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(54) Title: SIMIAN ADENOVIRUS NUCLEIC ACID AND AMINO ACID SEQUENCES, VECTORS CONTAINING SAME, AND METHODS OF USE

(57) Abstract: A recombinant vector comprises simian adenovirus sequences and a heterologous gene under the control of regulatory sequences. A cell line which expresses simian adenovirus gene(s) is also disclosed. Methods of using the vectors and cell lines are provided.

SIMIAN ADENOVIRUS NUCLEIC ACID AND AMINO ACID SEQUENCES, VECTORS CONTAINING SAME, AND METHODS OF USE

BACKGROUND OF THE INVENTION

Adenovirus is a double-stranded DNA virus with a genome size of about 36 kilobases (kb), which has been widely used for gene transfer applications due to its ability to achieve highly efficient gene transfer in a variety of target tissues and large transgene capacity. Conventionally, E1 genes of adenovirus are deleted and replaced with a transgene cassette consisting of the promoter of choice, cDNA sequence of the gene of interest and a poly A signal, resulting in a replication defective recombinant virus.

Adenoviruses have a characteristic morphology with an icosahedral capsid consisting of three major proteins, hexon (II), penton base (III) and a knobbed fibre (IV), along with a number of other minor proteins, VI, VIII, IX, IIIa and IVa2 [W.C. Russell, *J. Gen Virol.*, **81**:2573-2604 (Nov 2000)]. The virus genome is a linear, double-stranded DNA with a terminal protein attached covalently to the 5' termini, which have inverted terminal repeats (ITRs). The virus DNA is intimately associated with the highly basic protein VII and a small peptide termed mu. Another protein, V, is packaged with this DNA-protein complex and provides a structural link to the capsid via protein VI. The virus also contains a virus-encoded protease, which is necessary for processing of some of the structural proteins to produce mature infectious virus.

Recombinant adenoviruses have been described for delivery of molecules to host cells. See, US Patent 6,083,716, which describes the genome of two chimpanzee adenoviruses.

What is needed in the art are more effective vectors which avoid the effect of pre-existing immunity to selected adenovirus serotypes in the population and/or which are useful for repeat administration and for titer boosting by second vaccination, if required.

Summary of the Invention

The present invention provides the isolated nucleic acid sequences and amino acid sequences of six simian adenoviruses, vectors containing these sequences, and cell lines expressing simian adenovirus genes. Also provided are a number of methods for using the vectors and cells of the invention.

The methods of the invention involve delivering one or more selected heterologous gene(s) to a mammalian patient by administering a vector of the invention. Because the various vector constructs are derived from simian rather than from human adenoviruses, the immune system of the non-simian human or veterinary patient is not primed to respond immediately to the vector as a foreign antigen. Use of the compositions of this invention thus permits a more stable expression of the selected transgene when administered to a non-simian patient. Use of the compositions of this invention for vaccination permits presentation of a selected antigen for the elicitation of protective immune responses. Without wishing to be bound by theory, the ability of the adenoviruses of the invention to transduce human dendritic cells is at least partially responsible for the ability of the recombinant constructs of the invention to induce an immune response. The recombinant simian adenoviruses of this invention may also be used for producing heterologous gene products *in vitro*. Such gene products are themselves useful in a variety for a variety of purposes such as are described herein.

These and other embodiments and advantages of the invention are described in more detail below.

Brief Description of the Drawings

Fig. 1 provides an alignment of the amino acid sequences of the L1 and a portion of the L2 loops of the capsid protein hexon of the chimpanzee adenovirus C1 [SEQ ID NO:13], chimpanzee adenovirus C68 (Pan-9) [SEQ ID NO:14], and the novel Pan5 [SEQ ID NO:15], Pan6 [SEQ ID NO: 16] and Pan7 [SEQ ID NO: 17] chimpanzee adenovirus sequences of the invention. The intervening conserved region is part of the pedestal domain conserved between adenovirus serotypes.

Fig. 2 provides an alignment of the amino acid sequences of the fiber knob domains of chimpanzee C68 (Pan-9) [SEQ ID NO:18], Pan-6 [SEQ ID NO:19], Pan-7 [SEQ ID NO:20], and Pan-5 [SEQ ID NO:21] and the human adenoviruses serotypes 2 [SEQ ID NO:22] and 5 [SEQ ID NO:23].

DETAILED DESCRIPTION OF THE INVENTION

The invention provides novel nucleic acid and amino acid sequences from Ad Pan5 [SEQ ID NO:1-4, 15 and 21], Ad Pan6 [SEQ ID NO: 5-8, 16, 19], and Ad serotype

Pan7 [SEQ ID NO: 9-12, 17, 20], which were originally isolated from chimpanzee lymph nodes. In several instances throughout the specification, these adenoviruses are alternatively termed herein C5, C6 and C7, respectively. Also provided are sequences from adenovirus SV1 [SEQ ID NO: 24-28], which was originally isolated from the kidney cells of cynomolgus monkey. The invention also provides sequences of adenoviruses SV-25 [SEQ ID NO:29-33] and SV-39 [SEQ ID NO: 34-37], which were originally isolated from rhesus monkey kidney cells.

The present invention provides novel adenovirus vectors and packaging cell lines to produce those vectors for use in the *in vitro* production of recombinant proteins or fragments or other reagents. The invention further provides compositions for use in delivering a heterologous molecule for therapeutic or vaccine purposes. Such therapeutic or vaccine compositions contain the adenoviral vectors carrying an inserted heterologous molecule. In addition, novel sequences of the invention are useful in providing the essential helper functions required for production of recombinant adeno-associated viral (AAV) vectors. Thus, the invention provides helper constructs, methods and cell lines which use these sequences in such production methods.

The term "substantial homology" or "substantial similarity," when referring to a nucleic acid or fragment thereof, indicates that, when optimally aligned with appropriate nucleotide insertions or deletions with another nucleic acid (or its complementary strand), there is nucleotide sequence identity in at least about 95 to 99% of the aligned sequences.

The term "substantial homology" or "substantial similarity," when referring to amino acids or fragments thereof, indicates that, when optimally aligned with appropriate amino acid insertions or deletions with another amino acid (or its complementary strand), there is amino acid sequence identity in at least about 95 to 99% of the aligned sequences. Preferably, the homology is over full-length sequence, or a protein thereof, or a fragment thereof which is at least 8 amino acids, or more desirably, at least 15 amino acids in length. Examples of suitable fragments are described herein.

The term "percent sequence identity" or "identical" in the context of nucleic acid sequences refers to the residues in the two sequences that are the same when aligned for maximum correspondence. The length of sequence identity comparison may be over the full-length of the genome (e.g., about 36 kbp), the full-length of an open reading frame of a gene, protein, subunit, or enzyme [see, e.g., the tables providing the adenoviral coding

regions], or a fragment of at least about 500 to 5000 nucleotides, is desired. However, identity among smaller fragments, e.g. of at least about nine nucleotides, usually at least about 20 to 24 nucleotides, at least about 28 to 32 nucleotides, at least about 36 or more nucleotides, may also be desired. Similarly, "percent sequence identity" may be readily determined for amino acid sequences, over the full-length of a protein, or a fragment thereof. Suitably, a fragment is at least about 8 amino acids in length, and may be up to about 700 amino acids. Examples of suitable fragments are described herein.

Identity is readily determined using such algorithms and computer programs as are defined herein at default settings. Preferably, such identity is over the full length of the protein, enzyme, subunit, or over a fragment of at least about 8 amino acids in length. However, identity may be based upon shorter regions, where suited to the use to which the identical gene product is being put.

As described herein, alignments are performed using any of a variety of publicly or commercially available Multiple Sequence Alignment Programs, such as "Clustal W", accessible through Web Servers on the internet. Alternatively, Vector NTI utilities are also used. There are also a number of algorithms known in the art that can be used to measure nucleotide sequence identity, including those contained in the programs described above. As another example, polynucleotide sequences can be compared using Fasta, a program in GCG Version 6.1. Fasta provides alignments and percent sequence identity of the regions of the best overlap between the query and search sequences. For instance, percent sequence identity between nucleic acid sequences can be determined using Fasta with its default parameters (a word size of 6 and the NOPAM factor for the scoring matrix) as provided in GCG Version 6.1, herein incorporated by reference. Similarly programs are available for performing amino acid alignments. Generally, these programs are used at default settings, although one of skill in the art can alter these settings as needed. Alternatively, one of skill in the art can utilize another algorithm or computer program that provides at least the level of identity or alignment as that provided by the referenced algorithms and programs.

As used throughout this specification and the claims, the term "comprise" and its variants including, "comprises", "comprising", among other variants, is inclusive of other components, elements, integers, steps and the like. The term "consists of" or "consisting of" are exclusive of other components, elements, integers, steps and the like.

I. The Simian Adenovirus Sequences

The invention provides nucleic acid sequences and amino acid sequences of Pan5, Pan6, Pan7, SV1, SV25 and SV39, which are isolated from the other viral material with which they are associated in nature.

A. Nucleic Acid Sequences

The Pan5 nucleic acid sequences of the invention include nucleotides 1 to 36462 of SEQ ID NO:1. The Pan6 nucleic acid sequences of the invention include nucleotides 1 to 36604 of SEQ ID NO: 5. The Pan7 nucleic acid sequences of the invention include nucleotides 1 to 36535 of SEQ ID NO: 9. The SV1 nucleic acid sequences of the invention include nucleotides 1 to 34264 of SEQ ID NO: 24. The SV25 nucleic acid sequences of the invention include nucleotides 1 to 31044 of SEQ ID NO: 29. The SV39 nucleic acid sequences of the invention include nucleotides 1 to 34115 of SEQ ID NO: 34. See, Sequence Listing, which is incorporated by reference herein.

The nucleic acid sequences of the invention further encompass the strand which is complementary to the sequences of SEQ ID NO: 5, 9, 24, 29 and 34, as well as the RNA and cDNA sequences corresponding to the sequences of these sequences figures and their complementary strands. Further included in this invention are nucleic acid sequences which are greater than 95 to 98%, and more preferably about 99 to 99.9% homologous or identical to the Sequence Listing. Also included in the nucleic acid sequences of the invention are natural variants and engineered modifications of the sequences provided in SEQ ID NO: 5, 9, 24, 29 and 34 and their complementary strands. Such modifications include, for example, labels that are known in the art, methylation, and substitution of one or more of the naturally occurring nucleotides with a degenerate nucleotide.

The invention further encompasses fragments of the sequences of Pan5, Pan6, Pan7, SV1, SV25 and SV39, their complementary strand, cDNA and RNA complementary thereto. Suitable fragments are at least 15 nucleotides in length, and encompass functional fragments, i.e., fragments which are of biological interest. For example, a functional fragment can express a desired adenoviral product or may

be useful in production of recombinant viral vectors. Such fragments include the gene sequences and fragments listed in the tables below.

The following tables provide the transcript regions and open reading frames in the simian adenovirus sequences of the invention. For certain genes, the transcripts and open reading frames (ORFs) are located on the strand complementary to that presented in SEQ ID NO: 5, 9, 24, 29 and 34. See, e.g., E2b, E4 and E2a. The calculated molecular weights of the encoded proteins are also shown. Note that the E1a open reading frame Pan5 [nt 576-1436 of SEQ ID NO:1], Pan6 [nt 576 to 1437 of SEQ ID NO: 5] and Pan7 [nt 576 to 1437 of SEQ ID NO: 9] contain internal splice sites. These splice sites are noted in the following tables.

Ad Pan-5 [SEQ ID NO:1]				
Regions		Start (nt)	End (nt)	*M.W. (Daltons)*
ITR		1	120	-
E1a	Transcript	478		-
	13S	576-664,1233-1436		*28120*
	12S	576-1046, 1233-1436		*24389*
	9S	576-644,1233-1436		*9962*
	Transcript		1516	-
E1b	Transcript	1552		-
	Small T	1599	2171	*22317*
	Large T	1904	3412	*55595*
	IX	3492	3920	*14427*
	Transcript		3959	-
E2b	Transcript	10349		-
	PTP	10349	8451	*72930*
	Polymerase	8448	5083	*127237*
	IVa2	5604	3980	*50466*
	Transcript		3960	
28.1 kD		5155	5979	*28141*
Agnoprotein		7864	8580	*25755*
L1	Transcript	10849		-
	52/55D	10851	12025	
	IIIa	12050	13819	*65669*
	Transcript		13832	-
	Transcript	13894		-
L2	Penton	13898	15490	*59292*
	VII	15494	16078	*21478*
	V	16123	17166	*39568*
	Mu	17189	17422	*8524*
	transcript		17442	-
	Transcript	17488		-
L3	VI	17491	18222	*26192*
	Hexon	18315	21116	*104874*
	Endoprotease	20989	21783	*28304*
	transcript		21811	-

Ad Pan-5 (cont'd) [SEQ ID NO:1]				
Regions		Start (nt)	End (nt)	*M.W. (Daltons)*
E2a	Transcript	26782		-
	DBP	23386	21845	*57358*
	transcript		21788	-
L4	Transcript	23406		-
	100kD	23412	25805	*88223*
	33 kD homolog	25525	26356	*24538*
	VIII	26428	27111	*24768*
	transcript		27421	-
E3	Transcript	26788		-
	Orf #1	27112	27432	*12098*
	Orf #2	27386	28012	*23040*
	Orf #3	27994	28527	*19525*
	Orf #4	28557	29156	*22567*
	Orf #5	29169	29783	*22267*
	Orf #6	29798	30673	*31458*
	Orf #7	30681	30956	*10477*
	Orf #8	30962	31396	*16523*
	Orf #9	31389	31796	*15236*
	transcript		31837	-
L5	Transcript	32032		-
	Fiber	32035	33372	*47670*
	transcript		33443	-
E4	Transcript	36135		-
	Orf 7	33710	33462	*9191*
	Orf 6	34615	33710	*35005*
	Orf 4	34886	34521	*13878*
	Orf 3	35249	34896	*13641*
	Orf 2	35635	35246	*14584*
	Orf 1	36050	35676	*13772*
	Transcript		33437	-
ITR		36343	36462	-

Ad Pan-6 [SEQ ID NO: 5]				
Regions		Start (nt)	End (nt)	*M.W. (Daltons)*
ITR		1	123	-
E1a	transcript	478		-
	13S	576-1143, 1229-1437		*28291*
	12S	576-1050, 1229-1437		*24634*
	9S	576 – 645, 1229-1437		*10102*
	transcript		1516	-
E1b	transcript	1553		-
	Small T	1600	2172	*22315*
	LargeT	1905	3413	*55594*
	IX	3498	3926	*14427*
	transcript		3965	-
E2b	transcript	10341		-
	PTP	10340	8451	*72570*
	Polymerase	8445	5089	*126907*
	IVa2	5610	3986	*50452*
	transcript		3966	-
L1	transcript	10838		-
	52/55 kD	10840	12012	*44205*
	IIIa	12036	13799	*65460*
	Transcript		13812	-
28.1 kd		5161	5985	*28012*
Agnoprotein		7870	8580	*25382*
L2	transcript	13874		-
	Penton	13878	15467	*59314*
	VII	15471	16055	*21508*
	V	16100	17137	*39388*
	Mu	17160	17393	*8506*
	transcript		17415	-
L3	transcript	17466		-
	VI	17469	18188	*25860*
	Hexon	18284	21112	*106132*
	Endoprotease	21134	21754	*23445*
	transcript		21803	-
E2a	transcript	26780		-
	DBP	23375	21837	*57299*
	transcript		21780	-

Ad Pan-6 (cont'd) [SEQ ID NO:5]				
Regions		Start (nt)	End (nt)	*M.W. (Daltons)*
L4	Transcript	23398		-
	100kD	23404	25806	*88577*
	33 kD homolog	25523	26357	*24609*
	VIII	26426	27109	*24749*
	transcript		27419	-
E3	transcript	26786		-
	Orf #1	27110	27430	*12098*
	Orf #2	27384	28007	*22880*
	Orf #3	27989	28519	*19460*
	Orf #4	28553	29236	*25403*
	Orf #5	29249	29860	*22350*
	Orf #6	29875	30741	*31028*
	Orf #7	30749	31024	*10469*
	Orf #8	31030	31464	*16540*
	Orf #9	31457	31864	*15264*
	transcript		31907	-
L5	transcript	32159		
	Fiber	32162	33493	*47364*
	transcript		33574	-
E4	transcript	36276		-
	Orf 7	33841	33593	*9177*
	Orf 6	34746	33841	*35094*
	Orf 4	35017	34652	*13937*
	Orf 3	35380	35027	*13627*
	Orf 2	35766	35377	*14727*
	Orf 1	36181	35807	*13739*
	transcript		33558	-
ITR		36482	36604	-

Ad Pan-7 [SEQ ID NO:9]				
Regions		Start (nt)	End (nt)	*M.W. (Daltons)*
ITR		1	132	-
E1a	transcript	478		-
	13S	576 – 1143, 1229-1437		*28218*
	12S	576 – 1050, 1229- 1437		*24561*
	9S	576 – 645, 1229 – 1437		*10102*
	transcript		1516	-
E1b	transcript	1553		-
	Small T	1600	2178	*22559*
	LargeT	1905	3419	*55698*
	IVa2	3992	5616	*50210*
	transcript		3971	-
E2b	transcript	10341		-
	PTP	10340	8457	*72297*
	Polymerase	8451	5095	*126994*
	IX	3504	3932	*14441*
	transcript		3972	-
28.1kD		5167	5991	*28028*
Agnoprotein		7876	8586	*25424*
L1	transcript	10834		
	52/55 kD	10836	12011	*44302*
	IIIa	12035	13795	*65339*
	transcript		13808	-
L2	transcript	13870		-
	Penton	13874	15469	*59494*
	VII	15473	16057	*21339*
	V	16102	17139	*39414*
	Mu	17167	17400	*8506*
	transcript		17420	-
L3	transcript	17467		-
	VI	17470	18198	*26105*
	Hexon	18288	21086	*104763*
	Endoprotease	21106	21732	*23620*
	transcript		21781	-
E2a	transcript	26764		-
	DBP	23353	21815	*57199*
	transcript		21755	-

Ad Pan-7 (cont'd) [SEQ ID NO: 9]				
Regions		Start (nt)	End (nt)	*M.W. (Daltons)*
L4	transcript	23370		-
	100kD	23376	25781	*88520*
	33 kD homolog	25489	26338	*25155*
	VIII	26410	27093	*24749*
	transcript		27403	-
E3	transcript	26770		-
	Orf #1	27094	27414	*12056*
	Orf #2	27368	27988	*22667*
	Orf #3	27970	28500	*19462*
	Orf #4	28530	29150	*22999*
	Orf #5	29163	29777	*22224*
	Orf #6	29792	30679	*32153*
	Orf #7	30687	30962	*10511*
	Orf #8	30968	31399	*16388*
	Orf #9	31392	31799	*15205*
	transcript		31842	-
L5	transcript	32091		-
	Fiber	32094	33425	*47344*
	transcript		33517	-
E4	transcript	36208		-
	Orf 7	33784	33536	*9191*
	Orf 6	34689	33784	*35063*
	Orf 4	34960	34595	*13879*
	Orf 3	35323	34970	*13641*
	Orf 2	35709	35320	*14644*
	Orf 1	36123	35749	*13746*
	transcript		33501	-
ITR		36404	36535	-

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	Ad SV-1 [SEQ ID NO:24]		Ad SV-25 [SEQ ID NO:29]		Ad SV-39 [SEQ ID NO: 34]	
Region	Start	End	Start	End	Start	End
ITR	1	106	1	133	1	150
E1a	352	1120	-	-	404	1409
E1b	1301	2891	359	2273	1518	3877
E2b	9257	2882	9087	2754	10143	3868
E2a	24415	20281	24034	20086	25381	21228
E3	24974	27886	24791	25792	25790	29335
E4	33498	30881	30696	28163	33896	31157
ITR	34145	34264	30912	31044	33966	34115

	Ad SV-1 [SEQ ID NO:24]		Ad SV-25 [SEQ ID NO:29]		Ad SV-39 [SEQ ID NO: 34]	
Region	Start	End	Start	End	Start	End
ITR	1	106	1	133	1	150
L1	9513	12376	9343	12206	10416	13383
L2	12453	15858	12283	15696	13444	16877
L3	15910	20270	15748	20080	17783	21192
L4	21715	25603	21526	25420	22659	26427
L5	28059	30899	25320	28172	29513	31170
ITR	34145	34264	30912	31044	33966	34115

	protein	Ad SV-1, SEQ ID NO: 24		
		Start	End	*M.W.*
ITR		1	106	-
E1a	13S	459	953	*18039*
	12S			
E1b	Small T			
	LargeT	1301	2413	*42293*
	IX	2391	2885	*16882*
E2b	IVa2	4354	2924	*54087*
	Polymerase	6750	4027	*102883*
	PTP	9257	7371	*72413*
	Agno-protein	6850	7455	*20984*
L1	52/55 kD	9515	10642	*42675*
	IIIa	10663	12372	*636568*
L2	Penton	12454	13965	*56725*
	VII	13968	14531	*20397*
	V	14588	15625	*39374*
	Mu	15645	15857	*7568*
L3	VI	15911	16753	*30418*
	Hexon	16841	19636	*104494*
	Endoprotease	19645	20262	*23407*
2a	DBP	21700	20312	*52107*
L4	100kD	21721	24009	*85508*
	VIII	24591	25292	*25390*

	protein	Ad SV-1 (cont'd) SEQ ID NO: 24		
		Start	End	*M.W.*
E3	Orf #1	25292	25609	*11950*
	Orf #2	25563	26081	*18940*
	Orf #3	26084	26893	*30452*
	Orf #4	26908	27180	*10232*
	Orf #5	27177	17512	*12640*
	Orf #6	27505	27873	*13639*
L5	Fiber #2	28059	29150	*39472*
	Fiber #1	29183	30867	*61128*
E4	Orf 7	31098	30892	*7837*
	Orf 6	31982	31122	*33921*
	Orf 4	32277	31915	*14338*
	Orf 3	32629	32279	*13386*
	Orf 2	33018	32626	*14753*
	Orf 1	33423	33043	*14301*
ITR		34145	34264	

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	protein	Ad SV-25, SEQ ID NO:29			Ad SV-39, SEQ ID NO:34		
		Start	End	*M.W.*	Start	End	*M.W.*
ITR		1	133	-	1	150	-
E1a	13S				492	1355	*28585*
	12S				492	1355	*25003*
E1b	Small T	478	1030	*20274*	1518	2075	*21652*
	Large T	829	2244	*52310*	1823	3349	*55534*
	IX	2306	2716	*13854*	3434	3844	*14075*
E2b	IVa2	4208	2755	*54675*	3912	5141	*46164*
	Poly-merase	6581	3858	*102839*	7753	5033	*103988*
	PTP	9087	7207	*71326*	10143	8335	*69274*
	Agno-protein	6681	7139	*16025*	-	-	-
L1	52/55 kD	9345	10472	*42703*	10418	11608	*44232*
	IIIa	10493	12202	*63598*	11574	13364	*66078*
L2	Penton	12284	13801	*56949*	13448	14959	*56292*
	VII	13806	14369	*20369*	14960	15517	*20374*
	V	14426	15463	*39289*	15567	16628	*39676*
	Mu	15483	15695	*7598*	16650	16871	*7497*
L3	VI	15749	16591	*30347*	16925	17695	*28043*
	Hexon	16681	19446	*104035*	17785	20538	*102579*
	Endo-protease	19455	20072	*23338*	20573	21181	*22716*
2a	DBP	21511	20123	*52189*	22631	21231	*53160*
L4	100kD	21532	23829	*85970*	22659	25355	*100362*
	VIII	24408	25109	*25347*	25410	26108	*25229*

	protein	Ad SV-25, SEQ ID NO:29 (cont'd)			Ad SV-39, SEQ ID NO:34, (cont'd)		
		Start	End	*M.W.*	Start	End	*M.W.*
E3	Orf #1	25109	25426	*11890*	26375	27484	*42257*
	Orf #2				27580	28357	*29785*
	Orf #3				28370	28645	*10514*
	Orf #4				28863	29333	*18835*
	Orf #5						
	Orf #6						
L5	Fiber #2	25380	26423	*37529*			
	Fiber #1	26457	28136	*60707*	29515	31116	*56382*
E4	Orf 7				31441	31118	*11856*
	Orf 6	29255	28395	*33905*	32292	31438	*33437*
	Orf 4	29550	29188	*14399*	32587	32222	*13997*
	Orf 3	29902	29552	*13284*	32954	32607	*13353*
	Orf 2	30291	29899	*14853*	33348	32959	*14821*
	Orf 1	30316	30696	*14301*	33764	33378	*14235*
ITR		30912	31044		33966	34115	

The Pan5, Pan6, Pan7, SV1, SV25 and SV39 adenoviral nucleic acid sequences are useful as therapeutic agents and in construction of a variety of vector systems and host cells. As used herein, a vector includes any suitable nucleic acid molecule including, naked DNA, a plasmid, a virus, a cosmid, or an episome. These sequences and products may be used alone or in combination with other adenoviral sequences or fragments, or in combination with elements from other adenoviral or non-adenoviral sequences. The adenoviral sequences of the invention are also useful as antisense delivery vectors, gene therapy vectors, or vaccine vectors. Thus, the invention further provides nucleic acid molecules, gene delivery vectors, and host cells which contain the Ad sequences of the invention.

For example, the invention encompasses a nucleic acid molecule containing simian Ad ITR sequences of the invention. In another example, the invention provides a nucleic acid molecule containing simian Ad sequences of the invention encoding a desired Ad gene product. Still other nucleic acid molecule constructed using the sequences of the invention will be readily apparent to one of skill in the art, in view of the information provided herein.

In one embodiment, the simian Ad gene regions identified herein may be used in a variety of vectors for delivery of a heterologous molecule to a cell. For example, vectors are generated for expression of an adenoviral capsid protein (or fragment thereof) for purposes of generating a viral vector in a packaging host cell. Such vectors may be designed for expression in trans. Alternatively, such vectors are designed to provide cells which stably contain sequences which express desired adenoviral functions, e.g., one or more of E1a, E1b, the terminal repeat sequences, E2a, E2b, E4, E4ORF6 region.

In addition, the adenoviral gene sequences and fragments thereof are useful for providing the helper functions necessary for production of helper-dependent viruses (e.g., adenoviral vectors deleted of essential functions or adeno-associated viruses (AAV)). For such production methods, the simian adenoviral sequences of the invention are utilized in such a method in a manner similar to those described for the human Ad. However, due to the differences in sequences between the simian adenoviral sequences of the invention and those of human Ad, the use of the sequences of the invention essentially eliminate the possibility of homologous recombination with helper functions in a host cell carrying human Ad E1 functions, e.g., 293 cells, which may produce infectious adenoviral contaminants during rAAV production.

Methods of producing rAAV using adenoviral helper functions have been described at length in the literature with human adenoviral serotypes. See, e.g., US Patent 6,258,595 and the references cited therein. See, also, US Patent 5,871,982; WO 99/14354; WO 99/15685; WO 99/47691. These methods may also be used in production of non-human serotype AAV, including non-human primate AAV serotypes. The simian adenoviral gene sequences of the invention which provide the necessary helper functions (e.g., E1a, E1b, E2a and/or E4 ORF6) can be particularly useful in providing the necessary adenoviral function while minimizing or eliminating the possibility of

recombination with any other adenoviruses present in the rAAV-packaging cell which are typically of human origin. Thus, selected genes or open reading frames of the adenoviral sequences of the invention may be utilized in these rAAV production methods.

Alternatively, recombinant adenoviral simian vectors of the invention may be utilized in these methods. Such recombinant adenoviral simian vectors may include, e.g., a hybrid chimp Ad/AAV in which chimp Ad sequences flank a rAAV expression cassette composed of, e.g., AAV 3' and/or 5' ITRs and a transgene under the control of regulatory sequences which control its expression. One of skill in the art will recognize that still other simian adenoviral vectors and/or gene sequences of the invention will be useful for production of rAAV and other viruses dependent upon adenoviral helper.

In still another embodiment, nucleic acid molecules are designed for delivery and expression of selected adenoviral gene products in a host cell to achieve a desired physiologic effect. For example, a nucleic acid molecule containing sequences encoding an adenovirus E1a protein of the invention may be delivered to a subject for use as a cancer therapeutic. Optionally, such a molecule is formulated in a lipid-based carrier and preferentially targets cancer cells. Such a formulation may be combined with other cancer therapeutics (e.g., cisplatin, taxol, or the like). Still other uses for the adenoviral sequences provided herein will be readily apparent to one of skill in the art.

In addition, one of skill in the art will readily understand that the Ad sequences of the invention can be readily adapted for use for a variety of viral and non-viral vector systems for in vitro, ex vivo or in vivo delivery of therapeutic and immunogenic molecules. For example, the Pan5, Pan6, Pan7, SV1, SV25 and/or SV39 simian Ad genomes of the invention can be utilized in a variety of rAd and non-rAd vector systems. Such vectors systems may include, e.g., plasmids, lentiviruses, retroviruses, poxviruses, vaccinia viruses, and adeno-associated viral systems, among others. Selection of these vector systems is not a limitation of the present invention.

The invention further provides molecules useful for production of the simian and simian-derived proteins of the invention. Such molecules which carry polynucleotides including the simian Ad DNA sequences of the invention can be in the form of naked DNA, a plasmid, a virus or any other genetic element.

B. Simian Adenoviral Proteins of the Invention

The invention further provides gene products of the above adenoviruses, such as proteins, enzymes, and fragments thereof, which are encoded by the adenoviral nucleic acids of the invention. The invention further encompasses Pan5, Pan6 and Pan7, SV1, SV25 and SV39 proteins, enzymes, and fragments thereof, having the amino acid sequences encoded by these nucleic acid sequences which are generated by other methods. Such proteins include those encoded by the open reading frames identified in the tables above, in Figs. 1 and 2, and fragments thereof.

Thus, in one aspect, the invention provides unique simian adenoviral proteins which are substantially pure, i.e., are free of other viral and proteinaceous proteins. Preferably, these proteins are at least 10% homogeneous, more preferably 60% homogeneous, and most preferably 95% homogeneous.

In one embodiment, the invention provides unique simian-derived capsid proteins. As used herein, a simian-derived capsid protein includes any adenoviral capsid protein that contains a Pan5, Pan6, Pan7, SV1, SV25 or SV39 capsid protein or a fragment thereof, as defined above, including, without limitation, chimeric capsid proteins, fusion proteins, artificial capsid proteins, synthetic capsid proteins, and recombinantly capsid proteins, without limitation to means of generating these proteins.

Suitably, these simian-derived capsid proteins contain one or more Pan5, Pan6, Pan7, SV1, SV25 or SV39 regions or fragments thereof (e.g., a hexon, penton, fiber or fragment thereof) in combination with capsid regions or fragments thereof of different adenoviral serotypes, or modified simian capsid proteins or fragments, as described herein. A "modification of a capsid protein associated with altered tropism" as used herein includes an altered capsid protein, i.e, a penton, hexon or fiber protein region, or fragment thereof, such as the knob domain of the fiber region, or a polynucleotide encoding same, such that specificity is altered. The simian-derived capsid may be constructed with one or more of the simian Ad of the invention or another Ad serotypes which may be of human or non-human origin. Such Ad may be obtained from a variety of sources including the ATCC, commercial and academic sources, or the sequences of the Ad may be obtained from GenBank or other suitable sources.

The amino acid sequences of the simian adenoviruses penton proteins of the invention are provided herein. The AdPan5 penton protein is provided in SEQ ID

NO:2. The AdPan7 penton is provided in SEQ ID NO:6. The AdPan6 penton is provided in SEQ ID NO:10. The SV1 penton is provided in SEQ ID NO:25. The SV25 penton protein is provided in SEQ ID NO:30. The SV39 penton is provided in SEQ ID NO:35. Suitably, any of these penton proteins, or unique fragments thereof, may be utilized for a variety of purposes. Examples of suitable fragments include the penton having N-terminal and/or C-terminal truncations of about 50, 100, 150, or 200 amino acids, based upon the amino acid numbering provided above and in SEQ ID NO:2; SEQ ID NO:6; SEQ ID NO:25; SEQ ID NO:30, or SEQ ID NO:35. Other suitable fragments include shorter internal, C-terminal, or N-terminal fragments. Further, the penton protein may be modified for a variety of purposes known to those of skill in the art.

The invention further provides the amino acid sequences of the hexon protein of Pan5 [SEQ ID NO:3], Pan6 [SEQ ID NO:7], Pan 7 [SEQ ID NO:11], SV1 [SEQ ID NO:26], SV25 [SEQ ID NO:31], and/or SV39 [SEQ ID NO:36]. Suitably, this hexon protein, or unique fragments thereof, may be utilized for a variety of purposes. Examples of suitable fragments include the hexon having N-terminal and/or C-terminal truncations of about 50, 100, 150, 200, 300, 400, or 500 amino acids, based upon the amino acid numbering provided above and in SEQ ID NO: 3, 7, 11, 26, 31 and 36. Other suitable fragments include shorter internal, C-terminal, or N-terminal fragments. For example, one suitable fragment the loop region (domain) of the hexon protein, designated DE1 and FG1, or a hypervariable region thereof. Such fragments include the regions spanning amino acid residues about 125 to 443; about 138 to 441, or smaller fragments, such as those spanning about residue 138 to residue 163; about 170 to about 176; about 195 to about 203; about 233 to about 246; about 253 to about 264; about 287 to about 297; and about 404 to about 430 of the simian hexon proteins, with reference to SEQ ID NO: 3, 7, 11, 26, 31 or 36. Other suitable fragments may be readily identified by one of skill in the art. Further, the hexon protein may be modified for a variety of purposes known to those of skill in the art. Because the hexon protein is the determinant for serotype of an adenovirus, such artificial hexon proteins would result in adenoviruses having artificial serotypes. Other artificial capsid proteins can also be constructed using the chimp Ad penton sequences and/or fiber sequences of the invention and/or fragments thereof.

In one example, it may be desirable to generate an adenovirus having an altered hexon protein utilizing the sequences of a hexon protein of the invention. One suitable method for altering hexon proteins is described in US Patent 5,922,315, which is incorporated by reference. In this method, at least one loop region of the adenovirus hexon is changed with at least one loop region of another adenovirus serotype. Thus, at least one loop region of such an altered adenovirus hexon protein is a simian Ad hexon loop region of the invention (e.g. Pan7). In one embodiment, a loop region of the Pan7 hexon protein is replaced by a loop region from another adenovirus serotype. In another embodiment, the loop region of the Pan7 hexon is used to replace a loop region from another adenovirus serotype. Suitable adenovirus serotypes may be readily selected from among human and non-human serotypes, as described herein. Pan7 is selected for purposes of illustration only; the other simian Ad hexon proteins of the invention may be similarly altered, or used to alter another Ad hexon. The selection of a suitable serotype is not a limitation of the present invention. Still other uses for the hexon protein sequences of the invention will be readily apparent to those of skill in the art.

The invention further encompasses the fiber proteins of the simian adenoviruses of the invention. The fiber protein of AdPan 5 has the amino acid sequence of SEQ ID NO:4. The fiber protein AdPan6 has the amino acid sequence of SEQ ID NO: 8. The fiber protein of AdPan7 has the amino acid sequence of SEQ ID NO: 12. SV-1 has two fiber proteins; fiber 2 has the amino acid sequence of SEQ ID NO:27 and fiber 1 has the amino acid sequence of SEQ ID NO:28. SV-25 also has two fiber proteins; fiber 2 has the amino acid sequence of SEQ ID NO:32 and fiber 1 has the amino acid sequence of SEQ ID NO:33. The fiber protein of SV-39 has the amino acid sequence of SEQ ID NO:37.

Suitably, this fiber protein, or unique fragments thereof, may be utilized for a variety of purposes. One suitable fragment is the fiber knob, which spans about amino acids 247 to 425 of SEQ ID NO: 4, 8, 12, 28, 32, 33 and 37. See Fig. 2. Examples of other suitable fragments include the fiber having N-terminal and/or C-terminal truncations of about 50, 100, 150, or 200 amino acids, based upon the amino acid numbering provided above and in SEQ ID NO: 4, 8, 12, 28, 32, 33 and 37. Still other suitable fragments include internal fragments. Further, the fiber protein may be modified using a variety of techniques known to those of skill in the art.

The invention further encompasses unique fragments of the proteins of the invention which are at least 8 amino acids in length. However, fragments of other desired lengths can be readily utilized. In addition, the invention encompasses such modifications as may be introduced to enhance yield and/or expression of a Pan5, Pan6, Pan7, SV1, SV25 or SV39 gene product, e.g., construction of a fusion molecule in which all or a fragment of the Pan5, Pan6, Pan7, SV1, SV25 or SV39 gene product is fused (either directly or via a linker) with a fusion partner to enhance. Other suitable modifications include, without limitation, truncation of a coding region (e.g., a protein or enzyme) to eliminate a pre- or pro-protein ordinarily cleaved and to provide the mature protein or enzyme and/or mutation of a coding region to provide a secretable gene product. Still other modifications will be readily apparent to one of skill in the art. The invention further encompasses proteins having at least about 95% to 99% identity to the Pan5, Pan6, Pan7, SV1, SV25 or SV39 proteins provided herein.

As described herein, vectors of the invention containing the adenoviral capsid proteins of the invention are particularly well suited for use in applications in which the neutralizing antibodies diminish the effectiveness of other Ad serotype based vectors, as well as other viral vectors. The rAd vectors of the invention are particularly advantageous in readministration for repeat gene therapy or for boosting immune response (vaccine titers).

Under certain circumstances, it may be desirable to use one or more of the Pan5, Pan6, Pan7, SV1, SV25 and/or SV39 gene products (e.g., a capsid protein or a fragment thereof) to generate an antibody. The term "an antibody," as used herein, refers to an immunoglobulin molecule which is able to specifically bind to an epitope. Thus, the antibodies of the invention bind, preferably specifically and without cross-reactivity, to a Pan5, Pan6, Pan7, SV1, SV25 or SV39 epitope. The antibodies in the present invention exist in a variety of forms including, for example, high affinity polyclonal antibodies, monoclonal antibodies, synthetic antibodies, chimeric antibodies, recombinant antibodies and humanized antibodies. Such antibodies originate from immunoglobulin classes IgG, IgM, IgA, IgD and IgE.

Such antibodies may be generated using any of a number of methods know in the art. Suitable antibodies may be generated by well-known conventional techniques, e.g. Kohler and Milstein and the many known modifications thereof.

Similarly desirable high titer antibodies are generated by applying known recombinant techniques to the monoclonal or polyclonal antibodies developed to these antigens [see, e.g., PCT Patent Application No. PCT/GB85/00392; British Patent Application Publication No. GB2188638A; Amit *et al.*, 1986 *Science*, *233*:747-753; Queen *et al.*, 1989 *Proc. Nat'l. Acad. Sci. USA*, *86*:10029-10033; PCT Patent Application No. PCT/WO9007861; and Riechmann *et al.*, *Nature*, *332*:323-327 (1988); Huse *et al*, 1988a *Science*, *246*:1275-1281]. Alternatively, antibodies can be produced by manipulating the complementarity determining regions of animal or human antibodies to the antigen of this invention. See, e.g., E. Mark and Padlin, "Humanization of Monoclonal Antibodies", Chapter 4, The Handbook of Experimental Pharmacology, Vol. 113, The Pharmacology of Monoclonal Antibodies, Springer-Verlag (June, 1994); Harlow *et al.*, 1999, Using Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory Press, NY; Harlow *et al.*, 1989, Antibodies: A Laboratory Manual, Cold Spring Harbor, New York; Houston *et al.*, 1988, *Proc. Natl. Acad. Sci. USA 85*:5879-5883; and Bird *et al.*, 1988, *Science 242*:423-426. Further provided by the present invention are anti-idiotype antibodies (Ab2) and anti-anti-idiotype antibodies (Ab3). See, e.g., M. Wettendorff et al., "Modulation of anti-tumor immunity by anti-idiotypic antibodies." In Idiotypic Network and Diseases, ed. by J. Cerny and J. Hiernaux, 1990 *J. Am. Soc. Microbiol.*, Washington DC: pp. 203-229]. These anti-idiotype and anti-anti-idiotype antibodies are produced using techniques well known to those of skill in the art. These antibodies may be used for a variety of purposes, including diagnostic and clinical methods and kits.

Under certain circumstances, it may be desirable to introduce a detectable label or a tag onto a Pan5, Pan6, Pan7, SV1, SV25 or SV39 gene product, antibody or other construct of the invention. As used herein, a detectable label is a molecule which is capable, alone or upon interaction with another molecule, of providing a detectable signal. Most desirably, the label is detectable visually, e.g. by fluorescence, for ready use in immunohistochemical analyses or immunofluorescent microscopy. For example, suitable labels include fluorescein isothiocyanate (FITC), phycoerythrin (PE), allophycocyanin (APC), coriphosphine-O (CPO) or tandem dyes, PE-cyanin-5 (PC5), and PE-Texas Red (ECD). All of these fluorescent dyes are commercially available, and their uses known to the art. Other useful labels include a colloidal gold label. Still other useful labels include radioactive compounds or elements. Additionally, labels include a variety of enzyme

systems that operate to reveal a colorimetric signal in an assay, e.g., glucose oxidase (which uses glucose as a substrate) releases peroxide as a product which in the presence of peroxidase and a hydrogen donor such as tetramethyl benzidine (TMB) produces an oxidized TMB that is seen as a blue color. Other examples include horseradish peroxidase (HRP) or alkaline phosphatase (AP), and hexokinase in conjunction with glucose-6-phosphate dehydrogenase which reacts with ATP, glucose, and NAD+ to yield, among other products, NADH that is detected as increased absorbance at 340 nm wavelength.

Other label systems that are utilized in the methods of this invention are detectable by other means, e.g., colored latex microparticles [Bangs Laboratories, Indiana] in which a dye is embedded are used in place of enzymes to form conjugates with the target sequences provide a visual signal indicative of the presence of the resulting complex in applicable assays.

Methods for coupling or associating the label with a desired molecule are similarly conventional and known to those of skill in the art. Known methods of label attachment are described [see, for example, Handbook of Fluorescent probes and Research Chemicals, 6th Ed., R. P. M. Haugland, Molecular Probes, Inc., Eugene, OR, 1996; Pierce Catalog and Handbook, Life Science and Analytical Research Products, Pierce Chemical Company, Rockford, IL, 1994/1995]. Thus, selection of the label and coupling methods do not limit this invention.

The sequences, proteins, and fragments of the invention may be produced by any suitable means, including recombinant production, chemical synthesis, or other synthetic means. Suitable production techniques are well known to those of skill in the art. See, e.g., Sambrook et al, Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Press (Cold Spring Harbor, NY). Alternatively, peptides can also be synthesized by the well known solid phase peptide synthesis methods (Merrifield, *J. Am. Chem. Soc.*, **85**:2149 (1962); Stewart and Young, Solid Phase Peptide Synthesis (Freeman, San Francisco, 1969) pp. 27-62). These and other suitable production methods are within the knowledge of those of skill in the art and are not a limitation of the present invention.

In addition, one of skill in the art will readily understand that the Ad sequences of the invention can be readily adapted for use for a variety of viral and non-viral vector systems for *in vitro, ex vivo or in vivo* delivery of therapeutic and

immunogenic molecules. For example, in one embodiment, the simian Ad capsid proteins and other simian adenovirus proteins described herein are used for non-viral, protein-based delivery of genes, proteins, and other desirable diagnostic, therapeutic and immunogenic molecules. In one such embodiment, a protein of the invention is linked, directly or indirectly, to a molecule for targeting to cells with a receptor for adenoviruses. Preferably, a capsid protein such as a hexon, penton, fiber or a fragment thereof having a ligand for a cell surface receptor is selected for such targeting. Suitable molecules for delivery are selected from among the therapeutic molecules described herein and their gene products. A variety of linkers including, lipids, polyLys, and the like may be utilized as linkers. For example, the simian penton protein may be readily utilized for such a purpose by production of a fusion protein using the simian penton sequences in a manner analogous to that described in Medina-Kauwe LK, et al, *Gene Ther.* **2001** May; 8(10):795-803 and Medina-Kauwe LK, et al, *Gene Ther.* **2001** Dec; 8(23): 1753-1761. Alternatively, the amino acid sequences of simian Ad protein IX may be utilized for targeting vectors to a cell surface receptor, as described in US Patent Appln 20010047081. Suitable ligands include a CD40 antigen, an RGD-containing or polylysine-containing sequence, and the like. Still other simian Ad proteins, including, e.g., the hexon protein and/or the fiber protein, may be used for used for these and similar purposes.

Still other adenoviral proteins of the invention may be used as alone, or in combination with other adenoviral protein, for a variety of purposes which will be readily apparent to one of skill in the art. In addition, still other uses for the adenoviral proteins of the invention will be readily apparent to one of skill in the art.

II. Recombinant Adenoviral Vectors

The compositions of this invention include vectors that deliver a heterologous molecule to cells, either for therapeutic or vaccine purposes. As used herein, a vector may include any genetic element including, without limitation, naked DNA, a phage, transposon, cosmid, episome, plasmid, or a virus. Such vectors contain simian adenovirus DNA of Pan5, Pan6, Pan7, SV1, SV25 and/or SV39 and a minigene. By "minigene" is meant the combination of a selected heterologous gene and the other

regulatory elements necessary to drive translation, transcription and/or expression of the gene product in a host cell.

Typically, an adenoviral vector of the invention is designed such that the minigene is located in a nucleic acid molecule which contains other adenoviral sequences in the region native to a selected adenoviral gene. The minigene may be inserted into an existing gene region to disrupt the function of that region, if desired. Alternatively, the minigene may be inserted into the site of a partially or fully deleted adenoviral gene. For example, the minigene may be located in the site of such as the site of a functional E1 deletion or functional E3 deletion, among others that may be selected. The term "functionally deleted" or "functional deletion" means that a sufficient amount of the gene region is removed or otherwise damaged, e.g., by mutation or modification, so that the gene region is no longer capable of producing functional products of gene expression. If desired, the entire gene region may be removed. Other suitable sites for gene disruption or deletion are discussed elsewhere in the application.

For example, for a production vector useful for generation of a recombinant virus, the vector may contain the minigene and either the 5' end of the adenoviral genome or the 3' end of the adenoviral genome, or both the 5' and 3' ends of the adenoviral genome. The 5' end of the adenoviral genome contains the 5' cis-elements necessary for packaging and replication; i.e., the 5' inverted terminal repeat (ITR) sequences (which functions as origins of replication) and the native 5' packaging enhancer domains (that contain sequences necessary for packaging linear Ad genomes and enhancer elements for the E1 promoter). The 3' end of the adenoviral genome includes the 3' cis-elements (including the ITRs) necessary for packaging and encapsidation. Suitably, a recombinant adenovirus contains both 5' and 3' adenoviral cis-elements and the minigene is located between the 5' and 3' adenoviral sequences. Any adenoviral vector of the invention may also contain additional adenoviral sequences.

Suitably, these adenoviral vectors of the invention contain one or more adenoviral elements derived from an adenoviral genome of the invention. In one embodiment, the vectors contain adenoviral ITRs from Pan5, Pan6, Pan7, SV1, SV25 or SV39 and additional adenoviral sequences from the same adenoviral serotype. In another embodiment, the vectors contain adenoviral sequences that are derived from a different

adenoviral serotype than that which provides the ITRs. As defined herein, a pseudotyped adenovirus refers to an adenovirus in which the capsid protein of the adenovirus is from a different serotype than the serotype which provides the ITRs. The selection of the serotype of the ITRs and the serotype of any other adenoviral sequences present in vector is not a limitation of the present invention. A variety of adenovirus strains are available from the American Type Culture Collection, Manassas, Virginia, or available by request from a variety of commercial and institutional sources. Further, the sequences of many such strains are available from a variety of databases including, e.g., PubMed and GenBank. Homologous adenovirus vectors prepared from other simian or from human adenoviruses are described in the published literature [see, for example, US Patent No. 5,240,846]. The DNA sequences of a number of adenovirus types are available from GenBank, including type Ad5 [GenBank Accession No. M73260]. The adenovirus sequences may be obtained from any known adenovirus serotype, such as serotypes 2, 3, 4, 7, 12 and 40, and further including any of the presently identified human types. Similarly adenoviruses known to infect non-human animals (e.g., simians) may also be employed in the vector constructs of this invention. See, e.g., US Patent No. 6,083,716.

The viral sequences, helper viruses, if needed, and recombinant viral particles, and other vector components and sequences employed in the construction of the vectors described herein are obtained as described above. The DNA sequences of the Pan5, Pan6, Pan7, SV1, SV25 and/or SV39 simian adenovirus sequences of the invention are employed to construct vectors and cell lines useful in the preparation of such vectors.

Modifications of the nucleic acid sequences forming the vectors of this invention, including sequence deletions, insertions, and other mutations may be generated using standard molecular biological techniques and are within the scope of this invention.

A. The "Minigene"

The methods employed for the selection of the transgene, the cloning and construction of the "minigene" and its insertion into the viral vector are within the skill in the art given the teachings provided herein.

1. The transgene

The transgene is a nucleic acid sequence, heterologous to the vector sequences flanking the transgene, which encodes a polypeptide, protein, or other product, of interest. The nucleic acid coding sequence is operatively linked to regulatory

components in a manner which permits transgene transcription, translation, and/or expression in a host cell.

The composition of the transgene sequence will depend upon the use to which the resulting vector will be put. For example, one type of transgene sequence includes a reporter sequence, which upon expression produces a detectable signal. Such reporter sequences include, without limitation, DNA sequences encoding β-lactamase, β-galactosidase (LacZ), alkaline phosphatase, thymidine kinase, green fluorescent protein (GFP), chloramphenicol acetyltransferase (CAT), luciferase, membrane bound proteins including, for example, CD2, CD4, CD8, the influenza hemagglutinin protein, and others well known in the art, to which high affinity antibodies directed thereto exist or can be produced by conventional means, and fusion proteins comprising a membrane bound protein appropriately fused to an antigen tag domain from, among others, hemagglutinin or Myc. These coding sequences, when associated with regulatory elements which drive their expression, provide signals detectable by conventional means, including enzymatic, radiographic, colorimetric, fluorescence or other spectrographic assays, fluorescent activating cell sorting assays and immunological assays, including enzyme linked immunosorbent assay (ELISA), radioimmunoassay (RIA) and immunohistochemistry. For example, where the marker sequence is the LacZ gene, the presence of the vector carrying the signal is detected by assays for beta-galactosidase activity. Where the transgene is GFP or luciferase, the vector carrying the signal may be measured visually by color or light production in a luminometer.

However, desirably, the transgene is a non-marker sequence encoding a product which is useful in biology and medicine, such as proteins, peptides, RNA, enzymes, or catalytic RNAs. Desirable RNA molecules include tRNA, dsRNA, ribosomal RNA, catalytic RNAs, and antisense RNAs. One example of a useful RNA sequence is a sequence which extinguishes expression of a targeted nucleic acid sequence in the treated animal.

The transgene may be used for treatment, e.g., of genetic deficiencies, as a cancer therapeutic or vaccine, for induction of an immune response, and/or for prophylactic vaccine purposes. As used herein, induction of an immune response refers to the ability of a molecule (e.g., a gene product) to induce a T cell and/or a humoral immune response to the molecule. The invention further includes using multiple

transgenes, e.g., to correct or ameliorate a condition caused by a multi-subunit protein. In certain situations, a different transgene may be used to encode each subunit of a protein, or to encode different peptides or proteins. This is desirable when the size of the DNA encoding the protein subunit is large, e.g., for an immunoglobulin, the platelet-derived growth factor, or a dystrophin protein. In order for the cell to produce the multi-subunit protein, a cell is infected with the recombinant virus containing each of the different subunits. Alternatively, different subunits of a protein may be encoded by the same transgene. In this case, a single transgene includes the DNA encoding each of the subunits, with the DNA for each subunit separated by an internal ribozyme entry site (IRES). This is desirable when the size of the DNA encoding each of the subunits is small, e.g., the total size of the DNA encoding the subunits and the IRES is less than five kilobases. As an alternative to an IRES, the DNA may be separated by sequences encoding a 2A peptide, which self-cleaves in a post-translational event. See, e.g., M.L. Donnelly, *et al*, *J. Gen. Virol.*, **78**(Pt 1):13-21 (Jan 1997); Furler, S., *et al*, *Gene Ther.*, **8**(11):864-873 (June 2001); Klump H., *et al.*, *Gene Ther.*, **8**(10):811-817 (May 2001). This 2A peptide is significantly smaller than an IRES, making it well suited for use when space is a limiting factor. However, the selected transgene may encode any biologically active product or other product, e.g., a product desirable for study.

Suitable transgenes may be readily selected by one of skill in the art. The selection of the transgene is not considered to be a limitation of this invention.

2. Regulatory Elements

In addition to the major elements identified above for the minigene, the vector also includes conventional control elements necessary which are operably linked to the transgene in a manner that permits its transcription, translation and/or expression in a cell transfected with the plasmid vector or infected with the virus produced by the invention. As used herein, "operably linked" sequences include both expression control sequences that are contiguous with the gene of interest and expression control sequences that act in *trans* or at a distance to control the gene of interest.

Expression control sequences include appropriate transcription initiation, termination, promoter and enhancer sequences; efficient RNA processing signals such as splicing and polyadenylation (polyA) signals; sequences that stabilize cytoplasmic mRNA; sequences that enhance translation efficiency (i.e., Kozak consensus

sequence); sequences that enhance protein stability; and when desired, sequences that enhance secretion of the encoded product. A great number of expression control sequences, including promoters which are native, constitutive, inducible and/or tissue-specific, are known in the art and may be utilized.

Examples of constitutive promoters include, without limitation, the retroviral Rous sarcoma virus (RSV) LTR promoter (optionally with the RSV enhancer), the cytomegalovirus (CMV) promoter (optionally with the CMV enhancer) [see, e.g., Boshart *et al*, *Cell*, **41**:521-530 (1985)], the SV40 promoter, the dihydrofolate reductase promoter, the β-actin promoter, the phosphoglycerol kinase (PGK) promoter, and the EF1α promoter [Invitrogen].

Inducible promoters allow regulation of gene expression and can be regulated by exogenously supplied compounds, environmental factors such as temperature, or the presence of a specific physiological state, e.g., acute phase, a particular differentiation state of the cell, or in replicating cells only. Inducible promoters and inducible systems are available from a variety of commercial sources, including, without limitation, Invitrogen, Clontech and Ariad. Many other systems have been described and can be readily selected by one of skill in the art. For example, inducible promoters include the zinc-inducible sheep metallothionine (MT) promoter and the dexamethasone (Dex)-inducible mouse mammary tumor virus (MMTV) promoter. Other inducible systems include the T7 polymerase promoter system [WO 98/10088]; the ecdysone insect promoter [No *et al*, *Proc. Natl. Acad. Sci. USA*, **93**:3346-3351 (1996)], the tetracycline-repressible system [Gossen *et al*, *Proc. Natl. Acad. Sci. USA*, **89**:5547-5551 (1992)], the tetracycline-inducible system [Gossen *et al*, *Science*, **268**:1766-1769 (1995), see also Harvey *et al*, *Curr. Opin. Chem. Biol.*, **2**:512-518 (1998)]. Other systems include the FK506 dimer, VP16 or p65 using castradiol, diphenol murislerone, the RU486-inducible system [Wang *et al*, *Nat. Biotech.*, **15**:239-243 (1997) and Wang *et al*, *Gene Ther.*, **4**:432-441 (1997)] and the rapamycin-inducible system [Magari *et al*, *J. Clin. Invest.*, **100**:2865-2872 (1997)]. The effectiveness of some inducible promoters increases over time. In such cases one can enhance the effectiveness of such systems by inserting multiple repressors in tandem, e.g., TetR linked to a TetR by an IRES. Alternatively, one can wait at least 3 days before screening for the desired function. One can enhance expression of desired proteins by known means to enhance the effectiveness

of this system. For example, using the Woodchuck Hepatitis Virus Posttranscriptional Regulatory Element (WPRE).

In another embodiment, the native promoter for the transgene will be used. The native promoter may be preferred when it is desired that expression of the transgene should mimic the native expression. The native promoter may be used when expression of the transgene must be regulated temporally or developmentally, or in a tissue-specific manner, or in response to specific transcriptional stimuli. In a further embodiment, other native expression control elements, such as enhancer elements, polyadenylation sites or Kozak consensus sequences may also be used to mimic the native expression.

Another embodiment of the transgene includes a transgene operably linked to a tissue-specific promoter. For instance, if expression in skeletal muscle is desired, a promoter active in muscle should be used. These include the promoters from genes encoding skeletal β-actin, myosin light chain 2A, dystrophin, muscle creatine kinase, as well as synthetic muscle promoters with activities higher than naturally occurring promoters (see Li *et al.*, *Nat. Biotech.*, **17**:241-245 (1999)). Examples of promoters that are tissue-specific are known for liver (albumin, Miyatake *et al.*, *J. Virol.*, **71**:5124-32 (1997); hepatitis B virus core promoter, Sandig *et al.*, *Gene Ther.*, **3**:1002-9 (1996); alpha-fetoprotein (AFP), Arbuthnot *et al.*, *Hum. Gene Ther.*, 7:1503-14 (1996)), bone osteocalcin (Stein *et al.*, *Mol. Biol. Rep.*, **24**:185-96 (1997)); bone sialoprotein (Chen *et al.*, *J. Bone Miner. Res.*, **11**:654-64 (1996)), lymphocytes (CD2, Hansal *et al.*, *J. Immunol.*, **161**:1063-8 (1998); immunoglobulin heavy chain; T cell receptor chain), neuronal such as neuron-specific enolase (NSE) promoter (Andersen *et al.*, *Cell. Mol. Neurobiol.*, **13**:503-15 (1993)), neurofilament light-chain gene (Piccioli *et al.*, *Proc. Natl. Acad. Sci. USA*, **88**:5611-5 (1991)), and the neuron-specific vgf gene (Piccioli *et al.*, *Neuron*, **15**:373-84 (1995)), among others.

Optionally, vectors carrying transgenes encoding therapeutically useful or immunogenic products may also include selectable markers or reporter genes may include sequences encoding geneticin, hygromicin or purimycin resistance, among others. Such selectable reporters or marker genes (preferably located outside the viral genome to be packaged into a viral particle) can be used to signal the presence of the plasmids in bacterial cells, such as ampicillin resistance. Other components of the vector may include

an origin of replication. Selection of these and other promoters and vector elements are conventional and many such sequences are available [see, e.g., Sambrook et al, and references cited therein].

These vectors are generated using the techniques and sequences provided herein, in conjunction with techniques known to those of skill in the art. Such techniques include conventional cloning techniques of cDNA such as those described in texts [Sambrook et al, Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Press, Cold Spring Harbor, NY], use of overlapping oligonucleotide sequences of the adenovirus genomes, polymerase chain reaction, and any suitable method which provides the desired nucleotide sequence.

III. Production of the Recombinant Viral Particle

In one embodiment, the simian adenoviral plasmids (or other vectors) are used to produce recombinant adenoviral particles. In one embodiment, the recombinant adenoviruses are functionally deleted in the E1a or E1b genes, and optionally bearing other mutations, e.g., temperature-sensitive mutations or deletions in other genes. In other embodiments, it is desirable to retain an intact E1a and/or E1b region in the recombinant adenoviruses. Such an intact E1 region may be located in its native location in the adenoviral genome or placed in the site of a deletion in the native adenoviral genome (e.g., in the E3 region).

In the construction of useful simian adenovirus vectors for delivery of a gene to the human (or other mammalian) cell, a range of adenovirus nucleic acid sequences can be employed in the vectors. For example, all or a portion of the adenovirus delayed early gene E3 may be eliminated from the simian adenovirus sequence which forms a part of the recombinant virus. The function of simian E3 is believed to be irrelevant to the function and production of the recombinant virus particle. Simian adenovirus vectors may also be constructed having a deletion of at least the ORF6 region of the E4 gene, and more desirably because of the redundancy in the function of this region, the entire E4 region. Still another vector of this invention contains a deletion in the delayed early gene E2a. Deletions may also be made in any of the late genes L1 through L5 of the simian adenovirus genome. Similarly, deletions in the intermediate genes IX and IVa_2 may be useful for some purposes. Other deletions may be made in the other structural or non-

structural adenovirus genes. The above discussed deletions may be used individually, i.e., an adenovirus sequence for use in the present invention may contain deletions in only a single region. Alternatively, deletions of entire genes or portions thereof effective to destroy their biological activity may be used in any combination. For example, in one exemplary vector, the adenovirus sequence may have deletions of the E1 genes and the E4 gene, or of the E1, E2a and E3 genes, or of the E1 and E3 genes, or of E1, E2a and E4 genes, with or without deletion of E3, and so on. As discussed above, such deletions may be used in combination with other mutations, such as temperature-sensitive mutations, to achieve a desired result.

An adenoviral vector lacking any essential adenoviral sequences (e.g., E1a, E1b, E2a, E2b, E4 ORF6, L1, L2, L3, L4 and L5) may be cultured in the presence of the missing adenoviral gene products which are required for viral infectivity and propagation of an adenoviral particle. These helper functions may be provided by culturing the adenoviral vector in the presence of one or more helper constructs (e.g., a plasmid or virus) or a packaging host cell. See, for example, the techniques described for preparation of a "minimal" human Ad vector in International Patent Application WO96/13597, published May 9, 1996, and incorporated herein by reference.

1. Helper Viruses

Thus, depending upon the simian adenovirus gene content of the viral vectors employed to carry the minigene, a helper adenovirus or non-replicating virus fragment may be necessary to provide sufficient simian adenovirus gene sequences necessary to produce an infective recombinant viral particle containing the minigene. Useful helper viruses contain selected adenovirus gene sequences not present in the adenovirus vector construct and/or not expressed by the packaging cell line in which the vector is transfected. In one embodiment, the helper virus is replication-defective and contains a variety of adenovirus genes in addition to the sequences described above. Such a helper virus is desirably used in combination with an E1-expressing cell line.

Helper viruses may also be formed into poly-cation conjugates as described in Wu *et al*, *J. Biol. Chem.*, **264**:16985-16987 (1989); K. J. Fisher and J. M. Wilson, *Biochem. J.*, **299**:49 (April 1, 1994). Helper virus may optionally contain a second reporter minigene. A number of such reporter genes are known to the art. The presence of a reporter gene on the helper virus which is different from the transgene on

the adenovirus vector allows both the Ad vector and the helper virus to be independently monitored. This second reporter is used to enable separation between the resulting recombinant virus and the helper virus upon purification.

2. Complementation Cell Lines

To generate recombinant simian adenoviruses (Ad) deleted in any of the genes described above, the function of the deleted gene region, if essential to the replication and infectivity of the virus, must be supplied to the recombinant virus by a helper virus or cell line, i.e., a complementation or packaging cell line. In many circumstances, a cell line expressing the human E1 can be used to transcomplement the chimp Ad vector. This is particularly advantageous because, due to the diversity between the chimp Ad sequences of the invention and the human AdE1 sequences found in currently available packaging cells, the use of the current human E1-containing cells prevents the generation of replication-competent adenoviruses during the replication and production process. However, in certain circumstances, it will be desirable to utilize a cell line which expresses the E1 gene products can be utilized for production of an E1-deleted simian adenovirus. Such cell lines have been described. See, e.g., US Patent 6,083,716.

If desired, one may utilize the sequences provided herein to generate a packaging cell or cell line that expresses, at a minimum, the adenovirus E1 gene from Pan5, Pan6, Pan7, SV1, SV25 or SV39 under the transcriptional control of a promoter for expression in a selected parent cell line. Inducible or constitutive promoters may be employed for this purpose. Examples of such promoters are described in detail elsewhere in this specification. A parent cell is selected for the generation of a novel cell line expressing any desired AdPan5, Pan6, Pan7, SV1, SV25 or SV39 gene. Without limitation, such a parent cell line may be HeLa [ATCC Accession No. CCL 2], A549 [ATCC Accession No. CCL 185], HEK 293, KB [CCL 17], Detroit [e.g., Detroit 510, CCL 72] and WI-38 [CCL 75] cells, among others. These cell lines are all available from the American Type Culture Collection, 10801 University Boulevard, Manassas, Virginia 20110-2209. Other suitable parent cell lines may be obtained from other sources.

Such E1-expressing cell lines are useful in the generation of recombinant simian adenovirus E1 deleted vectors. Additionally, or alternatively, the invention provides cell lines that express one or more simian adenoviral gene products,

e.g., E1a, E1b, E2a, and/or E4 ORF6, can be constructed using essentially the same procedures for use in the generation of recombinant simian viral vectors. Such cell lines can be utilized to transcomplement adenovirus vectors deleted in the essential genes that encode those products, or to provide helper functions necessary for packaging of a helper-dependent virus (e.g., adeno-associated virus). The preparation of a host cell according to this invention involves techniques such as assembly of selected DNA sequences. This assembly may be accomplished utilizing conventional techniques. Such techniques include cDNA and genomic cloning, which are well known and are described in Sambrook et al., cited above, use of overlapping oligonucleotide sequences of the adenovirus genomes, combined with polymerase chain reaction, synthetic methods, and any other suitable methods which provide the desired nucleotide sequence.

In still another alternative, the essential adenoviral gene products are provided in *trans* by the adenoviral vector and/or helper virus. In such an instance, a suitable host cell can be selected from any biological organism, including prokaryotic (e.g., bacterial) cells, and eukaryotic cells, including, insect cells, yeast cells and mammalian cells. Particularly desirable host cells are selected from among any mammalian species, including, without limitation, cells such as A549, WEHI, 3T3, 10T1/2, HEK 293 cells or PERC6 (both of which express functional adenoviral E1) [Fallaux, FJ *et al*, (1998), *Hum Gene Ther*, **9**:1909-1917], Saos, C2C12, L cells, HT1080, HepG2 and primary fibroblast, hepatocyte and myoblast cells derived from mammals including human, monkey, mouse, rat, rabbit, and hamster. The selection of the mammalian species providing the cells is not a limitation of this invention; nor is the type of mammalian cell, i.e., fibroblast, hepatocyte, tumor cell, etc.

3. Assembly of Viral Particle and Transfection of a Cell Line

Generally, when delivering the vector comprising the minigene by transfection, the vector is delivered in an amount from about 5 μg to about 100 μg DNA, and preferably about 10 to about 50 μg DNA to about 1 x 10^4 cells to about 1 x 10^{13} cells, and preferably about 10^5 cells. However, the relative amounts of vector DNA to host cells may be adjusted, taking into consideration such factors as the selected vector, the delivery method and the host cells selected.

The vector may be any vector known in the art or disclosed above, including naked DNA, a plasmid, phage, transposon, cosmids, episomes, viruses, etc.

Introduction into the host cell of the vector may be achieved by any means known in the art or as disclosed above, including transfection, and infection. One or more of the adenoviral genes may be stably integrated into the genome of the host cell, stably expressed as episomes, or expressed transiently. The gene products may all be expressed transiently, on an episome or stably integrated, or some of the gene products may be expressed stably while others are expressed transiently. Furthermore, the promoters for each of the adenoviral genes may be selected independently from a constitutive promoter, an inducible promoter or a native adenoviral promoter. The promoters may be regulated by a specific physiological state of the organism or cell (i.e., by the differentiation state or in replicating or quiescent cells) or by exogenously-added factors, for example.

Introduction of the molecules (as plasmids or viruses) into the host cell may also be accomplished using techniques known to the skilled artisan and as discussed throughout the specification. In preferred embodiment, standard transfection techniques are used, e.g., $CaPO_4$ transfection or electroporation.

Assembly of the selected DNA sequences of the adenovirus (as well as the transgene and other vector elements into various intermediate plasmids, and the use of the plasmids and vectors to produce a recombinant viral particle are all achieved using conventional techniques. Such techniques include conventional cloning techniques of cDNA such as those described in texts [Sambrook et al, cited above], use of overlapping oligonucleotide sequences of the adenovirus genomes, polymerase chain reaction, and any suitable method which provides the desired nucleotide sequence. Standard transfection and co-transfection techniques are employed, e.g., $CaPO_4$ precipitation techniques. Other conventional methods employed include homologous recombination of the viral genomes, plaquing of viruses in agar overlay, methods of measuring signal generation, and the like.

For example, following the construction and assembly of the desired minigene-containing viral vector, the vector is transfected *in vitro* in the presence of a helper virus into the packaging cell line. Homologous recombination occurs between the helper and the vector sequences, which permits the adenovirus-transgene sequences in the vector to be replicated and packaged into virion capsids, resulting in the recombinant viral vector particles. The current method for producing such virus particles is transfection-based. However, the invention is not limited to such methods.

The resulting recombinant simian adenoviruses are useful in transferring a selected transgene to a selected cell. In *in vivo* experiments with the recombinant virus grown in the packaging cell lines, the E1-deleted recombinant simian adenoviral vectors of the invention demonstrate utility in transferring a transgene to a non-simian, preferably a human, cell.

IV. Use of the Recombinant Adenovirus Vectors

The recombinant simian adenovirus vectors of the invention are useful for gene transfer to a human or non-simian veterinary patient *in vitro, ex vivo,* and *in vivo*.

The recombinant adenovirus vectors described herein can be used as expression vectors for the production of the products encoded by the heterologous genes *in vitro*. For example, the recombinant adenoviruses containing a gene inserted into the location of an E1 deletion may be transfected into an E1-expressing cell line as described above. Alternatively, replication-competent adenoviruses may be used in another selected cell line. The transfected cells are then cultured in the conventional manner, allowing the recombinant adenovirus to express the gene product from the promoter. The gene product may then be recovered from the culture medium by known conventional methods of protein isolation and recovery from culture.

A Pan5, Pan6, Pan7, SV1, SV25 or SV39-derived recombinant simian adenoviral vector of the invention provides an efficient gene transfer vehicle that can deliver a selected transgene to a selected host cell *in vivo or ex vivo* even where the organism has neutralizing antibodies to one or more AAV serotypes. In one embodiment, the rAAV and the cells are mixed *ex vivo;* the infected cells are cultured using conventional methodologies; and the transduced cells are re-infused into the patient. These compositions are particularly well suited to gene delivery for therapeutic purposes and for immunization, including inducing protective immunity.

More commonly, the Pan 5, Pan6, Pan7, SV1, SV25, or SV39 recombinant adenoviral vectors of the invention will be utilized for delivery of therapeutic or immunogenic molecules, as described below. It will be readily understood for both applications, that the recombinant adenoviral vectors of the invention are particularly well suited for use in regimens involving repeat delivery of recombinant adenoviral vectors. Such regimens typically involve delivery of a series of viral vectors in which the viral

capsids are alternated. The viral capsids may be changed for each subsequent administration, or after a pre-selected number of administrations of a particular serotype capsid (e.g., one, two, three, four or more). Thus, a regimen may involve delivery of a rAd with a first simian capsid, delivery with a rAd with a second simian capsid, and delivery with a third simian capsid. A variety of other regimens which use the Ad capsids of the invention alone, in combination with one another, or in combination with other Ad serotypes will be apparent to those of skill in the art. Optionally, such a regimen may involve administration of rAd with capsids of other non-human primate adenoviruses, human adenoviruses, or artificial serotypes such as are described herein. Each phase of the regimen may involve administration of a series of injections (or other delivery routes) with a single Ad serotype capsid followed by a series with another Ad serotype capsid. Alternatively, the recombinant Ad vectors of the invention may be utilized in regimens involving other non-adenoviral-mediated delivery systems, including other viral systems, non-viral delivery systems, protein, peptides, and other biologically active molecules.

The following sections will focus on exemplary molecules which may be delivered via the adenoviral vectors of the invention.

A. Ad-Mediated Delivery of Therapeutic Molecules

In one embodiment, the above-described recombinant vectors are administered to humans according to published methods for gene therapy. A simian viral vector bearing the selected transgene may be administered to a patient, preferably suspended in a biologically compatible solution or pharmaceutically acceptable delivery vehicle. A suitable vehicle includes sterile saline. Other aqueous and non-aqueous isotonic sterile injection solutions and aqueous and non-aqueous sterile suspensions known to be pharmaceutically acceptable carriers and well known to those of skill in the art may be employed for this purpose.

The simian adenoviral vectors are administered in sufficient amounts to transduce the target cells and to provide sufficient levels of gene transfer and expression to provide a therapeutic benefit without undue adverse or with medically acceptable physiological effects, which can be determined by those skilled in the medical arts. Conventional and pharmaceutically acceptable routes of administration include, but are not limited to, direct delivery to the retina and other intraocular delivery methods, direct delivery to the liver, inhalation, intranasal, intravenous, intramuscular, intratracheal,

subcutaneous, intradermal, rectal, oral and other parenteral routes of administration. Routes of administration may be combined, if desired, or adjusted depending upon the transgene or the condition. The route of administration primarily will depend on the nature of the condition being treated.

Dosages of the viral vector will depend primarily on factors such as the condition being treated, the age, weight and health of the patient, and may thus vary among patients. For example, a therapeutically effective adult human or veterinary dosage of the viral vector is generally in the range of from about 100 µL to about 100 mL of a carrier containing concentrations of from about 1 x 10^6 to about 1 x 10^{15} particles, about 1 x 10^{11} to 1 x 10^{13} particles, or about 1 x 10^9 to 1x 10^{12} particles virus. Dosages will range depending upon the size of the animal and the route of administration. For example, a suitable human or veterinary dosage (for about an 80 kg animal) for intramuscular injection is in the range of about 1 x 10^9 to about 5 x 10^{12} particles per mL, for a single site. Optionally, multiple sites of administration may be delivered. In another example, a suitable human or veterinary dosage may be in the range of about 1 x 10^{11} to about 1 x 10^{15} particles for an oral formulation. One of skill in the art may adjust these doses, depending the route of administration, and the therapeutic or vaccinal application for which the recombinant vector is employed. The levels of expression of the transgene, or for an immunogen, the level of circulating antibody, can be monitored to determine the frequency of dosage administration. Yet other methods for determining the timing of frequency of administration will be readily apparent to one of skill in the art.

An optional method step involves the co-administration to the patient, either concurrently with, or before or after administration of the viral vector, of a suitable amount of a short acting immune modulator. The selected immune modulator is defined herein as an agent capable of inhibiting the formation of neutralizing antibodies directed against the recombinant vector of this invention or capable of inhibiting cytolytic T lymphocyte (CTL) elimination of the vector. The immune modulator may interfere with the interactions between the T helper subsets (T_{H1} or T_{H2}) and B cells to inhibit neutralizing antibody formation. Alternatively, the immune modulator may inhibit the interaction between T_{H1} cells and CTLs to reduce the occurrence of CTL elimination of the vector. A variety of useful immune modulators and dosages for use of same are disclosed, for example, in Yang *et al.*, *J. Virol.*, **70**(9) (Sept., 1996); International Patent

Application No. WO96/12406, published May 2, 1996; and International Patent Application No.PCT/US96/03035, all incorporated herein by reference.

1. Therapeutic Transgenes

Useful therapeutic products encoded by the transgene include hormones and growth and differentiation factors including, without limitation, insulin, glucagon, growth hormone (GH), parathyroid hormone (PTH), growth hormone releasing factor (GRF), follicle stimulating hormone (FSH), luteinizing hormone (LH), human chorionic gonadotropin (hCG), vascular endothelial growth factor (VEGF), angiopoietins, angiostatin, granulocyte colony stimulating factor (GCSF), erythropoietin (EPO), connective tissue growth factor (CTGF), basic fibroblast growth factor (bFGF), acidic fibroblast growth factor (aFGF), epidermal growth factor (EGF), transforming growth factor (TGF), platelet-derived growth factor (PDGF), insulin growth factors I and II (IGF-I and IGF-II), any one of the transforming growth factor superfamily, including TGF, activins, inhibins, or any of the bone morphogenic proteins (BMP) BMPs 1-15, any one of the heregluin/neuregulin/ARIA/neu differentiation factor (NDF) family of growth factors, nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF), neurotrophins NT-3 and NT-4/5, ciliary neurotrophic factor (CNTF), glial cell line derived neurotrophic factor (GDNF), neurturin, agrin, any one of the family of semaphorins/collapsins, netrin-1 and netrin-2, hepatocyte growth factor (HGF), ephrins, noggin, sonic hedgehog and tyrosine hydroxylase.

Other useful transgene products include proteins that regulate the immune system including, without limitation, cytokines and lymphokines such as thrombopoietin (TPO), interleukins (IL) IL-1 through IL-25 (including, e.g., IL-2, IL-4, IL-12 and IL-18), monocyte chemoattractant protein, leukemia inhibitory factor, granulocyte-macrophage colony stimulating factor, Fas ligand, tumor necrosis factors and, interferons, and, stem cell factor, flk-2/flt3 ligand. Gene products produced by the immune system are also useful in the invention. These include, without limitation, immunoglobulins IgG, IgM, IgA, IgD and IgE, chimeric immunoglobulins, humanized antibodies, single chain antibodies, T cell receptors, chimeric T cell receptors, single chain T cell receptors, class I and class II MHC molecules, as well as engineered immunoglobulins and MHC molecules. Useful gene products also include complement

regulatory proteins such as complement regulatory proteins, membrane cofactor protein (MCP), decay accelerating factor (DAF), CR1, CF2 and CD59.

Still other useful gene products include any one of the receptors for the hormones, growth factors, cytokines, lymphokines, regulatory proteins and immune system proteins. The invention encompasses receptors for cholesterol regulation, including the low density lipoprotein (LDL) receptor, high density lipoprotein (HDL) receptor, the very low density lipoprotein (VLDL) receptor, and the scavenger receptor. The invention also encompasses gene products such as members of the steroid hormone receptor superfamily including glucocorticoid receptors and estrogen receptors, Vitamin D receptors and other nuclear receptors. In addition, useful gene products include transcription factors such as *jun*, *fos*, max, mad, serum response factor (SRF), AP-1, AP2, *myb*, MyoD and myogenin, ETS-box containing proteins, TFE3, E2F, ATF1, ATF2, ATF3, ATF4, ZF5, NFAT, CREB, HNF-4, C/EBP, SP1, CCAAT-box binding proteins, interferon regulation factor (IRF-1), Wilms tumor protein, ETS-binding protein, STAT, GATA-box binding proteins, e.g., GATA-3, and the forkhead family of winged helix proteins.

Other useful gene products include, carbamoyl synthetase I, ornithine transcarbamylase, arginosuccinate synthetase, arginosuccinate lyase, arginase, fumarylacetacetate hydrolase, phenylalanine hydroxylase, alpha-1 antitrypsin, glucose-6-phosphatase, porphobilinogen deaminase, factor VIII, factor IX, cystathione beta-synthase, branched chain ketoacid decarboxylase, albumin, isovaleryl-coA dehydrogenase, propionyl CoA carboxylase, methyl malonyl CoA mutase, glutaryl CoA dehydrogenase, insulin, beta-glucosidase, pyruvate carboxylate, hepatic phosphorylase, phosphorylase kinase, glycine decarboxylase, H-protein, T-protein, a cystic fibrosis transmembrane regulator (CFTR) sequence, and a dystrophin cDNA sequence.

Other useful gene products include non-naturally occurring polypeptides, such as chimeric or hybrid polypeptides having a non-naturally occurring amino acid sequence containing insertions, deletions or amino acid substitutions. For example, single-chain engineered immunoglobulins could be useful in certain immunocompromised patients. Other types of non-naturally occurring gene sequences include antisense molecules and catalytic nucleic acids, such as ribozymes, which could be used to reduce overexpression of a target.

Reduction and/or modulation of expression of a gene are particularly desirable for treatment of hyperproliferative conditions characterized by hyperproliferating cells, as are cancers and psoriasis. Target polypeptides include those polypeptides which are produced exclusively or at higher levels in hyperproliferative cells as compared to normal cells. Target antigens include polypeptides encoded by oncogenes such as myb, myc, fyn, and the translocation gene bcr/abl, ras, src, P53, neu, trk and EGRF. In addition to oncogene products as target antigens, target polypeptides for anti-cancer treatments and protective regimens include variable regions of antibodies made by B cell lymphomas and variable regions of T cell receptors of T cell lymphomas which, in some embodiments, are also used as target antigens for autoimmune disease. Other tumor-associated polypeptides can be used as target polypeptides such as polypeptides which are found at higher levels in tumor cells including the polypeptide recognized by monoclonal antibody 17-1A and folate binding polypeptides.

Other suitable therapeutic polypeptides and proteins include those which may be useful for treating individuals suffering from autoimmune diseases and disorders by conferring a broad based protective immune response against targets that are associated with autoimmunity including cell receptors and cells which produce self-directed antibodies. T cell mediated autoimmune diseases include Rheumatoid arthritis (RA), multiple sclerosis (MS), Sjögren's syndrome, sarcoidosis, insulin dependent diabetes mellitus (IDDM), autoimmune thyroiditis, reactive arthritis, ankylosing spondylitis, scleroderma, polymyositis, dermatomyositis, psoriasis, vasculitis, Wegener's granulomatosis, Crohn's disease and ulcerative colitis. Each of these diseases is characterized by T cell receptors (TCRs) that bind to endogenous antigens and initiate the inflammatory cascade associated with autoimmune diseases.

The simian adenoviral vectors of the invention are particularly well suited for therapeutic regimens in which multiple adenoviral-mediated deliveries of transgenes is desired, e.g., in regimens involving redelivery of the same transgene or in combination regimens involving delivery of other transgenes. Such regimens may involve administration of a Pan5, Pan6, Pan7, SV1, SV25 or SV39 simian adenoviral vector, followed by re-administration with a vector from the same serotype adenovirus. Particularly desirable regimens involve administration of a Pan5, Pan6, Pan7, SV1, SV25 or SV39 simian adenoviral vector of the invention, in which the serotype of the viral

vector delivered in the first administration differs from the serotype of the viral vector utilized in one or more of the subsequent administrations. For example, a therapeutic regimen involves administration of a Pan5, Pan6, Pan7, SV1, SV25 or SV39 vector and repeat administration with one or more adenoviral vectors of the same or different serotypes. In another example, a therapeutic regimen involves administration of an adenoviral vector followed by repeat administration with a Pan5, Pan6, Pan7, SV1, SV25 or SV39 vector of the invention which differs from the serotype of the first delivered adenoviral vector, and optionally further administration with another vector which is the same or, preferably, differs from the serotype of the vector in the prior administration steps. These regimens are not limited to delivery of adenoviral vectors constructed using the Pan5, Pan6, Pan7, SV1, SV25 or SV39 simian serotypes of the invention. Rather, these regimens can readily utilize vectors other adenoviral serotypes, including, without limitation, other simian adenoviral serotypes (e.g., Pan9 or C68, C1, etc), other non-human primate adenoviral serotypes, or human adenoviral serotypes, in combination with one or more of the Pan5, Pan6, Pan7, SV1, SV25 or SV39 vectors of the invention. Examples of such simian, other non-human primate and human adenoviral serotypes are discussed elsewhere in this document. Further, these therapeutic regimens may involve either simultaneous or sequential delivery of Pan 5, Pan6, Pan7, SV1, SV25, and/or SV39 adenoviral vectors of the invention in combination with non-adenoviral vectors, non-viral vectors, and/or a variety of other therapeutically useful compounds or molecules. The present invention is not limited to these therapeutic regimens, a variety of which will be readily apparent to one of skill in the art.

B. Ad-Mediated Delivery of Immunogenic Transgenes

The recombinant simian adenoviruses may also be employed as immunogenic compositions. As used herein, an immunogenic composition is a composition to which a humoral (e.g., antibody) or cellular (e.g., a cytotoxic T cell) response is mounted to a transgene product delivered by the immunogenic composition following delivery to a mammal, and preferably a primate. The present invention provides a recombinant simian Ad that can contain in any of its adenovirus sequence deletions a gene encoding a desired immunogen. The simian adenovirus is likely to be better suited for use as a live recombinant virus vaccine in different animal species compared to an adenovirus of human origin, but is not limited to such a use. The

recombinant adenoviruses can be used as prophylactic or therapeutic vaccines against any pathogen for which the antigen(s) crucial for induction of an immune response and able to limit the spread of the pathogen has been identified and for which the cDNA is available.

Such vaccinal (or other immunogenic) compositions are formulated in a suitable delivery vehicle, as described above. Generally, doses for the immunogenic compositions are in the range defined above for therapeutic compositions. The levels of immunity of the selected gene can be monitored to determine the need, if any, for boosters. Following an assessment of antibody titers in the serum, optional booster immunizations may be desired.

Optionally, a vaccinal composition of the invention may be formulated to contain other components, including, e.g. adjuvants, stabilizers, pH adjusters, preservatives and the like. Such components are well known to those of skill in the vaccine art. Examples of suitable adjuvants include, without limitation, liposomes, alum, monophosphoryl lipid A, and any biologically active factor, such as cytokine, an interleukin, a chemokine, a ligands, and optimally combinations thereof. Certain of these biologically active factors can be expressed *in vivo*, e.g., via a plasmid or viral vector. For example, such an adjuvant can be administered with a priming DNA vaccine encoding an antigen to enhance the antigen-specific immune response compared with the immune response generated upon priming with a DNA vaccine encoding the antigen only.

The recombinant adenoviruses are administered in a "an immunogenic amount", that is, an amount of recombinant adenovirus that is effective in a route of administration to transfect the desired cells and provide sufficient levels of expression of the selected gene to induce an immune response. Where protective immunity is provided, the recombinant adenoviruses are considered to be vaccine compositions useful in preventing infection and/or recurrent disease.

Alternatively, or in addition, the vectors of the invention may contain a transgene encoding a peptide, polypeptide or protein which induces an immune response to a selected immunogen. The recombinant adenoviruses of this invention are expected to be highly efficacious at inducing cytolytic T cells and antibodies to the inserted heterologous antigenic protein expressed by the vector.

For example, immunogens may be selected from a variety of viral families. Example of desirable viral families against which an immune response would be desirable include, the picornavirus family, which includes the genera rhinoviruses, which are responsible for about 50% of cases of the common cold; the genera enteroviruses, which include polioviruses, coxsackieviruses, echoviruses, and human enteroviruses such as hepatitis A virus; and the genera apthoviruses, which are responsible for foot and mouth diseases, primarily in non-human animals. Within the picornavirus family of viruses, target antigens include the VP1, VP2, VP3, VP4, and VPG. Another viral family includes the calcivirus family, which encompasses the Norwalk group of viruses, which are an important causative agent of epidemic gastroenteritis. Still another viral family desirable for use in targeting antigens for inducing immune responses in humans and non-human animals is the togavirus family, which includes the genera alphavirus, which include Sindbis viruses, RossRiver virus, and Venezuelan, Eastern & Western Equine encephalitis, and rubivirus, including Rubella virus. The flaviviridae family includes dengue, yellow fever, Japanese encephalitis, St. Louis encephalitis and tick borne encephalitis viruses. Other target antigens may be generated from the Hepatitis C or the coronavirus family, which includes a number of non-human viruses such as infectious bronchitis virus (poultry), porcine transmissible gastroenteric virus (pig), porcine hemagglutinating encephalomyelitis virus (pig), feline infectious peritonitis virus (cats), feline enteric coronavirus (cat), canine coronavirus (dog), and human respiratory coronaviruses, which may cause the common cold and/or non-A, B or C hepatitis. Within the coronavirus family, target antigens include the E1 (also called M or matrix protein), E2 (also called S or Spike protein), E3 (also called HE or hemagglutin-elterose) glycoprotein (not present in all coronaviruses), or N (nucleocapsid). Still other antigens may be targeted against the rhabdovirus family, which includes the genera vesiculovirus (e.g., Vesicular Stomatitis Virus), and the general lyssavirus (e.g., rabies). Within the rhabdovirus family, suitable antigens may be derived from the G protein or the N protein. The family filoviridae, which includes hemorrhagic fever viruses such as Marburg and Ebola virus, may be a suitable source of antigens. The paramyxovirus family includes parainfluenza Virus Type 1, parainfluenza Virus Type 3, bovine parainfluenza Virus Type 3, rubulavirus (mumps virus), parainfluenza Virus Type 2, parainfluenza virus Type 4, Newcastle disease virus (chickens), rinderpest,

morbillivirus, which includes measles and canine distemper, and pneumovirus, which includes respiratory syncytial virus. The influenza virus is classified within the family orthomyxovirus and is a suitable source of antigen (e.g., the HA protein, the N1 protein). The bunyavirus family includes the genera bunyavirus (California encephalitis, La Crosse), phlebovirus (Rift Valley Fever), hantavirus (puremala is a hemahagin fever virus), nairovirus (Nairobi sheep disease) and various unassigned bungaviruses. The arenavirus family provides a source of antigens against LCM and Lassa fever virus. The reovirus family includes the genera reovirus, rotavirus (which causes acute gastroenteritis in children), orbiviruses, and cultivirus (Colorado Tick fever, Lebombo (humans), equine encephalosis, blue tongue).

The retrovirus family includes the sub-family oncorivirinal which encompasses such human and veterinary diseases as feline leukemia virus, HTLVI and HTLVII, lentivirinal (which includes human immunodeficiency virus (HIV), simian immunodeficiency virus (SIV), feline immunodeficiency virus (FIV), equine infectious anemia virus, and spumavirinal). Among the lentiviruses, many suitable antigens have been described and can readily be selected. Examples of suitable HIV and SIV antigens include, without limitation the gag, pol, Vif, Vpx, VPR, Env, Tat, Nef, and Rev proteins, as well as various fragments thereof. For example, suitable fragments of the Env protein may include any of its subunits such as the gp120, gp160, gp41, or smaller fragments thereof, e.g., of at least about 8 amino acids in length. Similarly, fragments of the tat protein may be selected. [See, US Patent 5,891,994 and US Patent 6,193,981.] See, also, the HIV and SIV proteins described in D.H. Barouch et al, J. Virol., 75(5):2462-2467 (March 2001), and R.R. Amara, et al, *Science*, **292**:69-74 (6 April 2001). In another example, the HIV and/or SIV immunogenic proteins or peptides may be used to form fusion proteins or other immunogenic molecules. See, e.g., the HIV-1 Tat and/or Nef fusion proteins and immunization regimens described in WO 01/54719, published August 2, 2001, and WO 99/16884, published April 8, 1999. The invention is not limited to the HIV and/or SIV immunogenic proteins or peptides described herein. In addition, a variety of modifications to these proteins have been described or could readily be made by one of skill in the art. See, e.g., the modified gag protein that is described in US Patent 5,972,596. Further, any desired HIV and/or SIV immunogens may be delivered alone or in combination. Such combinations may include expression from a single vector or from

multiple vectors. Optionally, another combination may involve delivery of one or more expressed immunogens with delivery of one or more of the immunogens in protein form. Such combinations are discussed in more detail below.

The papovavirus family includes the sub-family polyomaviruses (BKU and JCU viruses) and the sub-family papillomavirus (associated with cancers or malignant progression of papilloma). The adenovirus family includes viruses (EX, AD7, ARD, O.B.) which cause respiratory disease and/or enteritis. The parvovirus family feline parvovirus (feline enteritis), feline panleucopeniavirus, canine parvovirus, and porcine parvovirus. The herpesvirus family includes the sub-family alphaherpesvirinae, which encompasses the genera simplexvirus (HSVI, HSVII), varicellovirus (pseudorabies, varicella zoster) and the sub-family betaherpesvirinae, which includes the genera cytomegalovirus (HCMV, muromegalovirus) and the sub-family gammaherpesvirinae, which includes the genera lymphocryptovirus, EBV (Burkitts lymphoma), infectious rhinotracheitis, Marek's disease virus, and rhadinovirus. The poxvirus family includes the sub-family chordopoxvirinae, which encompasses the genera orthopoxvirus (Variola (Smallpox) and Vaccinia (Cowpox)), parapoxvirus, avipoxvirus, capripoxvirus, leporipoxvirus, suipoxvirus, and the sub-family entomopoxvirinae. The hepadnavirus family includes the Hepatitis B virus. One unclassified virus which may be suitable source of antigens is the Hepatitis delta virus. Still other viral sources may include avian infectious bursal disease virus and porcine respiratory and reproductive syndrome virus. The alphavirus family includes equine arteritis virus and various Encephalitis viruses.

The present invention may also encompass immunogens which are useful to immunize a human or non-human animal against other pathogens including bacteria, fungi, parasitic microorganisms or multicellular parasites which infect human and non-human vertebrates, or from a cancer cell or tumor cell. Examples of bacterial pathogens include pathogenic gram-positive cocci include pneumococci; staphylococci; and streptococci. Pathogenic gram-negative cocci include meningococcus; gonococcus. Pathogenic enteric gram-negative bacilli include enterobacteriaceae; pseudomonas, acinetobacteria and eikenella; melioidosis; salmonella; shigella; haemophilus; moraxella; *H. ducreyi* (which causes chancroid); brucella; *Franisella tularensis* (which causes tularemia); yersinia (pasteurella); streptobacillus moniliformis and spirillum; Gram-

positive bacilli include listeria monocytogenes; erysipelothrix rhusiopathiae; *Corynebacterium diphtheria* (diphtheria); cholera; *B. anthracis* (anthrax); donovanosis (granuloma inguinale); and bartonellosis. Diseases caused by pathogenic anaerobic bacteria include tetanus; botulism; other clostridia; tuberculosis; leprosy; and other mycobacteria. Pathogenic spirochetal diseases include syphilis; treponematoses: yaws, pinta and endemic syphilis; and leptospirosis. Other infections caused by higher pathogen bacteria and pathogenic fungi include actinomycosis; nocardiosis; cryptococcosis, blastomycosis, histoplasmosis and coccidioidomycosis; candidiasis, aspergillosis, and mucormycosis; sporotrichosis; paracoccidiodomycosis, petriellidiosis, torulopsosis, mycetoma and chromomycosis; and dermatophytosis. Rickettsial infections include Typhus fever, Rocky Mountain spotted fever, Q fever, and Rickettsialpox. Examples of mycoplasma and chlamydial infections include: mycoplasma pneumoniae; lymphogranuloma venereum; psittacosis; and perinatal chlamydial infections. Pathogenic eukaryotes encompass pathogenic protozoans and helminths and infections produced thereby include: amebiasis; malaria; leishmaniasis; trypanosomiasis; toxoplasmosis; *Pneumocystis carinii*; *Trichans*; *Toxoplasma gondii*; babesiosis; giardiasis; trichinosis; filariasis; schistosomiasis; nematodes; trematodes or flukes; and cestode (tapeworm) infections.

Many of these organisms and/or toxins produced thereby have been identified by the Centers for Disease Control [(CDC), Department of Heath and Human Services, USA], as agents which have potential for use in biological attacks. For example, some of these biological agents, include, *Bacillus anthracis* (anthrax), *Clostridium botulinum* and its toxin (botulism), *Yersinia pestis* (plague), variola major (smallpox), *Francisella tularensis* (tularemia), and viral hemorrhagic fevers [filoviruses (e.g., Ebola, Marburg], and arenaviruses [e.g., Lassa, Machupo]), all of which are currently classified as Category A agents; *Coxiella burnetti* (Q fever); Brucella species (brucellosis), *Burkholderia mallei* (glanders), *Burkholderia pseudomallei* (meloidosis), *Ricinus communis* and its toxin (ricin toxin), *Clostridium perfringens* and its toxin (epsilon toxin), *Staphylococcus* species and their toxins (enterotoxin B), *Chlamydia psittaci* (psittacosis), water safety threats (e.g., *Vibrio cholerae*, *Crytosporidium parvum*), Typhus fever (*Richettsia powazekii*), and viral encephalitis (alphaviruses, e.g., Venezuelan equine encephalitis; eastern equine encephalitis; western equine

encephalitis); all of which are currently classified as Category B agents; and Nipan virus and hantaviruses, which are currently classified as Category C agents. In addition, other organisms, which are so classified or differently classified, may be identified and/or used for such a purpose in the future. It will be readily understood that the viral vectors and other constructs described herein are useful to deliver antigens from these organisms, viruses, their toxins or other by-products, which will prevent and/or treat infection or other adverse reactions with these biological agents.

Administration of the vectors of the invention to deliver immunogens against the variable region of the T cells elicit an immune response including CTLs to eliminate those T cells. In RA, several specific variable regions of TCRs which are involved in the disease have been characterized. These TCRs include V-3, V-14, V-17 and Vα-17. Thus, delivery of a nucleic acid sequence that encodes at least one of these polypeptides will elicit an immune response that will target T cells involved in RA. In MS, several specific variable regions of TCRs which are involved in the disease have been characterized. These TCRs include V-7 and Vα-10. Thus, delivery of a nucleic acid sequence that encodes at least one of these polypeptides will elicit an immune response that will target T cells involved in MS. In scleroderma, several specific variable regions of TCRs which are involved in the disease have been characterized. These TCRs include V-6, V-8, V-14 and Vα-16, Vα-3C, Vα-7, Vα-14, Vα-15, Vα-16, Vα-28 and Vα-12. Thus, delivery of a recombinant simian adenovirus that encodes at least one of these polypeptides will elicit an immune response that will target T cells involved in scleroderma.

C. Ad-Mediated Delivery Methods

The therapeutic levels, or levels of immunity, of the selected gene can be monitored to determine the need, if any, for boosters. Following an assessment of CD8+ T cell response, or optionally, antibody titers, in the serum, optional booster immunizations may be desired. Optionally, the recombinant simian adenoviral vectors of the invention may be delivered in a single administration or in various combination regimens, e.g., in combination with a regimen or course of treatment involving other active ingredients or in a prime-boost regimen. A variety of such regimens have been described in the art and may be readily selected.

For example, prime-boost regimens may involve the administration of a DNA (e.g., plasmid) based vector to prime the immune system to second, booster, administration with a traditional antigen, such as a protein or a recombinant virus carrying the sequences encoding such an antigen. See, e.g., WO 00/11140, published March 2, 2000, incorporated by reference. Alternatively, an immunization regimen may involve the administration of a recombinant simian adenoviral vector of the invention to boost the immune response to a vector (either viral or DNA-based) carrying an antigen, or a protein. In still another alternative, an immunization regimen involves administration of a protein followed by booster with a vector encoding the antigen.

In one embodiment, the invention provides a method of priming and boosting an immune response to a selected antigen by delivering a plasmid DNA vector carrying said antigen, followed by boosting with a recombinant simian adenoviral vector of the invention. In one embodiment, the prime-boost regimen involves the expression of multiproteins from the prime and/or the boost vehicle. See, e.g., R.R. Amara, *Science*, **292**:69-74 (6 April 2001) which describes a multiprotein regimen for expression of protein subunits useful for generating an immune response against HIV and SIV. For example, a DNA prime may deliver the Gag, Pol, Vif, VPX and Vpr and Env, Tat, and Rev from a single transcript. Alternatively, the SIV Gag, Pol and HIV-1 Env is delivered in a recombinant adenovirus construct of the invention. Still other regimens are described in WO 99/16884 and WO 01/54719.

However, the prime-boost regimens are not limited to immunization for HIV or to delivery of these antigens. For example, priming may involve delivering with a first chimp vector of the invention followed by boosting with a second chimp vector, or with a composition containing the antigen itself in protein form. In one example, the prime-boost regimen can provide a protective immune response to the virus, bacteria or other organism from which the antigen is derived. In another desired embodiment, the prime-boost regimen provides a therapeutic effect that can be measured using convention assays for detection of the presence of the condition for which therapy is being administered.

The priming composition may be administered at various sites in the body in a dose dependent manner, which depends on the antigen to which the desired immune response is being targeted. The invention is not limited to the amount or situs of

injection(s) or to the pharmaceutical carrier. Rather, the regimen may involve a priming and/or boosting step, each of which may include a single dose or dosage that is administered hourly, daily, weekly or monthly, or yearly. As an example, the mammals may receive one or two doses containing between about 10 μg to about 50 μg of plasmid in carrier. A desirable amount of a DNA composition ranges between about 1 μg to about 10,000 μg of the DNA vector. Dosages may vary from about 1 μg to 1000 μg DNA per kg of subject body weight. The amount or site of delivery is desirably selected based upon the identity and condition of the mammal.

The dosage unit of the vector suitable for delivery of the antigen to the mammal is described herein. The vector is prepared for administration by being suspended or dissolved in a pharmaceutically or physiologically acceptable carrier such as isotonic saline; isotonic salts solution or other formulations that will be apparent to those skilled in such administration. The appropriate carrier will be evident to those skilled in the art and will depend in large part upon the route of administration. The compositions of the invention may be administered to a mammal according to the routes described above, in a sustained release formulation using a biodegradable biocompatible polymer, or by on-site delivery using micelles, gels and liposomes. Optionally, the priming step of this invention also includes administering with the priming composition, a suitable amount of an adjuvant, such as are defined herein.

Preferably, a boosting composition is administered about 2 to about 27 weeks after administering the priming composition to the mammalian subject. The administration of the boosting composition is accomplished using an effective amount of a boosting composition containing or capable of delivering the same antigen as administered by the priming DNA vaccine. The boosting composition may be composed of a recombinant viral vector derived from the same viral source (e.g., adenoviral sequences of the invention) or from another source. Alternatively, the "boosting composition" can be a composition containing the same antigen as encoded in the priming DNA vaccine, but in the form of a protein or peptide, which composition induces an immune response in the host. In another embodiment, the boosting composition contains a DNA sequence encoding the antigen under the control of a regulatory sequence directing its expression in a mammalian cell, e.g., vectors such as well-known bacterial or viral vectors. The primary requirements of the boosting composition are that the antigen

of the composition is the same antigen, or a cross-reactive antigen, as that encoded by the priming composition.

In another embodiment, the simian adenoviral vectors of the invention are also well suited for use in a variety of other immunization and therapeutic regimens. Such regimens may involve delivery of simian adenoviral vectors of the invention simultaneously or sequentially with Ad vectors of different serotype capsids, regimens in which adenoviral vectors of the invention are delivered simultaneously or sequentially with non-Ad vectors, regimens in which the adenoviral vectors of the invention are delivered simultaneously or sequentially with proteins, peptides, and/or other biologically useful therapeutic or immunogenic compounds. Such uses will be readily apparent to one of skill in the art.

The following examples illustrate the cloning of the simian adenoviruses and the construction of exemplary recombinant adenovirus vectors of the present invention. These examples are illustrative only, and do not limit the scope of the present invention.

Example 1 - Viral Propagation

The Pan5 [ATCC Accession No. VR-591], Pan6 [ATCC Accession No. VR-592], and Pan7 [ATCC Accession No. VR-593] viruses, originally isolated from lymph nodes from chimpanzees, were propagated in 293 cells [ATCC CRL1573]. Typically, these cells are cultured in Dulbecco's Modified Eagles Medium (DMEM; Sigma, St. Louis, MO.) supplemented with 10% fetal calf serum (FCS) [Sigma or Hyclone, Logan, UT] and 1 % Penicillin-Streptomycin (Sigma). Infection of 293 cells is carried out in DMEM supplemented with 2% FCS for the first 24 hours, after which FCS is added to bring the final concentration to 10%. Infected cells are harvested when 100% of the cells exhibit virus-induced cytopathic effect (CPE), and are then collected, and concentrated by centrifugation. Cell pellets are resuspended in 10 mM Tris (pH 8.0), and lysed by 3 cycles of freezing and thawing. Virus preparations are obtained following two ultra centrifugation steps on cesium chloride density gradients and stocks of virus are diluted to 1 to 5 x 10^{12} particles/ml in 10 mM Tris/100 mM NaCl/50% glycerol and stored at -70°C.

The ability of 293 cells to propagate these adenoviruses exceeded expectations which were based on knowledge of other non-human adenovirus serotypes.

Virus	Yield (virus particles produced in $8x10^8$ cells)
Pan5	8.8×10^{13}
Pan6	1.6×10^{14}
Pan7	8.8×10^{13}

Example 2 – Characterization of Viral Genomic DNA

Genomic DNA was isolated from the purified virus preparations of Example 1 and digested with HindIII or BamHI restriction enzymes following the manufacturers' recommendations. The results (not shown) revealed that that the Pan5, Pan6, Pan7 genomes of the invention and the published Pan 9 (C68) genome show different restriction patterns, and thus, are distinct from each other.

The nucleotide sequences of Pan5, Pan6 and Pan7 were determined. The nucleotide sequence of the top strand of Pan5 DNA is reported in SEQ ID NO: 1. The nucleotide sequence of the top strand of Pan6 DNA is reported in SEQ ID NO: 5. The nucleotide sequence of the top strand of Pan7 DNA is reported in SEQ ID NO: 9.

Regulatory and coding regions in the viral DNA sequences were identified by homology to known adenoviral sequences using the "Clustal W" program described above at conventional settings. See the tables above providing the adenoviral sequences. Open reading frames were translated and the predicted amino acid sequences examined for homology to previously described adenoviral protein sequences, Ad4, Ad5, Ad7, Ad12, and Ad40.

Analysis of the sequence revealed a genome organization that is similar to that present in human adenoviruses, with the greatest similarity to human Ad4. However, substantial differences in the hexon hypervariable regions were noted between the chimpanzee adenoviruses and other known adenoviruses, including AdHu4. These differences fit well with the serological cross-reactivity data that has been obtained (see below).

An alignment of a portion of the hexon sequences is shown in Fig. 1. The portion shown is from the region of the hexon that corresponds to the outwardly disposed extended loops DE1 and FG1 where the most variability between serotypes is observed.

An intervening portion that contributes to the base of the hexon (corresponding to residues 308-368 of the published AdC68 sequence; US Patent 6,083,716), and is highly conserved between serotypes, is also present. The following table summarizes the pair-wise comparisons of the amino acids in the hexon proteins.

Comparison		Hexon amino-acid Similarity (%)
#1	#2	
AdC5	AdC7	99.0
AdC5	AdC68	98.3
AdC5	AdC6	88.0
AdC5	AdC1	84.9
AdC6	AdC7	87.7
AdC6	AdC68	87.3
AdC6	AdC1	84.9
AdC7	AdC68	97.5
AdC7	AdC1	84.8
AdC68	AdC1	84.9

Analysis of the fiber knob domain (which is responsible for receptor binding) of the chimpanzee adenoviruses shows an overall similarity in structure (Fig. 2).

The degree of sequence similarity between the E1 proteins of huAd5 and C68 (see Tables below) is similar to that between huAd5 and Pan-5, Pan-6, and Pan-7.

Comparison		E1a (13S) amino-acid identity (%)
#1	#2	
AdHu5	AdC5	36.6
AdHu5	AdC6	28.5
AdHu5	AdC7	34.9
AdHu5	AdC68	35.6
AdHu5	AdC1	35.6
AdC5	AdC6	68.3
AdC5	AdC7	96.9
AdC5	AdC68	80.4
AdC5	AdC1	51.3
AdC6	AdC7	69.3
AdC6	AdC68	59.4
AdC6	AdC1	37.7
AdC7	AdC68	81.5
AdC7	AdC1	51.0
AdC68	AdC1	54.9

	Sequence Identity with human Ad5	
	E1b Small T Protein	E1b Large T Protein
C68	47.3%	55.8%
Pan-5	43.2%	54.5%
Pan-6	45.3%	54.5%
Pan-7	46.4%	53.8%

Replication-defective versions of AdC5, AdC6 and AdC7 were created by molecular cloning methods described in the following examples in which minigene cassettes were inserted into the place of the E1a and E1b genes. The molecular clones of the recombinant viruses were rescued and grown up in 293 cells for large-scale purification using the published CsCl sedimentation method [K. Fisher *et al.*, J. Virol., **70**:520 (1996)]. Vector yields were based on 50 plate (150 mm) preps in which approximately 1 x 10^9 293 cells were infected with the corresponding viruses. Yields were determined by measuring viral particle concentrations spectrophotometrically. After having constructed E1-deleted vectors, it was determined that HEK 293 cells (which express human adenovirus serotype 5 E1 functions) trans-complement the E1 deletions of the novel viral vectors and allow for the production of high titer stocks. Examples of virus yields for a few of these recombinant viruses are shown in the table below.

The transgenes for these vectors, β-galactosidase (LacZ), green fluorescent protein (GFP), alpha-1-anti-trypsin (A1AT), ebola glycoprotein (ebo), a soluble ebola glycoprotein variant lacking the transmembrane and cytoplasmic domains (sEbo), and three deletion mutants of the ebola glycoprotein (EboΔ2, EboΔ3, and EboΔ4), were expressed by the cytomegalovirus promoter (CMV). In the following table, ND indicates that the study has not yet been done.

Transgene	Viral backbone/Vector yield (Viral particles x 10^{13})			
	AdHu5	AdC7	**AdC68**	**AdC6**
CMVLacZ	1.5	1.4	3.3	6.1
CMVGFP	2.5	3.6	8	10
CMVA1AT	3.7	6	10	ND
CMVEbo	1.1	4.3	ND	ND
CMVsEbo	4.9	5.4	ND	ND
CMVEboΔ2	1	9.3	ND	ND
CMVEboΔ3	0.8	9.5	ND	ND
CMVEboΔ4	1.4	6.2	ND	ND

The ability of human adenovirus E1 to trans-complement the E1-deleted chimpanzee viruses of the invention is highly advantageous, as it permits the production of E1-deleted chimpanzee adenoviral vectors of the invention, while reducing or eliminating the risk of homologous recombination due to the differences in sequences between human Ad and the chimpanzee adenoviruses described herein.

Example 3 – Serological Studies of Pan 5, 6, and 7 Viruses

Because of the differences in the hexon hypervariable region, it was anticipated that the C5, C6, and C7 viruses would be serologically distinct from human adenoviruses, including AdHu4.

1. *Cross-Reactivity of Wild-type Viruses*

For screening of wild-type viruses in order to make a determination of antibody cross-reactivity, the replication competent viruses were used and inhibition of cytopathic effects (CPE) was measured. Briefly, preparations of adenoviruses (Adhu5, Pan-5, Pan-6, Pan-7 and AdC68) stored at $5x10^{12}$ particles/ml were diluted 1/600 for the assays. This concentration of virus was selected since it results in 100% CPE within 48 hours in the absence of neutralization. Prior to adding the virus to 293 cells ($4x10^4$ cells/well in a 96 well dish), 1:20 dilutions of sera were added. The assay is read as the presence or absence of CPE; full neutralization would read as no cytopathic effect. The results are summarized in the Table below. The fact that 9/36 human sera neutralized Adhu5 induced CPE is consistent with previous estimates of neutralizing antibodies in the human population. The numbers indicate the total individuals who showed neutralization (numerator) versus the total number screened (denominator). ND = not determined.

	Neutralization by 1/20 diln of serum		
	Human (N=36)	Rhesus (N=52)	Chimpanzee (N=20)
Adhu5	9/36	ND	ND
AdC68	1/36	0/52	12/20
Pan 5	0/36	0/52	10/20
Pan 6	0/36	0/52	9/20
Pan 7	0/36	0/52	12/20

Of all human sera screened, 35/36 were negative for neutralization to AdC68 while 36/36 were negative for neutralization to Pan-5, Pan-6 and Pan-7. Of 52 rhesus monkeys screened, none showed neutralization to any chimpanzee adenovirus; rhesus monkey is the preferred pre-clinical model for evaluating HIV vaccines. Between 9 to 12 out of 20 chimpanzees had substantial neutralization to one or another of the chimpanzee adenoviruses consistent with the fact these are indeed endemic chimpanzee-specific pathogens. Interestingly, there are chimpanzees with neutralizing antibodies only to Pan-5, Pan-6 or AdC68 supporting the hypothesis that several of these chimpanzee adenoviral vectors will not cross neutralize each other and are distinct serotypes.

The same assay was carried out for 20 chimpanzee serum samples. Fifty percent (50%) of the samples reacted serologically, in different degrees to Pan5; 40% to Pan6; 55% to Pan7 and 60% to C68. Among the positive serum samples, one of them had strong neutralizing activity to all four chimp viruses.

2. *Cross-neutralization with Recombinant Viruses*

High-titer polyclonal antibodies were obtained to each of the simian adenoviruses in order to more precisely gauge the degree of cross-neutralization among the different serotypes. This was done by intramuscular immunization of rabbits using a recombinant virus containing GFP based on previously the described C68 chimpanzee adenovirus as an adjuvant. The serum was then used to assay for neutralizing activity against each of the three chimpanzee adenoviruses of the invention, AdC5, AdC6 and AdC7. A rabbit was injected with $5x10^{12}$ viral particle per kg of C68CMVGFP vector intramuscularly and boosted 5 weeks later using the same dose. A bleed collected at the 9 week time point revealed extremely potent neutralizing activity against C68 as well as Pan-5 and Pan-7 but not against Pan-6 (see Table below), indicating that the administration of a C68 (or Pan-5 and Pan-7) based vaccine could be effectively followed by a boost using a vector based on Pan-6. However, it has been found that this level of inter-relatedness does not necessarily prevent with re-administration in a setting where antiviral antibody titers were not as high as was achieved in this rabbit. In the following table, + indicates 33% CPE; ++ indicates 66% CPE; +++ indicates 100% CPE.

Infection on 293 cells with virus:					
Pan5	Pan6	Pan7	Pan9(C68)	C68 GFP	Serum Dilution
-	+++	-	-	-	1/20
-	+++	-	-	-	1/40
-	+++	-	-	-	1/80
-	+++	-	-	-	1/160
-	+++	-	-	-	1/320
-	+++	-	-	-	1/640
-	+++	-	-	-	1/1,280
-	+++	-	-	-	1/2,560
-	+++	-	-	-	1/5,120
+	+++	-	-	-	1/10,240
+	+++	++	-	-	1/20,480
++	+++	+++	-	-	1/40,960
++	+++	+++	+	+	1/81,920
+++	+++	+++	++	++	1/163,840
+++	+++	+++	+++	+++	1/327,680
+++	+++	+++	+++	+++	1/665,360
+++	+++	+++	+++	+++	1/1,310,720
+++	+++	+++	+++	+++	1/2,621,440

3. *Quantitative Assay for Detection of Neutralizing Antibody*

The result was validated by a more quantitative-based assay for detecting neutralizing antibody, which is based on transduction of a GFP vector. Briefly, groups of C57BL/6 mice were immunized intramuscularly or intravenously with 5.0×10^{10} particles/ml Pan5, Pan6, Pan7 or C68. Sera from day 28 bleeds were tested for cross-neutralizing activity against C68CMVEGFP at dilutions of 1/20 and 1/80. In summary, when a pharmaceutical preparation of human immunoglobulin was tested for serological reactions to Pan 5, 6, and 7, and C68, some low levels of neutralizing activities against Pan 7 and C68 were detected. No neutralizing activity against Pan5 or Pan6 was detected. Serum samples from 36 human subjects were run for the same assay. Serum samples were tested at a 1/20 dilution. The results indicated that only one individual has clear neutralizing activity to C68. No neutralizing activity to Pan5, Pan6 or Pan7 was detected.

4. *In Vitro Cross-Neutralization*

Cross-neutralization of the simian adenoviruses by high-titer rabbit polyclonal antibodies raised against each of the adenoviruses Pan-5, Pan-6, Pan-7, and C68 was tested.

Rabbits were immunized with intra-muscular injections of 10^{13} particles of each of the chimpanzee adenoviruses and boosted 40 days later with the same dose with incomplete Freund's adjuvant. Sera were analyzed or the presence of neutralizing antibodies by incubating serial two-fold dilutions with 10^9 genome copies of each of the appropriate chimpanzee adenovirus vector expressing GFP and testing for the attenuation of GFP expression when applied to 293 cells. The serum dilution which produced a 50% reduction of GFP expression was scored as the neutralizing antibody titer against that particular virus.

The results are shown in the Table. The data are consistent with the expectation from sequence analysis of the hexon amino-acid sequences, which indicated that Ad Pan-6 was likely to be the most serologically distinct compared to the other chimpanzee adenoviruses.

	Infection of 293 cells with 10^9 genome copies of			
Serum from rabbit immunized with:	Ad Pan-5	Ad Pan-6	Ad Pan-7	Ad C68
Ad Pan-5	1/5120	<1/20	1/2560	1/2560
Ad Pan-6	No neutralization	1/20,480	<1/20	<1/20
Ad Pan-7	1/2560	1/160	1/163,840	1/2560
Ad C68	No neutralization	<1/20	<1/20	1/5120

In order to determine whether antibodies cross-reacting with the simian adenoviruses were likely to be of low prevalence in humans, simian adenoviruses SV1, SV39, and SV25 were tested for their ability to withstand neutralization when incubated with commercially available pooled human immunoglobulins (Ig). The same assay was also performed with Adhu5 and the chimpanzee adenoviruses Pan-5, Pan-6, Pan-7, and C68. In a further study, sera from mice has been immunized with one of the chimpanzee adenoviruses C5, C6, C7, and C68 and their ability to cross-neutralize the simian adenoviruses SV-15, SV-23, SA-17, and Baboon Adenovirus has been tested. No cross-reactivity was observed in any case.

Example 4 – Generation of Recombinant E1-Deleted Pan5 Vector

A modified pX plasmid was prepared by destroying the FspI site in the bla gene region of pX (Clontech) by site-directed mutagenesis. The resulting modified plasmid, termed pX', is a circular plasmid of 3000 bp which contains an f1 ori and an ampicillin resistance gene (AmpR-cds).

A. *Production of Pan-5 Adenovirus Plasmid*

A polylinker for sequential cloning of the Pan5 DNA fragments into pX' is created. The polylinker is substituted for the existing pX' polylinker following digestion with *MluI* and *EcoRI*. The blunt-*FseI* fragment of the Pan 5 is inserted into the *SmaI* and *FseI* sites of the polylinker. This fragment contains the 5' end

of the adenoviral genome (bp 1 to 3606, SEQ ID NO:1). The *SnaBI-FspI* fragment of Pan 5 (bp 455 to 3484, SEQ ID NO:1) is replaced with a short sequence flanked by *I-CeuI* and *PI-SceI* sites from pShuttle (Clontech), to eliminate the E1 region of the adenoviral genome. The *EcoRI*-blunt fragment of Pan5 (bp 28658 to 36462, SEQ ID NO:1) is inserted into the *EcoRI* and *EcoRV* sites of the polylinker (to provide the 3' end of the adenoviral genome); the *FseI-MluI* fragment (bp 3606 to 15135, SEQ ID NO:1) is inserted into the polylinker; and the *MluI-EcoRI* fragment is inserted into the polylinker (bp 15135 to 28658, SEQ ID NO:1). Optionally, a desired transgene is inserted into *I-CeuI* and *PI-SceI* sites of the newly created pX'Pan5ΔE1 vector.

B. *Alternative Method of Generating pX'Pan5ΔE1.*

The initial plasmid pX is derived from pAdX adenovirus plasmid available from Clontech, as described above. Thereafter, a *PacI-XhoI* region of pX' was deleted and the blunt-ended Pan5 polylinker was inserted into the *FspI* site to generate pX'PLNK (2994 bp). The 5'end-*FseI* region of Pan 5 (bp 1-3607, SEQ ID NO:1) was inserted into *SmaI* and *FseI* sites of pX'LNK to generate the pX'Pan5-5' plasmid (6591 bp). The *SnaBi-NdeI* region of pX'Pan5-5' was excised and replaced with the *Ceu/Sce* cassette, which had been PCR amplified from pRCS to create pX'Pan5-5'ΔE1 (4374 bp). Briefly, a sequence containing *I-CeuI* and *PI-SceI* rare cutter sites was PCR amplified from pRCS (3113bp). The 3' PCR primer was introduced an *NdeI* site into the PCR product.

To extend the Pan5 DNA in pX'Pan5-5'ΔE1 (4374 bp), the *FseI-MluI* region of Pan 5 (bp 3607-15135, SEQ ID NO:1) is added, to create pX'Pan5-5'Mlu (15900 bp). The remaining MluI-3' end of the Pan5 sequence (bp 15135-36462, SEQ ID NO:1) is added to the vector between the MluI and EcoRV sites of the vector polylinker to form pX'Pan5ΔE1 which contains the full-length Pan5 sequence containing a deletion in the E1 region.

C. Generation of Recombinant Viruses

To generate the recombinant adenoviruses from pX'Pan5ΔE1, the plasmid is co-transfected with a helper expressing E1, or from an E1-expressing packaging cell line, such as 293 cell line or a cell line prepared as described herein. The expression of E1 in the packaging cell permits the replication and packaging of

the Pan5ΔE1 into a virion capsid. In another embodiment, the packaging cell transfected with pX'Pan5ΔE1 is transfected with an adenovirus vector as described above bearing the transgene of interest. Homologous recombination occurs between the helper and the plasmid, which permits the adenovirus-transgene sequences in the vector to be replicated and packaged into virion capsids, resulting in the recombinant adenovirus.

Transfection is followed by an agar overlay for 2 weeks, after which the viruses are plaqued, expanded and screened for expression of the transgene. Several additional rounds of plaque purification are followed by another expansion of the cultures. Finally the cells are harvested, a virus extract prepared and the recombinant chimpanzee adenovirus containing the desired transgene is purified by buoyant density ultracentrifugation in a CsCl gradient or by alternative means known to those of skill in the art.

Example 5 – Generation of Recombinant E1-Deleted Pan6 Vector

A. Strategy for Construction of Pan-6 Adenoviral Plasmid

1. Cloning of terminal fragments

Pan 6 virus is deproteinated by pronase and proteanase K treatment and phenol extraction. Synthetic 12 bp Pme I linkers are ligated onto the viral DNA as described by Berkner and Sharp, *Nucleic Acids Research*, **11**: 6003 (1983). The viral DNA is then digested with Xba I to isolate a 5' terminal fragment (6043 bp). The Ad6 XbaI 5' fragment is then ligated into pX link at Sma I and Xba I sites to form pX-AdPan6-0-16.5. The viral DNA with Pme I linkers is also digested with Pac I to isolate the 6475 bp 3' terminal fragment and cloned into pX link at Pac I and Sma I sites, resulting in pXAdPan6-82-100.

2. *Deletion of E1 from the 5' clone*

To delete E1 (m.u.1.2-9), the BsiWi-Xba I fragment in pX-AdPan6-0-16.5 is replaced with a PCR fragment spanning m.u.9-16.7 fragment treated with BsiWi and Xba I, leading to pX-Ad-Pan6 m.u.0-1, 9-16.5 .

3. *Fusion of 5' and 3' clones and to create an anchor site to accept the middle Hind III fragment*

First, the 5' clone, pX-Ad-Pan6 m.u.0-1, 9-16.5, is further expanded by inserting the 2nd Xba I fragment (4350 bp, m.u.16.5 – 28) from Pan 6 genome into the Xba I site in the pX-Ad-Pan6 m.u.0-1, 9-16.5. This construct is named pXAd-Pan6-mu 0-1, 9-28.

Second, the 3' clone is also expanded by inserting the 15026 bp Mlu I/Pac I fragment covering m.u.41-82 from Pan 6 genome into the Mlu I/Pac I sites of pXAdPan6-82-100, generating pXAdPan6-m.u.41-100.

Then, a 8167 bp Hind III/Eco 47III Pan 6 fragment is isolated from pXAd-Pan6-mu 0-1, 9-28 and subcloned into pXAdPan6-m.u.41-100 at Hind III and Xba I blunt sites. This 5' and 3' fusion clone is called pXAdPan6mu0-1, 9-19.5, 64-100.

4. *Drop of the middle fragment of the genome into the fusion clone*

A 16335 bp Hind III fragment (m.u.19.5 – 64) from Pan 6 is inserted into Hind III site of pXAdPan6mu0-1, 9-19.5, 64-100 to form pXAdPan6-0-1, 9-100.

5. *Introduction of a PKGFP selective marker into the final construct for direct cloning the gene of interest and green/white selection of recombinant transformants.*

A minigene cassette that expresses GFP under a lac promoter and is flanked with recognition sites of rare intron encoding restriction enzymes, PI-Sce I and I-Ceu I, was isolated from pShuttle-pkGFP (bare) by Sap I and Dra III digestions followed by filling-in reaction. The pShuttle-pkGFP (bare) plasmid is 4126 bp in length, and contains a ColE1-Ori, a kanamycin resistance gene, plac, a LacZ promoter-GFPmut3-1 cds (Clontech), and a GFPmut3-1 cds (Clontech). This cassette is subcloned into Srf I cut and blunted pXAdPan6-0-1, 9-100. This final construct is called pX-Pan6-pkGFP mu.0-1, 9-100, which is useful for generating recombinant E1-deleted Pan 6 molecular clones carrying genes of interest by direct ligation and green/white selection in combination with the generic pShuttlepkGFP vectors.

B. Alternative Strategy for Generation of Pan-6 Plasmid

1. Cloning of 5' terminal fragment

The Pan 6 virus is deproteinated by pronase and proteanase K treatment and phenol extraction as described above and synthetic 12 bp Pme I linkers are ligated onto the viral DNA as described. The AdPan6 5' XbaI fragment is isolated and ligated into pX to form pX-AdPan6-0-16.5 (9022 bp) as described in Part A above.

2. Deletion of E1 from the 5' clone

To delete E1 (m.u. 1.2-9), pX-AdPan6-0-16.5 is digested with SnaBI and NdeI to remove the regions encoding the E1a and E1b proteins (3442-6310 bp). This vector is subsequently digested with BsiWI in preparation for blunting with the minigene cassette carrying a selective marker.

3. Introduction of a selective marker

A minigene cassette that expressed GFP under a lac promoter and which is flanked with recognition sites of rare intron encoding restriction enzymes, PI-XceI and I-CeuI, was isolated from pShuttle-pkGFP as described above. The DraIII-SapI fragment is then ligated with the digested pX-AdPan6-0-16.5 to form pX-AdPan6 MU 0-16.5ΔE1 (7749 bp).

4. Extension of Pan-6 Adenoviral Sequences

pX-AdPan6 MU 0-16.5ΔE1 was subjected to XbaI digestion to permit insertion of an XbaI-RsrII linker. An XbaI/RsrII digestion fragment from the AdPan6 genome was isolated (mu 28-100, 26240 bp) and ligated into the Xba/RsrII-digested pX-AdPan6 MU 0-16.5ΔE1 to provide pX-AdPan6 MU 0-1, 9-16.5, 28-100. A second XbaI fragment from the Pan6 genome (mu 16.5-28, 4350 bp) is then ligated into this plasmid to form pX-AdPan6 MU 0-1, 9-100 (38551 bp).

C. Generation of Recombinant Adenoviruses

To generate the recombinant adenoviruses from a E1-deleted Pan6 plasmid prepared as described in Parts A or b, the plasmid is co-transfected with a helper expressing E1, or from an E1-expressing packaging cell line, such as 293 cell line or a cell line prepared as described herein. The expression of E1 in the packaging cell permits the replication and packaging of the Pan6-pkGFP mu.0-1, 9-100 into a virion capsid. Alternatively, the packaging cell transfected with pX-Pan6-pkGFP mu.0-1, 9-100 is

transfected with an adenovirus vector as described above bearing another transgene of interest.

Example 6 – Generation of Recombinant E1-Deleted Pan7 Vector

A. Generation of Pan7 Plasmids

A synthetic linker containing the restriction sites PacI-SmaI-FseI-MluI-EcoRV-PacI was cloned into pBR322 that was cut with EcoRI and NdeI. The left end (bp1 to 3618) of Ad Pan7 was cloned into the linker between the SmaI and FseI sites. The adenovirus E1 was then excised from the cloned left end by cutting with SnaBI and NdeI and inserting an I-CeuI-GFP-PI-SceI cassette from pShuttle (Clontech) in its place. The resulting plasmid was cut with FseI and MluI and Ad Pan7 fragment FseI (bp 3618) to MluI (bp 155114 was inserted to extend the left end. The construct (pPan7pGFP) was completed by inserting the 21421 bp Ad Pan7 right end fragment from the MluI site (bp 15114) into the above plasmid between MluI and EcoRV to generate a complete molecular clone of E1 deleted adenovirus Pan7 suitable for the generation of recombinant adenoviruses. Optionally, a desired transgene is inserted into the I-CeuI and PI-SceI sites of the newly created pPan7 vector plasmid.

B. Construction of E1-Deleted Pan7 Viral Vectors

To generate the recombinant adenoviruses from pPan7ΔE1, the plasmid is co-transfected with a helper expressing E1, or from an E1-expressing packaging cell line, such as 293 cell line or a cell line prepared as described herein. The expression of E1 in the packaging cell permits the replication and packaging of the Pan7ΔE1 into a virion capsid. In another embodiment, the packaging cell transfected with pX'Pan7 ΔE1 is transfected with an adenovirus vector as described above bearing the transgene of interest. Homologous recombination occurs between the helper and the plasmid, which permits the adenovirus-transgene sequences in the vector to be replicated and packaged into virion capsids, resulting in the recombinant adenovirus. Transfection and purification is as described above.

Example 7 - Generation of Plasmid Vectors Expressing the E1 Genes

Plasmid vectors are constructed which encode the Pan5 E1 region gene, and these plasmids are used to generate stable cell lines expressing viral E1 proteins.

The E1 region of Pan5 is cloned into pX', essentially as described in Example 4 above, prior to replacement of this region with the fragment from pShuttle (Clontech). The expression plasmid contains the Pan5 adenoviral genome sequence spanning at least bp 1 to 3959 in the Pan5 genomic sequence. Thus, the expression plasmid contains the sequence encoding E1a and E1b of chimpanzee Ad Pan5 under the control of a heterologous promoter. Similar expression plasmids can be generated using the Ad Pan6 and AdPan 7 E1 regions, identified in the tables above.

Example 8 - Generation of Cell Lines Expressing Chimpanzee Adenovirus E1 Proteins

Cell lines expressing viral E1 proteins are generated by transfecting HeLa (ATCC Acc. No. CCL2) with the plasmid of Example 6. These cell lines are useful for the production of E1-deleted recombinant chimpanzee adenoviruses by co-transfection of genomic viral DNA and the expression plasmids described above. Transfection of these cell lines, as well as isolation and purification of recombinant chimpanzee adenoviruses therefrom are performed by methods conventional for other adenoviruses, i.e., human adenoviruses [see, e.g., Horwitz, cited above and other standard texts].

A. Cell lines expressing Pan5 E1 proteins

HeLa cells in 10cm dishes are transfected with 10 μg of pX-Pan51-E1 DNA using a Cellphect™ kit (Pharmacia, Uppsala, Sweden) and following the manufacturer's protocol. 22 hours post-transfection, the cells are subjected to a three minute glycerol shock (15% glycerol in Hepes Buffered Saline, pH 7.5) washed once in DMEM (HeLa) or F12K (A549; Life Technologies, Inc., Grand Island, NY) media supplemented with 10% FCS, 1% Pen-Strep, then incubated for six hours at 37°C in the above described media. The transfected cells are then split into duplicate 15cm plates at ratios of 1:20, 1:40, 1:80, 1:160, and 1:320. Following incubation at 37°C overnight, the media is supplemented with G418 (Life Technologies, Inc.) at a concentration of 1 μg/ml. The media is replaced every 5 days and clones are isolated 20 days post-transfection.

HeLa E1 cell clones are isolated and assayed for their ability to augment adeno-associated virus (AAV) infection and expression of recombinant LacZ protein as described below.

B. AAV Augmentation Assay for Screening E1 Expressing Cell Lines

AAV requires adenovirus-encoded proteins in order to complete its life cycle. The adenoviral E1 proteins as well as the E4 region-encoded ORF6 protein are necessary for the augmentation of AAV infection. An assay for E1 expression based on AAV augmentation is used. Briefly, the method for identifying adenoviral E1-expressing cells comprises the steps of infecting in separate cultures a putative adenovirus E1-expressing cell and a cell containing no adenovirus sequence, with both an adeno-associated virus (AAV) expressing a marker gene and an AAV expressing the ORF6 of the E4 gene of human adenovirus, for a suitable time. The marker gene activity in the resulting cells is measured and those cells with significantly greater measurable marker activity than the control cells are selected as confirmed E1-expressing cells. In the following experiment, the marker gene is a lacZ gene and the marker activity is the appearance of blue stain.

For example, the cell lines described above, as well as untransfected control cells (HeLa) are infected with 100 genomes per cell of an AAV vector bearing a marker gene, e.g., AV.LacZ [K. Fisher *et al.*, J. Virol., **70**:520 (1996)] and an AAV vector expressing the ORF6 region of human 5 (AV.orf6). The DNA sequence of the plasmid generates a novel recombinant adeno-associated virus (rAAV) containing the *LacZ* transgene and the Ad E4 ORF 6, which is an open reading frame whose expression product facilitates single-stranded (ss) to double-stranded (ds) conversion of rAAV genomic DNA. These vectors are incubated in medium containing 2% FCS and 1% Pen-Strep at 37°C for 4 hours, at which point an equal volume of medium containing 10% FCS is added. It should be understood by one of skill in the art that any marker gene (or reporter gene) may be employed in the first AAV vector of this assay, e.g., alkaline phosphatase, luciferase, and others. An antibody-enzyme assay can also be used to quantitate levels of antigen, where the marker expresses an antigen. The assay is not limited by the identity of the marker gene. Twenty to twenty-four hours post-infection, the cells are stained for LacZ activity using standard methods. After 4 hours the cells are observed microscopically and cell lines with significantly more blue cells than the A549 or HeLa cell controls are scored as positive.

Example 9 - Delivery of Transgene to Host Cell

The resulting recombinant chimpanzee adenovirus described in Example 4, 5 or 6 above is then employed to deliver the transgene to a mammalian, preferably human, cell. For example, following purification of the recombinant virus, human embryonic kidney 293 cells are infected at an MOI of 50 particles per cell. GFP expression was documented 24 hours post-infection.

A. Gene Transfer in Mouse Models via Pan-6, Pan-7, and Pan-9 vectors

Gene transfer efficiencies and toxicological profile of recombinant chimpanzee adenoviruses were compared in mouse liver directed gene transfer, mouse lung directed gene transfer, and mouse muscle directed gene transfer.

E1-deleted adenoviral vectors containing LacZ under the control of the CMV promoter were constructed using the techniques herein for human Ad5, chimpanzee Pan 6, chimpanzee Pan 7 and chimpanzee Pan 9 (C68). The vectors were delivered to immune-deficient NCR nude mice (80 for each study) as follows. For the liver study, 100 µl (1 x10^{11} particles) were injected into the tail vein. For the lung study, 50 µl (5 x10^{10} particles) were delivered intratracheally. For the muscle study, 25 µl (5 x10^{10}particles) were injected into tibialis anterior. The mice were sacrificed on days 3, 7, 14 and 28 post-vector injection (5 animals per group at each time point). At each necropsy, the liver/lung/muscle tissue was harvested and prepared for cryoblocks and paraffin embedding. The cryoblocks were sectioned for X-gal staining and the paraffin sections are H&E stained for histopathic analysis. At each time point, terminal bleeding was performed. Serum samples were subjected to liver function tests.

It was observed in this experiment the chimpanzee adenoviruses Pan-6, Pan-7, and Pan-9 were less efficient than huAd5 in gene transfer to the liver and to the lung. However, this may be desirable in certain circumstances, to reduce liver toxicity observed for huAd5. The gene transfer efficiency in muscle varied less between serotypes.

B. *Mouse study to feasibility of re-administration of adenovirus vectors by serotype switching between Adhu5, Pan-6, Pan-7, and Pan-9 vectors*

Mice were administered (C57/Bl6; 4/group) LacZ vectors based on huAd5, Pan-6, Pan-7, and Pan-9 (H5.040CMVLacZ, Pan6.000CMVLacZ, Pan7.000CMVLacZ, Pan9.000CMVLacZ; 10^{11}particles/injection) by tail vein. Thirty days later the mice were re-administered adenovirus vectors expressing α1-antitrypsin

(H5.040CMVhA1AT, Pan6.000CMVhA1AT, $1x10^{11}$ particles, Pan7.000CMVhA1AT, Pan9.000CMVhA1AT, 10^{11}particles/injection). Successful transduction by the re-administered vector is monitored by measuring serum α1-antitrypsin on days 3 and 7, following re-administration.

The ability of adenovirus vectors based on huAd5, Pan-6, Pan-7, and Pan-9 respectively to transduce the livers of mice in the presence of neutralizing antibodies to the other serotypes was determined. The results are tabulated here.

1st injection	2nd injection	Cross-neutralization
Adhu5	Adhu5	Yes (+ve control)
	Pan-6	No
	Pan-7	No
	Pan-9 (C68)	No
Pan-6	Adhu5	No
	Pan-6	Yes (+ve control)
	Pan-7	Yes
	Pan-9 (C68)	No
Pan-7	Adhu5	No
	Pan-6	Yes
	Pan-7	Yes (+ve control)
	Pan-9 (C68)	Yes

1st injection	2nd injection	Cross-neutralization
Pan-9 (C68)	Adhu5	No
	Pan-6	No
	Pan-7	Yes
	Pan-9 (C68)	Yes (+ve control)

Ability of vectors to transduce murine liver in the presence of neutralizing antibodies to other serotypes.

Thus, immunization with huAd5 does not prevent re-administration with either of the chimpanzee adenovirus vectors Pan-6, Pan-7, or Pan-9 (C68). This experiment also appears to indicate that Pan-7 is between Pan-6 and Pan-9 in the spectrum of antigenic relatedness and cross-reacts with both; however Pan-6 and Pan-9 do not neutralize each other. This is a surprising result based on homology comparisons, which indicates that Pan-6 is quite distinct from Pan-7 and Pan-9. Evaluation of antisera generated against Pan-9 indicated no cross-neutralization against Pan-6 but some neutralization against Pan-7, arguing that Pan-6 is distinct from the others.

Example 10 - Generation of Recombinant E1-Deleted SV-25 Vector

A plasmid was constructed containing the complete SV-25 genome except for an engineered E1 deletion. At the site of the E1 deletion recognition sites for the restriction enzymes I-CeuI and PI-SceI which would allow insertion of transgene from a shuttle plasmid where the transgene expression cassette is flanked by these two enzyme recognition sites were inserted.

A synthetic linker containing the restriction sites SwaI-SnaBI-SpeI-AflII-EcoRV-SwaI was cloned into pBR322 that was cut with EcoRI and NdeI. This was done by annealing together two synthetic oligomers SV25T (5'-AAT TTA AAT ACG TAG CGC ACT AGT CGC GCT AAG CGC GGA TAT CAT TTA AA-3', SEQ ID NO: 38) and SV25B (5'-TAT TTA AAT GAT ATC CGC GCT TAA GCG CGA CTA GTG CGC

TAC GTA TTT A-3', SEQ ID NO:39) and inserting it into pBR322 digested with EcoRI and NdeI. The left end (bp1 to 1057, SEQ ID NO:29) of Ad SV25 was cloned into the above linker between the SnaBI and SpeI sites. The right end (bp28059 to 31042, SEQ ID NO: 29) of Ad SV25 was cloned into the linker between the AflII and EcoRV sites. The adenovirus E1 was then excised between the EcoRI site (bp 547) to XhoI (bp 2031) from the cloned left end as follows. A PCR generated I-CeuI-PI-SceI cassette from pShuttle (Clontech) was inserted between the EcoRI and SpeI sites. The 10154 bp XhoI fragment of Ad SV-25 (bp2031 to 12185, SEQ ID NO:29) was then inserted into the SpeI site. The resulting plasmid was digested with HindIII and the construct (pSV25) was completed by inserting the 18344 bp Ad SV-25 HindIII fragment (bp11984 to 30328, SEQ ID NO:29) to generate a complete molecular clone of E1 deleted adenovirus SV25 suitable for the generation of recombinant adenoviruses. Optionally, a desired transgene is inserted into the I-CeuI and PI-SceI sites of the newly created pSV25 vector plasmid.

To generate an AdSV25 carrying a marker gene, a GFP (green fluorescent protein) expression cassette previously cloned in the plasmid pShuttle (Clontech) was excised with the restriction enzymes I-CeuI and PI-SceI and ligated into pSV25 (or another of the Ad chimp plasmids described herein) digested with the same enzymes. The resulting plasmid (pSV25GFP) was digested with SwaI to separate the bacterial plasmid backbone and transfected into the E1 complementing cell line HEK 293. About 10 days later, a cytopathic effect was observed indicating the presence of replicative virus. The successful generation of an Ad SV25 based adenoviral vector expressing GFP was confirmed by applying the supernatant from the transfected culture on to fresh cell cultures. The presence of secondarily infected cells was determined by observation of green fluorescence in a population of the cells.

Example 11 - Construction of E3 deleted Pan-5, Pan-6, Pan-7 and C68 vectors

In order to enhance the cloning capacity of the adenoviral vectors, the E3 region can be deleted because this region encodes genes that are not required for the propagation of the virus in culture. Towards this end, E3-deleted versions of Pan-5, Pan-6, Pan-7, and C68 have been made (a 3.5 kb Nru-AvrII fragment containing E31-9 is deleted).

A. *E3 deleted Pan5 based vector*

E1-deleted pPan5-pkGFP plasmid was treated with Avr II endonuclease to isolate a 5.8 kb fragment containing the E3 region and re-circulate pPan5-pkGFP with Avr II deletion to form construct pPan5-pkGFP-E3-Avr II. Subsequently, the 5.8 kb Avr II fragment was subcloned into pSL-Pan5-E3-Avr II for a further deletion of E3 region by Nru I digestion. This led to a plasmid pSL-Pan5-E3-deletion. The final construct pPan5-E3-pkGFP was produced by removing a 4.3 kb Avr II/Spe I fragment from pSL-Pan5-E3-deletion plasmid and inserting into pPan5-pkGFP-E3-Avr II at Avr II site. In this final construct, a 3.1 kb deletion in E3 region was accomplished.

B. *E3 deletion in Pan6 based vector*

E1-deleted pPan6- pkGFP molecular clone was digested with Sbf I and Not I to isolate 19.3 kb fragment and ligated back at Sbf I site. The resulting construct pPan6-Sbf I-E3 was treated with Eco 47 III and Swa I, generating pPan6-E3. Finally, 21 kb Sbf I fragment from Sbf I digestion of pPan6- pkGFP was subcloned into pPan6-E3 to create pPan6-E3-pkGFP with a 4 kb deletion in E3.

C. *E3 deleted Pan7 and Pan9 vectors*

The same strategy was used to achieve E3 deletions in both vectors. First, a 5.8 kb Avr II fragment spanning the E3 region was subcloned pSL-1180, followed by deletion of E3 by Nru I digestion. The resulting plasmids were treated with Spe I and Avr II to obtain 4.4 kb fragments and clone into pPan7- pkGFP and pPan9-pkGFP at Avr II sites to replace the original E3 containing Avr II fragments, respectively. The final pPan7-E3- pkGFP and pPan9-E3- pkGFP constructs have 3.5 kb E3-deletions.

Example 12 - Construction of E3- and E4-deleted Pan-7 vector

Although the deletion of the E1 region of adenoviruses (first generation adenovirus vectors) renders them replication-incompetent, expression of the adenoviral vector backbone genes is not fully abolished. Deletion of the E4 region considerably attenuates this residual gene expression and may confer a safety advantage. An E4-deleted Pan-7 vector containing a 2.5 kb deletion (a PvuII-AgeI fragment containing E4ORF1-ORF7 is deleted) has been constructed. High titer stocks of this virus were generated using a HEK 293-based cell line, which in addition to E1, expresses an essential E4 gene (orf 6).

1. *E4 deletion in the molecular clone of Pan7*

A 19 kb Xba I fragment was deleted from pPan7- pkGFP to create pPan7-Xba I from which a 2.5 kb E4 fragment was deleted by Age I and Pvu II partial digestion, resulting in pPan7-Xba I-E4. pPan7-E4- pkGFP plasmid was generated from pPan7-Xba I-E4 in two sequential cloning steps, adding 19 kb Xba I and 15 kb I-Ceu I/Mlu I fragments, both of which came from pPan7- pkGFP construct.

2. *Introduction of E3 and E4 deletions in Pan9 vector*

A 11 kb plasmid, pPan9-EcoRI, containing E4 region was created by retrieving 11 kb EcoRI fragment from pPan9 pkGFP after EcoRI digestion and self-ligation. E4 region was deleted from this construct by Age I digestion/filled in and Pvu II partial digestion and slef-ligation to generate pPan9-EcoR I-E4. A 23 kb EcoR I fragment was isolated from pPan9-pkGFP and inserted into pPan9-EcoR I-E4 at EcoR I site, followed by adding 5.8 kb Avr II fragment from pPan9-pkGFP, to form the final product pPan9-E3-E4- pkGF. Compared to the genome size of wild type Pan9, this E1-E3-E4-deleted vector could have a transgene capacity up to 8 kb.

3. *Introduction of minigene cassettes with genes of interest including reporter genes, glyco- and nuclear proteins of Ebo into molecular clones of Pan vectors*

A highly efficient direct cloning and green/white selection procedure was employed for creating molecular clones of recombinant viruses. Briefly, genes of interest were cloned into pShuttlepkGFP by screening white colonies for recombinants. Subsequently, the minigene cassettes were transferred into chimpanzee adenovirus backbone plasmids, pPanX-pkGFP with various deletions, easily by swapping with pkGFP cassette at I-Ceu I and PI-Sce I sites and screening a few white colonies for correct recombinants.

4. *Rescue of molecular clones of Pan vectors with multiple deletions in early regions and virus propagation*

For rescue of E1-E3-deleted molecular clones of chimpanzee adenovirus vectors, the clones were linearized with appropriate restriction enzymes and transfected into regular 293 cells. Once a full cytopathic effect (CPE) observed in the transfected

cells, crude lysate was harvested and expanded in 293 cells to large-scale infections. The viruses were purified by CsCl sedimentation method.

For E1-E4 and E1-E3-E4-deleted Pan vectors, 10-3 cells, a 293-based E1-E4-complementing cell line, were used for rescue and propagation of vectors. E4 ORF6 gene expression in 10-3 cells was induced by addition of 150 μM $ZnSO^4$ to the culture medium.

Example 13 - Vaccination with adenovirus vectors expressing wild type and variant EboZ GP.

AdHu5 or AdC7 vectors expressing Ebola envelope chimeras were produced for *in vivo* immunization experiments in C57BL/6 mice. Recombinant viruses with different viral backbones were created by molecular cloning method in which the minigene cassettes were inserted into the place of E1-deletions. The molecular clones of all recombinant viruses were rescued and grown up in 293 cells for large-scale purification using CsCl sedimentation method.
Five EboZ variants encoded by AdHu5 or AdPan7 (C7) were selected and produced to evaluate their relative immunogenicity following an intramuscular Ad injection. The wt Ebo, a soluble Ebo variant, EboΔ1, EboΔ2, EboΔ3, EboΔ4, EboΔ5S, EboΔ6S, EboΔ7S and EboΔ8S were evaluated in the initial vaccine studies. For the data summarized in the following table, the number of viral particles (per ml or total) produced and amplified from infected 293 cells was established by spectrophotometry reading.

Table: Production of Adhu5 or AdC7 Adenoviral vector encoding EboZ variant.

	HuAd5		AdC7	
Gene	Titer (VP x 10^{12}/ml)	Total yield (VP x 10^{12})	Titer (VP x 10^{12}/ml)	Total yield (VP x 10^{12})
Ebo wt	2.6	12	4.3	43
EboS	4.9	49	4.6	55
EboΔ2	2.1	9	5.8	93
EboΔ3	1.7	8	5.3	95
EboΔ4	3	12	4.1	62

Vector was administered intramuscularly (10^{11} genome copies/cell) in C57BL/6 mice and the presence of virus neutralizing antibody (VNA0 was evaluated 28 days later as a first measure of an immune response generated against the Ebola envelope glycoprotein. VNA is defined here as serum antibody able to inhibit transduction of HeLa cells mediated by HIV-based vector pseudotyped with the wild-type Ebola envelope.

VNA to the EboZ pseudotypes was detected with AdPan7 (C7) yielding higher titers than AdHu5. The EboZΔ3 elicited the highest VNA in terms of the transgene targets. For the data summarized in the following table, neutralizing antibody titers to HIV-EboZ-GFP pseudotypes (reciprocal dilution) are provided (N=5 animals/group).

	VNA Titers		
	EboZ wildtype	EboZs	EboZΔ3
AdHu5	12	16	12
AdC7	44	12	140

Example 14 – Pan7-mediated Expression of Ebola Proteins

Mouse studies to evaluate Pan-7 vectors expressing Ebola envelope proteins and the Ebola nuclear antigen have been initiated. These are directed towards evaluation of neutralizing antibodies in C57Bl/6 mice injected intramuscularly (IM) with Adhu5 or Pan-7 expressing each of 4 Ebola env constructs.

A. *Evaluation of CTL from C57Bl/6 mice injected IM with Adhu5 or Pan-7 expressing the Ebola env constructs.*

1. *Challenge experiment in mice with Ebola virus.*

Neutralizing antibody (NAB) responses to the Ebola envelope were analyzed by looking at immunized mouse sera mediated neutralization of a lentiviral (HIV) vector pseudotyped with the several constructs (eEbo, NTD2, NTD3, NTD4) of the Ebola envelope glycoprotein. C57BL/6 or BALB/c mice received a single intramuscular injection of 5×10^{10} particles per mouse of C7 (Ad Pan-7) encoding Ebola envelope variant. Neutralizing antibody was evaluated 30 days post-vaccination. Briefly, Ebola Zaire pseudotyped HIV vector encoding for ß-galactosidase (EboZ-HIV-LacZ) was incubated for 2 hr at 37°C with different dilution of heat inactivated mouse serum.. Following the incubation with serum, EboZ-HIV-LacZ was then used to infect HeLa cells for 16 hr at 37°C. Infectivity was revealed by X-gal staining of transduced HeLa cells positive for ß-galactosidase. Neutralizing titer represent the serum reciprocal dilution where a 50% decrease in the number of ß-galactosidase positive blue cells was observed. Sera were collected 30 days post-immunization, which consisted in a single intramuscular (I.M.) administration of 5×10^{10} particles/animal. Neutralizing antibody to Ebola pseudotyped HIV could be detected from all groups with antibody titers ranging from 20 for Ad-EboZ (Adhu5 expressing EboZ), Ad-NTD3 (Adhu5 expressing NTD3) and C7-sEbo (Ad Pan-7 expressing soluble EboZ) to over 130 for C7-NTD3 (Ad Pan-7 expressing soluble NTD3) and C7-NTD4 (Ad Pan-7 expressing soluble NTD3). The same immunization strategy in BALB/c mice resulted in lower neutralizing antibody titers for Ad- and C7-NTD2, and NTD4.

B. Cellular Immune Response

The cellular immune response to the Ebola envelope in C57BL/6 mice was evaluated 8 days after a single I.M. administration of 5×10^{10} particles of C7-LacZ or C7-Ebola envelope variant per animal. Mice were vaccinated I.M. with 5×10^{10} particles

of C7 encoding LacZ or Ebola envelope variant. Splenic lymphocytes from immunized mice were collected 8 days post vaccination and stimulated in vitro with feeder cells (splenic lymphocytes from untreated mice infected with human Adenovirus serotype 5 encoding for the wild-type Ebola envelope and irradiated). Standard 5-hr CTL assays were performed using ^{51}Cr-labeled syngenic C57 cells transfected with an expressor of EboZ.

A positive MHC-restricted cytotoxic T lymphocyte (CTL) response was observed from all AdPan-7 encoding for Ebola envelope variants with a higher response from NTD2, NTD3 or NTD4 immunized mice. Indeed, effector cells from C7 encoding Ebola envelope variant immunized mice recognized EboZ transfected target cells and gave recall CTL responses up to 30% specific lysis. Less than 5% lysis was seen with effector cells from naïve or LacZ immunized control mice confirming that lysis was specific for Ebola envelope antigens.

C. Protection Studies

The most direct means of evaluating C7 (Ad Pan-7) encoding for the EboZ variants as a successful vaccine in mice was to assess protection against weight loss and death following lethal challenge with mouse adapted Ebola Zaire virus. BALB/c mice were immunized with a single dose of 5 x 10^{10} particles per animal as performed previously and vaccinated animals were challenged with 200 LD_{50} of mouse adapted Ebola Zaire 21 days later. All control mice (vehicle and C7-LacZ) died between day 5 to day 9 post-challenge. In contrast, all vaccinated mice but one, (from the C7-sEbo group), survived the challenge with Ebola Zaire.

Weight loss was observed from mice vaccinated with C7-sEbo from day 4 to day 7. Signs of illness such as pilo-erection and from light to severe lethargy were also noted from mice vaccinated with C7-sEbo, NTD2 and NTD3 between day 4 to day 7. Mice immunized with C7-EboZ and C7-NTD4 did not show sign of illness. Overall, a single dose of C7-EboZ and C7-NTD4 completely protected immunized mice from illness and death possibly due to a significant T cell mediated immunity.

All documents recited above are incorporated herein by reference. Numerous modifications and variations of the present invention are included in the scope of the above-identified specification and are expected to be obvious to one of skill in the art. Such modifications and alterations to the compositions and processes of the present invention, such as selections of different minigenes or selection or dosage of the vectors or immune modulators are believed to be within the scope of the claims appended hereto.

WHAT IS CLAIMED IS:

1. An isolated simian adenovirus nucleic acid sequence selected from the group consisting of:

(a) Pan5 having the sequence of nucleic acids 1 to 36462 of SEQ ID NO:1;

(b) Pan6 having the sequence of nucleic acids 1 to 36604 of SEQ ID NO:5;

(c) Pan7 having the sequence of nucleic acids 1 to 36535 of SEQ ID NO:9;

(d) SV1 having the sequence of nucleic acids 1 to 34264 of SEQ ID NO: 24;

(e) SV25 having the sequence of nucleic acids 1 to 31044 of SEQ ID NO: 29;

(f) SV39 having the sequence of to nucleic acids 1 to 34115 of SEQ ID NO: 34, and

(g) a nucleic acid sequence complementary to the sequence of any of (a) to (f).

2. An isolated simian adenovirus serotype nucleic acid sequence selected from one or more of the group consisting of:

(a) 5' inverted terminal repeat (ITR) sequences;

(b) the adenovirus E1a region, or a fragment thereof selected from among the 13S, 12S and 9S regions;

(c) the adenovirus E1b region, or a fragment thereof selected from among the group consisting of the small T, large T, IX, and IVa2 regions;

(d) the E2b region;

(e) the L1 region, or a fragment thereof selected from among the group consisting of the 28.1 kD protein, polymerase, agnoprotein, 52/55 kD protein, and IIIa protein;

(f) the L2 region, or a fragment thereof selected from the group consisting of the penton, VII, VI, and Mu proteins;

(g) the L3 region, or a fragment thereof selected from the group consisting of the VI, hexon, or endoprotease;

(h) the 2a protein;

(i) the L4 region, or a fragment thereof selected from the group consisting of the 100 kD protein, the 33 kD homolog, and VIII;

(j) the E3 region, or a fragment thereof selected from the group consisting of E3 ORF1, E3 ORF2, E3 ORF3, E3 ORF4, E3 ORF5, E3 ORF6, E3 ORF7, E3 ORF8, and E3 ORF9;

(k) the L5 region, or a fragment thereof selected from a fiber protein;

(l) the E4 region, or a fragment thereof selected from the group consisting of E4 ORF7, E4 ORF6, E4 ORF4, E4 ORF3, E4 ORF2, and E4 ORF1;and

(m) the 3' ITR,

of any of Pan5 SEQ ID NO:1; Pan6 SEQ ID NO:5; Pan7 SEQ ID NO:9; SV1 SEQ ID NO: 24; SV25 SEQ ID NO: 29; and SV39 SEQ ID NO: 34, or sequence complementary to any of (a) to (m).

3. A simian adenovirus protein encoded by the nucleic acid sequence according to claim 2.

4. A nucleic acid molecule comprising a heterologous simian adenoviral sequence according to claim 2.

5. The nucleic acid molecule according to claim 4, wherein said simian adenoviral sequence encodes an adenoviral gene product and is operatively linked to regulatory control sequences which direct expression of the adenoviral gene product in a host cells.

6. The nucleic acid molecule according to claim 4 or 5, wherein said simian adenoviral sequence comprises the E1a region of Pan5 SEQ ID NO:1; Pan6 SEQ ID NO:5; Pan7 SEQ ID NO:9; SV1 SEQ ID NO: 24; SV25 SEQ ID NO: 29; and SV39 SEQ ID NO: 34.

7. A pharmaceutical composition comprising the nucleic acid molecule according to claim 6 and a physiologically compatible carrier.

8. An isolated simian adenoviral capsid protein selected from the group consisting of:

(a) a hexon protein of Pan5 SEQ ID NO:3, Pan6 SEQ ID NO:7, Pan7 SEQ ID NO:11, SV1 SEQ ID NO:26, SV25 SEQ ID NO:31or SV39 SEQ ID NO:36, or fragment thereof;

(b) a penton protein of Pan5 SEQ ID NO:2, Pan6 SEQ ID NO:6, Pan7 SEQ ID NO:10, SV1 SEQ ID NO:25, SV25 SEQ ID NO: 30 or SV39 SEQ ID NO:35;

(c) a fiber protein of Pan5 SEQ ID NO:4, Pan6 SEQ ID NO:8, Pan7 SEQ ID NO:12, SV1 SEQ ID NO: 27 and SEQ ID NO:28, SV25 SEQ ID NO: 32 and SEQ ID NO:33 or SV39 SEQ ID NO: 37, or a fragment thereof.

9. An artificial adenovirus serotype comprising a capsid protein according to claim 8 or a fragment thereof.

10. The artificial adenovirus serotype according to claim 9, wherein said capsid comprises a fragment of the hexon protein selected from the group consisting of Pan5 SEQ ID NO: 15, Pan6 SEQ ID NO:16 and Pan7 SEQ ID NO:17.

11. The artificial adenovirus serotype according to claim 9 or 10, wherein said capsid comprises a fragment of the fiber protein selected from the group consisting of Pan6 SEQ ID NO: 19, Pan7 SEQ ID NO:20 and Pan5 SEQ ID NO:21.

12. A nucleic acid molecule comprising a heterologous sequence encoding a protein according to claims 3 or 8 or an artificial adenovirus serotype according to any of claims 9 to 11.

13. A recombinant vector comprising a simian adenovirus sequence according to claim 2 or a nucleic acid molecule according to claim 4 or 12 and a heterologous gene operatively linked to sequences which direct expression of said gene in a host cell.

14. The recombinant vector according to claim 13, further comprising 5' and 3' adenovirus cis-elements necessary for replication and encapsidation.

15. The recombinant vector according to claim 13 or claim 14, wherein said vector is a virus.

16. The recombinant vector according to any of claims 13 to 15 wherein said vector lacks all or a part of the E1 gene.

17. A recombinant virus comprising a simian capsid protein according to claim 3 or an artificial adenovirus serotype according to any of claims 9 to 11.

18. A host cell comprising a nucleic acid molecule according to any of claims 4 to 6 or 12 , a recombinant vector according to any of claims 13 to 16, or a recombinant virus according to claim 17.

19. The host cell according to claim 18, wherein said host cell is stably transformed with the nucleic acid molecule or the recombinant vector.

20. The host cell according to claim 18 or claim 19, wherein said host cell expresses one or more adenoviral gene products from said nucleic acid molecule or recombinant vector, said adenoviral gene products selected from the group consisting of E1a, E1b, E2a, and E4 ORF6.

21. The host cell according to any of claims 18 to 20, wherein said host cell is stably transformed with a nucleic acid molecule comprising the simian adenovirus inverted terminal repeats.

22. A composition comprising a recombinant vector in a pharmaceutically acceptable carrier, said vector comprising a simian adenovirus sequence according to any of claims 1 or 2 and a selected heterologous gene operatively linked to regulatory sequences which direct expression of said gene in a host cell.

23. A method for delivering a heterologous gene to a mammalian cell comprising introducing into said cell an effective amount of the vector of any of claims 13 to 16 or a virus according to claim 17.

24. A method for repeat administration of a heterologous gene to a mammal comprising the steps of:

(a) introducing into said mammal a first vector which comprises the heterologous gene and

(b) introducing into said mammal a second vector which comprises the heterologous gene;

wherein at least the first virus or the second vector is a virus according to claim 17 and wherein the first and second recombinant vector are different.

25 . A method for producing a selected gene product comprising infecting a mammalian cell with the vector of any of claims 13 to 16 or a virus according to claim 17, culturing said cell under suitable conditions and recovering from said cell culture the expressed gene product.

26. A method for eliciting an immune response in a mammalian host against an infective agent comprising administering to said host an effective amount of the recombinant adenovirus of claim 17, wherein said heterologous gene encodes an antigen of the infective agent.

27. The method according to claim 26, comprising the step of priming the host with a DNA vaccine comprising the heterologous gene prior to administering the recombinant adenovirus .

28. A composition comprising a simian adenovirus capsid protein according to claim 8 linked to a heterologous molecule for delivery to a selected host cell.

29. A method for targeting a cell having an adenoviral receptor comprising delivering to a subject a composition according to claim 28.

FIGURE 1

```
Hu5     APKGAPNPCEWDEAATALEINLEEEDDDNEDEVDEQAEQQKTHVFGQAPYSGINITKEGIQIGVEGQT--
Pan-6   APKGAPNSSQWEQAKTG----------------------NGGTMETHTYGVAPMGGENITKDGLQIGTDVTANQ
Pan-5   APKGAPNTCQWTYKADG----------------------DTGTEKTYTYGNAPVQGISITKDGIQLGTDTDD--
Pan-7   APKGAPNTCQWTYKAG----------------------DTDTEKTYTYGNAPVQGISITKDGIQLGTDSDG--
Pan-9   APKGAPNTCQWTYKADG----------------------ETATEKTYTYGNAPVQGINITKDGIQLGTDTDD--

Hu5     --PKYADKTFQPEPQIGESQWYETEIN--HAAGRVLKKTTPMKPCYGSYAKPTNENGGQGILVKQQN--G
Pan-6   NKPIYADKTFQPEPQVGEENWQETEN---FYGGRALKKDTNMKPCYGSYARPTNEKGGQAKLKVGDDGVP
Pan-5   -QPIYADKTYQPEPQVGDAEWHDITGTDEKYGGRALKPDTKMKPCYGSFAKPTNKEGGQANVKTETG--G
Pan-7   -QAIYADETYQPEPQVGDAEWHDITGTDEKYGGRALKPDTKMKPCYGSFAKPTNKEGGQANVKTETG--G
Pan-9   -QPIYADKTYQPEPQVGDAEWHDITGTDEKYGGRALKPDTKMKPCYGSFAKPTNKEGGQANVKTGTG--T

Hu5     KLESQVEMQFFSTTEATAGNGDNLTPKVVLYSEDVDIETPDTHISYMPTIKEGNSRELMGQQSMPNRPNY
Pan-6   TKEFDIDLAFFDTPGGTVNGQDEYKADIVMYTENTYLETPDTHVVYKPGKDDASSEINLVQQSMPNRPNY
Pan-5   TKEYDIDMAFFDNRSAAAAG---LAPEIVLYTENVDLETPDTHIVYKAGTDDSSSSINLGQQSMPNRPNY
Pan-7   TKEYDIDMAFFDNRSAAAAG---LAPEIVLYTENVDLETPDTHIVYKAGTDDSSSSINLGQQSMPNRPNY
Pan-9   TKEYDIDMAFFDNRSAAAAG---LAPEIVLYTENVDLETPDTHIVYKAGTDDSSSSINLGQQAMPNRPNY

Hu5     IAFRDNFIGLMYYNSTGNMGVLAGQASQLNAVVDLQDRNTELSYQLLLDSIGDRTRYFSMWNQAVDSYDP
Pan-6   IGFRDNFIGLMYYNSTGNMGVLAGQASQLNAVVDLQDRNTELSYQLLLDSLGDRTRYFSMWNQAVDSYDP
Pan-5   IGFRDNFIGLMYYNSTGNMGVLAGQASQLNAVVDLQDRNTELSYQLLLDSLGDRTRYFSMWNQAVDSYDP
Pan-7   IGFRDNFIGLMYYNSTGNMGVLAGQASQLNAVVDLQDRNTELSYQLLLDSLGDRTRYFSMWNQAVDSYDP
Pan-9   IGFRDNFIGLMYYNSTGNMGVLAGQASQLNAVVDLQDRNTELSYQLLLDSLGDRTRYFSMWNQAVDSYDP

Hu5     DVRIIENHGTEDELPNYCFPLGGVINTETLTKVKPKTG----QENGWEKDATEFSDKNEIRVGNNFAMEI
Pan-6   DVRIIENHGVEDELPNYCFPLDGSGTNAAYQGVKVKDGQDGDVESEWENDDTVA-ARNQLCKGNIFAMEI
Pan-5   DVRIIENHGVEDELPNYCFPLDAVGRTDTYQGIKAN----GADQTTWTKDDTVN-DANELGKGNPFAMEI
Pan-7   DVRIIENHGVEDELPNYCFPLDAVGRTDTYQGIKAN----GDNQTTWTKDDTVN-DANELGKGNPFAMEI
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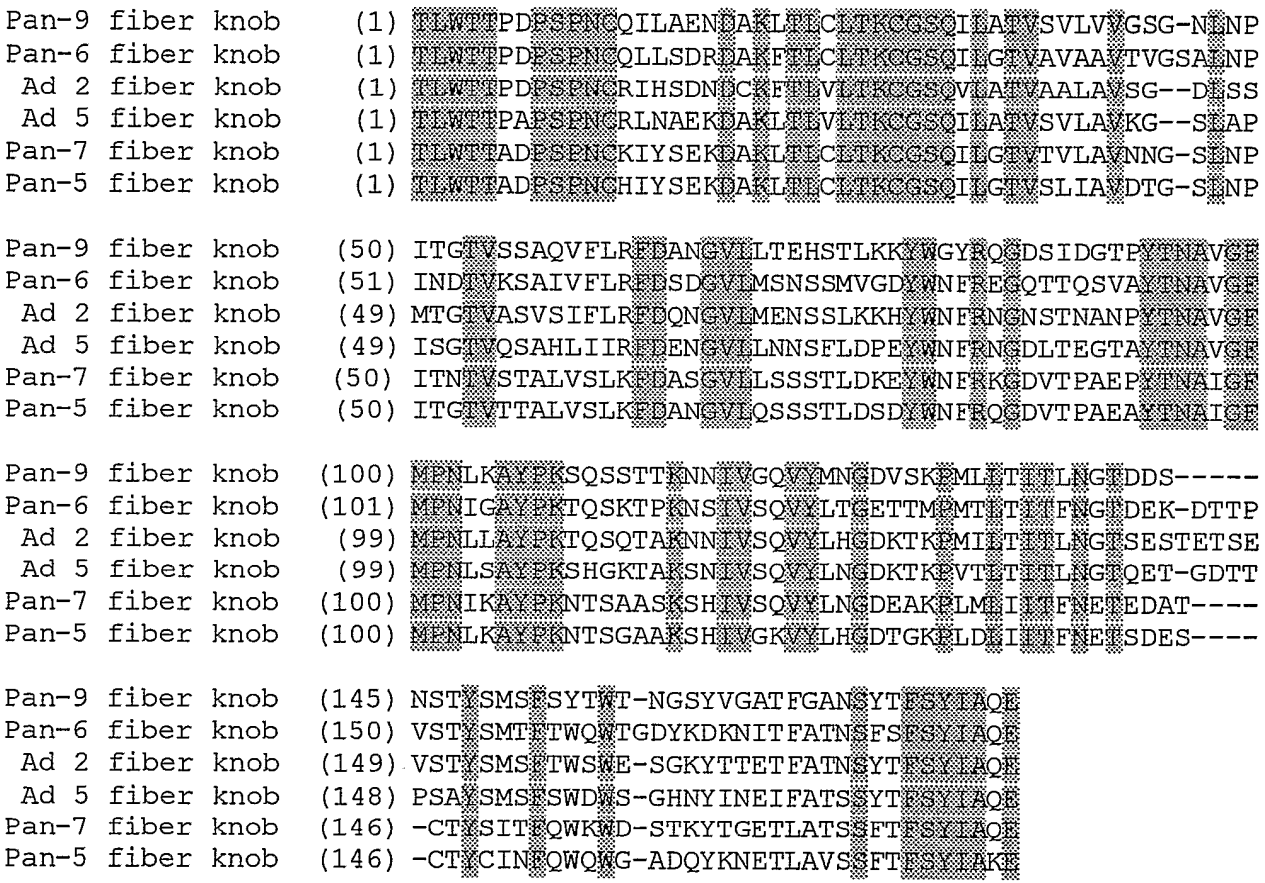
Fig. 2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Ad 2 fiber knob (1) TLWTTPDPSPNCRIHSDNDCKFTLVLTKCGSQVLATVAALAVSG--DLSS
Ad 5 fiber knob (1) TLWTTPAPSPNCRLNAEKDAKLTLVLTKCGSQILATVSVLAVKG--SLAP
Pan-7 fiber knob (1) TLWTTADPSPNCKIYSEKDAKLTLCLTKCGSQILGTVTVLAVNNG-SLNP
Pan-5 fiber knob (1) TLWTTADPSPNCHIYSEKDAKLTLCLTKCGSQILGTVSLIAVDTG-SLNP
Pan-9 fiber knob (50) ITGTVSSAQVFLRFDANGVLLTEHSTLKKYWGYRQGDSIDGTPYTNAVGF
Pan-6 fiber knob (51) INDTVKSAIVFLRFDSDGVLMSNSSMVGDYWNFREGQTTQSVAYTNAVGF
Ad 2 fiber knob (49) MTGTVASVSIFLRFDQNGVLMENSSLKKHYWNFRNGNSTNANPYTNAVGF
Ad 5 fiber knob (49) ISGTVQSAHLIIRFDENGVLLNNSFLDPEYWNFRNGDLTEGTAYTNAVGF
Pan-7 fiber knob (50) ITNTVSTALVSLKFDASGVLLSSSTLDKEYWNFRKGDVTPAEPYTNAIGF
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Ad 5 fiber knob (99) MPNLSAYPKSHGKTAKSNIVSQVYLNGDKTKPVTLTITLNGTQET-GDTT
Pan-7 fiber knob (100) MPNIKAYPKNTSAASKSHIVSQVYLNGDEAKPLMLIITFNETEDAT----
Pan-5 fiber knob (100) MPNLKAYPKNTSGAAKSHIVGKVYLHGDTGKPLDLIITFNETSDES----
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Pan-6 fiber knob (150) VSTYSMTTTWQWTGDYKDKNITFATNSFSFSYIAQE
Ad 2 fiber knob (149) VSTYSMSTTWSWE-SGKYTTETFATNSYTFSYIAQE
Ad 5 fiber knob (148) PSAYSMSFSWDWS-GHNYINEIFATSSYTFSYIAQE
Pan-7 fiber knob (146) -CTYSITFQWKWD-STKYTGETLATSSFTFSYIAQE
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SEQUENCE LISTING

<110> The Trustees of the University of Pennsylvania
Wilson, James M.
Gao, Guangping
Roy, Soumitra

<120> Simian Adenovirus Nucleic Acid and Amino Acid Sequences, Vectors Containing Same, and Methods of Use

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gcgcctgctg ggcgaggagg agtacctgaa cgactccttg cttcggcccg agcgcgagaa 13560

gaacttcccc aataacggga tagagagcct ggtggacaag atgagccgct ggaagacgta 13620

cgcgcacgag cacagggacg agccccgagc tagcagcagc accggcgcca cccgtagacg 13680

ccagcggcac gacaggcagc ggggtctggt gtgggacgat gaggattccg ccgacgacag 13740

cagcgtgttg gacttgggtg ggagtggtgg tggtaacccg ttcgctcacc tgcgcccccg 13800

tatcgggcgc ctgatgtaag aatctgaaaa aataaaagac ggtactcacc aaggccatgg 13860

cgaccagcgt gcgttcttct ctgttgtttg tagtagt atg atg agg cgc gtg tac 13915
Met Met Arg Arg Val Tyr
1 5

ccg gag ggt cct cct ccc tcg tac gag agc gtg atg cag cag gcg gtg 13963
Pro Glu Gly Pro Pro Pro Ser Tyr Glu Ser Val Met Gln Gln Ala Val
10 15 20

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gcg gcg gcg atg cag ccc ccg ctg gag gcg cct tac gtg ccc ccg cgg    14011
Ala Ala Ala Met Gln Pro Pro Leu Glu Ala Pro Tyr Val Pro Pro Arg
        25                  30                  35

tac ctg gcg cct acg gag ggg cgg aac agc att cgt tac tcg gag ctg    14059
Tyr Leu Ala Pro Thr Glu Gly Arg Asn Ser Ile Arg Tyr Ser Glu Leu
    40                  45                  50

gca ccc ttg tac gat acc acc cgg ttg tac ctg gtg gac aac aag tcg    14107
Ala Pro Leu Tyr Asp Thr Thr Arg Leu Tyr Leu Val Asp Asn Lys Ser
55                  60                  65                  70

gcg gac atc gcc tcg ctg aac tac cag aac gac cac agc aac ttc ctg    14155
Ala Asp Ile Ala Ser Leu Asn Tyr Gln Asn Asp His Ser Asn Phe Leu
                75                  80                  85

acc acc gtg gtg cag aac aac gat ttc acc ccc acg gag gcc agc acc    14203
Thr Thr Val Val Gln Asn Asn Asp Phe Thr Pro Thr Glu Ala Ser Thr
            90                  95                  100

cag acc atc aac ttt gac gag cgc tcg cgg tgg ggc ggc cag ctg aaa    14251
Gln Thr Ile Asn Phe Asp Glu Arg Ser Arg Trp Gly Gly Gln Leu Lys
        105                 110                 115

acc atc atg cac acc aac atg ccc aac gtg aac gag ttc atg tac agc    14299
Thr Ile Met His Thr Asn Met Pro Asn Val Asn Glu Phe Met Tyr Ser
    120                 125                 130

aac aag ttc aag gcg cgg gtg atg gtc tcg cgc aag acc ccc aac ggg    14347
Asn Lys Phe Lys Ala Arg Val Met Val Ser Arg Lys Thr Pro Asn Gly
135                 140                 145                 150

gtc aca gta aca gat ggt agt cag gac gag ctg acc tac gag tgg gtg    14395
Val Thr Val Thr Asp Gly Ser Gln Asp Glu Leu Thr Tyr Glu Trp Val
                155                 160                 165

gag ttt gag ctg ccc gag ggc aac ttc tcg gtg acc atg acc atc gat    14443
Glu Phe Glu Leu Pro Glu Gly Asn Phe Ser Val Thr Met Thr Ile Asp
            170                 175                 180

ctg atg aac aac gcc atc atc gac aac tac ttg gcg gtg ggg cgg cag    14491
Leu Met Asn Asn Ala Ile Ile Asp Asn Tyr Leu Ala Val Gly Arg Gln
        185                 190                 195

aac ggg gtg ctg gag agc gac atc ggc gtg aag ttc gac acg cgc aac    14539
Asn Gly Val Leu Glu Ser Asp Ile Gly Val Lys Phe Asp Thr Arg Asn
    200                 205                 210

ttc cgg ctg ggc tgg gac ccc gtg acc gag ctg gtg atg ccg ggc gtg    14587
Phe Arg Leu Gly Trp Asp Pro Val Thr Glu Leu Val Met Pro Gly Val
215                 220                 225                 230

tac acc aac gag gcc ttc cac ccc gac atc gtc ctg ctg ccc ggc tgc    14635
Tyr Thr Asn Glu Ala Phe His Pro Asp Ile Val Leu Leu Pro Gly Cys
                235                 240                 245
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ggc gtg gac ttc acc gag agc cgc ctc agc aac ctg ctg ggc atc cgc    14683
Gly Val Asp Phe Thr Glu Ser Arg Leu Ser Asn Leu Leu Gly Ile Arg
            250                 255                 260

aag cgg cag ccc ttc cag gag ggc ttc cag atc ctg tac gag gac ctg    14731
Lys Arg Gln Pro Phe Gln Glu Gly Phe Gln Ile Leu Tyr Glu Asp Leu
        265                 270                 275

gag ggg ggc aac atc ccc gcg ctg ctg gac gtg gac gcc tac gag aaa    14779
Glu Gly Gly Asn Ile Pro Ala Leu Leu Asp Val Asp Ala Tyr Glu Lys
    280                 285                 290

agc aag gag gat agc gcc gcc gcg gcg acc gca gcc gtg gcc acc gcc    14827
Ser Lys Glu Asp Ser Ala Ala Ala Ala Thr Ala Ala Val Ala Thr Ala
295                 300                 305                 310

tct acc gag gtg cgg ggc gat aat ttt gct agc gcc gcg aca ctg gca    14875
Ser Thr Glu Val Arg Gly Asp Asn Phe Ala Ser Ala Ala Thr Leu Ala
                315                 320                 325

gcg gcc gag gcg gct gaa acc gaa agt aag ata gtg atc cag ccg gtg    14923
Ala Ala Glu Ala Ala Glu Thr Glu Ser Lys Ile Val Ile Gln Pro Val
            330                 335                 340

gag aag gac agc aag gag agg agc tac aac gtg ctc gcg gac aag aaa    14971
Glu Lys Asp Ser Lys Glu Arg Ser Tyr Asn Val Leu Ala Asp Lys Lys
        345                 350                 355

aac acc gcc tac cgc agc tgg tac ctg gcc tac aac tac ggc gac ccc    15019
Asn Thr Ala Tyr Arg Ser Trp Tyr Leu Ala Tyr Asn Tyr Gly Asp Pro
    360                 365                 370

gag aag ggc gtg cgc tcc tgg acg ctg ctc acc acc tcg gac gtc acc    15067
Glu Lys Gly Val Arg Ser Trp Thr Leu Leu Thr Thr Ser Asp Val Thr
375                 380                 385                 390

tgc ggc gtg gag caa gtc tac tgg tcg ctg ccc gac atg atg caa gac    15115
Cys Gly Val Glu Gln Val Tyr Trp Ser Leu Pro Asp Met Met Gln Asp
                395                 400                 405

ccg gtc acc ttc cgc tcc acg cgt caa gtt agc aac tac ccg gtg gtg    15163
Pro Val Thr Phe Arg Ser Thr Arg Gln Val Ser Asn Tyr Pro Val Val
            410                 415                 420

ggc gcc gag ctc ctg ccc gtc tac tcc aag agc ttc ttc aac gag cag    15211
Gly Ala Glu Leu Leu Pro Val Tyr Ser Lys Ser Phe Phe Asn Glu Gln
        425                 430                 435

gcc gtc tac tcg cag cag ctg cgc gcc ttc acc tcg ctc acg cac gtc    15259
Ala Val Tyr Ser Gln Gln Leu Arg Ala Phe Thr Ser Leu Thr His Val
    440                 445                 450

ttc aac cgc ttc ccc gag aac cag atc ctc gtt cgc ccg ccc gcg ccc    15307
Phe Asn Arg Phe Pro Glu Asn Gln Ile Leu Val Arg Pro Pro Ala Pro
455                 460                 465                 470
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acc att acc acc gtc agt gaa aac gtt cct gct ctc aca gat cac ggg    15355
Thr Ile Thr Thr Val Ser Glu Asn Val Pro Ala Leu Thr Asp His Gly
                475                 480                 485

acc ctg ccg ctg cgc agc agt atc cgg gga gtc cag cgc gtg acc gtc    15403
Thr Leu Pro Leu Arg Ser Ser Ile Arg Gly Val Gln Arg Val Thr Val
            490                 495                 500

act gac gcc aga cgc cgc acc tgc ccc tac gtc tac aag gcc ctg ggc    15451
Thr Asp Ala Arg Arg Arg Thr Cys Pro Tyr Val Tyr Lys Ala Leu Gly
        505                 510                 515

gta gtc gcg ccg cgc gtc ctc tcg agc cgc acc ttc taa aaaatgtcca     15500
Val Val Ala Pro Arg Val Leu Ser Ser Arg Thr Phe
    520                 525                 530

ttctcatctc gcccagtaat aacaccggtt ggggcctgcg cgcgcccagc aagatgtacg  15560

gaggcgctcg ccaacgctcc acgcaacacc ccgtgcgcgt gcgcgggcac ttccgcgctc  15620

cctggggcgc cctcaagggc cgcgtgcgct cgcgcaccac cgtcgacgac gtgatcgacc  15680

aggtggtggc cgacgcgcgc aactacacgc ccgccgccgc gcccgtctcc accgtggacg  15740

ccgtcatcga cagcgtggtg gccgacgcgc gccggtacgc ccgcgccaag agccggcggc  15800

ggcgcatcgc ccggcggcac cggagcaccc ccgccatgcg cgcggcgcga gccttgctgc  15860

gcagggccag gcgcacggga cgcagggcca tgctcagggc ggccagacgc gcggcctccg  15920

gcagcagcag cgccggcagg acccgcagac gcgcggccac ggcggcggcg gcggccatcg  15980

ccagcatgtc ccgcccgcgg cgcggcaacg tgtactgggt gcgcgacgcc gccaccggtg  16040

tgcgcgtgcc cgtgcgcacc cgccccctc gcacttgaag atgctgactt cgcgatgttg  16100

atgtgtccca gcggcgagga ggatgtccaa gcgcaaattc aaggaagaga tgctccaggt  16160

catcgcgcct gagatctacg gcccggcggc ggtgaaggag gaaagaaagc cccgcaaact  16220

gaagcgggtc aaaaaggaca aaaaggagga ggaagatgtg gacggactgg tggagtttgt  16280

gcgcgagttc gccccccggc ggcgcgtgca gtggcgcggg cggaaagtga aaccggtgct  16340

gcgacccggc accacggtgg tcttcacgcc cggcgagcgt tccggctccg cctccaagcg  16400

ctcctacgac gaggtgtacg gggacgagga catcctcgag caggcggccg aacgtctggg  16460

cgagtttgct tacggcaagc gcagccgccc cgcgcccttg aaagaggagg cggtgtccat  16520

cccgctggac cacggcaacc ccacgccgag cctgaagccg gtgaccctgc agcaggtgct  16580

gcctggtgcg gcgccgcgcc ggggcttcaa gcgcgagggc ggcgaggatc tgtacccgac  16640

catgcagctg atggtgccca agcgccagaa gctggaggac gtgctggagc acatgaaggt  16700

ggaccccgag gtgcagcccg aggtcaaggt gcggcccatc aagcaggtgg ccccgggcct  16760
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gggcgtgcag accgtggaca tcaagatccc cacggagccc atggaaacgc agaccgagcc 16820

cgtgaagccc agcaccagca ccatggaggt gcagacggat ccctggatgc cggcaccggc 16880

ttccaccacc cgccgaagac gcaagtacgg cgcggccagc ctgctgatgc ccaactacgc 16940

gctgcatcct tccatcatcc ccacgccggg ctaccgcggc acgcgcttct accgcggcta 17000

caccagcagc cgccgccgca agaccaccac ccgccgccgc cgtcgtcgca cccgccgcag 17060

cagcaccgcg acttccgccg ccgccctggt gcggagagtg taccgcagcg ggcgcgagcc 17120

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agccgcgccg tagaaggctg acggggaacg ggctgcgtcg ccatcaccac cggcggcggc 17300

gcgccatcag caagcggttg gggggaggct tcctgcccgc gctgatgccc atcatcgccg 17360

cggcgatcgg ggcgatcccc ggcatagctt ccgtggcggt gcaggcctct cagcgccact 17420

gagacacagc ttggaaaatt tgtaataaaa aatggactga cgctcctggt cctgtgatgt 17480

gtgtttttag atggaagaca tcaatttttc gtccctggca ccgcgacacg gcacgcggcc 17540

gtttatgggc acctggagcg acatcggcaa cagccaactg aacgggggcg ccttcaattg 17600

gagcagtctc tggagcgggc ttaagaattt cgggtccacg ctcaaaacct atggcaacaa 17660

ggcgtggaac agcagcacag ggcaggcgct gagggaaaag ctgaaagagc agaacttcca 17720

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ctccacagtg gctaagcccc tgccgccggt ggccgtcgcg tcgcgcgccc cccgaggccg 18140

cccccaggcg aactggcaga gcactctgaa cagcatcgtg ggtctgggag tgcagagtgt 18200

gaagcgccgc cgctgctatt aaaagacact gtagcgctta acttgcttgt ctgtgtgtat 18260

atgtatgtcc gccgaccaga aggaggagga agaggcgcgt cgccgagttg caag atg 18317
Met

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gcc acc cca tcg atg ctg ccc cag tgg gcg tac atg cac atc gcc gga    18365
Ala Thr Pro Ser Met Leu Pro Gln Trp Ala Tyr Met His Ile Ala Gly
            535                 540                 545

cag gac gct tcg gag tac ctg agt ccg ggt ctg gtg cag ttc gcc cgc    18413
Gln Asp Ala Ser Glu Tyr Leu Ser Pro Gly Leu Val Gln Phe Ala Arg
        550                 555                 560

gcc aca gac acc tac ttc agt ctg ggg aac aag ttt agg aac ccc acg    18461
Ala Thr Asp Thr Tyr Phe Ser Leu Gly Asn Lys Phe Arg Asn Pro Thr
    565                 570                 575

gtg gcg ccc acg cac gat gtg acc acc gac cgc agc cag cgg ctg acg    18509
Val Ala Pro Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg Leu Thr
580                 585                 590                 595

ctg cgc ttc gtg ccc gtg gac cgc gag gac aac acc tac tcg tac aaa    18557
Leu Arg Phe Val Pro Val Asp Arg Glu Asp Asn Thr Tyr Ser Tyr Lys
                600                 605                 610

gtg cgc tac acg ctg gcc gtg ggc gac aac cgc gtg ctg gac atg gcc    18605
Val Arg Tyr Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met Ala
            615                 620                 625

agc acc tac ttt gac atc cgc ggc gtg ctg gat cgg ggc cct agc ttc    18653
Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro Ser Phe
        630                 635                 640

aaa ccc tac tcc ggc acc gct tac aac agc ctg gct ccc aag gga gcg    18701
Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ser Leu Ala Pro Lys Gly Ala
    645                 650                 655

ccc aac act tgc cag tgg aca tat aaa gct gat ggt gat act ggt aca    18749
Pro Asn Thr Cys Gln Trp Thr Tyr Lys Ala Asp Gly Asp Thr Gly Thr
660                 665                 670                 675

gaa aaa acc tat aca tat gga aat gcg cct gtg caa ggc att agt att    18797
Glu Lys Thr Tyr Thr Tyr Gly Asn Ala Pro Val Gln Gly Ile Ser Ile
                680                 685                 690

aca aaa gat ggt att caa ctt gga act gac act gat gat cag ccc att    18845
Thr Lys Asp Gly Ile Gln Leu Gly Thr Asp Thr Asp Asp Gln Pro Ile
            695                 700                 705

tat gca gat aaa act tat caa cca gag cct caa gtg ggt gat gct gaa    18893
Tyr Ala Asp Lys Thr Tyr Gln Pro Glu Pro Gln Val Gly Asp Ala Glu
        710                 715                 720

tgg cat gac atc act ggt act gat gaa aaa tat gga ggc aga gct ctc    18941
Trp His Asp Ile Thr Gly Thr Asp Glu Lys Tyr Gly Gly Arg Ala Leu
    725                 730                 735

aag cct gac acc aaa atg aag ccc tgc tat ggt tct ttt gcc aag cct    18989
Lys Pro Asp Thr Lys Met Lys Pro Cys Tyr Gly Ser Phe Ala Lys Pro
740                 745                 750                 755
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acc aat aaa gaa gga ggt cag gca aat gtg aaa acc gaa aca ggc ggt    19037
Thr Asn Lys Glu Gly Gly Gln Ala Asn Val Lys Thr Glu Thr Gly Gly
                760                 765                 770

acc aaa gaa tat gac att gac atg gca ttc ttc gat aat cga agt gca    19085
Thr Lys Glu Tyr Asp Ile Asp Met Ala Phe Phe Asp Asn Arg Ser Ala
            775                 780                 785

gct gcg gct ggc ctg gcc cca gaa att gtt ttg tat act gag aat gtg    19133
Ala Ala Ala Gly Leu Ala Pro Glu Ile Val Leu Tyr Thr Glu Asn Val
        790                 795                 800

gat ctg gaa act cca gat act cat att gta tac aag gcg ggc aca gat    19181
Asp Leu Glu Thr Pro Asp Thr His Ile Val Tyr Lys Ala Gly Thr Asp
    805                 810                 815

gac agc agc tct tct atc aat ttg ggt cag cag tcc atg ccc aac aga    19229
Asp Ser Ser Ser Ser Ile Asn Leu Gly Gln Gln Ser Met Pro Asn Arg
820                 825                 830                 835

ccc aac tac att ggc ttt aga gac aac ttt atc ggg ctc atg tac tac    19277
Pro Asn Tyr Ile Gly Phe Arg Asp Asn Phe Ile Gly Leu Met Tyr Tyr
                840                 845                 850

aac agc act ggc aac atg ggc gtg ctg gct ggt cag gcc tcc cag ctg    19325
Asn Ser Thr Gly Asn Met Gly Val Leu Ala Gly Gln Ala Ser Gln Leu
            855                 860                 865

aat gct gtg gtg gac ttg cag gac aga aac act gaa ctg tcc tac cag    19373
Asn Ala Val Val Asp Leu Gln Asp Arg Asn Thr Glu Leu Ser Tyr Gln
        870                 875                 880

ctc ttg ctt gac tct ctg ggc gac aga acc agg tat ttc agt atg tgg    19421
Leu Leu Leu Asp Ser Leu Gly Asp Arg Thr Arg Tyr Phe Ser Met Trp
    885                 890                 895

aat cag gcg gtg gac agc tat gac ccc gat gtg cgc att att gaa aat    19469
Asn Gln Ala Val Asp Ser Tyr Asp Pro Asp Val Arg Ile Ile Glu Asn
900                 905                 910                 915

cac ggt gtg gag gat gaa ctc cct aac tat tgc ttc ccc ctg gat gct    19517
His Gly Val Glu Asp Glu Leu Pro Asn Tyr Cys Phe Pro Leu Asp Ala
                920                 925                 930

gtg ggt aga act gat act tac cag gga att aag gcc aat ggt gct gat    19565
Val Gly Arg Thr Asp Thr Tyr Gln Gly Ile Lys Ala Asn Gly Ala Asp
            935                 940                 945

caa acc acc tgg acc aaa gat gat act gtt aat gat gct aat gaa ttg    19613
Gln Thr Thr Trp Thr Lys Asp Asp Thr Val Asn Asp Ala Asn Glu Leu
        950                 955                 960

ggc aag ggc aat cct ttc gcc atg gag atc aac atc cag gcc aac ctg    19661
Gly Lys Gly Asn Pro Phe Ala Met Glu Ile Asn Ile Gln Ala Asn Leu
    965                 970                 975
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tgg cgg aac ttc ctc tac gcg aac gtg gcg ctg tac ctg ccc gac tcc    19709
Trp Arg Asn Phe Leu Tyr Ala Asn Val Ala Leu Tyr Leu Pro Asp Ser
980                 985                 990                 995

tac aag tac acg ccg  gcc aac atc acg ctg  ccg acc aac acc aac      19754
Tyr Lys Tyr Thr Pro  Ala Asn Ile Thr Leu  Pro Thr Asn Thr Asn
                   1000                1005                1010

acc tac gat tac atg  aac ggc cgc gtg gtg  gcg ccc tcg ctg gtg      19799
Thr Tyr Asp Tyr Met  Asn Gly Arg Val Val  Ala Pro Ser Leu Val
                   1015                1020                1025

gac gcc tac atc aac  atc ggg gcg cgc tgg  tcg ctg gac ccc atg      19844
Asp Ala Tyr Ile Asn  Ile Gly Ala Arg Trp  Ser Leu Asp Pro Met
                   1030                1035                1040

gac aac gtc aac ccc  ttc aac cac cac cgc  aac gcg ggc ctg cgc      19889
Asp Asn Val Asn Pro  Phe Asn His His Arg  Asn Ala Gly Leu Arg
                   1045                1050                1055

tac cgc tcc atg ctc  ctg ggc aac ggg cgc  tac gtg ccc ttc cac      19934
Tyr Arg Ser Met Leu  Leu Gly Asn Gly Arg  Tyr Val Pro Phe His
                   1060                1065                1070

atc cag gtg ccc caa  aag ttc ttc gcc atc  aag agc ctc ctg ctc      19979
Ile Gln Val Pro Gln  Lys Phe Phe Ala Ile  Lys Ser Leu Leu Leu
                   1075                1080                1085

ctg ccc ggg tcc tac  acc tac gag tgg aac  ttc cgc aag gac gtc      20024
Leu Pro Gly Ser Tyr  Thr Tyr Glu Trp Asn  Phe Arg Lys Asp Val
                   1090                1095                1100

aac atg atc ctg cag  agc tcc ctc ggc aac  gac ctg cgc acg gac      20069
Asn Met Ile Leu Gln  Ser Ser Leu Gly Asn  Asp Leu Arg Thr Asp
                   1105                1110                1115

ggg gcc tcc atc gcc  ttc acc agc atc aac  ctc tac gcc acc ttc      20114
Gly Ala Ser Ile Ala  Phe Thr Ser Ile Asn  Leu Tyr Ala Thr Phe
                   1120                1125                1130

ttc ccc atg gcg cac  aac acc gcc tcc acg  ctc gag gcc atg ctg      20159
Phe Pro Met Ala His  Asn Thr Ala Ser Thr  Leu Glu Ala Met Leu
                   1135                1140                1145

cgc aac gac acc aac  gac cag tcc ttc aac  gac tac ctc tcg gcg      20204
Arg Asn Asp Thr Asn  Asp Gln Ser Phe Asn  Asp Tyr Leu Ser Ala
                   1150                1155                1160

gcc aac atg ctc tac  ccc atc ccg gcc aac  gcc acc aac gtg ccc      20249
Ala Asn Met Leu Tyr  Pro Ile Pro Ala Asn  Ala Thr Asn Val Pro
                   1165                1170                1175

atc tcc atc ccc tcg  cgc aac tgg gcc gcc  ttc cgc gga tgg tcc      20294
Ile Ser Ile Pro Ser  Arg Asn Trp Ala Ala  Phe Arg Gly Trp Ser
                   1180                1185                1190
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ttc acg cgc ctc aag  acc cgc gag acg ccc  tcg ctc ggc tcc ggg      20339
Phe Thr Arg Leu Lys  Thr Arg Glu Thr Pro  Ser Leu Gly Ser Gly
                1195                1200                1205

ttc gac ccc tac ttc  gtc tac tcg ggc tcc  atc ccc tac ctc gac      20384
Phe Asp Pro Tyr Phe  Val Tyr Ser Gly Ser  Ile Pro Tyr Leu Asp
                1210                1215                1220

ggc acc ttc tac ctc  aac cac acc ttc aag  aag gtc tcc atc acc      20429
Gly Thr Phe Tyr Leu  Asn His Thr Phe Lys  Lys Val Ser Ile Thr
                1225                1230                1235

ttc gac tcc tcc gtc  agc tgg ccc ggc aac  gac cgc ctc ctg acg      20474
Phe Asp Ser Ser Val  Ser Trp Pro Gly Asn  Asp Arg Leu Leu Thr
                1240                1245                1250

ccc aac gag ttc gaa  atc aag cgc acc gtc  gac gga gag ggg tac      20519
Pro Asn Glu Phe Glu  Ile Lys Arg Thr Val  Asp Gly Glu Gly Tyr
                1255                1260                1265

aac gtg gcc cag tgc  aac atg acc aag gac  tgg ttc ctg gtc cag      20564
Asn Val Ala Gln Cys  Asn Met Thr Lys Asp  Trp Phe Leu Val Gln
                1270                1275                1280

atg ctg gcc cac tac  aac atc ggc tac cag  ggc ttc tac gtg ccc      20609
Met Leu Ala His Tyr  Asn Ile Gly Tyr Gln  Gly Phe Tyr Val Pro
                1285                1290                1295

gag ggc tac aag gac  cgc atg tac tcc ttc  ttc cgc aac ttc cag      20654
Glu Gly Tyr Lys Asp  Arg Met Tyr Ser Phe  Phe Arg Asn Phe Gln
                1300                1305                1310

ccc atg agc cgc cag  gtc gtg gac gag gtc  aac tac aag gac tac      20699
Pro Met Ser Arg Gln  Val Val Asp Glu Val  Asn Tyr Lys Asp Tyr
                1315                1320                1325

cag gcc gtc acc ctg  gcc tac cag cac aac  aac tcg ggc ttc gtc      20744
Gln Ala Val Thr Leu  Ala Tyr Gln His Asn  Asn Ser Gly Phe Val
                1330                1335                1340

ggc tac ctc gcg ccc  acc atg cgc cag gga  cag ccc tac ccc gcc      20789
Gly Tyr Leu Ala Pro  Thr Met Arg Gln Gly  Gln Pro Tyr Pro Ala
                1345                1350                1355

aac tac ccc tac ccg  ctc atc ggc aag agc  gcc gtc gcc agc gtc      20834
Asn Tyr Pro Tyr Pro  Leu Ile Gly Lys Ser  Ala Val Ala Ser Val
                1360                1365                1370

acc cag aaa aag ttc  ctc tgc gac cgg gtc  atg tgg cgc atc ccc      20879
Thr Gln Lys Lys Phe  Leu Cys Asp Arg Val  Met Trp Arg Ile Pro
                1375                1380                1385

ttc tcc agc aac ttc  atg tcc atg ggc gcg  ctc acc gac ctc ggc      20924
Phe Ser Ser Asn Phe  Met Ser Met Gly Ala  Leu Thr Asp Leu Gly
                1390                1395                1400
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cag aac atg ctc tac  gcc aac tcc gcc cac  gcg cta gac atg aat      20969
Gln Asn Met Leu Tyr  Ala Asn Ser Ala His  Ala Leu Asp Met Asn
                1405                1410                1415

ttc gaa gtc gac ccc  atg gat gag tcc acc  ctt ctc tat gtt gtc      21014
Phe Glu Val Asp Pro  Met Asp Glu Ser Thr  Leu Leu Tyr Val Val
                1420                1425                1430

ttc gaa gtc ttc gac  gtc gtc cga gtg cac  cag ccc cac cgc ggc      21059
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Val Ile Glu Ala Val  Tyr Leu Arg Thr Pro  Phe Ser Ala Gly Asn
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Ala Thr Thr

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Leu  Asp Ser Ser Gly Lys  Leu Ile Ser Asn Thr  Ala Thr Lys Ala
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1745                 1750                 1755

agt  cag att ctg ggc act  gtt tcc ctc ata gct  gtt gat act ggc     32967
Ser  Gln Ile Leu Gly Thr  Val Ser Leu Ile Ala  Val Asp Thr Gly
1760                 1765                 1770

agt  tta aat ccc ata aca  gga aca gta acc act  gct ctt gtc tca     33012
Ser  Leu Asn Pro Ile Thr  Gly Thr Val Thr Thr  Ala Leu Val Ser
1775                 1780                 1785

ctt  aaa ttc gat gca aat  gga gtt ttg caa agc  agc tca aca cta     33057
Leu  Lys Phe Asp Ala Asn  Gly Val Leu Gln Ser  Ser Ser Thr Leu
1790                 1795                 1800

gac  tca gac tat tgg aat  ttc aga cag gga gat  gtt aca cct gct     33102
Asp  Ser Asp Tyr Trp Asn  Phe Arg Gln Gly Asp  Val Thr Pro Ala
1805                 1810                 1815

gaa  gcc tat act aat gct  ata ggt ttc atg ccc  aat cta aaa gca     33147
Glu  Ala Tyr Thr Asn Ala  Ile Gly Phe Met Pro  Asn Leu Lys Ala
1820                 1825                 1830

tac  cct aaa aac aca agt  gga gct gca aaa agt  cac att gtt ggg     33192
Tyr  Pro Lys Asn Thr Ser  Gly Ala Ala Lys Ser  His Ile Val Gly
1835                 1840                 1845

aaa  gtg tac cta cat ggg  gat aca ggc aaa cca  ctg gac ctc att     33237
Lys  Val Tyr Leu His Gly  Asp Thr Gly Lys Pro  Leu Asp Leu Ile
1850                 1855                 1860

att  act ttc aat gaa aca  agt gat gaa tct tgc  act tac tgt att     33282
Ile  Thr Phe Asn Glu Thr  Ser Asp Glu Ser Cys  Thr Tyr Cys Ile
1865                 1870                 1875

aac  ttt caa tgg cag tgg  ggg gct gat caa tat  aaa aat gaa aca     33327
Asn  Phe Gln Trp Gln Trp  Gly Ala Asp Gln Tyr  Lys Asn Glu Thr
1880                 1885                 1890

ctt  gcc gtc agt tca ttc  acc ttt tcc tat att  gct aaa gaa taa     33372
Leu  Ala Val Ser Ser Phe  Thr Phe Ser Tyr Ile  Ala Lys Glu
1895                 1900                 1905

accccactct gtaccccatc tctgtctatg gaaaaaactc tgaaacacaa aataaaataa  33432

agttcaagtg ttttattgat tcaacagttt tacaggattc gagcagttat ttttcctcca  33492

ccctcccagg acatggaata caccaccctc tccccccgca cagccttgaa catctgaatg  33552

ccattggtga tggacatgct tttggtctcc acgttccaca cagtttcaga gcgagccagt  33612

ctcgggtcgg tcagggagat gaaaccctcc gggcactccc gcatctgcac ctcacagctc  33672
```

aacagctgag gattgtcctc ggtggtcggg atcacggtta tctggaagaa gcagaagagc 33732

ggcggtggga atcatagtcc gcgaacggga tcggccggtg gtgtcgcatc aggccccgca 33792

gcagtcgctg tcgccgccgc tccgtcaagc tgctgctcag ggggtccggg tccagggact 33852

ccctcagcat gatgcccacg gccctcagca tcagtcgtct ggtgcggcgg gcgcagcagc 33912

gcatgcggat ctcgctcagg tcgctgcagt acgtgcaaca caggaccacc aggttgttca 33972

acagtccata gttcaacacg ctccagccga aactcatcgc gggaaggatg ctacccacgt 34032

ggccgtcgta ccagatcctc aggtaaatca agtggcgccc cctccagaac acgctgccca 34092

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ggttgaacat gcagccccgg atgatcctgc ggaaccacag ggccagcacc gccccgcccg 34212

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cagaacctgg tccgggcgct gcacaccgat cgccggcggc ggtcccggcg cttggaacgc 34692

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ccaaaagttt gaggtatatt attgatgatg 36462

<210> 2
<211> 530
<212> PRT
<213> chimpanzee adenovirus serotype Pan5

<400> 2

Met Met Arg Arg Val Tyr Pro Glu Gly Pro Pro Pro Ser Tyr Glu Ser
1 5 10 15

Val Met Gln Gln Ala Val Ala Ala Ala Met Gln Pro Pro Leu Glu Ala
20 25 30

Pro Tyr Val Pro Pro Arg Tyr Leu Ala Pro Thr Glu Gly Arg Asn Ser
35 40 45

Ile Arg Tyr Ser Glu Leu Ala Pro Leu Tyr Asp Thr Thr Arg Leu Tyr
50 55 60

```
Leu Val Asp Asn Lys Ser Ala Asp Ile Ala Ser Leu Asn Tyr Gln Asn
65                  70                  75                  80

Asp His Ser Asn Phe Leu Thr Thr Val Val Gln Asn Asn Asp Phe Thr
                85                  90                  95

Pro Thr Glu Ala Ser Thr Gln Thr Ile Asn Phe Asp Glu Arg Ser Arg
            100                 105                 110

Trp Gly Gly Gln Leu Lys Thr Ile Met His Thr Asn Met Pro Asn Val
        115                 120                 125

Asn Glu Phe Met Tyr Ser Asn Lys Phe Lys Ala Arg Val Met Val Ser
    130                 135                 140

Arg Lys Thr Pro Asn Gly Val Thr Val Thr Asp Gly Ser Gln Asp Glu
145                 150                 155                 160

Leu Thr Tyr Glu Trp Val Glu Phe Glu Leu Pro Glu Gly Asn Phe Ser
                165                 170                 175

Val Thr Met Thr Ile Asp Leu Met Asn Asn Ala Ile Ile Asp Asn Tyr
            180                 185                 190

Leu Ala Val Gly Arg Gln Asn Gly Val Leu Glu Ser Asp Ile Gly Val
        195                 200                 205

Lys Phe Asp Thr Arg Asn Phe Arg Leu Gly Trp Asp Pro Val Thr Glu
    210                 215                 220

Leu Val Met Pro Gly Val Tyr Thr Asn Glu Ala Phe His Pro Asp Ile
225                 230                 235                 240

Val Leu Leu Pro Gly Cys Gly Val Asp Phe Thr Glu Ser Arg Leu Ser
                245                 250                 255

Asn Leu Leu Gly Ile Arg Lys Arg Gln Pro Phe Gln Glu Gly Phe Gln
            260                 265                 270

Ile Leu Tyr Glu Asp Leu Glu Gly Gly Asn Ile Pro Ala Leu Leu Asp
        275                 280                 285

Val Asp Ala Tyr Glu Lys Ser Lys Glu Asp Ser Ala Ala Ala Ala Thr
    290                 295                 300

Ala Ala Val Ala Thr Ala Ser Thr Glu Val Arg Gly Asp Asn Phe Ala
305                 310                 315                 320

Ser Ala Ala Thr Leu Ala Ala Ala Glu Ala Ala Glu Thr Glu Ser Lys
                325                 330                 335

Ile Val Ile Gln Pro Val Glu Lys Asp Ser Lys Glu Arg Ser Tyr Asn
            340                 345                 350
```

```
Val Leu Ala Asp Lys Lys Asn Thr Ala Tyr Arg Ser Trp Tyr Leu Ala
        355                 360                 365

Tyr Asn Tyr Gly Asp Pro Glu Lys Gly Val Arg Ser Trp Thr Leu Leu
    370                 375                 380

Thr Thr Ser Asp Val Thr Cys Gly Val Glu Gln Val Tyr Trp Ser Leu
385                 390                 395                 400

Pro Asp Met Met Gln Asp Pro Val Thr Phe Arg Ser Thr Arg Gln Val
                405                 410                 415

Ser Asn Tyr Pro Val Val Gly Ala Glu Leu Leu Pro Val Tyr Ser Lys
            420                 425                 430

Ser Phe Phe Asn Glu Gln Ala Val Tyr Ser Gln Gln Leu Arg Ala Phe
        435                 440                 445

Thr Ser Leu Thr His Val Phe Asn Arg Phe Pro Glu Asn Gln Ile Leu
    450                 455                 460

Val Arg Pro Pro Ala Pro Thr Ile Thr Thr Val Ser Glu Asn Val Pro
465                 470                 475                 480

Ala Leu Thr Asp His Gly Thr Leu Pro Leu Arg Ser Ser Ile Arg Gly
                485                 490                 495

Val Gln Arg Val Thr Val Thr Asp Ala Arg Arg Arg Thr Cys Pro Tyr
            500                 505                 510

Val Tyr Lys Ala Leu Gly Val Val Ala Pro Arg Val Leu Ser Ser Arg
        515                 520                 525

Thr Phe
    530
```

<210> 3
<211> 933
<212> PRT
<213> chimpanzee adenovirus serotype Pan5

<400> 3

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Met Ala Thr Pro Ser Met Leu Pro Gln Trp Ala Tyr Met His Ile Ala
1               5                   10                  15

Gly Gln Asp Ala Ser Glu Tyr Leu Ser Pro Gly Leu Val Gln Phe Ala
            20                  25                  30

Arg Ala Thr Asp Thr Tyr Phe Ser Leu Gly Asn Lys Phe Arg Asn Pro
        35                  40                  45

Thr Val Ala Pro Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg Leu
    50                  55                  60
```

```
Thr Leu Arg Phe Val Pro Val Asp Arg Glu Asp Asn Thr Tyr Ser Tyr
65                  70                  75                  80

Lys Val Arg Tyr Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met
                85                  90                  95

Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro Ser
            100                 105                 110

Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ser Leu Ala Pro Lys Gly
        115                 120                 125

Ala Pro Asn Thr Cys Gln Trp Thr Tyr Lys Ala Asp Gly Asp Thr Gly
    130                 135                 140

Thr Glu Lys Thr Tyr Thr Tyr Gly Asn Ala Pro Val Gln Gly Ile Ser
145                 150                 155                 160

Ile Thr Lys Asp Gly Ile Gln Leu Gly Thr Asp Thr Asp Asp Gln Pro
                165                 170                 175

Ile Tyr Ala Asp Lys Thr Tyr Gln Pro Glu Pro Gln Val Gly Asp Ala
            180                 185                 190

Glu Trp His Asp Ile Thr Gly Thr Asp Glu Lys Tyr Gly Gly Arg Ala
        195                 200                 205

Leu Lys Pro Asp Thr Lys Met Lys Pro Cys Tyr Gly Ser Phe Ala Lys
    210                 215                 220

Pro Thr Asn Lys Glu Gly Gly Gln Ala Asn Val Lys Thr Glu Thr Gly
225                 230                 235                 240

Gly Thr Lys Glu Tyr Asp Ile Asp Met Ala Phe Phe Asp Asn Arg Ser
                245                 250                 255

Ala Ala Ala Ala Gly Leu Ala Pro Glu Ile Val Leu Tyr Thr Glu Asn
            260                 265                 270

Val Asp Leu Glu Thr Pro Asp Thr His Ile Val Tyr Lys Ala Gly Thr
        275                 280                 285

Asp Asp Ser Ser Ser Ser Ile Asn Leu Gly Gln Gln Ser Met Pro Asn
    290                 295                 300

Arg Pro Asn Tyr Ile Gly Phe Arg Asp Asn Phe Ile Gly Leu Met Tyr
305                 310                 315                 320

Tyr Asn Ser Thr Gly Asn Met Gly Val Leu Ala Gly Gln Ala Ser Gln
                325                 330                 335

Leu Asn Ala Val Val Asp Leu Gln Asp Arg Asn Thr Glu Leu Ser Tyr
            340                 345                 350

Gln Leu Leu Leu Asp Ser Leu Gly Asp Arg Thr Arg Tyr Phe Ser Met
        355                 360                 365
```

```
Trp Asn Gln Ala Val Asp Ser Tyr Asp Pro Asp Val Arg Ile Ile Glu
    370                 375                 380

Asn His Gly Val Glu Asp Glu Leu Pro Asn Tyr Cys Phe Pro Leu Asp
385                 390                 395                 400

Ala Val Gly Arg Thr Asp Thr Tyr Gln Gly Ile Lys Ala Asn Gly Ala
                405                 410                 415

Asp Gln Thr Thr Trp Thr Lys Asp Asp Thr Val Asn Asp Ala Asn Glu
            420                 425                 430

Leu Gly Lys Gly Asn Pro Phe Ala Met Glu Ile Asn Ile Gln Ala Asn
        435                 440                 445

Leu Trp Arg Asn Phe Leu Tyr Ala Asn Val Ala Leu Tyr Leu Pro Asp
    450                 455                 460

Ser Tyr Lys Tyr Thr Pro Ala Asn Ile Thr Leu Pro Thr Asn Thr Asn
465                 470                 475                 480

Thr Tyr Asp Tyr Met Asn Gly Arg Val Val Ala Pro Ser Leu Val Asp
                485                 490                 495

Ala Tyr Ile Asn Ile Gly Ala Arg Trp Ser Leu Asp Pro Met Asp Asn
            500                 505                 510

Val Asn Pro Phe Asn His His Arg Asn Ala Gly Leu Arg Tyr Arg Ser
        515                 520                 525

Met Leu Leu Gly Asn Gly Arg Tyr Val Pro Phe His Ile Gln Val Pro
    530                 535                 540

Gln Lys Phe Phe Ala Ile Lys Ser Leu Leu Leu Leu Pro Gly Ser Tyr
545                 550                 555                 560

Thr Tyr Glu Trp Asn Phe Arg Lys Asp Val Asn Met Ile Leu Gln Ser
                565                 570                 575

Ser Leu Gly Asn Asp Leu Arg Thr Asp Gly Ala Ser Ile Ala Phe Thr
            580                 585                 590

Ser Ile Asn Leu Tyr Ala Thr Phe Phe Pro Met Ala His Asn Thr Ala
        595                 600                 605

Ser Thr Leu Glu Ala Met Leu Arg Asn Asp Thr Asn Asp Gln Ser Phe
    610                 615                 620

Asn Asp Tyr Leu Ser Ala Ala Asn Met Leu Tyr Pro Ile Pro Ala Asn
625                 630                 635                 640

Ala Thr Asn Val Pro Ile Ser Ile Pro Ser Arg Asn Trp Ala Ala Phe
                645                 650                 655

Arg Gly Trp Ser Phe Thr Arg Leu Lys Thr Arg Glu Thr Pro Ser Leu
            660                 665                 670
```

```
Gly Ser Gly Phe Asp Pro Tyr Phe Val Tyr Ser Gly Ser Ile Pro Tyr
        675                 680                 685

Leu Asp Gly Thr Phe Tyr Leu Asn His Thr Phe Lys Lys Val Ser Ile
    690                 695                 700

Thr Phe Asp Ser Ser Val Ser Trp Pro Gly Asn Asp Arg Leu Leu Thr
705                 710                 715                 720

Pro Asn Glu Phe Glu Ile Lys Arg Thr Val Asp Gly Glu Gly Tyr Asn
                725                 730                 735

Val Ala Gln Cys Asn Met Thr Lys Asp Trp Phe Leu Val Gln Met Leu
            740                 745                 750

Ala His Tyr Asn Ile Gly Tyr Gln Gly Phe Tyr Val Pro Glu Gly Tyr
        755                 760                 765

Lys Asp Arg Met Tyr Ser Phe Phe Arg Asn Phe Gln Pro Met Ser Arg
    770                 775                 780

Gln Val Val Asp Glu Val Asn Tyr Lys Asp Tyr Gln Ala Val Thr Leu
785                 790                 795                 800

Ala Tyr Gln His Asn Asn Ser Gly Phe Val Gly Tyr Leu Ala Pro Thr
                805                 810                 815

Met Arg Gln Gly Gln Pro Tyr Pro Ala Asn Tyr Pro Tyr Pro Leu Ile
            820                 825                 830

Gly Lys Ser Ala Val Ala Ser Val Thr Gln Lys Lys Phe Leu Cys Asp
        835                 840                 845

Arg Val Met Trp Arg Ile Pro Phe Ser Ser Asn Phe Met Ser Met Gly
    850                 855                 860

Ala Leu Thr Asp Leu Gly Gln Asn Met Leu Tyr Ala Asn Ser Ala His
865                 870                 875                 880

Ala Leu Asp Met Asn Phe Glu Val Asp Pro Met Asp Glu Ser Thr Leu
                885                 890                 895

Leu Tyr Val Val Phe Glu Val Phe Asp Val Val Arg Val His Gln Pro
            900                 905                 910

His Arg Gly Val Ile Glu Ala Val Tyr Leu Arg Thr Pro Phe Ser Ala
        915                 920                 925

Gly Asn Ala Thr Thr
    930
```

<210> 4
<211> 445
<212> PRT
<213> chimpanzee adenovirus serotype Pan5

<400> 4

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Met Ser Lys Lys Arg Val Arg Val Asp Asp Asp Phe Asp Pro Val Tyr
1               5                  10                  15

Pro Tyr Asp Ala Asp Asn Ala Pro Thr Val Pro Phe Ile Asn Pro Pro
            20                  25                  30

Phe Val Ser Ser Asp Gly Phe Gln Glu Lys Pro Leu Gly Val Leu Ser
        35                  40                  45

Leu Arg Leu Ala Asp Pro Val Thr Thr Lys Asn Gly Glu Ile Thr Leu
    50                  55                  60

Lys Leu Gly Asp Gly Val Asp Leu Asp Ser Ser Gly Lys Leu Ile Ser
65                  70                  75                  80

Asn Thr Ala Thr Lys Ala Ala Ala Pro Leu Ser Phe Ser Asn Asn Thr
                85                  90                  95

Ile Ser Leu Asn Met Asp Thr Pro Phe Tyr Asn Asn Asn Gly Lys Leu
            100                 105                 110

Gly Met Lys Val Thr Ala Pro Leu Lys Ile Leu Asp Thr Asp Leu Leu
        115                 120                 125

Lys Thr Leu Val Val Ala Tyr Gly Gln Gly Leu Gly Thr Asn Thr Thr
    130                 135                 140

Gly Ala Leu Val Ala Gln Leu Ala Ser Pro Leu Ala Phe Asp Ser Asn
145                 150                 155                 160

Ser Lys Ile Ala Leu Asn Leu Gly Asn Gly Pro Leu Lys Val Asp Ala
                165                 170                 175

Asn Arg Leu Asn Ile Asn Cys Asn Arg Gly Leu Tyr Val Thr Thr Thr
            180                 185                 190

Lys Asp Ala Leu Glu Ala Asn Ile Ser Trp Ala Asn Ala Met Thr Phe
        195                 200                 205

Ile Gly Asn Ala Met Gly Val Asn Ile Asp Thr Gln Lys Gly Leu Gln
    210                 215                 220

Phe Gly Thr Thr Ser Thr Val Ala Asp Val Lys Asn Ala Tyr Pro Ile
225                 230                 235                 240

Gln Ile Lys Leu Gly Ala Gly Leu Thr Phe Asp Ser Thr Gly Ala Ile
                245                 250                 255

Val Ala Trp Asn Lys Asp Asp Asp Lys Leu Thr Leu Trp Thr Thr Ala
            260                 265                 270

Asp Pro Ser Pro Asn Cys His Ile Tyr Ser Glu Lys Asp Ala Lys Leu
        275                 280                 285
```

```
Thr Leu Cys Leu Thr Lys Cys Gly Ser Gln Ile Leu Gly Thr Val Ser
    290                 295                 300

Leu Ile Ala Val Asp Thr Gly Ser Leu Asn Pro Ile Thr Gly Thr Val
305                 310                 315                 320

Thr Thr Ala Leu Val Ser Leu Lys Phe Asp Ala Asn Gly Val Leu Gln
                325                 330                 335

Ser Ser Ser Thr Leu Asp Ser Asp Tyr Trp Asn Phe Arg Gln Gly Asp
            340                 345                 350

Val Thr Pro Ala Glu Ala Tyr Thr Asn Ala Ile Gly Phe Met Pro Asn
        355                 360                 365

Leu Lys Ala Tyr Pro Lys Asn Thr Ser Gly Ala Ala Lys Ser His Ile
    370                 375                 380

Val Gly Lys Val Tyr Leu His Gly Asp Thr Gly Lys Pro Leu Asp Leu
385                 390                 395                 400

Ile Ile Thr Phe Asn Glu Thr Ser Asp Glu Ser Cys Thr Tyr Cys Ile
                405                 410                 415

Asn Phe Gln Trp Gln Trp Gly Ala Asp Gln Tyr Lys Asn Glu Thr Leu
            420                 425                 430

Ala Val Ser Ser Phe Thr Phe Ser Tyr Ile Ala Lys Glu
        435                 440                 445
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<210> 5
<211> 36604
<212> DNA
<213> chimpanzee adenovirus serotype Pan6

<220>
<221> CDS
<222> (13878)..(15467)
<223> L2 Penton

<220>
<221> CDS
<222> (18284)..(21112)
<223> L3 Hexon

<220>
<221> CDS
<222> (32162)..(33493)
<223> L5 Fiber

<400> 5

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ggaaatgagg tgtttctggg cggatgcaag tgaaaacggg ccattttcgc gcgaaaactg 300

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Phe Gln Glu Gly Phe Gln Ile Leu Tyr Glu Asp Leu Glu Gly Gly Asn
        270                 275                 280

atc ccc gcg ctc ttg gat gtc gaa gcc tac gag aaa agc aag gag gat    14774
Ile Pro Ala Leu Leu Asp Val Glu Ala Tyr Glu Lys Ser Lys Glu Asp
    285                 290                 295

agc acc gcc gcg gcg acc gca gcc gtg gcc acc gcc tct acc gag gtg    14822
Ser Thr Ala Ala Ala Thr Ala Ala Val Ala Thr Ala Ser Thr Glu Val
300                 305                 310                 315

cgg ggc gat aat ttt gct agc gct gcg gca gcg gcc gag gcg gct gaa    14870
Arg Gly Asp Asn Phe Ala Ser Ala Ala Ala Ala Ala Glu Ala Ala Glu
                320                 325                 330

acc gaa agt aag ata gtc atc cag ccg gtg gag aag gac agc aag gac    14918
Thr Glu Ser Lys Ile Val Ile Gln Pro Val Glu Lys Asp Ser Lys Asp
            335                 340                 345

agg agc tac aac gtg ctc gcg gac aag aaa aac acc gcc tac cgc agc    14966
Arg Ser Tyr Asn Val Leu Ala Asp Lys Lys Asn Thr Ala Tyr Arg Ser
        350                 355                 360

tgg tac ctg gcc tac aac tac ggc gac ccc gag aag ggc gtg cgc tcc    15014
Trp Tyr Leu Ala Tyr Asn Tyr Gly Asp Pro Glu Lys Gly Val Arg Ser
    365                 370                 375

tgg acg ctg ctc acc acc tcg gac gtc acc tgc ggc gtg gag caa gtc    15062
Trp Thr Leu Leu Thr Thr Ser Asp Val Thr Cys Gly Val Glu Gln Val
380                 385                 390                 395

tac tgg tcg ctg ccc gac atg atg caa gac ccg gtc acc ttc cgc tcc    15110
Tyr Trp Ser Leu Pro Asp Met Met Gln Asp Pro Val Thr Phe Arg Ser
                400                 405                 410

acg cgt caa gtt agc aac tac ccg gtg gtg ggc gcc gag ctc ctg ccc    15158
Thr Arg Gln Val Ser Asn Tyr Pro Val Val Gly Ala Glu Leu Leu Pro
            415                 420                 425

gtc tac tcc aag agc ttc ttc aac gag cag gcc gtc tac tcg cag cag    15206
Val Tyr Ser Lys Ser Phe Phe Asn Glu Gln Ala Val Tyr Ser Gln Gln
        430                 435                 440
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ctg cgc gcc ttc acc tcg ctc acg cac gtc ttc aac cgc ttc ccc gag    15254
Leu Arg Ala Phe Thr Ser Leu Thr His Val Phe Asn Arg Phe Pro Glu
    445                 450                 455

aac cag atc ctc gtc cgc ccg ccc gcg ccc acc att acc acc gtc agt    15302
Asn Gln Ile Leu Val Arg Pro Pro Ala Pro Thr Ile Thr Thr Val Ser
460                 465                 470                 475

gaa aac gtt cct gct ctc aca gat cac ggg acc ctg ccg ctg cgc agc    15350
Glu Asn Val Pro Ala Leu Thr Asp His Gly Thr Leu Pro Leu Arg Ser
                480                 485                 490

agt atc cgg gga gtc cag cgc gtg acc gtc act gac gcc aga cgc cgc    15398
Ser Ile Arg Gly Val Gln Arg Val Thr Val Thr Asp Ala Arg Arg Arg
            495                 500                 505

acc tgc ccc tac gtc tac aag gcc ctg ggc gta gtc gcg ccg cgc gtc    15446
Thr Cys Pro Tyr Val Tyr Lys Ala Leu Gly Val Val Ala Pro Arg Val
        510                 515                 520

ctc tcg agc cgc acc ttc taa aaaatgtcca ttctcatctc gcccagtaat       15497
Leu Ser Ser Arg Thr Phe
    525
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aacaccggtt ggggcctgcg cgcgcccagc aagatgtacg gaggcgctcg ccaacgctcc  15557

acgcaacacc ccgtgcgcgt gcgcgggcac ttccgcgctc cctggggcgc cctcaagggc  15617

cgcgtgcgct cgcgcaccac cgtcgacgac gtgatcgacc aggtggtggc cgacgcgcgc  15677

aactacacgc ccgccgccgc gcccgtctcc accgtggacg ccgtcatcga cagcgtggtg  15737

gccgacgcgc gccggtacgc ccgcaccaag agccggcggc ggcgcatcgc ccggcggcac  15797

cggagcaccc ccgccatgcg cgcggcgcga gccttgctgc gcagggccag gcgcacggga  15857

cgcagggcca tgctcagggc ggccagacgc gcggcctccg gcagcagcag cgccggcagg  15917

acccgcagac gcgcggccac ggcggcggcg gcggccatcg ccagcatgtc ccgcccgcgg  15977

cgcggcaacg tgtactgggt gcgcgacgcc gccaccggtg tgcgcgtgcc cgtgcgcacc  16037

cgcccccctc gcacttgaag atgctgactt cgcgatgttg atgtgtccca gcggcgagga  16097

ggatgtccaa gcgcaaatac aaggaagaga tgctccaggt catcgcgcct gagatctacg  16157

gccccgcggc ggcggtgaag gaggaaagaa agccccgcaa actgaagcgg gtcaaaaagg  16217

acaaaaagga ggaggaagat gacggactgg tggagtttgt gcgcgagttc gccccccggc  16277

ggcgcgtgca gtggcgcggg cggaaagtga aaccggtgct gcggcccggc accacggtgg  16337

tcttcacgcc cggcgagcgt tccggctccg cctccaagcg ctcctacgac gaggtgtacg  16397

gggacgagga catcctcgag caggcggtcg agcgtctggg cgagtttgcg tacggcaagc  16457

gcagccgccc cgcgcccttg aaagaggagg cggtgtccat cccgctggac cacggcaacc  16517
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ccacgccgag cctgaagccg gtgaccctgc agcaggtgct accgagcgcg gcgccgcgcc 16577

ggggcttcaa gcgcgagggc ggcgaggatc tgtacccgac catgcagctg atggtgccca 16637

agcgccagaa gctggaggac gtgctggagc acatgaaggt ggaccccgag gtgcagcccg 16697

aggtcaaggt gcggcccatc aagcaggtgg ccccgggcct gggcgtgcag accgtggaca 16757

tcaagatccc cacggagccc atggaaacgc agaccgagcc cgtgaagccc agcaccagca 16817

ccatggaggt gcagacggat ccctggatgc cagcaccagc ttccaccagc actcgccgaa 16877

gacgcaagta cggcgcggcc agcctgctga tgcccaacta cgcgctgcat ccttccatca 16937

tccccacgcc gggctaccgc ggcacgcgct tctaccgcgg ctacaccagc agccgccgcc 16997

gcaagaccac cacccgccgc cgtcgtcgca gccgccgcag cagcaccgcg acttccgcct 17057

tggtgcggag agtgtatcgc agcgggcgcg agcctctgac cctgccgcgc gcgcgctacc 17117

acccgagcat cgccatttaa ctaccgcctc ctacttgcag atatggccct cacatgccgc 17177

ctccgcgtcc ccattacggg ctaccgagga agaaagccgc gccgtagaag gctgacgggg 17237

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ggcttcctgc ccgcgctgat ccccatcatc gccgcggcga tcggggcgat ccccggcata 17357

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aacagccgcc tggacgcggt cccgcccgcg gggtccgtgg agatgcccca ggtggaggag 17837

gagctgcctc ccctggacaa gcgcggcgac aagcgaccgc gtcccgacgc ggaggagacg 17897

ctgctgacgc acacggacga gccgcccccg tacgaggagg cggtgaaact gggcctgccc 17957

accacgcggc ccgtggcgcc tctggccacc ggagtgctga aacccagcag cagccagccc 18017

gcgaccctgg acttgcctcc gcctcgcccc tccacagtgg ctaagcccct gccgccggtg 18077

gccgtcgcgt cgcgcgcccc ccgaggccgc ccccaggcga actggcagag cactctgaac 18137

agcatcgtgg gtctgggagt gcagagtgtg aagcgccgcc gctgctatta aaagacactg 18197

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tagcgcttaa cttgcttgtc tgtgtgtata tgtatgtccg ccgaccagaa ggaggagtgt  18257

gaagaggcgc gtcgccgagt tgcaag atg gcc acc cca tcg atg ctg ccc cag   18310
                             Met Ala Thr Pro Ser Met Leu Pro Gln
                             530                 535

tgg gcg tac atg cac atc gcc gga cag gac gct tcg gag tac ctg agt    18358
Trp Ala Tyr Met His Ile Ala Gly Gln Asp Ala Ser Glu Tyr Leu Ser
    540                 545                 550

ccg ggt ctg gtg cag ttc gcc cgc gcc aca gac acc tac ttc agt ctg    18406
Pro Gly Leu Val Gln Phe Ala Arg Ala Thr Asp Thr Tyr Phe Ser Leu
555                 560                 565                 570

ggg aac aag ttt agg aac ccc acg gtg gcg ccc acg cac gat gtg acc    18454
Gly Asn Lys Phe Arg Asn Pro Thr Val Ala Pro Thr His Asp Val Thr
                575                 580                 585

acc gac cgc agc cag cgg ctg acg ctg cgc ttc gtg ccc gtg gac cgc    18502
Thr Asp Arg Ser Gln Arg Leu Thr Leu Arg Phe Val Pro Val Asp Arg
            590                 595                 600

gag gac aac acc tac tcg tac aaa gtg cgc tac acg ctg gcc gtg ggc    18550
Glu Asp Asn Thr Tyr Ser Tyr Lys Val Arg Tyr Thr Leu Ala Val Gly
        605                 610                 615

gac aac cgc gtg ctg gac atg gcc agc acc tac ttt gac atc cgc ggc    18598
Asp Asn Arg Val Leu Asp Met Ala Ser Thr Tyr Phe Asp Ile Arg Gly
    620                 625                 630

gtg ctg gac cgg ggc cct agc ttc aaa ccc tac tct ggc acc gcc tac    18646
Val Leu Asp Arg Gly Pro Ser Phe Lys Pro Tyr Ser Gly Thr Ala Tyr
635                 640                 645                 650

aac agc cta gct ccc aag gga gct ccc aat tcc agc cag tgg gag caa    18694
Asn Ser Leu Ala Pro Lys Gly Ala Pro Asn Ser Ser Gln Trp Glu Gln
                655                 660                 665

gca aaa aca ggc aat ggg gga act atg gaa aca cac aca tat ggt gtg    18742
Ala Lys Thr Gly Asn Gly Gly Thr Met Glu Thr His Thr Tyr Gly Val
            670                 675                 680

gcc cca atg ggc gga gag aat att aca aaa gat ggt ctt caa att gga    18790
Ala Pro Met Gly Gly Glu Asn Ile Thr Lys Asp Gly Leu Gln Ile Gly
        685                 690                 695

act gac gtt aca gcg aat cag aat aaa cca att tat gcc gac aaa aca    18838
Thr Asp Val Thr Ala Asn Gln Asn Lys Pro Ile Tyr Ala Asp Lys Thr
    700                 705                 710

ttt caa cca gaa ccg caa gta gga gaa gaa aat tgg caa gaa act gaa    18886
Phe Gln Pro Glu Pro Gln Val Gly Glu Glu Asn Trp Gln Glu Thr Glu
715                 720                 725                 730

aac ttt tat ggc ggt aga gct ctt aaa aaa gac aca aac atg aaa cct    18934
Asn Phe Tyr Gly Gly Arg Ala Leu Lys Lys Asp Thr Asn Met Lys Pro
                735                 740                 745
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tgc tat ggc tcc tat gct aga ccc acc aat gaa aaa gga ggt caa gct    18982
Cys Tyr Gly Ser Tyr Ala Arg Pro Thr Asn Glu Lys Gly Gly Gln Ala
            750                 755                 760

aaa ctt aaa gtt gga gat gat gga gtt cca acc aaa gaa ttc gac ata    19030
Lys Leu Lys Val Gly Asp Asp Gly Val Pro Thr Lys Glu Phe Asp Ile
        765                 770                 775

gac ctg gct ttc ttt gat act ccc ggt ggc acc gtg aac ggt caa gac    19078
Asp Leu Ala Phe Phe Asp Thr Pro Gly Gly Thr Val Asn Gly Gln Asp
    780                 785                 790

gag tat aaa gca gac att gtc atg tat acc gaa aac acg tat ttg gaa    19126
Glu Tyr Lys Ala Asp Ile Val Met Tyr Thr Glu Asn Thr Tyr Leu Glu
795                 800                 805                 810

act cca gac acg cat gtg gta tac aaa cca ggc aag gat gat gca agt    19174
Thr Pro Asp Thr His Val Val Tyr Lys Pro Gly Lys Asp Asp Ala Ser
                815                 820                 825

tct gaa att aac ctg gtt cag cag tct atg ccc aac aga ccc aac tac    19222
Ser Glu Ile Asn Leu Val Gln Gln Ser Met Pro Asn Arg Pro Asn Tyr
            830                 835                 840

att ggg ttc agg gac aac ttt atc ggt ctt atg tac tac aac agc act    19270
Ile Gly Phe Arg Asp Asn Phe Ile Gly Leu Met Tyr Tyr Asn Ser Thr
        845                 850                 855

ggc aat atg ggt gtg ctt gct ggt cag gcc tcc cag ctg aat gct gtg    19318
Gly Asn Met Gly Val Leu Ala Gly Gln Ala Ser Gln Leu Asn Ala Val
    860                 865                 870

gtt gat ttg caa gac aga aac acc gag ctg tcc tac cag ctc ttg ctt    19366
Val Asp Leu Gln Asp Arg Asn Thr Glu Leu Ser Tyr Gln Leu Leu Leu
875                 880                 885                 890

gac tct ttg ggt gac aga acc cgg tat ttc agt atg tgg aac cag gcg    19414
Asp Ser Leu Gly Asp Arg Thr Arg Tyr Phe Ser Met Trp Asn Gln Ala
                895                 900                 905

gtg gac agt tat gac ccc gat gtg cgc atc atc gaa aac cat ggt gtg    19462
Val Asp Ser Tyr Asp Pro Asp Val Arg Ile Ile Glu Asn His Gly Val
            910                 915                 920

gag gat gaa ttg cca aac tat tgc ttc ccc ttg gac ggc tct ggc act    19510
Glu Asp Glu Leu Pro Asn Tyr Cys Phe Pro Leu Asp Gly Ser Gly Thr
        925                 930                 935

aac gcc gca tac caa ggt gtg aaa gta aaa gat ggt caa gat ggt gat    19558
Asn Ala Ala Tyr Gln Gly Val Lys Val Lys Asp Gly Gln Asp Gly Asp
    940                 945                 950

gtt gag agt gaa tgg gaa aat gac gat act gtt gca gct cga aat caa    19606
Val Glu Ser Glu Trp Glu Asn Asp Asp Thr Val Ala Ala Arg Asn Gln
955                 960                 965                 970
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tta tgt aaa ggt aac att ttc gcc atg gag att aat ctc cag gct aac    19654
Leu Cys Lys Gly Asn Ile Phe Ala Met Glu Ile Asn Leu Gln Ala Asn
                975                 980                 985

ctg tgg aga agt ttc ctc tac tcg aac gtg gcc ctg tac ctg  ccc gac   19702
Leu Trp Arg Ser Phe Leu Tyr Ser Asn Val Ala Leu Tyr Leu  Pro Asp
            990                 995                1000

tcc tac aag  tac acg ccg acc aac  gtc acg ctg ccg acc  aac acc     19747
Ser Tyr Lys  Tyr Thr Pro Thr Asn  Val Thr Leu Pro Thr  Asn Thr
        1005                1010                1015

aac acc tac  gat tac atg aat ggc  aga gtg aca cct ccc  tcg ctg     19792
Asn Thr Tyr  Asp Tyr Met Asn Gly  Arg Val Thr Pro Pro  Ser Leu
        1020                1025                1030

gta gac gcc  tac ctc aac atc ggg  gcg cgc tgg tcg ctg  gac ccc     19837
Val Asp Ala  Tyr Leu Asn Ile Gly  Ala Arg Trp Ser Leu  Asp Pro
        1035                1040                1045

atg gac aac  gtc aac ccc ttc aac  cac cac cgc aac gcg  ggc ctg     19882
Met Asp Asn  Val Asn Pro Phe Asn  His His Arg Asn Ala  Gly Leu
        1050                1055                1060

cgc tac cgc  tcc atg ctc ctg ggc  aac ggg cgc tac gtg  ccc ttc     19927
Arg Tyr Arg  Ser Met Leu Leu Gly  Asn Gly Arg Tyr Val  Pro Phe
        1065                1070                1075

cac atc cag  gtg ccc caa aag ttt  ttc gcc atc aag agc  ctc ctg     19972
His Ile Gln  Val Pro Gln Lys Phe  Phe Ala Ile Lys Ser  Leu Leu
        1080                1085                1090

ctc ctg ccc  ggg tcc tac acc tac  gag tgg aac ttc cgc  aag gac     20017
Leu Leu Pro  Gly Ser Tyr Thr Tyr  Glu Trp Asn Phe Arg  Lys Asp
        1095                1100                1105

gtc aac atg  atc ctg cag agc tcc  cta ggc aac gac ctg  cgc acg     20062
Val Asn Met  Ile Leu Gln Ser Ser  Leu Gly Asn Asp Leu  Arg Thr
        1110                1115                1120

gac ggg gcc  tcc atc gcc ttc acc  agc atc aac ctc tac  gcc acc     20107
Asp Gly Ala  Ser Ile Ala Phe Thr  Ser Ile Asn Leu Tyr  Ala Thr
        1125                1130                1135

ttc ttc ccc  atg gcg cac aac acc  gcc tcc acg ctc gag  gcc atg     20152
Phe Phe Pro  Met Ala His Asn Thr  Ala Ser Thr Leu Glu  Ala Met
        1140                1145                1150

ctg cgc aac  gac acc aac gac cag  tcc ttc aac gac tac  ctc tcg     20197
Leu Arg Asn  Asp Thr Asn Asp Gln  Ser Phe Asn Asp Tyr  Leu Ser
        1155                1160                1165

gcg gcc aac  atg ctc tac ccc atc  ccg gcc aac gcc acc  aac gtg     20242
Ala Ala Asn  Met Leu Tyr Pro Ile  Pro Ala Asn Ala Thr  Asn Val
        1170                1175                1180
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ccc atc tcc  atc ccc tcg cgc aac  tgg gcc gcc ttc cgc  gga tgg     20287
Pro Ile Ser  Ile Pro Ser Arg Asn  Trp Ala Ala Phe Arg  Gly Trp
        1185                 1190                 1195

tcc ttc acg  cgc ctg aag acc cgc  gag acg ccc tcg ctc  ggc tcc     20332
Ser Phe Thr  Arg Leu Lys Thr Arg  Glu Thr Pro Ser Leu  Gly Ser
        1200                 1205                 1210

ggg ttc gac  ccc tac ttc gtc tac  tcg ggc tcc atc ccc  tac cta     20377
Gly Phe Asp  Pro Tyr Phe Val Tyr  Ser Gly Ser Ile Pro  Tyr Leu
        1215                 1220                 1225

gac ggc acc  ttc tac ctc aac cac  acc ttc aag aag gtc  tcc atc     20422
Asp Gly Thr  Phe Tyr Leu Asn His  Thr Phe Lys Lys Val  Ser Ile
        1230                 1235                 1240

acc ttc gac  tcc tcc gtc agc tgg  ccc ggc aac gac cgc  ctc ctg     20467
Thr Phe Asp  Ser Ser Val Ser Trp  Pro Gly Asn Asp Arg  Leu Leu
        1245                 1250                 1255

acg ccc aac  gag ttc gaa atc aag  cgc acc gtc gac gga  gag gga     20512
Thr Pro Asn  Glu Phe Glu Ile Lys  Arg Thr Val Asp Gly  Glu Gly
        1260                 1265                 1270

tac aac gtg  gcc cag tgc aac atg  acc aag gac tgg ttc  ctg gtc     20557
Tyr Asn Val  Ala Gln Cys Asn Met  Thr Lys Asp Trp Phe  Leu Val
        1275                 1280                 1285

cag atg ctg  gcc cac tac aac atc  ggc tac cag ggc ttc  tac gtg     20602
Gln Met Leu  Ala His Tyr Asn Ile  Gly Tyr Gln Gly Phe  Tyr Val
        1290                 1295                 1300

ccc gag ggc  tac aag gac cgc atg  tac tcc ttc ttc cgc  aac ttc     20647
Pro Glu Gly  Tyr Lys Asp Arg Met  Tyr Ser Phe Phe Arg  Asn Phe
        1305                 1310                 1315

cag ccc atg  agc cgc cag gtc gtg  gac gag gtc aac tac  aag gac     20692
Gln Pro Met  Ser Arg Gln Val Val  Asp Glu Val Asn Tyr  Lys Asp
        1320                 1325                 1330

tac cag gcc  gtc acc ctg gcc tac  cag cac aac aac tcg  ggc ttc     20737
Tyr Gln Ala  Val Thr Leu Ala Tyr  Gln His Asn Asn Ser  Gly Phe
        1335                 1340                 1345

gtc ggc tac  ctc gcg ccc acc atg  cgc cag ggc cag ccc  tac ccc     20782
Val Gly Tyr  Leu Ala Pro Thr Met  Arg Gln Gly Gln Pro  Tyr Pro
        1350                 1355                 1360

gcc aac tac  ccc tac ccg ctc atc  ggc aag agc gcc gtc  gcc agc     20827
Ala Asn Tyr  Pro Tyr Pro Leu Ile  Gly Lys Ser Ala Val  Ala Ser
        1365                 1370                 1375

gtc acc cag  aaa aag ttc ctc tgc  gac cgg gtc atg tgg  cgc atc     20872
Val Thr Gln  Lys Lys Phe Leu Cys  Asp Arg Val Met Trp  Arg Ile
        1380                 1385                 1390
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ccc ttc tcc  agc aac ttc atg tcc  atg ggc gcg ctc acc  gac ctc     20917
Pro Phe Ser  Ser Asn Phe Met Ser  Met Gly Ala Leu Thr  Asp Leu
        1395                 1400                 1405

ggc cag aac  atg ctc tac gcc aac  tcc gcc cac gcg cta  gac atg     20962
Gly Gln Asn  Met Leu Tyr Ala Asn  Ser Ala His Ala Leu  Asp Met
        1410                 1415                 1420

aat ttc gaa  gtc gac ccc atg gat  gag tcc acc ctt ctc  tat gtt     21007
Asn Phe Glu  Val Asp Pro Met Asp  Glu Ser Thr Leu Leu  Tyr Val
        1425                 1430                 1435

gtc ttc gaa  gtc ttc gac gtc gtc  cga gtg cac cag ccc  cac cgc     21052
Val Phe Glu  Val Phe Asp Val Val  Arg Val His Gln Pro  His Arg
        1440                 1445                 1450

ggc gtc atc  gaa gcc gtc tac ctg  cgc acg ccc ttc tcg  gcc ggc     21097
Gly Val Ile  Glu Ala Val Tyr Leu  Arg Thr Pro Phe Ser  Ala Gly
        1455                 1460                 1465

aac gcc acc  acc taa gccgctcttg cttcttgcaa gatgacggcg ggctccggcg   21152
Asn Ala Thr  Thr
        1470
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agcaggagct cagggccatc ctccgcgacc tgggctgcgg gccctgcttc ctgggcacct  21212

tcgacaagcg cttccctgga ttcatggccc cgcacaagct ggcctgcgcc atcgtgaaca  21272

cggccggccg cgagaccggg ggcgagcact ggctggcctt cgcctggaac ccgcgctccc  21332

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ccctggaaaa gtccacccag accgtgcagg gtccgcgctc ggccgcctgc gggctcttct  21512

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ccatgaactt actgacgggg gtgcccaacg gcatgctcca gtcgccccag gtggaaccca  21632

ccctgcgccg caaccaggaa gcgctctacc gcttcctcaa tgcccactcc gcctactttc  21692

gctcccaccg cgcgcgcatc gagaaggcca ccgccttcga ccgcatgaat caagacatgt  21752

aaaaaaccgg tgtgtgtatg tgaatgcttt attcataata aacagcacat gtttatgcca  21812

ccttctctga ggctctgact ttatttagaa atcgaagggg ttctgccggc tctcggcatg  21872

gcccgcgggc agggatacgt tgcggaactg gtacttgggc agccacttga actcggggat  21932

cagcagcttg ggcacgggga ggtcggggaa cgagtcgctc cacagcttgc gcgtgagttg  21992

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cgcgcgagag ttgcggtaca cggggttgca gcactggaac accatcaggg ccgggtgctt  22112

cacgcttgcc agcaccgtcg cgtcggtgat gccctccacg tccagatcct cggcgttggc  22172
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catcccgaag ggggtcatct tgcaggtctg ccgccccatg ctgggcacgc agccgggctt 22232

gtggttgcaa tcgcagtgca gggggatcag catcatctgg gcctgctcgg agctcatgcc 22292

cgggtacatg gccttcatga aagcctccag ctggcggaag gcctgctgcg ccttgccgcc 22352

ctcggtgaag aagaccccgc aggacttgct agagaactgg ttggtggcgc agccggcgtc 22412

gtgcacgcag cagcgcgcgt cgttgttggc cagctgcacc acgctgcgcc cccagcggtt 22472

ctgggtgatc ttggcccggt tggggttctc cttcagcgcg cgctgcccgt tctcgctcgc 22532

cacatccatc tcgatagtgt gctccttctg gatcatcacg gtcccgtgca ggcaccgcag 22592

cttgccctcg gcttcggtgc agccgtgcag ccacagcgcg cagccggtgc actcccagtt 22652

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Phe  Gln Glu Lys Pro Leu  Gly Val Leu Ser Leu  Arg Leu Ala Asp
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Pro  Val Thr Thr Lys Asn  Gly Glu Ile Thr Leu  Lys Leu Gly Glu
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<210> 6
<211> 529
<212> PRT
<213> chimpanzee adenovirus serotype Pan6

<400> 6

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Pro Tyr Val Pro Pro Arg Tyr Leu Ala Pro Thr Glu Gly Arg Asn Ser
        35                  40                  45

Ile Arg Tyr Ser Glu Leu Ala Pro Leu Tyr Asp Thr Thr Arg Leu Tyr
    50                  55                  60

Leu Val Asp Asn Lys Ser Ala Asp Ile Ala Ser Leu Asn Tyr Gln Asn
65                  70                  75                  80

Asp His Ser Asn Phe Leu Thr Thr Val Val Gln Asn Asn Asp Phe Thr
                85                  90                  95

Pro Thr Glu Ala Ser Thr Gln Thr Ile Asn Phe Asp Glu Arg Ser Arg
            100                 105                 110

Trp Gly Gly Gln Leu Lys Thr Ile Met His Thr Asn Met Pro Asn Val
        115                 120                 125

Asn Glu Phe Met Tyr Ser Asn Lys Phe Lys Ala Arg Val Met Val Ser
    130                 135                 140

Arg Lys Thr Pro Asn Gly Val Asp Asp Asp Tyr Asp Gly Ser Gln Asp
145                 150                 155                 160

Glu Leu Thr Tyr Glu Trp Val Glu Phe Glu Leu Pro Glu Gly Asn Phe
                165                 170                 175

Ser Val Thr Met Thr Ile Asp Leu Met Asn Asn Ala Ile Ile Asp Asn
            180                 185                 190

Tyr Leu Ala Val Gly Arg Gln Asn Gly Val Leu Glu Ser Asp Ile Gly
        195                 200                 205

Val Lys Phe Asp Thr Arg Asn Phe Arg Leu Gly Trp Asp Pro Val Thr
    210                 215                 220

Glu Leu Val Met Pro Gly Val Tyr Thr Asn Glu Ala Phe His Pro Asp
225                 230                 235                 240

Ile Val Leu Leu Pro Gly Cys Gly Val Asp Phe Thr Glu Ser Arg Leu
                245                 250                 255

Ser Asn Leu Leu Gly Ile Arg Lys Arg Gln Pro Phe Gln Glu Gly Phe
            260                 265                 270

Gln Ile Leu Tyr Glu Asp Leu Glu Gly Gly Asn Ile Pro Ala Leu Leu
        275                 280                 285
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Asp Val Glu Ala Tyr Glu Lys Ser Lys Glu Asp Ser Thr Ala Ala Ala
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Thr Ala Ala Val Ala Thr Ala Ser Thr Glu Val Arg Gly Asp Asn Phe
305                 310                 315                 320

Ala Ser Ala Ala Ala Ala Ala Glu Ala Ala Glu Thr Glu Ser Lys Ile
                325                 330                 335

Val Ile Gln Pro Val Glu Lys Asp Ser Lys Asp Arg Ser Tyr Asn Val
            340                 345                 350

Leu Ala Asp Lys Lys Asn Thr Ala Tyr Arg Ser Trp Tyr Leu Ala Tyr
        355                 360                 365

Asn Tyr Gly Asp Pro Glu Lys Gly Val Arg Ser Trp Thr Leu Leu Thr
    370                 375                 380

Thr Ser Asp Val Thr Cys Gly Val Glu Gln Val Tyr Trp Ser Leu Pro
385                 390                 395                 400

Asp Met Met Gln Asp Pro Val Thr Phe Arg Ser Thr Arg Gln Val Ser
                405                 410                 415

Asn Tyr Pro Val Val Gly Ala Glu Leu Leu Pro Val Tyr Ser Lys Ser
            420                 425                 430

Phe Phe Asn Glu Gln Ala Val Tyr Ser Gln Gln Leu Arg Ala Phe Thr
        435                 440                 445

Ser Leu Thr His Val Phe Asn Arg Phe Pro Glu Asn Gln Ile Leu Val
    450                 455                 460

Arg Pro Pro Ala Pro Thr Ile Thr Thr Val Ser Glu Asn Val Pro Ala
465                 470                 475                 480

Leu Thr Asp His Gly Thr Leu Pro Leu Arg Ser Ser Ile Arg Gly Val
                485                 490                 495

Gln Arg Val Thr Val Thr Asp Ala Arg Arg Arg Thr Cys Pro Tyr Val
            500                 505                 510

Tyr Lys Ala Leu Gly Val Val Ala Pro Arg Val Leu Ser Ser Arg Thr
        515                 520                 525

Phe
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<210> 7
<211> 942
<212> PRT
<213> chimpanzee adenovirus serotype Pan6

<400> 7

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Gly Gln Asp Ala Ser Glu Tyr Leu Ser Pro Gly Leu Val Gln Phe Ala
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Arg Ala Thr Asp Thr Tyr Phe Ser Leu Gly Asn Lys Phe Arg Asn Pro
        35                  40                  45

Thr Val Ala Pro Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg Leu
    50                  55                  60

Thr Leu Arg Phe Val Pro Val Asp Arg Glu Asp Asn Thr Tyr Ser Tyr
65                  70                  75                  80

Lys Val Arg Tyr Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met
                85                  90                  95

Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro Ser
            100                 105                 110

Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ser Leu Ala Pro Lys Gly
        115                 120                 125

Ala Pro Asn Ser Ser Gln Trp Glu Gln Ala Lys Thr Gly Asn Gly Gly
    130                 135                 140

Thr Met Glu Thr His Thr Tyr Gly Val Ala Pro Met Gly Gly Glu Asn
145                 150                 155                 160

Ile Thr Lys Asp Gly Leu Gln Ile Gly Thr Asp Val Thr Ala Asn Gln
                165                 170                 175

Asn Lys Pro Ile Tyr Ala Asp Lys Thr Phe Gln Pro Glu Pro Gln Val
            180                 185                 190

Gly Glu Glu Asn Trp Gln Glu Thr Glu Asn Phe Tyr Gly Gly Arg Ala
        195                 200                 205

Leu Lys Lys Asp Thr Asn Met Lys Pro Cys Tyr Gly Ser Tyr Ala Arg
    210                 215                 220

Pro Thr Asn Glu Lys Gly Gly Gln Ala Lys Leu Lys Val Gly Asp Asp
225                 230                 235                 240

Gly Val Pro Thr Lys Glu Phe Asp Ile Asp Leu Ala Phe Phe Asp Thr
                245                 250                 255

Pro Gly Gly Thr Val Asn Gly Gln Asp Glu Tyr Lys Ala Asp Ile Val
            260                 265                 270

Met Tyr Thr Glu Asn Thr Tyr Leu Glu Thr Pro Asp Thr His Val Val
        275                 280                 285

Tyr Lys Pro Gly Lys Asp Asp Ala Ser Ser Glu Ile Asn Leu Val Gln
    290                 295                 300

Gln Ser Met Pro Asn Arg Pro Asn Tyr Ile Gly Phe Arg Asp Asn Phe
305                 310                 315                 320
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Ile Gly Leu Met Tyr Tyr Asn Ser Thr Gly Asn Met Gly Val Leu Ala
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Gly Gln Ala Ser Gln Leu Asn Ala Val Val Asp Leu Gln Asp Arg Asn
            340                 345                 350

Thr Glu Leu Ser Tyr Gln Leu Leu Leu Asp Ser Leu Gly Asp Arg Thr
        355                 360                 365

Arg Tyr Phe Ser Met Trp Asn Gln Ala Val Asp Ser Tyr Asp Pro Asp
    370                 375                 380

Val Arg Ile Ile Glu Asn His Gly Val Glu Asp Glu Leu Pro Asn Tyr
385                 390                 395                 400

Cys Phe Pro Leu Asp Gly Ser Gly Thr Asn Ala Ala Tyr Gln Gly Val
                405                 410                 415

Lys Val Lys Asp Gly Gln Asp Gly Asp Val Glu Ser Glu Trp Glu Asn
            420                 425                 430

Asp Asp Thr Val Ala Ala Arg Asn Gln Leu Cys Lys Gly Asn Ile Phe
        435                 440                 445

Ala Met Glu Ile Asn Leu Gln Ala Asn Leu Trp Arg Ser Phe Leu Tyr
    450                 455                 460

Ser Asn Val Ala Leu Tyr Leu Pro Asp Ser Tyr Lys Tyr Thr Pro Thr
465                 470                 475                 480

Asn Val Thr Leu Pro Thr Asn Thr Asn Thr Tyr Asp Tyr Met Asn Gly
                485                 490                 495

Arg Val Thr Pro Pro Ser Leu Val Asp Ala Tyr Leu Asn Ile Gly Ala
            500                 505                 510

Arg Trp Ser Leu Asp Pro Met Asp Asn Val Asn Pro Phe Asn His His
        515                 520                 525

Arg Asn Ala Gly Leu Arg Tyr Arg Ser Met Leu Leu Gly Asn Gly Arg
    530                 535                 540

Tyr Val Pro Phe His Ile Gln Val Pro Gln Lys Phe Phe Ala Ile Lys
545                 550                 555                 560

Ser Leu Leu Leu Leu Pro Gly Ser Tyr Thr Tyr Glu Trp Asn Phe Arg
                565                 570                 575

Lys Asp Val Asn Met Ile Leu Gln Ser Ser Leu Gly Asn Asp Leu Arg
            580                 585                 590

Thr Asp Gly Ala Ser Ile Ala Phe Thr Ser Ile Asn Leu Tyr Ala Thr
        595                 600                 605

Phe Phe Pro Met Ala His Asn Thr Ala Ser Thr Leu Glu Ala Met Leu
    610                 615                 620
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```
Arg Asn Asp Thr Asn Asp Gln Ser Phe Asn Asp Tyr Leu Ser Ala Ala
625                 630                 635                 640

Asn Met Leu Tyr Pro Ile Pro Ala Asn Ala Thr Asn Val Pro Ile Ser
                645                 650                 655

Ile Pro Ser Arg Asn Trp Ala Ala Phe Arg Gly Trp Ser Phe Thr Arg
            660                 665                 670

Leu Lys Thr Arg Glu Thr Pro Ser Leu Gly Ser Gly Phe Asp Pro Tyr
        675                 680                 685

Phe Val Tyr Ser Gly Ser Ile Pro Tyr Leu Asp Gly Thr Phe Tyr Leu
    690                 695                 700

Asn His Thr Phe Lys Lys Val Ser Ile Thr Phe Asp Ser Ser Val Ser
705                 710                 715                 720

Trp Pro Gly Asn Asp Arg Leu Leu Thr Pro Asn Glu Phe Glu Ile Lys
                725                 730                 735

Arg Thr Val Asp Gly Glu Gly Tyr Asn Val Ala Gln Cys Asn Met Thr
            740                 745                 750

Lys Asp Trp Phe Leu Val Gln Met Leu Ala His Tyr Asn Ile Gly Tyr
        755                 760                 765

Gln Gly Phe Tyr Val Pro Glu Gly Tyr Lys Asp Arg Met Tyr Ser Phe
    770                 775                 780

Phe Arg Asn Phe Gln Pro Met Ser Arg Gln Val Val Asp Glu Val Asn
785                 790                 795                 800

Tyr Lys Asp Tyr Gln Ala Val Thr Leu Ala Tyr Gln His Asn Asn Ser
                805                 810                 815

Gly Phe Val Gly Tyr Leu Ala Pro Thr Met Arg Gln Gly Gln Pro Tyr
            820                 825                 830

Pro Ala Asn Tyr Pro Tyr Pro Leu Ile Gly Lys Ser Ala Val Ala Ser
        835                 840                 845

Val Thr Gln Lys Lys Phe Leu Cys Asp Arg Val Met Trp Arg Ile Pro
    850                 855                 860

Phe Ser Ser Asn Phe Met Ser Met Gly Ala Leu Thr Asp Leu Gly Gln
865                 870                 875                 880

Asn Met Leu Tyr Ala Asn Ser Ala His Ala Leu Asp Met Asn Phe Glu
                885                 890                 895

Val Asp Pro Met Asp Glu Ser Thr Leu Leu Tyr Val Val Phe Glu Val
            900                 905                 910

Phe Asp Val Val Arg Val His Gln Pro His Arg Gly Val Ile Glu Ala
        915                 920                 925
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Val Tyr Leu Arg Thr Pro Phe Ser Ala Gly Asn Ala Thr Thr
930 935 940

<210> 8
<211> 443
<212> PRT
<213> chimpanzee adenovirus serotype Pan6

<400> 8

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Pro Tyr Asp Ala Asp Asn Ala Pro Thr Val Pro Phe Ile Asn Pro Pro
20 25 30

Phe Val Ser Ser Asp Gly Phe Gln Glu Lys Pro Leu Gly Val Leu Ser
35 40 45

Leu Arg Leu Ala Asp Pro Val Thr Thr Lys Asn Gly Glu Ile Thr Leu
50 55 60

Lys Leu Gly Glu Gly Val Asp Leu Asp Ser Ser Gly Lys Leu Ile Ser
65 70 75 80

Asn Thr Ala Thr Lys Ala Ala Ala Pro Leu Ser Ile Ser Asn Asn Thr
85 90 95

Ile Ser Leu Lys Thr Ala Ala Pro Phe Tyr Asn Asn Asn Gly Thr Leu
100 105 110

Ser Leu Asn Val Ser Thr Pro Leu Ala Val Phe Pro Thr Phe Asn Thr
115 120 125

Leu Gly Ile Ser Leu Gly Asn Gly Leu Gln Thr Ser Asn Lys Leu Leu
130 135 140

Thr Val Gln Leu Thr His Pro Leu Thr Phe Ser Ser Asn Ser Ile Thr
145 150 155 160

Val Lys Thr Asp Lys Gly Leu Tyr Ile Asn Ser Ser Gly Asn Arg Gly
165 170 175

Leu Glu Ala Asn Ile Ser Leu Lys Arg Gly Leu Val Phe Asp Gly Asn
180 185 190

Ala Ile Ala Thr Tyr Ile Gly Asn Gly Leu Asp Tyr Gly Ser Tyr Asp
195 200 205

Ser Asp Gly Lys Thr Arg Pro Val Ile Thr Lys Ile Gly Ala Gly Leu
210 215 220

Asn Phe Asp Ala Asn Lys Ala Ile Ala Val Lys Leu Gly Thr Gly Leu
225 230 235 240

```
Ser Phe Asp Ser Ala Gly Ala Leu Thr Ala Gly Asn Lys Gln Asp Asp
                245                 250                 255

Lys Leu Thr Leu Trp Thr Thr Pro Asp Pro Ser Pro Asn Cys Gln Leu
            260                 265                 270

Leu Ser Asp Arg Asp Ala Lys Phe Thr Leu Cys Leu Thr Lys Cys Gly
        275                 280                 285

Ser Gln Ile Leu Gly Thr Val Ala Val Ala Ala Val Thr Val Gly Ser
    290                 295                 300

Ala Leu Asn Pro Ile Asn Asp Thr Val Lys Ser Ala Ile Val Phe Leu
305                 310                 315                 320

Arg Phe Asp Ser Asp Gly Val Leu Met Ser Asn Ser Ser Met Val Gly
                325                 330                 335

Asp Tyr Trp Asn Phe Arg Glu Gly Gln Thr Thr Gln Ser Val Ala Tyr
            340                 345                 350

Thr Asn Ala Val Gly Phe Met Pro Asn Ile Gly Ala Tyr Pro Lys Thr
        355                 360                 365

Gln Ser Lys Thr Pro Lys Asn Ser Ile Val Ser Gln Val Tyr Leu Thr
    370                 375                 380

Gly Glu Thr Thr Met Pro Met Thr Leu Thr Ile Thr Phe Asn Gly Thr
385                 390                 395                 400

Asp Glu Lys Asp Thr Thr Pro Val Ser Thr Tyr Ser Met Thr Phe Thr
                405                 410                 415

Trp Gln Trp Thr Gly Asp Tyr Lys Asp Lys Asn Ile Thr Phe Ala Thr
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Asn Ser Phe Ser Phe Ser Tyr Ile Ala Gln Glu
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<210> 9
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<223> L5 Fiber

<400> 9

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Ser Tyr Glu Ser Val Met Gln Gln Ala Val Ala Ala Ala Met Gln Pro
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Pro Leu Glu Ala Pro Tyr Val Pro Pro Arg Tyr Leu Ala Pro Thr Glu
    30                  35                  40

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Gly Arg Asn Ser Ile Arg Tyr Ser Glu Leu Ala Pro Leu Tyr Asp Thr
45                  50                  55                  60

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Thr Arg Leu Tyr Leu Val Asp Asn Lys Ser Ala Asp Ile Ala Ser Leu
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Asn Tyr Gln Asn Asp His Ser Asn Phe Leu Thr Thr Val Val Gln Asn
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Asn Asp Phe Thr Pro Thr Glu Ala Ser Thr Gln Thr Ile Asn Phe Asp
        95                  100                 105

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Glu Arg Ser Arg Trp Gly Gly Gln Leu Lys Thr Ile Met His Thr Asn
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atg ccc aac gtg aac gag ttc atg tac agc aac aag ttc aag gcg cgg    14293
Met Pro Asn Val Asn Glu Phe Met Tyr Ser Asn Lys Phe Lys Ala Arg
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Val Met Val Ser Arg Lys Thr Pro Asn Gly Val Ala Val Asp Glu Asn
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Tyr Asp Gly Ser Gln Asp Glu Leu Thr Tyr Glu Trp Val Glu Phe Glu
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Asn Ala Ile Ile Asp Asn Tyr Leu Ala Val Gly Arg Gln Asn Gly Val
    190                 195                 200

ctg gag agc gac atc ggc gtg aag ttc gac acg cgc aac ttc cgg ctg    14533
Leu Glu Ser Asp Ile Gly Val Lys Phe Asp Thr Arg Asn Phe Arg Leu
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ggc tgg gac ccc gtg acc gag ctg gtg atg ccg ggc gtg tac acc aac    14581
Gly Trp Asp Pro Val Thr Glu Leu Val Met Pro Gly Val Tyr Thr Asn
                225                 230                 235

gag gcc ttc cac ccc gac atc gtc ctg ctg ccc ggc tgc ggc gtg gac    14629
Glu Ala Phe His Pro Asp Ile Val Leu Leu Pro Gly Cys Gly Val Asp
            240                 245                 250

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Phe Thr Glu Ser Arg Leu Ser Asn Leu Leu Gly Ile Arg Lys Arg Gln
        255                 260                 265

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Pro Phe Gln Glu Gly Phe Gln Ile Leu Tyr Glu Asp Leu Glu Gly Gly
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Asn Ile Pro Ala Leu Leu Asp Val Glu Ala Tyr Glu Lys Ser Lys Glu
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Glu Ala Ala Ala Ala Ala Thr Ala Ala Val Ala Thr Ala Ser Thr Glu
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Val Arg Gly Asp Asn Phe Ala Ser Ala Ala Ala Val Ala Glu Ala Ala
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Glu Thr Glu Ser Lys Ile Val Ile Gln Pro Val Glu Lys Asp Ser Lys
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Asp Arg Ser Tyr Asn Val Leu Ala Asp Lys Lys Asn Thr Ala Tyr Arg
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Ser Thr Arg Gln Val Ser Asn Tyr Pro Val Val Gly Ala Glu Leu Leu
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Pro Val Tyr Ser Lys Ser Phe Phe Asn Glu Gln Ala Val Tyr Ser Gln
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Gln Leu Arg Ala Phe Thr Ser Leu Thr His Val Phe Asn Arg Phe Pro
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Ser Glu Asn Val Pro Ala Leu Thr Asp His Gly Thr Leu Pro Leu Arg
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Arg Thr Cys Pro Tyr Val Tyr Lys Ala Leu Gly Val Val Ala Pro Arg
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                              Met Ala Thr Pro Ser Met Leu Pro
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cag tgg gcg tac atg cac atc gcc gga cag gac gct tcg gag tac ctg    18359
Gln Trp Ala Tyr Met His Ile Ala Gly Gln Asp Ala Ser Glu Tyr Leu
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agt ccg ggt ctg gtg cag ttc gcc cgc gcc aca gac acc tac ttc agt    18407
Ser Pro Gly Leu Val Gln Phe Ala Arg Ala Thr Asp Thr Tyr Phe Ser
                560                 565                 570

ctg ggg aac aag ttt agg aac ccc acg gtg gcg ccc acg cac gat gtg    18455
Leu Gly Asn Lys Phe Arg Asn Pro Thr Val Ala Pro Thr His Asp Val
            575                 580                 585

acc acc gac cgc agc cag cgg ctg acg ctg cgc ttc gtg ccc gtg gac    18503
Thr Thr Asp Arg Ser Gln Arg Leu Thr Leu Arg Phe Val Pro Val Asp
        590                 595                 600

cgc gag gac aac acc tac tcg tac aaa gtg cgc tac acg ctg gcc gtg    18551
Arg Glu Asp Asn Thr Tyr Ser Tyr Lys Val Arg Tyr Thr Leu Ala Val
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ggc gac aac cgc gtg ctg gac atg gcc agc acc tac ttt gac atc cgc    18599
Gly Asp Asn Arg Val Leu Asp Met Ala Ser Thr Tyr Phe Asp Ile Arg
620                 625                 630                 635

ggc gtg ctg gat cgg ggg ccc agc ttc aaa ccc tac tcc ggc acc gcc    18647
Gly Val Leu Asp Arg Gly Pro Ser Phe Lys Pro Tyr Ser Gly Thr Ala
                640                 645                 650

tac aac agc ctg gct ccc aag gga gcg ccc aac act tgc cag tgg aca    18695
Tyr Asn Ser Leu Ala Pro Lys Gly Ala Pro Asn Thr Cys Gln Trp Thr
            655                 660                 665

tat aaa gct ggt gat act gat aca gaa aaa acc tat aca tat gga aat    18743
Tyr Lys Ala Gly Asp Thr Asp Thr Glu Lys Thr Tyr Thr Tyr Gly Asn
        670                 675                 680

gca cct gtg caa ggc att agc att aca aag gat ggt att caa ctt gga    18791
Ala Pro Val Gln Gly Ile Ser Ile Thr Lys Asp Gly Ile Gln Leu Gly
    685                 690                 695
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act gac agc gat ggt cag gca atc tat gca gac gaa act tat caa cca    18839
Thr Asp Ser Asp Gly Gln Ala Ile Tyr Ala Asp Glu Thr Tyr Gln Pro
700                 705                 710                 715

gag cct caa gtg ggt gat gct gaa tgg cat gac atc act ggt act gat    18887
Glu Pro Gln Val Gly Asp Ala Glu Trp His Asp Ile Thr Gly Thr Asp
                720                 725                 730

gaa aaa tat gga ggc aga gct ctt aag cct gac acc aaa atg aag cct    18935
Glu Lys Tyr Gly Gly Arg Ala Leu Lys Pro Asp Thr Lys Met Lys Pro
            735                 740                 745

tgc tat ggt tct ttt gcc aag cct acc aat aaa gaa gga ggc cag gca    18983
Cys Tyr Gly Ser Phe Ala Lys Pro Thr Asn Lys Glu Gly Gly Gln Ala
        750                 755                 760

aat gtg aaa acc gaa aca ggc ggt acc aaa gaa tat gac att gac atg    19031
Asn Val Lys Thr Glu Thr Gly Gly Thr Lys Glu Tyr Asp Ile Asp Met
    765                 770                 775

gca ttc ttc gat aat cga agt gca gct gcc gcc ggc cta gcc cca gaa    19079
Ala Phe Phe Asp Asn Arg Ser Ala Ala Ala Ala Gly Leu Ala Pro Glu
780                 785                 790                 795

att gtt ttg tat act gag aat gtg gat ctg gaa act cca gat acc cat    19127
Ile Val Leu Tyr Thr Glu Asn Val Asp Leu Glu Thr Pro Asp Thr His
                800                 805                 810

att gta tac aag gca ggt aca gat gac agt agc tct tct atc aat ttg    19175
Ile Val Tyr Lys Ala Gly Thr Asp Asp Ser Ser Ser Ser Ile Asn Leu
            815                 820                 825

ggt cag cag tcc atg ccc aac aga ccc aac tac att ggc ttc aga gac    19223
Gly Gln Gln Ser Met Pro Asn Arg Pro Asn Tyr Ile Gly Phe Arg Asp
        830                 835                 840

aac ttt atc ggt ctg atg tac tac aac agc act ggc aat atg ggt gta    19271
Asn Phe Ile Gly Leu Met Tyr Tyr Asn Ser Thr Gly Asn Met Gly Val
    845                 850                 855

ctg gct gga cag gcc tcc cag ctg aat gct gtg gtg gac ttg cag gac    19319
Leu Ala Gly Gln Ala Ser Gln Leu Asn Ala Val Val Asp Leu Gln Asp
860                 865                 870                 875

aga aac acc gaa ctg tcc tac cag ctc ttg ctt gac tct ctg ggt gac    19367
Arg Asn Thr Glu Leu Ser Tyr Gln Leu Leu Leu Asp Ser Leu Gly Asp
                880                 885                 890

aga acc agg tat ttc agt atg tgg aat cag gcg gtg gac agt tat gac    19415
Arg Thr Arg Tyr Phe Ser Met Trp Asn Gln Ala Val Asp Ser Tyr Asp
            895                 900                 905

ccc gat gtg cgc att att gaa aat cac ggt gtg gag gat gaa ctt cct    19463
Pro Asp Val Arg Ile Ile Glu Asn His Gly Val Glu Asp Glu Leu Pro
        910                 915                 920
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aac tat tgc ttc ccc ctg gat gct gtg ggt aga act gat act tac cag    19511
Asn Tyr Cys Phe Pro Leu Asp Ala Val Gly Arg Thr Asp Thr Tyr Gln
    925                 930                 935

gga att aag gcc aat ggt gat aat caa acc acc tgg acc aaa gat gat    19559
Gly Ile Lys Ala Asn Gly Asp Asn Gln Thr Thr Trp Thr Lys Asp Asp
940                 945                 950                 955

act gtt aat gat gct aat gaa ttg ggc aag ggc aat cct ttc gcc atg    19607
Thr Val Asn Asp Ala Asn Glu Leu Gly Lys Gly Asn Pro Phe Ala Met
                960                 965                 970

gag atc aac atc cag gcc aac ctg tgg cgg aac ttc ctc tac gcg aac    19655
Glu Ile Asn Ile Gln Ala Asn Leu Trp Arg Asn Phe Leu Tyr Ala Asn
            975                 980                 985

gtg gcg ctg tac ctg ccc gac tcc tac aag tac acg ccg  gcc aac atc   19703
Val Ala Leu Tyr Leu Pro Asp Ser Tyr Lys Tyr Thr Pro  Ala Asn Ile
        990                 995                 1000

acg ctg  ccc acc aac acc aac  acc tac gat tac atg  aac ggc cgc     19748
Thr Leu  Pro Thr Asn Thr Asn  Thr Tyr Asp Tyr Met  Asn Gly Arg
    1005                1010                1015

gtg gtg  gcg ccc tcg ctg gtg  gac gcc tac atc aac  atc ggg gcg     19793
Val Val  Ala Pro Ser Leu Val  Asp Ala Tyr Ile Asn  Ile Gly Ala
    1020                1025                1030

cgc tgg  tcg ctg gac ccc atg  gac aac gtc aac ccc  ttc aac cac     19838
Arg Trp  Ser Leu Asp Pro Met  Asp Asn Val Asn Pro  Phe Asn His
    1035                1040                1045

cac cgc  aac gcg ggc ctg cga  tac cgc tcc atg ctc  ctg ggc aac     19883
His Arg  Asn Ala Gly Leu Arg  Tyr Arg Ser Met Leu  Leu Gly Asn
    1050                1055                1060

ggg cgc  tac gtg ccc ttc cac  atc cag gtg ccc caa  aag ttt ttc     19928
Gly Arg  Tyr Val Pro Phe His  Ile Gln Val Pro Gln  Lys Phe Phe
    1065                1070                1075

gcc atc  aag agc ctc ctg ctc  ctg ccc ggg tcc tac  acc tac gag     19973
Ala Ile  Lys Ser Leu Leu Leu  Leu Pro Gly Ser Tyr  Thr Tyr Glu
    1080                1085                1090

tgg aac  ttc cgc aag gac gtc  aac atg atc ctg cag  agc tcc ctc     20018
Trp Asn  Phe Arg Lys Asp Val  Asn Met Ile Leu Gln  Ser Ser Leu
    1095                1100                1105

ggc aac  gac ctg cgc acg gac  ggg gcc tcc atc gcc  ttc acc agc     20063
Gly Asn  Asp Leu Arg Thr Asp  Gly Ala Ser Ile Ala  Phe Thr Ser
    1110                1115                1120

atc aac  ctc tac gcc acc ttc  ttc ccc atg gcg cac  aac acc gcc     20108
Ile Asn  Leu Tyr Ala Thr Phe  Phe Pro Met Ala His  Asn Thr Ala
    1125                1130                1135
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tcc acg  ctc gag gcc atg ctg  cgc aac gac acc aac  gac cag tcc     20153
Ser Thr  Leu Glu Ala Met Leu  Arg Asn Asp Thr Asn  Asp Gln Ser
    1140                 1145                 1150

ttc aac  gac tac ctc tcg gcg  gcc aac atg ctc tac  ccc atc ccg     20198
Phe Asn  Asp Tyr Leu Ser Ala  Ala Asn Met Leu Tyr  Pro Ile Pro
    1155                 1160                 1165

gcc aac  gcc acc aac gtg ccc  atc tcc atc ccc tcg  cgc aac tgg     20243
Ala Asn  Ala Thr Asn Val Pro  Ile Ser Ile Pro Ser  Arg Asn Trp
    1170                 1175                 1180

gcc gcc  ttc cgc ggc tgg tcc  ttc acg cgc ctc aag  acc cgc gag     20288
Ala Ala  Phe Arg Gly Trp Ser  Phe Thr Arg Leu Lys  Thr Arg Glu
    1185                 1190                 1195

acg ccc  tcg ctc ggc tcc ggg  ttc gac ccc tac ttc  gtc tac tcg     20333
Thr Pro  Ser Leu Gly Ser Gly  Phe Asp Pro Tyr Phe  Val Tyr Ser
    1200                 1205                 1210

ggc tcc  atc ccc tac ctc gac  ggc acc ttc tac ctc  aac cac acc     20378
Gly Ser  Ile Pro Tyr Leu Asp  Gly Thr Phe Tyr Leu  Asn His Thr
    1215                 1220                 1225

ttc aag  aag gtc tcc atc acc  ttc gac tcc tcc gtc  agc tgg ccc     20423
Phe Lys  Lys Val Ser Ile Thr  Phe Asp Ser Ser Val  Ser Trp Pro
    1230                 1235                 1240

ggc aac  gac cgc ctc ctg acg  ccc aac gag ttc gaa  atc aag cgc     20468
Gly Asn  Asp Arg Leu Leu Thr  Pro Asn Glu Phe Glu  Ile Lys Arg
    1245                 1250                 1255

acc gtc  gac gga gag ggg tac  aac gtg gcc cag tgc  aac atg acc     20513
Thr Val  Asp Gly Glu Gly Tyr  Asn Val Ala Gln Cys  Asn Met Thr
    1260                 1265                 1270

aag gac  tgg ttc ctg gtc cag  atg ctg gcc cac tac  aac atc ggc     20558
Lys Asp  Trp Phe Leu Val Gln  Met Leu Ala His Tyr  Asn Ile Gly
    1275                 1280                 1285

tac cag  ggc ttc tac gtg ccc  gag ggc tac aag gac  cgc atg tac     20603
Tyr Gln  Gly Phe Tyr Val Pro  Glu Gly Tyr Lys Asp  Arg Met Tyr
    1290                 1295                 1300

tcc ttc  ttc cgc aac ttc cag  ccc atg agc cgc cag  gtc gtg gac     20648
Ser Phe  Phe Arg Asn Phe Gln  Pro Met Ser Arg Gln  Val Val Asp
    1305                 1310                 1315

gag gtc  aac tac aag gac tac  cag gcc gtc acc ctg  gcc tac cag     20693
Glu Val  Asn Tyr Lys Asp Tyr  Gln Ala Val Thr Leu  Ala Tyr Gln
    1320                 1325                 1330

cac aac  aac tcg ggc ttc gtc  ggc tac ctc gcg ccc  acc atg cgc     20738
His Asn  Asn Ser Gly Phe Val  Gly Tyr Leu Ala Pro  Thr Met Arg
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Gln Gly  Gln Pro Tyr Pro Ala  Asn Tyr Pro Tyr Pro  Leu Ile Gly
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aag agc  gcc gtc gcc agc gtc  acc cag aaa aag ttc  ctc tgc gac     20828
Lys Ser  Ala Val Ala Ser Val  Thr Gln Lys Lys Phe  Leu Cys Asp
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cgg gtc  atg tgg cgc atc ccc  ttc tcc agc aac ttc  atg tcc atg     20873
Arg Val  Met Trp Arg Ile Pro  Phe Ser Ser Asn Phe  Met Ser Met
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ggc gcg  ctc acc gac ctc ggc  cag aac atg ctc tac  gcc aac tcc     20918
Gly Ala  Leu Thr Asp Leu Gly  Gln Asn Met Leu Tyr  Ala Asn Ser
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gcc cac  gcg cta gac atg aat  ttc gaa gtc gac ccc  atg gat gag     20963
Ala His  Ala Leu Asp Met Asn  Phe Glu Val Asp Pro  Met Asp Glu
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tcc acc  ctt ctc tat gtt gtc  ttc gaa gtc ttc gac  gtc gtc cga     21008
Ser Thr  Leu Leu Tyr Val Val  Phe Glu Val Phe Asp  Val Val Arg
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gtg cac  cag ccc cac cgc ggc  gtc atc gag gcc gtc  tac ctg cgc     21053
Val His  Gln Pro His Arg Gly  Val Ile Glu Ala Val  Tyr Leu Arg
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Thr Pro  Phe Ser Ala Gly Asn  Ala Thr Thr
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Phe  Asp Pro Val Tyr Pro  Tyr Asp Ala Asp Asn  Ala Pro Thr Val
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Pro  Phe Ile Asn Pro Pro  Phe Val Ser Ser Asp  Gly Phe Gln Glu
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Lys  Pro Leu Gly Val Leu  Ser Leu Arg Leu Ala  Asp Pro Val Thr
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Thr  Lys Asn Gly Glu Ile  Thr Leu Lys Leu Gly  Glu Gly Val Asp
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Leu  Asp Ser Ser Gly Lys  Leu Ile Ser Asn Thr  Ala Thr Lys Ala
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cgcgcacttc ctcaaacgcc caaactgccg tcatttccgg gttcccacgc tacgtcatcg 36375

gaattcgact ttcaaattcc gtcgaccgtt aaaaacgtca cccgccccgc ccctaacggt 36435

cgcccgtctc tcggccaatc accttcctcc ctccccaaat tcaaacagct catttgcata 36495

ttaacgcgca ccaaaagttt gaggtatatt attgatgatg 36535

<210> 10
<211> 531
<212> PRT
<213> chimpanzee adenovirus serotype Pan7

<400> 10

Met Met Arg Arg Val Tyr Pro Glu Gly Pro Pro Pro Ser Tyr Glu Ser
1 5 10 15

Val Met Gln Gln Ala Val Ala Ala Ala Met Gln Pro Pro Leu Glu Ala
20 25 30

Pro Tyr Val Pro Pro Arg Tyr Leu Ala Pro Thr Glu Gly Arg Asn Ser
35 40 45

Ile Arg Tyr Ser Glu Leu Ala Pro Leu Tyr Asp Thr Thr Arg Leu Tyr
50 55 60

Leu Val Asp Asn Lys Ser Ala Asp Ile Ala Ser Leu Asn Tyr Gln Asn
65 70 75 80

Asp His Ser Asn Phe Leu Thr Thr Val Val Gln Asn Asn Asp Phe Thr
85 90 95

Pro Thr Glu Ala Ser Thr Gln Thr Ile Asn Phe Asp Glu Arg Ser Arg
100 105 110

Trp Gly Gly Gln Leu Lys Thr Ile Met His Thr Asn Met Pro Asn Val
115 120 125

Asn Glu Phe Met Tyr Ser Asn Lys Phe Lys Ala Arg Val Met Val Ser
130 135 140

Arg Lys Thr Pro Asn Gly Val Ala Val Asp Glu Asn Tyr Asp Gly Ser
145 150 155 160

Gln Asp Glu Leu Thr Tyr Glu Trp Val Glu Phe Glu Leu Pro Glu Gly
165 170 175

Asn Phe Ser Val Thr Met Thr Ile Asp Leu Met Asn Asn Ala Ile Ile
180 185 190

Asp Asn Tyr Leu Ala Val Gly Arg Gln Asn Gly Val Leu Glu Ser Asp
195 200 205

Ile Gly Val Lys Phe Asp Thr Arg Asn Phe Arg Leu Gly Trp Asp Pro
210 215 220

Val Thr Glu Leu Val Met Pro Gly Val Tyr Thr Asn Glu Ala Phe His
225 230 235 240

Pro Asp Ile Val Leu Leu Pro Gly Cys Gly Val Asp Phe Thr Glu Ser
245 250 255

Arg Leu Ser Asn Leu Leu Gly Ile Arg Lys Arg Gln Pro Phe Gln Glu
260 265 270

```
Gly Phe Gln Ile Leu Tyr Glu Asp Leu Glu Gly Gly Asn Ile Pro Ala
        275                 280                 285

Leu Leu Asp Val Glu Ala Tyr Glu Lys Ser Lys Glu Glu Ala Ala Ala
    290                 295                 300

Ala Ala Thr Ala Ala Val Ala Thr Ala Ser Thr Glu Val Arg Gly Asp
305                 310                 315                 320

Asn Phe Ala Ser Ala Ala Ala Val Ala Glu Ala Ala Glu Thr Glu Ser
                325                 330                 335

Lys Ile Val Ile Gln Pro Val Glu Lys Asp Ser Lys Asp Arg Ser Tyr
            340                 345                 350

Asn Val Leu Ala Asp Lys Lys Asn Thr Ala Tyr Arg Ser Trp Tyr Leu
        355                 360                 365

Ala Tyr Asn Tyr Gly Asp Pro Glu Lys Gly Val Arg Ser Trp Thr Leu
    370                 375                 380

Leu Thr Thr Ser Asp Val Thr Cys Gly Val Glu Gln Val Tyr Trp Ser
385                 390                 395                 400

Leu Pro Asp Met Met Gln Asp Pro Val Thr Phe Arg Ser Thr Arg Gln
                405                 410                 415

Val Ser Asn Tyr Pro Val Val Gly Ala Glu Leu Leu Pro Val Tyr Ser
            420                 425                 430

Lys Ser Phe Phe Asn Glu Gln Ala Val Tyr Ser Gln Gln Leu Arg Ala
        435                 440                 445

Phe Thr Ser Leu Thr His Val Phe Asn Arg Phe Pro Glu Asn Gln Ile
    450                 455                 460

Leu Val Arg Pro Pro Ala Pro Thr Ile Thr Thr Val Ser Glu Asn Val
465                 470                 475                 480

Pro Ala Leu Thr Asp His Gly Thr Leu Pro Leu Arg Ser Ser Ile Arg
                485                 490                 495

Gly Val Gln Arg Val Thr Val Thr Asp Ala Arg Arg Arg Thr Cys Pro
            500                 505                 510

Tyr Val Tyr Lys Ala Leu Gly Val Val Ala Pro Arg Val Leu Ser Ser
        515                 520                 525

Arg Thr Phe
    530
```

<210> 11
<211> 932
<212> PRT
<213> chimpanzee adenovirus serotype Pan7

<400> 11

```
Met Ala Thr Pro Ser Met Leu Pro Gln Trp Ala Tyr Met His Ile Ala
1               5                  10                  15

Gly Gln Asp Ala Ser Glu Tyr Leu Ser Pro Gly Leu Val Gln Phe Ala
            20                  25                  30

Arg Ala Thr Asp Thr Tyr Phe Ser Leu Gly Asn Lys Phe Arg Asn Pro
        35                  40                  45

Thr Val Ala Pro Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg Leu
    50                  55                  60

Thr Leu Arg Phe Val Pro Val Asp Arg Glu Asp Asn Thr Tyr Ser Tyr
65                  70                  75                  80

Lys Val Arg Tyr Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met
                85                  90                  95

Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro Ser
            100                 105                 110

Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ser Leu Ala Pro Lys Gly
        115                 120                 125

Ala Pro Asn Thr Cys Gln Trp Thr Tyr Lys Ala Gly Asp Thr Asp Thr
    130                 135                 140

Glu Lys Thr Tyr Thr Tyr Gly Asn Ala Pro Val Gln Gly Ile Ser Ile
145                 150                 155                 160

Thr Lys Asp Gly Ile Gln Leu Gly Thr Asp Ser Asp Gly Gln Ala Ile
                165                 170                 175

Tyr Ala Asp Glu Thr Tyr Gln Pro Glu Pro Gln Val Gly Asp Ala Glu
            180                 185                 190

Trp His Asp Ile Thr Gly Thr Asp Glu Lys Tyr Gly Gly Arg Ala Leu
        195                 200                 205

Lys Pro Asp Thr Lys Met Lys Pro Cys Tyr Gly Ser Phe Ala Lys Pro
    210                 215                 220

Thr Asn Lys Glu Gly Gly Gln Ala Asn Val Lys Thr Glu Thr Gly Gly
225                 230                 235                 240

Thr Lys Glu Tyr Asp Ile Asp Met Ala Phe Phe Asp Asn Arg Ser Ala
                245                 250                 255

Ala Ala Ala Gly Leu Ala Pro Glu Ile Val Leu Tyr Thr Glu Asn Val
            260                 265                 270

Asp Leu Glu Thr Pro Asp Thr His Ile Val Tyr Lys Ala Gly Thr Asp
        275                 280                 285
```

```
Asp Ser Ser Ser Ser Ile Asn Leu Gly Gln Gln Ser Met Pro Asn Arg
    290                 295                 300

Pro Asn Tyr Ile Gly Phe Arg Asp Asn Phe Ile Gly Leu Met Tyr Tyr
305                 310                 315                 320

Asn Ser Thr Gly Asn Met Gly Val Leu Ala Gly Gln Ala Ser Gln Leu
                325                 330                 335

Asn Ala Val Val Asp Leu Gln Asp Arg Asn Thr Glu Leu Ser Tyr Gln
            340                 345                 350

Leu Leu Leu Asp Ser Leu Gly Asp Arg Thr Arg Tyr Phe Ser Met Trp
        355                 360                 365

Asn Gln Ala Val Asp Ser Tyr Asp Pro Asp Val Arg Ile Ile Glu Asn
    370                 375                 380

His Gly Val Glu Asp Glu Leu Pro Asn Tyr Cys Phe Pro Leu Asp Ala
385                 390                 395                 400

Val Gly Arg Thr Asp Thr Tyr Gln Gly Ile Lys Ala Asn Gly Asp Asn
                405                 410                 415

Gln Thr Thr Trp Thr Lys Asp Asp Thr Val Asn Asp Ala Asn Glu Leu
            420                 425                 430

Gly Lys Gly Asn Pro Phe Ala Met Glu Ile Asn Ile Gln Ala Asn Leu
        435                 440                 445

Trp Arg Asn Phe Leu Tyr Ala Asn Val Ala Leu Tyr Leu Pro Asp Ser
    450                 455                 460

Tyr Lys Tyr Thr Pro Ala Asn Ile Thr Leu Pro Thr Asn Thr Asn Thr
465                 470                 475                 480

Tyr Asp Tyr Met Asn Gly Arg Val Val Ala Pro Ser Leu Val Asp Ala
                485                 490                 495

Tyr Ile Asn Ile Gly Ala Arg Trp Ser Leu Asp Pro Met Asp Asn Val
            500                 505                 510

Asn Pro Phe Asn His His Arg Asn Ala Gly Leu Arg Tyr Arg Ser Met
        515                 520                 525

Leu Leu Gly Asn Gly Arg Tyr Val Pro Phe His Ile Gln Val Pro Gln
    530                 535                 540

Lys Phe Phe Ala Ile Lys Ser Leu Leu Leu Leu Pro Gly Ser Tyr Thr
545                 550                 555                 560

Tyr Glu Trp Asn Phe Arg Lys Asp Val Asn Met Ile Leu Gln Ser Ser
                565                 570                 575

Leu Gly Asn Asp Leu Arg Thr Asp Gly Ala Ser Ile Ala Phe Thr Ser
            580                 585                 590
```

```
Ile Asn Leu Tyr Ala Thr Phe Phe Pro Met Ala His Asn Thr Ala Ser
        595                 600                 605

Thr Leu Glu Ala Met Leu Arg Asn Asp Thr Asn Asp Gln Ser Phe Asn
    610                 615                 620

Asp Tyr Leu Ser Ala Ala Asn Met Leu Tyr Pro Ile Pro Ala Asn Ala
625                 630                 635                 640

Thr Asn Val Pro Ile Ser Ile Pro Ser Arg Asn Trp Ala Ala Phe Arg
                645                 650                 655

Gly Trp Ser Phe Thr Arg Leu Lys Thr Arg Glu Thr Pro Ser Leu Gly
            660                 665                 670

Ser Gly Phe Asp Pro Tyr Phe Val Tyr Ser Gly Ser Ile Pro Tyr Leu
        675                 680                 685

Asp Gly Thr Phe Tyr Leu Asn His Thr Phe Lys Lys Val Ser Ile Thr
    690                 695                 700

Phe Asp Ser Ser Val Ser Trp Pro Gly Asn Asp Arg Leu Leu Thr Pro
705                 710                 715                 720

Asn Glu Phe Glu Ile Lys Arg Thr Val Asp Gly Glu Gly Tyr Asn Val
                725                 730                 735

Ala Gln Cys Asn Met Thr Lys Asp Trp Phe Leu Val Gln Met Leu Ala
            740                 745                 750

His Tyr Asn Ile Gly Tyr Gln Gly Phe Tyr Val Pro Glu Gly Tyr Lys
        755                 760                 765

Asp Arg Met Tyr Ser Phe Phe Arg Asn Phe Gln Pro Met Ser Arg Gln
    770                 775                 780

Val Val Asp Glu Val Asn Tyr Lys Asp Tyr Gln Ala Val Thr Leu Ala
785                 790                 795                 800

Tyr Gln His Asn Asn Ser Gly Phe Val Gly Tyr Leu Ala Pro Thr Met
                805                 810                 815

Arg Gln Gly Gln Pro Tyr Pro Ala Asn Tyr Pro Tyr Pro Leu Ile Gly
            820                 825                 830

Lys Ser Ala Val Ala Ser Val Thr Gln Lys Lys Phe Leu Cys Asp Arg
        835                 840                 845

Val Met Trp Arg Ile Pro Phe Ser Ser Asn Phe Met Ser Met Gly Ala
    850                 855                 860

Leu Thr Asp Leu Gly Gln Asn Met Leu Tyr Ala Asn Ser Ala His Ala
865                 870                 875                 880

Leu Asp Met Asn Phe Glu Val Asp Pro Met Asp Glu Ser Thr Leu Leu
                885                 890                 895
```

```
Tyr Val Val Phe Glu Val Phe Asp Val Val Arg Val His Gln Pro His
            900                 905                 910

Arg Gly Val Ile Glu Ala Val Tyr Leu Arg Thr Pro Phe Ser Ala Gly
        915                 920                 925

Asn Ala Thr Thr
    930
```

<210> 12
<211> 443
<212> PRT
<213> chimpanzee adenovirus serotype Pan7

<400> 12

```
Met Ser Lys Lys Arg Val Arg Val Asp Asp Asp Phe Asp Pro Val Tyr
1               5                   10                  15

Pro Tyr Asp Ala Asp Asn Ala Pro Thr Val Pro Phe Ile Asn Pro Pro
            20                  25                  30

Phe Val Ser Ser Asp Gly Phe Gln Glu Lys Pro Leu Gly Val Leu Ser
        35                  40                  45

Leu Arg Leu Ala Asp Pro Val Thr Thr Lys Asn Gly Glu Ile Thr Leu
    50                  55                  60

Lys Leu Gly Glu Gly Val Asp Leu Asp Ser Ser Gly Lys Leu Ile Ser
65                  70                  75                  80

Asn Thr Ala Thr Lys Ala Ala Ala Pro Leu Ser Phe Ser Asn Asn Thr
                85                  90                  95

Ile Ser Leu Asn Met Asp Thr Pro Leu Tyr Thr Lys Asp Gly Lys Leu
            100                 105                 110

Ser Leu Gln Val Ser Pro Pro Leu Asn Ile Leu Lys Ser Thr Ile Leu
        115                 120                 125

Asn Thr Leu Ala Val Ala Tyr Gly Ser Gly Leu Gly Leu Ser Gly Gly
    130                 135                 140

Thr Ala Leu Ala Val Gln Leu Ala Ser Pro Leu Thr Phe Asp Glu Lys
145                 150                 155                 160

Gly Asn Ile Lys Ile Asn Leu Ala Ser Gly Pro Leu Thr Val Asp Ala
                165                 170                 175

Ser Arg Leu Ser Ile Asn Cys Lys Arg Gly Val Thr Val Thr Thr Ser
            180                 185                 190

Gly Asp Ala Ile Glu Ser Asn Ile Ser Trp Pro Lys Gly Ile Arg Phe
        195                 200                 205
```

```
Glu Gly Asn Gly Ile Ala Ala Asn Ile Gly Arg Gly Leu Glu Phe Gly
    210                 215                 220

Thr Thr Ser Thr Glu Thr Asp Val Thr Asp Ala Tyr Pro Ile Gln Val
225                 230                 235                 240

Lys Leu Gly Thr Gly Leu Thr Phe Asp Ser Thr Gly Ala Ile Val Ala
                245                 250                 255

Trp Asn Lys Glu Asp Asp Lys Leu Thr Leu Trp Thr Thr Ala Asp Pro
            260                 265                 270

Ser Pro Asn Cys Lys Ile Tyr Ser Glu Lys Asp Ala Lys Leu Thr Leu
        275                 280                 285

Cys Leu Thr Lys Cys Gly Ser Gln Ile Leu Gly Thr Val Thr Val Leu
    290                 295                 300

Ala Val Asn Asn Gly Ser Leu Asn Pro Ile Thr Asn Thr Val Ser Thr
305                 310                 315                 320

Ala Leu Val Ser Leu Lys Phe Asp Ala Ser Gly Val Leu Leu Ser Ser
                325                 330                 335

Ser Thr Leu Asp Lys Glu Tyr Trp Asn Phe Arg Lys Gly Asp Val Thr
            340                 345                 350

Pro Ala Glu Pro Tyr Thr Asn Ala Ile Gly Phe Met Pro Asn Ile Lys
        355                 360                 365

Ala Tyr Pro Lys Asn Thr Ser Ala Ala Ser Lys Ser His Ile Val Ser
    370                 375                 380

Gln Val Tyr Leu Asn Gly Asp Glu Ala Lys Pro Leu Met Leu Ile Ile
385                 390                 395                 400

Thr Phe Asn Glu Thr Glu Asp Ala Thr Cys Thr Tyr Ser Ile Thr Phe
                405                 410                 415

Gln Trp Lys Trp Asp Ser Thr Lys Tyr Thr Gly Glu Thr Leu Ala Thr
            420                 425                 430

Ser Ser Phe Thr Phe Ser Tyr Ile Ala Gln Glu
        435                 440
```

<210> 13
<211> 338
<212> PRT
<213> simian serotype C1

<400> 13

```
Ala Pro Lys Gly Ala Pro Asn Thr Ser Gln Trp Leu Asp Lys Gly Val
1               5                   10                  15
```

```
Thr Thr Thr Asp Asn Asn Thr Glu Asn Gly Asp Glu Glu Asp Glu Val
            20                  25                  30

Ala Glu Glu Gly Glu Glu Glu Lys Gln Ala Thr Tyr Thr Phe Gly Asn
        35                  40                  45

Ala Pro Val Lys Ala Glu Ala Glu Ile Thr Lys Glu Gly Leu Pro Ile
    50                  55                  60

Gly Leu Glu Val Pro Ser Glu Gly Asp Pro Lys Pro Ile Tyr Ala Asp
65                  70                  75                  80

Lys Leu Tyr Gln Pro Glu Pro Gln Val Gly Glu Glu Ser Trp Thr Asp
                85                  90                  95

Thr Asp Gly Thr Asp Glu Lys Tyr Gly Gly Arg Ala Leu Lys Pro Glu
            100                 105                 110

Thr Lys Met Lys Pro Cys Tyr Gly Ser Phe Ala Lys Pro Thr Asn Val
        115                 120                 125

Lys Gly Gly Gln Ala Lys Val Lys Lys Val Glu Glu Gly Lys Val Glu
    130                 135                 140

Tyr Asp Ile Asp Met Asn Phe Phe Asp Leu Arg Ser Gln Lys Thr Gly
145                 150                 155                 160

Leu Lys Pro Lys Ile Val Met Tyr Ala Glu Asn Val Asp Leu Glu Thr
                165                 170                 175

Pro Asp Thr His Val Val Tyr Lys Pro Gly Ala Ser Asp Ala Ser Ser
            180                 185                 190

His Ala Asn Leu Gly Gln Gln Ser Met Pro Asn Arg Pro Asn Tyr Ile
        195                 200                 205

Gly Phe Arg Asp Asn Phe Ile Gly Leu Met Tyr Tyr Asn Ser Thr Gly
    210                 215                 220

Asn Met Gly Val Leu Ala Gly Gln Ala Ser Gln Leu Asn Ala Val Val
225                 230                 235                 240

Asp Leu Gln Asp Arg Asn Thr Glu Leu Ser Tyr Gln Leu Leu Leu Asp
                245                 250                 255

Ser Leu Gly Asp Arg Thr Arg Tyr Phe Ser Met Trp Asn Gln Ala Val
            260                 265                 270

Asp Ser Tyr Asp Pro Asp Val Arg Val Ile Glu Asn His Gly Val Glu
        275                 280                 285

Asp Glu Leu Pro Asn Tyr Cys Phe Pro Leu Asp Gly Val Gly Pro Arg
    290                 295                 300

Thr Asp Ser Tyr Lys Gly Ile Glu Thr Asn Gly Asp Glu Asn Thr Thr
305                 310                 315                 320
```

```
Trp Lys Asp Leu Asp Pro Asn Gly Ile Ser Glu Leu Ala Lys Gly Asn
                325                 330                 335

Pro Phe


<210>  14
<211>  315
<212>  PRT
<213>  chimpanzee adenovirus Pan-9

<400>  14

Ala Pro Lys Gly Ala Pro Asn Thr Cys Gln Trp Thr Tyr Lys Ala Asp
1               5                   10                  15

Gly Glu Thr Ala Thr Glu Lys Thr Tyr Thr Tyr Gly Asn Ala Pro Val
            20                  25                  30

Gln Gly Ile Asn Ile Thr Lys Asp Gly Ile Gln Leu Gly Thr Asp Thr
        35                  40                  45

Asp Asp Gln Pro Ile Tyr Ala Asp Lys Thr Tyr Gln Pro Glu Pro Gln
    50                  55                  60

Val Gly Asp Ala Glu Trp His Asp Ile Thr Gly Thr Asp Glu Lys Tyr
65                  70                  75                  80

Gly Gly Arg Ala Leu Lys Pro Asp Thr Lys Met Lys Pro Cys Tyr Gly
                85                  90                  95

Ser Phe Ala Lys Pro Thr Asn Lys Glu Gly Gly Gln Ala Asn Val Lys
            100                 105                 110

Thr Gly Thr Gly Thr Thr Lys Glu Tyr Asp Ile Asp Met Ala Phe Phe
        115                 120                 125

Asp Asn Arg Ser Ala Ala Ala Ala Gly Leu Ala Pro Glu Ile Val Leu
    130                 135                 140

Tyr Thr Glu Asn Val Asp Leu Glu Thr Pro Asp Thr His Ile Val Tyr
145                 150                 155                 160

Lys Ala Gly Thr Asp Asp Ser Ser Ser Ser Ile Asn Leu Gly Gln Gln
                165                 170                 175

Ala Met Pro Asn Arg Pro Asn Tyr Ile Gly Phe Arg Asp Asn Phe Ile
            180                 185                 190

Gly Leu Met Tyr Tyr Asn Ser Thr Gly Asn Met Gly Val Leu Ala Gly
        195                 200                 205

Gln Ala Ser Gln Leu Asn Ala Val Val Asp Leu Gln Asp Arg Asn Thr
    210                 215                 220
```

```
Glu Leu Ser Tyr Gln Leu Leu Leu Asp Ser Leu Gly Asp Arg Thr Arg
225                 230                 235                 240

Tyr Phe Ser Met Trp Asn Gln Ala Val Asp Ser Tyr Asp Pro Asp Val
                245                 250                 255

Arg Ile Ile Glu Asn His Gly Val Glu Asp Glu Leu Pro Asn Tyr Cys
            260                 265                 270

Phe Pro Leu Asp Ala Val Gly Arg Thr Asp Thr Tyr Gln Gly Ile Lys
        275                 280                 285

Ala Asn Gly Thr Asp Gln Thr Thr Trp Thr Lys Asp Asp Ser Val Asn
    290                 295                 300

Asp Ala Asn Glu Ile Gly Lys Gly Asn Pro Phe
305                 310                 315
```

<210> 15
<211> 315
<212> PRT
<213> chimpanzee adenovirus Pan-5

<400> 15

```
Ala Pro Lys Gly Ala Pro Asn Thr Cys Gln Trp Thr Tyr Lys Ala Asp
1               5                   10                  15

Gly Asp Thr Gly Thr Glu Lys Thr Tyr Thr Tyr Gly Asn Ala Pro Val
            20                  25                  30

Gln Gly Ile Ser Ile Thr Lys Asp Gly Ile Gln Leu Gly Thr Asp Thr
        35                  40                  45

Asp Asp Gln Pro Ile Tyr Ala Asp Lys Thr Tyr Gln Pro Glu Pro Gln
    50                  55                  60

Val Gly Asp Ala Glu Trp His Asp Ile Thr Gly Thr Asp Glu Lys Tyr
65                  70                  75                  80

Gly Gly Arg Ala Leu Lys Pro Asp Thr Lys Met Lys Pro Cys Tyr Gly
                85                  90                  95

Ser Phe Ala Lys Pro Thr Asn Lys Glu Gly Gly Gln Ala Asn Val Lys
            100                 105                 110

Thr Glu Thr Gly Gly Thr Lys Glu Tyr Asp Ile Asp Met Ala Phe Phe
        115                 120                 125

Asp Asn Arg Ser Ala Ala Ala Ala Gly Leu Ala Pro Glu Ile Val Leu
    130                 135                 140

Tyr Thr Glu Asn Val Asp Leu Glu Thr Pro Asp Thr His Ile Val Tyr
145                 150                 155                 160
```

```
Lys Ala Gly Thr Asp Asp Ser Ser Ser Ser Ile Asn Leu Gly Gln Gln
                165                 170                 175

Ser Met Pro Asn Arg Pro Asn Tyr Ile Gly Phe Arg Asp Asn Phe Ile
            180                 185                 190

Gly Leu Met Tyr Tyr Asn Ser Thr Gly Asn Met Gly Val Leu Ala Gly
        195                 200                 205

Gln Ala Ser Gln Leu Asn Ala Val Val Asp Leu Gln Asp Arg Asn Thr
    210                 215                 220

Glu Leu Ser Tyr Gln Leu Leu Leu Asp Ser Leu Gly Asp Arg Thr Arg
225                 230                 235                 240

Tyr Phe Ser Met Trp Asn Gln Ala Val Asp Ser Tyr Asp Pro Asp Val
                245                 250                 255

Arg Ile Ile Glu Asn His Gly Val Glu Asp Glu Leu Pro Asn Tyr Cys
            260                 265                 270

Phe Pro Leu Asp Ala Val Gly Arg Thr Asp Thr Tyr Gln Gly Ile Lys
        275                 280                 285

Ala Asn Gly Ala Asp Gln Thr Thr Trp Thr Lys Asp Asp Thr Val Asn
    290                 295                 300

Asp Ala Asn Glu Leu Gly Lys Gly Asn Pro Phe
305                 310                 315
```

<210> 16
<211> 324
<212> PRT
<213> chimpanzee adenovirus Pan-6

<400> 16

```
Ala Pro Lys Gly Ala Pro Asn Ser Ser Gln Trp Glu Gln Ala Lys Thr
1               5                   10                  15

Gly Asn Gly Gly Thr Met Glu Thr His Thr Tyr Gly Val Ala Pro Met
            20                  25                  30

Gly Gly Glu Asn Ile Thr Lys Asp Gly Leu Gln Ile Gly Thr Asp Val
        35                  40                  45

Thr Ala Asn Gln Asn Lys Pro Ile Tyr Ala Asp Lys Thr Phe Gln Pro
    50                  55                  60

Glu Pro Gln Val Gly Glu Glu Asn Trp Gln Glu Thr Glu Asn Phe Tyr
65                  70                  75                  80

Gly Gly Arg Ala Leu Lys Lys Asp Thr Lys Met Lys Pro Cys Tyr Gly
                85                  90                  95
```

```
Ser Tyr Ala Arg Pro Thr Asn Glu Lys Gly Gly Gln Ala Lys Leu Lys
            100                 105                 110

Val Gly Asp Asp Gly Val Pro Thr Lys Glu Phe Asp Ile Asp Leu Ala
        115                 120                 125

Phe Phe Asp Thr Pro Gly Gly Thr Val Asn Gly Gln Asp Glu Tyr Lys
    130                 135                 140

Ala Asp Ile Val Met Tyr Thr Glu Asn Thr Tyr Leu Glu Thr Pro Asp
145                 150                 155                 160

Thr His Val Val Tyr Lys Pro Gly Lys Asp Asp Ala Ser Ser Glu Ile
                165                 170                 175

Asn Leu Val Gln Gln Ser Met Pro Asn Arg Pro Asn Tyr Ile Gly Phe
            180                 185                 190

Arg Asp Asn Phe Ile Gly Leu Met Tyr Tyr Asn Ser Thr Gly Asn Met
        195                 200                 205

Gly Val Leu Ala Gly Gln Ala Ser Gln Leu Asn Ala Val Val Asp Leu
    210                 215                 220

Gln Asp Arg Asn Thr Glu Leu Ser Tyr Gln Leu Leu Leu Asp Ser Leu
225                 230                 235                 240

Gly Asp Arg Thr Arg Tyr Phe Ser Met Trp Asn Gln Ala Val Asp Ser
                245                 250                 255

Tyr Asp Pro Asp Val Arg Ile Ile Glu Asn His Gly Val Glu Asp Glu
            260                 265                 270

Leu Pro Asn Tyr Cys Phe Pro Leu Asp Gly Ser Gly Thr Asn Ala Ala
        275                 280                 285

Tyr Gln Gly Val Lys Val Lys Asp Gly Gln Asp Gly Asp Val Glu Ser
    290                 295                 300

Glu Trp Glu Asn Asp Asp Thr Val Ala Ala Arg Asn Gln Leu Cys Lys
305                 310                 315                 320

Gly Asn Ile Phe
```

<210> 17
<211> 314
<212> PRT
<213> chimpanzee adenovirus Pan-7

<400> 17

```
Ala Pro Lys Gly Ala Pro Asn Thr Cys Gln Trp Thr Tyr Lys Ala Gly
1               5                   10                  15

Asp Thr Asp Thr Glu Lys Thr Tyr Thr Tyr Gly Asn Ala Pro Val Gln
            20                  25                  30
```

```
Gly Ile Ser Ile Thr Lys Asp Gly Ile Gln Leu Gly Thr Asp Ser Asp
        35                  40                  45

Gly Gln Ala Ile Tyr Ala Asp Glu Thr Tyr Gln Pro Glu Pro Gln Val
    50                  55                  60

Gly Asp Ala Glu Trp His Asp Ile Thr Gly Thr Asp Glu Lys Tyr Gly
65                  70                  75                  80

Gly Arg Ala Leu Lys Pro Asp Thr Lys Met Lys Pro Cys Tyr Gly Ser
                85                  90                  95

Phe Ala Lys Pro Thr Asn Lys Glu Gly Gly Gln Ala Asn Val Lys Thr
            100                 105                 110

Glu Thr Gly Gly Thr Lys Glu Tyr Asp Ile Asp Met Ala Phe Phe Asp
        115                 120                 125

Asn Arg Ser Ala Ala Ala Ala Gly Leu Ala Pro Glu Ile Val Leu Tyr
    130                 135                 140

Thr Glu Asn Val Asp Leu Glu Thr Pro Asp Thr His Ile Val Tyr Lys
145                 150                 155                 160

Ala Gly Thr Asp Asp Ser Ser Ser Ser Ile Asn Leu Gly Gln Gln Ser
                165                 170                 175

Met Pro Asn Arg Pro Asn Tyr Ile Gly Phe Arg Asp Asn Phe Ile Gly
            180                 185                 190

Leu Met Tyr Tyr Asn Ser Thr Gly Asn Met Gly Val Leu Ala Gly Gln
        195                 200                 205

Ala Ser Gln Leu Asn Ala Val Val Asp Leu Gln Asp Arg Asn Thr Glu
    210                 215                 220

Leu Ser Tyr Gln Leu Leu Leu Asp Ser Leu Gly Asp Arg Thr Arg Tyr
225                 230                 235                 240

Phe Ser Met Trp Asn Gln Ala Val Asp Ser Tyr Asp Pro Asp Val Arg
                245                 250                 255

Ile Ile Glu Asn His Gly Val Glu Asp Glu Leu Pro Asn Tyr Cys Phe
            260                 265                 270

Pro Leu Asp Ala Val Gly Arg Thr Asp Thr Tyr Gln Gly Ile Lys Ala
        275                 280                 285

Asn Gly Asp Asn Gln Thr Thr Trp Thr Lys Asp Asp Thr Val Asn Asp
    290                 295                 300

Ala Asn Glu Leu Gly Lys Gly Asn Pro Phe
305                 310
```

<210> 18
<211> 179
<212> PRT
<213> chimpanzee adenovirus Pan9

<400> 18

Thr Leu Trp Thr Thr Pro Asp Pro Ser Pro Asn Cys Gln Ile Leu Ala
1 5 10 15

Glu Asn Asp Ala Lys Leu Thr Leu Cys Leu Thr Lys Cys Gly Ser Gln
20 25 30

Ile Leu Ala Thr Val Ser Val Leu Val Val Gly Ser Gly Asn Leu Asn
35 40 45

Pro Ile Thr Gly Thr Val Ser Ser Ala Gln Val Phe Leu Arg Phe Asp
50 55 60

Ala Asn Gly Val Leu Leu Thr Glu His Ser Thr Leu Lys Lys Tyr Trp
65 70 75 80

Gly Tyr Arg Gln Gly Asp Ser Ile Asp Gly Thr Pro Tyr Thr Asn Ala
85 90 95

Val Gly Phe Met Pro Asn Leu Lys Ala Tyr Pro Lys Ser Gln Ser Ser
100 105 110

Thr Thr Lys Asn Asn Ile Val Gly Gln Val Tyr Met Asn Gly Asp Val
115 120 125

Ser Lys Pro Met Leu Leu Thr Ile Thr Leu Asn Gly Thr Asp Asp Ser
130 135 140

Asn Ser Thr Tyr Ser Met Ser Phe Ser Tyr Thr Trp Thr Asn Gly Ser
145 150 155 160

Tyr Val Gly Ala Thr Phe Gly Ala Asn Ser Tyr Thr Phe Ser Tyr Ile
165 170 175

Ala Gln Glu

<210> 19
<211> 185
<212> PRT
<213> chimpanzee adenovirus Pan6

<400> 19

Thr Leu Trp Thr Thr Pro Asp Pro Ser Pro Asn Cys Gln Leu Leu Ser
1 5 10 15

Asp Arg Asp Ala Lys Phe Thr Leu Cys Leu Thr Lys Cys Gly Ser Gln
20 25 30

```
Ile Leu Gly Thr Val Ala Val Ala Ala Val Thr Val Gly Ser Ala Leu
        35                  40                  45

Asn Pro Ile Asn Asp Thr Val Lys Ser Ala Ile Val Phe Leu Arg Phe
    50                  55                  60

Asp Ser Asp Gly Val Leu Met Ser Asn Ser Ser Met Val Gly Asp Tyr
65                  70                  75                  80

Trp Asn Phe Arg Glu Gly Gln Thr Thr Gln Ser Val Ala Tyr Thr Asn
                85                  90                  95

Ala Val Gly Phe Met Pro Asn Ile Gly Ala Tyr Pro Lys Thr Gln Ser
            100                 105                 110

Lys Thr Pro Lys Asn Ser Ile Val Ser Gln Val Tyr Leu Thr Gly Glu
        115                 120                 125

Thr Thr Met Pro Met Thr Leu Thr Ile Thr Phe Asn Gly Thr Asp Glu
    130                 135                 140

Lys Asp Thr Thr Pro Val Ser Thr Tyr Ser Met Thr Phe Thr Trp Gln
145                 150                 155                 160

Trp Thr Gly Asp Tyr Lys Asp Lys Asn Ile Thr Phe Ala Thr Asn Ser
                165                 170                 175

Phe Ser Phe Ser Tyr Ile Ala Gln Glu
            180                 185
```

<210> 20
<211> 179
<212> PRT
<213> chimpanzee adenovirus Pan7

<400> 20

```
Thr Leu Trp Thr Thr Ala Asp Pro Ser Pro Asn Cys Lys Ile Tyr Ser
1               5                   10                  15

Glu Lys Asp Ala Lys Leu Thr Leu Cys Leu Thr Lys Cys Gly Ser Gln
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Pro Ile Thr Asn Thr Val Ser Thr Ala Leu Val Ser Leu Lys Phe Asp
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cgatacgtgc agcagtccgt gagtctgtac ttgatgcggg agggcgccac cgcttccacg 11700

gctttagaca tgacggctcg gaacatggaa ccgtcctttt actccgccca ccggccgttc 11760

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tttcttcctc tctttcttcc tcggcgcggc aga atg aga aga gcg gtg aga gtc   12474
                                    Met Arg Arg Ala Val Arg Val
                                    1               5

acg ccg gcg gcg tat gag ggt ccg ccc cct tct tac gaa agc gtg atg    12522
Thr Pro Ala Ala Tyr Glu Gly Pro Pro Pro Ser Tyr Glu Ser Val Met
        10                  15                  20

gga tca gcg aac gtg ccg gcc acg ctg gag gcg cct tac gtt cct ccc    12570
Gly Ser Ala Asn Val Pro Ala Thr Leu Glu Ala Pro Tyr Val Pro Pro
    25                  30                  35

aga tac ctg gga cct acg gag ggc aga aac agc atc cgt tac tcc gag    12618
Arg Tyr Leu Gly Pro Thr Glu Gly Arg Asn Ser Ile Arg Tyr Ser Glu
40                  45                  50                  55

ctg gca ccc ctg tac gat acc acc aag gtg tac ctg gtg gac aac aag    12666
Leu Ala Pro Leu Tyr Asp Thr Thr Lys Val Tyr Leu Val Asp Asn Lys
                60                  65                  70

tcg gcg gac atc gcc tcc ctg aat tat caa aac gat cac agc aat ttt    12714
Ser Ala Asp Ile Ala Ser Leu Asn Tyr Gln Asn Asp His Ser Asn Phe
            75                  80                  85

ctg act acc gtg gtg cag aac aat gac ttc acc ccg acg gag gcg ggc    12762
Leu Thr Thr Val Val Gln Asn Asn Asp Phe Thr Pro Thr Glu Ala Gly
        90                  95                  100

acg cag acc att aac ttt gac gag cgt tcc cgc tgg ggc ggt cag ctg    12810
Thr Gln Thr Ile Asn Phe Asp Glu Arg Ser Arg Trp Gly Gly Gln Leu
    105                 110                 115

aaa acc atc ctg cac acc aac atg ccc aac atc aac gag ttc atg tcc    12858
Lys Thr Ile Leu His Thr Asn Met Pro Asn Ile Asn Glu Phe Met Ser
120                 125                 130                 135
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acc aac aag ttc agg gcc agg ctg atg gtt aaa aag gct gaa aac cag    12906
Thr Asn Lys Phe Arg Ala Arg Leu Met Val Lys Lys Ala Glu Asn Gln
                140                 145                 150

cct ccc gag tac gaa tgg ttt gag ttc acc att ccc gag ggc aac tat    12954
Pro Pro Glu Tyr Glu Trp Phe Glu Phe Thr Ile Pro Glu Gly Asn Tyr
            155                 160                 165

tcc gag acc atg act atc gat ctg atg aac aat gcg atc gtg gac aat    13002
Ser Glu Thr Met Thr Ile Asp Leu Met Asn Asn Ala Ile Val Asp Asn
        170                 175                 180

tac ctg caa gtg ggg agg cag aac ggg gta ttg gaa agc gat atc ggc    13050
Tyr Leu Gln Val Gly Arg Gln Asn Gly Val Leu Glu Ser Asp Ile Gly
    185                 190                 195

gta aaa ttt gat acc aga aac ttc cga ctg ggg tgg gat ccc gtg acc    13098
Val Lys Phe Asp Thr Arg Asn Phe Arg Leu Gly Trp Asp Pro Val Thr
200                 205                 210                 215

aag ctg gtg atg cca ggc gtg tac acc aac gag gct ttt cac ccc gac    13146
Lys Leu Val Met Pro Gly Val Tyr Thr Asn Glu Ala Phe His Pro Asp
                220                 225                 230

atc gtg ctg ctg ccg ggg tgc ggt gtg gac ttc act cag agc cgt ttg    13194
Ile Val Leu Leu Pro Gly Cys Gly Val Asp Phe Thr Gln Ser Arg Leu
            235                 240                 245

agt aac ctg tta ggg atc aga aag cgc cgc ccc ttc caa gag ggc ttt    13242
Ser Asn Leu Leu Gly Ile Arg Lys Arg Arg Pro Phe Gln Glu Gly Phe
        250                 255                 260

cag atc atg tat gag gac ctg gaa gga ggt aac att cca ggt ttg cta    13290
Gln Ile Met Tyr Glu Asp Leu Glu Gly Gly Asn Ile Pro Gly Leu Leu
    265                 270                 275

gac gtg ccg gcg tat gaa gag agt gtt aaa cag gcg gag gcg cag gga    13338
Asp Val Pro Ala Tyr Glu Glu Ser Val Lys Gln Ala Glu Ala Gln Gly
280                 285                 290                 295

cga gag att cga ggc gac acc ttt gcc acg gaa cct cac gaa ctg gta    13386
Arg Glu Ile Arg Gly Asp Thr Phe Ala Thr Glu Pro His Glu Leu Val
                300                 305                 310

ata aaa cct ctg gaa caa gac agt aaa aaa cgg agt tac aac att ata    13434
Ile Lys Pro Leu Glu Gln Asp Ser Lys Lys Arg Ser Tyr Asn Ile Ile
            315                 320                 325

tcc ggc act atg aat acc ttg tac cgg agc tgg ttt ctg gct tac aac    13482
Ser Gly Thr Met Asn Thr Leu Tyr Arg Ser Trp Phe Leu Ala Tyr Asn
        330                 335                 340

tac ggg gat ccc gaa aag gga gtg aga tca tgg acc ata ctc acc acc    13530
Tyr Gly Asp Pro Glu Lys Gly Val Arg Ser Trp Thr Ile Leu Thr Thr
    345                 350                 355
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acg gac gtg acc tgc ggc tcg cag caa gtg tac tgg tcc ctg ccg gat    13578
Thr Asp Val Thr Cys Gly Ser Gln Gln Val Tyr Trp Ser Leu Pro Asp
360                 365                 370                 375

atg atg caa gac ccg gtc acc ttc cgc ccc tcc acc caa gtc agc aac    13626
Met Met Gln Asp Pro Val Thr Phe Arg Pro Ser Thr Gln Val Ser Asn
                380                 385                 390

ttc ccg gtg gtg ggc acc gag ctg ctg ccc gtc cat gcc aag agc ttc    13674
Phe Pro Val Val Gly Thr Glu Leu Leu Pro Val His Ala Lys Ser Phe
            395                 400                 405

tac aac gaa cag gcc gtc tac tcg caa ctc att cgc cag tcc acc gcg    13722
Tyr Asn Glu Gln Ala Val Tyr Ser Gln Leu Ile Arg Gln Ser Thr Ala
        410                 415                 420

ctt acc cac gtg ttc aat cgc ttt ccc gag aac cag att ctg gtg cgc    13770
Leu Thr His Val Phe Asn Arg Phe Pro Glu Asn Gln Ile Leu Val Arg
    425                 430                 435

cct ccc gct cct acc att acc acc gtc agt gaa aac gtt ccc gcc ctc    13818
Pro Pro Ala Pro Thr Ile Thr Thr Val Ser Glu Asn Val Pro Ala Leu
440                 445                 450                 455

aca gat cac gga acc ctg ccg ctg cgc agc agt atc agt gga gtt cag    13866
Thr Asp His Gly Thr Leu Pro Leu Arg Ser Ser Ile Ser Gly Val Gln
                460                 465                 470

cgc gtg acc atc acc gac gcc aga cgt cga acc tgt ccc tac gtt tac    13914
Arg Val Thr Ile Thr Asp Ala Arg Arg Arg Thr Cys Pro Tyr Val Tyr
            475                 480                 485

aaa gct ctt ggc gta gtg gct cct aaa gtg ctc tct agt cgc acc ttc    13962
Lys Ala Leu Gly Val Val Ala Pro Lys Val Leu Ser Ser Arg Thr Phe
        490                 495                 500

taa acatgtccat cctcatctct cccgataaca acaccggctg gggactgggc         14015

tccggcaaga tgtacggcgg agccaaaagg cgctccagtc agcacccagt tcgagttcgg  14075

ggccacttcc gtgctccctg gggagcttac aagcgaggac tctcgggccg aacggcggta  14135

gacgatacca tagatgccgt gattgccgac gcccgccggt acaaccccgg accggtcgct  14195

agcgccgcct ccaccgtgga ttccgtgatc gacagcgtgg tagctggcgc tcgggcctat  14255

gctcgccgca agaggcggct gcatcggaga cgtcgcccca ccgccgccat gctggcagcc  14315

agggccgtgc tgaggcgggc ccggagggta ggcagaaggg ctatgcgccg cgctgccgcc  14375

aacgccgccg ccgggagggc ccgccgacag gctgcccgcc aggctgctgc cgccatcgct  14435

agcatggcca gacccaggag agggaacgtg tactgggtgc gcgattctgt gacgggagtc  14495

cgagtgccgg tgcgcagccg acctccccga agttagaaga tccaagctgc gaagacggcg  14555

gtactgagtc tccctgttgt tatcagccca acatgagcaa gcgcaagttt aaagaagaac  14615
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ccttgaaaga gggcgcctct ccaccctacc caatgacaaa accgatcgcg cctatggctc  16475

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gagtgaaaag cctgaaacgc cgccgttgct attattaaaa gtgtagctaa aaaatttccc  16775

gttgtatacg cctcctatgt taccgccaga gacgcgtgac tgtcgccgcg agcgccgctt  16835

tcaag atg gcc acc cca tcg atg atg ccg cag tgg tct tac atg cac atc  16885
      Met Ala Thr Pro Ser Met Met Pro Gln Trp Ser Tyr Met His Ile
          505                 510                 515

gcc ggg cag gac gcc tcg gag tac ctg agc ccc ggt ctc gtg cag ttc    16933
Ala Gly Gln Asp Ala Ser Glu Tyr Leu Ser Pro Gly Leu Val Gln Phe
    520                 525                 530

gcc cgc gcc acc gac acc tac ttc agc ttg gga aac aag ttt aga aac    16981
Ala Arg Ala Thr Asp Thr Tyr Phe Ser Leu Gly Asn Lys Phe Arg Asn
535                 540                 545                 550

ccc acc gtg gcc ccc acc cac gat gta acc acg gac cgc tcg caa agg    17029
Pro Thr Val Ala Pro Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg
                555                 560                 565

ctg acc ctg cgt ttt gtg ccc gta gac cgg gag gac acc gcg tac tct    17077
Leu Thr Leu Arg Phe Val Pro Val Asp Arg Glu Asp Thr Ala Tyr Ser
            570                 575                 580

tac aaa gtg cgc tac acg ctg gcc gta ggg gac aac cga gtg ctg gac    17125
Tyr Lys Val Arg Tyr Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp
        585                 590                 595

atg gcc agc acc tac ttt gac atc cgg gga gtg ctg gat cgc ggt ccc    17173
Met Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro
    600                 605                 610

agt ttt aag ccc tac tcg ggt acc gcg tac aat tcc ctg gct ccc aag    17221
Ser Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ser Leu Ala Pro Lys
615                 620                 625                 630

ggc gct ccc aac cct gca gaa tgg acg aat tca gac agc aaa gtt aaa    17269
Gly Ala Pro Asn Pro Ala Glu Trp Thr Asn Ser Asp Ser Lys Val Lys
                635                 640                 645

gtg agg gca cag gcg cct ttt gtt agc tcg tat ggt gct aca gcg att    17317
Val Arg Ala Gln Ala Pro Phe Val Ser Ser Tyr Gly Ala Thr Ala Ile
            650                 655                 660
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aca aaa gag ggt att cag gtg gga gta acc tta aca gac tcc gga tca    17365
Thr Lys Glu Gly Ile Gln Val Gly Val Thr Leu Thr Asp Ser Gly Ser
        665                 670                 675

aca cca cag tat gca gat aaa acg tat cag cct gag ccg caa att gga    17413
Thr Pro Gln Tyr Ala Asp Lys Thr Tyr Gln Pro Glu Pro Gln Ile Gly
    680                 685                 690

gaa cta cag tgg aac agc gat gtt gga acc gat gac aaa ata gca gga    17461
Glu Leu Gln Trp Asn Ser Asp Val Gly Thr Asp Asp Lys Ile Ala Gly
695                 700                 705                 710

aga gtg cta aag aaa aca acg ccc atg ttc cct tgt tac ggc tca tat    17509
Arg Val Leu Lys Lys Thr Thr Pro Met Phe Pro Cys Tyr Gly Ser Tyr
                715                 720                 725

gcc agg ccc act aat gaa aaa gga gga cag gca aca ccg tcc gct agt    17557
Ala Arg Pro Thr Asn Glu Lys Gly Gly Gln Ala Thr Pro Ser Ala Ser
            730                 735                 740

caa gac gtg caa aat ccc gaa tta caa ttt ttt gcc tct act aat gtc    17605
Gln Asp Val Gln Asn Pro Glu Leu Gln Phe Phe Ala Ser Thr Asn Val
        745                 750                 755

gcc aat aca cca aaa gca gtt cta tat gcg gag gac gtg tca att gaa    17653
Ala Asn Thr Pro Lys Ala Val Leu Tyr Ala Glu Asp Val Ser Ile Glu
    760                 765                 770

gcg cca gac act cac ttg gtg ttc aaa cca aca gtc act gaa ggc att    17701
Ala Pro Asp Thr His Leu Val Phe Lys Pro Thr Val Thr Glu Gly Ile
775                 780                 785                 790

aca agt tca gag gct cta ctg acc caa caa gct gct ccc aac cgt cca    17749
Thr Ser Ser Glu Ala Leu Leu Thr Gln Gln Ala Ala Pro Asn Arg Pro
                795                 800                 805

aac tac ata gcc ttt aga gat aat ttt att ggt ctc atg tac tac aat    17797
Asn Tyr Ile Ala Phe Arg Asp Asn Phe Ile Gly Leu Met Tyr Tyr Asn
            810                 815                 820

agc aca ggt aac atg gga gta ctg gca ggc cag gct tct cag cta aat    17845
Ser Thr Gly Asn Met Gly Val Leu Ala Gly Gln Ala Ser Gln Leu Asn
        825                 830                 835

gca gtt gtt gac ctg caa gac aga aat act gag ctg tcc tac caa ctc    17893
Ala Val Val Asp Leu Gln Asp Arg Asn Thr Glu Leu Ser Tyr Gln Leu
    840                 845                 850

atg ttg gac gcc ctc gga gac cgc agt cgg tac ttt tct atg tgg aac    17941
Met Leu Asp Ala Leu Gly Asp Arg Ser Arg Tyr Phe Ser Met Trp Asn
855                 860                 865                 870

caa gct gtg gat agt tac gat cct gat gta aga atc ata gaa aac cat    17989
Gln Ala Val Asp Ser Tyr Asp Pro Asp Val Arg Ile Ile Glu Asn His
                875                 880                 885
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ggc gta gaa gat gaa ttg cct aat tat tgc ttt cct ttg gga ggc atg    18037
Gly Val Glu Asp Glu Leu Pro Asn Tyr Cys Phe Pro Leu Gly Gly Met
            890                 895                 900

gca gta acc gac acc tac tcg cct ata aag gtt aat gga gga ggc aat    18085
Ala Val Thr Asp Thr Tyr Ser Pro Ile Lys Val Asn Gly Gly Gly Asn
        905                 910                 915

gga tgg gaa gcc aat aac ggc gtt ttc acc gaa aga gga gtg gaa ata    18133
Gly Trp Glu Ala Asn Asn Gly Val Phe Thr Glu Arg Gly Val Glu Ile
    920                 925                 930

ggt tca ggg aac atg ttt gcc atg gag att aac ctg caa gcc aac cta    18181
Gly Ser Gly Asn Met Phe Ala Met Glu Ile Asn Leu Gln Ala Asn Leu
935                 940                 945                 950

tgg cgt agc ttt ctg tac tcc aat att ggg ctg tac ctg cca gac tct    18229
Trp Arg Ser Phe Leu Tyr Ser Asn Ile Gly Leu Tyr Leu Pro Asp Ser
                955                 960                 965

ctc aaa atc act cct gac aac atc aca ctc cca gag aac aaa aac acc    18277
Leu Lys Ile Thr Pro Asp Asn Ile Thr Leu Pro Glu Asn Lys Asn Thr
            970                 975                 980

tat cag tat atg aac ggt cgc gtg acg cca ccc ggg ctg gtt gac acc    18325
Tyr Gln Tyr Met Asn Gly Arg Val Thr Pro Pro Gly Leu Val Asp Thr
        985                 990                 995

tac gtt  aac gtg ggc gcg cgc  tgg tcc ccc gat gtc  atg gac agt     18370
Tyr Val  Asn Val Gly Ala Arg  Trp Ser Pro Asp Val  Met Asp Ser
    1000                1005                1010

att aac  cct ttt aat cac cac  cgc aac gcc gga ctc  cgc tac cgt     18415
Ile Asn  Pro Phe Asn His His  Arg Asn Ala Gly Leu  Arg Tyr Arg
    1015                1020                1025

tcc atg  ctc ctg gga aac gga  cgc tac gtg ccc ttc  cac atc cag     18460
Ser Met  Leu Leu Gly Asn Gly  Arg Tyr Val Pro Phe  His Ile Gln
    1030                1035                1040

gtg ccc  cag aaa ttc ttt gca  att aaa aac ctg ctg  ctg ctc ccc     18505
Val Pro  Gln Lys Phe Phe Ala  Ile Lys Asn Leu Leu  Leu Leu Pro
    1045                1050                1055

ggt tcc  tac acc tac gag tgg  aac ttc cgc aag gac  gtg aac atg     18550
Gly Ser  Tyr Thr Tyr Glu Trp  Asn Phe Arg Lys Asp  Val Asn Met
    1060                1065                1070

atc ttg  cag agc tcg ctg ggc  aat gac ctg cga gtg  gac ggg gcc     18595
Ile Leu  Gln Ser Ser Leu Gly  Asn Asp Leu Arg Val  Asp Gly Ala
    1075                1080                1085

agc atc  cgc ttc gac agc atc  aac ctg tac gcc aac  ttt ttc ccc     18640
Ser Ile  Arg Phe Asp Ser Ile  Asn Leu Tyr Ala Asn  Phe Phe Pro
    1090                1095                1100
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atg gcc  cac aac acg gcc tcc  acc ctg gaa gcc atg  ctg cgc aac     18685
Met Ala  His Asn Thr Ala Ser  Thr Leu Glu Ala Met  Leu Arg Asn
    1105                 1110                 1115

gac acc  aac gac caa tct ttc  aac gac tac ctg tgc  gcg gcc aac     18730
Asp Thr  Asn Asp Gln Ser Phe  Asn Asp Tyr Leu Cys  Ala Ala Asn
    1120                 1125                 1130

atg ctg  tac ccc atc ccc gcc  aac gcc acc agc gtg  ccc atc tcc     18775
Met Leu  Tyr Pro Ile Pro Ala  Asn Ala Thr Ser Val  Pro Ile Ser
    1135                 1140                 1145

att ccc  tct cgc aac tgg gca  gcc ttc agg ggc tgg  agt ttc acc     18820
Ile Pro  Ser Arg Asn Trp Ala  Ala Phe Arg Gly Trp  Ser Phe Thr
    1150                 1155                 1160

cgc ctc  aaa acc aag gag acc  ccc tcg ctg ggc tcc  ggg ttc gac     18865
Arg Leu  Lys Thr Lys Glu Thr  Pro Ser Leu Gly Ser  Gly Phe Asp
    1165                 1170                 1175

ccc tac  ttc gtc tac tcc ggc  tcc atc ccc tac ctg  gac ggc acc     18910
Pro Tyr  Phe Val Tyr Ser Gly  Ser Ile Pro Tyr Leu  Asp Gly Thr
    1180                 1185                 1190

ttc tac  ctc aac cat act ttc  aaa aag gtg tca atc  atg ttc gac     18955
Phe Tyr  Leu Asn His Thr Phe  Lys Lys Val Ser Ile  Met Phe Asp
    1195                 1200                 1205

tcc tcc  gtc agc tgg ccc ggc  aac gac cgt ctg ctg  acg ccc aac     19000
Ser Ser  Val Ser Trp Pro Gly  Asn Asp Arg Leu Leu  Thr Pro Asn
    1210                 1215                 1220

gag ttc  gaa atc aag cgt tcg  gtg gac ggt gaa ggg  tac aac gtg     19045
Glu Phe  Glu Ile Lys Arg Ser  Val Asp Gly Glu Gly  Tyr Asn Val
    1225                 1230                 1235

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Ala Gln  Ser Asn Met Thr Lys  Asp Trp Phe Leu Ile  Gln Met Leu
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agc cac  tac aac atc ggc tac  cag ggc ttc tac gtg  ccc gaa aat     19135
Ser His  Tyr Asn Ile Gly Tyr  Gln Gly Phe Tyr Val  Pro Glu Asn
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tac aag  gac cgc atg tac tct  ttc ttc aga aac ttc  caa ccc atg     19180
Tyr Lys  Asp Arg Met Tyr Ser  Phe Phe Arg Asn Phe  Gln Pro Met
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agc cgc  caa att gta gat tca  acg gct tac act aat  tat cag gat     19225
Ser Arg  Gln Ile Val Asp Ser  Thr Ala Tyr Thr Asn  Tyr Gln Asp
    1285                 1290                 1295

gtg aaa  ctg cca tac cag cat  aac aac tca ggg ttc  gtg ggc tac     19270
Val Lys  Leu Pro Tyr Gln His  Asn Asn Ser Gly Phe  Val Gly Tyr
    1300                 1305                 1310
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Met Gly  Pro Thr Met Arg Glu  Gly Gln Ala Tyr Pro  Ala Asn Tyr
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ccc tat  ccc ctg att ggg gcc  acc gcc gtg ccc agc  ctc acg cag     19360
Pro Tyr  Pro Leu Ile Gly Ala  Thr Ala Val Pro Ser  Leu Thr Gln
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aaa aag  ttc ctc tgc gac cgg  gtg atg tgg agg atc  ccc ttc tct     19405
Lys Lys  Phe Leu Cys Asp Arg  Val Met Trp Arg Ile  Pro Phe Ser
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agc aac  ttc atg tct atg ggc  tcc ctc acc gac ctg  ggg cag aac     19450
Ser Asn  Phe Met Ser Met Gly  Ser Leu Thr Asp Leu  Gly Gln Asn
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atg ctg  tac gcc aac tcc gct  cac gcc ttg gat atg  acc ttt gag     19495
Met Leu  Tyr Ala Asn Ser Ala  His Ala Leu Asp Met  Thr Phe Glu
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gtg gat  ccc atg gat gag ccc  acg ctt ctc tat gtt  ctg ttt gaa     19540
Val Asp  Pro Met Asp Glu Pro  Thr Leu Leu Tyr Val  Leu Phe Glu
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Val Phe  Asp Val Val Arg Ile  His Gln Pro His Arg  Gly Val Ile
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gag gcc  gtc tac ctg cgc aca  cct ttc tct gcc ggt  aac gcc acc     19630
Glu Ala  Val Tyr Leu Arg Thr  Pro Phe Ser Ala Gly  Asn Ala Thr
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Thr
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                                    Met  Lys Arg Thr Arg Val  Asp
                                    1435                1440

gaa gac ttc aac  ccc gtc tac ccc tat  gac acc aca acc act  cct     28124
Glu Asp Phe Asn  Pro Val Tyr Pro Tyr  Asp Thr Thr Thr Thr  Pro
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gca gtt ccc ttt  ata tca ccc ccc ttt  gta aac agc gat ggt  ctt     28169
Ala Val Pro Phe  Ile Ser Pro Pro Phe  Val Asn Ser Asp Gly  Leu
            1460                1465                1470

cag gaa aac ccc  cca ggt gtt tta agt  ctg cga ata gct aaa  ccc     28214
Gln Glu Asn Pro  Pro Gly Val Leu Ser  Leu Arg Ile Ala Lys  Pro
            1475                1480                1485

cta tat ttc gac  atg gag aga aaa cta  gcc ctt tca ctt gga  aga     28259
Leu Tyr Phe Asp  Met Glu Arg Lys Leu  Ala Leu Ser Leu Gly  Arg
            1490                1495                1500

ggg ttg aca att  acc gcc gcc gga caa  tta gaa agt acg cag  agc     28304
Gly Leu Thr Ile  Thr Ala Ala Gly Gln  Leu Glu Ser Thr Gln  Ser
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gta caa acc aac  cca ccg ttg ata att  acc aac aac aac aca  ctg     28349
Val Gln Thr Asn  Pro Pro Leu Ile Ile  Thr Asn Asn Asn Thr  Leu
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Val Leu Gly Tyr  Ser Ser Pro Leu Arg  Val Thr Asp Asn Lys  Leu
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aca ttt aac ttc  aca tca cca ctc cgt  tat gaa aat gaa aac  ctt     28484
Thr Phe Asn Phe  Thr Ser Pro Leu Arg  Tyr Glu Asn Glu Asn  Leu
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act ttt aac tat  aca gag cct ctt aaa  ctt ata aat aac agc  ctt     28529
Thr Phe Asn Tyr  Thr Glu Pro Leu Lys  Leu Ile Asn Asn Ser  Leu
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gcc att gac atc  aat tcc tca aaa ggc  ctt agt agc gtc gga  ggc     28574
Ala Ile Asp Ile  Asn Ser Ser Lys Gly  Leu Ser Ser Val Gly  Gly
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Ser Leu Ala Val  Asn Leu Ser Ser Asp  Leu Lys Phe Asp Ser  Asn
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gga tcc ata gct  ttt ggc ata caa acc  ctg tgg acc gct ccg  acc     28664
Gly Ser Ile Ala  Phe Gly Ile Gln Thr  Leu Trp Thr Ala Pro  Thr
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tcg act ggc aac  tgc acc gtc tac agc  gag ggc gat tcc cta  ctt     28709
Ser Thr Gly Asn  Cys Thr Val Tyr Ser  Glu Gly Asp Ser Leu  Leu
            1640                 1645                 1650

agt ctc tgt tta  acc aaa tgc gga gct  cac gtc tta gga agt  gta     28754
Ser Leu Cys Leu  Thr Lys Cys Gly Ala  His Val Leu Gly Ser  Val
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agt tta acc ggt  tta aca gga acc ata  acc caa atg act gat  att     28799
Ser Leu Thr Gly  Leu Thr Gly Thr Ile  Thr Gln Met Thr Asp  Ile
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Ser Val Thr Ile  Gln Phe Thr Phe Asp  Asn Asn Gly Lys Leu  Leu
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Ser Ser Pro Leu  Ile Asn Asn Ala Phe  Ser Ile Arg Gln Asn  Asp
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agt acg gcc tca  aac cct acc tac aac  gcc ctg gcg ttt atg  cct     28934
Ser Thr Ala Ser  Asn Pro Thr Tyr Asn  Ala Leu Ala Phe Met  Pro
            1715                 1720                 1725

aac agt acc ata  tat gca aga ggg gga  ggt ggt gaa cca cga  aac     28979
Asn Ser Thr Ile  Tyr Ala Arg Gly Gly  Gly Gly Glu Pro Arg  Asn
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Ile Ile Leu Thr  Val Thr Tyr Asn Ser  Val Ala Thr Gly Tyr  Ser
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Leu Ser Phe Lys  Trp Thr Ala Leu Ala  Arg Glu Lys Phe Ala  Thr
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cca aca acc tcg  ttt tgc tac att aca  gaa caa taa aaccgtgtac       29160
Pro Thr Thr Ser  Phe Cys Tyr Ile Thr  Glu Gln
            1790                 1795

cccaccgttt cgttttttc ag atg aaa cgg  gcg aga gtt gat gaa  gac      29209
                         Met Lys Arg  Ala Arg Val Asp Glu  Asp
                                 1800                 1805

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Phe Asn Pro Val  Tyr Pro Tyr Asp Pro  Pro His Ala Pro Val  Met
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Pro Phe Ile Thr  Pro Pro Phe Thr Ser  Ser Asp Gly Leu Gln  Glu
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Lys Pro Leu Gly  Val Leu Ser Leu Asn  Tyr Arg Asp Pro Ile  Thr
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Thr Gln Asn Glu  Ser Leu Thr Ile Lys  Leu Gly Asn Gly Leu  Thr
            1855                 1860                 1865

cta gac aac cag  gga caa cta aca tca  acc gct ggc gaa gta  gaa      29434
Leu Asp Asn Gln  Gly Gln Leu Thr Ser  Thr Ala Gly Glu Val  Glu
            1870                 1875                 1880

cct cca ctc act  aac gct aac aac aaa  ctt gca ctg gtc tat  agc      29479
Pro Pro Leu Thr  Asn Ala Asn Asn Lys  Leu Ala Leu Val Tyr  Ser
            1885                 1890                 1895

gat cct tta gca  gta aag cgc aac agc  cta acc tta tcg cac  acc      29524
Asp Pro Leu Ala  Val Lys Arg Asn Ser  Leu Thr Leu Ser His  Thr
            1900                 1905                 1910

gct ccc ctt gtt  att gct gat aac tct  tta gca ttg caa gtt  tca      29569
Ala Pro Leu Val  Ile Ala Asp Asn Ser  Leu Ala Leu Gln Val  Ser
            1915                 1920                 1925

gag cct att ttt  ata aat gac aag gac  aaa cta gcc ctg caa  aca      29614
Glu Pro Ile Phe  Ile Asn Asp Lys Asp  Lys Leu Ala Leu Gln  Thr
            1930                 1935                 1940
```

```
gcc gcg ccc ctt  gta act aac gct ggc  acc ctt cgc tta caa  agc      29659
Ala Ala Pro Leu  Val Thr Asn Ala Gly  Thr Leu Arg Leu Gln  Ser
            1945                 1950                 1955

gcc gcc cct tta  ggc att gca gac caa  acc cta aaa ctc ctg  ttt      29704
Ala Ala Pro Leu  Gly Ile Ala Asp Gln  Thr Leu Lys Leu Leu  Phe
            1960                 1965                 1970

acc aac cct ttg  tac ttg cag aat aac  ttt ctc acg tta gcc  att      29749
Thr Asn Pro Leu  Tyr Leu Gln Asn Asn  Phe Leu Thr Leu Ala  Ile
            1975                 1980                 1985

gaa cga ccc ctt  gcc att acc aat act  gga aag ctg gct cta  cag      29794
Glu Arg Pro Leu  Ala Ile Thr Asn Thr  Gly Lys Leu Ala Leu  Gln
            1990                 1995                 2000

ctc tcc cca ccg  cta caa aca gca gac  aca ggc ttg act ttg  caa      29839
Leu Ser Pro Pro  Leu Gln Thr Ala Asp  Thr Gly Leu Thr Leu  Gln
            2005                 2010                 2015

acc aac gtg cca  tta act gta agc aac  ggg acc cta ggc tta  gcc      29884
Thr Asn Val Pro  Leu Thr Val Ser Asn  Gly Thr Leu Gly Leu  Ala
            2020                 2025                 2030

ata aag cgc cca  ctt att att cag gac  aac aac ttg ttt ttg  gac      29929
Ile Lys Arg Pro  Leu Ile Ile Gln Asp  Asn Asn Leu Phe Leu  Asp
            2035                 2040                 2045

ttc aga gct ccc  ctg cgt ctt ttc aac  agc gac cca gta cta  ggg      29974
Phe Arg Ala Pro  Leu Arg Leu Phe Asn  Ser Asp Pro Val Leu  Gly
            2050                 2055                 2060

ctt aac ttt tac  acc cct ctt gcg gta  cgc gat gag gcg ctc  act      30019
Leu Asn Phe Tyr  Thr Pro Leu Ala Val  Arg Asp Glu Ala Leu  Thr
            2065                 2070                 2075

gtt aac aca ggc  cgc ggc ctc aca gtg  agt tac gat ggt tta  att      30064
Val Asn Thr Gly  Arg Gly Leu Thr Val  Ser Tyr Asp Gly Leu  Ile
            2080                 2085                 2090

tta aat ctt ggt  aag gat ctt cgc ttt  gac aac aac acc gtt  tct      30109
Leu Asn Leu Gly  Lys Asp Leu Arg Phe  Asp Asn Asn Thr Val  Ser
            2095                 2100                 2105

gtc gct ctt agt  gct gct ttg cct tta  caa tac act gat cag  ctt      30154
Val Ala Leu Ser  Ala Ala Leu Pro Leu  Gln Tyr Thr Asp Gln  Leu
            2110                 2115                 2120

cgc ctt aac gtg  ggc gct ggg ctg cgt  tac aat cca gtg agt  aag      30199
Arg Leu Asn Val  Gly Ala Gly Leu Arg  Tyr Asn Pro Val Ser  Lys
            2125                 2130                 2135

aaa ttg gac gtg  aac ccc aat caa aac  aag ggt tta acc tgg  gaa      30244
Lys Leu Asp Val  Asn Pro Asn Gln Asn  Lys Gly Leu Thr Trp  Glu
            2140                 2145                 2150
```

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aat gac tac ctc  att gta aag cta gga  aat gga tta ggt ttt  gat     30289
Asn Asp Tyr Leu  Ile Val Lys Leu Gly  Asn Gly Leu Gly Phe  Asp
            2155                 2160                 2165

ggc gat gga aac  ata gct gtt tct cct  caa gtt aca tcg cct  gac     30334
Gly Asp Gly Asn  Ile Ala Val Ser Pro  Gln Val Thr Ser Pro  Asp
            2170                 2175                 2180

acc tta tgg acc  act gcc gac cca tcc  ccc aat tgt tcc atc  tac     30379
Thr Leu Trp Thr  Thr Ala Asp Pro Ser  Pro Asn Cys Ser Ile  Tyr
            2185                 2190                 2195

act gat tta gat  gcc aaa atg tgg ctc  tcg ttg gta aaa caa  ggg     30424
Thr Asp Leu Asp  Ala Lys Met Trp Leu  Ser Leu Val Lys Gln  Gly
            2200                 2205                 2210

ggt gtg gtt cac  ggt tct gtt gct tta  aaa gca ttg aaa gga  acc     30469
Gly Val Val His  Gly Ser Val Ala Leu  Lys Ala Leu Lys Gly  Thr
            2215                 2220                 2225

cta ttg agt cct  acg gaa agc gcc att  gtt att ata cta cat  ttt     30514
Leu Leu Ser Pro  Thr Glu Ser Ala Ile  Val Ile Ile Leu His  Phe
            2230                 2235                 2240

gac aat tat gga  gtg cga att ctc aat  tat ccc act ttg ggc  act     30559
Asp Asn Tyr Gly  Val Arg Ile Leu Asn  Tyr Pro Thr Leu Gly  Thr
            2245                 2250                 2255

caa ggc acg ttg  gga aat aat gca act  tgg ggt tat agg cag  gga     30604
Gln Gly Thr Leu  Gly Asn Asn Ala Thr  Trp Gly Tyr Arg Gln  Gly
            2260                 2265                 2270

gaa tct gca gac  act aat gta ctc aat  gca cta gca ttt atg  ccc     30649
Glu Ser Ala Asp  Thr Asn Val Leu Asn  Ala Leu Ala Phe Met  Pro
            2275                 2280                 2285

agt tca aaa agg  tac cca aga ggg cgt  gga agc gaa gtt cag  aat     30694
Ser Ser Lys Arg  Tyr Pro Arg Gly Arg  Gly Ser Glu Val Gln  Asn
            2290                 2295                 2300

caa act gtg ggc  tac act tgt ata cag  ggt gac ttt tct atg  ccc     30739
Gln Thr Val Gly  Tyr Thr Cys Ile Gln  Gly Asp Phe Ser Met  Pro
            2305                 2310                 2315

gta ccg tac caa  ata cag tac aac tat  gga cca act ggc tac  tcc     30784
Val Pro Tyr Gln  Ile Gln Tyr Asn Tyr  Gly Pro Thr Gly Tyr  Ser
            2320                 2325                 2330

ttt aaa ttt att  tgg aga act gtt tca  aga caa cca ttt gac  atc     30829
Phe Lys Phe Ile  Trp Arg Thr Val Ser  Arg Gln Pro Phe Asp  Ile
            2335                 2340                 2345

cca tgc tgt ttt  ttc tct tac att acg  gaa gaa taa aacaactttt      30875
Pro Cys Cys Phe  Phe Ser Tyr Ile Thr  Glu Glu
            2350                 2355

tctttttatt ttctttttat tttacacgca cagtaaggct tcctccaccc ttccatctca  30935
```

cagcatacac cagcctctcc cccttcatgg cagtaaactg ttgtgagtca gtccggtatt 30995

tgggagttaa gatccaaaca gtctctttgg tgatgaaaca tggatccgtg atggacacaa 31055

atccctggga caggttctcc aacgtttcgg taaaaaactg catgccgccc tacaaaacaa 31115

acaggttcag gctctccacg ggttatctcc ccgatcaaac tcagacagag taaaggtgcg 31175

atgatgttcc actaaaccac gcaggtggcg ctgtctgaac ctctcggtgc gactcctgtg 31235

aggctggtaa gaagttagat tgtccagcag cctcacagca tggatcatca gtctacgagt 31295

gcgtctggcg cagcagcgca tctgaatctc actgagattc cggcaagaat cgcacaccat 31355

cacaatcagg ttgttcatga tcccatagct gaacacgctc cagccaaagc tcattcgctc 31415

caacagcgcc accgcgtgtc cgtccaacct tactttaaca taaatcaggt gtctgccgcg 31475

tacaaacatg ctacccgcat acagaacctc ccggggcaaa cccctgttca ccacctgcct 31535

gtaccaggga aacctcacat ttatcaggga gccatagata gccattttaa accaattagc 31595

taacaccgcc ccaccagctc tacactgaag agaaccggga gagttacaat gacagtgaat 31655

aatccatctc tcataacccc taatggtctg atggaaatcc agatctaacg tggcacagca 31715

gatacacact ttcatataca ttttcatcac atgtttttcc caggccgtta aaatacaatc 31775

ccaatacacg ggccactcct gcagtacaat aaagctaata caagatggta tactcctcac 31835

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gcagcgatac cgtctgtcgc gttgcatcgt agaccaggga ccgacgcact tcctcgtact 32015

tgtagtagca gaaccacgtc cgctgccagc acgtctccaa gtaacgccgg tccctgcgtc 32075

gctcacgctc cctcctcaac gcaaagtgca accactcttg taatccacac agatccctct 32135

cggcctccgg ggcgatgcac acctcaaacc tacagatgtc tcggtacagt tccaaacacg 32195

tagtgagggc gagttccaac caagacagac agcctgatct atcccgacac actggaggtg 32255

gaggaagaca cggaagaggc atgttattcc aagcgattca ccaacgggtc gaaatgaaga 32315

tcccgaagat gacaacggtc gcctccggag ccctgatgga atttaacagc cagatcaaac 32375

attatgcgat tttccaggct atcaatcgcg gcctccaaaa gagcctggac ccgcacttcc 32435

acaaacacca gcaaagcaaa agcgttatta tcaaactctt cgatcatcaa gctgcaggac 32495

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agacacacca tcatgactgc aagatatcgg gctcctgaga cacctgcagc agatttaaca 32675

gacccaggtc aggttgctct ccgcgatcgc gaatctccat ccgcaaagtc atttgcaaat 32735

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gctcctttaa aaagtccagt acttctatat tcagttcgtg caagtactga agcaactgtg 32975

cgggaatatg cacagcaaaa aaaatagggc ggctcagata catgttgacc taaaataaaa 33035

agaatcatta aactaaagaa gcctggcgaa cggtgggata tatgacacgc tccagcagca 33095

ggcaagcaac cggctgtccc cgggaaccgc ggtaaaattc atccgaatga ttaaaaagaa 33155

caacagagac ttcccaccat gtactcggtt ggatctcctg agcacagagc aataccccc 33215

tcacattcat atccgctaca gaaaaaaaac gtcccagata cccagcggga atatccaacg 33275

acagctgcaa agacagcaaa acaatccctc tgggagcaat cacaaaatcc tccggtgaaa 33335

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aatgcacata aatatgttca tcagccattg ccccgtctta ccgcgtaaac agccacgaaa 33455

aaatcgagct aaaatccacc caacagccta tagctatata tacactccac ccaatgacgc 33515

taataccgca ccacccacga ccaaagttca cccacaccca caaaacccgc gaaaatccag 33575

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cacgtcaccc cggccccgcc tcgctcctcc ccgctcatta tcatattggc acgtttccag 33755

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ggtgaaaaaa gcacatacat attagaataa ccctgttgct ggggcaaaaa ggcccgtcgt 33875

cccagcaaat gcacataaat atgttcatca gccattgccc cgtcttaccg cgtaaacagc 33935

cacgaaaaaa tcgagctaaa atccacccaa cagcctatag ctatatatac actccaccca 33995

atgacgctaa taccgcacca cccacgacca aagttcaccc acacccacaa aacccgcgaa 34055

aatccagcgc cgtcagcact tccgcaattt cagtctcaca acgtcacttc cgcgcgcctt 34115

ttcactttcc cacacacgcc cttcgcccgc ccgccctcgc gccaccccgc gtcaccccac 34175

gtcaccgcac gtcaccccgg ccccgcctcg ctcctccccg ctcattatca tattggcacg 34235

tttccagaat aaggtatatt attgatgca 34264

<210> 25
<211> 503
<212> PRT
<213> simian adenovirus SV-1

<400> 25

```
Met Arg Arg Ala Val Arg Val Thr Pro Ala Ala Tyr Glu Gly Pro Pro
1               5                  10                  15

Pro Ser Tyr Glu Ser Val Met Gly Ser Ala Asn Val Pro Ala Thr Leu
            20                  25                  30

Glu Ala Pro Tyr Val Pro Pro Arg Tyr Leu Gly Pro Thr Glu Gly Arg
        35                  40                  45

Asn Ser Ile Arg Tyr Ser Glu Leu Ala Pro Leu Tyr Asp Thr Thr Lys
    50                  55                  60

Val Tyr Leu Val Asp Asn Lys Ser Ala Asp Ile Ala Ser Leu Asn Tyr
65                  70                  75                  80

Gln Asn Asp His Ser Asn Phe Leu Thr Thr Val Val Gln Asn Asn Asp
                85                  90                  95

Phe Thr Pro Thr Glu Ala Gly Thr Gln Thr Ile Asn Phe Asp Glu Arg
            100                 105                 110

Ser Arg Trp Gly Gly Gln Leu Lys Thr Ile Leu His Thr Asn Met Pro
        115                 120                 125

Asn Ile Asn Glu Phe Met Ser Thr Asn Lys Phe Arg Ala Arg Leu Met
    130                 135                 140

Val Lys Lys Ala Glu Asn Gln Pro Pro Glu Tyr Glu Trp Phe Glu Phe
145                 150                 155                 160

Thr Ile Pro Glu Gly Asn Tyr Ser Glu Thr Met Thr Ile Asp Leu Met
                165                 170                 175

Asn Asn Ala Ile Val Asp Asn Tyr Leu Gln Val Gly Arg Gln Asn Gly
            180                 185                 190

Val Leu Glu Ser Asp Ile Gly Val Lys Phe Asp Thr Arg Asn Phe Arg
        195                 200                 205

Leu Gly Trp Asp Pro Val Thr Lys Leu Val Met Pro Gly Val Tyr Thr
    210                 215                 220

Asn Glu Ala Phe His Pro Asp Ile Val Leu Leu Pro Gly Cys Gly Val
225                 230                 235                 240

Asp Phe Thr Gln Ser Arg Leu Ser Asn Leu Leu Gly Ile Arg Lys Arg
                245                 250                 255

Arg Pro Phe Gln Glu Gly Phe Gln Ile Met Tyr Glu Asp Leu Glu Gly
            260                 265                 270
```

```
Gly Asn Ile Pro Gly Leu Leu Asp Val Pro Ala Tyr Glu Glu Ser Val
        275                 280                 285

Lys Gln Ala Glu Ala Gln Gly Arg Glu Ile Arg Gly Asp Thr Phe Ala
    290                 295                 300

Thr Glu Pro His Glu Leu Val Ile Lys Pro Leu Glu Gln Asp Ser Lys
305                 310                 315                 320

Lys Arg Ser Tyr Asn Ile Ile Ser Gly Thr Met Asn Thr Leu Tyr Arg
                325                 330                 335

Ser Trp Phe Leu Ala Tyr Asn Tyr Gly Asp Pro Glu Lys Gly Val Arg
            340                 345                 350

Ser Trp Thr Ile Leu Thr Thr Thr Asp Val Thr Cys Gly Ser Gln Gln
        355                 360                 365

Val Tyr Trp Ser Leu Pro Asp Met Met Gln Asp Pro Val Thr Phe Arg
    370                 375                 380

Pro Ser Thr Gln Val Ser Asn Phe Pro Val Val Gly Thr Glu Leu Leu
385                 390                 395                 400

Pro Val His Ala Lys Ser Phe Tyr Asn Glu Gln Ala Val Tyr Ser Gln
                405                 410                 415

Leu Ile Arg Gln Ser Thr Ala Leu Thr His Val Phe Asn Arg Phe Pro
            420                 425                 430

Glu Asn Gln Ile Leu Val Arg Pro Pro Ala Pro Thr Ile Thr Thr Val
        435                 440                 445

Ser Glu Asn Val Pro Ala Leu Thr Asp His Gly Thr Leu Pro Leu Arg
    450                 455                 460

Ser Ser Ile Ser Gly Val Gln Arg Val Thr Ile Thr Asp Ala Arg Arg
465                 470                 475                 480

Arg Thr Cys Pro Tyr Val Tyr Lys Ala Leu Gly Val Val Ala Pro Lys
                485                 490                 495

Val Leu Ser Ser Arg Thr Phe
            500
```

<210> 26
<211> 931
<212> PRT
<213> simian adenovirus SV-1

<400> 26

```
Met Ala Thr Pro Ser Met Met Pro Gln Trp Ser Tyr Met His Ile Ala
1               5                   10                  15
```

```
Gly Gln Asp Ala Ser Glu Tyr Leu Ser Pro Gly Leu Val Gln Phe Ala
            20                  25                  30

Arg Ala Thr Asp Thr Tyr Phe Ser Leu Gly Asn Lys Phe Arg Asn Pro
        35                  40                  45

Thr Val Ala Pro Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg Leu
    50                  55                  60

Thr Leu Arg Phe Val Pro Val Asp Arg Glu Asp Thr Ala Tyr Ser Tyr
65                  70                  75                  80

Lys Val Arg Tyr Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met
                85                  90                  95

Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro Ser
            100                 105                 110

Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ser Leu Ala Pro Lys Gly
        115                 120                 125

Ala Pro Asn Pro Ala Glu Trp Thr Asn Ser Asp Ser Lys Val Lys Val
    130                 135                 140

Arg Ala Gln Ala Pro Phe Val Ser Ser Tyr Gly Ala Thr Ala Ile Thr
145                 150                 155                 160

Lys Glu Gly Ile Gln Val Gly Val Thr Leu Thr Asp Ser Gly Ser Thr
                165                 170                 175

Pro Gln Tyr Ala Asp Lys Thr Tyr Gln Pro Glu Pro Gln Ile Gly Glu
            180                 185                 190

Leu Gln Trp Asn Ser Asp Val Gly Thr Asp Asp Lys Ile Ala Gly Arg
        195                 200                 205

Val Leu Lys Lys Thr Thr Pro Met Phe Pro Cys Tyr Gly Ser Tyr Ala
    210                 215                 220

Arg Pro Thr Asn Glu Lys Gly Gly Gln Ala Thr Pro Ser Ala Ser Gln
225                 230                 235                 240

Asp Val Gln Asn Pro Glu Leu Gln Phe Phe Ala Ser Thr Asn Val Ala
                245                 250                 255

Asn Thr Pro Lys Ala Val Leu Tyr Ala Glu Asp Val Ser Ile Glu Ala
            260                 265                 270

Pro Asp Thr His Leu Val Phe Lys Pro Thr Val Thr Glu Gly Ile Thr
        275                 280                 285

Ser Ser Glu Ala Leu Leu Thr Gln Gln Ala Ala Pro Asn Arg Pro Asn
    290                 295                 300

Tyr Ile Ala Phe Arg Asp Asn Phe Ile Gly Leu Met Tyr Tyr Asn Ser
305                 310                 315                 320
```

```
Thr Gly Asn Met Gly Val Leu Ala Gly Gln Ala Ser Gln Leu Asn Ala
                325                 330                 335

Val Val Asp Leu Gln Asp Arg Asn Thr Glu Leu Ser Tyr Gln Leu Met
            340                 345                 350

Leu Asp Ala Leu Gly Asp Arg Ser Arg Tyr Phe Ser Met Trp Asn Gln
        355                 360                 365

Ala Val Asp Ser Tyr Asp Pro Asp Val Arg Ile Ile Glu Asn His Gly
    370                 375                 380

Val Glu Asp Glu Leu Pro Asn Tyr Cys Phe Pro Leu Gly Gly Met Ala
385                 390                 395                 400

Val Thr Asp Thr Tyr Ser Pro Ile Lys Val Asn Gly Gly Gly Asn Gly
                405                 410                 415

Trp Glu Ala Asn Asn Gly Val Phe Thr Glu Arg Gly Val Glu Ile Gly
            420                 425                 430

Ser Gly Asn Met Phe Ala Met Glu Ile Asn Leu Gln Ala Asn Leu Trp
        435                 440                 445

Arg Ser Phe Leu Tyr Ser Asn Ile Gly Leu Tyr Leu Pro Asp Ser Leu
    450                 455                 460

Lys Ile Thr Pro Asp Asn Ile Thr Leu Pro Glu Asn Lys Asn Thr Tyr
465                 470                 475                 480

Gln Tyr Met Asn Gly Arg Val Thr Pro Pro Gly Leu Val Asp Thr Tyr
                485                 490                 495

Val Asn Val Gly Ala Arg Trp Ser Pro Asp Val Met Asp Ser Ile Asn
            500                 505                 510

Pro Phe Asn His His Arg Asn Ala Gly Leu Arg Tyr Arg Ser Met Leu
        515                 520                 525

Leu Gly Asn Gly Arg Tyr Val Pro Phe His Ile Gln Val Pro Gln Lys
    530                 535                 540

Phe Phe Ala Ile Lys Asn Leu Leu Leu Leu Pro Gly Ser Tyr Thr Tyr
545                 550                 555                 560

Glu Trp Asn Phe Arg Lys Asp Val Asn Met Ile Leu Gln Ser Ser Leu
                565                 570                 575

Gly Asn Asp Leu Arg Val Asp Gly Ala Ser Ile Arg Phe Asp Ser Ile
            580                 585                 590

Asn Leu Tyr Ala Asn Phe Phe Pro Met Ala His Asn Thr Ala Ser Thr
        595                 600                 605

Leu Glu Ala Met Leu Arg Asn Asp Thr Asn Asp Gln Ser Phe Asn Asp
    610                 615                 620
```

```
Tyr Leu Cys Ala Ala Asn Met Leu Tyr Pro Ile Pro Ala Asn Ala Thr
625                 630                 635                 640

Ser Val Pro Ile Ser Ile Pro Ser Arg Asn Trp Ala Ala Phe Arg Gly
                645                 650                 655

Trp Ser Phe Thr Arg Leu Lys Thr Lys Glu Thr Pro Ser Leu Gly Ser
            660                 665                 670

Gly Phe Asp Pro Tyr Phe Val Tyr Ser Gly Ser Ile Pro Tyr Leu Asp
        675                 680                 685

Gly Thr Phe Tyr Leu Asn His Thr Phe Lys Lys Val Ser Ile Met Phe
    690                 695                 700

Asp Ser Ser Val Ser Trp Pro Gly Asn Asp Arg Leu Leu Thr Pro Asn
705                 710                 715                 720

Glu Phe Glu Ile Lys Arg Ser Val Asp Gly Glu Gly Tyr Asn Val Ala
                725                 730                 735

Gln Ser Asn Met Thr Lys Asp Trp Phe Leu Ile Gln Met Leu Ser His
            740                 745                 750

Tyr Asn Ile Gly Tyr Gln Gly Phe Tyr Val Pro Glu Asn Tyr Lys Asp
        755                 760                 765

Arg Met Tyr Ser Phe Phe Arg Asn Phe Gln Pro Met Ser Arg Gln Ile
    770                 775                 780

Val Asp Ser Thr Ala Tyr Thr Asn Tyr Gln Asp Val Lys Leu Pro Tyr
785                 790                 795                 800

Gln His Asn Asn Ser Gly Phe Val Gly Tyr Met Gly Pro Thr Met Arg
                805                 810                 815

Glu Gly Gln Ala Tyr Pro Ala Asn Tyr Pro Tyr Pro Leu Ile Gly Ala
            820                 825                 830

Thr Ala Val Pro Ser Leu Thr Gln Lys Lys Phe Leu Cys Asp Arg Val
        835                 840                 845

Met Trp Arg Ile Pro Phe Ser Ser Asn Phe Met Ser Met Gly Ser Leu
    850                 855                 860

Thr Asp Leu Gly Gln Asn Met Leu Tyr Ala Asn Ser Ala His Ala Leu
865                 870                 875                 880

Asp Met Thr Phe Glu Val Asp Pro Met Asp Glu Pro Thr Leu Leu Tyr
                885                 890                 895

Val Leu Phe Glu Val Phe Asp Val Val Arg Ile His Gln Pro His Arg
            900                 905                 910
```

```
Gly Val Ile Glu Ala Val Tyr Leu Arg Thr Pro Phe Ser Ala Gly Asn
        915                 920                 925

Ala Thr Thr
    930
```

<210> 27
<211> 363
<212> PRT
<213> simian adenovirus SV-1

<400> 27

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Met Lys Arg Thr Arg Val Asp Glu Asp Phe Asn Pro Val Tyr Pro Tyr
1               5                  10                  15

Asp Thr Thr Thr Thr Pro Ala Val Pro Phe Ile Ser Pro Pro Phe Val
            20                  25                  30

Asn Ser Asp Gly Leu Gln Glu Asn Pro Pro Gly Val Leu Ser Leu Arg
        35                  40                  45

Ile Ala Lys Pro Leu Tyr Phe Asp Met Glu Arg Lys Leu Ala Leu Ser
    50                  55                  60

Leu Gly Arg Gly Leu Thr Ile Thr Ala Ala Gly Gln Leu Glu Ser Thr
65                  70                  75                  80

Gln Ser Val Gln Thr Asn Pro Pro Leu Ile Ile Thr Asn Asn Asn Thr
                85                  90                  95

Leu Thr Leu Arg His Ser Pro Pro Leu Asn Leu Thr Asp Asn Ser Leu
            100                 105                 110

Val Leu Gly Tyr Ser Ser Pro Leu Arg Val Thr Asp Asn Lys Leu Thr
        115                 120                 125

Phe Asn Phe Thr Ser Pro Leu Arg Tyr Glu Asn Glu Asn Leu Thr Phe
    130                 135                 140

Asn Tyr Thr Glu Pro Leu Lys Leu Ile Asn Asn Ser Leu Ala Ile Asp
145                 150                 155                 160

Ile Asn Ser Ser Lys Gly Leu Ser Ser Val Gly Gly Ser Leu Ala Val
                165                 170                 175

Asn Leu Ser Ser Asp Leu Lys Phe Asp Ser Asn Gly Ser Ile Ala Phe
            180                 185                 190

Gly Ile Gln Thr Leu Trp Thr Ala Pro Thr Ser Thr Gly Asn Cys Thr
        195                 200                 205

Val Tyr Ser Glu Gly Asp Ser Leu Leu Ser Leu Cys Leu Thr Lys Cys
    210                 215                 220
```

```
Gly Ala His Val Leu Gly Ser Val Ser Leu Thr Gly Leu Thr Gly Thr
225                 230                 235                 240

Ile Thr Gln Met Thr Asp Ile Ser Val Thr Ile Gln Phe Thr Phe Asp
                245                 250                 255

Asn Asn Gly Lys Leu Leu Ser Ser Pro Leu Ile Asn Asn Ala Phe Ser
            260                 265                 270

Ile Arg Gln Asn Asp Ser Thr Ala Ser Asn Pro Thr Tyr Asn Ala Leu
        275                 280                 285

Ala Phe Met Pro Asn Ser Thr Ile Tyr Ala Arg Gly Gly Gly Gly Glu
    290                 295                 300

Pro Arg Asn Asn Tyr Tyr Val Gln Thr Tyr Leu Arg Gly Asn Val Gln
305                 310                 315                 320

Lys Pro Ile Ile Leu Thr Val Thr Tyr Asn Ser Val Ala Thr Gly Tyr
                325                 330                 335

Ser Leu Ser Phe Lys Trp Thr Ala Leu Ala Arg Glu Lys Phe Ala Thr
            340                 345                 350

Pro Thr Thr Ser Phe Cys Tyr Ile Thr Glu Gln
        355                 360
```

<210> 28
<211> 560
<212> PRT
<213> simian adenovirus SV-1

<400> 28

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Met Lys Arg Ala Arg Val Asp Glu Asp Phe Asn Pro Val Tyr Pro Tyr
1               5                   10                  15

Asp Pro Pro His Ala Pro Val Met Pro Phe Ile Thr Pro Pro Phe Thr
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Tyr Arg Asp Pro Ile Thr Thr Gln Asn Glu Ser Leu Thr Ile Lys Leu
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Gly Asn Gly Leu Thr Leu Asp Asn Gln Gly Gln Leu Thr Ser Thr Ala
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Gly Glu Val Glu Pro Pro Leu Thr Asn Ala Asn Asn Lys Leu Ala Leu
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Val Tyr Ser Asp Pro Leu Ala Val Lys Arg Asn Ser Leu Thr Leu Ser
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His Thr Ala Pro Leu Val Ile Ala Asp Asn Ser Leu Ala Leu Gln Val
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Ala Ala Pro Leu Val Thr Asn Ala Gly Thr Leu Arg Leu Gln Ser Ala
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Ala Pro Leu Gly Ile Ala Asp Gln Thr Leu Lys Leu Leu Phe Thr Asn
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Pro Leu Tyr Leu Gln Asn Asn Phe Leu Thr Leu Ala Ile Glu Arg Pro
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Leu Ala Ile Thr Asn Thr Gly Lys Leu Ala Leu Gln Leu Ser Pro Pro
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Leu Gln Thr Ala Asp Thr Gly Leu Thr Leu Gln Thr Asn Val Pro Leu
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Thr Val Ser Asn Gly Thr Leu Gly Leu Ala Ile Lys Arg Pro Leu Ile
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Ile Gln Asp Asn Asn Leu Phe Leu Asp Phe Arg Ala Pro Leu Arg Leu
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Phe Asn Ser Asp Pro Val Leu Gly Leu Asn Phe Tyr Thr Pro Leu Ala
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Val Arg Asp Glu Ala Leu Thr Val Asn Thr Gly Arg Gly Leu Thr Val
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Ser Tyr Asp Gly Leu Ile Leu Asn Leu Gly Lys Asp Leu Arg Phe Asp
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Asn Asn Thr Val Ser Val Ala Leu Ser Ala Ala Leu Pro Leu Gln Tyr
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Thr Asp Gln Leu Arg Leu Asn Val Gly Ala Gly Leu Arg Tyr Asn Pro
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Val Ser Lys Lys Leu Asp Val Asn Pro Asn Gln Asn Lys Gly Leu Thr
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Trp Glu Asn Asp Tyr Leu Ile Val Lys Leu Gly Asn Gly Leu Gly Phe
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Asp Gly Asp Gly Asn Ile Ala Val Ser Pro Gln Val Thr Ser Pro Asp
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Thr Leu Trp Thr Thr Ala Asp Pro Ser Pro Asn Cys Ser Ile Tyr Thr
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Asp Leu Asp Ala Lys Met Trp Leu Ser Leu Val Lys Gln Gly Gly Val
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Val Arg Ile Leu Asn Tyr Pro Thr Leu Gly Thr Gln Gly Thr Leu Gly
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Asn Asn Ala Thr Trp Gly Tyr Arg Gln Gly Glu Ser Ala Asp Thr Asn
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Val Leu Asn Ala Leu Ala Phe Met Pro Ser Ser Lys Arg Tyr Pro Arg
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Gly Arg Gly Ser Glu Val Gln Asn Gln Thr Val Gly Tyr Thr Cys Ile
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Gln Gly Asp Phe Ser Met Pro Val Pro Tyr Gln Ile Gln Tyr Asn Tyr
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cgatcgcgcc actatctcca gtctgctgac ccccaacact cgcctgctgc tgctcttgat 11220

cgcaccgttt accaacagta gcactatcag ccgtgactcg tacctgggtc atctcatcac 11280

tctgtaccgc gaggccatcg gccaggctca gatcgacgag catacgtatc aggagattac 11340

taacgtgagc cgtgccctgg gtcaggaaga taccggcagc ctggaagcca cgttgaactt 11400

tttgctaacc aaccggaggc aaaaaatacc ctcccagttc acgttaagcg ccgaggagga 11460

gaggattctg cgatacgtgc agcagtccgt gagcctgtac ttgatgcgcg agggcgccac 11520

cgcttccacg gctttagaca tgacggctcg gaacatggaa ccgtcctttt actccgccca 11580

ccggccgttc attaaccgtc tgatggacta cttccatcgc gcggccgcca tgaacgggga 11640

gtacttcacc aatgccatcc tgaatccgca ttggatgccc ccgtccggct tctacaccgg 11700

ggagtttgac ctgcccgaag ccgacgacgg ctttctgtgg gacgacgtgt ccgatagcat 11760

tttcacgccg gctaatcgcc gattccagaa gaaggagggc ggagacgagc tccccctctc 11820

cagcgtggaa gcggcctcaa ggggagagag tccctttcca agtctgtctt ccgccagtag 11880

cggtcgggta acgcgtccac ggttgccggg ggagagcgac tacctgaacg acccccttgct 11940

gcgaccggct agaaagaaaa attttcccaa taacggggtg gaaagcttgg tggataaaat 12000

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gaatcgttgg aagacgtacg cccaggagca gcgggagtgg gaggacagtc agccgcggcc  12060

gctggtaccg ccgcattggc gtcgccagag agaagacccg gacgactccg cagacgatag  12120

tagcgtgttg gacctgggag ggagcggagc caaccccttt gctcacttgc aacccaaggg  12180

gcgctcgagt cgcctgtatt aataaaaaag acgcggaaac ttaccagagc catggccaca  12240

gcgtgtgtgc tttcttcctc tctttcttcc tcggcgcggc aga atg aga aga gcg     12295
                                                Met Arg Arg Ala
                                                1

gtg aga gtc acg ccg gcg gcg tat gag ggc ccg ccc cct tct tac gaa     12343
Val Arg Val Thr Pro Ala Ala Tyr Glu Gly Pro Pro Pro Ser Tyr Glu
5                   10                  15                  20

agc gtg atg gga tca gcg aac gtg ccg gcc acg ctg gag gcg cct tac     12391
Ser Val Met Gly Ser Ala Asn Val Pro Ala Thr Leu Glu Ala Pro Tyr
                25                  30                  35

gtt cct ccc aga tac ctg gga cct acg gag ggc aga aac agc atc cgt     12439
Val Pro Pro Arg Tyr Leu Gly Pro Thr Glu Gly Arg Asn Ser Ile Arg
            40                  45                  50

tac tcc gag ctg gcg ccc ctg tac gat acc acc aag gtg tac ctg gtg     12487
Tyr Ser Glu Leu Ala Pro Leu Tyr Asp Thr Thr Lys Val Tyr Leu Val
        55                  60                  65

gac aac aag tcg gcg gac atc gcc tcc ctg aat tac caa aac gat cac     12535
Asp Asn Lys Ser Ala Asp Ile Ala Ser Leu Asn Tyr Gln Asn Asp His
    70                  75                  80

agt aac ttt ctg act acc gtg gtg cag aac aat gac ttc acc ccg acg     12583
Ser Asn Phe Leu Thr Thr Val Val Gln Asn Asn Asp Phe Thr Pro Thr
85                  90                  95                  100

gag gcg ggc acg cag acc att aac ttt gac gag cgt tcc cgc tgg ggc     12631
Glu Ala Gly Thr Gln Thr Ile Asn Phe Asp Glu Arg Ser Arg Trp Gly
                105                 110                 115

ggt cag ctg aaa acc atc ctg cac acc aac atg ccc aac atc aac gag     12679
Gly Gln Leu Lys Thr Ile Leu His Thr Asn Met Pro Asn Ile Asn Glu
            120                 125                 130

ttc atg tcc acc aac aag ttc agg gct aag ctg atg gta gaa aaa agt     12727
Phe Met Ser Thr Asn Lys Phe Arg Ala Lys Leu Met Val Glu Lys Ser
        135                 140                 145

aat gcg gaa act cgg cag ccc cga tac gag tgg ttc gag ttt acc att     12775
Asn Ala Glu Thr Arg Gln Pro Arg Tyr Glu Trp Phe Glu Phe Thr Ile
    150                 155                 160

cca gag ggc aac tat tcc gaa act atg act atc gat ctc atg aat aac     12823
Pro Glu Gly Asn Tyr Ser Glu Thr Met Thr Ile Asp Leu Met Asn Asn
165                 170                 175                 180
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gcg atc gtg gac aat tac ctg caa gtg ggg aga cag aac ggg gtg ctg    12871
Ala Ile Val Asp Asn Tyr Leu Gln Val Gly Arg Gln Asn Gly Val Leu
               185                 190                 195

gaa agc gat atc ggc gtg aaa ttc gat acc aga aac ttc cga ctg ggg    12919
Glu Ser Asp Ile Gly Val Lys Phe Asp Thr Arg Asn Phe Arg Leu Gly
            200                 205                 210

tgg gat ccc gtg acc aag ctg gtg atg cca ggc gtg tac acc aac gag    12967
Trp Asp Pro Val Thr Lys Leu Val Met Pro Gly Val Tyr Thr Asn Glu
        215                 220                 225

gct ttt cac ccg gac atc gtg ctg ctg ccg ggg tgc ggt gtg gac ttc    13015
Ala Phe His Pro Asp Ile Val Leu Leu Pro Gly Cys Gly Val Asp Phe
    230                 235                 240

act cag agc cgt ttg agt aac ctg tta gga att aga aag cgc cgc ccc    13063
Thr Gln Ser Arg Leu Ser Asn Leu Leu Gly Ile Arg Lys Arg Arg Pro
245                 250                 255                 260

ttc caa gag ggc ttt caa atc atg tat gag gac ctg gag gga ggt aat    13111
Phe Gln Glu Gly Phe Gln Ile Met Tyr Glu Asp Leu Glu Gly Gly Asn
               265                 270                 275

ata ccc gcc tta ctg gac gtg tcg aag tac gaa gct agc ata caa cgc    13159
Ile Pro Ala Leu Leu Asp Val Ser Lys Tyr Glu Ala Ser Ile Gln Arg
            280                 285                 290

gcc aaa gcg gag ggt aga gag att cgg gga gac acc ttt gcg gta gct    13207
Ala Lys Ala Glu Gly Arg Glu Ile Arg Gly Asp Thr Phe Ala Val Ala
        295                 300                 305

ccc cag gac ctg gaa ata gtg cct tta act aaa gac agc aaa gac aga    13255
Pro Gln Asp Leu Glu Ile Val Pro Leu Thr Lys Asp Ser Lys Asp Arg
    310                 315                 320

agc tac aat att ata aac aac acg acg gac acc ctg tat cgg agc tgg    13303
Ser Tyr Asn Ile Ile Asn Asn Thr Thr Asp Thr Leu Tyr Arg Ser Trp
325                 330                 335                 340

ttt ctg gct tac aac tac gga gac ccc gag aaa gga gtg aga tca tgg    13351
Phe Leu Ala Tyr Asn Tyr Gly Asp Pro Glu Lys Gly Val Arg Ser Trp
               345                 350                 355

acc ata ctc acc acc acg gac gtg acc tgt ggc tcg cag caa gtg tac    13399
Thr Ile Leu Thr Thr Thr Asp Val Thr Cys Gly Ser Gln Gln Val Tyr
            360                 365                 370

tgg tcc ctg ccg gat atg atg caa gac ccg gtc acc ttc cgc ccc tcc    13447
Trp Ser Leu Pro Asp Met Met Gln Asp Pro Val Thr Phe Arg Pro Ser
        375                 380                 385

acc caa gtc agc aac ttc ccg gtg gtg ggc acc gag ctg ctg ccc gtc    13495
Thr Gln Val Ser Asn Phe Pro Val Val Gly Thr Glu Leu Leu Pro Val
    390                 395                 400
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cat gcc aag agc ttc tac aac gag cag gcc gtc tac tcg caa ctt att    13543
His Ala Lys Ser Phe Tyr Asn Glu Gln Ala Val Tyr Ser Gln Leu Ile
405                 410                 415                 420

cgc cag tcc acc gcg ctt acc cac gtg ttc aat cgc ttt ccc gag aac    13591
Arg Gln Ser Thr Ala Leu Thr His Val Phe Asn Arg Phe Pro Glu Asn
                425                 430                 435

cag att ctg gtg cgc cct ccc gct cct acc att acc acc gtc agt gaa    13639
Gln Ile Leu Val Arg Pro Pro Ala Pro Thr Ile Thr Thr Val Ser Glu
            440                 445                 450

aac gtt ccc gcc ctc aca gat cac gga acc ctg ccg ctg cgc agc agt    13687
Asn Val Pro Ala Leu Thr Asp His Gly Thr Leu Pro Leu Arg Ser Ser
        455                 460                 465

atc agt gga gtt cag cgc gtg acc atc acc gac gcc aga cgt cga acc    13735
Ile Ser Gly Val Gln Arg Val Thr Ile Thr Asp Ala Arg Arg Arg Thr
    470                 475                 480

tgc ccc tac gtt tac aaa gcg ctt ggc gtg gtg gct cct aaa gtt ctt    13783
Cys Pro Tyr Val Tyr Lys Ala Leu Gly Val Val Ala Pro Lys Val Leu
485                 490                 495                 500

tct agt cgc acc ttc taa aaacatgtcc atcctcatct ctcccgataa          13831
Ser Ser Arg Thr Phe
                505

caacaccggc tggggactgg gctccggcaa gatgtacggc ggagccaaaa ggcgctccag  13891

tcagcaccca gttcgagttc ggggccactt ccgcgctcct tggggagctt acaagcgagg  13951

actctcgggt cgaacggctg tagacgatac catagatgcc gtgattgccg acgcccgccg  14011

gtacaacccc ggaccggtcg ctagcgccgc ctccaccgtg gattccgtga tcgacagcgt  14071

ggtagccggc gctcgggcct atgctcgccg caagaggcgg ctgcatcgga gacgtcgccc  14131

caccgccgcc atgctggcag ccagggccgt gctgaggcgg gcccggaggg caggcagaag  14191

ggctatgcgc cgcgctgccg ccaacgccgc cgccgggagg gcccgccgac aggctgcccg  14251

ccaggctgcc gctgccatcg ctagcatggc cagacccagg agagggaacg tgtactgggt  14311

gcgtgattct gtgacgggag tccgagtgcc ggtgcgcagc cgacctcccc gaagttagaa  14371

gatccaagct gcgaagacgg cggtactgag tctccctgtt gttatcagcc caacatgagc  14431

aagcgcaagt ttaaagaaga actgctgcag acgctggtgc ctgagatcta tggccctccg  14491

gacgtgaagc cagacattaa gccccgcgat atcaagcgtg ttaaaaagcg ggaaaagaaa  14551

gaggaactcg cggtggtaga cgatggcgga gtggaattta ttaggagttt cgccccgcga  14611

cgcagggttc aatggaaagg gcggcgggta caacgcgttt tgaggccggg caccgcggta  14671

gtttttaccc cgggagagcg gtcggccgtt aggggtttca aaaggcagta cgacgaggtg  14731
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tacggcgacg aggacatatt ggaacaggcg gctcaacaga tcggagaatt tgcctacgga 14791

aagcgttcgc gtcgcgaaga cctggccatc gccttagaca gcggcaaccc cacgcccagc 14851

ctcaaacccg tgacgctgca gcaggtgctt cccgtgagcg ccagcacgga cagcaagagg 14911

gggattaaga gagaaatgga agatctgcat cccaccatcc aactcatggt ccctaaacgg 14971

cagaggctgg aagaggtcct ggagaagatg aaagtggacc ccagcataga gccggatgta 15031

aaagtcagac ctattaagga agtggccccc ggtcttgggg tgcaaacggt ggacattcaa 15091

atccccgtca ccaccgcttc aaccgccgtg gaagctatgg aaacgcaaac ggagacccct 15151

gccgcgatcg gtaccaggga agtggcgttg caaacggagc cttggtacga atacgcagcc 15211

cctcggcgtc agaggcgttc cgctcgttac ggccccgcca acgccatcat gccagaatat 15271

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ggaacccgcc gccgaacccg tcgccgccgc cgctcccgtc gcgctctggc ccccgtgtcg 15391

gtgcggcgtg tgacccgccg gggaaagaca gtcgtcattc ccaacccgcg ttaccaccct 15451

agcatccttt aataactctg ccgttttgca gatggctctg acttgccgcg tgcgccttcc 15511

cgttccgcac tatcgaggaa gatctcgtcg taggagaggc atgacgggca gtggtcgccg 15571

gcgggctttg cgcaggcgca tgaaaggcgg aattttaccc gccctgatac ccataattgc 15631

cgccgccatc ggtgccatac ccggcgttgc ttcagtggcg ttgcaagcag ctcgtaataa 15691

ataaacaaag gcttttgcac ttatgacctg gtcctgacta ttttatgcag aaagagcatg 15751

gaagacatca attttacgtc gctggctccg cggcacggct cgcggccgct catgggcacc 15811

tggaacgaca tcggcaccag tcagctcaac gggggcgctt tcaattgggg gagcctttgg 15871

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agtgctggtc agatgctccg agataaactg aaggacacca acttccaaga aaaagtggtc 15991

aatggggtgg tgaccggcat ccacggcgcg gtagatctcg ccaaccaagc ggtgcagaaa 16051

gagattgaca ggcgtttgga aagctcgcgg gtgccgccgc agagagggga tgaggtggag 16111

gtcgaggaag tagaagtaga ggaaaagctg cccccgctgg agaaagttcc cggtgcgcct 16171

ccgagaccgc agaagcggcc caggccagaa ctagaagaga ctctggtgac ggagagcaag 16231

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actaagccga tcgcacccat ggctcgaccg gtgtacggca aggattacaa gcccgtcacg 16351

ctagagctgc ccccaccgcc ccccacgcgc ccgaccgtcc ccccccctgcc gactccgtcg 16411

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gcggccgcgg cgggacccgt gtccgcacca tccgctgtgc ctctgccagc cgcccgtcca  16471

gtggccgtgg ccactgccag aaaccccaga ggccagagag gagccaactg gcaaagcacg  16531

ctgaacagca tcgtgggcct gggagtgaaa agcctgaaac gccgccgttg ctattattaa  16591

aaaagtgtag ctaaaaagtc tcccgttgta tacgcctcct atgttaccgc cagagacgag  16651

tgactgtcgc cgcgagcgcc gctttcaag atg gcc acc cca tcg atg atg ccg     16704
                                Met Ala Thr Pro Ser Met Met Pro
                                                    510

cag tgg tct tac atg cac atc gcc ggc cag gac gcc tcg gag tac ctg     16752
Gln Trp Ser Tyr Met His Ile Ala Gly Gln Asp Ala Ser Glu Tyr Leu
    515                 520                 525

agt ccc ggc ctc gtg cag ttt gcc cgc gcc acc gac acc tac ttc agc     16800
Ser Pro Gly Leu Val Gln Phe Ala Arg Ala Thr Asp Thr Tyr Phe Ser
530                 535                 540                 545

ttg gga aac aag ttt aga aac ccc acc gtg gcc ccc acc cac gat gtg     16848
Leu Gly Asn Lys Phe Arg Asn Pro Thr Val Ala Pro Thr His Asp Val
                550                 555                 560

acc acg gac cgc tcg cag agg ctg acc ctg cgc ttt gtg ccc gta gac     16896
Thr Thr Asp Arg Ser Gln Arg Leu Thr Leu Arg Phe Val Pro Val Asp
            565                 570                 575

cgg gag gac acc gcg tac tct tac aaa gtg cgc tac acg ttg gcc gta     16944
Arg Glu Asp Thr Ala Tyr Ser Tyr Lys Val Arg Tyr Thr Leu Ala Val
        580                 585                 590

ggg gac aac cga gtg ctg gac atg gcc agc acc tac ttt gac atc cgg     16992
Gly Asp Asn Arg Val Leu Asp Met Ala Ser Thr Tyr Phe Asp Ile Arg
    595                 600                 605

ggg gtg ctg gat cgg ggt ccc agc ttc aag ccc tat tcc ggc acc gct     17040
Gly Val Leu Asp Arg Gly Pro Ser Phe Lys Pro Tyr Ser Gly Thr Ala
610                 615                 620                 625

tac aac tcc ctg gcc ccc aag gga gct ccc aac ccc tcg gaa tgg acg     17088
Tyr Asn Ser Leu Ala Pro Lys Gly Ala Pro Asn Pro Ser Glu Trp Thr
                630                 635                 640

gac act tcc gac aac aaa ctt aaa gca tat gct cag gct ccc tac cag     17136
Asp Thr Ser Asp Asn Lys Leu Lys Ala Tyr Ala Gln Ala Pro Tyr Gln
            645                 650                 655

agt caa gga ctt aca aag gat ggt att cag gtt ggg cta gtt gtg aca     17184
Ser Gln Gly Leu Thr Lys Asp Gly Ile Gln Val Gly Leu Val Val Thr
        660                 665                 670

gag tca gga caa aca ccc caa tat gca aac aaa gtg tac caa ccc gag     17232
Glu Ser Gly Gln Thr Pro Gln Tyr Ala Asn Lys Val Tyr Gln Pro Glu
    675                 680                 685
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cca caa att ggg gaa aac caa tgg aat tta gaa caa gaa gat aaa gcg    17280
Pro Gln Ile Gly Glu Asn Gln Trp Asn Leu Glu Gln Glu Asp Lys Ala
690                 695                 700                 705

gcg gga aga gtc cta aag aaa gat acc cct atg ttt ccc tgc tat ggg    17328
Ala Gly Arg Val Leu Lys Lys Asp Thr Pro Met Phe Pro Cys Tyr Gly
                710                 715                 720

tca tat gcc agg ccc aca aac gaa caa gga ggg cag gca aaa aac caa    17376
Ser Tyr Ala Arg Pro Thr Asn Glu Gln Gly Gly Gln Ala Lys Asn Gln
            725                 730                 735

gaa gta gat tta cag ttt ttt gcc act ccg ggc gac acc cag aac acg    17424
Glu Val Asp Leu Gln Phe Phe Ala Thr Pro Gly Asp Thr Gln Asn Thr
        740                 745                 750

gct aaa gtg gta ctt tat gct gaa aat gtc aac ctg gaa act cca gat    17472
Ala Lys Val Val Leu Tyr Ala Glu Asn Val Asn Leu Glu Thr Pro Asp
    755                 760                 765

act cac tta gtg ttt aaa ccc gat gac gac agc acc agt tca aaa ctt    17520
Thr His Leu Val Phe Lys Pro Asp Asp Asp Ser Thr Ser Ser Lys Leu
770                 775                 780                 785

ctt ctt ggg cag cag gct gca cct aac aga ccc aac tac ata ggt ttt    17568
Leu Leu Gly Gln Gln Ala Ala Pro Asn Arg Pro Asn Tyr Ile Gly Phe
                790                 795                 800

aga gat aat ttt att ggt tta atg tac tac aat agc act gga aac atg    17616
Arg Asp Asn Phe Ile Gly Leu Met Tyr Tyr Asn Ser Thr Gly Asn Met
            805                 810                 815

ggc gtg ctg gcc gga cag gct tct caa ttg aat gcc gta gtc gac ttg    17664
Gly Val Leu Ala Gly Gln Ala Ser Gln Leu Asn Ala Val Val Asp Leu
        820                 825                 830

cag gac aga aac acc gag ttg tcc tac cag ctg atg ctg gac gca ctg    17712
Gln Asp Arg Asn Thr Glu Leu Ser Tyr Gln Leu Met Leu Asp Ala Leu
    835                 840                 845

ggg gat cgc agc cga tat ttt tca atg tgg aat cag gca gta gac agc    17760
Gly Asp Arg Ser Arg Tyr Phe Ser Met Trp Asn Gln Ala Val Asp Ser
850                 855                 860                 865

tat gac cca gac gtt aga att ata gaa aac cac gga gtg gaa gac gaa    17808
Tyr Asp Pro Asp Val Arg Ile Ile Glu Asn His Gly Val Glu Asp Glu
                870                 875                 880

ctg cca aac tat tgt ttt cct ctg gga gga atg gtg gtg act gac aat    17856
Leu Pro Asn Tyr Cys Phe Pro Leu Gly Gly Met Val Val Thr Asp Asn
            885                 890                 895

tac aac tct gtg acg cct caa aat gga ggc agt gga aat aca tgg cag    17904
Tyr Asn Ser Val Thr Pro Gln Asn Gly Gly Ser Gly Asn Thr Trp Gln
        900                 905                 910
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gca gac aat act aca ttt agt caa aga gga gcg cag att ggc tcc gga    17952
Ala Asp Asn Thr Thr Phe Ser Gln Arg Gly Ala Gln Ile Gly Ser Gly
    915                 920                 925

aac atg ttt gcc ctg gaa att aac cta cag gcc aac ctc tgg cgc ggc    18000
Asn Met Phe Ala Leu Glu Ile Asn Leu Gln Ala Asn Leu Trp Arg Gly
930                 935                 940                 945

ttc ttg tat tcc aat att ggg ttg tat ctt cca gac tct ctg aaa atc    18048
Phe Leu Tyr Ser Asn Ile Gly Leu Tyr Leu Pro Asp Ser Leu Lys Ile
                950                 955                 960

acc ccc gac aac atc acg ctg cca gaa aac aaa aac act tat cag tac    18096
Thr Pro Asp Asn Ile Thr Leu Pro Glu Asn Lys Asn Thr Tyr Gln Tyr
            965                 970                 975

atg aac ggt cgc gta acg cca ccc ggg ctc ata gac acc tat gta aac    18144
Met Asn Gly Arg Val Thr Pro Pro Gly Leu Ile Asp Thr Tyr Val Asn
        980                 985                 990

gtg ggc gcg cgc tgg tcc ccc  gat gtc atg gac agc  att aac ccc ttc  18192
Val Gly Ala Arg Trp Ser Pro  Asp Val Met Asp Ser  Ile Asn Pro Phe
    995                 1000                1005

aac  cac cac cgt aac gcg  ggc ttg cgc tac cgc  tcc atg ctc ttg     18237
Asn  His His Arg Asn Ala  Gly Leu Arg Tyr Arg  Ser Met Leu Leu
1010                1015                1020

ggc  aac ggc cgt tat gtg  cct ttt cac att cag  gtg ccc caa aaa     18282
Gly  Asn Gly Arg Tyr Val  Pro Phe His Ile Gln  Val Pro Gln Lys
1025                1030                1035

ttc  ttt gcc att aaa aac  ctg ctg ctt ctc ccc  ggt tcc tat acc     18327
Phe  Phe Ala Ile Lys Asn  Leu Leu Leu Leu Pro  Gly Ser Tyr Thr
1040                1045                1050

tat  gag tgg aac ttc cgc  aag gat gtc aac atg  atc ctg cag agc     18372
Tyr  Glu Trp Asn Phe Arg  Lys Asp Val Asn Met  Ile Leu Gln Ser
1055                1060                1065

tcg  ctg ggt aat gac ctg  cga gtg gac ggg gcc  agc ata cgc ttt     18417
Ser  Leu Gly Asn Asp Leu  Arg Val Asp Gly Ala  Ser Ile Arg Phe
1070                1075                1080

gac  agc att aac ctg tat  gcc aac ttt ttt ccc  atg gcc cac aac     18462
Asp  Ser Ile Asn Leu Tyr  Ala Asn Phe Phe Pro  Met Ala His Asn
1085                1090                1095

acg  gcc tct acc ctg gaa  gcc atg ctg cgc aac  gac acc aat gac     18507
Thr  Ala Ser Thr Leu Glu  Ala Met Leu Arg Asn  Asp Thr Asn Asp
1100                1105                1110

cag  tcc ttc aac gac tac  ctg tgc gcg gct aac  atg ctg tac ccc     18552
Gln  Ser Phe Asn Asp Tyr  Leu Cys Ala Ala Asn  Met Leu Tyr Pro
1115                1120                1125
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atc  ccc gcc aac gcc acc  agc gtg ccc att tct  att cct tct cgg     18597
Ile  Pro Ala Asn Ala Thr  Ser Val Pro Ile Ser  Ile Pro Ser Arg
1130                 1135                 1140

aac  tgg gct gcc ttc agg  ggc tgg agt ttt act  cgc ctc aaa acc     18642
Asn  Trp Ala Ala Phe Arg  Gly Trp Ser Phe Thr  Arg Leu Lys Thr
1145                 1150                 1155

aag  gag act ccc tcg ctg  ggc tcc ggt ttt gac  ccc tac ttt gtt     18687
Lys  Glu Thr Pro Ser Leu  Gly Ser Gly Phe Asp  Pro Tyr Phe Val
1160                 1165                 1170

tac  tcc ggc tcc att ccc  tac cta gat ggc acc  ttt tac ctc aac     18732
Tyr  Ser Gly Ser Ile Pro  Tyr Leu Asp Gly Thr  Phe Tyr Leu Asn
1175                 1180                 1185

cac  act ttc aaa aag gtg  tct att atg ttt gac  tcc tcg gtt agc     18777
His  Thr Phe Lys Lys Val  Ser Ile Met Phe Asp  Ser Ser Val Ser
1190                 1195                 1200

tgg  ccc ggc aac gac cgc  ctg cta acg ccc aac  gag ttc gaa att     18822
Trp  Pro Gly Asn Asp Arg  Leu Leu Thr Pro Asn  Glu Phe Glu Ile
1205                 1210                 1215

aag  cgt tcc gtg gac ggt  gaa ggg tac aac gtg  gcc cag agc aac     18867
Lys  Arg Ser Val Asp Gly  Glu Gly Tyr Asn Val  Ala Gln Ser Asn
1220                 1225                 1230

atg  acc aag gac tgg ttt  cta att caa atg ctc  agt cac tat aat     18912
Met  Thr Lys Asp Trp Phe  Leu Ile Gln Met Leu  Ser His Tyr Asn
1235                 1240                 1245

ata  ggt tac cag ggc ttc  tat gtg ccc gag aac  tac aag gac cgc     18957
Ile  Gly Tyr Gln Gly Phe  Tyr Val Pro Glu Asn  Tyr Lys Asp Arg
1250                 1255                 1260

atg  tac tcc ttc ttc cgc  aac ttc caa cca atg  agc cgg cag gtg     19002
Met  Tyr Ser Phe Phe Arg  Asn Phe Gln Pro Met  Ser Arg Gln Val
1265                 1270                 1275

gta  gat acc gtg act tat  aca gac tac aaa gat  gtc aag ctc ccc     19047
Val  Asp Thr Val Thr Tyr  Thr Asp Tyr Lys Asp  Val Lys Leu Pro
1280                 1285                 1290

tac  caa cac aac aac tca  ggg ttc gtg ggc tac  atg gga ccc acc     19092
Tyr  Gln His Asn Asn Ser  Gly Phe Val Gly Tyr  Met Gly Pro Thr
1295                 1300                 1305

atg  cga gag gga cag gcc  tac ccg gcc aac tat  ccc tac ccc ctg     19137
Met  Arg Glu Gly Gln Ala  Tyr Pro Ala Asn Tyr  Pro Tyr Pro Leu
1310                 1315                 1320

atc  gga gag act gcc gta  ccc agc ctc acg cag  aaa aag ttc ctc     19182
Ile  Gly Glu Thr Ala Val  Pro Ser Leu Thr Gln  Lys Lys Phe Leu
1325                 1330                 1335
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tgc  gac cgg gtg atg tgg  agg ata ccc ttc tct  agc aac ttt atg     19227
Cys  Asp Arg Val Met Trp  Arg Ile Pro Phe Ser  Ser Asn Phe Met
1340                 1345                 1350

tcg  atg ggc tcc ctc acc  gac ctg ggg cag aac  atg ctg tac gcc     19272
Ser  Met Gly Ser Leu Thr  Asp Leu Gly Gln Asn  Met Leu Tyr Ala
1355                 1360                 1365

aac  tcc gct cac gcc ttg  gac atg act ttt gag  gtg gat ccc atg     19317
Asn  Ser Ala His Ala Leu  Asp Met Thr Phe Glu  Val Asp Pro Met
1370                 1375                 1380

gat  gag ccc acg ctt ctc  tat gtt ctg ttt gaa  gtc ttc gac gtg     19362
Asp  Glu Pro Thr Leu Leu  Tyr Val Leu Phe Glu  Val Phe Asp Val
1385                 1390                 1395

gtg  cgc atc cac cag ccg  cac cgc ggc gtc atc  gag gcc gtc tac     19407
Val  Arg Ile His Gln Pro  His Arg Gly Val Ile  Glu Ala Val Tyr
1400                 1405                 1410

ctg  cgc aca cct ttc tct  gcc ggt aac gcc acc  acc taa agaagctgat  19456
Leu  Arg Thr Pro Phe Ser  Ala Gly Asn Ala Thr  Thr
1415                 1420                 1425

gggttccagc gaacaggagt tgcaggccat tgttcgcgac ctgggctgcg ggccctgctt  19516

tttgggcacc ttcgacaagc gttttcccgg attcatgtcc ccccacaagc cggcctgcgc  19576

catcgttaac acggccggac gggagacagg gggggtgcac tggctcgcct tcgcctggaa  19636

cccgcgcaac cgcacctgct acctgttcga ccctttttggt ttctccgacg aaaggctgaa  19696

gcagatctac caattcgagt acgaggggct cctcaagcgc agcgctctgg cctccacgcc  19756

cgaccactgc gtcaccctgg aaaagtccac ccagacggtc caggggcccc tctcggccgc  19816

ctgcgggctt ttctgttgca tgtttttgca cgccttcgtg cactggcctc acacccccat  19876

ggagcgcaac cccaccatgg atctgctcac cggagtgccc aacagcatgc ttcacagtcc  19936

ccaggtcgcc cccaccctgc gtcgcaatca ggaccacctg tatcgctttc tggggaaaca  19996

ctctgcctat ttccgccgcc accggcagcg catcgaacag gccacggcct tcgaaagcat  20056

gagccaaaga gtgtaatcaa taaaaaccgt ttttatttga catgatacgc gcttctggcg  20116

tttttattaa aaatcgaagg gttcgaggga ggggtcctcg tgcccgctgg ggagggacac  20176

gttgcggtac tggaatcggg cgctccaacg aaactcgggg atcaccagcc gcggcagggc  20236

cacgtcttcc atgttctgct tccaaaactg tcgcaccagc tgcagggctc ccatcacgtc  20296

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ggggttggca cactggaaca ccaacacgct ggggttgtgg atactagcca gggccgtcgg  20416

gtcggtcacc tccgatgcat ccagatcctc ggcattgctc agggcgaacg gggtcagctt  20476
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gcacatctgc cgcccgatct ggggtaccag gtcgcgcttg ttgaggcagt cgcagcgcag 20536

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tctcacctca tcgacgcctt caccgcccgg cctctcctgg tagaaaccga acgcgggatc 25336

actaccatca ccctgttctg catctgcccc acgcccggat tac atg aag atc tgt 25391
Met Lys Ile Cys
1430

gtt gtc atc ttt gcg ctc agt tta ata aaa act gaa ctt ttt gcc 25436
Val Val Ile Phe Ala Leu Ser Leu Ile Lys Thr Glu Leu Phe Ala
1435 1440 1445

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gta cct tca acg cca  cgc gtt gtt tct cct  tgt gaa aaa acc cca      25481
Val Pro Ser Thr Pro  Arg Val Val Ser Pro  Cys Glu Lys Thr Pro
                1450                1455                1460

gga gtc ctt aac tta  cac ata gca aaa ccc  ttg tat ttt acc ata      25526
Gly Val Leu Asn Leu  His Ile Ala Lys Pro  Leu Tyr Phe Thr Ile
                1465                1470                1475

gaa aaa caa cta gcc  ctt tca att gga aaa  ggg tta aca att tct      25571
Glu Lys Gln Leu Ala  Leu Ser Ile Gly Lys  Gly Leu Thr Ile Ser
                1480                1485                1490

gct aca gga cag ttg  gaa agc aca gca agc  gta cag gac agc gct      25616
Ala Thr Gly Gln Leu  Glu Ser Thr Ala Ser  Val Gln Asp Ser Ala
                1495                1500                1505

aca cca ccc cta cgt  ggt att tcc cct tta  aag ctg aca gac aac      25661
Thr Pro Pro Leu Arg  Gly Ile Ser Pro Leu  Lys Leu Thr Asp Asn
                1510                1515                1520

ggt tta aca tta agc  tat tca gat ccc ctg  cgt gtg gta ggt gac      25706
Gly Leu Thr Leu Ser  Tyr Ser Asp Pro Leu  Arg Val Val Gly Asp
                1525                1530                1535

caa ctt acg ttt aat  ttt act tct cca cta  cgt tac gaa aat ggc      25751
Gln Leu Thr Phe Asn  Phe Thr Ser Pro Leu  Arg Tyr Glu Asn Gly
                1540                1545                1550

agt ctt aca ttc aac  tac act tct ccc atg  aca cta ata aac aac      25796
Ser Leu Thr Phe Asn  Tyr Thr Ser Pro Met  Thr Leu Ile Asn Asn
                1555                1560                1565

agt ctt gct att aac  gtc aat acc tcc aaa  ggc ctc agt agt gac      25841
Ser Leu Ala Ile Asn  Val Asn Thr Ser Lys  Gly Leu Ser Ser Asp
                1570                1575                1580

aac ggc aca ctc gct  gta aat gtt act cca  gat ttt aga ttt aac      25886
Asn Gly Thr Leu Ala  Val Asn Val Thr Pro  Asp Phe Arg Phe Asn
                1585                1590                1595

agc tct ggt gcc tta  act ttt ggc ata caa  agt cta tgg act ttt      25931
Ser Ser Gly Ala Leu  Thr Phe Gly Ile Gln  Ser Leu Trp Thr Phe
                1600                1605                1610

cca acc aaa act cct  aac tgt acc gtg ttt  acc gaa agt gac tcc      25976
Pro Thr Lys Thr Pro  Asn Cys Thr Val Phe  Thr Glu Ser Asp Ser
                1615                1620                1625

ctg ctg agt ctt tgc  ttg act aaa tgc gga  gct cac gta ctt gga      26021
Leu Leu Ser Leu Cys  Leu Thr Lys Cys Gly  Ala His Val Leu Gly
                1630                1635                1640

agc gtg agt tta agc  gga gtg gca gga acc  atg cta aaa atg acc      26066
Ser Val Ser Leu Ser  Gly Val Ala Gly Thr  Met Leu Lys Met Thr
                1645                1650                1655
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cac act tct gtt acc  gtt cag ttt tcg ttt  gat gac agt ggt aaa      26111
His Thr Ser Val Thr  Val Gln Phe Ser Phe  Asp Asp Ser Gly Lys
                1660                1665                1670

cta ata ttc tct cca  ctt gcg aac aac act  tgg ggt gtt cga caa      26156
Leu Ile Phe Ser Pro  Leu Ala Asn Asn Thr  Trp Gly Val Arg Gln
                1675                1680                1685

agc gag agt ccg ttg  ccc aac cca tcc ttc  aac gct ctc acg ttt      26201
Ser Glu Ser Pro Leu  Pro Asn Pro Ser Phe  Asn Ala Leu Thr Phe
                1690                1695                1700

atg cca aac agt acc  att tat tct aga gga  gca agt aac gaa cct      26246
Met Pro Asn Ser Thr  Ile Tyr Ser Arg Gly  Ala Ser Asn Glu Pro
                1705                1710                1715

caa aac aat tat tat  gtc cag acg tat ctt  aga ggc aac gtg cga      26291
Gln Asn Asn Tyr Tyr  Val Gln Thr Tyr Leu  Arg Gly Asn Val Arg
                1720                1725                1730

aag cca att cta cta  act gtt acc tac aac  tca gtt aat tca gga      26336
Lys Pro Ile Leu Leu  Thr Val Thr Tyr Asn  Ser Val Asn Ser Gly
                1735                1740                1745

tat tcc tta act ttt  aaa tgg gat gct gtc  gcc aat gaa aaa ttt      26381
Tyr Ser Leu Thr Phe  Lys Trp Asp Ala Val  Ala Asn Glu Lys Phe
                1750                1755                1760

gcc act cct aca tct  tcg ttt tgc tat gtt  gca gag caa taa          26423
Ala Thr Pro Thr Ser  Ser Phe Cys Tyr Val  Ala Glu Gln
                1765                1770

aaccctgtta ccccaccgtc tcgttttttt cag atg aaa  cga gcg aga gtt      26474
                                        Met Lys  Arg Ala Arg Val
                                            1775

gat  gaa gac ttc aac cca  gtg tac cct tat gac  ccc cca tac gct     26519
Asp  Glu Asp Phe Asn Pro  Val Tyr Pro Tyr Asp  Pro Pro Tyr Ala
1780                1785                1790

ccc  gtc atg ccc ttc att  act ccg cct ttt acc  tcc tcg gat ggg     26564
Pro  Val Met Pro Phe Ile  Thr Pro Pro Phe Thr  Ser Ser Asp Gly
1795                1800                1805

ttg  cag gaa aaa cca ctt  gga gtg tta agt tta  aac tac agg gat     26609
Leu  Gln Glu Lys Pro Leu  Gly Val Leu Ser Leu  Asn Tyr Arg Asp
1810                1815                1820

ccc  att act aca caa aat  ggg tct ctc acg tta  aaa cta gga aac     26654
Pro  Ile Thr Thr Gln Asn  Gly Ser Leu Thr Leu  Lys Leu Gly Asn
1825                1830                1835

ggc  ctc act cta aac aac  cag gga cag tta aca  tca act gct ggc     26699
Gly  Leu Thr Leu Asn Asn  Gln Gly Gln Leu Thr  Ser Thr Ala Gly
1840                1845                1850
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gaa  gtg gag cct ccg ctc  act aat gct aac aac  aaa ctt gca cta     26744
Glu  Val Glu Pro Pro Leu  Thr Asn Ala Asn Asn  Lys Leu Ala Leu
1855                 1860                 1865

gcc  tat agc gaa cca tta  gca gta aaa agc aac  cgc cta act cta     26789
Ala  Tyr Ser Glu Pro Leu  Ala Val Lys Ser Asn  Arg Leu Thr Leu
1870                 1875                 1880

tca  cac acc gct ccc ctt  gtc atc gct aat aat  tct tta gcg ttg     26834
Ser  His Thr Ala Pro Leu  Val Ile Ala Asn Asn  Ser Leu Ala Leu
1885                 1890                 1895

caa  gtt tca gag cct att  ttt gta aat gac gat  gac aag cta gcc     26879
Gln  Val Ser Glu Pro Ile  Phe Val Asn Asp Asp  Asp Lys Leu Ala
1900                 1905                 1910

ctg  cag aca gcc gcc ccc  ctt gta acc aac gct  ggc acc ctt cgc     26924
Leu  Gln Thr Ala Ala Pro  Leu Val Thr Asn Ala  Gly Thr Leu Arg
1915                 1920                 1925

tta  cag agc gct gcc cct  tta gga ttg gtt gaa  aat act ctt aaa     26969
Leu  Gln Ser Ala Ala Pro  Leu Gly Leu Val Glu  Asn Thr Leu Lys
1930                 1935                 1940

ctg  ctg ttt tct aaa ccc  ttg tat ttg caa aat  gat ttt ctt gca     27014
Leu  Leu Phe Ser Lys Pro  Leu Tyr Leu Gln Asn  Asp Phe Leu Ala
1945                 1950                 1955

tta  gcc att gaa cgc ccc  ctg gct gta gca gcc  gca ggt act ctg     27059
Leu  Ala Ile Glu Arg Pro  Leu Ala Val Ala Ala  Ala Gly Thr Leu
1960                 1965                 1970

acc  cta caa ctt act cct  cca tta aag act aac  gat gac ggg cta     27104
Thr  Leu Gln Leu Thr Pro  Pro Leu Lys Thr Asn  Asp Asp Gly Leu
1975                 1980                 1985

aca  cta tcc aca gtc gag  cca tta act gta aaa  aac gga aac cta     27149
Thr  Leu Ser Thr Val Glu  Pro Leu Thr Val Lys  Asn Gly Asn Leu
1990                 1995                 2000

ggc  ttg caa ata tcg cgc  cct tta gtt gtt caa  aac aac ggc ctt     27194
Gly  Leu Gln Ile Ser Arg  Pro Leu Val Val Gln  Asn Asn Gly Leu
2005                 2010                 2015

tcg  ctt gct att acc ccc  ccg ctg cgt ttg ttt  aac agc gac ccc     27239
Ser  Leu Ala Ile Thr Pro  Pro Leu Arg Leu Phe  Asn Ser Asp Pro
2020                 2025                 2030

gtt  ctt ggt ttg ggc ttc  act ttt ccc cta gct  gtc aca aac aac     27284
Val  Leu Gly Leu Gly Phe  Thr Phe Pro Leu Ala  Val Thr Asn Asn
2035                 2040                 2045

ctc  ctc tcc tta aac atg  gga gac gga gtt aaa  ctt acc tat aat     27329
Leu  Leu Ser Leu Asn Met  Gly Asp Gly Val Lys  Leu Thr Tyr Asn
2050                 2055                 2060
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aaa  cta aca gcc aat ttg  ggt agg gat tta caa  ttt gaa aac ggt     27374
Lys  Leu Thr Ala Asn Leu  Gly Arg Asp Leu Gln  Phe Glu Asn Gly
2065                 2070                 2075

gcg  att gcc gta acg ctt  act gcc gaa tta cct  ttg caa tac act     27419
Ala  Ile Ala Val Thr Leu  Thr Ala Glu Leu Pro  Leu Gln Tyr Thr
2080                 2085                 2090

aac  aaa ctt caa ctg aat  att gga gct ggc ctt  cgt tac aat gga     27464
Asn  Lys Leu Gln Leu Asn  Ile Gly Ala Gly Leu  Arg Tyr Asn Gly
2095                 2100                 2105

gcc  agc aga aaa cta gat  gta aac att aac caa  aat aaa ggc tta     27509
Ala  Ser Arg Lys Leu Asp  Val Asn Ile Asn Gln  Asn Lys Gly Leu
2110                 2115                 2120

act  tgg gac aac gat gca  gtt att ccc aaa cta  gga tcg ggc tta     27554
Thr  Trp Asp Asn Asp Ala  Val Ile Pro Lys Leu  Gly Ser Gly Leu
2125                 2130                 2135

caa  ttt gac cct aat ggc  aac atc gct gtt atc  cct gaa acc gtg     27599
Gln  Phe Asp Pro Asn Gly  Asn Ile Ala Val Ile  Pro Glu Thr Val
2140                 2145                 2150

aag  ccg caa acg tta tgg  acg act gca gat ccc  tcg cct aac tgc     27644
Lys  Pro Gln Thr Leu Trp  Thr Thr Ala Asp Pro  Ser Pro Asn Cys
2155                 2160                 2165

tca  gtg tac cag gac ttg  gat gcc agg ctg tgg  ctc gct ctt gtt     27689
Ser  Val Tyr Gln Asp Leu  Asp Ala Arg Leu Trp  Leu Ala Leu Val
2170                 2175                 2180

aaa  agt ggc gac atg gtg  cat gga agc att gcc  cta aaa gcc cta     27734
Lys  Ser Gly Asp Met Val  His Gly Ser Ile Ala  Leu Lys Ala Leu
2185                 2190                 2195

aaa  ggg acg ttg cta aat  cct aca gcc agc tac  att tcc att gtg     27779
Lys  Gly Thr Leu Leu Asn  Pro Thr Ala Ser Tyr  Ile Ser Ile Val
2200                 2205                 2210

ata  tat ttt tac agc aac  gga gtc agg cgt acc  aac tat cca acg     27824
Ile  Tyr Phe Tyr Ser Asn  Gly Val Arg Arg Thr  Asn Tyr Pro Thr
2215                 2220                 2225

ttt  gac aac gaa ggc acc  tta gct aac agc gcc  act tgg gga tac     27869
Phe  Asp Asn Glu Gly Thr  Leu Ala Asn Ser Ala  Thr Trp Gly Tyr
2230                 2235                 2240

cga  cag ggg caa tct gct  aac act aat gtg acc  aat gcc act gaa     27914
Arg  Gln Gly Gln Ser Ala  Asn Thr Asn Val Thr  Asn Ala Thr Glu
2245                 2250                 2255

ttt  atg ccc agc tca agc  agg tac ccc gtg aat  aaa gga gac aac     27959
Phe  Met Pro Ser Ser Ser  Arg Tyr Pro Val Asn  Lys Gly Asp Asn
2260                 2265                 2270
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```
att  caa aat caa tct ttt  tca tac acc tgt att  aaa gga gat ttt     28004
Ile  Gln Asn Gln Ser Phe  Ser Tyr Thr Cys Ile  Lys Gly Asp Phe
2275                 2280                 2285

gct  atg cct gtc ccg ttc  cgt gta aca tat aat  cac gcc ctg gaa     28049
Ala  Met Pro Val Pro Phe  Arg Val Thr Tyr Asn  His Ala Leu Glu
2290                 2295                 2300

ggg  tat tcc ctt aag ttc  acc tgg cgc gtt gta  gcc aat cag gcc     28094
Gly  Tyr Ser Leu Lys Phe  Thr Trp Arg Val Val  Ala Asn Gln Ala
2305                 2310                 2315

ttt  gat att cct tgc tgt  tca ttt tca tac atc  aca gaa taa         28136
Phe  Asp Ile Pro Cys Cys  Ser Phe Ser Tyr Ile  Thr Glu
2320                 2325                 2330

aaaaccactt tttcatttta atttcttttt attttacacg aacagtgaga cttcctccac  28196

ccttccattt gacagcatac accagcctct ccccccttcat agcagtaaac tgttgtgaat  28256

cagtccggta tttgggagtt aaaatccaaa cagtctcttt ggtgatgaaa cgtcgatcag  28316

taatggacac aaatccctgg gacaggtttt ccaacgtttc ggtgaaaaac tgcacaccgc  28376

cctacaaaac aaacaggttc aggctctcca cgggttatct ccccgatcaa actcagacag  28436

ggtaaaggtg cggtggtgtt ccactaaacc acgcaggtgg cgctgtctga acctctcggt  28496

gcgactcctg tgaggctggt aagaagttag attgtccagt agcctcacag catgtatcat  28556

cagtctacga gtgcgtctgg cgcagcagcg catctgaatc tcactgagat tccggcaaga  28616

atcgcacacc atcacaatca ggttgttcat gatcccatag ctgaacacgc tccagccaaa  28676

gctcattcgc tccaacagcg ccaccgcgtg tccgtccaac cttactttaa cataaatcag  28736

gtgtctgccg cgtacaaaca tgctacccac atacagaact tcccggggca ggcccctgtt  28796

caccacctgt ctgtaccagg gaaacctcac atttatcagg gagccataga tggccatttt  28856

aaaccaatta gctaataccg ccccaccagc tctacactga agagaaccgg gagagttaca  28916

atgacagtga ataatccatc tctcataacc cctgatggtc tgatgaaaat ctagatctaa  28976

cgtggcacaa caaatacaca ctttcatata cattttcata acatgttttt cccaggccgt  29036

taaaatacaa tcccaataca cgggccactc ctgcagtaca ataaagctaa tacaagatgg  29096

tatactcctc acctcactga cactgtgcat gttcatattt tcacattcta agtaccgaga  29156

gttctcctct acagcagcac tgctgcggtc ctcacaaggt ggtagctggt gatgattgta  29216

gggggccagt ctgcagcgat accgtctgtc gcgttgcatc gtagaccagg aaccgacgca  29276

cctcctcgta cttgtggtag cagaaccacg tccgctgcca gcacgtctcc acgtaacgcc  29336

ggtccctgcg tcgctcacgc tccctcctca atgcaaagtg caaccactct tgtaatccac  29396
```

acagatccct ctcggcctcc ggggtgatgc acacctcaaa cctacagatg tctcggtaca 29456

gttccaaaca cgtagtgagg gcgagttcca accaagacag acagcctgat ctatcccgac 29516

acactggagg tggaggaaga cacggaagag gcatgttatt ccaagcgatt caccaacggg 29576

tcgaaatgaa gatcccgaag atgacaacgg tcgcctccgg agccctgatg gaatttaaca 29636

gccagatcaa acgttatgcg attctccaag ctatcgatcg ccgcttccaa aagagcctgg 29696

acccgcactt ccacaaacac cagcaaagca aaagcactat tatcaaactc ttcaatcatc 29756

aagctgcagg actgtacaat gcctaagtaa ttttcgtttc tccactcgcg aatgatgtcg 29816

cggcagatag tctgaaggtt catcccgtgc agggtaaaaa gctccgaaag ggcgccctct 29876

acagccatgc gtagacacac catcatgact gcaagatatc gggctcctga gacacctgca 29936

gcagatttaa cagatcaagg tcaggttgct ctccgcgatc acgaatctcc atccgcaagg 29996

tcatttgcaa aaaattaaat aaatctatgc cgactagatc tgtcaactcc gcattaggaa 30056

ccaaatcagg tgtggctacg cagcacaaaa gttccaggga tggtgccaaa ctcactagaa 30116

ccgctcccga gtaacaaaac tgatgaatgg gagtaacaca gtgtaaaatg tgcaaccaaa 30176

aatcactaag gtgctccttt aaaaagtcca gtacttctat attcagtccg tgcaagtact 30236

gaagcaactg tgcgggaata tgcacaacaa aaaaaatagg gcggctcaga tacatgttga 30296

cctaaaataa aaagaatcat taaactaaag aagcttggcg aacggtggga taaatgacac 30356

gctccagcag cagacaggca accggctgtc cccgggaacc gcggtaaaat tcatccgaat 30416

gattaaaaag aacaacagaa acttcccacc atgtactcgg ttggatctcc tgagcacaca 30476

gcaatacccc cctcacattc atgtccgcca cagaaaaaaa acgtcccaga tacccagcgg 30536

ggatatccaa cgacagctgc aaagacagca aaacaatccc tctgggagcg atcacaaaat 30596

cctccggtga aaaaagcaca tacatattag aataaccctg ttgctggggc aaaaaggccc 30656

ggcgtcccag caaatgcaca taaatatgtt catcagccat tgccccgtct taccgcgtaa 30716

tcagccacga aaaaatcgag ctaaaattca cccaacagcc tatagctata tatacactcc 30776

gcccaatgac gctaataccg caccacccac gaccaaagtt cacccacacc cacaaaaccc 30836

gcgaaaatcc agcgccgtca gcacttccgc aatttcagtc tcacaacgtc acttccgcgc 30896

gccttttcac attcccacac acacccgcgc ccttcgcccc gccctcgcgc caccccgcgt 30956

caccgcacgt caccccggcc ccgcctcgct cctccccgct cattatcata ttggcacgtt 31016

tccagaataa ggtatattat tgatgatg 31044

<210> 30
<211> 505
<212> PRT
<213> simian adenovirus SV-25

<400> 30

Met Arg Arg Ala Val Arg Val Thr Pro Ala Ala Tyr Glu Gly Pro Pro
1 5 10 15

Pro Ser Tyr Glu Ser Val Met Gly Ser Ala Asn Val Pro Ala Thr Leu
20 25 30

Glu Ala Pro Tyr Val Pro Pro Arg Tyr Leu Gly Pro Thr Glu Gly Arg
35 40 45

Asn Ser Ile Arg Tyr Ser Glu Leu Ala Pro Leu Tyr Asp Thr Thr Lys
50 55 60

Val Tyr Leu Val Asp Asn Lys Ser Ala Asp Ile Ala Ser Leu Asn Tyr
65 70 75 80

Gln Asn Asp His Ser Asn Phe Leu Thr Thr Val Val Gln Asn Asn Asp
85 90 95

Phe Thr Pro Thr Glu Ala Gly Thr Gln Thr Ile Asn Phe Asp Glu Arg
100 105 110

Ser Arg Trp Gly Gly Gln Leu Lys Thr Ile Leu His Thr Asn Met Pro
115 120 125

Asn Ile Asn Glu Phe Met Ser Thr Asn Lys Phe Arg Ala Lys Leu Met
130 135 140

Val Glu Lys Ser Asn Ala Glu Thr Arg Gln Pro Arg Tyr Glu Trp Phe
145 150 155 160

Glu Phe Thr Ile Pro Glu Gly Asn Tyr Ser Glu Thr Met Thr Ile Asp
165 170 175

Leu Met Asn Asn Ala Ile Val Asp Asn Tyr Leu Gln Val Gly Arg Gln
180 185 190

Asn Gly Val Leu Glu Ser Asp Ile Gly Val Lys Phe Asp Thr Arg Asn
195 200 205

Phe Arg Leu Gly Trp Asp Pro Val Thr Lys Leu Val Met Pro Gly Val
210 215 220

Tyr Thr Asn Glu Ala Phe His Pro Asp Ile Val Leu Leu Pro Gly Cys
225 230 235 240

Gly Val Asp Phe Thr Gln Ser Arg Leu Ser Asn Leu Leu Gly Ile Arg
245 250 255

```
Lys Arg Arg Pro Phe Gln Glu Gly Phe Gln Ile Met Tyr Glu Asp Leu
            260                 265                 270

Glu Gly Gly Asn Ile Pro Ala Leu Leu Asp Val Ser Lys Tyr Glu Ala
        275                 280                 285

Ser Ile Gln Arg Ala Lys Ala Glu Gly Arg Glu Ile Arg Gly Asp Thr
    290                 295                 300

Phe Ala Val Ala Pro Gln Asp Leu Glu Ile Val Pro Leu Thr Lys Asp
305                 310                 315                 320

Ser Lys Asp Arg Ser Tyr Asn Ile Ile Asn Asn Thr Thr Asp Thr Leu
                325                 330                 335

Tyr Arg Ser Trp Phe Leu Ala Tyr Asn Tyr Gly Asp Pro Glu Lys Gly
            340                 345                 350

Val Arg Ser Trp Thr Ile Leu Thr Thr Thr Asp Val Thr Cys Gly Ser
        355                 360                 365

Gln Gln Val Tyr Trp Ser Leu Pro Asp Met Met Gln Asp Pro Val Thr
    370                 375                 380

Phe Arg Pro Ser Thr Gln Val Ser Asn Phe Pro Val Val Gly Thr Glu
385                 390                 395                 400

Leu Leu Pro Val His Ala Lys Ser Phe Tyr Asn Glu Gln Ala Val Tyr
                405                 410                 415

Ser Gln Leu Ile Arg Gln Ser Thr Ala Leu Thr His Val Phe Asn Arg
            420                 425                 430

Phe Pro Glu Asn Gln Ile Leu Val Arg Pro Pro Ala Pro Thr Ile Thr
        435                 440                 445

Thr Val Ser Glu Asn Val Pro Ala Leu Thr Asp His Gly Thr Leu Pro
    450                 455                 460

Leu Arg Ser Ser Ile Ser Gly Val Gln Arg Val Thr Ile Thr Asp Ala
465                 470                 475                 480

Arg Arg Arg Thr Cys Pro Tyr Val Tyr Lys Ala Leu Gly Val Val Ala
                485                 490                 495

Pro Lys Val Leu Ser Ser Arg Thr Phe
            500                 505
```

<210> 31
<211> 921
<212> PRT
<213> simian adenovirus SV-25

<400> 31

```
Met Ala Thr Pro Ser Met Met Pro Gln Trp Ser Tyr Met His Ile Ala
1               5                   10                  15
```

```
Gly Gln Asp Ala Ser Glu Tyr Leu Ser Pro Gly Leu Val Gln Phe Ala
            20                  25                  30

Arg Ala Thr Asp Thr Tyr Phe Ser Leu Gly Asn Lys Phe Arg Asn Pro
        35                  40                  45

Thr Val Ala Pro Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg Leu
    50                  55                  60

Thr Leu Arg Phe Val Pro Val Asp Arg Glu Asp Thr Ala Tyr Ser Tyr
65                  70                  75                  80

Lys Val Arg Tyr Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met
                85                  90                  95

Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Leu Asp Arg Gly Pro Ser
            100                 105                 110

Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ser Leu Ala Pro Lys Gly
        115                 120                 125

Ala Pro Asn Pro Ser Glu Trp Thr Asp Thr Ser Asp Asn Lys Leu Lys
    130                 135                 140

Ala Tyr Ala Gln Ala Pro Tyr Gln Ser Gln Gly Leu Thr Lys Asp Gly
145                 150                 155                 160

Ile Gln Val Gly Leu Val Val Thr Glu Ser Gly Gln Thr Pro Gln Tyr
                165                 170                 175

Ala Asn Lys Val Tyr Gln Pro Glu Pro Gln Ile Gly Glu Asn Gln Trp
            180                 185                 190

Asn Leu Glu Gln Glu Asp Lys Ala Ala Gly Arg Val Leu Lys Lys Asp
        195                 200                 205

Thr Pro Met Phe Pro Cys Tyr Gly Ser Tyr Ala Arg Pro Thr Asn Glu
    210                 215                 220

Gln Gly Gly Gln Ala Lys Asn Gln Glu Val Asp Leu Gln Phe Phe Ala
225                 230                 235                 240

Thr Pro Gly Asp Thr Gln Asn Thr Ala Lys Val Val Leu Tyr Ala Glu
                245                 250                 255

Asn Val Asn Leu Glu Thr Pro Asp Thr His Leu Val Phe Lys Pro Asp
            260                 265                 270

Asp Asp Ser Thr Ser Ser Lys Leu Leu Leu Gly Gln Gln Ala Ala Pro
        275                 280                 285

Asn Arg Pro Asn Tyr Ile Gly Phe Arg Asp Asn Phe Ile Gly Leu Met
    290                 295                 300
```

Tyr Tyr Asn Ser Thr Gly Asn Met Gly Val Leu Ala Gly Gln Ala Ser
305 310 315 320

Gln Leu Asn Ala Val Val Asp Leu Gln Asp Arg Asn Thr Glu Leu Ser
325 330 335

Tyr Gln Leu Met Leu Asp Ala Leu Gly Asp Arg Ser Arg Tyr Phe Ser
340 345 350

Met Trp Asn Gln Ala Val Asp Ser Tyr Asp Pro Asp Val Arg Ile Ile
355 360 365

Glu Asn His Gly Val Glu Asp Glu Leu Pro Asn Tyr Cys Phe Pro Leu
370 375 380

Gly Gly Met Val Val Thr Asp Asn Tyr Asn Ser Val Thr Pro Gln Asn
385 390 395 400

Gly Gly Ser Gly Asn Thr Trp Gln Ala Asp Asn Thr Thr Phe Ser Gln
405 410 415

Arg Gly Ala Gln Ile Gly Ser Gly Asn Met Phe Ala Leu Glu Ile Asn
420 425 430

Leu Gln Ala Asn Leu Trp Arg Gly Phe Leu Tyr Ser Asn Ile Gly Leu
435 440 445

Tyr Leu Pro Asp Ser Leu Lys Ile Thr Pro Asp Asn Ile Thr Leu Pro
450 455 460

Glu Asn Lys Asn Thr Tyr Gln Tyr Met Asn Gly Arg Val Thr Pro Pro
465 470 475 480

Gly Leu Ile Asp Thr Tyr Val Asn Val Gly Ala Arg Trp Ser Pro Asp
485 490 495

Val Met Asp Ser Ile Asn Pro Phe Asn His His Arg Asn Ala Gly Leu
500 505 510

Arg Tyr Arg Ser Met Leu Leu Gly Asn Gly Arg Tyr Val Pro Phe His
515 520 525

Ile Gln Val Pro Gln Lys Phe Phe Ala Ile Lys Asn Leu Leu Leu Leu
530 535 540

Pro Gly Ser Tyr Thr Tyr Glu Trp Asn Phe Arg Lys Asp Val Asn Met
545 550 555 560

Ile Leu Gln Ser Ser Leu Gly Asn Asp Leu Arg Val Asp Gly Ala Ser
565 570 575

Ile Arg Phe Asp Ser Ile Asn Leu Tyr Ala Asn Phe Phe Pro Met Ala
580 585 590

His Asn Thr Ala Ser Thr Leu Glu Ala Met Leu Arg Asn Asp Thr Asn
595 600 605

```
Asp Gln Ser Phe Asn Asp Tyr Leu Cys Ala Ala Asn Met Leu Tyr Pro
    610                 615                 620

Ile Pro Ala Asn Ala Thr Ser Val Pro Ile Ser Ile Pro Ser Arg Asn
625                 630                 635                 640

Trp Ala Ala Phe Arg Gly Trp Ser Phe Thr Arg Leu Lys Thr Lys Glu
                645                 650                 655

Thr Pro Ser Leu Gly Ser Gly Phe Asp Pro Tyr Phe Val Tyr Ser Gly
            660                 665                 670

Ser Ile Pro Tyr Leu Asp Gly Thr Phe Tyr Leu Asn His Thr Phe Lys
        675                 680                 685

Lys Val Ser Ile Met Phe Asp Ser Ser Val Ser Trp Pro Gly Asn Asp
    690                 695                 700

Arg Leu Leu Thr Pro Asn Glu Phe Glu Ile Lys Arg Ser Val Asp Gly
705                 710                 715                 720

Glu Gly Tyr Asn Val Ala Gln Ser Asn Met Thr Lys Asp Trp Phe Leu
                725                 730                 735

Ile Gln Met Leu Ser His Tyr Asn Ile Gly Tyr Gln Gly Phe Tyr Val
            740                 745                 750

Pro Glu Asn Tyr Lys Asp Arg Met Tyr Ser Phe Phe Arg Asn Phe Gln
        755                 760                 765

Pro Met Ser Arg Gln Val Val Asp Thr Val Thr Tyr Thr Asp Tyr Lys
    770                 775                 780

Asp Val Lys Leu Pro Tyr Gln His Asn Asn Ser Gly Phe Val Gly Tyr
785                 790                 795                 800

Met Gly Pro Thr Met Arg Glu Gly Gln Ala Tyr Pro Ala Asn Tyr Pro
                805                 810                 815

Tyr Pro Leu Ile Gly Glu Thr Ala Val Pro Ser Leu Thr Gln Lys Lys
            820                 825                 830

Phe Leu Cys Asp Arg Val Met Trp Arg Ile Pro Phe Ser Ser Asn Phe
        835                 840                 845

Met Ser Met Gly Ser Leu Thr Asp Leu Gly Gln Asn Met Leu Tyr Ala
    850                 855                 860

Asn Ser Ala His Ala Leu Asp Met Thr Phe Glu Val Asp Pro Met Asp
865                 870                 875                 880

Glu Pro Thr Leu Leu Tyr Val Leu Phe Glu Val Phe Asp Val Val Arg
                885                 890                 895

Ile His Gln Pro His Arg Gly Val Ile Glu Ala Val Tyr Leu Arg Thr
            900                 905                 910
```

Pro Phe Ser Ala Gly Asn Ala Thr Thr
915 920

<210> 32
<211> 347
<212> PRT
<213> simian adenovirus SV-25

<400> 32

Met Lys Ile Cys Val Val Ile Phe Ala Leu Ser Leu Ile Lys Thr Glu
1 5 10 15

Leu Phe Ala Val Pro Ser Thr Pro Arg Val Val Ser Pro Cys Glu Lys
20 25 30

Thr Pro Gly Val Leu Asn Leu His Ile Ala Lys Pro Leu Tyr Phe Thr
35 40 45

Ile Glu Lys Gln Leu Ala Leu Ser Ile Gly Lys Gly Leu Thr Ile Ser
50 55 60

Ala Thr Gly Gln Leu Glu Ser Thr Ala Ser Val Gln Asp Ser Ala Thr
65 70 75 80

Pro Pro Leu Arg Gly Ile Ser Pro Leu Lys Leu Thr Asp Asn Gly Leu
85 90 95

Thr Leu Ser Tyr Ser Asp Pro Leu Arg Val Val Gly Asp Gln Leu Thr
100 105 110

Phe Asn Phe Thr Ser Pro Leu Arg Tyr Glu Asn Gly Ser Leu Thr Phe
115 120 125

Asn Tyr Thr Ser Pro Met Thr Leu Ile Asn Asn Ser Leu Ala Ile Asn
130 135 140

Val Asn Thr Ser Lys Gly Leu Ser Ser Asp Asn Gly Thr Leu Ala Val
145 150 155 160

Asn Val Thr Pro Asp Phe Arg Phe Asn Ser Ser Gly Ala Leu Thr Phe
165 170 175

Gly Ile Gln Ser Leu Trp Thr Phe Pro Thr Lys Thr Pro Asn Cys Thr
180 185 190

Val Phe Thr Glu Ser Asp Ser Leu Leu Ser Leu Cys Leu Thr Lys Cys
195 200 205

Gly Ala His Val Leu Gly Ser Val Ser Leu Ser Gly Val Ala Gly Thr
210 215 220

Met Leu Lys Met Thr His Thr Ser Val Thr Val Gln Phe Ser Phe Asp
225 230 235 240

```
Asp Ser Gly Lys Leu Ile Phe Ser Pro Leu Ala Asn Asn Thr Trp Gly
                245                 250                 255

Val Arg Gln Ser Glu Ser Pro Leu Pro Asn Pro Ser Phe Asn Ala Leu
            260                 265                 270

Thr Phe Met Pro Asn Ser Thr Ile Tyr Ser Arg Gly Ala Ser Asn Glu
        275                 280                 285

Pro Gln Asn Asn Tyr Tyr Val Gln Thr Tyr Leu Arg Gly Asn Val Arg
    290                 295                 300

Lys Pro Ile Leu Leu Thr Val Thr Tyr Asn Ser Val Asn Ser Gly Tyr
305                 310                 315                 320

Ser Leu Thr Phe Lys Trp Asp Ala Val Ala Asn Glu Lys Phe Ala Thr
                325                 330                 335

Pro Thr Ser Ser Phe Cys Tyr Val Ala Glu Gln
            340                 345
```

<210> 33
<211> 559
<212> PRT
<213> simian adenovirus SV-25

<400> 33

```
Met Lys Arg Ala Arg Val Asp Glu Asp Phe Asn Pro Val Tyr Pro Tyr
1               5                   10                  15

Asp Pro Pro Tyr Ala Pro Val Met Pro Phe Ile Thr Pro Pro Phe Thr
            20                  25                  30

Ser Ser Asp Gly Leu Gln Glu Lys Pro Leu Gly Val Leu Ser Leu Asn
        35                  40                  45

Tyr Arg Asp Pro Ile Thr Thr Gln Asn Gly Ser Leu Thr Leu Lys Leu
    50                  55                  60

Gly Asn Gly Leu Thr Leu Asn Asn Gln Gly Gln Leu Thr Ser Thr Ala
65                  70                  75                  80

Gly Glu Val Glu Pro Pro Leu Thr Asn Ala Asn Asn Lys Leu Ala Leu
                85                  90                  95

Ala Tyr Ser Glu Pro Leu Ala Val Lys Ser Asn Arg Leu Thr Leu Ser
            100                 105                 110

His Thr Ala Pro Leu Val Ile Ala Asn Asn Ser Leu Ala Leu Gln Val
        115                 120                 125

Ser Glu Pro Ile Phe Val Asn Asp Asp Asp Lys Leu Ala Leu Gln Thr
    130                 135                 140
```

```
Ala Ala Pro Leu Val Thr Asn Ala Gly Thr Leu Arg Leu Gln Ser Ala
145                 150                 155                 160

Ala Pro Leu Gly Leu Val Glu Asn Thr Leu Lys Leu Leu Phe Ser Lys
                165                 170                 175

Pro Leu Tyr Leu Gln Asn Asp Phe Leu Ala Leu Ala Ile Glu Arg Pro
            180                 185                 190

Leu Ala Val Ala Ala Ala Gly Thr Leu Thr Leu Gln Leu Thr Pro Pro
        195                 200                 205

Leu Lys Thr Asn Asp Asp Gly Leu Thr Leu Ser Thr Val Glu Pro Leu
    210                 215                 220

Thr Val Lys Asn Gly Asn Leu Gly Leu Gln Ile Ser Arg Pro Leu Val
225                 230                 235                 240

Val Gln Asn Asn Gly Leu Ser Leu Ala Ile Thr Pro Pro Leu Arg Leu
                245                 250                 255

Phe Asn Ser Asp Pro Val Leu Gly Leu Gly Phe Thr Phe Pro Leu Ala
            260                 265                 270

Val Thr Asn Asn Leu Leu Ser Leu Asn Met Gly Asp Gly Val Lys Leu
        275                 280                 285

Thr Tyr Asn Lys Leu Thr Ala Asn Leu Gly Arg Asp Leu Gln Phe Glu
    290                 295                 300

Asn Gly Ala Ile Ala Val Thr Leu Thr Ala Glu Leu Pro Leu Gln Tyr
305                 310                 315                 320

Thr Asn Lys Leu Gln Leu Asn Ile Gly Ala Gly Leu Arg Tyr Asn Gly
                325                 330                 335

Ala Ser Arg Lys Leu Asp Val Asn Ile Asn Gln Asn Lys Gly Leu Thr
            340                 345                 350

Trp Asp Asn Asp Ala Val Ile Pro Lys Leu Gly Ser Gly Leu Gln Phe
        355                 360                 365

Asp Pro Asn Gly Asn Ile Ala Val Ile Pro Glu Thr Val Lys Pro Gln
    370                 375                 380

Thr Leu Trp Thr Thr Ala Asp Pro Ser Pro Asn Cys Ser Val Tyr Gln
385                 390                 395                 400

Asp Leu Asp Ala Arg Leu Trp Leu Ala Leu Val Lys Ser Gly Asp Met
                405                 410                 415

Val His Gly Ser Ile Ala Leu Lys Ala Leu Lys Gly Thr Leu Leu Asn
            420                 425                 430

Pro Thr Ala Ser Tyr Ile Ser Ile Val Ile Tyr Phe Tyr Ser Asn Gly
        435                 440                 445
```

```
Val Arg Arg Thr Asn Tyr Pro Thr Phe Asp Asn Glu Gly Thr Leu Ala
    450                 455                 460

Asn Ser Ala Thr Trp Gly Tyr Arg Gln Gly Gln Ser Ala Asn Thr Asn
465                 470                 475                 480

Val Thr Asn Ala Thr Glu Phe Met Pro Ser Ser Ser Arg Tyr Pro Val
                485                 490                 495

Asn Lys Gly Asp Asn Ile Gln Asn Gln Ser Phe Ser Tyr Thr Cys Ile
            500                 505                 510

Lys Gly Asp Phe Ala Met Pro Val Pro Phe Arg Val Thr Tyr Asn His
        515                 520                 525

Ala Leu Glu Gly Tyr Ser Leu Lys Phe Thr Trp Arg Val Val Ala Asn
    530                 535                 540

Gln Ala Phe Asp Ile Pro Cys Cys Ser Phe Ser Tyr Ile Thr Glu
545                 550                 555
```

<210> 34
<211> 34115
<212> DNA
<213> simian adenovirus SV-39

<220>
<221> CDS
<222> (13448)..(14959)
<223> L2 Penton

<220>
<221> CDS
<222> (17785)..(20538)
<223> L3 Hexon

<220>
<221> CDS
<222> (29515)..(31116)
<223> L5 Fiber #1

<400> 34

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catcatcaat ataacaccgc aagatggcga ccgagttaac atgcaaatga ggtgggcgga     60

gttacgcgac ctttgtcttg ggaacgcgga agtgggcgcg gcgggtttcg gggaggagcg    120

cggggcgggg cgggcgtgtc gcgcggcggt gacgcgccgg ggacccggaa attgagtagt    180

ttttattcat tttgcaagtt tttctgtaca ttttggcgcg aaaactgaaa cgaggaagtg    240

aaaagtgaaa aatgccgagg tagtcaccgg gtggagatct gacctttgcc gtgtggagtt    300

tacccgctga cgtgtgggtt tcggtctcta ttttttcact gtggttttcc gggtacggtc    360
```

aaaggtcccc attttatgac tccacgtcag ctgatcgcta gggtatttaa tgcgcctcag 420

accgtcaaga ggccactctt gagtgccggc gagaagagtt ttctcctccg cgttccgcca 480

actgtgaaaa aatgaggaac ttcttgctat ctccggggct gccagcgacc gtagccgccg 540

agctgttgga ggacattgtt accggagctc tgggagacga tcctcaggtg atttctcact 600

tttgtgaaga ttttagtctt catgatctct atgatattga tccgggtgtt gaggggcaag 660

aggatgaatg gctggagtct gtggatgggt tttttccgga cgctatgctg ctagaggctg 720

atttgccacc acctcacaac tctcacactg agcccgagtc agctgctatt cctgaattgt 780

catcaggtga acttgacttg gcttgttacg agactatgcc tccggagtcg gatgaggagg 840

acagcgggat cagcgatccc acggctttta tggtctctaa ggcgattgct atactaaaag 900

aagatgatga tggcgatgat ggatttcgac tggacgctcc ggcggtgccg gggagagact 960

gtaagtcctg tgaataccac cgggatcgta ccggagaccc gtctatgttg tgttctctgt 1020

gttatctccg tcttaacgct gcttttgtct acagtaagtg ttttgtgctt ttttaccctg 1080

tggctttgtt gagtttattt ttttctgtgt ctcatagggt gttgtttatt ataggtcctg 1140

tttcagatgt ggaggaacct gatagtacta ctggaaatga ggaggaaaag ccctccccgc 1200

cgaaactaac tcagcgctgc agacctaata ttttgagacc ctcggcccag cgtgtgtcat 1260

cccggaaacg tgctgctgtt aattgcatag aagatttatt ggaagagccc actgaacctt 1320

tggacttgtc cttaaagcga ccccgcccgc agtagggcgc ggtgccagtt ttttctctct 1380

agcttccggg tgactcagtg caataaaaat tttcttggca acaggtgtat gtgtttactt 1440

tacgggcggg aagggattag gggagtataa agctggaggg gaaaaatctg aggctgtcag 1500

atcgagtgag aagttccatg gacttgtacg agagcctaga gaatctaagt tctttgcgac 1560

gtttgctgga ggaggcctcc gacagaacct cttacatttg gaggtttctg ttcggttccc 1620

ctctgagtcg ctttttgcac cgggtgaagc gagagcacct gacggaattt gatgggcttt 1680

tagagcagct gcctggactg tttgattctt tgaatctcgg ccaccggacg ctgctagagg 1740

agaggctttt tccacaattg gacttttcct ctccaggccg tctgtgttca gcgcttgctt 1800

ttgctgtaca tctgttggac agatggaacg agcagacgca gctcagcccg ggttacactc 1860

tggacttcct gacgctatgc ctatggaagt tcggaatcag gaggggggagg aagctgtacg 1920

ggcgcttggt ggagaggcat ccgtctctgc gccagcagcg tctgcaagct caagtgctgc 1980

tgaggcggga ggatctggaa gccatttcgg aggaggagag cggcatggaa gagaagaatc 2040

cgagagcggg gctggaccct ccggcggagg agtaggggggg ataccggacc cttttcctga 2100

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Leu Glu Gly Gly Asn Ile Pro Ala Leu Leu Asp Val Pro Ala Tyr Glu
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gag agc atc gcc aac gca agg gag gcg gcg atc agg ggc gat aat ttc    14353
Glu Ser Ile Ala Asn Ala Arg Glu Ala Ala Ile Arg Gly Asp Asn Phe
            290                 295                 300
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gcg gcg cag ccc cag gcg gct cca acc ata aaa ccc gtt ttg gaa gac    14401
Ala Ala Gln Pro Gln Ala Ala Pro Thr Ile Lys Pro Val Leu Glu Asp
        305                 310                 315

tcc aaa ggg cgg agc tac aac gta ata gcc aac acc aac aac acg gct    14449
Ser Lys Gly Arg Ser Tyr Asn Val Ile Ala Asn Thr Asn Asn Thr Ala
    320                 325                 330

tac agg agc tgg tat ctg gct tat aac tac ggc gac ccg gag aag ggg    14497
Tyr Arg Ser Trp Tyr Leu Ala Tyr Asn Tyr Gly Asp Pro Glu Lys Gly
335                 340                 345                 350

gtt agg gcc tgg acc ctg ctc acc act ccg gac gtg acg tgc ggt tca    14545
Val Arg Ala Trp Thr Leu Leu Thr Thr Pro Asp Val Thr Cys Gly Ser
                355                 360                 365

gag cag gtc tac tgg tcg ctg cct gac atg tac gtg gac cct gtg acg    14593
Glu Gln Val Tyr Trp Ser Leu Pro Asp Met Tyr Val Asp Pro Val Thr
            370                 375                 380

ttt cgc tcc acg cag caa gtt agc aac tac cca gtg gtg gga gcg gag    14641
Phe Arg Ser Thr Gln Gln Val Ser Asn Tyr Pro Val Val Gly Ala Glu
        385                 390                 395

ctt atg ccg att cac agc aag agc ttt tac aac gag cag gcc gtc tac    14689
Leu Met Pro Ile His Ser Lys Ser Phe Tyr Asn Glu Gln Ala Val Tyr
    400                 405                 410

tca cag ctc att cgt cag acc acc gcc cta acg cac gtt ttc aac cgc    14737
Ser Gln Leu Ile Arg Gln Thr Thr Ala Leu Thr His Val Phe Asn Arg
415                 420                 425                 430

ttc ccc gag aac caa atc cta gtg cga cct cca gcg ccc acc atc acc    14785
Phe Pro Glu Asn Gln Ile Leu Val Arg Pro Pro Ala Pro Thr Ile Thr
                435                 440                 445

acc gtc agc gag aac gtg ccc gct cta acc gat cac ggg acg ctg cct    14833
Thr Val Ser Glu Asn Val Pro Ala Leu Thr Asp His Gly Thr Leu Pro
            450                 455                 460

ttg cag aac agc atc cgc gga gtt cag cga gtt acc atc acg gac gcc    14881
Leu Gln Asn Ser Ile Arg Gly Val Gln Arg Val Thr Ile Thr Asp Ala
        465                 470                 475

cgt cgt cgg acc tgt ccc tac gtc tac aaa gcc ttg gga atc gtg gcc    14929
Arg Arg Arg Thr Cys Pro Tyr Val Tyr Lys Ala Leu Gly Ile Val Ala
    480                 485                 490

ccg cgc gtc ctg tcg agt cgc act ttc tag atgtccatcc tcatctctcc      14979
Pro Arg Val Leu Ser Ser Arg Thr Phe
495                 500

cagcaacaat accggttggg gtctgggcgt gaccaaaatg tacggaggcg ccaaacgacg  15039

gtccccacaa catcccgtgc gagtgcgcgg gcactttaga gccccatggg ggtcgcacac  15099

gcgcgggcgc accggccgaa ccaccgtcga cgacgtgatc gatagcgtgg tggccgacgc  15159
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ccgcaactac cagcccgctc gatccacggt ggacgaagtc atcgacggcg tggtggccga 15219

cgccagggcc tacgcccgca gaaagtctcg tctgcgccgc cgccgttcgc taaagcgccc 15279

cacggccgcc atgaaagccg ctcgctctct gctgcgtcgc gcacgtatcg tgggtcgccg 15339

cgccgccaga cgcgcagccg ccaacgccgc cgccggccga gtgcgccgcc gggccgccca 15399

gcaggccgcc gccgccatct ccagtctatc cgccccccga cgcgggaatg tgtactgggt 15459

cagggactcg gccaccggcg tgcgagttcc cgtgagaacc cgtcctcctc gtccctgaat 15519

aaaaagttct aagcccaatc ggtgttccgt tgtgtgttca gctcgtcatg accaaacgca 15579

agtttaaaga ggagctgctg caagcgctgg tccccgaaat ctatgcgccg gcgccggacg 15639

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gcgccgcaca ggcggtagag gccatgcaga ccgacgtggg gatgatgacg gacctgcccg 16299

cagctgctgc cgccgtggcc agcgccgcga cgcaaacgga agccggcatg cagaccgacc 16359

cgtggacgga ggcgcccgtg cagccggcca gaagacgcgt cagacggacg tacggccccg 16419

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gcacggcacg cggccgtata tggggacgtg gagcgagatc ggcacgaacc agatgaacgg  17019

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cgccaactgg cagaccaccc tcaacagtat tgtcggactg ggggtgaagt ctctgaagcg  17679

ccgtcgctgt ttttaaagca caatttatta aacgagtagc cctgtcttaa tccatcgttg  17739

tatgtgtgcc tatatcacgc gttcagagcc tgaccgtccg tcaag atg gcc act ccg  17796
                                                Met Ala Thr Pro
                                                    505

tcg atg atg ccg cag tgg tcg tac atg cac atc gcc ggg cag gac gcc    17844
Ser Met Met Pro Gln Trp Ser Tyr Met His Ile Ala Gly Gln Asp Ala
        510                 515                 520

tcg gag tac ctg agc ccg ggt ctg gtg cag ttt gcc cgt gcg acg gaa    17892
Ser Glu Tyr Leu Ser Pro Gly Leu Val Gln Phe Ala Arg Ala Thr Glu
    525                 530                 535

acc tac ttc tca ctg ggc aac aag ttc agg aac ccc acc gtg gcg ccc    17940
Thr Tyr Phe Ser Leu Gly Asn Lys Phe Arg Asn Pro Thr Val Ala Pro
540                 545                 550                 555

acc cac gac gtc acc acc gat cgg tcc cag cga ctg aca atc cgc ttc    17988
Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg Leu Thr Ile Arg Phe
                560                 565                 570

gtc ccc gtg gac aag gaa gac acc gct tac tcc tac aaa acc cgc ttc    18036
Val Pro Val Asp Lys Glu Asp Thr Ala Tyr Ser Tyr Lys Thr Arg Phe
            575                 580                 585

acg ctg gcc gtg ggc gac aac cgg gtg cta gac atg gcc agt acc tac    18084
Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met Ala Ser Thr Tyr
        590                 595                 600
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ttt gac atc cgc ggc gtg atc gac cgc gga cct agc ttc aag cct tac    18132
Phe Asp Ile Arg Gly Val Ile Asp Arg Gly Pro Ser Phe Lys Pro Tyr
    605                 610                 615

tcc ggc acg gct tac aac tca ctg gct ccc aaa ggg gcg ccc aac aac    18180
Ser Gly Thr Ala Tyr Asn Ser Leu Ala Pro Lys Gly Ala Pro Asn Asn
620                 625                 630                 635

agc caa tgg aac gcc aca gat aac ggg aac aag cca gtg tgt ttt gct    18228
Ser Gln Trp Asn Ala Thr Asp Asn Gly Asn Lys Pro Val Cys Phe Ala
                640                 645                 650

cag gca gct ttt ata ggt caa agc att aca aaa gac gga gtg caa ata    18276
Gln Ala Ala Phe Ile Gly Gln Ser Ile Thr Lys Asp Gly Val Gln Ile
            655                 660                 665

cag aac tca gaa aat caa cag gct gct gcc gac aaa act tac caa cca    18324
Gln Asn Ser Glu Asn Gln Gln Ala Ala Ala Asp Lys Thr Tyr Gln Pro
        670                 675                 680

gag cct caa att gga gtt tcc acc tgg gat acc aac gtt acc agt aac    18372
Glu Pro Gln Ile Gly Val Ser Thr Trp Asp Thr Asn Val Thr Ser Asn
    685                 690                 695

gct gcc gga cga gtg tta aaa gcc acc act ccc atg ctg cca tgt tac    18420
Ala Ala Gly Arg Val Leu Lys Ala Thr Thr Pro Met Leu Pro Cys Tyr
700                 705                 710                 715

ggt tca tat gcc aat ccc act aat cca aac ggg ggt cag gca aaa aca    18468
Gly Ser Tyr Ala Asn Pro Thr Asn Pro Asn Gly Gly Gln Ala Lys Thr
                720                 725                 730

gaa gga gac att tcg cta aac ttt ttc aca aca act gcg gca gca gac    18516
Glu Gly Asp Ile Ser Leu Asn Phe Phe Thr Thr Thr Ala Ala Ala Asp
            735                 740                 745

aat aat ccc aaa gtg gtt ctt tac agc gaa gat gta aac ctt caa gcc    18564
Asn Asn Pro Lys Val Val Leu Tyr Ser Glu Asp Val Asn Leu Gln Ala
        750                 755                 760

ccc gat act cac tta gta tat aag cca acg gtg gga gaa aac gtt atc    18612
Pro Asp Thr His Leu Val Tyr Lys Pro Thr Val Gly Glu Asn Val Ile
    765                 770                 775

gcc gca gaa gcc ctg cta acg cag cag gcg tgt ccc aac aga gca aac    18660
Ala Ala Glu Ala Leu Leu Thr Gln Gln Ala Cys Pro Asn Arg Ala Asn
780                 785                 790                 795

tac ata ggt ttc cga gat aac ttt atc ggt tta atg tat tat aac agc    18708
Tyr Ile Gly Phe Arg Asp Asn Phe Ile Gly Leu Met Tyr Tyr Asn Ser
                800                 805                 810

aca ggg aac atg gga gtt ctg gca ggt cag gcc tcg cag tta aac gca    18756
Thr Gly Asn Met Gly Val Leu Ala Gly Gln Ala Ser Gln Leu Asn Ala
            815                 820                 825
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gtt gta gac ctg caa gat cga aac acg gaa ctg tcc tat cag cta atg    18804
Val Val Asp Leu Gln Asp Arg Asn Thr Glu Leu Ser Tyr Gln Leu Met
        830                 835                 840

cta gat gct ctg ggt gac aga act cga tat ttc tca atg tgg aat cag    18852
Leu Asp Ala Leu Gly Asp Arg Thr Arg Tyr Phe Ser Met Trp Asn Gln
    845                 850                 855

gcc gtg gac agc tac gat cca gac gtt agg att atc gag aac cat ggg    18900
Ala Val Asp Ser Tyr Asp Pro Asp Val Arg Ile Ile Glu Asn His Gly
860                 865                 870                 875

gtg gaa gac gag ctg ccc aat tac tgt ttt cca ctc cca ggc atg ggt    18948
Val Glu Asp Glu Leu Pro Asn Tyr Cys Phe Pro Leu Pro Gly Met Gly
                880                 885                 890

att ttt aac tcc tac aag ggg gta aaa cca caa aat ggc ggt aat ggt    18996
Ile Phe Asn Ser Tyr Lys Gly Val Lys Pro Gln Asn Gly Gly Asn Gly
            895                 900                 905

aac tgg gaa gca aac ggg gac cta tca aat gcc aat gag atc gct tta    19044
Asn Trp Glu Ala Asn Gly Asp Leu Ser Asn Ala Asn Glu Ile Ala Leu
        910                 915                 920

gga aac att ttt gcc atg gaa att aac ctc cac gca aac ctg tgg cgc    19092
Gly Asn Ile Phe Ala Met Glu Ile Asn Leu His Ala Asn Leu Trp Arg
    925                 930                 935

agc ttc ttg tac agc aat gtg gcg ctg tac ctg cca gac agc tat aaa    19140
Ser Phe Leu Tyr Ser Asn Val Ala Leu Tyr Leu Pro Asp Ser Tyr Lys
940                 945                 950                 955

ttc act ccc gct aac atc act ctg ccc gcc aac caa aac acc tac gag    19188
Phe Thr Pro Ala Asn Ile Thr Leu Pro Ala Asn Gln Asn Thr Tyr Glu
                960                 965                 970

tat atc aac ggg cgc gtc act tct cca acc ctg gtg gac acc ttt gtt    19236
Tyr Ile Asn Gly Arg Val Thr Ser Pro Thr Leu Val Asp Thr Phe Val
            975                 980                 985

aac att gga gcc cga tgg tcg ccg gat ccc atg gac aac  gtc aac ccc    19284
Asn Ile Gly Ala Arg Trp Ser Pro Asp Pro Met Asp Asn  Val Asn Pro
        990                 995                 1000

ttt aac  cat cac cgg aac gcg  ggc ctc cgt tac cgc  tcc atg ctg      19329
Phe Asn  His His Arg Asn Ala  Gly Leu Arg Tyr Arg  Ser Met Leu
    1005                1010                1015

ctg gga  aat gga cgc gtg gtg  cct ttc cac ata caa  gtg ccg caa      19374
Leu Gly  Asn Gly Arg Val Val  Pro Phe His Ile Gln  Val Pro Gln
    1020                1025                1030

aaa ttt  ttc gcg att aag aac  ctc ctg ctt ttg ccc  ggc tcc tac      19419
Lys Phe  Phe Ala Ile Lys Asn  Leu Leu Leu Leu Pro  Gly Ser Tyr
    1035                1040                1045
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act tac  gag tgg agc ttc aga  aaa gac gtg aac atg  att ctg cag     19464
Thr Tyr  Glu Trp Ser Phe Arg  Lys Asp Val Asn Met  Ile Leu Gln
    1050                 1055                 1060

agc acc  ctg ggc aat gat ctt  cga gtg gac ggg gcc  agc gtc cgc     19509
Ser Thr  Leu Gly Asn Asp Leu  Arg Val Asp Gly Ala  Ser Val Arg
    1065                 1070                 1075

att gac  agc gtc aac ttg tac  gcc aac ttt ttc ccc  atg gcg cac     19554
Ile Asp  Ser Val Asn Leu Tyr  Ala Asn Phe Phe Pro  Met Ala His
    1080                 1085                 1090

aac acc  gct tct acc ttg gaa  gcc atg ctg cga aac  gac acc aac     19599
Asn Thr  Ala Ser Thr Leu Glu  Ala Met Leu Arg Asn  Asp Thr Asn
    1095                 1100                 1105

gac cag  tcg ttt aac gac tac  ctc agc gcg gcc aac  atg ctt tat     19644
Asp Gln  Ser Phe Asn Asp Tyr  Leu Ser Ala Ala Asn  Met Leu Tyr
    1110                 1115                 1120

ccc att  ccg gcc aac gcc acc  aac gtt ccc att tcc  att ccc tcc     19689
Pro Ile  Pro Ala Asn Ala Thr  Asn Val Pro Ile Ser  Ile Pro Ser
    1125                 1130                 1135

cgc aac  tgg gcg gcc ttc cgg  gga tgg agc ttc acc  cgc ctt aaa     19734
Arg Asn  Trp Ala Ala Phe Arg  Gly Trp Ser Phe Thr  Arg Leu Lys
    1140                 1145                 1150

gcc aag  gaa acg cct tcc ttg  ggc tcc ggc ttt gac  ccc tac ttt     19779
Ala Lys  Glu Thr Pro Ser Leu  Gly Ser Gly Phe Asp  Pro Tyr Phe
    1155                 1160                 1165

gtg tac  tca ggc acc att cct  tac ctg gac ggc agc  ttt tac ctc     19824
Val Tyr  Ser Gly Thr Ile Pro  Tyr Leu Asp Gly Ser  Phe Tyr Leu
    1170                 1175                 1180

aac cac  act ttc aaa cgt ctg  tcc atc atg ttc gat  tct tcc gta     19869
Asn His  Thr Phe Lys Arg Leu  Ser Ile Met Phe Asp  Ser Ser Val
    1185                 1190                 1195

agt tgg  ccg ggc aac gac cgc  ctc ctg acg ccg aac  gag ttc gaa     19914
Ser Trp  Pro Gly Asn Asp Arg  Leu Leu Thr Pro Asn  Glu Phe Glu
    1200                 1205                 1210

att aag  cgc att gtg gac ggg  gaa ggc tac aac gtg  gct caa agt     19959
Ile Lys  Arg Ile Val Asp Gly  Glu Gly Tyr Asn Val  Ala Gln Ser
    1215                 1220                 1225

aac atg  acc aaa gac tgg ttt  tta att caa atg ctc  agc cac tac     20004
Asn Met  Thr Lys Asp Trp Phe  Leu Ile Gln Met Leu  Ser His Tyr
    1230                 1235                 1240

aac atc  ggc tac caa ggc ttc  tat gtt ccc gag ggc  tac aag gat     20049
Asn Ile  Gly Tyr Gln Gly Phe  Tyr Val Pro Glu Gly  Tyr Lys Asp
    1245                 1250                 1255
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cgg atg  tat tct ttc ttc cga  aac ttt cag ccc atg  agc cgc cag      20094
Arg Met  Tyr Ser Phe Phe Arg  Asn Phe Gln Pro Met  Ser Arg Gln
    1260                 1265                 1270

gtg ccg  gat ccc acc gct gcc  ggc tat caa gcc gtt  ccc ctg ccc      20139
Val Pro  Asp Pro Thr Ala Ala  Gly Tyr Gln Ala Val  Pro Leu Pro
    1275                 1280                 1285

aga caa  cac aac aac tcg ggc  ttt gtg ggg tac atg  ggc ccg acc      20184
Arg Gln  His Asn Asn Ser Gly  Phe Val Gly Tyr Met  Gly Pro Thr
    1290                 1295                 1300

atg cgc  gaa gga cag cca tac  ccg gcc aac tac ccc  tat ccc ctg      20229
Met Arg  Glu Gly Gln Pro Tyr  Pro Ala Asn Tyr Pro  Tyr Pro Leu
    1305                 1310                 1315

atc ggc  gct acc gcc gtc ccc  gcc att acc cag aaa  aag ttt ttg      20274
Ile Gly  Ala Thr Ala Val Pro  Ala Ile Thr Gln Lys  Lys Phe Leu
    1320                 1325                 1330

tgc gac  cgc gtc atg tgg cgc  ata cct ttt tcc agc  aac ttt atg      20319
Cys Asp  Arg Val Met Trp Arg  Ile Pro Phe Ser Ser  Asn Phe Met
    1335                 1340                 1345

tca atg  ggg gcc ctg acc gac  ctc gga cag aac atg  ctt tac gct      20364
Ser Met  Gly Ala Leu Thr Asp  Leu Gly Gln Asn Met  Leu Tyr Ala
    1350                 1355                 1360

aac tcc  gcc cat gcc ctg gat  atg act ttt gag gtg  gac ccc atg      20409
Asn Ser  Ala His Ala Leu Asp  Met Thr Phe Glu Val  Asp Pro Met
    1365                 1370                 1375

aac gag  ccc acg ttg ctg tac  atg ctt ttt gag gtg  ttc gac gtg      20454
Asn Glu  Pro Thr Leu Leu Tyr  Met Leu Phe Glu Val  Phe Asp Val
    1380                 1385                 1390

gtc aga  gtg cac cag ccg cac  cgc ggt att atc gag  gcc gtg tac      20499
Val Arg  Val His Gln Pro His  Arg Gly Ile Ile Glu  Ala Val Tyr
    1395                 1400                 1405

ctg cgc  acc ccc ttc tct gcg  ggc aat gcc acc aca  taa gccgctgaac  20548
Leu Arg  Thr Pro Phe Ser Ala  Gly Asn Ala Thr Thr
    1410                 1415                 1420

tagctggttt ttaccccaga tcccatgggc tccacggaag acgaactgcg ggccattgtg  20608

cgagacctgg gctgcggacc ctacttcctg ggcacctttg acaagcggtt tcccgggttc  20668

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Phe  Asn Pro Val Tyr Pro  Tyr Gly Tyr Ser Thr  Pro Thr Asp Val
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Asp  Gly Lys Leu Val Gly  Glu Gly Gln Ala Ile  Leu Ala Asn Leu
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Pro  Leu Gln Ile Thr Asn  Asn Thr Ile Ser Leu  Arg Phe Gly Asn
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aca  ctt gcc ttg aat gac  aat aat gaa ctc caa  acc aca cta aaa     29856
Thr  Leu Ala Leu Asn Asp  Asn Asn Glu Leu Gln  Thr Thr Leu Lys
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Ser  Ser Ser Pro Leu Lys  Ile Thr Asp Gln Thr  Leu Ser Leu Asn
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Ile  Gly Asp Ser Leu Ala  Ile Lys Asp Asp Lys  Leu Glu Ser Ala
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ctt  caa gcg acc ctc cca  ctc tcc att agc aac  aac acc atc agc     29991
Leu  Gln Ala Thr Leu Pro  Leu Ser Ile Ser Asn  Asn Thr Ile Ser
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ctc  aac gtg ggc acc gga  ctc acc ata aat gga  aac gtt tta caa     30036
Leu  Asn Val Gly Thr Gly  Leu Thr Ile Asn Gly  Asn Val Leu Gln
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gct  gtt ccc tta aat gct  cta agt ccc cta act  att tcc aac aat     30081
Ala  Val Pro Leu Asn Ala  Leu Ser Pro Leu Thr  Ile Ser Asn Asn
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Asn  Ile Ser Leu Arg Tyr  Gly Ser Ser Leu Thr  Val Leu Asn Asn
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tcc  aac aac tca att tct  ctc aac act cta tct  ccg ttt aga atc     30216
Ser  Asn Asn Ser Ile Ser  Leu Asn Thr Leu Ser  Pro Phe Arg Ile
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gag  aat ggt ttc ctc acg  ctc tat ttg gga aca  aaa tct ggc ttg     30261
Glu  Asn Gly Phe Leu Thr  Leu Tyr Leu Gly Thr  Lys Ser Gly Leu
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Leu  Val Gln Asn Ser Gly  Leu Lys Val Gln Ala  Gly Tyr Gly Leu
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caa  gta aca gac acc aat  gct ctc aca tta aga  tat ctc gct cca     30351
Gln  Val Thr Asp Thr Asn  Ala Leu Thr Leu Arg  Tyr Leu Ala Pro
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Phe  Asp Thr Gly Asn Gly  Leu Thr Leu Ser Glu  Asn Lys Leu Ala
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gta  gct gca ggt agt ggt  cta act ttt aga gat  ggt gcc ttg gta     30576
Val  Ala Ala Gly Ser Gly  Leu Thr Phe Arg Asp  Gly Ala Leu Val
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gcc  acg gga acc gca ttt  acg caa aca ctg tgg  act acg gct gat     30621
Ala  Thr Gly Thr Ala Phe  Thr Gln Thr Leu Trp  Thr Thr Ala Asp
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Pro  Ser Pro Asn Cys Thr  Ile Ile Gln Asp Arg  Asp Thr Lys Phe
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Cys  Asn Met Tyr Val Ser  Thr Phe Leu Arg Gly  Asn Pro Gln Arg
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Pro  Ile Val Leu Asn Ile  Thr Phe Asn Asn Gln  Thr Ser Gly Phe
1910                 1915                 1920

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gctcagagca gcggctatat actctacctg tgacgtcaag aaccgaaagt caaaagttca 33876

cccggcgcgc ccgaaaaaac ccgcgaaaat ccacccaaaa agcccgcgaa aaacacttcc 33936

gtataaaatt tccgggttac cggcgcgtca ccgccgcgcg acacgcccgc cccgccccgc 33996

gctcctcccc gaaacccgcc gcgcccactt ccgcgttccc aagacaaagg tcgcgtaact 34056

ccgcccacct catttgcatg ttaactcggt cgccatcttg cggtgttata ttgatgatg 34115

<210> 35
<211> 503
<212> PRT
<213> simian adenovirus SV-39

<400> 35

Met Arg Arg Ala Val Ala Val Pro Ser Ala Ala Met Ala Leu Gly Pro
1 5 10 15

Pro Pro Ser Tyr Glu Ser Val Met Ala Ala Ala Thr Leu Gln Ala Pro
20 25 30

Leu Glu Asn Pro Tyr Val Pro Pro Arg Tyr Leu Glu Pro Thr Gly Gly
35 40 45

Arg Asn Ser Ile Arg Tyr Ser Glu Leu Thr Pro Leu Tyr Asp Thr Thr
50 55 60

Arg Leu Tyr Leu Val Asp Asn Lys Ser Ala Asp Ile Ala Thr Leu Asn
65 70 75 80

Tyr Gln Asn Asp His Ser Asn Phe Leu Thr Ser Val Val Gln Asn Ser
85 90 95

Asp Tyr Thr Pro Ala Glu Ala Ser Thr Gln Thr Ile Asn Leu Asp Asp
100 105 110

Arg Ser Arg Trp Gly Gly Asp Leu Lys Thr Ile Leu His Thr Asn Met
115 120 125

Pro Asn Val Asn Glu Phe Met Phe Thr Asn Ser Phe Arg Ala Lys Leu
130 135 140

Met Val Ala His Glu Ala Asp Lys Asp Pro Val Tyr Glu Trp Val Gln
145 150 155 160

```
Leu Thr Leu Pro Glu Gly Asn Phe Ser Glu Ile Met Thr Ile Asp Leu
                165                 170                 175

Met Asn Asn Ala Ile Ile Asp His Tyr Leu Ala Val Ala Arg Gln Gln
            180                 185                 190

Gly Val Lys Glu Ser Glu Ile Gly Val Lys Phe Asp Thr Arg Asn Phe
        195                 200                 205

Arg Leu Gly Trp Asp Pro Glu Thr Gly Leu Val Met Pro Gly Val Tyr
    210                 215                 220

Thr Asn Glu Ala Phe His Pro Asp Val Val Leu Leu Pro Gly Cys Gly
225                 230                 235                 240

Val Asp Phe Thr Tyr Ser Arg Leu Asn Asn Leu Leu Gly Ile Arg Lys
                245                 250                 255

Arg Met Pro Phe Gln Glu Gly Phe Gln Ile Leu Tyr Glu Asp Leu Glu
            260                 265                 270

Gly Gly Asn Ile Pro Ala Leu Leu Asp Val Pro Ala Tyr Glu Glu Ser
        275                 280                 285

Ile Ala Asn Ala Arg Glu Ala Ala Ile Arg Gly Asp Asn Phe Ala Ala
    290                 295                 300

Gln Pro Gln Ala Ala Pro Thr Ile Lys Pro Val Leu Glu Asp Ser Lys
305                 310                 315                 320

Gly Arg Ser Tyr Asn Val Ile Ala Asn Thr Asn Asn Thr Ala Tyr Arg
                325                 330                 335

Ser Trp Tyr Leu Ala Tyr Asn Tyr Gly Asp Pro Glu Lys Gly Val Arg
            340                 345                 350

Ala Trp Thr Leu Leu Thr Thr Pro Asp Val Thr Cys Gly Ser Glu Gln
        355                 360                 365

Val Tyr Trp Ser Leu Pro Asp Met Tyr Val Asp Pro Val Thr Phe Arg
    370                 375                 380

Ser Thr Gln Gln Val Ser Asn Tyr Pro Val Val Gly Ala Glu Leu Met
385                 390                 395                 400

Pro Ile His Ser Lys Ser Phe Tyr Asn Glu Gln Ala Val Tyr Ser Gln
                405                 410                 415

Leu Ile Arg Gln Thr Thr Ala Leu Thr His Val Phe Asn Arg Phe Pro
            420                 425                 430

Glu Asn Gln Ile Leu Val Arg Pro Pro Ala Pro Thr Ile Thr Thr Val
        435                 440                 445

Ser Glu Asn Val Pro Ala Leu Thr Asp His Gly Thr Leu Pro Leu Gln
    450                 455                 460
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```
Asn Ser Ile Arg Gly Val Gln Arg Val Thr Ile Thr Asp Ala Arg Arg
465                 470                 475                 480

Arg Thr Cys Pro Tyr Val Tyr Lys Ala Leu Gly Ile Val Ala Pro Arg
                485                 490                 495

Val Leu Ser Ser Arg Thr Phe
            500


<210>  36
<211>  917
<212>  PRT
<213>  simian adenovirus SV-39

<400>  36

Met Ala Thr Pro Ser Met Met Pro Gln Trp Ser Tyr Met His Ile Ala
1               5                   10                  15

Gly Gln Asp Ala Ser Glu Tyr Leu Ser Pro Gly Leu Val Gln Phe Ala
            20                  25                  30

Arg Ala Thr Glu Thr Tyr Phe Ser Leu Gly Asn Lys Phe Arg Asn Pro
        35                  40                  45

Thr Val Ala Pro Thr His Asp Val Thr Thr Asp Arg Ser Gln Arg Leu
    50                  55                  60

Thr Ile Arg Phe Val Pro Val Asp Lys Glu Asp Thr Ala Tyr Ser Tyr
65                  70                  75                  80

Lys Thr Arg Phe Thr Leu Ala Val Gly Asp Asn Arg Val Leu Asp Met
                85                  90                  95

Ala Ser Thr Tyr Phe Asp Ile Arg Gly Val Ile Asp Arg Gly Pro Ser
            100                 105                 110

Phe Lys Pro Tyr Ser Gly Thr Ala Tyr Asn Ser Leu Ala Pro Lys Gly
        115                 120                 125

Ala Pro Asn Asn Ser Gln Trp Asn Ala Thr Asp Asn Gly Asn Lys Pro
    130                 135                 140

Val Cys Phe Ala Gln Ala Ala Phe Ile Gly Gln Ser Ile Thr Lys Asp
145                 150                 155                 160

Gly Val Gln Ile Gln Asn Ser Glu Asn Gln Gln Ala Ala Ala Asp Lys
                165                 170                 175

Thr Tyr Gln Pro Glu Pro Gln Ile Gly Val Ser Thr Trp Asp Thr Asn
            180                 185                 190

Val Thr Ser Asn Ala Ala Gly Arg Val Leu Lys Ala Thr Thr Pro Met
        195                 200                 205
```

Leu Pro Cys Tyr Gly Ser Tyr Ala Asn Pro Thr Asn Pro Asn Gly Gly
210 215 220

Gln Ala Lys Thr Glu Gly Asp Ile Ser Leu Asn Phe Phe Thr Thr Thr
225 230 235 240

Ala Ala Ala Asp Asn Asn Pro Lys Val Val Leu Tyr Ser Glu Asp Val
245 250 255

Asn Leu Gln Ala Pro Asp Thr His Leu Val Tyr Lys Pro Thr Val Gly
260 265 270

Glu Asn Val Ile Ala Ala Glu Ala Leu Leu Thr Gln Gln Ala Cys Pro
275 280 285

Asn Arg Ala Asn Tyr Ile Gly Phe Arg Asp Asn Phe Ile Gly Leu Met
290 295 300

Tyr Tyr Asn Ser Thr Gly Asn Met Gly Val Leu Ala Gly Gln Ala Ser
305 310 315 320

Gln Leu Asn Ala Val Val Asp Leu Gln Asp Arg Asn Thr Glu Leu Ser
325 330 335

Tyr Gln Leu Met Leu Asp Ala Leu Gly Asp Arg Thr Arg Tyr Phe Ser
340 345 350

Met Trp Asn Gln Ala Val Asp Ser Tyr Asp Pro Asp Val Arg Ile Ile
355 360 365

Glu Asn His Gly Val Glu Asp Glu Leu Pro Asn Tyr Cys Phe Pro Leu
370 375 380

Pro Gly Met Gly Ile Phe Asn Ser Tyr Lys Gly Val Lys Pro Gln Asn
385 390 395 400

Gly Gly Asn Gly Asn Trp Glu Ala Asn Gly Asp Leu Ser Asn Ala Asn
405 410 415

Glu Ile Ala Leu Gly Asn Ile Phe Ala Met Glu Ile Asn Leu His Ala
420 425 430

Asn Leu Trp Arg Ser Phe Leu Tyr Ser Asn Val Ala Leu Tyr Leu Pro
435 440 445

Asp Ser Tyr Lys Phe Thr Pro Ala Asn Ile Thr Leu Pro Ala Asn Gln
450 455 460

Asn Thr Tyr Glu Tyr Ile Asn Gly Arg Val Thr Ser Pro Thr Leu Val
465 470 475 480

Asp Thr Phe Val Asn Ile Gly Ala Arg Trp Ser Pro Asp Pro Met Asp
485 490 495

Asn Val Asn Pro Phe Asn His His Arg Asn Ala Gly Leu Arg Tyr Arg
500 505 510

Ser Met Leu Leu Gly Asn Gly Arg Val Val Pro Phe His Ile Gln Val
515 520 525

Pro Gln Lys Phe Phe Ala Ile Lys Asn Leu Leu Leu Leu Pro Gly Ser
530 535 540

Tyr Thr Tyr Glu Trp Ser Phe Arg Lys Asp Val Asn Met Ile Leu Gln
545 550 555 560

Ser Thr Leu Gly Asn Asp Leu Arg Val Asp Gly Ala Ser Val Arg Ile
565 570 575

Asp Ser Val Asn Leu Tyr Ala Asn Phe Phe Pro Met Ala His Asn Thr
580 585 590

Ala Ser Thr Leu Glu Ala Met Leu Arg Asn Asp Thr Asn Asp Gln Ser
595 600 605

Phe Asn Asp Tyr Leu Ser Ala Ala Asn Met Leu Tyr Pro Ile Pro Ala
610 615 620

Asn Ala Thr Asn Val Pro Ile Ser Ile Pro Ser Arg Asn Trp Ala Ala
625 630 635 640

Phe Arg Gly Trp Ser Phe Thr Arg Leu Lys Ala Lys Glu Thr Pro Ser
645 650 655

Leu Gly Ser Gly Phe Asp Pro Tyr Phe Val Tyr Ser Gly Thr Ile Pro
660 665 670

Tyr Leu Asp Gly Ser Phe Tyr Leu Asn His Thr Phe Lys Arg Leu Ser
675 680 685

Ile Met Phe Asp Ser Ser Val Ser Trp Pro Gly Asn Asp Arg Leu Leu
690 695 700

Thr Pro Asn Glu Phe Glu Ile Lys Arg Ile Val Asp Gly Glu Gly Tyr
705 710 715 720

Asn Val Ala Gln Ser Asn Met Thr Lys Asp Trp Phe Leu Ile Gln Met
725 730 735

Leu Ser His Tyr Asn Ile Gly Tyr Gln Gly Phe Tyr Val Pro Glu Gly
740 745 750

Tyr Lys Asp Arg Met Tyr Ser Phe Phe Arg Asn Phe Gln Pro Met Ser
755 760 765

Arg Gln Val Pro Asp Pro Thr Ala Ala Gly Tyr Gln Ala Val Pro Leu
770 775 780

Pro Arg Gln His Asn Asn Ser Gly Phe Val Gly Tyr Met Gly Pro Thr
785 790 795 800

Met Arg Glu Gly Gln Pro Tyr Pro Ala Asn Tyr Pro Tyr Pro Leu Ile
805 810 815

```
Gly Ala Thr Ala Val Pro Ala Ile Thr Gln Lys Lys Phe Leu Cys Asp
            820                 825                 830

Arg Val Met Trp Arg Ile Pro Phe Ser Ser Asn Phe Met Ser Met Gly
        835                 840                 845

Ala Leu Thr Asp Leu Gly Gln Asn Met Leu Tyr Ala Asn Ser Ala His
    850                 855                 860

Ala Leu Asp Met Thr Phe Glu Val Asp Pro Met Asn Glu Pro Thr Leu
865                 870                 875                 880

Leu Tyr Met Leu Phe Glu Val Phe Asp Val Val Arg Val His Gln Pro
                885                 890                 895

His Arg Gly Ile Ile Glu Ala Val Tyr Leu Arg Thr Pro Phe Ser Ala
            900                 905                 910

Gly Asn Ala Thr Thr
        915
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<210> 37
<211> 533
<212> PRT
<213> simian adenovirus SV-39

<400> 37

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Met Lys Arg Ala Lys Val Glu Glu Gly Phe Asn Pro Val Tyr Pro Tyr
1               5                   10                  15

Gly Tyr Ser Thr Pro Thr Asp Val Ala Pro Pro Phe Val Ala Ser Asp
            20                  25                  30

Gly Leu Gln Glu Asn Pro Pro Gly Val Leu Ser Leu Lys Ile Ser Lys
        35                  40                  45

Pro Leu Thr Phe Asn Ala Ser Lys Ala Leu Ser Leu Ala Ile Gly Pro
    50                  55                  60

Gly Leu Lys Ile Gln Asp Gly Lys Leu Val Gly Glu Gly Gln Ala Ile
65                  70                  75                  80

Leu Ala Asn Leu Pro Leu Gln Ile Thr Asn Asn Thr Ile Ser Leu Arg
                85                  90                  95

Phe Gly Asn Thr Leu Ala Leu Asn Asp Asn Asn Glu Leu Gln Thr Thr
            100                 105                 110

Leu Lys Ser Ser Ser Pro Leu Lys Ile Thr Asp Gln Thr Leu Ser Leu
        115                 120                 125

Asn Ile Gly Asp Ser Leu Ala Ile Lys Asp Asp Lys Leu Glu Ser Ala
    130                 135                 140
```

```
Leu Gln Ala Thr Leu Pro Leu Ser Ile Ser Asn Asn Thr Ile Ser Leu
145                 150                 155                 160

Asn Val Gly Thr Gly Leu Thr Ile Asn Gly Asn Val Leu Gln Ala Val
                165                 170                 175

Pro Leu Asn Ala Leu Ser Pro Leu Thr Ile Ser Asn Asn Asn Ile Ser
            180                 185                 190

Leu Arg Tyr Gly Ser Ser Leu Thr Val Leu Asn Asn Glu Leu Gln Ser
        195                 200                 205

Asn Leu Thr Val His Ser Pro Leu Lys Leu Asn Ser Asn Asn Ser Ile
    210                 215                 220

Ser Leu Asn Thr Leu Ser Pro Phe Arg Ile Glu Asn Gly Phe Leu Thr
225                 230                 235                 240

Leu Tyr Leu Gly Thr Lys Ser Gly Leu Leu Val Gln Asn Ser Gly Leu
                245                 250                 255

Lys Val Gln Ala Gly Tyr Gly Leu Gln Val Thr Asp Thr Asn Ala Leu
            260                 265                 270

Thr Leu Arg Tyr Leu Ala Pro Leu Thr Ile Pro Asp Ser Gly Ser Glu
        275                 280                 285

Gln Gly Ile Leu Lys Val Asn Thr Gly Gln Gly Leu Ser Val Asn Gln
    290                 295                 300

Ala Gly Ala Leu Glu Thr Ser Leu Gly Gly Gly Leu Lys Tyr Ala Asp
305                 310                 315                 320

Asn Lys Ile Thr Phe Asp Thr Gly Asn Gly Leu Thr Leu Ser Glu Asn
                325                 330                 335

Lys Leu Ala Val Ala Ala Gly Ser Gly Leu Thr Phe Arg Asp Gly Ala
            340                 345                 350

Leu Val Ala Thr Gly Thr Ala Phe Thr Gln Thr Leu Trp Thr Thr Ala
        355                 360                 365

Asp Pro Ser Pro Asn Cys Thr Ile Ile Gln Asp Arg Asp Thr Lys Phe
    370                 375                 380

Thr Leu Ala Leu Thr Ile Ser Gly Ser Gln Val Leu Gly Thr Val Ser
385                 390                 395                 400

Ile Ile Gly Val Lys Gly Pro Leu Ser Ser Ser Ile Pro Ser Ala Thr
                405                 410                 415

Val Thr Val Gln Leu Asn Phe Asp Ser Asn Gly Ala Leu Leu Ser Ser
            420                 425                 430

Ser Ser Leu Lys Gly Tyr Trp Gly Tyr Arg Gln Gly Pro Ser Ile Asp
        435                 440                 445
```

```
Pro Tyr Pro Ile Ile Asn Ala Leu Asn Phe Met Pro Asn Ser Leu Ala
    450                 455                 460

Tyr Pro Pro Gly Gln Glu Ile Gln Ala Lys Cys Asn Met Tyr Val Ser
465                 470                 475                 480

Thr Phe Leu Arg Gly Asn Pro Gln Arg Pro Ile Val Leu Asn Ile Thr
                485                 490                 495

Phe Asn Asn Gln Thr Ser Gly Phe Ser Ile Arg Phe Thr Trp Thr Asn
            500                 505                 510

Leu Thr Thr Gly Glu Ala Phe Ala Met Pro Pro Cys Thr Phe Ser Tyr
        515                 520                 525

Ile Ala Glu Gln Gln
    530
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<210> 38
<211> 50
<212> DNA
<213> Artificial sequence

<220>
<223> oligomer SV25T

<400> 38
aatttaaata cgtagcgcac tagtcgcgct aagcgcggat atcatttaaa 50

<210> 39
<211> 49
<212> DNA
<213> Artificial sequence

<220>
<223> oligomer SV25B

<400> 39
tatttaaatg atatccgcgc ttaagcgcga ctagtgcgct acgtattta 49