcagcg gcagtggatc tgggacacag ttcactctca ccatcagcgg cgtgcagtgt 240

gacgatgctg ccacttacta ctgtcaaggc acttattata gtagtggttg gtacactgct 300

ttcggcggag ggaccgaggt ggtggtcaaa cgt 333

<210> SEQ ID NO 713
<211> LENGTH: 69
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 713

gcagccgtgc tgacccagac accatcgccc gtgtctgcag ctgtgggagg cacagtcacc 60

atcaattgc 69

<210> SEQ ID NO 714
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 714

caggccagtc agagcattgg tagcgactta gcc 33

<210> SEQ ID NO 715

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<211> LENGTH: 45
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 715

tggtatcagc agaaaccagg gcagcctccc aagctcctga tctat 45

<210> SEQ ID NO 716
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 716

gatgcatcca ctctggcatc t 21

<210> SEQ ID NO 717
<211> LENGTH: 96
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 717

ggggtcccat cgcggttcag cggcagtgga tctgggacac agttcactct caccatcagc 60

ggcgtgcagt gtgacgatgc tgccacttac tactgt 96

<210> SEQ ID NO 718
<211> LENGTH: 36
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 718

caaggcactt attatagtag tggttggtac actgct 36

<210> SEQ ID NO 719
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 719

ttcggcggag ggaccgaggt ggtggtcaaa cgt 33

<210> SEQ ID NO 720
<211> LENGTH: 318
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 720

acggtagcgg ccccatctgt cttcatcttc ccgccatctg atgagcagtt gaaatctgga 60

actgcctctg ttgtgtgcct gctgaataac ttctatccca gagaggccaa agtacagtgg 120

aaggtggata acgccctcca atcgggtaac tcccaggaga gtgtcacaga gcaggacagc 180

aaggacagca cctacagcct cagcagcacc ctgacgctga gcaaagcaga ctacgagaaa 240

cacaaagtct acgcctgcga agtcacccat cagggcctga gctcgcccgt cacaaagagc 300

ttcaacaggg gagagtgt 318

<210> SEQ ID NO 721

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<211> LENGTH: 447
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 721

Gln Gln Leu Glu Gln Ser Gly Gly Gly Ala Glu Gly Gly Leu Val Lys
1 5 10 15

Pro Gly Gly Ser Leu Glu Leu Cys Cys Lys Ala Ser Gly Phe Ser Leu
20 25 30

Ser Ser Thr Tyr Trp Met Cys Trp Val Arg Gln Ala Pro Gly Lys Gly
35 40 45

Leu Glu Trp Ile Gly Cys Ile Tyr Thr Gly Ser Gly Ser Thr Asp Tyr
50 55 60

Ala Ser Trp Val Asn Gly Gln Phe Thr Leu Ser Arg Asp Ile Asp Gln
65 70 75 80

Ser Thr Gly Cys Leu Gln Leu Asn Ser Leu Thr Val Ala Asp Thr Ala
85 90 95

Met Tyr Tyr Cys Thr Lys Asn Phe Asp Leu Trp Gly Pro Gly Thr Leu
100 105 110

Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
115 120 125

Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys
130 135 140

Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
145 150 155 160

Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
165 170 175

Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
180 185 190

Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn
195 200 205

Thr Lys Val Asp Ala Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His
210 215 220

Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val
225 230 235 240

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
245 250 255

Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
260 265 270

Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
275 280 285

Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser
290 295 300

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
305 310 315 320

Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile
325 330 335

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
340 345 350

Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
355 360 365

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Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
    370                 375                 380

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
385                 390                 395                 400

Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
                405                 410                 415

Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
            420                 425                 430

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
        435                 440                 445


<210> SEQ ID NO 722
<211> LENGTH: 117
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 722

Gln Gln Leu Glu Gln Ser Gly Gly Gly Ala Glu Gly Gly Leu Val Lys
1               5                   10                  15

Pro Gly Gly Ser Leu Glu Leu Cys Cys Lys Ala Ser Gly Phe Ser Leu
            20                  25                  30

Ser Ser Thr Tyr Trp Met Cys Trp Val Arg Gln Ala Pro Gly Lys Gly
        35                  40                  45

Leu Glu Trp Ile Gly Cys Ile Tyr Thr Gly Ser Gly Ser Thr Asp Tyr
    50                  55                  60

Ala Ser Trp Val Asn Gly Gln Phe Thr Leu Ser Arg Asp Ile Asp Gln
65                  70                  75                  80

Ser Thr Gly Cys Leu Gln Leu Asn Ser Leu Thr Val Ala Asp Thr Ala
                85                  90                  95

Met Tyr Tyr Cys Thr Lys Asn Phe Asp Leu Trp Gly Pro Gly Thr Leu
            100                 105                 110

Val Thr Val Ser Ser
        115


<210> SEQ ID NO 723
<211> LENGTH: 33
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 723

Gln Gln Leu Glu Gln Ser Gly Gly Gly Ala Glu Gly Gly Leu Val Lys
1               5                   10                  15

Pro Gly Gly Ser Leu Glu Leu Cys Cys Lys Ala Ser Gly Phe Ser Leu
            20                  25                  30

Ser


<210> SEQ ID NO 724
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 724

Ser Thr Tyr Trp Met Cys
1               5
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<210> SEQ ID NO 725
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 725

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
1 5 10

<210> SEQ ID NO 726
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 726

Cys Ile Tyr Thr Gly Ser Gly Ser Thr Asp Tyr Ala Ser Trp Val Asn
1 5 10 15

Gly

<210> SEQ ID NO 727
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 727

Gln Phe Thr Leu Ser Arg Asp Ile Asp Gln Ser Thr Gly Cys Leu Gln
1 5 10 15

Leu Asn Ser Leu Thr Val Ala Asp Thr Ala Met Tyr Tyr Cys Thr Lys
20 25 30

<210> SEQ ID NO 728
<211> LENGTH: 4
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 728

Asn Phe Asp Leu
1

<210> SEQ ID NO 729
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 729

Trp Gly Pro Gly Thr Leu Val Thr Val Ser Ser
1 5 10

<210> SEQ ID NO 730
<211> LENGTH: 330
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 730

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15

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Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
            20                  25                  30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
        35                  40                  45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
    50                  55                  60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65                  70                  75                  80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Ala
                85                  90                  95

Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
            100                 105                 110

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
        115                 120                 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
    130                 135                 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145                 150                 155                 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
                165                 170                 175

Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
            180                 185                 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
        195                 200                 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
    210                 215                 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
225                 230                 235                 240

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
                245                 250                 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
            260                 265                 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
        275                 280                 285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
    290                 295                 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305                 310                 315                 320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
                325                 330


<210> SEQ ID NO 731
<211> LENGTH: 1341
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 731

cagcagctgg agcagtccgg aggaggagcc gaaggaggcc tggtcaagcc tgggggatcc     60

ctggaactct gctgcaaggc ctctggattc tccctcagta gcacctactg gatgtgctgg    120

gtccgccagg ctccagggaa ggggctggag tggattggat gcatttatac tggtagtggt    180
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agcacagact acgcgagctg ggtgaatggc caattcactc tctccagaga catcgaccag 240

agcacaggtt gcctacaact gaacagtctg acagtcgcgg acacggccat gtattactgt 300

acgaaaaatt ttgacttgtg gggcccgggc accctggtca ccgtctcgag cgcctccacc 360

aagggcccat cggtcttccc cctggcaccc tcctccaaga gcacctctgg gggcacagcg 420

gccctgggct gcctggtcaa ggactacttc cccgaaccgg tgacggtgtc gtggaactca 480

ggcgccctga ccagcggcgt gcacaccttc ccggctgtcc tacagtcctc aggactctac 540

tccctcagca gcgtggtgac cgtgccctcc agcagcttgg gcacccagac ctacatctgc 600

aacgtgaatc acaagcccag caacaccaag gtggacgcga gagttgagcc caaatcttgt 660

gacaaaactc acacatgccc accgtgccca gcacctgaac tcctgggggg accgtcagtc 720

ttcctcttcc ccccaaaacc caaggacacc ctcatgatct cccggacccc tgaggtcaca 780

tgcgtggtgg tggacgtgag ccacgaagac cctgaggtca agttcaactg gtacgtggac 840

ggcgtggagg tgcataatgc caagacaaag ccgcgggagg agcagtacgc cagcacgtac 900

cgtgtggtca gcgtcctcac cgtcctgcac caggactggc tgaatggcaa ggagtacaag 960

tgcaaggtct ccaacaaagc cctcccagcc cccatcgaga aaaccatctc caaagccaaa 1020

gggcagcccc gagaaccaca ggtgtacacc ctgcccccat cccgggagga gatgaccaag 1080

aaccaggtca gcctgacctg cctggtcaaa ggcttctatc ccagcgacat cgccgtggag 1140

tgggagagca atgggcagcc ggagaacaac tacaagacca cgcctcccgt gctggactcc 1200

gacggctcct tcttcctcta cagcaagctc accgtggaca agagcaggtg gcagcagggg 1260

aacgtcttct catgctccgt gatgcatgag gctctgcaca accactacac gcagaagagc 1320

ctctccctgt ctccgggtaa a 1341

<210> SEQ ID NO 732
<211> LENGTH: 351
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 732

cagcagctgg agcagtccgg aggaggagcc gaaggaggcc tggtcaagcc tgggggatcc 60

ctggaactct gctgcaaggc ctctggattc tccctcagta gcacctactg gatgtgctgg 120

gtccgccagg ctccagggaa ggggctggag tggattggat gcatttatac tggtagtggt 180

agcacagact acgcgagctg ggtgaatggc caattcactc tctccagaga catcgaccag 240

agcacaggtt gcctacaact gaacagtctg acagtcgcgg acacggccat gtattactgt 300

acgaaaaatt ttgacttgtg gggcccgggc accctggtca ccgtctcgag c 351

<210> SEQ ID NO 733
<211> LENGTH: 99
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 733

cagcagctgg agcagtccgg aggaggagcc gaaggaggcc tggtcaagcc tgggggatcc 60

ctggaactct gctgcaaggc ctctggattc tccctcagt 99

<210> SEQ ID NO 734

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<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 734

agcacctact ggatgtgc 18

<210> SEQ ID NO 735
<211> LENGTH: 42
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 735

tgggtccgcc aggctccagg gaaggggctg gagtggattg ga 42

<210> SEQ ID NO 736
<211> LENGTH: 51
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 736

tgcatttata ctggtagtgg tagcacagac tacgcgagct gggtgaatgg c 51

<210> SEQ ID NO 737
<211> LENGTH: 96
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 737

caattcactc tctccagaga catcgaccag agcacaggtt gcctacaact gaacagtctg 60

acagtcgcgg acacggccat gtattactgt acgaaa 96

<210> SEQ ID NO 738
<211> LENGTH: 12
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 738

aattttgact tg 12

<210> SEQ ID NO 739
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 739

tggggcccgg gcaccctggt caccgtctcg agc 33

<210> SEQ ID NO 740
<211> LENGTH: 990
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 740

gcctccacca agggcccatc ggtcttcccc ctggcaccct cctccaagag cacctctggg 60

ggcacagcgg ccctgggctg cctggtcaag gactacttcc ccgaaccggt gacggtgtcg 120

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tggaactcag gcgccctgac cagcggcgtg cacaccttcc cggctgtcct acagtcctca    180

ggactctact ccctcagcag cgtggtgacc gtgccctcca gcagcttggg cacccagacc    240

tacatctgca acgtgaatca caagcccagc aacaccaagg tggacgcgag agttgagccc    300

aaatcttgtg acaaaactca cacatgccca ccgtgcccag cacctgaact cctgggggga    360

ccgtcagtct tcctcttccc cccaaaaccc aaggacaccc tcatgatctc ccggacccct    420

gaggtcacat gcgtggtggt ggacgtgagc cacgaagacc ctgaggtcaa gttcaactgg    480

tacgtggacg gcgtggaggt gcataatgcc aagacaaagc cgcgggagga gcagtacgcc    540

agcacgtacc gtgtggtcag cgtcctcacc gtcctgcacc aggactggct gaatggcaag    600

gagtacaagt gcaaggtctc caacaaagcc ctcccagccc ccatcgagaa aaccatctcc    660

aaagccaaag ggcagccccg agaaccacag gtgtacaccc tgcccccatc ccgggaggag    720

atgaccaaga accaggtcag cctgacctgc ctggtcaaag gcttctatcc cagcgacatc    780

gccgtggagt gggagagcaa tgggcagccg gagaacaact acaagaccac gcctcccgtg    840

ctggactccg acggctcctt cttcctctac agcaagctca ccgtggacaa gagcaggtgg    900

cagcagggga acgtcttctc atgctccgtg atgcatgagg ctctgcacaa ccactacacg    960

cagaagagcc tctccctgtc tccgggtaaa                                     990
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<210> SEQ ID NO 741
<211> LENGTH: 220
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 741

```
Ala Gln Val Leu Thr Gln Thr Pro Ser Ser Val Ser Ala Ala Val Gly
1               5                   10                  15

Gly Thr Val Thr Ile Asn Cys Gln Ser Ser Pro Ser Val Tyr Ser Asn
            20                  25                  30

Asn Tyr Leu Ser Trp Phe Gln Gln Lys Pro Gly Gln Pro Pro Lys Gly
        35                  40                  45

Leu Ile Ala Asp Ala Ser Thr Leu Ala Ser Gly Val Pro Ser Arg Phe
    50                  55                  60

Lys Gly Ser Gly Ser Gly Thr Gln Phe Thr Leu Thr Ile Ser Gly Val
65                  70                  75                  80

Gln Cys Asp Asp Ala Ala Ala Tyr Tyr Cys Leu Gly Tyr Tyr Asp Cys
                85                  90                  95

Gly Ser Thr Asp Cys His Ala Phe Gly Gly Gly Thr Glu Val Val Val
            100                 105                 110

Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp
        115                 120                 125

Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn
    130                 135                 140

Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu
145                 150                 155                 160

Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp
                165                 170                 175

Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr
            180                 185                 190
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Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser
        195                 200                 205

Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
    210                 215                 220


<210> SEQ ID NO 742
<211> LENGTH: 114
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 742

Ala Gln Val Leu Thr Gln Thr Pro Ser Ser Val Ser Ala Ala Val Gly
1               5                   10                  15

Gly Thr Val Thr Ile Asn Cys Gln Ser Ser Pro Ser Val Tyr Ser Asn
            20                  25                  30

Asn Tyr Leu Ser Trp Phe Gln Gln Lys Pro Gly Gln Pro Pro Lys Gly
        35                  40                  45

Leu Ile Ala Asp Ala Ser Thr Leu Ala Ser Gly Val Pro Ser Arg Phe
    50                  55                  60

Lys Gly Ser Gly Ser Gly Thr Gln Phe Thr Leu Thr Ile Ser Gly Val
65                  70                  75                  80

Gln Cys Asp Asp Ala Ala Ala Tyr Tyr Cys Leu Gly Tyr Tyr Asp Cys
                85                  90                  95

Gly Ser Thr Asp Cys His Ala Phe Gly Gly Gly Thr Glu Val Val Val
            100                 105                 110

Lys Arg


<210> SEQ ID NO 743
<211> LENGTH: 23
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 743

Ala Gln Val Leu Thr Gln Thr Pro Ser Ser Val Ser Ala Ala Val Gly
1               5                   10                  15

Gly Thr Val Thr Ile Asn Cys
            20


<210> SEQ ID NO 744
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 744

Gln Ser Ser Pro Ser Val Tyr Ser Asn Asn Tyr Leu Ser
1               5                   10


<210> SEQ ID NO 745
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 745

Trp Phe Gln Gln Lys Pro Gly Gln Pro Pro Lys Gly Leu Ile Ala
1               5                   10                  15
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<210> SEQ ID NO 746
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 746

Asp Ala Ser Thr Leu Ala Ser
1 5

<210> SEQ ID NO 747
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 747

Gly Val Pro Ser Arg Phe Lys Gly Ser Gly Ser Gly Thr Gln Phe Thr
1 5 10 15

Leu Thr Ile Ser Gly Val Gln Cys Asp Asp Ala Ala Ala Tyr Tyr Cys
20 25 30

<210> SEQ ID NO 748
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 748

Leu Gly Tyr Tyr Asp Cys Gly Ser Thr Asp Cys His Ala
1 5 10

<210> SEQ ID NO 749
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 749

Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg
1 5 10

<210> SEQ ID NO 750
<211> LENGTH: 106
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 750

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
1 5 10 15

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
20 25 30

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
35 40 45

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
50 55 60

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
65 70 75 80

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
85 90 95

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Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
100 105

<210> SEQ ID NO 751
<211> LENGTH: 660
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 751

gcccaagtgc tgacccagac tccatcctcc gtgtctgcag ctgtgggagg cacagtcacc 60

atcaattgcc agtccagtcc gagtgtttat agtaacaact acttatcctg gtttcagcag 120

aaaccagggc agcctcccaa aggcctgatc gctgatgcat ccactctggc atctggggtc 180

ccatcgcggt tcaaaggcag tggatctggg acacagttca ctctcaccat cagcggcgtg 240

cagtgtgacg atgctgccgc ttactactgt ctaggctatt atgattgtgg tagtactgat 300

tgtcatgctt tcggcggagg gaccgaggtg gtggtcaaac gtacggtagc ggccccatct 360

gtcttcatct tcccgccatc tgatgagcag ttgaaatctg gaactgcctc tgttgtgtgc 420

ctgctgaata acttctatcc cagagaggcc aaagtacagt ggaaggtgga taacgccctc 480

caatcgggta actcccagga gagtgtcaca gagcaggaca gcaaggacag cacctacagc 540

ctcagcagca ccctgacgct gagcaaagca gactacgaga aacacaaagt ctacgcctgc 600

gaagtcaccc atcagggcct gagctcgccc gtcacaaaga gcttcaacag gggagagtgt 660

<210> SEQ ID NO 752
<211> LENGTH: 342
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 752

gcccaagtgc tgacccagac tccatcctcc gtgtctgcag ctgtgggagg cacagtcacc 60

atcaattgcc agtccagtcc gagtgtttat agtaacaact acttatcctg gtttcagcag 120

aaaccagggc agcctcccaa aggcctgatc gctgatgcat ccactctggc atctggggtc 180

ccatcgcggt tcaaaggcag tggatctggg acacagttca ctctcaccat cagcggcgtg 240

cagtgtgacg atgctgccgc ttactactgt ctaggctatt atgattgtgg tagtactgat 300

tgtcatgctt tcggcggagg gaccgaggtg gtggtcaaac gt 342

<210> SEQ ID NO 753
<211> LENGTH: 69
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 753

gcccaagtgc tgacccagac tccatcctcc gtgtctgcag ctgtgggagg cacagtcacc 60

atcaattgc 69

<210> SEQ ID NO 754
<211> LENGTH: 39
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 754

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cagtccagtc cgagtgttta tagtaacaac tacttatcc 39

<210> SEQ ID NO 755
<211> LENGTH: 45
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 755

tggtttcagc agaaaccagg gcagcctccc aaaggcctga tcgct 45

<210> SEQ ID NO 756
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 756

gatgcatcca ctctggcatc t 21

<210> SEQ ID NO 757
<211> LENGTH: 96
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 757

ggggtcccat cgcggttcaa aggcagtgga tctgggacac agttcactct caccatcagc 60

ggcgtgcagt gtgacgatgc tgccgcttac tactgt 96

<210> SEQ ID NO 758
<211> LENGTH: 39
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 758

ctaggctatt atgattgtgg tagtactgat tgtcatgct 39

<210> SEQ ID NO 759
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 759

ttcggcggag ggaccgaggt ggtggtcaaa cgt 33

<210> SEQ ID NO 760
<211> LENGTH: 318
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 760

acggtagcgg ccccatctgt cttcatcttc ccgccatctg atgagcagtt gaaatctgga 60

actgcctctg ttgtgtgcct gctgaataac ttctatccca gagaggccaa agtacagtgg 120

aaggtggata acgccctcca atcgggtaac tcccaggaga gtgtcacaga gcaggacagc 180

aaggacagca cctacagcct cagcagcacc ctgacgctga gcaaagcaga ctacgagaaa 240

cacaaagtct acgcctgcga agtcacccat cagggcctga gctcgcccgt cacaaagagc 300

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ttcaacaggg gagagtgt 318

<210> SEQ ID NO 761
<211> LENGTH: 447
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 761

Gln Gln Leu Glu Gln Ser Gly Gly Gly Ala Glu Gly Gly Leu Val Lys
1 5 10 15

Pro Gly Gly Ser Leu Glu Leu Cys Cys Lys Ala Ser Gly Phe Ser Leu
20 25 30

Thr Thr Ser His Trp Met Cys Trp Val Arg Gln Ala Pro Gly Lys Gly
35 40 45

Leu Asn Trp Ile Gly Cys Ile Ser Ala Gly Ser Gly Asp Ala Asp Tyr
50 55 60

Ala Thr Trp Val Asp Ala Gln Phe Thr Leu Ser Arg Asp Ile Asp Gln
65 70 75 80

Asn Thr Gly Cys Leu Gln Leu Asn Ser Leu Thr Pro Ala Asp Thr Ala
85 90 95

Met Tyr Tyr Cys Thr Ile Asn Phe Glu Leu Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
115 120 125

Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys
130 135 140

Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
145 150 155 160

Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
165 170 175

Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
180 185 190

Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn
195 200 205

Thr Lys Val Asp Ala Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His
210 215 220

Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val
225 230 235 240

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
245 250 255

Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
260 265 270

Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
275 280 285

Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser
290 295 300

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
305 310 315 320

Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile
325 330 335

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Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
            340                 345                 350

Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
        355                 360                 365

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
    370                 375                 380

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
385                 390                 395                 400

Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
                405                 410                 415

Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
            420                 425                 430

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
        435                 440                 445


<210> SEQ ID NO 762
<211> LENGTH: 117
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 762

Gln Gln Leu Glu Gln Ser Gly Gly Gly Ala Glu Gly Gly Leu Val Lys
1               5                   10                  15

Pro Gly Gly Ser Leu Glu Leu Cys Cys Lys Ala Ser Gly Phe Ser Leu
            20                  25                  30

Thr Thr Ser His Trp Met Cys Trp Val Arg Gln Ala Pro Gly Lys Gly
        35                  40                  45

Leu Asn Trp Ile Gly Cys Ile Ser Ala Gly Ser Gly Asp Ala Asp Tyr
    50                  55                  60

Ala Thr Trp Val Asp Ala Gln Phe Thr Leu Ser Arg Asp Ile Asp Gln
65                  70                  75                  80

Asn Thr Gly Cys Leu Gln Leu Asn Ser Leu Thr Pro Ala Asp Thr Ala
                85                  90                  95

Met Tyr Tyr Cys Thr Ile Asn Phe Glu Leu Trp Gly Gln Gly Thr Leu
            100                 105                 110

Val Thr Val Ser Ser
        115


<210> SEQ ID NO 763
<211> LENGTH: 33
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 763

Gln Gln Leu Glu Gln Ser Gly Gly Gly Ala Glu Gly Gly Leu Val Lys
1               5                   10                  15

Pro Gly Gly Ser Leu Glu Leu Cys Cys Lys Ala Ser Gly Phe Ser Leu
            20                  25                  30

Thr


<210> SEQ ID NO 764
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus
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<400> SEQUENCE: 764

Thr Ser His Trp Met Cys
1 5

<210> SEQ ID NO 765
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 765

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Asn Trp Ile Gly
1 5 10

<210> SEQ ID NO 766
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 766

Cys Ile Ser Ala Gly Ser Gly Asp Ala Asp Tyr Ala Thr Trp Val Asp
1 5 10 15

Ala

<210> SEQ ID NO 767
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 767

Gln Phe Thr Leu Ser Arg Asp Ile Asp Gln Asn Thr Gly Cys Leu Gln
1 5 10 15

Leu Asn Ser Leu Thr Pro Ala Asp Thr Ala Met Tyr Tyr Cys Thr Ile
20 25 30

<210> SEQ ID NO 768
<211> LENGTH: 4
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 768

Asn Phe Glu Leu
1

<210> SEQ ID NO 769
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 769

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
1 5 10

<210> SEQ ID NO 770
<211> LENGTH: 330
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

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<400> SEQUENCE: 770

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65 70 75 80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Ala
85 90 95

Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
100 105 110

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
115 120 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
130 135 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145 150 155 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
165 170 175

Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
180 185 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
195 200 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
210 215 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
225 230 235 240

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
245 250 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
260 265 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
275 280 285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
290 295 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305 310 315 320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
325 330

<210> SEQ ID NO 771
<211> LENGTH: 1341
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 771

cagcagctgg agcagtccgg aggaggagcc gaaggaggcc tggtcaagcc tgggggatcc 60

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ctggaactct gctgcaaagc ctctggattc tccctcacta cgagccactg gatgtgttgg 120

gtccgccagg ctccagggaa ggggctgaat tggattggat gcattagtgc cggtagtggt 180

gacgcagact acgcgacctg ggtggatgcc caattcactc tctccagaga catcgaccag 240

aacacaggtt gcctacaatt gaacagtctg acacccgcgg acacggccat gtattactgt 300

acgataaatt ttgagttgtg gggccaaggc accctggtca ccgtctcgag cgcctccacc 360

aagggcccat cggtcttccc cctggcaccc tcctccaaga gcacctctgg gggcacagcg 420

gccctgggct gcctggtcaa ggactacttc cccgaaccgg tgacggtgtc gtggaactca 480

ggcgccctga ccagcggcgt gcacaccttc ccggctgtcc tacagtcctc aggactctac 540

tccctcagca gcgtggtgac cgtgccctcc agcagcttgg gcacccagac ctacatctgc 600

aacgtgaatc acaagcccag caacaccaag gtggacgcga gagttgagcc caaatcttgt 660

gacaaaactc acacatgccc accgtgccca gcacctgaac tcctgggggg accgtcagtc 720

ttcctcttcc ccccaaaacc caaggacacc ctcatgatct cccggacccc tgaggtcaca 780

tgcgtggtgg tggacgtgag ccacgaagac cctgaggtca agttcaactg gtacgtggac 840

ggcgtggagg tgcataatgc caagacaaag ccgcgggagg agcagtacgc cagcacgtac 900

cgtgtggtca gcgtcctcac cgtcctgcac caggactggc tgaatggcaa ggagtacaag 960

tgcaaggtct ccaacaaagc cctcccagcc cccatcgaga aaaccatctc caaagccaaa 1020

gggcagcccc gagaaccaca ggtgtacacc ctgcccccat cccgggagga gatgaccaag 1080

aaccaggtca gcctgacctg cctggtcaaa ggcttctatc ccagcgacat cgccgtggag 1140

tgggagagca atgggcagcc ggagaacaac tacaagacca cgcctcccgt gctggactcc 1200

gacggctcct tcttcctcta cagcaagctc accgtggaca agagcaggtg gcagcagggg 1260

aacgtcttct catgctccgt gatgcatgag gctctgcaca accactacac gcagaagagc 1320

ctctccctgt ctccgggtaa a 1341

<210> SEQ ID NO 772
<211> LENGTH: 351
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 772

cagcagctgg agcagtccgg aggaggagcc gaaggaggcc tggtcaagcc tgggggatcc 60

ctggaactct gctgcaaagc ctctggattc tccctcacta cgagccactg gatgtgttgg 120

gtccgccagg ctccagggaa ggggctgaat tggattggat gcattagtgc cggtagtggt 180

gacgcagact acgcgacctg ggtggatgcc caattcactc tctccagaga catcgaccag 240

aacacaggtt gcctacaatt gaacagtctg acacccgcgg acacggccat gtattactgt 300

acgataaatt ttgagttgtg gggccaaggc accctggtca ccgtctcgag c 351

<210> SEQ ID NO 773
<211> LENGTH: 99
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 773

cagcagctgg agcagtccgg aggaggagcc gaaggaggcc tggtcaagcc tgggggatcc 60

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ctggaactct gctgcaaagc ctctggattc tccctcact 99

<210> SEQ ID NO 774
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 774

acgagccact ggatgtgt 18

<210> SEQ ID NO 775
<211> LENGTH: 42
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 775

tgggtccgcc aggctccagg gaaggggctg aattggattg ga 42

<210> SEQ ID NO 776
<211> LENGTH: 51
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 776

tgcattagtg ccggtagtgg tgacgcagac tacgcgacct gggtggatgc c 51

<210> SEQ ID NO 777
<211> LENGTH: 96
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 777

caattcactc tctccagaga catcgaccag aacacaggtt gcctacaatt gaacagtctg 60

acacccgcgg acacggccat gtattactgt acgata 96

<210> SEQ ID NO 778
<211> LENGTH: 12
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 778

aattttgagt tg 12

<210> SEQ ID NO 779
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 779

tggggccaag gcaccctggt caccgtctcg agc 33

<210> SEQ ID NO 780
<211> LENGTH: 990
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 780

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gcctccacca agggcccatc ggtcttcccc ctggcaccct cctccaagag cacctctggg     60

ggcacagcgg ccctgggctg cctggtcaag gactacttcc ccgaaccggt gacggtgtcg    120

tggaactcag gcgccctgac cagcggcgtg cacaccttcc cggctgtcct acagtcctca    180

ggactctact ccctcagcag cgtggtgacc gtgccctcca gcagcttggg cacccagacc    240

tacatctgca acgtgaatca caagcccagc aacaccaagg tggacgcgag agttgagccc    300

aaatcttgtg acaaaactca cacatgccca ccgtgcccag cacctgaact cctgggggga    360

ccgtcagtct tcctcttccc cccaaaaccc aaggacaccc tcatgatctc ccggacccct    420

gaggtcacat gcgtggtggt ggacgtgagc cacgaagacc ctgaggtcaa gttcaactgg    480

tacgtggacg gcgtggaggt gcataatgcc aagacaaagc cgcgggagga gcagtacgcc    540

agcacgtacc gtgtggtcag cgtcctcacc gtcctgcacc aggactggct gaatggcaag    600

gagtacaagt gcaaggtctc caacaaagcc ctcccagccc ccatcgagaa aaccatctcc    660

aaagccaaag ggcagccccg agaaccacag gtgtacaccc tgccccatc ccgggaggag    720

atgaccaaga accaggtcag cctgacctgc ctggtcaaag gcttctatcc cagcgacatc    780

gccgtggagt gggagagcaa tgggcagccg gagaacaact acaagaccac gcctcccgtg    840

ctggactccg acggctcctt cttcctctac agcaagctca ccgtggacaa gagcaggtgg    900

cagcagggga acgtcttctc atgctccgtg atgcatgagg ctctgcacaa ccactacacg    960

cagaagagcc tctccctgtc tccgggtaaa                                     990
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<210> SEQ ID NO 781
<211> LENGTH: 219
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 781

Ala Gln Val Leu Thr Gln Thr Pro Ser Ser Val Ser Ala Ala Val Gly
1               5                   10                  15

Gly Thr Val Thr Ile Asn Cys Gln Ser Ser Pro Ser Val Tyr Ser Ser
            20                  25                  30

Tyr Leu Ser Trp Phe Gln Gln Lys Pro Gly Gln Pro Pro Lys Phe Leu
        35                  40                  45

Ile Tyr Glu Ala Ser Lys Leu Ala Ser Gly Val Pro Ser Arg Phe Ser
    50                  55                  60

Gly Ser Gly Ser Gly Thr Gln Phe Thr Leu Thr Ile Ser Gly Val Gln
65                  70                  75                  80

Cys Ser Asp Ala Ala Thr Tyr Tyr Cys Leu Gly Ala Tyr Asp Cys Gly
                85                  90                  95

Arg Thr Asp Cys His Ala Phe Gly Gly Gly Thr Glu Val Val Val Lys
            100                 105                 110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
        115                 120                 125

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
    130                 135                 140

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
145                 150                 155                 160

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
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                165                 170                 175

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
            180                 185                 190

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
        195                 200                 205

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
    210                 215


<210> SEQ ID NO 782
<211> LENGTH: 113
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 782

Ala Gln Val Leu Thr Gln Thr Pro Ser Ser Val Ser Ala Ala Val Gly
1               5                   10                  15

Gly Thr Val Thr Ile Asn Cys Gln Ser Ser Pro Ser Val Tyr Ser Ser
            20                  25                  30

Tyr Leu Ser Trp Phe Gln Gln Lys Pro Gly Gln Pro Pro Lys Phe Leu
        35                  40                  45

Ile Tyr Glu Ala Ser Lys Leu Ala Ser Gly Val Pro Ser Arg Phe Ser
    50                  55                  60

Gly Ser Gly Ser Gly Thr Gln Phe Thr Leu Thr Ile Ser Gly Val Gln
65                  70                  75                  80

Cys Ser Asp Ala Ala Thr Tyr Tyr Cys Leu Gly Ala Tyr Asp Cys Gly
                85                  90                  95

Arg Thr Asp Cys His Ala Phe Gly Gly Gly Thr Glu Val Val Val Lys
            100                 105                 110

Arg


<210> SEQ ID NO 783
<211> LENGTH: 23
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 783

Ala Gln Val Leu Thr Gln Thr Pro Ser Ser Val Ser Ala Ala Val Gly
1               5                   10                  15

Gly Thr Val Thr Ile Asn Cys
            20


<210> SEQ ID NO 784
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 784

Gln Ser Ser Pro Ser Val Tyr Ser Ser Tyr Leu Ser
1               5                   10


<210> SEQ ID NO 785
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 785
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Trp Phe Gln Gln Lys Pro Gly Gln Pro Pro Lys Phe Leu Ile Tyr
1               5                   10                  15


<210> SEQ ID NO 786
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 786

Glu Ala Ser Lys Leu Ala Ser
1               5


<210> SEQ ID NO 787
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 787

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Gln Phe Thr
1               5                   10                  15

Leu Thr Ile Ser Gly Val Gln Cys Ser Asp Ala Ala Thr Tyr Tyr Cys
            20                  25                  30


<210> SEQ ID NO 788
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 788

Leu Gly Ala Tyr Asp Cys Gly Arg Thr Asp Cys His Ala
1               5                   10


<210> SEQ ID NO 789
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 789

Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg
1               5                   10


<210> SEQ ID NO 790
<211> LENGTH: 106
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 790

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
1               5                   10                  15

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
            20                  25                  30

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
        35                  40                  45

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
    50                  55                  60

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
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65 70 75 80

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
85 90 95

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
100 105

<210> SEQ ID NO 791
<211> LENGTH: 657
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 791

gcccaagtgc tgacccagac tccatcctcc gtgtctgcag ctgtgggagg cacagtcacc 60

atcaattgcc agtccagtcc gagtgtttat agtagctact tatcctggtt tcagcagaaa 120

ccagggcagc ctcccaagtt cctgatctac gaagcatcca aactggcatc tggggtccca 180

tcgcggttca gcggcagtgg atctgggaca cagttcactc tcaccatcag cggcgtgcag 240

tgtagcgatg ctgccactta ctactgtctt ggcgcgtatg attgtggtcg tactgattgt 300

catgctttcg gcggagggac cgaggtggtg gtcaaacgta cggtagcggc cccatctgtc 360

ttcatcttcc cgccatctga tgagcagttg aaatctggaa ctgcctctgt tgtgtgcctg 420

ctgaataact tctatcccag agaggccaaa gtacagtgga aggtggataa cgccctccaa 480

tcgggtaact cccaggagag tgtcacagag caggacagca aggacagcac ctacagcctc 540

agcagcaccc tgacgctgag caaagcagac tacgagaaac acaaagtcta cgcctgcgaa 600

gtcacccatc agggcctgag ctcgcccgtc acaaagagct tcaacagggg agagtgt 657

<210> SEQ ID NO 792
<211> LENGTH: 339
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 792

gcccaagtgc tgacccagac tccatcctcc gtgtctgcag ctgtgggagg cacagtcacc 60

atcaattgcc agtccagtcc gagtgtttat agtagctact tatcctggtt tcagcagaaa 120

ccagggcagc ctcccaagtt cctgatctac gaagcatcca aactggcatc tggggtccca 180

tcgcggttca gcggcagtgg atctgggaca cagttcactc tcaccatcag cggcgtgcag 240

tgtagcgatg ctgccactta ctactgtctt ggcgcgtatg attgtggtcg tactgattgt 300

catgctttcg gcggagggac cgaggtggtg gtcaaacgt 339

<210> SEQ ID NO 793
<211> LENGTH: 69
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 793

gcccaagtgc tgacccagac tccatcctcc gtgtctgcag ctgtgggagg cacagtcacc 60

atcaattgc 69

<210> SEQ ID NO 794

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<211> LENGTH: 36
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 794

cagtccagtc cgagtgttta tagtagctac ttatcc 36

<210> SEQ ID NO 795
<211> LENGTH: 45
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 795

tggtttcagc agaaaccagg gcagcctccc aagttcctga tctac 45

<210> SEQ ID NO 796
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 796

gaagcatcca aactggcatc t 21

<210> SEQ ID NO 797
<211> LENGTH: 96
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 797

ggggtcccat cgcggttcag cggcagtgga tctgggacac agttcactct caccatcagc 60

ggcgtgcagt gtagcgatgc tgccacttac tactgt 96

<210> SEQ ID NO 798
<211> LENGTH: 39
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 798

cttggcgcgt atgattgtgg tcgtactgat tgtcatgct 39

<210> SEQ ID NO 799
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 799

ttcggcggag ggaccgaggt ggtggtcaaa cgt 33

<210> SEQ ID NO 800
<211> LENGTH: 318
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 800

acggtagcgg ccccatctgt cttcatcttc ccgccatctg atgagcagtt gaaatctgga 60

actgcctctg ttgtgtgcct gctgaataac ttctatccca gagaggccaa agtacagtgg 120

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aaggtggata acgccctcca atcgggtaac tcccaggaga gtgtcacaga gcaggacagc    180

aaggacagca cctacagcct cagcagcacc ctgacgctga gcaaagcaga ctacgagaaa    240

cacaaagtct acgcctgcga agtcacccat cagggcctga gctcgcccgt cacaaagagc    300

ttcaacaggg gagagtgt                                                  318


<210> SEQ ID NO 801
<211> LENGTH: 447
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 801

Gln Gln Leu Glu Gln Ser Gly Gly Gly Ala Glu Gly Gly Leu Val Lys
1               5                   10                  15

Pro Gly Gly Ser Leu Lys Leu Ser Cys Lys Ala Ser Gly Phe Thr Ile
            20                  25                  30

Ser Arg Asp Tyr Trp Ile Cys Trp Val Arg Gln Ala Pro Gly Lys Gly
        35                  40                  45

Leu Glu Trp Ile Gly Cys Ile Ser Ala Gly Gly Gly Ser Thr Asp Tyr
    50                  55                  60

Ala Asn Trp Val Asn Gly Arg Phe Thr Leu Ser Arg Asp Ile Asp Gln
65                  70                  75                  80

Ser Thr Gly Cys Leu Gln Leu Asn Ser Leu Thr Asp Ala Asp Thr Ala
                85                  90                  95

Met Tyr Tyr Cys Ala Gly Asn Leu Glu Ile Trp Gly Gln Gly Thr Leu
            100                 105                 110

Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
        115                 120                 125

Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys
    130                 135                 140

Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
145                 150                 155                 160

Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
                165                 170                 175

Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
            180                 185                 190

Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn
        195                 200                 205

Thr Lys Val Asp Ala Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His
    210                 215                 220

Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val
225                 230                 235                 240

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
                245                 250                 255

Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
            260                 265                 270

Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
        275                 280                 285

Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser
    290                 295                 300

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
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305                 310                 315                 320

Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile
                325                 330                 335

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
            340                 345                 350

Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
        355                 360                 365

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
    370                 375                 380

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
385                 390                 395                 400

Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
                405                 410                 415

Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
            420                 425                 430

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
        435                 440                 445


<210> SEQ ID NO 802
<211> LENGTH: 117
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 802

Gln Gln Leu Glu Gln Ser Gly Gly Gly Ala Glu Gly Gly Leu Val Lys
1               5                   10                  15

Pro Gly Gly Ser Leu Lys Leu Ser Cys Lys Ala Ser Gly Phe Thr Ile
            20                  25                  30

Ser Arg Asp Tyr Trp Ile Cys Trp Val Arg Gln Ala Pro Gly Lys Gly
        35                  40                  45

Leu Glu Trp Ile Gly Cys Ile Ser Ala Gly Gly Gly Ser Thr Asp Tyr
    50                  55                  60

Ala Asn Trp Val Asn Gly Arg Phe Thr Leu Ser Arg Asp Ile Asp Gln
65                  70                  75                  80

Ser Thr Gly Cys Leu Gln Leu Asn Ser Leu Thr Asp Ala Asp Thr Ala
                85                  90                  95

Met Tyr Tyr Cys Ala Gly Asn Leu Glu Ile Trp Gly Gln Gly Thr Leu
            100                 105                 110

Val Thr Val Ser Ser
        115


<210> SEQ ID NO 803
<211> LENGTH: 33
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 803

Gln Gln Leu Glu Gln Ser Gly Gly Gly Ala Glu Gly Gly Leu Val Lys
1               5                   10                  15

Pro Gly Gly Ser Leu Lys Leu Ser Cys Lys Ala Ser Gly Phe Thr Ile
            20                  25                  30

Ser
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<210> SEQ ID NO 804
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 804

Arg Asp Tyr Trp Ile Cys
1 5

<210> SEQ ID NO 805
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 805

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
1 5 10

<210> SEQ ID NO 806
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 806

Cys Ile Ser Ala Gly Gly Gly Ser Thr Asp Tyr Ala Asn Trp Val Asn
1 5 10 15

Gly

<210> SEQ ID NO 807
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 807

Arg Phe Thr Leu Ser Arg Asp Ile Asp Gln Ser Thr Gly Cys Leu Gln
1 5 10 15

Leu Asn Ser Leu Thr Asp Ala Asp Thr Ala Met Tyr Tyr Cys Ala Gly
20 25 30

<210> SEQ ID NO 808
<211> LENGTH: 4
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 808

Asn Leu Glu Ile
1

<210> SEQ ID NO 809
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 809

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
1 5 10

<210> SEQ ID NO 810
<211> LENGTH: 330

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<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 810

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65 70 75 80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Ala
85 90 95

Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
100 105 110

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
115 120 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
130 135 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145 150 155 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
165 170 175

Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
180 185 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
195 200 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
210 215 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
225 230 235 240

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
245 250 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
260 265 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
275 280 285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
290 295 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305 310 315 320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
325 330

<210> SEQ ID NO 811
<211> LENGTH: 1341
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:

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<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 811

cagcagctgg agcagtccgg aggaggagcc gaaggaggcc tggtcaagcc tgggggatcc 60

ctgaaactct cctgcaaagc ctctggattc accatcagta gggactactg gatatgttgg 120

gtccgccagg ctccagggaa ggggctggag tggattggat gcattagtgc tggtggtggt 180

agcacagact acgcgaactg ggtgaatggc cgattcactc tctccagaga catcgaccag 240

agcacaggtt gccttcaact gaacagtctg acagacgcgg acacggccat gtattactgt 300

gcgggaaatc tagagatctg gggccaaggg accctggtca ccgtctcgag cgcctccacc 360

aagggcccat cggtcttccc cctggcaccc tcctccaaga gcacctctgg gggcacagcg 420

gccctgggct gcctggtcaa ggactacttc cccgaaccgg tgacggtgtc gtggaactca 480

ggcgccctga ccagcggcgt gcacaccttc ccggctgtcc tacagtcctc aggactctac 540

tccctcagca gcgtggtgac cgtgccctcc agcagcttgg gcacccagac ctacatctgc 600

aacgtgaatc acaagcccag caacaccaag gtggacgcga gagttgagcc caaatcttgt 660

gacaaaactc acacatgccc accgtgccca gcacctgaac tcctgggggg accgtcagtc 720

ttcctcttcc ccccaaaacc caaggacacc ctcatgatct cccggacccc tgaggtcaca 780

tgcgtggtgg tggacgtgag ccacgaagac cctgaggtca agttcaactg gtacgtggac 840

ggcgtggagg tgcataatgc caagacaaag ccgcgggagg agcagtacgc cagcacgtac 900

cgtgtggtca gcgtcctcac cgtcctgcac caggactggc tgaatggcaa ggagtacaag 960

tgcaaggtct ccaacaaagc cctcccagcc cccatcgaga aaaccatctc caaagccaaa 1020

gggcagcccc gagaaccaca ggtgtacacc ctgcccccat cccgggagga gatgaccaag 1080

aaccaggtca gcctgacctg cctggtcaaa ggcttctatc ccagcgacat cgccgtggag 1140

tgggagagca atgggcagcc ggagaacaac tacaagacca cgcctcccgt gctggactcc 1200

gacggctcct tcttcctcta cagcaagctc accgtggaca agagcaggtg gcagcagggg 1260

aacgtcttct catgctccgt gatgcatgag gctctgcaca accactacac gcagaagagc 1320

ctctccctgt ctccgggtaa a 1341

<210> SEQ ID NO 812
<211> LENGTH: 351
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 812

cagcagctgg agcagtccgg aggaggagcc gaaggaggcc tggtcaagcc tgggggatcc 60

ctgaaactct cctgcaaagc ctctggattc accatcagta gggactactg gatatgttgg 120

gtccgccagg ctccagggaa ggggctggag tggattggat gcattagtgc tggtggtggt 180

agcacagact acgcgaactg ggtgaatggc cgattcactc tctccagaga catcgaccag 240

agcacaggtt gccttcaact gaacagtctg acagacgcgg acacggccat gtattactgt 300

gcgggaaatc tagagatctg gggccaaggg accctggtca ccgtctcgag c 351

<210> SEQ ID NO 813
<211> LENGTH: 99
<212> TYPE: DNA

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<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 813

cagcagctgg agcagtccgg aggaggagcc gaaggaggcc tggtcaagcc tgggggatcc 60

ctgaaactct cctgcaaagc ctctggattc accatcagt 99

<210> SEQ ID NO 814
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 814

agggactact ggatatgt 18

<210> SEQ ID NO 815
<211> LENGTH: 42
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 815

tgggtccgcc aggctccagg gaaggggctg gagtggattg ga 42

<210> SEQ ID NO 816
<211> LENGTH: 51
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 816

tgcattagtg ctggtggtgg tagcacagac tacgcgaact gggtgaatgg c 51

<210> SEQ ID NO 817
<211> LENGTH: 96
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 817

cgattcactc tctccagaga catcgaccag agcacaggtt gccttcaact gaacagtctg 60

acagacgcgg acacggccat gtattactgt gcggga 96

<210> SEQ ID NO 818
<211> LENGTH: 12
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 818

aatctagaga tc 12

<210> SEQ ID NO 819
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 819

tggggccaag ggaccctggt caccgtctcg agc 33

<210> SEQ ID NO 820
<211> LENGTH: 990
<212> TYPE: DNA

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<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 820

gcctccacca agggcccatc ggtcttcccc ctggcaccct cctccaagag cacctctggg 60

ggcacagcgg ccctgggctg cctggtcaag gactacttcc ccgaaccggt gacggtgtcg 120

tggaactcag gcgccctgac cagcggcgtg cacaccttcc cggctgtcct acagtcctca 180

ggactctact ccctcagcag cgtggtgacc gtgccctcca gcagcttggg cacccagacc 240

tacatctgca acgtgaatca caagcccagc aacaccaagg tggacgcgag agttgagccc 300

aaatcttgtg acaaaactca cacatgccca ccgtgcccag cacctgaact cctgggggga 360

ccgtcagtct tcctcttccc cccaaaaccc aaggacaccc tcatgatctc ccggacccct 420

gaggtcacat gcgtggtggt ggacgtgagc cacgaagacc ctgaggtcaa gttcaactgg 480

tacgtggacg gcgtggaggt gcataatgcc aagacaaagc cgcgggagga gcagtacgcc 540

agcacgtacc gtgtggtcag cgtcctcacc gtcctgcacc aggactggct gaatggcaag 600

gagtacaagt gcaaggtctc caacaaagcc ctcccagccc ccatcgagaa aaccatctcc 660

aaagccaaag ggcagccccg agaaccacag gtgtacaccc tgccccatc ccgggaggag 720

atgaccaaga accaggtcag cctgacctgc ctggtcaaag gcttctatcc cagcgacatc 780

gccgtggagt gggagagcaa tgggcagccg gagaacaact acaagaccac gcctcccgtg 840

ctggactccg acggctcctt cttcctctac agcaagctca ccgtggacaa gagcaggtgg 900

cagcagggga acgtcttctc atgctccgtg atgcatgagg ctctgcacaa ccactacacg 960

cagaagagcc tctccctgtc tccgggtaaa 990

<210> SEQ ID NO 821
<211> LENGTH: 220
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 821

Ala Gln Val Leu Thr Gln Thr Pro Ser Ser Val Ser Ala Ala Val Gly
1 5 10 15

Gly Thr Val Thr Ile Asn Cys Gln Ser Ser Pro Ser Ile Tyr Ser Gly
20 25 30

Ala Phe Leu Ser Trp Phe Gln Gln Lys Pro Gly Gln Pro Pro Lys Phe
35 40 45

Leu Ile Tyr Glu Ala Ser Lys Leu Ala Ser Gly Val Pro Ser Arg Phe
50 55 60

Ser Gly Ser Gly Ser Gly Thr Gln Phe Thr Leu Thr Ile Ser Asp Val
65 70 75 80

Gln Cys Asp Asp Ala Ala Thr Tyr Tyr Cys Leu Gly Phe Tyr Asp Cys
85 90 95

Ser Ser Val Asp Cys His Ala Phe Gly Gly Gly Thr Glu Val Val Val
100 105 110

Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp
115 120 125

Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn
130 135 140

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Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu
145                 150                 155                 160

Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp
                165                 170                 175

Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr
            180                 185                 190

Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser
        195                 200                 205

Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
    210                 215                 220


<210> SEQ ID NO 822
<211> LENGTH: 114
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 822

Ala Gln Val Leu Thr Gln Thr Pro Ser Ser Val Ser Ala Ala Val Gly
1               5                   10                  15

Gly Thr Val Thr Ile Asn Cys Gln Ser Ser Pro Ser Ile Tyr Ser Gly
            20                  25                  30

Ala Phe Leu Ser Trp Phe Gln Gln Lys Pro Gly Gln Pro Pro Lys Phe
        35                  40                  45

Leu Ile Tyr Glu Ala Ser Lys Leu Ala Ser Gly Val Pro Ser Arg Phe
    50                  55                  60

Ser Gly Ser Gly Ser Gly Thr Gln Phe Thr Leu Thr Ile Ser Asp Val
65                  70                  75                  80

Gln Cys Asp Asp Ala Ala Thr Tyr Tyr Cys Leu Gly Phe Tyr Asp Cys
                85                  90                  95

Ser Ser Val Asp Cys His Ala Phe Gly Gly Gly Thr Glu Val Val Val
            100                 105                 110

Lys Arg


<210> SEQ ID NO 823
<211> LENGTH: 23
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 823

Ala Gln Val Leu Thr Gln Thr Pro Ser Ser Val Ser Ala Ala Val Gly
1               5                   10                  15

Gly Thr Val Thr Ile Asn Cys
            20


<210> SEQ ID NO 824
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 824

Gln Ser Ser Pro Ser Ile Tyr Ser Gly Ala Phe Leu Ser
1               5                   10


<210> SEQ ID NO 825
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<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 825

Trp Phe Gln Gln Lys Pro Gly Gln Pro Pro Lys Phe Leu Ile Tyr
1 5 10 15

<210> SEQ ID NO 826
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 826

Glu Ala Ser Lys Leu Ala Ser
1 5

<210> SEQ ID NO 827
<211> LENGTH: 32
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 827

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Gln Phe Thr
1 5 10 15

Leu Thr Ile Ser Asp Val Gln Cys Asp Asp Ala Ala Thr Tyr Tyr Cys
20 25 30

<210> SEQ ID NO 828
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 828

Leu Gly Phe Tyr Asp Cys Ser Ser Val Asp Cys His Ala
1 5 10

<210> SEQ ID NO 829
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 829

Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg
1 5 10

<210> SEQ ID NO 830
<211> LENGTH: 106
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 830

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
1 5 10 15

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
20 25 30

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
35 40 45

-continued

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
50 55 60

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
65 70 75 80

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
85 90 95

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
100 105

<210> SEQ ID NO 831
<211> LENGTH: 660
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 831

gcccaagtgc tgacccagac tccatcctcc gtgtctgcag ctgtgggagg cacagtcacc 60

atcaattgcc agtccagtcc gagtatttat agtggcgcct ttttatcctg gtttcagcag 120

aaaccagggc agcctcccaa gttcctgatc tacgaagcct ccaaactggc atctggggtc 180

ccatcgcggt tcagtggcag tggatctggg acacagttca ctctcaccat cagcgacgta 240

cagtgtgacg atgctgccac ttactactgt ctaggctttt atgattgtag cagtgttgat 300

tgccatgctt tcggcggagg gaccgaggtg gtggtcaaac gtacggtagc ggccccatct 360

gtcttcatct tcccgccatc tgatgagcag ttgaaatctg gaactgcctc tgttgtgtgc 420

ctgctgaata acttctatcc cagagaggcc aaagtacagt ggaaggtgga taacgccctc 480

caatcgggta actcccagga gagtgtcaca gagcaggaca gcaaggacag cacctacagc 540

ctcagcagca ccctgacgct gagcaaagca gactacgaga aacacaaagt ctacgcctgc 600

gaagtcaccc atcagggcct gagctcgccc gtcacaaaga gcttcaacag gggagagtgt 660

<210> SEQ ID NO 832
<211> LENGTH: 342
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 832

gcccaagtgc tgacccagac tccatcctcc gtgtctgcag ctgtgggagg cacagtcacc 60

atcaattgcc agtccagtcc gagtatttat agtggcgcct ttttatcctg gtttcagcag 120

aaaccagggc agcctcccaa gttcctgatc tacgaagcct ccaaactggc atctggggtc 180

ccatcgcggt tcagtggcag tggatctggg acacagttca ctctcaccat cagcgacgta 240

cagtgtgacg atgctgccac ttactactgt ctaggctttt atgattgtag cagtgttgat 300

tgccatgctt tcggcggagg gaccgaggtg gtggtcaaac gt 342

<210> SEQ ID NO 833
<211> LENGTH: 69
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 833

gcccaagtgc tgacccagac tccatcctcc gtgtctgcag ctgtgggagg cacagtcacc 60

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atcaattgc 69

<210> SEQ ID NO 834
<211> LENGTH: 39
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 834

cagtccagtc cgagtattta tagtggcgcc tttttatcc 39

<210> SEQ ID NO 835
<211> LENGTH: 45
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 835

tggtttcagc agaaaccagg gcagcctccc aagttcctga tctac 45

<210> SEQ ID NO 836
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 836

gaagcctcca aactggcatc t 21

<210> SEQ ID NO 837
<211> LENGTH: 96
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 837

ggggtcccat cgcggttcag tggcagtgga tctgggacac agttcactct caccatcagc 60

gacgtacagt gtgacgatgc tgccacttac tactgt 96

<210> SEQ ID NO 838
<211> LENGTH: 39
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 838

ctaggctttt atgattgtag cagtgttgat tgccatgct 39

<210> SEQ ID NO 839
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 839

ttcggcggag ggaccgaggt ggtggtcaaa cgt 33

<210> SEQ ID NO 840
<211> LENGTH: 318
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 840

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acggtagcgg ccccatctgt cttcatcttc ccgccatctg atgagcagtt gaaatctgga 60

actgcctctg ttgtgtgcct gctgaataac ttctatccca gagaggccaa agtacagtgg 120

aaggtggata acgccctcca atcgggtaac tcccaggaga gtgtcacaga gcaggacagc 180

aaggacagca cctacagcct cagcagcacc ctgacgctga gcaaagcaga ctacgagaaa 240

cacaaagtct acgcctgcga agtcacccat cagggcctga gctcgcccgt cacaaagagc 300

ttcaacaggg gagagtgt 318

<210> SEQ ID NO 841

<400> SEQUENCE: 841

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<210> SEQ ID NO 842

<400> SEQUENCE: 842

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<210> SEQ ID NO 843

<400> SEQUENCE: 843

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<210> SEQ ID NO 844

<400> SEQUENCE: 844

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<210> SEQ ID NO 845

<400> SEQUENCE: 845

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<210> SEQ ID NO 846

<400> SEQUENCE: 846

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<210> SEQ ID NO 847

<400> SEQUENCE: 847

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<210> SEQ ID NO 848

<400> SEQUENCE: 848

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<210> SEQ ID NO 849

<400> SEQUENCE: 849

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<210> SEQ ID NO 850

<400> SEQUENCE: 850

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<210> SEQ ID NO 851

<400> SEQUENCE: 851

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<210> SEQ ID NO 852

<400> SEQUENCE: 852

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<210> SEQ ID NO 853

<400> SEQUENCE: 853

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<210> SEQ ID NO 854

<400> SEQUENCE: 854

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<210> SEQ ID NO 855

<400> SEQUENCE: 855

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<210> SEQ ID NO 856

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<210> SEQ ID NO 857

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<210> SEQ ID NO 858

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<210> SEQ ID NO 859

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<210> SEQ ID NO 860

<400> SEQUENCE: 860

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<210> SEQ ID NO 861

<400> SEQUENCE: 861

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<210> SEQ ID NO 862

<400> SEQUENCE: 862

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<210> SEQ ID NO 863

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<210> SEQ ID NO 870

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<210> SEQ ID NO 871

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<210> SEQ ID NO 872

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<210> SEQ ID NO 873

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<210> SEQ ID NO 874

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<210> SEQ ID NO 876

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<210> SEQ ID NO 877

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<210> SEQ ID NO 878

<400> SEQUENCE: 878

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<210> SEQ ID NO 879

<400> SEQUENCE: 879

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<210> SEQ ID NO 880

<400> SEQUENCE: 880

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<210> SEQ ID NO 881
<211> LENGTH: 442
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 881

Gln Glu Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Glu Gly

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1               5                   10                  15

Ser Leu Thr Leu Thr Cys Thr Ala Ser Gly Phe Asp Phe Ser Ser Asn
            20                  25                  30

Ala Met Cys Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile
        35                  40                  45

Gly Ser Ile Tyr Asn Ala Asp Gly Lys Asn Tyr Tyr Ala Ile Trp Ala
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Thr Ser Ser Thr Thr Val Thr Leu
65                  70                  75                  80

Gln Met Thr Ser Leu Thr Ala Ala Asp Thr Ala Thr Tyr Phe Cys Ala
                85                  90                  95

Arg Asp Phe Asp Leu Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
            100                 105                 110

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
        115                 120                 125

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
    130                 135                 140

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
145                 150                 155                 160

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
                165                 170                 175

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
            180                 185                 190

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Ala
        195                 200                 205

Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
    210                 215                 220

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
225                 230                 235                 240

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
                245                 250                 255

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
            260                 265                 270

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
        275                 280                 285

Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
    290                 295                 300

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
305                 310                 315                 320

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
                325                 330                 335

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
            340                 345                 350

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
        355                 360                 365

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
    370                 375                 380

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
385                 390                 395                 400

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
                405                 410                 415
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Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
420 425 430

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440

<210> SEQ ID NO 882
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 882

Gln Glu Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Glu Gly
1 5 10 15

Ser Leu Thr Leu Thr Cys Thr Ala Ser Gly Phe Asp Phe Ser Ser Asn
20 25 30

Ala Met Cys Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Ser Ile Tyr Asn Ala Asp Gly Lys Asn Tyr Tyr Ala Ile Trp Ala
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Thr Ser Ser Thr Thr Val Thr Leu
65 70 75 80

Gln Met Thr Ser Leu Thr Ala Ala Asp Thr Ala Thr Tyr Phe Cys Ala
85 90 95

Arg Asp Phe Asp Leu Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
100 105 110

<210> SEQ ID NO 883
<211> LENGTH: 30
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 883

Gln Glu Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Glu Gly
1 5 10 15

Ser Leu Thr Leu Thr Cys Thr Ala Ser Gly Phe Asp Phe Ser
20 25 30

<210> SEQ ID NO 884
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 884

Ser Asn Ala Met Cys
1 5

<210> SEQ ID NO 885
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 885

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
1 5 10

<210> SEQ ID NO 886

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<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 886

Ser Ile Tyr Asn Ala Asp Gly Lys Asn Tyr Tyr Ala Ile Trp Ala Lys
1 5 10 15

Gly

<210> SEQ ID NO 887
<211> LENGTH: 31
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 887

Arg Phe Thr Ile Ser Arg Thr Ser Ser Thr Thr Val Thr Leu Gln Met
1 5 10 15

Thr Ser Leu Thr Ala Ala Asp Thr Ala Thr Tyr Phe Cys Ala Arg
20 25 30

<210> SEQ ID NO 888
<211> LENGTH: 4
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 888

Asp Phe Asp Leu
1

<210> SEQ ID NO 889
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 889

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
1 5 10

<210> SEQ ID NO 890
<211> LENGTH: 330
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 890

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65 70 75 80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Ala
85 90 95

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Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
100 105 110

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
115 120 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
130 135 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145 150 155 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
165 170 175

Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
180 185 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
195 200 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
210 215 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
225 230 235 240

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
245 250 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
260 265 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
275 280 285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
290 295 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305 310 315 320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
325 330

<210> SEQ ID NO 891
<211> LENGTH: 1326
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 891

caggagcagc tggtggagtc cgggggaggc ctggtccagc ctgagggatc cctgacactc 60

acctgcacag cctctggatt cgacttcagt agcaatgcaa tgtgctgggt ccgccaggct 120

ccagggaagg gcctggagtg gatcggatcc atttataatg ctgatggtaa gaattattac 180

gcgatttggg cgaaaggccg attcaccatc tccagaacct cgtcgaccac ggtgactctg 240

caaatgacca gtctgacagc cgcggacacg gccacctatt tctgtgcgag agactttgac 300

ttgtggggcc agggcaccct cgtcaccgtc tcgagcgcct ccaccaaggg cccatcggtc 360

ttcccctgg caccctcctc caagagcacc tctgggggca cagcggccct gggctgcctg 420

gtcaaggact acttccccga accggtgacg gtgtcgtgga actcaggcgc cctgaccagc 480

ggcgtgcaca ccttcccggc tgtcctacag tcctcaggac tctactccct cagcagcgtg 540

gtgaccgtgc cctccagcag cttgggcacc cagacctaca tctgcaacgt gaatcacaag 600

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cccagcaaca ccaaggtgga cgcgagagtt gagcccaaat cttgtgacaa aactcacaca 660

tgcccaccgt gcccagcacc tgaactcctg gggggaccgt cagtcttcct cttccccca 720

aaacccaagg acaccctcat gatctcccgg acccctgagg tcacatgcgt ggtggtggac 780

gtgagccacg aagaccctga ggtcaagttc aactggtacg tggacggcgt ggaggtgcat 840

aatgccaaga caaagccgcg ggaggagcag tacgccagca cgtaccgtgt ggtcagcgtc 900

ctcaccgtcc tgcaccagga ctggctgaat ggcaaggagt acaagtgcaa ggtctccaac 960

aaagccctcc cagccccat cgagaaaacc atctccaaag ccaaagggca gccccgagaa 1020

ccacaggtgt acaccctgcc cccatcccgg gaggagatga ccaagaacca ggtcagcctg 1080

acctgcctgg tcaaaggctt ctatcccagc gacatcgccg tggagtggga gagcaatggg 1140

cagccggaga acaactacaa gaccacgcct cccgtgctgg actccgacgg ctccttcttc 1200

ctctacagca agctcaccgt ggacaagagc aggtggcagc aggggaacgt cttctcatgc 1260

tccgtgatgc atgaggctct gcacaaccac tacacgcaga agagcctctc cctgtctccg 1320

ggtaaa 1326

<210> SEQ ID NO 892
<211> LENGTH: 336
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 892

caggagcagc tggtggagtc cgggggaggc ctggtccagc ctgagggatc cctgacactc 60

acctgcacag cctctggatt cgacttcagt agcaatgcaa tgtgctgggt ccgccaggct 120

ccagggaagg gcctggagtg gatcggatcc atttataatg ctgatggtaa gaattattac 180

gcgatttggg cgaaaggccg attcaccatc tccagaacct cgtcgaccac ggtgactctg 240

caaatgacca gtctgacagc cgcggacacg gccacctatt tctgtgcgag agactttgac 300

ttgtggggcc agggcaccct cgtcaccgtc tcgagc 336

<210> SEQ ID NO 893
<211> LENGTH: 90
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 893

caggagcagc tggtggagtc cgggggaggc ctggtccagc ctgagggatc cctgacactc 60

acctgcacag cctctggatt cgacttcagt 90

<210> SEQ ID NO 894
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 894

agcaatgcaa tgtgc 15

<210> SEQ ID NO 895
<211> LENGTH: 42
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

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<400> SEQUENCE: 895

tgggtccgcc aggctccagg gaagggcctg gagtggatcg ga 42

<210> SEQ ID NO 896
<211> LENGTH: 51
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 896

tccatttata atgctgatgg taagaattat tacgcgattt gggcgaaagg c 51

<210> SEQ ID NO 897
<211> LENGTH: 93
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 897

cgattcacca tctccagaac ctcgtcgacc acggtgactc tgcaaatgac cagtctgaca 60

gccgcggaca cggccaccta tttctgtgcg aga 93

<210> SEQ ID NO 898
<211> LENGTH: 12
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 898

gactttgact tg 12

<210> SEQ ID NO 899
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 899

tggggccagg gcaccctcgt caccgtctcg agc 33

<210> SEQ ID NO 900
<211> LENGTH: 990
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 900

gcctccacca agggcccatc ggtcttcccc ctggcaccct cctccaagag cacctctggg 60

ggcacagcgg ccctgggctg cctggtcaag gactacttcc ccgaaccggt gacggtgtcg 120

tggaactcag gcgccctgac cagcggcgtg cacaccttcc cggctgtcct acagtcctca 180

ggactctact ccctcagcag cgtggtgacc gtgccctcca gcagcttggg cacccagacc 240

tacatctgca acgtgaatca caagcccagc aacaccaagg tggacgcgag agttgagccc 300

aaatcttgtg acaaaactca cacatgccca ccgtgcccag cacctgaact cctgggggga 360

ccgtcagtct tcctcttccc cccaaaaccc aaggacaccc tcatgatctc ccggacccct 420

gaggtcacat gcgtggtggt ggacgtgagc cacgaagacc ctgaggtcaa gttcaactgg 480

tacgtggacg gcgtggaggt gcataatgcc aagacaaagc cgcgggagga gcagtacgcc 540

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agcacgtacc gtgtggtcag cgtcctcacc gtcctgcacc aggactggct gaatggcaag 600

gagtacaagt gcaaggtctc caacaaagcc ctcccagccc ccatcgagaa aaccatctcc 660

aaagccaaag ggcagccccg agaaccacag gtgtacaccc tgcccccatc ccgggaggag 720

atgaccaaga accaggtcag cctgacctgc ctggtcaaag gcttctatcc cagcgacatc 780

gccgtggagt gggagagcaa tgggcagccg gagaacaact acaagaccac gcctcccgtg 840

ctggactccg acggctcctt cttcctctac agcaagctca ccgtggacaa gagcaggtgg 900

cagcagggga acgtcttctc atgctccgtg atgcatgagg ctctgcacaa ccactacacg 960

cagaagagcc tctccctgtc tccgggtaaa 990

<210> SEQ ID NO 901
<211> LENGTH: 219
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 901

Ala Ala Val Leu Thr Gln Thr Pro Ser Pro Val Ser Ala Ala Val Gly
1 5 10 15

Gly Thr Val Thr Ile Asn Cys Gln Ser Ser Gln Ser Val Tyr Asp Asn
20 25 30

Asp Trp Leu Ala Trp Phe Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu
35 40 45

Leu Ile Tyr Leu Thr Ser Thr Leu Ala Ser Gly Val Pro Ser Arg Phe
50 55 60

Ser Gly Ser Gly Ser Gly Thr Gln Phe Thr Leu Thr Ile Ser Gly Val
65 70 75 80

Gln Cys Asp Asp Ala Ala Thr Tyr Tyr Cys Leu Gly Gly Tyr Asp Glu
85 90 95

Asp Gly Asp Thr His Val Phe Gly Gly Gly Thr Glu Val Val Val Lys
100 105 110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
115 120 125

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
130 135 140

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
145 150 155 160

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
165 170 175

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
180 185 190

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
195 200 205

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> SEQ ID NO 902
<211> LENGTH: 113
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

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<400> SEQUENCE: 902

Ala Ala Val Leu Thr Gln Thr Pro Ser Pro Val Ser Ala Ala Val Gly
1 5 10 15

Gly Thr Val Thr Ile Asn Cys Gln Ser Ser Gln Ser Val Tyr Asp Asn
20 25 30

Asp Trp Leu Ala Trp Phe Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu
35 40 45

Leu Ile Tyr Leu Thr Ser Thr Leu Ala Ser Gly Val Pro Ser Arg Phe
50 55 60

Ser Gly Ser Gly Ser Gly Thr Gln Phe Thr Leu Thr Ile Ser Gly Val
65 70 75 80

Gln Cys Asp Asp Ala Ala Thr Tyr Tyr Cys Leu Gly Gly Tyr Asp Glu
85 90 95

Asp Gly Asp Thr His Val Phe Gly Gly Gly Thr Glu Val Val Val Lys
100 105 110

Arg

<210> SEQ ID NO 903
<211> LENGTH: 23
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 903

Ala Ala Val Leu Thr Gln Thr Pro Ser Pro Val Ser Ala Ala Val Gly
1 5 10 15

Gly Thr Val Thr Ile Asn Cys
20

<210> SEQ ID NO 904
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 904

Gln Ser Ser Gln Ser Val Tyr Asp Asn Asp Trp Leu Ala
1 5 10

<210> SEQ ID NO 905
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 905

Trp Phe Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr
1 5 10 15

<210> SEQ ID NO 906
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 906

Leu Thr Ser Thr Leu Ala Ser
1 5

<210> SEQ ID NO 907
<211> LENGTH: 32
<212> TYPE: PRT

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<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 907

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Gln Phe Thr
1 5 10 15

Leu Thr Ile Ser Gly Val Gln Cys Asp Asp Ala Ala Thr Tyr Tyr Cys
20 25 30

<210> SEQ ID NO 908
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 908

Leu Gly Gly Tyr Asp Glu Asp Gly Asp Thr His Val
1 5 10

<210> SEQ ID NO 909
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 909

Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg
1 5 10

<210> SEQ ID NO 910
<211> LENGTH: 106
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 910

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
1 5 10 15

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
20 25 30

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
35 40 45

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
50 55 60

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
65 70 75 80

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
85 90 95

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
100 105

<210> SEQ ID NO 911
<211> LENGTH: 657
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 911

gcagccgtgc tgacccagac accatcgccc gtgtctgcag ctgtgggagg cacagtcacc 60

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atcaattgcc agtccagtca gagtgtttat gataacgact ggttagcctg gttccagcag 120

aaaccagggc agcctcccaa gctcctgatc tatctgacat ccactctggc atctggagtc 180

ccatcgcggt tcagcggcag tggatctggg acacagttca ctctcaccat cagtggtgtg 240

cagtgtgacg atgctgccac ttactactgt ctaggcggct atgatgaaga tggtgatacg 300

catgttttcg gcggagggac cgaggtggtg gtcaaacgta cggtagcggc cccatctgtc 360

ttcatcttcc cgccatctga tgagcagttg aaatctggaa ctgcctctgt tgtgtgcctg 420

ctgaataact tctatcccag agaggccaaa gtacagtgga aggtggataa cgccctccaa 480

tcgggtaact cccaggagag tgtcacagag caggacagca aggacagcac ctacagcctc 540

agcagcaccc tgacgctgag caaagcagac tacgagaaac acaaagtcta cgcctgcgaa 600

gtcacccatc agggcctgag ctcgcccgtc acaaagagct tcaacagggg agagtgt 657

<210> SEQ ID NO 912
<211> LENGTH: 339
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 912

gcagccgtgc tgacccagac accatcgccc gtgtctgcag ctgtgggagg cacagtcacc 60

atcaattgcc agtccagtca gagtgtttat gataacgact ggttagcctg gttccagcag 120

aaaccagggc agcctcccaa gctcctgatc tatctgacat ccactctggc atctggagtc 180

ccatcgcggt tcagcggcag tggatctggg acacagttca ctctcaccat cagtggtgtg 240

cagtgtgacg atgctgccac ttactactgt ctaggcggct atgatgaaga tggtgatacg 300

catgttttcg gcggagggac cgaggtggtg gtcaaacgt 339

<210> SEQ ID NO 913
<211> LENGTH: 69
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 913

gcagccgtgc tgacccagac accatcgccc gtgtctgcag ctgtgggagg cacagtcacc 60

atcaattgc 69

<210> SEQ ID NO 914
<211> LENGTH: 39
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 914

cagtccagtc agagtgttta tgataacgac tggttagcc 39

<210> SEQ ID NO 915
<211> LENGTH: 45
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 915

tggttccagc agaaaccagg gcagcctccc aagctcctga tctat 45

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<210> SEQ ID NO 916
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 916

ctgacatcca ctctggcatc t 21

<210> SEQ ID NO 917
<211> LENGTH: 96
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 917

ggagtcccat cgcggttcag cggcagtgga tctgggacac agttcactct caccatcagt 60

ggtgtgcagt gtgacgatgc tgccacttac tactgt 96

<210> SEQ ID NO 918
<211> LENGTH: 36
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 918

ctaggcggct atgatgaaga tggtgatacg catgtt 36

<210> SEQ ID NO 919
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 919

ttcggcggag ggaccgaggt ggtggtcaaa cgt 33

<210> SEQ ID NO 920
<211> LENGTH: 318
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 920

acggtagcgg ccccatctgt cttcatcttc ccgccatctg atgagcagtt gaaatctgga 60

actgcctctg ttgtgtgcct gctgaataac ttctatccca gagaggccaa agtacagtgg 120

aaggtggata acgccctcca atcgggtaac tcccaggaga gtgtcacaga gcaggacagc 180

aaggacagca cctacagcct cagcagcacc ctgacgctga gcaaagcaga ctacgagaaa 240

cacaaagtct acgcctgcga agtcacccat cagggcctga gctcgcccgt cacaaagagc 300

ttcaacaggg gagagtgt 318

<210> SEQ ID NO 921
<211> LENGTH: 447
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 921

Gln Ser Val Glu Glu Ser Gly Gly Arg Leu Val Thr Pro Gly Thr Pro

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1               5                   10                  15

Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Asn Asn Tyr Ala
            20                  25                  30

Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
        35                  40                  45

Ile Met Gly Val Asn Asp Ile Thr Tyr Tyr Ala Ser Trp Ala Lys Gly
    50                  55                  60

Arg Phe Thr Ile Ser Lys Thr Ser Thr Thr Val Asp Leu Lys Met Thr
65                  70                  75                  80

Ser Leu Thr Thr Glu Asp Thr Ala Thr Tyr Phe Cys Thr Arg Glu Ile
                85                  90                  95

Arg Asp Asp Gly Asp Ser Ser Asp Lys Leu Trp Gly Pro Gly Thr Leu
            100                 105                 110

Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
        115                 120                 125

Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys
    130                 135                 140

Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
145                 150                 155                 160

Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
                165                 170                 175

Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
            180                 185                 190

Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn
        195                 200                 205

Thr Lys Val Asp Ala Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His
    210                 215                 220

Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val
225                 230                 235                 240

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
                245                 250                 255

Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
            260                 265                 270

Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
        275                 280                 285

Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser
    290                 295                 300

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
305                 310                 315                 320

Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile
                325                 330                 335

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
            340                 345                 350

Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
        355                 360                 365

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
    370                 375                 380

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
385                 390                 395                 400

Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
                405                 410                 415
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Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
420 425 430

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> SEQ ID NO 922
<211> LENGTH: 117
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 922

Gln Ser Val Glu Glu Ser Gly Gly Arg Leu Val Thr Pro Gly Thr Pro
1 5 10 15

Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Asn Asn Tyr Ala
20 25 30

Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
35 40 45

Ile Met Gly Val Asn Asp Ile Thr Tyr Tyr Ala Ser Trp Ala Lys Gly
50 55 60

Arg Phe Thr Ile Ser Lys Thr Ser Thr Thr Val Asp Leu Lys Met Thr
65 70 75 80

Ser Leu Thr Thr Glu Asp Thr Ala Thr Tyr Phe Cys Thr Arg Glu Ile
85 90 95

Arg Asp Asp Gly Asp Ser Ser Asp Lys Leu Trp Gly Pro Gly Thr Leu
100 105 110

Val Thr Val Ser Ser
115

<210> SEQ ID NO 923
<211> LENGTH: 29
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 923

Gln Ser Val Glu Glu Ser Gly Gly Arg Leu Val Thr Pro Gly Thr Pro
1 5 10 15

Leu Thr Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Asn
20 25

<210> SEQ ID NO 924
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 924

Asn Tyr Ala Met Ser
1 5

<210> SEQ ID NO 925
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 925

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly
1 5 10

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<210> SEQ ID NO 926
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 926

Ile Met Gly Val Asn Asp Ile Thr Tyr Tyr Ala Ser Trp Ala Lys Gly
1 5 10 15

<210> SEQ ID NO 927
<211> LENGTH: 30
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 927

Arg Phe Thr Ile Ser Lys Thr Ser Thr Thr Val Asp Leu Lys Met Thr
1 5 10 15

Ser Leu Thr Thr Glu Asp Thr Ala Thr Tyr Phe Cys Thr Arg
20 25 30

<210> SEQ ID NO 928
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 928

Glu Ile Arg Asp Asp Gly Asp Ser Ser Asp Lys Leu
1 5 10

<210> SEQ ID NO 929
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 929

Trp Gly Pro Gly Thr Leu Val Thr Val Ser Ser
1 5 10

<210> SEQ ID NO 930
<211> LENGTH: 330
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 930

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65 70 75 80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Ala

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                85                  90                  95

Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
            100                 105                 110

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
        115                 120                 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
    130                 135                 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145                 150                 155                 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
                165                 170                 175

Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
            180                 185                 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
        195                 200                 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
    210                 215                 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
225                 230                 235                 240

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
                245                 250                 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
            260                 265                 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
        275                 280                 285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
    290                 295                 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305                 310                 315                 320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
                325                 330


<210> SEQ ID NO 931
<211> LENGTH: 1341
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 931

cagtcggtgg aggagtccgg gggtcgcctg gtcacgcctg ggacacccct gacactcacc     60

tgcaccgtct ctggattctc cctcaataac tatgcaatga gctgggtccg ccaggctcca    120

gggaaggggc tggaatggat cggaatcatg ggtgttaatg atatcacata ctacgcgagc    180

tgggcgaaag gccgattcac catctccaaa acctcgacca cggtggatct gaaaatgacc    240

agtctgacaa ccgaggacac ggccacctat ttctgtacta gagagatccg tgatgatggt    300

gatagttctg ataagttgtg gggcccgggc accctcgtca ccgtctcgag cgcctccacc    360

aagggcccat cggtcttccc cctggcaccc tcctccaaga gcacctctgg gggcacagcg    420

gccctgggct gcctggtcaa ggactacttc cccgaaccgg tgacggtgtc gtggaactca    480

ggcgccctga ccagcggcgt gcacaccttc ccggctgtcc tacagtcctc aggactctac    540

tccctcagca gcgtggtgac cgtgccctcc agcagcttgg gcacccagac ctacatctgc    600
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aacgtgaatc acaagcccag caacaccaag gtggacgcga gagttgagcc caaatcttgt 660

gacaaaactc acacatgccc accgtgccca gcacctgaac tcctgggggg accgtcagtc 720

ttcctcttcc ccccaaaacc caaggacacc ctcatgatct cccggacccc tgaggtcaca 780

tgcgtggtgg tggacgtgag ccacgaagac cctgaggtca agttcaactg gtacgtggac 840

ggcgtggagg tgcataatgc caagacaaag ccgcgggagg agcagtacgc cagcacgtac 900

cgtgtggtca gcgtcctcac cgtcctgcac caggactggc tgaatggcaa ggagtacaag 960

tgcaaggtct ccaacaaagc cctcccagcc cccatcgaga aaaccatctc caaagccaaa 1020

gggcagcccc gagaaccaca ggtgtacacc ctgcccccat cccgggagga gatgaccaag 1080

aaccaggtca gcctgacctg cctggtcaaa ggcttctatc ccagcgacat cgccgtggag 1140

tgggagagca atgggcagcc ggagaacaac tacaagacca cgcctcccgt gctggactcc 1200

gacggctcct tcttcctcta cagcaagctc accgtggaca agagcaggtg gcagcagggg 1260

aacgtcttct catgctccgt gatgcatgag gctctgcaca accactacac gcagaagagc 1320

ctctccctgt ctccgggtaa a 1341

<210> SEQ ID NO 932
<211> LENGTH: 351
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 932

cagtcggtgg aggagtccgg gggtcgcctg gtcacgcctg ggacacccct gacactcacc 60

tgcaccgtct ctggattctc cctcaataac tatgcaatga gctgggtccg ccaggctcca 120

gggaaggggc tggaatggat cggaatcatg ggtgttaatg atatcacata ctacgcgagc 180

tgggcgaaag gccgattcac catctccaaa acctcgacca cggtggatct gaaaatgacc 240

agtctgacaa ccgaggacac ggccacctat ttctgtacta gagagatccg tgatgatggt 300

gatagttctg ataagttgtg gggcccgggc accctcgtca ccgtctcgag c 351

<210> SEQ ID NO 933
<211> LENGTH: 87
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 933

cagtcggtgg aggagtccgg gggtcgcctg gtcacgcctg ggacacccct gacactcacc 60

tgcaccgtct ctggattctc cctcaat 87

<210> SEQ ID NO 934
<211> LENGTH: 15
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 934

aactatgcaa tgagc 15

<210> SEQ ID NO 935
<211> LENGTH: 42
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

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<400> SEQUENCE: 935

tgggtccgcc aggctccagg gaaggggctg gaatggatcg ga 42

<210> SEQ ID NO 936
<211> LENGTH: 48
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 936

atcatgggtg ttaatgatat cacatactac gcgagctggg cgaaaggc 48

<210> SEQ ID NO 937
<211> LENGTH: 90
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 937

cgattcacca tctccaaaac ctcgaccacg gtggatctga aaatgaccag tctgacaacc 60

gaggacacgg ccacctattt ctgtactaga 90

<210> SEQ ID NO 938
<211> LENGTH: 36
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 938

gagatccgtg atgatggtga tagttctgat aagttg 36

<210> SEQ ID NO 939
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 939

tggggcccgg gcaccctcgt caccgtctcg agc 33

<210> SEQ ID NO 940
<211> LENGTH: 990
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 940

gcctccacca agggcccatc ggtcttcccc ctggcaccct cctccaagag cacctctggg 60

ggcacagcgg ccctgggctg cctggtcaag gactacttcc ccgaaccggt gacggtgtcg 120

tggaactcag gcgccctgac cagcggcgtg cacaccttcc cggctgtcct acagtcctca 180

ggactctact ccctcagcag cgtggtgacc gtgccctcca gcagcttggg cacccagacc 240

tacatctgca acgtgaatca caagcccagc aacaccaagg tggacgcgag agttgagccc 300

aaatcttgtg acaaaactca cacatgccca ccgtgcccag cacctgaact cctgggggga 360

ccgtcagtct tcctcttccc cccaaaaccc aaggacaccc tcatgatctc ccggaccccct 420

gaggtcacat gcgtggtggt ggacgtgagc cacgaagacc ctgaggtcaa gttcaactgg 480

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agcacgtacc gtgtggtcag cgtcctcacc gtcctgcacc aggactggct gaatggcaag 600

gagtacaagt gcaaggtctc caacaaagcc ctcccagccc ccatcgagaa aaccatctcc 660

aaagccaaag ggcagccccg agaaccacag gtgtacaccc tgcccccatc ccgggaggag 720

atgaccaaga accaggtcag cctgacctgc ctggtcaaag gcttctatcc cagcgacatc 780

gccgtggagt gggagagcaa tgggcagccg gagaacaact acaagaccac gcctcccgtg 840

ctggactccg acggctcctt cttcctctac agcaagctca ccgtggacaa gagcaggtgg 900

cagcagggga acgtcttctc atgctccgtg atgcatgagg ctctgcacaa ccactacacg 960

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<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 941

Ala Ile Lys Met Thr Gln Thr Pro Ser Ser Val Ser Ala Ala Val Gly
1 5 10 15

Gly Thr Val Thr Ile Asn Cys Gln Ala Ser Glu Asp Ile Tyr Thr Asn
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Asn Leu Leu Ile
35 40 45

Tyr Asp Ala Ser Asp Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Asp Gly Thr Gln Phe Thr Leu Thr Ile Ser Ala Val Gln Cys
65 70 75 80

Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gly Val Ala Trp Ser Ser Asn
85 90 95

Thr Gly Tyr Gly Ser Ala Phe Gly Gly Gly Thr Glu Val Val Val Lys
100 105 110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
115 120 125

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
130 135 140

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
145 150 155 160

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
165 170 175

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
180 185 190

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
195 200 205

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> SEQ ID NO 942
<211> LENGTH: 113
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

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<400> SEQUENCE: 942

Ala Ile Lys Met Thr Gln Thr Pro Ser Ser Val Ser Ala Ala Val Gly
1 5 10 15

Gly Thr Val Thr Ile Asn Cys Gln Ala Ser Glu Asp Ile Tyr Thr Asn
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Asn Leu Leu Ile
35 40 45

Tyr Asp Ala Ser Asp Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Asp Gly Thr Gln Phe Thr Leu Thr Ile Ser Ala Val Gln Cys
65 70 75 80

Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gly Val Ala Trp Ser Ser Asn
85 90 95

Thr Gly Tyr Gly Ser Ala Phe Gly Gly Gly Thr Glu Val Val Val Lys
100 105 110

Arg

<210> SEQ ID NO 943
<211> LENGTH: 23
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 943

Ala Ile Lys Met Thr Gln Thr Pro Ser Ser Val Ser Ala Ala Val Gly
1 5 10 15

Gly Thr Val Thr Ile Asn Cys
20

<210> SEQ ID NO 944
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 944

Gln Ala Ser Glu Asp Ile Tyr Thr Asn Leu Ala
1 5 10

<210> SEQ ID NO 945
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 945

Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Asn Leu Leu Ile Tyr
1 5 10 15

<210> SEQ ID NO 946
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 946

Asp Ala Ser Asp Leu Ala Ser
1 5

<210> SEQ ID NO 947
<211> LENGTH: 32

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<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 947

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Asp Gly Thr Gln Phe Thr
1 5 10 15

Leu Thr Ile Ser Ala Val Gln Cys Glu Asp Ala Ala Thr Tyr Tyr Cys
20 25 30

<210> SEQ ID NO 948
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 948

Gln Gly Val Ala Trp Ser Ser Asn Thr Gly Tyr Gly Ser Ala
1 5 10

<210> SEQ ID NO 949
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 949

Phe Gly Gly Gly Thr Glu Val Val Val Lys Arg
1 5 10

<210> SEQ ID NO 950
<211> LENGTH: 106
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 950

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
1 5 10 15

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
20 25 30

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
35 40 45

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
50 55 60

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
65 70 75 80

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
85 90 95

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
100 105

<210> SEQ ID NO 951
<211> LENGTH: 657
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 951

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atcaattgcc aggccagtga ggacatttac accaatttag cctggtatca gcagaaacca 120

gggcagcctc ccaacctcct gatctatgat gcatccgatc tggcatctgg ggtcccgtcg 180

cggttcagcg gcagtggaga tgggacacag ttcactctca ccatcagcgc cgtgcagtgt 240

gaagatgctg ccacttacta ctgtcaaggt gttgcttgga gtagtaatac tggttatggt 300

tccgctttcg gcggagggac cgaggtggtg gtcaaacgta cggtagcggc cccatctgtc 360

ttcatcttcc cgccatctga tgagcagttg aaatctggaa ctgcctctgt tgtgtgcctg 420

ctgaataact tctatcccag agaggccaaa gtacagtgga aggtggataa cgccctccaa 480

tcgggtaact cccaggagag tgtcacagag caggacagca aggacagcac ctacagcctc 540

agcagcaccc tgacgctgag caaagcagac tacgagaaac acaaagtcta cgcctgcgaa 600

gtcacccatc agggcctgag ctcgcccgtc acaaagagct tcaacagggg agagtgt 657

<210> SEQ ID NO 952
<211> LENGTH: 339
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 952

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atcaattgcc aggccagtga ggacatttac accaatttag cctggtatca gcagaaacca 120

gggcagcctc ccaacctcct gatctatgat gcatccgatc tggcatctgg ggtcccgtcg 180

cggttcagcg gcagtggaga tgggacacag ttcactctca ccatcagcgc cgtgcagtgt 240

gaagatgctg ccacttacta ctgtcaaggt gttgcttgga gtagtaatac tggttatggt 300

tccgctttcg gcggagggac cgaggtggtg gtcaaacgt 339

<210> SEQ ID NO 953
<211> LENGTH: 69
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 953

gccatcaaaa tgacccagac tccatcctcc gtgtctgcag ctgtgggagg cacagtcacc 60

atcaattgc 69

<210> SEQ ID NO 954
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 954

caggccagtg aggacattta caccaattta gcc 33

<210> SEQ ID NO 955
<211> LENGTH: 45
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 955

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<210> SEQ ID NO 956
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 956

gatgcatccg atctggcatc t 21

<210> SEQ ID NO 957
<211> LENGTH: 96
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 957

ggggtcccgt cgcggttcag cggcagtgga gatgggacac agttcactct caccatcagc 60

gccgtgcagt gtgaagatgc tgccacttac tactgt 96

<210> SEQ ID NO 958
<211> LENGTH: 42
<212> TYPE: DNA
<213> ORGANISM: Oryctolagus cuniculus

<400> SEQUENCE: 958

caaggtgttg cttggagtag taatactggt tatggttccg ct 42

<210> SEQ ID NO 959
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 959

ttcggcggag ggaccgaggt ggtggtcaaa cgt 33

<210> SEQ ID NO 960
<211> LENGTH: 318
<212> TYPE: DNA
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 960

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actgcctctg ttgtgtgcct gctgaataac ttctatccca gagaggccaa agtacagtgg 120

aaggtggata acgccctcca atcgggtaac tcccaggaga gtgtcacaga gcaggacagc 180

aaggacagca cctacagcct cagcagcacc ctgacgctga gcaaagcaga ctacgagaaa 240

cacaaagtct acgcctgcga agtcacccat cagggcctga gctcgcccgt cacaaagagc 300

ttcaacaggg gagagtgt 318

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<210> SEQ ID NO 1241
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<212> TYPE: PRT
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<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (38)..(38)
<223> OTHER INFORMATION: AMIDATION

<400> SEQUENCE: 1241

His Ser Asp Gly Ile Phe Thr Asp Ser Tyr Ser Arg Tyr Arg Lys Gln
1 5 10 15

Met Ala Val Lys Lys Tyr Leu Ala Ala Val Leu Gly Lys Arg Tyr Lys
            20 25 30

Gln Arg Val Lys Asn Lys
        35

<210> SEQ ID NO 1242
<211> LENGTH: 27
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

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<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (27)..(27)
<223> OTHER INFORMATION: AMIDATION

<400> SEQUENCE: 1242

His Ser Asp Gly Ile Phe Thr Asp Ser Tyr Ser Arg Tyr Arg Lys Gln
1 5 10 15

Met Ala Val Lys Lys Tyr Leu Ala Ala Val Leu
20 25

<210> SEQ ID NO 1243
<211> LENGTH: 28
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (28)..(28)
<223> OTHER INFORMATION: AMIDATION

<400> SEQUENCE: 1243

His Ser Asp Ala Val Phe Thr Asp Asn Tyr Thr Arg Leu Arg Lys Gln
1 5 10 15

Met Ala Val Lys Lys Tyr Leu Asn Ser Ile Leu Asn
20 25

<210> SEQ ID NO 1244
<211> LENGTH: 330
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 1244

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65 70 75 80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95

Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
100 105 110

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
115 120 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
130 135 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145 150 155 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
165 170 175

Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
180 185 190

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His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
        195                 200                 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
    210                 215                 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
225                 230                 235                 240

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
                245                 250                 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
            260                 265                 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
        275                 280                 285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
    290                 295                 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305                 310                 315                 320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
                325                 330


<210> SEQ ID NO 1245
<211> LENGTH: 330
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 1245

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1               5                   10                  15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
            20                  25                  30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
        35                  40                  45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
    50                  55                  60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65                  70                  75                  80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Ala
                85                  90                  95

Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
            100                 105                 110

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
        115                 120                 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
    130                 135                 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145                 150                 155                 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
                165                 170                 175

Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
            180                 185                 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
        195                 200                 205
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Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
    210                 215                 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
225                 230                 235                 240

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
                245                 250                 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
            260                 265                 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
        275                 280                 285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
    290                 295                 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305                 310                 315                 320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
                325                 330


<210> SEQ ID NO 1246
<211> LENGTH: 330
<212> TYPE: PRT
<213> ORGANISM: Artificial
<220> FEATURE:
<223> OTHER INFORMATION: Humanized antibody sequence

<400> SEQUENCE: 1246

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1               5                   10                  15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
            20                  25                  30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
        35                  40                  45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
    50                  55                  60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65                  70                  75                  80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
                85                  90                  95

Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
            100                 105                 110

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
        115                  120                 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
    130                 135                 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145                 150                 155                 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
                165                 170                 175

Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
            180                 185                 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
        195                 200                 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
    210                 215                 220
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Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
225                 230                 235                 240

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
                245                 250                 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
            260                 265                 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
        275                 280                 285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
    290                 295                 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305                 310                 315                 320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
                325                 330
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1. An antibody or antibody fragment selected from the following:

(a) a human, humanized or chimerized anti-human Pituitary Adenylate Cyclase-Activating Polypeptide ("PACAP") antibody or antibody fragment that antagonizes, inhibits, neutralizes or blocks at least one biological effect associated with human PACAP;

(b) a human, humanized or chimerized anti-PACAP antibody or antibody fragment that specifically competes for binding to human PACAP with an antibody selected from the group consisting of Ab1, Ab2, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab1.H, Ab5, Ab7, Ab11, Ab12, Ab4, Ab3, Ab6, Ab8, and Ab9 or an antigen-binding fragment of any one of the foregoing;

(c) a human, humanized or chimerized anti-PACAP antibody or antibody fragment that specifically binds to at least one linear or conformational epitope bound by an anti-PACAP antibody selected from the group consisting of Ab1, Ab2, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab1.H, Ab5, Ab7, Ab11, Ab12, Ab4, Ab3, Ab6, Ab8, and Ab9 or an antigen-binding fragment of any one of the foregoing;

(d) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing claims which binds to the identical epitopes as any one of Ab1, Ab2, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab1.H, Ab5, Ab7, Ab11, Ab12, Ab4, Ab3, Ab6, Ab8, and Ab9 or an antigen-binding fragment of any one of the foregoing;

(e) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing claims that specifically binds to an epitope on human PACAP or a fragment or variant thereof containing the corresponding amino acid residues wherein said epitope is selected from the group consisting of:

(i) at least one of residues 7, 10, 13, and 14 of a human PACAP;

(ii) at least one of residues 5, 6, 8, 10, and 13 of a human PACAP;

(iii) at least one of residues 6, 8, 9, 10, and 13 of a human PACAP;

(iv) at least one of residues 5, 6, 8, 9, 10, and 13 of a human PACAP;

(v) at least one of residues 7, 10, 12, 13, 14, and 17 of a human PACAP;

(vi) at least one of residues 5, 6, 8, 9, 10, 12, and 13 of a human PACAP;

(vii) at least one of residues 5, 6, 8, 9, 10, 13, and 14 of a human PACAP;

(viii) at least one of residues 6, 8, 10, 11, 13, 14, and 18 of a human PACAP;

(ix) at least one of residues 8, 9, 10, 13, 14, 17, and 18 of a human PACAP;

(x) at least one of residues 3, 4, 5, 6, 7, 10, 13, and 14 of a human PACAP;

(xi) at least one of residues 5, 6, 8, 9, 10, 12, 13, and 14 of a human PACAP;

(xii) at least one of residues 5, 6, 9, 10, 12, 13, 14, and 17 of a human PACAP;

(xiii) at least one of residues 6, 8, 10, 11, 13, 14, 18, and 22 of a human PACAP;

(xiv) at least one of residues 8, 9, 10, 11, 12, 13, 14, 17, and 21 of a human PACAP;

(xv) at least one of residues 4, 5, 6, 8, 9, 10, 12, 13, 14, and 17 of a human PACAP;

(xvi) at least two of the residues of any one of (i)-(xv);

(xvii) at least three of the residues of any one of (i)-(xv);

(xviii) at least four of the residues of any one of (i)-(xv);

(xix) at least five of the residues of any one of (ii)-(xv);

(xx) at least six of the residues of any one of (iv)-(xv);

(xxi) at least seven of the residues of any one of (vi)-(xv);

(xxii) at least eight of the residues of any one of (x)-(xv);

(xxiii) at least nine of the residues of (xiv) or (xv);

(xxiv) all ten residues of (xv);

(f) a human, humanized or chimerized anti-PACAP human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing which specifically binds to an epitope on human PACAP, or a fragment or variant thereof containing the corresponding amino acid residues that includes residues 8 and/or 14 of human PACAP;

(g) human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing, which specifically binds to an epitope on human PACAP or a fragment or variant thereof containing the corresponding amino acid residues, wherein said epitope consists of the residues of any one of (i)-(xv) as set forth in claim (e);

(h) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing, which specifically binds to an epitope on human PACAP (or a fragment or variant thereof containing the corresponding amino acid residues) that is present in human wild-type PACAP38 and in human wild-type human PACAP27;

(i) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing wherein said epitope is identified by alanine scanning, e.g., as disclosed in Example 12;

(j) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing which does not bind to or does not appreciably bind to human Vasoactive Intestinal Peptide ("VIP");

(k) The human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing which has a K_D for human PACAP which is at least 10, 100, 1000, 10,000 or 100,000 fold lower (stronger) than the K_D of said antibody or antibody fragment to human VI;

(l) human, humanized or chimerized anti-PACAP antibody or antibody fragment of any of the foregoing which inhibits or neutralizes at least one biological effect elicited by human PACAP;

(m) The human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing which comprises one or more of the following:

(1) inhibits, blocks or prevents PACAP activation of at least one of PAC1 receptor ("PAC1-R"), vasoactive intestinal peptide receptor type 1 ("VPAC1-R"), and/or vasoactive intestinal peptide receptor type 2 ("VPAC2-R");

(2) inhibits, blocks or prevents PACAP activation of each of PAC1-R, VPAC1-R, and VPAC2-R;

(3) inhibits, blocks or prevents PACAP activation of PAC1-R;

(4) is capable of inhibiting PACAP binding to at least one of PAC1-R, VPAC1-R, and/or VPAC2-R;

(5) is capable of inhibiting PACAP binding to each of PAC1-R, VPAC1-R, and/or VPAC2-R;

(6) is capable of inhibiting PACAP binding to PAC1-R-expressing cells;

(7) is capable of inhibiting PACAP binding to VPAC1-R-expressing cells;

(8) is capable of inhibiting PACAP binding to VPAC2-R-expressing cells;

(9) inhibits PACAP binding to the cell surface, e.g. via a glycosaminoglycan ("GAG");

(10) does not inhibit PACAP-mediated binding of such antibody to the cell surface, e.g., via a GAG;

(11) inhibits, blocks or prevents PACAP-induced cAMP production; and/or

(12) when administered to a subject reduces PACAP-induced vasodilation;

(n) human, humanized or chimerized anti-PACAP antibody or antibody fragment of any of the foregoing which inhibits or neutralizes at least one biological effect elicited by human PACAP;

(o) a human, humanized or chimerized anti-PACAP antibody or antibody fragment of any of the foregoing which is substantially non-immunogenic in human subjects;

(p) a human, humanized or chimerized anti-PACAP antibody or antibody fragment of any of the foregoing which is suitable for treating a human subject having an acute, episodic or chronic condition associated with increased vasodilation, mast cell degranulation and/or neuronal activation;

(q) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising at least 2 complementarity determining regions ("CDRs") of an anti-PACAP antibody selected from Ab1, Ab2, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab1.H, Ab5, Ab7, Ab11, Ab12, Ab4, Ab3, Ab6, Ab8, or Ab9, preferably CDR3 and/or the V_L CDR3;

(r) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing, comprising at least 3 CDRs of an anti-PACAP antibody selected from Ab1, Ab2, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab1.H, Ab5, Ab7, Ab11, Ab12, Ab4, Ab3, Ab6, Ab8, or Ab9;

(s) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing, comprising at least 4 CDRs of an anti-PACAP antibody selected from Ab1, Ab2, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab1.H, Ab5, Ab7, Ab11, Ab12, Ab4, Ab3, Ab6, Ab8, or Ab9;

(t) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising at least 5 CDRs of an anti-PACAP antibody selected from Ab1, Ab2, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab1.H, Ab5, Ab7, Ab11, Ab12, Ab4, Ab3, Ab6, Ab8, or Ab9;

(u) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising all 6 CDRs of an anti-PACAP antibody selected from Ab1, Ab2, Ab13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab1.H, Ab5, Ab7, Ab11, Ab12, Ab4, Ab3, Ab6, Ab8, or Ab9;

(v) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a variable heavy chain comprising the CDR1 sequence consisting of SEQ ID NO: 4; a CDR2 sequence consisting of SEQ ID NO: 6; and a CDR3 sequence consisting of SEQ ID NO: 8; and/or

(2) a variable light chain comprising the CDR1 sequence consisting of SEQ ID NO: 24; a CDR2 sequence consisting of SEQ ID NO: 26; and a CDR3 sequence consisting of SEQ ID NO: 28;

(w) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any one of the foregoing comprising:

(1) a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 2, and/or

(2) a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 22;

(x) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any one of the foregoing comprising:

(1) a variable heavy chain having the amino acid sequence of SEQ ID NO: 2, and/or

(1) a variable light chain having the amino acid sequence of SEQ ID NO: 22;

(y) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any one of the foregoing comprising:

(1) a heavy chain having the amino acid sequence of SEQ ID NO: 1, and/or

(2) a light chain having the amino acid sequence of SEQ ID NO: 21;

(z) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any one of the foregoing comprising: comprising:

(1) a variable heavy chain comprising the CDR1 sequence consisting of SEQ ID NO: 44; a CDR2 sequence consisting of SEQ ID NO: 46; and a CDR3 sequence consisting of SEQ ID NO: 48; and/or

(2) a variable light chain comprising the CDR1 sequence consisting of SEQ ID NO: 64; a CDR2 sequence consisting of SEQ ID NO: 66; and a CDR3 sequence consisting of SEQ ID NO: 68;

(aa) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any one of the foregoing comprising:

(1) a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 42, and/or

(2) a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 62;

(bb) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any one of the foregoing comprising:

(1) a variable heavy chain having the amino acid sequence of SEQ ID NO: 42, and/or

(2) a variable light chain having the amino acid sequence of SEQ ID NO: 62;

(cc) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any one of the foregoing comprising:

(1) a heavy chain having the amino acid sequence of SEQ ID NO: 41, and/or

(2) a light chain having the amino acid sequence of SEQ ID NO: 61;

(dd) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any one of the foregoing comprising:

(1) a variable heavy chain comprising the CDR1 sequence consisting of SEQ ID NO: 84; a CDR2 sequence consisting of SEQ ID NO: 86; and a CDR3 sequence consisting of SEQ ID NO: 88; and/or

(2) a variable light chain comprising the CDR1 sequence consisting of SEQ ID NO: 104; a CDR2 sequence consisting of SEQ ID NO: 106; and a CDR3 sequence consisting of SEQ ID NO: 108;

(ee) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any one of the foregoing comprising: comprising:

(1) a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 82 and/or

(2) a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 102;

(ff) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a variable heavy chain having the amino acid sequence of SEQ ID NO: 82, and/or

(2) a variable light chain having the amino acid sequence of SEQ ID NO: 102;

(gg) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a heavy chain having the amino acid sequence of SEQ ID NO: 81, and/or

(2) a light chain having the amino acid sequence of SEQ ID NO: 101;

(hh) human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a variable heavy chain comprising the CDR1 sequence consisting of SEQ ID NO: 124; a CDR2 sequence consisting of SEQ ID NO: 126; and a CDR3 sequence consisting of SEQ ID NO: 128; and/or

(2) a variable light chain comprising the CDR1 sequence consisting of SEQ ID NO: 144; a CDR2 sequence consisting of SEQ ID NO: 146; and a CDR3 sequence consisting of SEQ ID NO: 148;

(ii) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 122 and/or

(2) a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 142;

(jj) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a variable heavy chain having the amino acid sequence of SEQ ID NO: 122, and/or

(2) a variable light chain having the amino acid sequence of SEQ ID NO: 142;

(kk) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a heavy chain having the amino acid sequence of SEQ ID NO: 121, and/or

(2) a light chain having the amino acid sequence of SEQ ID NO: 141;

(ll) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a variable heavy chain comprising the CDR1 sequence consisting of SEQ ID NO: 164; a CDR2

sequence consisting of SEQ ID NO: 166; and a CDR3 sequence consisting of SEQ ID NO: 168; and/or

(2) a variable light chain comprising the CDR1 sequence consisting of SEQ ID NO: 184;

a CDR2 sequence consisting of SEQ ID NO: 186; and a CDR3 sequence consisting of SEQ ID NO: 188;

(mm) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 162, and/or

(2) a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 182;

(nn) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a variable heavy chain having the amino acid sequence of SEQ ID NO: 162, and/or

(2) a variable light chain having the amino acid sequence of SEQ ID NO: 182;

(oo) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a heavy chain having the amino acid sequence of SEQ ID NO: 161, and/or

(2) a light chain having the amino acid sequence of SEQ ID NO: 181;

(pp) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a variable heavy chain comprising the CDR1 sequence consisting of SEQ ID NO: 204; a CDR2 sequence consisting of SEQ ID NO: 206; and a CDR3 sequence consisting of SEQ ID NO: 208; and/or

(2) a variable light chain comprising the CDR1 sequence consisting of SEQ ID NO: 224; a CDR2 sequence consisting of SEQ ID NO: 226; and a CDR3 sequence consisting of SEQ ID NO: 228;

(qq) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 202 and/or

(2) a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 222;

(rr) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a variable heavy chain having the amino acid sequence of SEQ ID NO: 202, and/or

(2) a variable light chain having the amino acid sequence of SEQ ID NO: 222;

(ss) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a heavy chain having the amino acid sequence of SEQ ID NO: 201, and/or

(2) a light chain having the amino acid sequence of SEQ ID NO: 221;

(tt) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a variable heavy chain comprising the CDR1 sequence consisting of SEQ ID NO: 244; a CDR2 sequence consisting of SEQ ID NO: 246; and a CDR3 sequence consisting of SEQ ID NO: 248; and/or

(2) a variable light chain comprising the CDR1 sequence consisting of SEQ ID NO: 264; a CDR2 sequence consisting of SEQ ID NO: 266; and a CDR3 sequence consisting of SEQ ID NO: 268;

(uu) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 242, and/or

(2) a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 262;

(vv) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a variable heavy chain having the amino acid sequence of SEQ ID NO: 242, and/or

(2) a variable light chain having the amino acid sequence of SEQ ID NO: 262;

(ww) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a heavy chain having the amino acid sequence of SEQ ID NO: 241, and/or

(2) a light chain having the amino acid sequence of SEQ ID NO: 261;

(xx) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a variable heavy chain comprising the CDR1 sequence consisting of SEQ ID NO: 284; a CDR2 sequence consisting of SEQ ID NO: 286; and a CDR3 sequence consisting of SEQ ID NO: 288; and/or

(2) the variable light chain comprising a CDR1 sequence consisting of SEQ ID NO: 304; a CDR2 sequence consisting of SEQ ID NO: 306; and a CDR3 sequence consisting of SEQ ID NO: 308;

(yy) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 282, and/or

(2) a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 302;

(zz) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a variable heavy chain having the amino acid sequence of SEQ ID NO: 282, and/or

(2) a variable light chain having the amino acid sequence of SEQ ID NO: 302;

(aaa) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a heavy chain having the amino acid sequence of SEQ ID NO: 281, and/or

(2) a light chain having the amino acid sequence of SEQ ID NO: 301;

(bbb) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a variable heavy chain comprising the CDR1 sequence consisting of SEQ ID NO: 324; a CDR2 sequence consisting of SEQ ID NO: 326; and a CDR3 sequence consisting of SEQ ID NO: 328; and/or

(2) a variable light chain comprising the CDR1 sequence consisting of SEQ ID NO: 344; a CDR2 sequence consisting of SEQ ID NO: 346; and a CDR3 sequence consisting of SEQ ID NO: 348;

(ccc) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 322, and/or

(2) a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 342;

(ddd) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a variable heavy chain having the amino acid sequence of SEQ ID NO: 322, and/or

(2) a variable light chain having the amino acid sequence of SEQ ID NO: 342;

(eee) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a heavy chain having the amino acid sequence of SEQ ID NO: 321, and/or

(2) a light chain having the amino acid sequence of SEQ ID NO: 341;

(fff) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a variable heavy chain comprising the CDR1 sequence consisting of SEQ ID NO: 364; a CDR2 sequence consisting of SEQ ID NO: 366; and a CDR3 sequence consisting of SEQ ID NO: 368; and/or

(2) a variable light chain comprising the CDR1 sequence consisting of SEQ ID NO: 384; a CDR2 sequence consisting of SEQ ID NO: 386; and a CDR3 sequence consisting of SEQ ID NO: 388;

(ggg) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 362, and/or

(2) a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 382;

(hhh) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a variable heavy chain having the amino acid sequence of SEQ ID NO: 362, and/or

(2) a variable light chain having the amino acid sequence of SEQ ID NO: 382;

(iii) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a heavy chain having the amino acid sequence of SEQ ID NO: 361, and/or

(2) a light chain having the amino acid sequence of SEQ ID NO: 381;

(jjj) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) the variable heavy chain comprising the CDR1 sequence consisting of SEQ ID NO: 484; the CDR2 sequence consisting of SEQ ID NO: 486; and the CDR3 sequence consisting of SEQ ID NO: 488; and/or

(2) the variable light chain comprising the CDR1 sequence consisting of SEQ ID NO: 504; the CDR2 sequence consisting of SEQ ID NO: 506; and the CDR3 sequence consisting of SEQ ID NO: 508;

(kkk) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 482, and/or

(2) a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 502;

(lll) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a variable heavy chain having the amino acid sequence of SEQ ID NO: 482, and/or

(2) a variable light chain having the amino acid sequence of SEQ ID NO: 502;

(mmm) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a heavy chain having the amino acid sequence of SEQ ID NO: 481, and/or

(2) a light chain having the amino acid sequence of SEQ ID NO: 501;

(nnn) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a variable heavy chain comprising the CDR1 sequence consisting of SEQ ID NO: 524; a CDR2 sequence consisting of SEQ ID NO: 526; and a CDR3 sequence consisting of SEQ ID NO: 528; and/or

(2) a variable light chain comprising the CDR1 sequence consisting of SEQ ID NO: 544; a CDR2 sequence consisting of SEQ ID NO: 546; and a CDR3 sequence consisting of SEQ ID NO: 548;

(ooo) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:
(1) a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 522, and/or
(2) a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 542;

(ppp) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:
(1) a variable heavy chain having the amino acid sequence of SEQ ID NO: 522, and/or
(2) a variable light chain having the amino acid sequence of SEQ ID NO: 542;

(qqq) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:
(1) a heavy chain having the amino acid sequence of SEQ ID NO: 521, and/or
(2) a light chain having the amino acid sequence of SEQ ID NO: 541;

(rrr) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:
(1) a variable heavy chain comprising the CDR1 sequence consisting of SEQ ID NO: 564; a CDR2 sequence consisting of SEQ ID NO: 566; and a CDR3 sequence consisting of SEQ ID NO: 568; and/or
(2) a variable light chain comprising the CDR1 sequence consisting of SEQ ID NO: 584; a CDR2 sequence consisting of SEQ ID NO: 586; and a CDR3 sequence consisting of SEQ ID NO: 588;

(sss) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:
(a) a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 562, and/or
(b) a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 582;

(ttt) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:
(a) a variable heavy chain having the amino acid sequence of SEQ ID NO: 562, and/or
(b) a variable light chain having the amino acid sequence of SEQ ID NO: 582;

(uuu) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:
(1) a heavy chain having the amino acid sequence of SEQ ID NO: 561, and/or
(2) a light chain having the amino acid sequence of SEQ ID NO: 581;

(vvv) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:
(1) a variable heavy chain comprising the CDR1 sequence consisting of SEQ ID NO: 604; a CDR2 sequence consisting of SEQ ID NO: 606; and a CDR3 sequence consisting of SEQ ID NO: 608; and/or
(2) a variable light chain comprising the CDR1 sequence consisting of SEQ ID NO: 624; a CDR2 sequence consisting of SEQ ID NO: 626; and a CDR3 sequence consisting of SEQ ID NO: 628;

(www) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:
(1) a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 602 and/or
(2) a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 622;

(xxx) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:
(1) a variable heavy chain having the amino acid sequence of SEQ ID NO: 602, and/or
(2) a variable light chain having the amino acid sequence of SEQ ID NO: 622;

(yyy) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:
(1) a heavy chain having the amino acid sequence of SEQ ID NO: 601, and/or
(2) a light chain having the amino acid sequence of SEQ ID NO: 621;

(zzz) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:
(1) the variable heavy chain comprising the CDR1 sequence consisting of SEQ ID NO: 644; the CDR2 sequence consisting of SEQ ID NO: 646; and the CDR3 sequence consisting of SEQ ID NO: 648; and/or
(2) the variable light chain comprising the CDR1 sequence consisting of SEQ ID NO: 664; the CDR2 sequence consisting of SEQ ID NO: 666; and the CDR3 sequence consisting of SEQ ID NO: 668;

(aaaa) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:
(1) a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 642, and/or
(2) a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 662;

(bbbb) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:
(1) a variable heavy chain having the amino acid sequence of SEQ ID NO: 642, and/or
(2) a variable light chain having the amino acid sequence of SEQ ID NO: 662;

(cccc) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:
(1) a heavy chain having the amino acid sequence of SEQ ID NO: 641, and/or

(2) a light chain having the amino acid sequence of SEQ ID NO: 661;

(dddd) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) the variable heavy chain comprising the CDR1 sequence consisting of SEQ ID NO: 684; the CDR2 sequence consisting of SEQ ID NO: 686; and the CDR3 sequence consisting of SEQ ID NO: 688; and/or

(2) the variable light chain comprising the CDR1 sequence consisting of SEQ ID NO: 704; the CDR2 sequence consisting of SEQ ID NO: 706; and the CDR3 sequence consisting of SEQ ID NO: 708;

(eeee) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 682, and/or

(2) a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 702;

(ffff) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a variable heavy chain having the amino acid sequence of SEQ ID NO: 682, and/or

(2) a variable light chain having the amino acid sequence of SEQ ID NO: 702;

(gggg) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a heavy chain having the amino acid sequence of SEQ ID NO: 681, and/or

(2) a light chain having the amino acid sequence of SEQ ID NO: 701;

(hhhh) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a variable heavy chain comprising the CDR1 sequence consisting of SEQ ID NO: 724; a CDR2 sequence consisting of SEQ ID NO: 726; and a CDR3 sequence consisting of SEQ ID NO: 728; and/or

(2) a variable light chain comprising the CDR1 sequence consisting of SEQ ID NO: 744; a CDR2 sequence consisting of SEQ ID NO: 746; and a CDR3 sequence consisting of SEQ ID NO: 748;

(iiii) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 722 and/or

(2) a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 742;

(jjjj) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a variable heavy chain having the amino acid sequence of SEQ ID NO: 722, and/or

(2) a variable light chain having the amino acid sequence of SEQ ID NO: 742;

(kkkk) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a heavy chain having the amino acid sequence of SEQ ID NO: 721, and/or

(2) a light chain having the amino acid sequence of SEQ ID NO: 741;

(llll) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a variable heavy chain comprising the CDR1 sequence consisting of SEQ ID NO: 764; a CDR2 sequence consisting of SEQ ID NO: 766; and a CDR3 sequence consisting of SEQ ID NO: 768; and/or

(2) a variable light chain comprising the CDR1 sequence consisting of SEQ ID NO: 784; a CDR2 sequence consisting of SEQ ID NO: 786; and a CDR3 sequence consisting of SEQ ID NO: 788;

(mmmm) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 762, and/or

(2) a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 782;

(nnnn) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a variable heavy chain having the amino acid sequence of SEQ ID NO: 762, and/or

(2) a variable light chain having the amino acid sequence of SEQ ID NO: 782;

(oooo) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a heavy chain having the amino acid sequence of SEQ ID NO: 761, and/or

(2) a light chain having the amino acid sequence of SEQ ID NO: 781;

(pppp) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) the variable heavy chain comprising the CDR1 sequence consisting of SEQ ID NO: 804; the CDR2 sequence consisting of SEQ ID NO: 806; and the CDR3 sequence consisting of SEQ ID NO: 808; and/or

(2) the variable light chain comprising the CDR1 sequence consisting of SEQ ID NO: 824; the CDR2 sequence consisting of SEQ ID NO: 826; and the CDR3 sequence consisting of SEQ ID NO: 828;

(qqqq) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a variable heavy chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 802, and/or

(2) a variable light chain comprising an amino acid sequence with at least 80, 85, 90, 95, 96, 97, 98, or 99% sequence identity to SEQ ID NO: 822;

(rrrr) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(1) a variable heavy chain having the amino acid sequence of SEQ ID NO: 802, and/or

(2) a variable light chain having the amino acid sequence of SEQ ID NO: 822;

(ssss) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising:

(a) a heavy chain having the amino acid sequence of SEQ ID NO: 801, and/or

(b) a light chain having the amino acid sequence of SEQ ID NO: 821;

(tttt) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing selected from the group consisting of scFvs, camelbodies, nanobodies, Immunoglobulin New Antigen Receptor ("IgNAR"), fragment antigen binding ("Fab") fragments, Fab' fragments, MetMab like antibodies, monovalent antibody fragments, and F(ab')2 fragments;

(uuuu) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising, wherein the antibody or antibody fragment substantially or entirely lacks N-glycosylation and/or O-glycosylation;

(vvvv) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising wherein the antibody or antibody fragment comprises a human constant domain;

(wwww) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising an IgG1, IgG2, IgG3, or IgG4 antibody;

(xxxx) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising an Fc region that has been modified to alter at least one of effector function, half-life, proteolysis, or glycosylation;

(yyyy) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising an Fc region which contains one or more mutations that alters or eliminates N- and/or O-glycosylation;

(zzzz) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing wherein the antibody or antibody fragment binds to PACAP with a binding affinity (K_D) of less than or equal to 5×10^{-5}M, 10^{-5}M, 5×10^{-6} M, 10^{-6} M, 5×10^{-7}M, 10^{-7}M, 5×10^{-8}M, 10^{-8} M, 5×10^{-9} M, 10^{-9} M, 5×10^{-10} M, 10^{-10} M, 5×10^{-11}M, 10^{-11} M, 5×10^{-12}M, 10^{-12} M, 5×10^{-13} M, or 10^{-13} M, e.g., as determined by ELISA, bio-layer interferometry ("BLI"), KINEXA or surface plasmon resonance at 25° or 37° C.;

(aaaaa) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing wherein the antibody or antibody fragment binds to PACAP with a binding affinity (K_D) of less than or equal to 5×10^{-10} M, 10^{-10} M, 5×10^{-11} M, 10^{-11} M, 5×10^{-12}M, or 10^{-12} M;

(bbbbb) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing comprising, which binds to PACAP with an off-rate (k_{off}) of less than or equal to 5×10^{-4} s^{-1}, 10^{-4} s^{-1}, 5×10^{-5} s^{-1}, or 10^{-5} s^{-1};

(ccccc) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing wherein the antibody or antibody fragment is directly or indirectly attached to a detectable label or therapeutic agent;

(ddddd) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing which when administered to a subject inhibits or neutralizes at least one biological effect elicited by PACAP;

(eeeee) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing which neutralizes or inhibits PACAP activation of at least one of PAC1-R, VPAC1-R, or VPAC2-R;

(fffff) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing which neutralizes or inhibits PACAP activation of each of PAC1-R, VPAC1-R, and VPAC2-R;

(ggggg) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing which neutralizes or inhibits PACAP activation of PAC1-R;

(hhhhh) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing which is capable of inhibiting or preventing PACAP binding to at least one of PAC1-R, VPAC1-R, or VPAC2-R;

(iiiii) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing which is capable of inhibiting or preventing PACAP binding to each of PAC1-R, VPAC1-R, and VPAC2-R;

(jjjjj) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing which is capable of inhibiting or preventing PACAP binding to PAC1-R-expressing cells, VPAC1-R-expressing cells, and/or VPAC2-R-expressing cells;

(kkkkk) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing which inhibits or blocks PACAP-induced cAMP production;

(lllll) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing which when administered to a subject reduces PACAP-induced vasodilation, mast cell degranulation and/or neuronal activation;

(mmmmm) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing wherein the antibody or antibody fragment binds to PACAP with a K_D that is less than about 100 nM;

(nnnnn) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing wherein the antibody or antibody fragment binds to PACAP with a K_D that is less than about 40 nM;

(ooooo) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing wherein the antibody or antibody fragment binds to PACAP with a K_D that is less than about 100 pM;

(ppppp) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing, wherein the antibody or antibody fragment binds to PACAP with a K_D that is less than about 50 pM;

(qqqqq) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing wherein the antibody or antibody fragment binds to PACAP with a K_D that is less than about 25 pM;

(rrrrr) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing wherein the antibody or antibody fragment binds to PACAP with a K_D that is between about 10 pM and about 100 pM;

(sssss) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing which has stronger affinity for PACAP as compared to VIP and/or does not bind to VIP, wherein the affinity of said antibody or antibody fragment to PACAP optionally is at least 10-fold, 30-fold, 100-fold, 300-fold, 1000-fold, 3000-fold, 10000-fold, 30000-fold, 100000-fold, 300000-fold, 1000000-fold, 3000000-fold, 10000000-fold, 30000000-fold or more stronger than the affinity of said antibody or antibody fragment to VIP;

(ttttt) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing wherein the antibody or antibody fragment is attached to at least one effector moiety optionally wherein said effector moiety comprises a chemical linker;

(uuuuu) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing wherein the antibody or antibody fragment is attached to one or more detectable moieties; optionally wherein said detectable moiety comprises a fluorescent dye, enzyme, substrate, bioluminescent material, radioactive material, chemiluminescent moiety, or mixtures thereof; or

(wwwww) a human, humanized or chimerized anti-PACAP antibody or antibody fragment according to any of the foregoing wherein the antibody or antibody fragment is attached to one or more functional moieties;

2-128. (canceled)

129. An anti-idiotypic antibody produced against an anti-PACAP antibody or antibody fragment according claim **1**, which optionally, neutralizes one or more biological effects of the anti-PACAP antibody to which it binds.

130. A method of using the anti-idiotypic antibody of claim **129** to monitor the in vivo levels of said anti-PACAP antibody or antibody fragment in a subject or to neutralize the in vivo effects of said anti-PACAP antibody in a subject.

131. A composition suitable for therapeutic, prophylactic, or a diagnostic use comprising a therapeutically, prophylactically or diagnostically effective amount of at least one anti-PACAP antibody or antibody fragment or anti-idiotypic antibody according to claim **1** or **129**.

132. The composition of claim **131**, which is

(i) suitable for subcutaneous, intravenous, intramuscular, topical, oral, inhalatory, intranasal, intrabuccal, vaginal, anal, transdermal, intraperitoneal, or intrathecal administration;

(ii) suitable for subcutaneous intravenous or intramuscular administration;

(iii) is lyophilized;

(iv) further comprising a pharmaceutically acceptable diluent, carrier, solubilizer, emulsifier, preservative, or mixture thereof;

(v) further comprising at least one other active agent, optionally selected from the group consisting of a chemotherapeutic, an analgesic, an anti-inflammatory, an immunosuppressant, a cytokine, an antiproliferative, an antiemetic and a cytotoxin;

(vi) is lyophilized, stabilized, and/or formulated for administration by injection.

133-138. (canceled)

139. An isolated nucleic acid sequence or nucleic acid sequences encoding an anti-PACAP antibody or antibody fragment or anti-idiotypic antibody according claim **1** or a vector or vectors containing the isolated nucleic acid sequence or sequences or a host cell containing the isolated nucleic acid sequence or sequences or vector or vectors.

140-141. (canceled)

142. The host cell of claim **139**, which is a mammalian, bacterial, fungal, yeast, avian, amphibian, plant or insect cell, e.g., a filamentous fungus or a CHO cell or a yeast selected from the following genera: *Arxiozyma; Ascobotryozyma; Citeromyces; Debaryomyces; Dekkera; Eremothecium; Issatchenkia; Kazachstania; Kluyveromyces; Kodamaea; Lodderomyces; Pachysolen; Pichia; Saccharomyces; Saturnispora; Tetrapisispora; Torulaspora; Williopsis*; and *Zygosaccharomyces*, optionally *Pichia*, and further optionally a *Pichia* selected from *Pichia pastoris, Pichia methanolica* and *Hansenula polymorpha* (*Pichia angusta*).

143-146. (canceled)

147. A method of expressing an anti-PACAP antibody or antibody fragment comprising culturing the host cell according to claim **139** or **142** under conditions that provide for expression of said antibody or antibody fragment, optionally a polyploid yeast cell or CHO cell that stably expresses and secretes said antibody or antibody fragment, optionally made by a method that comprises: (i) introducing at least one expression vector containing one or more heterologous polynucleotides encoding said antibody operably linked to a promoter and a signal sequence into a haploid yeast cell; (ii) producing by mating or spheroplast fusion a polyploid yeast from said first and/or second haploid yeast cell; (iii) selecting polyploid yeast cells, optionally *Pichia*, that stably express said antibody; and (iv) producing stable polyploid yeast cultures from said polyploid yeast cells that stably express said antibody into the culture medium.

148-150. (canceled)

151. A method selected from the following:

(i) blocking, inhibiting, blocking or neutralizing one or more biological effects associated with PACAP in a subject comprising administering to said subject a therapeutically or prophylactically effective amount of a human, humanized or chimerized anti-PACAP antibody or antibody fragment that antagonizes, inhibits, neutralizes or blocks at least one biological effect associated with human PACAP;

(ii) blocking, inhibiting, or neutralizing one or more biological effects associated with pituitary adenylate cyclase-activating peptide ("PACAP") in a subject comprising administering to a subject a therapeutically or prophylactically effective amount of a human, humanized or chimerized anti-PACAP antibody or antibody fragment that antagonizes, inhibits, neutralizes or blocks at least one biological effect associated with human PACAP and that does not substantially interact with (bind) Vasoactive Intestinal Peptide ("VIP");

(iii) blocking, inhibiting, or neutralizing one or more biological effects, e.g., vasomotor effects, associated with pituitary adenylate cyclase-activating peptide ("PACAP") in a subject comprising administering to a subject a therapeutically or prophylactically effective amount of a human, humanized or chimerized anti-PACAP antibody or antibody fragment that comprises one or more of the following:

(a) inhibits, blocks or neutralizes at least one biological effect elicited by PACAP;

(b) neutralizes or inhibits PACAP activation of at least one of PAC1 receptor ("PAC1-R"), vasoactive intestinal peptide receptor type 1 ("VPAC1-R"), and/or vasoactive intestinal peptide receptor type 2 ("VPAC2-R");

(c) inhibits, blocks or neutralizes PACAP activation of each of PAC1-R, VPAC1-R, and VPAC2-R; (d) neutralizes or inhibits PACAP activation of PAC1-R;

(d) is capable of inhibiting PACAP binding to at least one of PAC1-R, VPAC1-R, and/or VPAC2-R;

(e) is capable of inhibiting PACAP binding to each of PAC1-R, VPAC1-R, and/or VPAC2-R;

(f) is capable of inhibiting PACAP binding to PAC1-R-expressing cells;

(g) is capable of inhibiting PACAP binding to VPAC1-R and/or VPAC2-R-expressing cells;

(h) does not inhibit PACAP-mediated binding of such antibody to the cell surface, e.g., via a glycosaminoglycan ("GAG");

(i) inhibits PACAP binding to the cell surface, e.g. via a glycosaminoglycan "GAG");

(j) inhibits PACAP-induced cyclic adenosine monophosphate ("cAMP") production; and/or

(k) when administered to a subject reduces PACAP-induced vasodilation, mast cell degranulation and/or neuronal activation;

(iv) blocking, inhibiting, or neutralizing vasodilation, e.g., vasodilation of the dural arteries, which is associated with or elicited by pituitary adenylate cyclase-activating peptide ("PACAP") in a subject comprising administering to a subject a therapeutically or prophylactically effective amount of a human, humanized or chimerized anti-PACAP antibody or antibody fragment that blocks, inhibits, or neutralizes vasodilation associated with, or elicited by PACAP;

(v) treating or preventing the onset, frequency, severity or duration of headache or migraine in a subject comprising administering to a subject in need thereof an effective amount of a human, humanized or chimerized anti-human Pituitary Adenylate Cyclase-Activating Polypeptide ("PACAP") antibody or antibody fragment that elicits one or more of the following effects:

(a) inhibits or neutralizes at least one biological effect elicited by PACAP;

(b) neutralizes or inhibits PACAP activation of at least one of PAC1 receptor ("PAC1-R"), vasoactive intestinal peptide receptor type 1 ("VPAC1-R"), and/or vasoactive intestinal peptide receptor type 2 ("VPAC2-R");

(c) neutralizes or inhibits PACAP activation of each of PAC1-R, VPAC1-R, and VPAC2-R;

(d) neutralizes or inhibits PACAP activation of PAC1-R; (e) is capable of inhibiting PACAP binding to at least one of PAC1-R, VPAC1-R, and/or VPAC2-R; (f) is capable of inhibiting PACAP binding to each of PAC1-R, VPAC1-R, and/or VPAC2-R;

(e) is capable of inhibiting PACAP binding to PAC1-R-expressing cells;

(f) is capable of inhibiting PACAP binding to VPAC1-R and/or VPAC2-R-expressing cells;

(g) does not inhibit PACAP-mediated binding of such antibody to the cell surface, e.g., via a GAG;

(h) inhibits PACAP binding to the cell surface, e.g. via a glycosaminoglycan ("GAG");

(i) inhibits PACAP-induced cyclic adenosine monophosphate ("cAMP") production; and/or

(j) when administered to a subject reduces PACAP-induced vasodilation, mast cell degranulation and/or neuronal activation; wherein the headache or migraine is optionally selected from migraine with aura, migraine without aura, hemiplegic migraine, cluster headache, migrainous neuralgia, chronic headache, chronic migraine, medication overuse headache, and tension headache;

(vi) treating a human subject having an acute, episodic or chronic condition associated with at least one of increased vasodilation, mast cell degranulation and neuronal activation or a combination of any of the foregoing comprising administering to a subject in need thereof an effective amount of an antagonistic human, humanized or chimerized anti-human Pituitary Adenylate Cyclase-Activating Polypeptide ("PACAP") antibody or antibody fragment;

(vii) The method of any one of (i)-(vi), which is effected by the administration of a therapeutically or prophylactically effective amount of at least one human, humanized or chimerized anti-PACAP antibody or antibody fragment according to claim **1**

(viii) The method of any one of (i)-(vii), wherein the anti-PACAP antibody is a human antibody or antibody fragment;

(ix) The method of any one of (i)-(vii), wherein the anti-PACAP antibody is a humanized antibody or antibody fragment;

(x). The method of any one of (i)-(vii), wherein the anti-PACAP antibody is a chimeric antibody or antibody fragment;

(xi) The method of any one of (i)-(x), wherein the anti-PACAP antibody or antibody fragment binds to PACAP27 and/or PACAP38 and blocks PACAP27 and/or PACAP38 binding to PAC1-R, VPAC1-R, and/or VPAC2-R;

(xii) the method of any one of (i)-(vi), wherein the anti-PACAP antibody or antibody fragment binds to PACAP27 and/or PACAP38 and blocks PACAP27 and/or PACAP38 binding to each of PAC1-R, VPAC1-R, and VPAC2-R;

(xiii) the method of any one of (i)-(vi), wherein the anti-PACAP antibody or antibody fragment binds to PACAP27 and/or PACAP38 and blocks PACAP27 and/or PACAP38 binding to PAC1-R-expressing cells;

(xiv) the method of any one of (i)-(vi), wherein the affinity of said antibody or antibody fragment to PACAP is at least 10-fold, 30-fold, 100-fold, 300-fold, 1000-fold, 3000-fold, 10000-fold, 30000-fold, 100000-fold, 300000-fold, 1000000-fold, 3000000-fold, 10000000-fold, 30000000-fold or more stronger than the affinity of said antibody or antibody fragment to VIP;

(xv) the method of any one of (i)-(xiv), wherein the subject has a condition selected from the group consisting of migraine with aura, migraine without aura, hemiplegic migraines, cluster headaches, migrainous neuralgia, chronic headaches, tension headaches, general headaches, hot flush, chronic paroxysmal hemicrania, secondary headaches due to an underlying structural problem in the head, secondary headaches due to an underlying structural problem in the neck, cranial neuralgia, sinus headaches, headache associated with sinusitis, allergy-induced headaches, allergy-induced migraines, trigeminal neuralgia, post-herpetic neuralgia, phantom limb pain, fibromyalgia, reflex sympathetic dystrophy, pain, chronic pain, inflammatory pain, post-operative incision pain, post-surgical pain, trauma-related pain, lower back pain, eye pain, tooth pain, complex regional pain syndrome, cancer pain, primary or metastatic bone cancer pain, fracture pain, osteoporotic fracture pain, pain resulting from burn, gout joint pain, pain associated with sickle cell crises, pain associated with temporomandibular disorders, cirrhosis, hepatitis, neurogenic pain, neuropathic pain, nociceptic pain, visceral pain, menstrual pain, ovarialgia, osteoarthritis pain, rheumatoid arthritis pain, diabetic neuropathy, sciatica, dyspepsia, irritable bowel syndrome, inflammatory bowel disease, Crohn's disease, ileitis, ulcerative colitis, renal colic, dysmenorrhea, cystitis, interstitial cystitis, menstrual period, labor, menopause, pancreatitis, schizophrenia, depression, post-traumatic stress disorder ("PTSD"), anxiety disorders, autoimmune diabetes, Sjögren's syndrome, multiple sclerosis, overactive bladder, bronchial hyperreactivity, asthma, stroke, bronchitis, bronchodilation, emphysema, chronic obstructive pulmonary disease ("COPD"), inflammatory dermatitis, adenocarcinoma in glandular tissue, blastoma in embryonic tissue of organs, carcinoma in epithelial tissue, leukemia in tissues that form blood cells, lymphoma in lymphatic tissue, myeloma in bone marrow, sarcoma in connective or supportive tissue, adrenal cancer, AIDS-related lymphoma, anemia, bladder cancer, bone cancer, brain cancer, breast cancer, carcinoid tumors, cervical cancer, chemotherapy, colon cancer, cytopenia, endometrial cancer, esophageal cancer, gastric cancer, head cancer, neck cancer, hepatobiliary cancer, kidney cancer, leukemia, liver cancer, lung cancer, lymphoma, Hodgkin's disease, non-Hodgkin's, nervous system tumors, oral cancer, ovarian cancer, pancreatic cancer, prostate cancer, rectal cancer, skin cancer, stomach cancer, testicular cancer, thyroid cancer, urethral cancer, cancer of bone marrow, multiple myeloma, tumors that metastasize to the bone, tumors infiltrating the nerve and hollow viscus, tumors near neural structures; optionally the cancer pain comprises visceral pain, preferably visceral pain which arises from pancreatic cancer and/or metastases in the abdomen, optionally the cancer pain comprises somatic pain, preferably somatic pain due to one or more of metastasis in the bone, postsurgical pain, sarcomas cancer of the connective tissue, cancer of bone tissue, cancer of blood-forming cells of the bone marrow, multiple myeloma, leukemia, primary or secondary bone cancer, acne vulgaris, atopic dermatitis, urticaria, keloids, hypertrophic scars and rosacea, endothelial dysfunction, Raynaud's syndrome, coronary heart disease ("CHD"), coronary artery disease ("CAD"), heart failure, peripheral arterial disease ("PAD"), diabetes, pulmonary hypertension ("PH"), connective tissue disorder, allergic dermatitis, psoriasis, pruritus, neurogenic cutaneous redness, erythema, sarcoidosis, shock, sepsis, opiate withdrawal syndrome, morphine tolerance, and epilepsy;

(xvi) the method of any one of (i)-(xv), wherein the subject has a condition selected from the group consisting of migraine, headache and a pain associated disease or condition, optionally a headache or migraine is selected from the group consisting of migraine with aura, migraine without aura, hemiplegic migraine, cluster headache, migrainous neuralgia, chronic headache, chronic migraine, medication overuse headache, and tension headache;

(xvii) the method of any one of (i)-(xv), wherein the subject has a ocular disorder associated with photophobia selected from the group consisting of achromatopsia, aniridia, photophobia caused by an anticholinergic drug, aphakia, buphthalmos, cataracts, cone dystrophy, congenital abnormalities of the eye, viral conjunctivitis, corneal abrasion, corneal dystrophy, corneal ulcer, disruption of the corneal epithelium, ectopia lentis, endophthalmitis, eye trauma caused by disease, eye trauma caused by injury, eye trauma caused by infection, chalazion, episcleritis, glaucoma, keratoconus, optic nerve hypoplasia, hydrophthalmos, congenital glaucoma iritis, optic neuritis, pigment dispersion syndrome, pupillary dilation, retinal detachment, scarring of the cornea, sclera and uveitis;

(xviii) the method of any one of (i)-(xv), wherein the subject has a nervous system-related or neurological condition associated with photophobia selected from the group consisting of autism spectrum disorders, Chiari malformation, dyslexia, encephalitis, meningitis, subarachnoid hemorrhage, tumor of the posterior cranial fossa, ankylosing spondylitis, albinism, ariboflavinosis, benzodiazepines, chemotherapy, chikungunya, cystinosis, Ehlers-Danlos syndrome, hangover, influenza, infectious mononucleosis, magnesium deficiency, mercury poisoning, migraine, rabies, and tyrosinemia type II;

(xix) the method of any one of (i)-(xviii), wherein the subject has a photophobia associated disorder selected from the group consisting of migraine with aura, migraine without aura, iritis, uveitis, meningitis, depression, bipolar disorder, cluster headache or anther trigeminal autonomic cephalalgia ("TAC") or blepharospasm, depression, agoraphobia and bipolar disorder;

(xx) the method of any one of (i)-(xix), wherein the antibody is a human, humanized, or chimerized anti-PACAP antibody or antibody fragment; or

(xxi) the method of any one of (i)-(xx), wherein the anti-PACAP antibody or antibody fragment is a human, humanized, or chimerized anti-PACAP antibody or antibody fragment according to claim **1**.

152-261. (canceled)

262. Any of the methods of claim **151**, wherein:

(i) the anti-PACAP antibody or antibody fragment binds to PACAP with a K_D that is between about 10 pM and about 100 pM;

(ii) the method further comprises administering separately or co-administering another agent, optionally selected from a chemotherapeutic, an analgesic, an anti-inflammatory, an immunosuppressant, a cytokine, an antiproliferative, an antiemetic or a cytotoxin or a non-steroidal anti-inflammatory drug ("NSAID"), an opioid analgesic, another antibody or a non-antibody biologic or an anti-NGF antibody or antibody fragment or an anti-Calcitonin Gene-Related Peptide ("CGRP") antibody or antibody fragment and/or an anti-CGRP receptor antibody or antibody fragment or is a cyclooxygenase 1 and/or cyclooxygenase 2 inhibitor or is a NSAID is selected from the group consisting of (1) propionic acid derivatives including ibuprofen, naproxen, naprosyn, diclofenac, and ketoprofen; (2) acetic acid derivatives including tolmetin and sulindac; (3) fenamic acid derivatives including mefenamic acid and meclofenamic acid; (4) biphenylcarboxylic acid derivatives including diflunisal and flufenisal; and (5) oxicams including piroxim, sudoxicam, and isoxicam or is an opioid analgesic selected from the group consisting of codeine, dihydrocodeine, diacetylmorphine, hydrocodone, hydromorphone, levorphanol, oxymorphone, alfentanil, buprenorphine, butorphanol, fentanyl, sufentanil, meperidine, methadone, nalbuphine, propoxyphene, pentazocine, and pharmaceutically acceptable salts thereof or is morphine or a morphine derivative or pharmaceutically acceptable salt thereof;

(iii) the method comprises the combined administration of the opioid analgesic and the anti-PACAP antibody or antigen binding fragment which increase the analgesic effect as compared to either the opioid analgesic or the anti-PACAP antibody or antigen binding fragment administered alone;

(iv) the treated subject has previously received an anti-CGRP antibody or antibody fragment and/or an anti-CGRP receptor antibody or antibody fragment;

(v) the treated subject is a migraineur who did not adequately respond to anti-CGRP antibody and/or an anti-CGRP receptor antibody or antibody fragment treatment;

(vi) the subject has previously received at least one anti-CGRP antibody or antibody fragment and/or an anti-CGRP receptor antibody or antibody fragment administration and has elicited an immune response to the anti-CGRP antibody or antibody fragment and/or the anti-CGRP receptor antibody or antibody fragment; or

(vii) the method of any of the foregoing wherein the antibody or antigen binding fragment thereof ameliorates or treats one or more conditions associated with PACAP expression in a subject in need thereof, said condition selected from the group consisting of: migraine with aura, migraine without aura, hemiplegic migraines, cluster headaches, migrainous neuralgia, chronic headaches, tension headaches, general headaches, hot flush, chronic paroxysmal hemicrania, secondary headaches due to an underlying structural problem in the head, secondary headaches due to an underlying structural problem in the neck, cranial neuralgia, sinus headaches, headache associated with sinusitis, allergy-induced headaches, allergy-induced migraines, trigeminal neuralgia, post-herpetic neuralgia, phantom limb pain, fibromyalgia, reflex sympathetic dystrophy, pain, chronic pain, inflammatory pain, post-operative incision pain, post-surgical pain, trauma-related pain, lower back pain, eye pain, tooth pain, complex regional pain syndrome, cancer pain, primary or metastatic bone cancer pain, fracture pain, osteoporotic fracture pain, pain resulting from burn, gout joint pain, pain associated with sickle cell crises, pain associated with temporomandibular disorders, cirrhosis, hepatitis, neurogenic pain, neuropathic pain, nociceptic pain, visceral pain, menstrual pain, ovarialgia, osteoarthritis pain, rheumatoid arthritis pain, diabetic neuropathy, sciatica, dyspepsia, irritable bowel syndrome, inflammatory bowel disease, Crohn's disease, ileitis, ulcerative colitis, renal colic, dysmenorrhea, cystitis, interstitial cystitis, menstrual period, labor, menopause, pancreatitis, schizophrenia, depression, post-traumatic stress disorder, anxiety disorders, autoimmune diabetes, Sjögren's syndrome, multiple sclerosis, overactive bladder, bronchial hyperreactivity, asthma, stroke, bronchitis, bronchodilation, emphysema, chronic obstructive pulmonary disease ("COPD"), inflammatory dermatitis, adenocarcinoma in glandular tissue, blastoma in embryonic tissue of organs, carcinoma in epithelial tissue, leukemia in tissues that form blood cells, lymphoma in lymphatic tissue, myeloma in bone marrow, sarcoma in connective or supportive tissue, adrenal cancer, AIDS-related lymphoma, anemia, bladder cancer, bone cancer, brain cancer, breast cancer, carcinoid tumors, cervical cancer, chemotherapy, colon cancer, cytopenia, endometrial cancer, esophageal cancer, gastric cancer, head cancer, neck cancer, hepatobiliary cancer, kidney cancer, leukemia, liver cancer, lung cancer, lymphoma, Hodgkin's disease, non-Hodgkin's, nervous system tumors, oral cancer, ovarian cancer, pancreatic cancer, prostate cancer, rectal cancer, skin cancer, stomach cancer, testicular cancer, thyroid cancer, urethral cancer, cancer of bone marrow, multiple myeloma, tumors that metastasize to the bone, tumors infiltrating the nerve and hollow viscus, tumors near neural structures, acne vulgaris, atopic dermatitis, urticaria, keloids, hypertrophic scars and rosacea, endothelial dysfunction, Raynaud's syndrome, coronary heart disease ("CHD"), coronary artery disease ("CAD"), heart failure, peripheral arterial disease ("PAD"), diabetes, pulmonary hypertension ("PH"), connective tissue disorder, allergic dermatitis, psoriasis, pruritus, neurogenic cutaneous redness, erythema, sarcoidosis, shock, sepsis, opiate withdrawal syndrome, morphine tolerance, and epilepsy.

263-277. (canceled)

278. An anti-PACAP antibody or antibody fragment or a method according to claim **1** or **262** which:

(i) inhibits the effects of PACAP on vasodilation;

(ii) inhibits the effects of PACAP on cAMP production;

(iii) inhibits the effects of PACAP on PLC resulting in reduced Ca^{++} and PLD levels;

(v) inhibits the effects of PACAP on adenylate cyclase activity;

(vi) inhibits the effects of PACAP on its binding to any or all of PAC1-R, VPAC1-R or VPAC2-R;

(vii) inhibits the effects of PACAP on neurodevelopment;

(viii) inhibits the effects of PACAP on neuroprotection;

(ix) inhibits the effects of PACAP on neuromodulation;

(x) inhibits the effects of PACAP on neurogenic inflammation;

(xi) inhibits the effects of PACAP on nociception;

(xii) modulates the interaction of PACAP with binding the cell surface, e.g. via at least one glycosaminoglycan ("GAG"); optionally wherein said at least one GAG comprises one or more of heparin, chondroitin, keratin, and hyaluronic acid;

(xiii) blocks or inhibits receptor-independent cellular uptake of PACAP38 and/or PACAP27; or it

(xiv) inhibits or blocks GAG-dependent uptake of PACAP38 and/or PACAP27 by cells.

279-291. (canceled)

292. A method of therapy or prophylaxis which comprises the administration of an anti-PACAP antibody or antibody fragment according to claim **1**.

293. A composition for use in human therapy containing an anti-PACAP antibody or antibody fragment according to claim **1**.

294. The composition of claim **293**, which:

(i) contains another active agent, e.g., selected from a chemotherapeutic, an analgesic, an anti-inflammatory, an immunosuppressant, a cytokine, an antiproliferative, an antiemetic or a cytotoxin, optionally the analgesic is a non-steroidal anti-inflammatory drug ("NSAID"), an opioid analgesic, another antibody or a non-antibody biologic, the other antibody is an anti-NGF antibody or antibody fragment, the other antibody is an anti-Calcitonin Gene-Related Peptide ("CGRP") antibody or antibody fragment and/or an anti-CGRP receptor antibody or antibody fragment, optionally the NSAID is a cyclooxygenase 1 and/or cyclooxygenase 2 inhibitor, the NSAID is selected from the group consisting of (1) propionic acid derivatives including ibuprofen, naproxen, naprosyn, diclofenac, and ketoprofen; (2) acetic acid derivatives including tolmetin and sulindac; (3) fenamic acid derivatives including mefenamic acid and meclofenamic acid; (4) biphenylcarboxylic acid derivatives including diflunisal and flufenisal; and (5) oxicams including piroxim, sudoxicam, and isoxicam, the opioid analgesic is selected from the group consisting of codeine, dihydrocodeine, diacetylmorphine, hydrocodone, hydromorphone, levorphanol, oxymorphone, alfentanil, buprenorphine, butorphanol, fentanyl, sufentanil, meperidine, methadone, nalbuphine, propoxyphene, pentazocine, and pharmaceutically acceptable salts thereof, the opioid analgesic is morphine or a morphine derivative or pharmaceutically acceptable salt thereof, the opioid analgesic and the anti-PACAP antibody or antigen binding fragment increase the analgesic effect as compared to either the opioid analgesic or the anti-PACAP antibody or antigen binding fragment administered alone, the anti-PACAP antibody or fragment and another active agent combined therewith or administered in combination elicit a synergistic or additive effect on the treatment or prevention of a PACAP associated effect, e.g., migraine or on pain.

295-311. (canceled)

312. A composition for use in human therapy containing an anti-PACAP antibody or antibody fragment according to claim **278**.

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