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(54) EVOKING PROTECTION AGAINST STREPTOTOCCUS PNEUMONIAE INCORPORATING B-CELL AND T-CELL PNEUMOCOCCAL PROTEIN ANTIGENS AND PNEUMOCOCCAL POLYSACCHARIDES DELIVERED CONCOMITANTLY

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(57) ABSTRACT

This disclosure is directed to compositions that combine the polysaccharide-specific antibody protection afforded by the conventional vaccines through carrier effects provided by one or more pneumococcal common T-cell antigen(s) together with *Streptococcus pneumoniae*-specific Th-17 responses elicited by the pneumococcal carrier common T-cell antigen. The disclosed compositions are useful for pan-serotypic protection against NP carriage, and antibody responses against common pneumococcal virulence factors, potentially useful for pan-serotype protection against *Streptococcus pneumoniae* invasive diseases.

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CROSS-REFERENCE TO RELATED APPLICATION

[0001] This application claims the benefit of Provisional Application No. 61/879,040, filed Sep. 17, 2013, which is expressly incorporated herein by reference in its entirety.

STATEMENT REGARDING SEQUENCE LISTING

[0002] The sequence listing associated with this application is provided in text format in lieu of a paper copy and is hereby incorporated by reference into the specification. The name of the text file containing the sequence listing is 52641_Sequence_final_2014-09-16.txt. The text file is 288 KB, was created on Sep. 16, 2014, and is being submitted via EFS-Web with the filing of the specification.

TECHNICAL FIELD

[0003] The present disclosure generally relates to immunogenic compositions and vaccine formulations and their methods of use for stimulating a host response against *Streptococcus pneumoniae* antigens.

BACKGROUND

[0004] Pneumococcal disease continues to be a leading cause of sickness and death in the United States and throughout the world. Each year, millions of cases of pneumonia, meningitis, bacteremia, and otitis media are attributed to infection with the pathogen *Streptococcus pneumoniae*. *S. pneumoniae* is a Gram-positive encapsulated coccus that colonizes the nasopharynx in about 5-10% of healthy adults and 20-40% of healthy children. Normal colonization becomes infectious when *S. pneumoniae* is carried into the Eustachian tubes, nasal sinuses, lungs, bloodstream, meninges, joint spaces, bones and peritoneal cavity. *S. pneumoniae* has several virulence factors that enable the organism to evade the immune system. Examples include a polysaccharide capsule that reduces phagocytosis by host immune cells, proteases that inhibit complement-mediated opsonization, and proteins that cause lysis of host cells. In the polysaccharide capsule, the presence of complex polysaccharides forms the basis for dividing pneumococci into different serotypes. To date, more than 90 serotypes of *S. pneumoniae* have been identified.

[0005] Various pharmaceutical compositions have been used to harness an immune response against infection by *S. pneumoniae*. A polyvalent pneumococcal vaccine, PPV-23, was developed for preventing pneumonia and other invasive diseases due to *S. pneumoniae* in the adult and aging populations. The vaccine contains capsular polysaccharides (CPs) from 23 serotypes of *S. pneumoniae*. As T cell-independent antigens, these CPs induce only short-lived antibody responses without immunological memory, thus necessitating repeated doses, which increases the risk of immunological tolerance. The antibodies raised against *S. pneumoniae*, termed anticapsular antibodies, are recognized as generally protective in adult and immunocompetent individuals. Also, carriage of pneumococci, wherein the bacteria are colonized in a subject's nasopharynx without causing symptoms of an active infection but are capable of being transferred to others, is not affected. Accordingly, this vaccine strategy does not promote indirect, or "herd" immunity. Furthermore, children under 2 years of age and immunocompromised individuals, including the elderly, do not respond well to T cell-independent antigens and, therefore, are not afforded optimal protection by PPV-23.

[0006] PREVNAR®, another *S. pneumoniae* vaccine, includes bacterial polysaccharides from seven *S. pneumoniae* strains conjugated to the mutated diphtheria toxin protein CRM_{197}. This vaccine induces both B and T cell immune responses. However, because it only protects against 7 pneumococcal serotypes, serotype replacement can render PREVNAR® less effective. Serotype emergence or replacement has already been demonstrated in several clinical trials and epidemiologic studies, necessitating development of different formulations of these vaccines. An example is the recently introduced PREVNAR 13®, directed to 13 pneumococcal serotypes. Furthermore, the two PREVNAR® conjugated formulations are expensive to manufacture, greatly limiting their availability in the developing world. PPV-23, which consists of 23 purified, but nonconjugated polysaccharides, has broader coverage, but does not provide protection to children under the age of 2 years, a population which is at the highest risk for pneumococcal disease.

[0007] Accordingly, *S. pneumoniae* remains a major health concern, especially in very young, elderly, or immunocompromised patients. DNA and protein sequence information for *S. pneumoniae* has been known for some time facilitating research into alternative antigens or vaccine strategies. However, a major problem remains regarding how to elicit an immune response that is long-lived, is effective in all age groups, and is effective across a large spectrum of serotypes.

[0008] Thus, there remains a need to design more effective pharmaceutical compositions and methods than the current strategies offer. In particular, such compositions and methods need to incorporate combinations of antigens that elicit a balanced and enduring immune response against multiple *S. pneumoniae* serotypes in an effort to ameliorate symptoms of septic infections and to reduce carriage. The present disclosure provides an approach addresses this and related needs.

SUMMARY

[0009] This summary is provided to introduce a selection of concepts in a simplified form that are further described below in the Detailed Description. This summary is not intended to identify key features of the claimed subject matter, nor is it intended to be used as an aid in determining the scope of the claimed subject matter.

[0010] In one aspect, the present disclosure provides an immunogenic composition, vaccine formulation, and/or method of use that incorporates a novel combination of B cell and T cell antigens. The composition comprises i) a capsular polysaccharide (CP) component capable of stimulating B cell responses, and ii) a polypeptide component with at least a first polypeptide antigen and a second polypeptide antigen. The first polypeptide antigen is capable of inducing a T cell response, while the second polypeptide antigen is capable of inducing a B cell response. At least a portion of the CP component is conjugated to at least a portion of the polypeptide component that includes the first polypeptide antigen.

[0011] In some embodiments, the CP component comprises a plurality CP antigens derived from different *S. pneumoniae* serotypes. In some embodiments, the plurality of different *S. pneumoniae* CPs are derived from a plurality of *S. pneumoniae* serotypes comprising serotypes 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19F, 19A, 20, 22F, 23F, and/or 33F. In some embodiments, the different *S. pneumoniae* CPs are derived from a plurality of *S. pneumoniae* comprising serotypes 1, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and/or 23F.

[0012] In some embodiments, the first polypeptide antigen is capable of inducing a T_H17 cell response. In certain embodiments, the first polypeptide antigen has an amino acid sequence at least 90% identical to the polypeptide sequence of an antigen listed in Table 2, or any immunogenic fragment thereof. In some embodiments, the first polypeptide antigen has an amino acid sequence with at least 90% identity to SEQ ID NO:22 or SEQ ID NO:36, or any immunogenic fragment thereof.

[0013] In some embodiments, the second polypeptide antigen has an amino acid sequence at least 90% identical to the polypeptide sequence of an antigen listed in Table 1, or any immunogenic fragment thereof. In some embodiments, the second polypeptide antigen has an amino acid sequence with at least 90% identity to SEQ ID NO:90, or an antigenic fragment thereof, and comprises an L(Leu)460D(Asp) substitution.

[0014] In some embodiments, the first and second polypeptide antigens are linked. In certain embodiments, the first and second polypeptide antigens are domains of the same fusion polypeptide molecule. Thus, in further embodiments, at least a portion of the CPs is conjugated to the second polypeptide antigen.

[0015] In some additional embodiments, the first and second polypeptide antigens are separate polypeptide molecules.

[0016] In some embodiments, the immunogenic composition further comprises an adjuvant. In some embodiments, the adjuvant is an aluminum or aluminum salt-based adjuvant.

[0017] In some embodiments, the immunogenic composition is incorporated into a particle formulation.

[0018] In some embodiments, the administration of a therapeutically effective amount of the immunogenic composition to a subject in need results in reduced mucosal carriage of *S. pneumoniae* in the subject.

[0019] In some embodiments, the subject is a mammal, such as a mouse or human.

DETAILED DESCRIPTION

[0020] The present disclosure provides immunogenic formulations and methods for generating an effective response against a broad spectrum of *S. pneumoniae* serotypes by targeting a plurality of target immune cell types.

[0021] Existing conjugated polysaccharide vaccines prevent many invasive pneumococcal diseases caused by vaccine-type strains. However, increased rates of disease caused by serotypes not covered by current vaccines have made creating a vaccine incorporating conserved pneumococcal protein antigens a priority. A vaccine based on noncapsular protein antigens that are well-conserved amongst the greater than 90 known pneumococcal serotypes would prevent immunologic escape through serotype replacement.

[0022] Expanded availability of pneumococcal genomic information has facilitated development of genome-based approaches for protein antigen identification. Efforts thus far have focused on identifying surface-exposed proteins that can be bound by circulating antibodies and thereby direct clearance of the pathogen through mechanisms similar to polysaccharide-based vaccines. However, it is currently unknown whether antibodies elicited against pneumococcal protein antigens will be as effective as anticapsular antibodies in providing protective immunity against targeted pneumococcus serotypes in humans.

[0023] During childhood, the incidence of pneumococcal disease caused by a broad range of serotypes declines years before natural acquisition of anticapsular antibodies suggesting other mechanisms provide natural immunity to pneumococcus. Studies in mice have shown that acquired immunity to pneumococcal colonization, either after mucosal exposure to live bacteria or elicited by intranasal immunization with killed unencapsulated pneumococcal whole-cell antigen (WCA), is antibody independent and $CD4^+$ T cell dependent. This immunity was unchanged in mice that genetically lacked antibodies, IFNγ, or IL-4, but was completely abrogated in mice treated with neutralizing CD4 or IL-17A antibody or in mice genetically lacking the IL-17A receptor. This identifies the likely effector cells as IL-17A-producing $CD4^+$ T_H17 cells. A similar role for IL-17 signaling in pathogen clearance has been observed in mouse models of infection for at least 12 other mucosal pathogens, indicating this pathway plays a general role in clearance of pathogens at mucosal surfaces. Furthermore, humans lacking T_H17 cells because of genetic mutation are highly susceptible to mucosal infections by pathogens such as *Staphylococcus aureus, Haemophilus influenzae* and *S. pneumoniae* (Milner et al., 2008, Nature, 452:773-776), indicating that T_H17 likely play an important role in natural immunity to important mucosal pathogens of humans.

[0024] Accordingly, the present disclosure provides for a multi-component vaccine, immunogenic compounds, and methods of use, that incorporate a polypeptide antigen component and a polysaccharide component. The polypeptide component comprises one or more polypeptide antigens that induce T_H17 cells. In some embodiments, these polypeptide antigens are useful to obtain responses against a broad spectrum of *S. pneumoniae* serotypes because they are not limited to particular serotypes defined by specific capsular polysaccharides. A T_H17-specific polypeptide component provides the additional benefit of enhanced protection against mucosal colonization and/or infection. This protection complements the enhanced protection provided by the traditional polysaccharide antigens and/or recognized surface-exposed polypeptide antigens that induce neutralizing antibody responses that can provide protection against invasive pneumococcal disease in an individual. Furthermore, combating the colonization of *S. pneumoniae* at mucosal surfaces, such as in the nasopharynx, contributes to protection against (or reduction of) asymptomatic carriage of pan-serotypic *S. pneumoniae*. A reduction in nasopharyngeal carriage, which may be related to IL-17 induction, provides an advantage at the host population level because of reduced transmission rates from vaccinated individuals, who may have otherwise been a carrier/transmitter. Thus, the vaccine formulations and associated methods that target, in part, a T_H17 cell response, can provide benefits beyond the subject receiving administration thereof to other members of the community. Accordingly in certain embodiments, the vaccine composition or immunogenic composition induces a T_H17 cell response greater than that induced by a control unrelated antigen (for example, the HSV-2 protein ICP47 with the gene name US12) after contacting T_H17 cells.

[0025] In some embodiments, the vaccine composition or immunogenic composition also induces a B-cell response that results in the production of antibodies specific for an *S. pneumoniae* antigen. In some embodiments, the polypeptide component comprises one or more polypeptide antigens that induce a B-cell response. In certain embodiments the polysaccharide component comprises one or more capsular polysaccharides (CPs) from *S. pneumoniae* serotypes that induce a B-cell response. In some embodiments, the one or more CPs are unconjugated. In some embodiments, the CPs are conjugated to a protein carrier. In some embodiments, the protein carrier induces a T-cell response, for example, a T_H17 cell response. The protein carrier can be any polypeptide described herein as part of the polypeptide component.

[0026] In a preferred embodiment, the vaccine composition or immunogenic composition induces a coordinate or concurrent increase in both a T_H17 cell response and a B-cell response. In some embodiments, the vaccine formulation inhibits infection by *S. pneumoniae* in an uninfected subject. In certain embodiments, the vaccine formulation reduces occurrence, duration or severity of *S. pneumoniae* nasopharyngeal colonization in an individual infected by *S. pneumoniae*. In some embodiments, the vaccine formulation inhibits development of sepsis in an individual infected by *S. pneumoniae*. In some embodiments, the vaccine formulation inhibits development of invasive diseases such as pneumonia, meningitis, otitis media, sinusitis or infection of other sites or organs with *S. pneumoniae.*

A. Polysaccharide Antigens

[0027] The present embodiments incorporate one or more pneumococcal capsular polysaccharide (CPs) antigens into the vaccines and/or immunogenic compositions, and methods disclosed herein. As described above, CPs-based vaccines have been widely used to promote protective immunity against various specific serotypes of *S. pneumoniae*. Protective immunity is mainly dependent on the specific CPs used and the subject's production of anticapsular antibodies specific for the CP antigens. An unconjugated polyvalent vaccine, PPV-23 (PNEUMOVAX® 23, Merck Sharp & Dohme Corp., Whitestation, N.J.) incorporates CP antigens from *S. pneumoniae* serotypes 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19F, 19A, 20, 22F, 23F, and 33F. The combination of these CPs has been estimated to cover (i.e., induce antibodies in healthy individuals against) approximately 90% of the serious pneumococcal invasive disease serotypes in Western industrialized countries. However, it will be understood that CPs obtained from any *S. pneumoniae* serotype isolate are encompassed by the present disclosure.

[0028] Many of these polysaccharides are obtainable from the ATCC as lyophilized bulk powders. One preferred form of these polysaccharides is disclosed in U.S. Pat. No. 5,847,112, incorporated herein by reference. Alternatively, CPs can be isolated from bacterial cultures of *S. pneumoniae*. In this regard, the approach to isolation of the polysaccharides depends somewhat on the physical characteristics of the given CP. However, in general, the bacteria are cultured and the CPs are recovered according to known methods (see, e.g., Williams, C. A., and Chase, M. W., Methods in Immunology and Immunochemistry, Vol. I, Academic Press (1967)). In one embodiment, each pneumococcal serotype is grown in a soy-based medium. The individual CPs are then purified through standard steps including centrifugation, precipitation, and ultra-filtration. See, e.g., U.S. Pat. Pub. No. 2008/0286838 and U.S. Pat. No. 5,847,112, each of which are incorporated herein by reference.

[0029] Following a large scale culture of the bacteria in appropriate nutrient media known in the art to support Pneumococcal growth, a bactericidal, such as phenol or toluene, is added to kill the organisms. Alcohol fractionation of the polysaccharide is then conducted in two stages: a low alcohol stage to precipitate cellular debris and other unwanted impurities, and a water-miscible-alcohol stage to precipitate the capsular polysaccharides while leaving additional impurities in the supernatant fluid. Resuspension in an aqueous medium is followed by removal of contaminating proteins and nucleic acids by known methods such as nuclease or proteolytic digestion and/or solvent extraction. The crude polysaccharide is recovered by alcohol precipitation and drying to form a powder of the crude CPs. See, e.g, Example 3 of U.S. Pat. No. 5,623,057, incorporated herein by reference. These preparations can be useful, for example, for the inclusion of unconjugated CP antigens into the vaccines and immunogenic compounds of the present disclosure.

[0030] Capsular polysaccharides found to be poorly immunogenic by themselves have been shown to have improved immunogenicity when conjugated to an immunogenic carrier protein. Additionally, unconjugated CPs are poor inducers of T-cell immune responses. Accordingly, in some embodiments of the present disclosure, the CPs can be conjugated to a carrier protein or multiple carrier proteins. Carrier proteins are preferably proteins that are non-toxic and obtainable in a sufficient amount and purity. In some embodiments, the carrier proteins are themselves antigens, B-cell antigens or antigens capable of eliciting a T_H17 cell response. In some embodiments, the carrier protein is an antigen capable of eliciting a T_H17 cell response

[0031] Nonlimiting examples of carrier proteins for CP conjugation include DT (Diphtheria toxoid), TT (tetanus toxoid) or fragment C of TT, pertussis toxoid, cholera toxoid, *E. coli* LT, endotoxin A from *Pseudomonas aeruginosa*, and diptheria CRM_{197}. Bacterial outer membrane proteins can also be used, such as outer membrane complex c (OMPC) (e.g., outer membrane complex (OMPC) of *Neisseria meningitides* B), porins, transferrin binding proteins, pneumococcal surface protein A (PspA; see WO 2002/091998), pneumococcal adhesin protein (PsaA), C5a peptidase from Group A or Group B *streptococcus*, or *Haemophilus influenzae* protein D, pneumococcal pneumolysin (Kuo et al., 1995, Infect. Immun. 63:2706-2713) including pneumolysoid L460D (see, e.g., US 2009/0285846), pneumolysin (ply) detoxified in some fashion, for example dPLY-GMBS (see WO 2004/081515) or dPLY-formol, PhtX, including PhtA, PhtB, PhtD, PhtE and fusions of Pht proteins, for example PhtDE fusions, PhtBE fusions (see WO 2001/98334 and WO 2003/54007). Other proteins useful as carrier proteins for CP conjugate compositions include ovalbumin, keyhole limpet hemocyanin (KLH), bovine serum albumin (BSA) or purified protein derivative of tuberculin (PPD), PorB (from *N. meningitidis*), PD) (*H. influenzae* protein D; see, e.g., EP0594610B), or immunologically functional equivalents thereof, synthetic peptides (see EP0378881B and EP0427347B), heat shock proteins (see WO 93/17712 and WO 94/03208), pertussis proteins (see WO 1998/58668 and EP0471177B), cytokines, lymphokines, growth factors or hormones (see WO 1991/01146), artificial proteins comprising multiple human $CD4^+$ T cell epitopes from various pathogen derived antigens (See Falugi et al., 2001, Eur. J. Immunol. 31:3816-3824) such as N19 protein (see Baraldoi et al., 2004, Infect. Immun. 72:4884-4887), iron uptake proteins (see WO 2001/172337), toxin A or B of *C. dfficile* (see WO 2000/61761), and flagellin (see Ben-Yedidia et al., 1998, Immunol. Lett. 64:9). CRM_{197}, for example, is a non-toxic variant (i.e., toxoid) of diphtheria toxin. In one embodiment, CRM_{197} is isolated from cultures of *Corynebacterium diphtheria* strain C7 (β 197) grown in casamino acids and yeast extract-based medium.

[0032] Well-known examples of CP-conjugate vaccine compositions include PREVNAR® (Wyeth LLC/Pfizer, NY, N.Y.), a heptavalent CP conjugate vaccine that includes CPs from *S. pneumoniae* strains 4, 6B, 9V, 14, 18C, 19F, and 23F conjugated to CRM_{197} of *Corynebacterium diphtheriae*; PREVNAR 13® (Wyeth LLC/Pfizer, NY, N.Y.) with the seven CPs of PREVNAR® plus six additional CPs from *S. pneumoniae* strains 1, 3, 5, 6A, 19A and 7F; and SYNFLORIX™ (GSK, Brentford, UK) a vaccine with the seven CPs of PREVNAR® plus CPs from *S. pneumoniae* strains 1, 5, and 7F, with eight of the CPs conjugated to a protein carrier from *Haemophilus influenzae*.

[0033] Vaccines and immunogenic compositions that incorporate multivalent conjugated CPs can include those with mixtures of different CP-protein conjugates, each conjugate prepared separately with a given CP subtype (i.e., from different serotypes). Alternatively or in addition, multivalent vaccines can include conjugates wherein several different CP subtypes are all conjugated to a given protein at one time or sequentially.

[0034] Crude CP extracts are often highly viscous and poorly soluble resulting in conjugates that are largely insoluble and unfilterable. Furthermore, the conjugation process from crude extracts results in poor yield and removal of unconjugated CPs, which is important for dosing reasons, is difficult for full length CPs. Thus, additional processing of prepared CPs can promote more efficient and effective incorporation into CP-protein conjugates. U.S. Pat. No. 5,623,057, incorporated herein by reference, provides an exemplary, non-limiting approach to preparing *S. pneumoniae* CPs useful for inclusion in protein-conjugate vaccines and immunogenic compositions. Disclosed herein are processing steps that can be employed in addition to the crude extract preparations described above that can facilitate and optimize the conjugation of CPs for vaccine formulations. Briefly, the dry, crude, capsular polysaccharide as prepared above can be purified, for example, by anion-exchange chromatography or other chromatographic procedure, prior to, or after partial hydrolysis. The chromatographic adsorption-desorption can be used either positively or negatively. Regardless of any purification steps, the CPs can be directly subjected to partial thermal hydrolysis, high-energy sonic hydrolysis, or other hydrolytic means, such as chemical, enzymatic or physical (e.g., a high pressure cell) means, which are known. A target endpoint of hydrolysis, conveniently measured by solution viscosity or high-performance size exclusion chromatography, is predetermined for each polysaccharide on a pilot scale such that antigenicity of the polysaccharide is not abrogated. For CPs that require more complex structure to retain antigenicity, a more gentle size reduction is achievable by sonic or physical shear means. Finally, the hydrolyzed CPs can be fractionated according to size and purity. Fractionation can be accomplished using differential alcohol solubility or chromatography using a size exclusion resin.

[0035] Many different schemes are available to those skilled in the art for preparing conjugates of polysaccharides and other moieties. Generally, the CPs are chemically activated to make the saccharides capable of reacting with the carrier protein. Once activated, each CP is separately conjugated to a carrier protein to form a glycoconjugate.

[0036] In one embodiment, the chemical activation of the polysaccharides and subsequent conjugation to the carrier protein are achieved by means described in U.S. Pat. No. 4,365,170, U.S. Pat. No. 4,673,574 and U.S. Pat. No. 4,902,506, each of which is incorporated herein by reference. Briefly, the chemistry entails the activation of pneumococcal polysaccharide by reaction with any oxidizing agent which oxidizes a terminal hydroxyl group to an aldehyde, such as periodate (including sodium periodate, potassium periodate, or periodic acid). The reaction leads to a random oxidative cleavage of vicinal hydroxyl groups of the carbohydrates with the formation of reactive aldehyde groups.

[0037] Coupling to the protein carrier (e.g., CRM_{197}) can be by reductive amination via direct amination to the lysyl groups of the protein. For example, conjugation is carried out by reacting a mixture of the activated polysaccharide and carrier protein with a reducing agent such as sodium cyanoborohydride. Unreacted aldehydes are then capped with the addition of a strong reducing agent, such as sodium borohydride.

[0038] In another embodiment, the conjugation method can rely on activation of the saccharide with 1-cyano-4-dimethylamino pyridinium tetrafluoroborate (CDAP) to form a cyanate ester. The activated saccharide can thus be coupled directly or via a spacer (linker) group to an amino group on the carrier protein. For example, the spacer could be cystamine or cysteamine to give a thiolated polysaccharide which could be coupled to the carrier via a thioether linkage obtained after reaction with a maleimide-activated carrier protein (for example using GMBS) or a haloacetylated carrier protein (for example using iodoacetimide, e.g., ethyl iodoacetimide HCl or N-succinimidyl bromoacetate or SIAB, or SIA, or SBAP). Preferably, the cyanate ester (optionally made by CDAP chemistry) is coupled with hexane diamine or adipic acid dihydrazide (ADH) and the amino-derivatised saccharide is conjugated to the carrier protein using carbodiimide (e.g., EDAC or EDC) chemistry via a carboxyl group on the protein carrier. Such conjugates are described in, for example, WO 1993/15760, WO 1995/08348, WO 1996/29094, Chu et al., 1983, Infect. Immunity 40:245-256, and the like.

[0039] Other suitable techniques use carbodiimides, hydrazides, active esters, norborane, p-nitrobenzoic acid, N-hydroxysuccinimide, S—NHS, EDC, TSTU. Many conjugation agents are described in WO 1998/42721, incorporated herein by reference in its entirety. Conjugation can involve a carbonyl linker which can be formed by reaction of a free hydroxyl group of the saccharide with 1,1'-carbonyldiimidazole (CDI) (see Bethell et al., 1979, J. Biol. Chem. 254:2572-2574; Hearn et al., 1981, J. Chromatogr. 218:509-518) followed by reaction of with a protein to form a carbamate linkage. This can involve reduction of the anomeric terminus to a primary hydroxyl group, optional protection/deprotection of the primary hydroxyl group, reaction of the primary hydroxyl group with CDI to form a CDI carbamate intermediate and coupling the CDI carbamate intermediate with an amino group on a protein.

[0040] After conjugation of the capsular polysaccharide to the carrier protein, the polysaccharide-protein conjugates are purified (enriched with respect to the amount of polysaccharide-protein conjugate) by one or more of a variety of techniques. Examples of these techniques are well known to the skilled artisan and include concentration/diafiltration operations, ultrafiltration, precipitation/elution, column chromatography, and depth filtration. See, e.g., U.S. Pat. No. 6,146, 902, incorporated herein by reference.

B. Polypeptide Antigens

[0041] 1. B-Cell Antigens

[0042] In some embodiments the vaccine or immunogenic composition comprises at least one *S. pneumoniae* antigen that is predominantly an antibody target. Exemplary antibody protein antigens are shown in Table 1. In some embodiments, this antigen is Pneumococcal surface adhesin A (PsaA) (SEQ ID NO:1) or fragments or variants thereof. In some embodiments, fragments or variants of PspA comprise proline-rich segments with the non-proline block (PR+NPB), for example the CD2 sequence (SEQ ID NO:2). In some embodiments, fragments or variants of PspA comprise proline-rich segments with the non-proline block and 10, 20 30, 40 or more additional amino acids of PspA sequence, for example the H70 sequence (SEQ ID NO:7). In some embodiments, the *S. pneumoniae* antigen that is predominantly an antibody target comprises a pneumolysoid. In some embodiments, the pneumolysoid is L460 pneumolysoid. These antibody target antigens are described in more detail below.

TABLE 1

Exemplary *S. pneumoniae* protein antigens are predominantly antibody targets

Locus tag name and description	Protein SEQ ID No.
PspA	1
PR + NRB from PspA with coiled-coil	2
CD2	3
PR + NRB from PspA w/o coiled-coil	4
PR only with coiled-coil	5
PR only w/o coiled-coil	6
H70 (PR + NRB from PspA aa 290-410)	7
Non-proline Block (NPB)	8
Non-proline Block (NPB)	9
Non-proline Block (NPB)	10
S. pneumoniae protein pneumolysin	90

[0043] In some embodiments, vaccines or pharmaceutical compositions comprising an *S. pneumoniae* polypeptide includes a fusion protein containing at least one *S. pneumoniae* antigen that is a B-Cell/antibody antigen. In some instances, the known *S. pneumoniae* antigens are predominantly antibody targets. In some instances, the known *S. pneumoniae* antigens protect from *S. pneumoniae* colonization, or from *S. pneumonia*-induced sepsis. One appropriate art-recognized class of *S. pneumoniae* antigen is Pneumococcal surface protein A (PspA) (SEQ ID NO:1) and derivatives of PspA. Derivatives of PspA include proline-rich segments with the non-proline block (PR+NPB, further described below as well as in Daniels, C. C. et al. (2010) Infect. Immun. 78:2163-72) and related constructs comprising all or a fragment of the proline-rich region of PspA (e.g., regions containing one or more of the sequences PAPAP (SEQ ID NO:91), PKP, PKEPEQ (SEQ ID NO:92) and PEKP and optionally including a non-proline block). H70 (SEQ ID NO:7) is one exemplary sequence which includes the proline-rich region and non-proline-block encompassing amino acids 290-410 PspA. An example of the non-proline-block has the exemplary sequence EKSADQQAEEDIYARRSEEEYNRLTQQQ (SEQ ID NO:8), which generally has no proline residues in an otherwise proline-rich area of the non-coiled region of PspA. Other embodiments of non-proline block (NPB) sequences include SEQ ID NOS:8 and 9 and PspA and its derivatives can include genes expressing similar proline-rich structures (i.e., PKP, PKEPEQ (SEQ ID NO:92) and PEKP), with or without the NPB. The amino acids at ether end of the NPB mark the boundaries of the proline-rich region. In one example, the amino-terminal boundary to the PR-region is DLKKAVNE (SEQ ID NO:11), and the carboxyterminal boundary is (K/G)TGW(K/G)QENGMW (SEQ ID NO:12). Peptides containing the NPB are particularly immunogenic, suggesting that the NPB can be an important epitope. Exemplary immunogenic PspA polypeptide derivatives containing the coiled-coil structure include SEQ ID NOS:2 and 5. Particular embodiments of the immunogenic PspA polypeptide derivatives lacking the coiled-coil structure have the amino acid sequences shown as SEQ ID NOS:3, 4 and 6. Immunogenic PspA polypeptides SEQ ID NO:1-4 include both PR and NPB sequences (PR+NPB). Immunogenic PspA polypeptides of SEQ ID NOS:5 and 6 include only a PR sequence (PR only) and lack the NPB.

[0044] Another appropriate art-recognized class of *S. pneumoniae* antigen are the pneumolysoids. Pneumolysoids have homology to the *S. pneumoniae* protein pneumolysin (PLY), but have reduced toxicity compared to pneumolysin. Pneumolysin is a key component in the pathogenesis of streptococcal pneumonia. The use of pneumolysin (or its homologues) as a part of a vaccine for *S. pneumoniae* lung infections and otitis media is becoming increasingly important due to the described drawbacks of typical CP-based strategies. A pneumolysin mutant (referred to as "Pd-B") contains a single mutation at position 433 (wherein the native tryptophan residue has been changed to a phenylalanine). This mutation in pneumolysin is in the conserved undecapeptide of Domain 4, the structure within the cholesterol-dependent cytolysins (CDCs), which has long been thought to mediate binding to mammalian membranes. Other mutants of pneumolysin are described in U.S. Pat. No. 6,716,432, for example. Mutations are sought typically to provide an antigen with lower toxicity than native pneumolysin, but that still have a relative effective antigenicity so as to stimulate effective antibody response. See, e.g., U.S. Pat. No. 8,128,939.

[0045] Pneumolysoids encompassed by the present disclosure, thus, can be naturally occurring or engineered derivatives of pneumolysin. In some embodiments, a pneumolysoid has at least 70%, 80%, 85%, 90%, 95%, 97%, 98%, or 99% identity to the amino acid sequence of native pneumolysin, as set forth herein as SEQ ID NO:9, or a fragment thereof. In some embodiments, the pneumolysoid demonstrates less than ½, ⅕, 1/10, 1/20, 1/50, 1/100, 1/200, 1/500, or 1/1000 the toxicity of pneumolysin in an assay for one or both of hemolytic activity towards erythrocytes and inhibition of polymorphonuclear leukocytes. Both assays are described in Saunders et al., 1989, Infect. Immun. 57:2547-2552. Exemplary pneumolysoids include PdT (a triple mutant further described in Berry et al., 1995, Infect. Immun. 63:1969-1974); Pd-A and Pd-B (Paton et al., 1991, Infect. Immun. 59:2297-2304); rPd2 and rPd3 (Ferreira et al., 2006, FEMS Immunol. Med. Microbiol. 46:291-297); Ply8, δPLY, L460D (see, e.g., U.S. Pub.

No. 2009/0285846 and L. Mitchell, Protective Immune Responses to *Streptococcus pneumoniae* Pneumolysoids, ASM2011 conference abstract, 2011), or a variant thereof. In some embodiments, the pneumolysin has a mutation in the catalytic domain, such as at amino acid 428 or 433 or the vicinity. In some embodiments, pneumolysin mutants can have substitutions at position 460, 370 and/or 406 of pneumolysin, as well as substitutions in one or more of three residues that flank either side of positions 370, 406 or 460, including positions 367, 368, 369, 371, 372, 373, 403, 404, 405, 407, 408, 409, 457, 458, 459, 461, 462, and 463. For example, these residues may be substituted with a negatively-charged amino acid, glutamate, or aspartate (except in position 403, which already comprises aspartate), or a positively charged amino acid lysine, arginine, or histidine (except in positions 367 and 407, which already comprise histidine residues). Alternatively, these residues may be substituted with any other natural amino acid (including gly, ala, leu, ile, val, pro, trp, asn, gin, phe, tyr, met, cys, thr, or ser) which abrogates the binding activity, pore-forming, and hemolytic activity of the mutant. See U.S. Pat. No. 8,128,939, incorporated herein by reference in its entirety.

[0046] Other appropriate *S. pneumoniae* antigens to serve as B-cell/antibody target antigens include PhtX, including PhtA, PhtB, PhtD, PhtE, Choline-binding proteins PcpA and CbpA and derivatives thereof (Ogunniyi et al., 2001. Infect. Immun. 69:5997-6003); caseinolytic protease; sortase A (SrtA); pilus 1 KrgA adhesin; PpmA; PrtA; PavA; LytA; Stk-PR; PcsB; and RrgB and derivatives thereof:

[0047] 2. T_H17 Cell Antigens

[0048] As described above, the subset of T cells expressing IL-17A, i.e., T_H17 cells, have been identified as playing an important role in natural immunity to mucosal pathogens, such as *S. pneumoniae*. Accordingly, the vaccines and immunogenic compositions described herein include a polypeptide component directed to inducing a T_H17 response to *S. pneumoniae*. This component contributes the advantages of preventing or lowering mucosal colonization and carriage against a wide spectrum of *S. pneumoniae* serotypes.

[0049] Immunogenic polypeptide antigens that induce T_H17 cells can be identified according to known methods. Extensive genomic information for *S. pneumoniae* is known that can assist prediction of effective T cell antigens. For example, the *S. pneumoniae* ATCC 700669 complete genome sequence is available under GenBank accession number FM211187.1 (incorporated herein by reference) and polypeptide sequences are linked therein. Several known algorithms and computational tools can be used to predict immunogenicity of known or predicted polypeptide sequences, such as EpiMatrix (produced by EpiVax), PEP-VAC (Promiscuous EPitope-based VACcine, hosted by Dana Farber Cancer Institute on the world wide web), MHCPred (which uses a partial least squares approach and is hosted by The Jenner Institute on the world wide web), and Immune Epitope Database algorithms available on the world wide web. Additionally, immunogenic portions can be identified by various methods, including protein microarrays, ELISPOT/ELISA techniques, and/or specific assays on different deletion mutants (e.g., fragments) of the polypeptide in question.

[0050] In one illustrative example, as reported in more detail in Moffitt, et al., 2011, Cell Host & Microbe, 9:158-165, incorporated herein by reference, a library containing 2207 of the predicted 2233 open reading frames predicted in the *S. pneumoniae* genome was cloned and expressed with an in-frame 1 cell epitope. The final validated library of expressed and MH-IC-presented peptides was estimated to reflect 95% of the total proteome sequence of *S. pneumoniae*. Macrophages presenting the *S. pneumoniae* peptides were screened against $CD4^+$ T cells isolated from mice that had been immunized with a killed *S. pneumoniae* whole cell vaccine, and peptides inducing IL-17 expression (i.e., T_H17 induction) were identified. Bioinformatic analyses assisted the identification of top candidates by identifying amino acid sequences that had no homology with human proteins and low conservation with protein sequences of other bacteria. Additionally, to assess whether the identified antigens are well-presented during pneumococcal exposure, the IL-17A responses of experimentally colonized mice were evaluated in vitro by stimulating splenocytes isolated from mice previously intranasally inoculated with *S. pneumoniae* with purified antigens. Finally, the purified antigens were used to stimulate human PBMCs isolated from healthy adult donors to determine whether humans prime T_{11}17 cells specifically for the selected antigens during the course of natural exposure to *S. pneumoniae*.

[0051] Thus, polypeptide antigens indicated as effective antigens for stimulating T_H17 cells using approaches such as that described in Moffitt, et al., 2011, are useful in this aspect of the disclosure. Exemplary T_H17 polypeptide antigens are listed below in Table 2. These and additional T_H17 polypeptide antigens are listed in Tables 1 and 2 of U.S. Pub. No. US20120189649, incorporated herein by reference in its entirety.

TABLE 2

Exemplary immunogenic polypeptides useful for stimulating T_H17 cells.

Locus tag name and description	Protein SEQ ID NO:	DNA GenGank Accession No.
SP0024	13	NC_003028.3|:27381-27878
SP0882	14	NC_003028.3|:83 1804-832628
SP0882N	15	
SP0882 with exogenous signal sequence	16	
SP0882N with exogenous signal sequence	17	
SP0148 lacking signal sequence	18	
SP0148 including signal sequence	19	NC_003028.3|:145,513-146,343*
SP1072	20	NC_003028.3|:1008420-1010180
SP2108 including signal sequence	21	NC_003028.3|:2020750-2022021
SP2108 lacking signal sequence	22	
SP0641M	23	
SP0641	24	NC_003028.3|:2020750-2022021
SP0641N	25	
SP0882 consensus	26	
SP0882N consensus	27	
SP0882 consensus with exogenous leader	28	
SP0882N consensus with exogenous leader	29	
SP0148 consensus lacking signal sequence	30	
SP0148 consensus including signal sequence	31	
SP2108 consensus lacking signal sequence	32	
SP2108 consensus including signal sequence	33	

TABLE 2-continued

Exemplary immunogenic polypeptides useful for stimulating T_H17 cells.

Locus tag name and description	Protein SEQ ID NO:	DNA GenGank Accession No.
SP1634	34	NC_003028.3|:1534348-1535421
SP0314	35	NC_003028.3|:287483-290683
SP1912	36	NC_003028.3|:824672-1824971
SP1912L	37	
SP0641.1	38	
SP1912 consensus	39	
SP0641N consensus	40	
SP0641M consensus	41	

*The database sequence incorrectly lists TTG (encoding Leu) at nucleotide positions 541-543. The correct sequence is TTC at that codon and encodes Phe.

[0052] 3. Fusion Proteins

[0053] In some embodiments, one or more, e.g., two, three, four, or more polypeptides from Table 1 and/or Table 2 or immunogenic fragments or variants thereof are provided in a mixture. In some embodiments, the mixture contains both full-length polypeptides and/or fragments resulting from processing, or partial processing, of signal sequences by an expression host, e.g., *E. coli*, an insect cell line (e.g., the baculovirus expression system), or a mammalian (e.g., human or Chinese Hamster Ovary) cell line. In some embodiments, rather than being in a simple physical mixture, two, three, four, or more polypeptides from Table 1 and/or Table 2, or immunogenic fragments or variants thereof are covalently bound to each other, e.g., as a fusion protein.

[0054] Thus, in some embodiments, two or more of the antigens are fused or linked. For example, in some embodiments, the vaccine or immunogenic composition comprises fusion proteins. An exemplary fusion protein includes a first portion that primarily elicits a T-cell response and a second portion that primarily elicits a B-cell (e.g., antibody) response, or vice versa. In certain embodiments, the fusion proteins include one, two or more of the polypeptides (or genes) described herein as a B-cell antigen and a T-cell antigen listed in Table 1 and/or Table 2. In certain embodiments, the fusion protein includes a polypeptide or gene listed in Table 1 fused to a polypeptide or gene listed in Table 2.

[0055] In some embodiments, the fusion protein comprises an N-terminal peptide and a C-terminal peptide. In some embodiments, the N-terminal peptide comprises an immunogenic polypeptide that induces a T_H17 response, for example, any polypeptide described herein for this purpose. Some examples include the polypeptides having an amino acid sequence comprising SEQ ID NOS:13-41, or immunogenic fragments or variants thereof. In these embodiments, the C-terminal peptide can comprise an *S. pneumoniae* antigen that is predominantly an antibody target as described herein or immunogenic fragments or variants thereof. In other embodiments, the N-terminal peptide comprises an *S. pneumoniae* antigen that is predominantly an antibody target, as described herein, and the C-terminal peptide can comprise an immunogenic polypeptide that induces a T_H17 response, for example, the polypeptide having an amino acid sequence comprising SEQ ID NOS: 13-41, or immunogenic fragments or variants thereof.

[0056] In some embodiments, the antigenic peptides at the N-terminal and the C-terminal are directly bound to each other. In other embodiments, the antigenic peptides at the N-terminal and the C-terminal are linked via a linker peptide. The length of and/or amino acids that comprise a linker, when present, can be adjusted to obtain a more flexible or rigid linker. Exemplary peptide linkers are shown as SEQ ID NOS: 42-44. A linker can generally be from 1-40, such as 10-30 and specifically 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acids in length.

[0057] An illustrative, nonlimiting list of potential fusion proteins is set forth in Table 3.

TABLE 3

Immunogenic fusion proteins for *S. pneumoniae* vaccine formulations.

Locus tag name	DNA SEQ ID NO:	Protein SEQ ID NO:
SP2108/SP0148	45	46
SP0148/SP2108	47	48
SP2108/SP1912	49	50
SP0148/SP1912	51	52
SP2108/SP1912/SP0148	53	54
SP0148/SP1912/SP2108	55	56
SP2108/SP0148/SP1912	57	58
SP0148/SP2108/SP1912	59	60
SP0148/CD2	61	62
SP0148/H70	63	64
SP2108/CD2	65	66
SP2108/H70	67	68
SP0148/LC/CD2	69	70
SP0148/ LC/H70	71	72
SP2108/LC/CD2	73	74
SP2108/LC/H70	75	76
SP0148/LR/CD2	77	78
SP0148/LR/H70	79	80
SP2108/LR/CD2	81	82
SP2108/LR/H70	83	84

[0058] 4. General Characteristics of Protein Antigens

[0059] As described, the vaccine and immunogenic compositions of the present disclosure incorporate a protein component with one or more polypeptides that serve as effective antigens for T cells and for B cells. Thus, the polypeptides of the present disclosure, and fragments and variants thereof, are immunogenic. This includes instances where the polypeptides are fused, mixed, or coordinately administered with other polypeptide or polysaccharide antigens, adjuvants, or carriers. These polypeptides can be immunogenic in mammals, for example mice, guinea pigs, or humans. An immunogenic polypeptide is typically one capable of raising a significant immune response in an assay or in a subject. The immune response can be innate, humoral, cell-mediated, and/or mucosal (combining elements of innate, humoral and cell-mediated immunity). For instance, an immunogenic polypeptide can induce the production of IL-17 produced by antigen-specific T cells. Alternatively or additionally, an immunogenic polypeptide can (i) induce production of antibodies, e.g., neutralizing antibodies, that bind to the polypeptide and/or the whole bacteria, (ii) induce T_H17 immunity, (iii) activate the $CD4^+$ T cell response, for example by stimulating antigen-specific $CD4^+$ T cells and/or increasing localization of $CD4^+$ T cells to the site of infection or reinfection, (iv) activate the $CD8^+$ T cell response, for example by increasing $CD8^+$ T cells and/or increasing localization of $CD8^+$ T cells to the site of infection or reinfection, (v) induce THil immunity, and/or (vi) activate innate immunity. In some embodiments, an immunogenic polypeptide causes the production of a detectable amount of antibody specific to that antigen.

[0060] In certain embodiments, polypeptides have less than 20%, 30%, 40%, 50%, 60% or 70% identity to human autoantigens and/or gut commensal bacteria (e.g., certain *Bacteroides, Clostridium, Fusobacterium, Eubacterium, Ruminococcus, Peptococcus, Peptostreptococcus, Bifidobacterium, Escherichia* and *Lactobacillus* species). Examples of human autoantigens include insulin, proliferating cell nuclear antigen, cytochrome P450, and myelin basic protein.

[0061] A polypeptide can comprise one or more immunogenic portions and one or more nonimmunogenic portions. The immunogenic portions can be identified by various methods, including protein microarrays, ELISPOT/ELISA techniques, T cell cloning and/or specific assays on different deletion mutants (e.g., fragments) of the polypeptide in question. Immunogenic portions can also be identified by computer algorithms. Some such algorithms, like EpiMatrix (produced by EpiVax), use a computational matrix approach. Other computational tools for identifying antigenic epitopes include PEPVAC (Promiscuous EPitope-based VACcine, hosted by Dana Farber Cancer Institute on the world wide web), MI ICPred (which uses a partial least squares approach and is hosted by The Jenner Institute on the world wide web), and Immune Epitope Database algorithms which is also available on the world wide web. An immunogenic fragment of a polypeptide described herein comprises at least one immunogenic portion, as measured experimentally or identified by algorithm.

[0062] Thus, in some aspects, this application provides an immunogenic fragment of an antigen described herein. The fragments, in some instances, are close in size to the full-length polypeptide or equivalent to the polypeptides listed in Table 1 or Table 2. For example, they can lack at most one, two, three, four, five, ten, twenty, or thirty amino acids from one or both termini. In certain embodiments, the polypeptide is 100-500 amino acids in length, or 150-450, or 200-400, or 250-250 amino acids in length. In some embodiments, the polypeptide is 100-200, 150-250, 200-300, 250-350, 300-400, 350-450, or 400-500 amino acids in length. In certain embodiments, the fragments result from processing, or partial processing, of signal sequences by an expression host, e.g., *E. coli*, an insect cell line (e.g., the baculovirus expression system), or a mammalian (e.g., human or Chinese Hamster Ovary) cell line. The fragments described above or sub-fragments thereof (e.g., fragments of 8-50, 8-30, or 8-20 amino acid residues) preferably have one of the biological activities described herein, such as inducing the production of IL-17. For example, the fragments can induce increased IL-17 production by at least 1.5 fold or 2 fold, or more (e.g., either as an absolute measure or relative to an immunologically inactive protein). A fragment can be used as the polypeptide in the vaccines described herein and can be fused to another protein, protein fragment or other antigen.

[0063] Individual strains of *S. pneumoniae* contain numerous mutations relative to each other, and some of these result in different protein sequences between the different strains. One of skill in the art can readily substitute an amino acid sequence, or a portion thereof, with the homologous amino acid sequence from a different *S. pneumoniae* strain for any amino acid antigen described herein. In certain aspects, this application encompasses immunogenic polypeptides with at least 90%, 95%, 97%, 98%, 99%, or 99.5% identity to the polypeptides of Table 1, 2, or 3, any other polypeptide antigen sequence described herein, or an immunogenic fragment thereof. Serotypic variation can be used to design such variants of the polypeptides of Tables 1, 2, and/or 3. In some cases, the polypeptide antigen is at least 70%, 80%, 85%, 90%, 95%, 97%, 98%, or 99% identical to the corresponding wild-type *S. pneumoniae* protein. Sequences of the polypeptides described herein, and nucleic acids that encode them, are known; see, for example, the *S. pneumoniae* ATCC 700669 complete genome sequence under GenBank accession number FM211187.1 and linked polypeptide sequences therein.

[0064] An immunogenic composition can also comprise portions of the *Streptococcus* polypeptides, including fusion proteins, for example deletion mutants, truncation mutants, oligonucleotides, and peptide fragments. In some embodiments, the portions of said polypeptides are immunogenic. The immunogenicity of a portion of a protein is readily determined using the same assays that are used to determine the immunogenicity of the full-length protein. In some embodiments, the portion of the polypeptide has substantially the same immunogenicity as the full-length proteins. In some embodiments, the immunogenicity is no more than 10%, 20%, 30%, 40%, or 50% less than that of the full-length protein (e.g., polypeptides of Table 1, 2, or 3, or otherwise described herein). The peptide fragments can be, for example, linear, circular, or branched.

[0065] In some embodiments, the fragment is a truncated fragment of any of SEQ ID NOS:1-41, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, and 84, having from 1-5, 1-10, or 1-20 amino acid residues removed from the N-terminus, C-terminus, or both. In some such embodiments, the same number of residues is removed from the N-terminus and the C-terminus, while in other embodiments, a different number of residues is removed from the N-terminus compared to the C-terminus.

[0066] Some embodiments of the vaccine formulations and immunogenic compositions described herein include an immunogenic polypeptide, including fusion proteins, (e.g., a polypeptide of Table 1, 2, or 3, or otherwise described herein) that contains a membrane translocating sequence (MTS), to facilitate introduction of the polypeptide into the mammalian cell and subsequent stimulation of the cell-mediated immune response. Exemplary membrane translocating sequences include a hydrophobic region in the signal sequence of Kaposi fibroblast growth factor, the MTS of α-synuclein, β-synuclein, or γ-synuclein, the third helix of the Antennapedia homeodomain, SN50, integrin β3 h-region, HIV Tat, pAntp, PR-39, abaecin, apidaecin, Bac5, Bac7, *P. berghei* CS protein, and those MTSs described, for example, in U.S. Pat. Nos. 6,248,558, 6,432,680, and 6,248,558.

[0067] In certain embodiments, an antigen (e.g., a polypeptide of Tables 1, 2, or 3, or a fragment thereof) is covalently bound to another molecule. This can, for example, increase the half-life, solubility, bioavailability, or immunogenicity of the antigen. Molecules that can be covalently bound to the antigen include a carbohydrate, biotin, poly(ethylene glycol) (PEG), polysialic acid, N-propionylated polysialic acid, polysaccharides, and PLGA. There are many different types of PEG, ranging from molecular weights of below 300 g/mol to over 10,000,000 g/mol. PEG chains can be linear, branched, or with comb or star geometries. In some embodiments, the naturally produced form of a protein is covalently bound to a moiety that stimulates the immune system. An example of such a moiety is a lipid moiety. In some instances, lipid moieties are recognized by a Toll-like receptor (TLR) such as TLR-2 or TLR-4, and activate the innate immune system.

[0068] In certain embodiments, vaccines or pharmaceutical compositions comprising an *S. pneumoniae* polypeptide, including a fusion protein comprising an *S. pneumoniae* polypeptide, contain at least one lipidated polypeptide. In some embodiments, the protein or fusion protein is lipidated. In certain embodiments, the protein or fusion protein is lipidated on the N-terminal peptide. Conjugation to the lipid moiety can be direct or indirect (e.g., via a linker). The lipid moiety can be synthetic or naturally produced. In certain embodiments, a polypeptide from Table 1, 2, or 3 can be chemically conjugated to a lipid moiety. In certain embodiments, a construct can comprise a gene or polypeptide from Table 1, 2, or 3, or an immunogenic fragment or variant thereof, and a lipidation sequence including a lipobox motif. A canonical lipobox motif is shown as SEQ ID NO:85. A lipidation sequence can be N-terminal or C-terminal to the protein, and can be embedded in a signal or other sequence, or in a fusion protein. Exemplary lipidation sequences include the signal sequence of SP2108 (SEQ ID NO:86) and the signal sequence of the *E. coli* gene RlpB (SEQ ID NO:87). A signal sequence can be, for example, an *E. coli* or *S. pneumoniae* signal sequence. Exemplary *E. coli* signal sequences include the mlpA signal sequence (Lin et al., 1978, Proc. Natl. Acad. Sci. U.S.A. 75:4891-4895), the lamB signal sequence (Emr et al., 1978, Proc. Natl. Acad. Sci. U.S.A. 75:5802-5806), the MBP signal sequence (Bassford, 1979, J. Bacteriol. 139:19-31). Lpp is an exemplary *E. coli* signal sequence that directs lipidation (Cullen et al., 2003, Plasmid. 49:18-29.) *E. coli* signal sequences that direct lipidation are also described in Legrain et al., 1995, Protein Expr. Purif 6:570-578), e.g., the signal sequence of the gene RlpB (SEQ ID NO:87). Numerous *S. pneumoniae* signal sequences are known in the art. One such signal sequence is SEQ ID NO:86.

[0069] In certain embodiments, vaccines or pharmaceutical compositions comprising an *S. pneumoniae* polypeptide including a fusion protein can comprise a polypeptide from Table 1 and/or 2, or an immunogenic fragment or variant thereof, and a tag. A tag can be N-terminal or C-terminal. For instance, tags can be added to the polypeptide to facilitate purification, detection, solubility, or confer other desirable characteristics on the protein. For instance, a purification tag can be a peptide, oligopeptide, or polypeptide that can be used in affinity purification. Examples include His, GST, TAP, FLAG, myc, HA, MBP, VSV-G, thioredoxin, V5, avidin, streptavidin, BCCP, Calmodulin, Nus, S tags, lipoprotein D, and β galactosidase. Particular exemplary His tags include HIHHHHH (SEQ ID NO:88) and MSYYHHHHHH (SEQ ID NO:89). In other embodiments, the polypeptide is free of tags such as protein purification tags, and is purified by a method not relying on affinity for a purification tag. In some embodiments, the fused portion is short. This, in some instances, the fusion protein comprises no more than 1, 2, 3, 4, 5, 10, or 20 additional amino acids on one or both termini of polypeptide from Table 1 and/or 2.

C. Additional Components of Vaccine and Immunogenic Compositions

[0070] In certain embodiments, the vaccine or immunogenic composition comprises a plurality of antigens described herein and one or more of the following: an adjuvant (e.g., a vaccine delivery system and/or immunostimulatory compound), stabilizer, buffer, surfactant, controlled release component, salt, and/or a preservative.

[0071] 1. Carriers/Adjuvants

[0072] The vaccine formulations and immunogenic compositions described herein can include an adjuvant. Adjuvants can be broadly separated into two classes, based on their principal mechanisms of action: vaccine delivery systems and immunostimulatory compounds (see, e.g., Singh et al., Curr. HIV Res. 1:309-320, 2003).

[0073] Vaccine delivery systems are often advantageously particle formulations. Examples of particle formulations include emulsions, microparticles, immune-stimulating complexes (ISCOMs), nanoparticles, which can be, for example, particles and/or matrices, and liposomes, and the like. Such formulations are often effective for delivery of intact antigens, or collections of different antigenic vaccine components that work in concert, to promote robust immune responses.

[0074] Oil emulsion compositions suitable fbor use as adjuvants/carriers in the present disclosure include squalene-water emulsions, such as MF59 (5% Squalene, 0.5% Tween 80, and 0.5% Span 85, formulated into submicron particles using a micro fluidizer). See, e.g., WO2009016515.

[0075] Microparticles (i.e., a particle of ~100 nm to ~150 μm in diameter, more preferably ~200 nm to ~30 μm in diameter, and most preferably ~500 nm to ~10 μm in diameter) can be formed from materials that are biodegradable and non-toxic (e.g., a poly(α-hydroxy acid), a polyhydroxybutyric acid, a polyorthoester, a polyanhydride, a polycaprolactone, etc.). Poly(lactide-co-glycolide)-based microparticles are known as effective carriers, which are optionally treated to have a negatively-charged surface (e.g., with SDS) or a positively-charged surface (e.g., with a cationic detergent, such as CTAB).

[0076] Nanoparticles have been shown to be effective delivery vehicles for vaccine compositions and can enhance the immune response. Individual nanoparticles are typically between 1 and 100 nanometers. In some embodiments, the nanoparticles are solid and can have the vaccine components conjugated to the surface. In other embodiments, the nanoparticles, such as liposomes, can be formed around and thus encapsulating mixtures of vaccine components. Liposome vesicles, for example, can be formed around the vaccine components using pure phospholipid or a mixture of phospholipids and phosphoglycerides according to known methods. See, e.g., U.S. Pub. No. 2006/0189554. In some embodiments, protein antigens, such as T_H17 cell protein antigen or B cell protein antigen, can be lapidated to facilitate their incorporation into the nanoparticle. Moreover CP antigens can be conjugated to the lipid nanoparticle coats according to known methods.

[0077] In addition, or alternatively, an adjuvant is provided to generate a signal to the immune system so that it generates a response to the antigen, wherein the antigen drives the specificity of the response to the pathogen. Such "immunostimulatory" compound adjuvants are sometimes derived from pathogens and can represent pathogen associated molecular patterns (PAMP), e.g., lipopolysaccharides (LPS), monophosphoryl lipid (MPL), or CpG-containing DNA, which activate cells of the innate immune system.

[0078] Such immunostimulatory compound adjuvants can be classified as organic and inorganic. Preferred inorganic adjuvants include aluminum salts (alum) such as aluminum phosphate, amorphous aluminum hydroxyphosphate sulfate, and aluminum hydroxide, which are commonly used in human vaccines and are easily adapted to new vaccine technologies.

[0079] Organic adjuvants comprise organic molecules including macromolecules. An example of an organic adjuvant is cholera toxin.

[0080] Known adjuvants can also be selected on the basis of the response they induce. In some embodiments, the adjuvant induces the activation of T_H1 cells or T_H2 cells. In other embodiments, the adjuvant induces the activation of B cells. In yet other embodiments, the adjuvant induces the activation of antigen-presenting cells. These categories are not mutually exclusive; in some cases, an adjuvant activates more than one type of cell.

[0081] In certain embodiments, the adjuvant can induce the activation of T_H17 cells. It can promote the $CD4^+$ or $CD8^+$ T cells to secrete IL-17. In some embodiments, an adjuvant that induces the activation of T_H17 cells is one that produces at least a 2-fold, and in some cases a 10-fold, experimental sample-to-control ratio in the following assay. In the assay, an experimenter compares the IL-17 levels secreted by two populations of cells: (1) cells from animals immunized with the adjuvant and a polypeptide known to induce T_H17 activation, and (2) cells from animals treated with the adjuvant and an irrelevant (control) polypeptide. An adjuvant that induces the activation of T_H17 cells can cause the cells of population (1) to produce more than 2-fold, or more than 10-fold more IL-17 than the cells of population (2). IL-17 can be measured, for example, by ELISA or ELISPOT. Certain toxins, such as cholera toxin and labile toxin (produced by enterotoxigenic *E. coli*, or ETEC), activate a T_H17 response. Thus, in some embodiments, the adjuvant is a toxin. One form of labile toxin is produced by Intercell. Mutant derivates of labile toxin that are active as adjuvants but significantly less toxic can be used as well. Exemplary detoxified mutant derivatives of labile toxin include mutants lacking ADP-ribosyltransferase activity. Particular detoxified mutant derivatives of labile toxin include LTK7 (Douce et al, 1995, Proc. Natl. Acad. Sci. USA 92:1644-1648) and LTK63 (Williams et al., 2004, J. Immunol. 173:7435-7443), LT-G192 (Douce et al., 1999, Infect. Immun. 67:4400-4406), and LTR72 (Giuliani et al., 1998, J. Exp. Med. 187:1123-1132).

[0082] In some embodiments, the adjuvant comprises a VLP (virus-like particle). One such adjuvant platform, Alphavirus replicons, induces the activation of T_H17 cells using alphavirus and is produced by Alphavax. In certain embodiments of the Alphavirus replicon system, alphavirus can be engineered to express an antigen of interest, a cytokine of interest (for example, IL-17 or a cytokine that stimulates IL-17 production), or both, and can be produced in a helper cell line. More detailed information can be found in U.S. Pat. No. 5,643,576 and U.S. Pat. No. 6,783,939.

[0083] In some embodiments, a vaccine formulation is administered to a patient in combination with a nucleic acid encoding a cytokine. Certain classes of adjuvants activate toll-like receptors (TLRs) in order to activate a T_H17 response. TLRs are well known proteins that can be found on leukocyte membranes, and recognize foreign antigens (including microbial antigens). Administering a known TLR ligand together with an antigen of interest (for instance, as a fusion protein) can promote the development of an immune response specific to the antigen of interest. One exemplary adjuvant that activates TLRs comprises Monophosphoryl Lipid A (MPL). Traditionally, MPL has been produced as a detoxified lipopolysaccharide (LPS) endotoxin obtained from gram negative bacteria, such as *S. minnesota*. In particular, sequential acid and base hydrolysis of LPS produces an immunoactive lipid A fraction (which is MPL), and lacks the saccharide groups and all but one of the phosphates present in LPS. A number of synthetic TLR agonists (in particular, TLR-4 agonists) are disclosed in Evans et al., 2003, Expert Rev. Vaccines 2:219-229. Like MPL adjuvants, these synthetic compounds activate the innate immune system via TLR-4. Another type of TLR agonist is a synthetic phospholipid dimer, for example E6020 (Ishizaka et al., 2007, Expert Rev. Vaccines 6:773-784). Various TLR agonists (including TLR-4 agonists) have been produced and/or sold by, for example, the Infectious Disease Research Institute (IRDI), Corixa, Esai, Avanti Polar Lipids, Inc., and Sigma Aldrich. Another exemplary adjuvant that activates TLRs comprises a mixture of MPL, Trehalose Dicoynomycolate (TDM), and dioctadecyldimethylammonium bromide (DDA). Another TLR-activating adjuvant is R848 (resiquimod).

[0084] In some embodiments, the adjuvant is or comprises a saponin. Typically, the saponin is a triterpene glycoside, such as those isolated from the bark of the *Quillaja saponaria* tree. A saponin extract from a biological source can be further fractionated (e.g., by chromatography) to isolate the portions of the extract with the best adjuvant activity and with acceptable toxicity. Typical fractions of extract from *Quillaja saponaria* tree used as adjuvants are known as fractions A and C.

[0085] A particular form of saponins that can be used in vaccine formulations described herein is immunostimulating complexes (ISCOMs). ISCOMs are an art-recognized class of adjuvants, that generally comprise *Quillaja* saponin fractions and lipids (e.g., cholesterol and phospholipids such as phosphatidyl choline). In certain embodiments, an ISCOM is assembled together with a polypeptide of interest. However, different saponin fractions can be used in different ratios. In addition, the different saponin fractions can either exist together in the same particles or have substantially only one fraction per particle (such that the indicated ratio of fractions A and C are generated by mixing together particles with the different fractions). In this context, "substantially" refers to less than 20%, 15%, 10%, 5%, 4%, 3%, 2% or even 1%. Such adjuvants can comprise fraction A and fraction C mixed into a ratio of 70-95 A:30-5 C, such as 70 A:30 C to 75 A:5 C, 75 A:5 C to 80 A:20 C, 80 A:20 C to 85 A:15C, 85 A:15 C to 90 A:10 C, 90 A:10 C to 95 A:5 C, or 95 A:5 C to 99 A:1 C.

[0086] In certain embodiments, combinations of adjuvants are used. For example, in some embodiments an adjuvant that promotes a B cell response to the protein and/or CP antigens, such as aluminum, can be combined with an adjuvant that promotes a T cell response, such as TLR agonists. Three exemplary combinations of adjuvants are MPL and alum, E6020 and alum, and MPL and an ISCOM.

[0087] An adjuvant can be covalently bound to an antigen. In some embodiments, the adjuvant can comprise a protein which induces inflammatory responses through activation of antigen presenting cells (APCs). In some embodiments, one or more of these proteins can be recombinantly fused with an antigen of choice, such that the resultant fusion molecule promotes dendritic cell maturation, activates dendritic cells to produce cytokines and chemokines, and ultimately, enhances presentation of the antigen to naïve T cells and initiation of T cell responses (see for example, Wu et al., 2005, Cancer Res. 65:4947-4954). In certain embodiments, a polypeptide, including a fusion protein, described herein is presented in the context of the trivalent conjugate system, comprising a fusion protein of *S. pneumoniae* Pneumococcal surface adhesin A (PsaA) with the pneumolysoid PdT and a cell wall polysaccharide (PsaA:PdT-CPs), described in Lu et al., 2009, Infect. Immun. 77:2076-2083. The pneumolysin derivative PdT carries three amino acid substitutions (W433F, D385N, and C428G) which render the molecule nontoxic but do not interfere with its TLR-4-mediated inflammatory properties. Conjugation of a polysaccharide to the fusion of a polypeptide to the TLR-4-agonist PdT enhances immunological response to the polypeptide. In some embodiments, one or more polypeptides described herein are used in place of PsaA in the trivalent conjugate. The trivalent conjugate system typically includes alum and is usually administered parenterally. Other exemplary adjuvants that can be covalently bound to antigens comprise polysaccharides, pneumolysin, synthetic peptides, lipopeptides, and nucleic acids.

[0088] Typically, the same adjuvant or mixture of adjuvants is present in each dose of a vaccine. Optionally, however, an adjuvant can be administered with the first dose of vaccine and not with subsequent doses (i.e., booster shots). Alternatively, a strong adjuvant can be administered with the first dose of vaccine and a weaker adjuvant or lower dose of the strong adjuvant can be administered with subsequent doses. The adjuvant can be administered before the administration of the antigen, concurrent with the administration of the antigen or after the administration of the antigen to a subject (sometimes within 1, 2, 6, or 12 hours, and sometimes within 1, 2, or 5 days). Certain adjuvants are appropriate for human patients, non-human animals, or both.

[0089] 2. Additional Components

[0090] In addition to the antigens and the adjuvants described above, a vaccine formulation or immunogenic composition can include one or more additional components, such as a stabilizer, buffer, surfactant, controlled release component, salt, and/or preservative.

[0091] In certain embodiments, the vaccine formulation or immunogenic composition can include one or more stabilizers such as sugars (such as sucrose, trehalose, glucose, or fructose), phosphate (such as sodium phosphate dibasic, potassium phosphate monobasic, dibasic potassium phosphate, or monosodium phosphate), glutamate (such as monosodium L-glutamate), gelatin (such as processed gelatin, hydrolyzed gelatin, or porcine gelatin), amino acids (such as arginine, asparagine, histidine, L-histidine, alanine, valine, leucine, isoleucine, serine, threonine, lysine, phenylalanine, tyrosine, and the alkyl esters thereof), inosine, or sodium borate.

[0092] In certain embodiments, the vaccine formulation or immunogenic composition includes one or more buffers such as a mixture of sodium bicarbonate and ascorbic acid. In some embodiments, the vaccine formulation can be administered in saline, such as phosphate buffered saline (PBS), or distilled water.

[0093] In certain embodiments, the vaccine formulation or immunogenic composition includes one or more surfactants such as, for example, polysorbate 80 (Tween 80), Triton X-100, Polyethylene glycol tert-octylphenyl ether t-Octylphenoxypolyethoxyethanol 4-(1,1,3,3-Tetramethylbutyl) phenylpolyethylene glycol (TRITON X-100); Polyoxyethylenesorbitan monolaurate Polyethylene glycol sorbitan monolaurate (TWEEN 20); 4-(1,1,3,3-Tetramethylbutyl) phenol polymer with formaldehyde and oxirane (TYLOXAPOL); and the like. A surfactant can be ionic or nonionic.

[0094] In certain embodiments, the vaccine formulation or immunogenic composition includes one or more salts such, for example, as sodium chloride, ammonium chloride, calcium chloride, or potassium chloride.

[0095] In certain embodiments, a preservative is included in the vaccine or immunogenic composition. In other embodiments, no preservative is used. A preservative is most often used in multi-dose vaccine vials, and is less often needed in single-dose vaccine vials. In certain embodiments, the preservative is, for example, 2-phenoxyethanol, methyl and propyl parabens, benzyl alcohol, thiomersal, and/or sorbic acid.

[0096] In certain embodiments, the vaccine formulation or immunogenic composition is a controlled release formulation.

D. Use of Vaccines and Immunogenic Compositions

[0097] The *S. pneumoniae* vaccines described herein can be used for prophylactic and/or therapeutic treatment of *S. pneumoniae*. Accordingly, this application provides a method for treating a subject suffering from or susceptible to *S. pneumoniae* infection, comprising administering an effective amount of any of the vaccine formulations described herein. In some aspects, the method inhibits *S. pneumoniae* colonization in an individual. In some aspects, the method reduces or prevents nasopharyngeal carriage in an individual. In some aspects, the method inhibits *S. pneumoniae* symptoms, invasive disease or sequelae, such as sepsis, pneumonia, meningitis, otitis media, sinusitis or infection of other sites or organs with *S. pneumoniae*. The subject receiving the vaccination can be a male or a female, and can be a child or adult. In some embodiments, the subject being treated is a human. In other embodiments, the subject is a non-human animal.

[0098] 1. Prophylactic Use

[0099] In prophylactic embodiments, the vaccine is administered to a subject to induce an immune response that can help protect against the establishment of *S. pneumoniae*, for example by protecting against colonization, the first and necessary step in disease progression. Thus, in some aspects, the method inhibits infection by *S. pneumoniae* in a non-colonized or uninfected subject. In another aspect, the method can reduce or eliminate the nasopharyngeal carriage by an individual. In another aspect, the method can reduce the duration of colonization in an individual who is already colonized.

[0100] In some embodiments, the vaccine compositions of the present disclosure confer protective immunity, allowing a vaccinated individual to exhibit delayed onset of symptoms or sequelae, or reduced severity of symptoms or sequelae, as the result of his or her exposure to the vaccine. In certain embodiments, the reduction in severity of symptoms or sequelae is at least 25%, 40%, 50%, 60%, 70%, 80%, or even 90%. In particular embodiments, vaccinated individuals can display no symptoms or sequelae upon contact with *S. pneumoniae*, do not become colonized by *S. pneumoniae*, or demonstrate reduced colonization/duration of colonization. Protective immunity is typically achieved by one or more of the following mechanisms: mucosal, humoral, and/or cellular immunity. Mucosal immunity is primarily the result of secretory IgA (sIGA) antibodies on mucosal surfaces of the respiratory, gastrointestinal, and genitourinary tracts. The sIGA antibodies are generated after a series of events mediated by antigen-processing cells, B and T lymphocytes, that result in sIGA production by B lymphocytes on mucosa-lined tissues of the body. Humoral immunity is typically the result of IgG antibodies and IgM antibodies in serum. Cellular immunity can be achieved through cytotoxic T lymphocytes or through delayed-type hypersensitivity that involves macrophages and T lymphocytes, as well as other mechanisms involving T cells without a requirement for antibodies. In particular, cellular mucosal immunity can be mediated by T_H1 or T_H17 cells.

[0101] Essentially any individual has a certain risk of becoming infected with *S. pneumoniae*. However, certain sub-populations have an increased risk of infection. In some embodiments, a vaccine formulation as described herein (e.g., a composition comprising one or more polysaccharides antigens and one or more polypeptides capable of inducing a B cell and T cell response) is administered to patients that are immunocompromised.

[0102] An immunocompromising condition arising from a medical treatment is likely to expose the individual in question to a higher risk of infection with *S. pneumoniae*. It is possible to treat an infection prophylactically in an individual having the immunocompromised condition before or during treatments known to compromise immune function. By prophylactically treating with an antigenic composition (e.g., including one or more polypeptide antigens capable of inducing a B cell and/or T cell response, and one or more polysaccharide antigens), before or during a treatment known to compromise immune function, it is possible to prevent a subsequent *S. pneumoniae* infection or to reduce the risk of the individual contracting an infection due to the immunocompromised condition. Should the individual contract an *S. pneumoniae* infection e.g., following a treatment leading to an immunocompromised condition it is also possible to treat the infection by administering to the individual an antigen composition.

[0103] The following groups are at increased risk of pneumococcal disease or its complications, and therefore it is advantageous for subjects falling into one or more of these groups to receive a vaccine formulation described herein: children, especially those from 1 month to 5 years old or 2 months to 2 years old; children who are at least 2 years of age with asplenia, splenic dysfunction or sickle-cell disease; children who are at least 2 years of age with nephrotic syndrome, chronic cerebrospinal fluid leak, HIV infection or other conditions associated with immunosuppression.

[0104] In another embodiment, at least one dose of the pneumococcal combined antigen composition is given to adults in the following groups at increased risk of pneumococcal disease or its complications: all persons 65 years of age; adults with asplenia, splenic dysfunction or sickle-cell disease; adults with the following conditions: chronic cardiorespiratory disease, cirrhosis, alcoholism, chronic renal disease, nephrotic syndrome, diabetes mellitus, chronic cerebrospinal fluid leak, HIV infection, AIDS and other conditions associated with immunosuppression (e.g., Hodgkin's disease, lymphoma, multiple myeloma, immunosuppression for organ transplantation), individuals with cochlear implants; individuals with long-term health problems such as heart disease and lung disease, as well as individuals who are taking any drug or treatment that lowers the body's resistance to infection, such as long-term steroids, certain cancer drugs, radiation therapy; Alaskan natives and certain Native American populations.

[0105] 2. Therapeutic Use

[0106] In therapeutic applications, the vaccine can be administered to a patient suffering from *S. pneumoniae* infection, in an amount sufficient to treat the patient. Treating the patient, in this case, refers to reducing *S. pneumoniae* symptoms and/or bacterial load and/or sequelae in an infected individual. Some individuals remain asymptomatic upon colonization but can carry a mucosal infection that can be transmitted to other individuals. Accordingly, in some embodiments, treatment refers to eliminating or reducing the mucosal bacterial load, or to reducing the duration of nasopharyngeal carriage. In some embodiments, treating the patient refers to reducing the infectivity of the patient to other individuals. In some embodiments, treating the patient refers to reducing the duration of symptoms or sequelae. In some embodiments, treating the patient refers to reducing the intensity of symptoms or sequelae. In some embodiments, the vaccine reduces transmissibility of *S. pneumoniae* from the vaccinated patient. In certain embodiments, the reductions described above are at least 25%, 30%, 40%, 50%, 60%, 70%, 80%, or even 90%.

[0107] In therapeutic embodiments, the vaccine is administered to an individual post-infection. The vaccine can be administered shortly after infection, e.g., before symptoms or sequelae manifest, or can be administered during or after manifestation of symptoms or sequelae.

[0108] A therapeutic *S. pneumoniae* vaccine can reduce the intensity and/or duration of the various symptoms or sequelae of *S. pneumoniae* infection. Symptoms or sequelae of *S. pneumoniae* infection can take many forms. In some cases, an infected patient develops pneumonia, acute sinusitis, otitis media (ear infection), meningitis, bacteremia, sepsis, osteomyelitis, septic arthritis, endocarditis, peritonitis, pericarditis, cellulitis, or brain abscess.

[0109] Sepsis is a rare but life-threatening complication of *S. pneumoniae* infection, where the bacterium invades the bloodstream and systemic inflammation results. Typically, fever is observed and white blood cell count increases. A further description of sepsis is found in Goldstein, B., et al., 2005, Pediatr. Crit. Care Med. 6:2-8.

[0110] 3. Assaying Vaccination/Immunogenic Composition Efficacy

[0111] The efficacy of the vaccines and immunogenic compositions disclosed herein can be determined in a number of ways, in addition to the clinical outcomes described above. First, one can assay IL-17 levels (particularly IL-17A) by stimulating T cells derived from the subject after administration/vaccination. The IL-17 levels can be compared to IL-17 levels in the same subject before vaccination. Increased IL-17 (e.g., IL-17A) levels, such as a 1.5 fold, 2-fold, 5-fold, 10-fold, 20-fold, 50-fold 20 or 100-fold or more increase, would indicate an increased response to the vaccine. Alternatively (or in combination), one can assay neutrophils in the presence of T cells or antibodies from the patient for pneumococcal killing. Increased pneumococcal killing, such as a 1.5 fold, 2-fold, 5-fold, 10-fold, 20-fold, 50-fold, or 100-fold or more increase, would indicate an increased response to the vaccine. In addition, one can measure T_H17 cell activation, where increased T_H17 cell activation, such as a 1.5-fold, 2-fold, 5-fold, 10-fold, 20-fold, 50-fold or 100-fold or more increase, correlates with an increased response to the vaccine or immunogenic compositions. One can also measure levels of an antibody specific to the vaccine, where increased levels of the specific antibody, such as a 1.5-fold, 2-fold, 5-fold, 10-fold, 20-fold, 50-fold, or 100-fold or more increase, are correlated with increased vaccine or immunogenic composition efficacy. In certain embodiments, two or more of these assays are used. For example, one can measure IL-17 levels and the levels of vaccine-specific antibody. Alternatively, one can follow epidemiological markers such as incidence of, severity of, or duration of pneumococcal infection in vaccinated individuals compared to unvaccinated individuals.

[0112] The efficacy of the B-cell-directed antigen can be tested by measuring antibody titers against the B cell protein antigen, such as PspA or L460D pneumolysin or CP according to known assays. Some additional illustrative assays include testing for pneumolysin toxin neutralizing antibody responses, opsonophagocytic assay responses, and passive transfer of protection to mice against challenge with *S. pneumoniae*. These tests have the advantage establishing the quality of the antibody response, i.e., the efficacy of the antibodies produced in actually combating the *S. pneumoniae*, as opposed to merely establishing elevated levels of antibodies with unknown efficacy.

[0113] Vaccine efficacy can also be assayed in various model systems such as mouse models for pneumococcal carriage or disease. For instance, BALB/c or C57BL/6 strains of mice can be used. After administering the test vaccine to a subject (as a single dose or multiple doses), a challenge dose of *S. pneumoniae* is administered. In some cases, a challenge dose administered intranasally is sufficient to cause *S. pneumoniae* colonization (especially nasal colonization) in an unvaccinated animal, and in some cases a challenge dose administered via aspiration is sufficient to cause sepsis and a high rate of lethality in unvaccinated animals. One can then measure the reduction in colonization or the reduction in lethality in vaccinated animals.

[0114] Vaccine efficacy for specifically preventing or reducing nasopharyngeal carriage can be also assayed in available model systems as described above. In some embodiments, after administering the test vaccine to a model animal (in a single dose or multiple doses), at least one challenge dose of *S. pneumoniae* is administered intranasally, where the dose is sufficient to cause mucosal colonization in an unvaccinated animal. After sufficient time to allow establishment, the nasopharyngeal chamber is flushed and bacterial levels assayed from the obtained wash solution (e.g., CFU resulting per volume wash or using quantitative polymerase chain reaction (PCR) techniques directed to known *S. pneumoniae* genes). Furthermore, nasopharyngeal carriage can be monitored in humans receiving administrations of the described vaccine compositions. For example, carriage or carriage load can be assayed in individuals by obtaining mucosal samples using a deep nasopharyngeal swab technique. In one embodiment, a sterile swab with a flexible aluminum shaft and a dry calcium alginate tip is inserted into the nostril, and passed into the nasopharynx to a distance equal to that from the subject's nose to the tip of the ear. The sample can be stored in an appropriate medium, such as skim milk-tryptone-glucose-glycerol (STGG) medium, for quantification and/or identification assays. Nasopharyngeal carriage (i.e., presence of *S. pneumoniae* in the nasopharyngeal chamber) or carriage load can be assayed by known methods, including direct culturing techniques, detection of fluorescently labeled bacteria, quantitative PCR techniques directed to *S. pneumnoniae* genes, or commercially available kits such as BinaxNOW® (Alere, Waltham, Mass.).

[0115] 4. Use of Immunogenic Compositions Against *S. pneumoniae* Infection

[0116] The immunogenic compositions of the present disclosure are designed to elicit an immune response against *S. pneumoniae*. Compositions described herein (e.g., ones comprising one or more polypeptides, including fusion proteins, and one or more polysaccharide antigens) can stimulate an antibody response or a cell-mediated immune response, or both, in the mammal to which it is administered. In some embodiments, the composition stimulates a T_H1-biased $CD4^+$ T cell response, a T_H17-biased $CD4^+$ T cell response and/or a $CD8^+$ T cell response. In some embodiments, the composition stimulates an antibody response. In some embodiments, the composition stimulates a T_H1-biased $CD4^+$ T cell response, T_H17-biased $CD4^+$ T cell response and/or a $CD8^+$ T cell response, and an antibody response.

[0117] In certain embodiments, the composition (e.g., one comprising one or more polypeptides, including fusion proteins, and one or more polysaccharide antigens) includes a cytokine such as IL-17, to provide additional stimulation to the immune system of the mammal.

[0118] While not wishing to be bound by theory, in some embodiments a T_H17 cell response is desirable in mounting an immune response to the compositions disclosed herein, e.g., ones comprising one or more polypeptides, including fusion proteins, and one or more polysaccharide antigens. In certain embodiments, an active T_H17 response is beneficial in clearing a pneumococcal infection. For instance, mice lacking the IL-17A receptor show decreased whole cell vaccine-based protection from a pneumococcal challenge (Lu et al., 2008, PLoS Pathog. 4.9:e1000159).

[0119] Thus, provided herein is a method of increasing IL-17 production by administering the compositions described herein (e.g., ones comprising one or more polypeptides described herein) to a subject. Furthermore, this application provides a method of activating T_H17 cells by administering said compositions to a subject. In certain embodiments, increased IL-17A levels contribute to increased pneumococcal killing by neutrophils or neutrophil-like cells, for instance by inducing recruitment and activation of neutrophils of neutrophil-like cells. In certain embodiments, this pneumococcal killing is independent of antibodies and complement. However, specific antibody production and complement activation can be useful additional mechanisms that contribute to clearing of a pneumococcal infection.

[0120] Immunogenic compositions containing immunogenic polypeptides and one or more lipid polysaccharides, together with a pharmaceutical carrier are also provided.

E. Doses/Routes of Administration/Formulation

[0121] 1. Dosage Forms, Amounts, and Timing

[0122] The amount of antigen in each vaccine or immunogenic composition dose is selected as an effective amount, which induces a prophylactic or therapeutic response against one, more or all of the antigens presented, as described above, in either a single dose or over multiple doses. Preferably, the dose is without significant adverse side effects in typical vaccines. Such amount will vary depending upon which specific antigens are employed. Generally, it is expected that a dose will comprise 1-100 μg of each protein antigen in the polypeptide component, for instance between 1-10 μg of each protein antigen. In some embodiments, the vaccine formulation comprises 1-250 μg, such as 1-100 μg, of the total polypeptide component; 1-250 μg, such as 1-100 μg, of the total CP antigen component; and 1-250 μg, such as 1-100 μg, of the adjuvant/carrier component. In some embodiments, the appropriate amount of protein and/or CP antigen component to be delivered will depend on the age, weight, and health (e.g., immunocompromised status) of a subject. When present, typically an adjuvant will be present in amounts from 1 μg-250 μg per dose, for example 50-150 μg, 75-125 μg or 100 μg.

[0123] In some embodiments, only one dose of the vaccine is administered to achieve the results described above. In other embodiments, following an initial vaccination, subjects receive one or more boost vaccinations, for a total of two, three, four or five vaccinations. Advantageously, the number is three or fewer. A boost vaccination can be administered, for example, about 1 month, 2 months, 4 months, 6 months, or 12 months after the initial vaccination, such that one vaccination regimen involves administration at 0, 0.5-2, and 4-8 months. It can be advantageous to administer split doses of vaccines which can be administered by the same or different routes. The vaccines and immunogenic compositions described herein can take on a variety of dosage forms. In certain embodiments, the composition is provided in solid or powdered (e.g., lyophilized) form; it also can be provided in solution form. In certain embodiments, a dosage form is provided as a dose of lyophilized composition and at least one separate sterile container of diluent or adjuvant.

[0124] In some embodiments, the composition, or discrete component thereof, (e.g., CP, B cell peptide antigen, and/or T cell peptide antigen) will be administered in a dose escalation manner in subsequence administrations, such that successive administrations of the composition contain a higher concentration of composition than previous administrations. In some embodiments, the composition will be administered in a manner such that successive administrations of the composition contain a lower concentration of composition than previous administrations.

[0125] In therapeutic applications, compositions are administered to a patient suffering from a disease in an amount sufficient to treat the patient. Therapeutic applications of a composition described herein include reducing transmissibility, slowing disease progression, reducing bacterial viability or replication, or inhibiting the expression of proteins required for toxicity, such as by 90%, 80%, 70%, 60%, 50%, 40%, 30%, 20%, or 10% of the levels at which they would occur in individuals who are not treated with the composition.

[0126] In prophylactic embodiments, compositions are administered to a human or other mammal to induce an immune response that can inhibit the establishment of an infectious disease or other condition. In some embodiments, a composition can partially block the bacterium from establishing an infection.

[0127] In some embodiments, the compositions are administered in combination with antibiotics. This co-administration is particularly appropriate when the pharmaceutical composition is administered to a patient who has recently been exposed (or is suspected of having been recently exposed) to *S. pneumoniae*. Many antibiotics are used to treat pneumococcal infections, including penicillin, amoxicillin, amoxicillin/clavulanate, cefuroxime, cefotaxime, ceftriaxone, and vancomycin. The appropriate antibiotic can be selected based on the type and severity of the infection, as well as any known antibiotic resistance of the infection (Jacobs, 1999, Am. J. Med. 106:19S-25S).

[0128] 2. Routes of Administration

[0129] The vaccine formulations and pharmaceutical compositions herein can be delivered by administration to an individual, typically by systemic administration (e.g., intramuscular, intradermal, subcutaneous, subdermal, transdermal, intravenous, intraperitoneal, intracranial, intranasal, mucosal, anal, vaginal, oral, buccal route or they can be inhaled) or they can be administered by topical application. In some embodiments, the route of administration is intramuscular. In other embodiments, the route of administration is subcutaneous. In yet other embodiments, the route of administration is mucosal. In certain embodiments, the route of administration is transdermal or intradermal.

[0130] Certain routes of administration are particularly appropriate for vaccine formulations and immunogenic compositions comprising specified adjuvants. In particular, transdermal administration is one suitable route of administration for *S. pneumoniae* vaccines comprising toxins (e.g., cholera toxin or labile toxin); in other embodiments, the administration is intranasal. Vaccines formulated with Alphavirus replicons can be administered, for example, by the intramuscular or the subcutaneous route. Vaccines comprising Monophosphory Lipid A (MPL), Trehalose Dicoynomycolate (TDM), and dioctadecyldimethylammonium bromide (DDA) are suitable (inter alia) for intramuscular and subcutaneous administration. A vaccine comprising resiquimod can be administered topically or subcutaneously, for example.

[0131] 3. Formulations

[0132] The vaccine formulation or immunogenic composition can be suitable for administration to a human patient, and vaccine or immunogenic composition preparation can conform to USFDA guidelines. In some embodiments, the vaccine formulation or immunogenic composition is suitable for administration to a non-human animal. In some embodiments, the vaccine or immunogenic composition is substantially free of either endotoxins or exotoxins. Endotoxins can include pyrogens, such as some lipopolysaccharide (LPS) molecules not used herein as antigens. The vaccine or immunogenic composition can also be substantially free of inactive protein fragments which may cause a fever or other side effects. In some embodiments, the composition contains less than 1%, less than 0.1%, less than 0.01%, less than 0.001%, or less than 0.0001% of endotoxins, exotoxins, and/or inactive protein fragments. In some embodiments, the vaccine or immunogenic composition has lower levels of pyrogens than industrial water, tap water, or distilled water. Other vaccine or immunogenic composition components can be purified using methods known in the art, such as ion-exchange chromatography, ultrafiltration, or distillation. In other embodiments, the pyrogens can be inactivated or destroyed prior to administration to a patient. Raw materials for vaccines, such as water, buffers, salts and other chemicals can also be screened and depyrogenated. All materials in the vaccine can be sterile, and each lot of the vaccine can be tested for sterility. Thus, in certain embodiments the endotoxin levels in the vaccine fall below the levels set by the USFDA, for example 0.2 endotoxin (EU)/kg of product for an intrathecal injectable composition; 5 EU/kg of product for a non-intrathecal injectable composition, and 0.25-0.5 EU/mL for sterile water.

[0133] In certain embodiments, the preparation comprises less than 50%, 20%, 10%, or 5% (by dry weight) contaminating protein. In certain embodiments, the desired molecule is present in the substantial absence of other biological macromolecules, such as other proteins (particularly other proteins which can substantially mask, diminish, confuse or alter the characteristics of the component proteins either as purified preparations or in their function in the subject reconstituted mixture). In certain embodiments, at least 80%, 90%, 95%, 99%, or 99.8% (by dry weight) of biological macromolecules of the same type present (but water, buffers, and other small molecules, especially molecules having a molecular weight of less than 5000, can be present). In some embodiments, the vaccine or immunogenic composition comprising purified subunit proteins contains less than 5%, 2%, 1%, 0.5%, 0.2%, 0.1% of protein from host cells in which the subunit proteins were expressed, relative to the amount of purified subunit. In some embodiments, the desired polypeptides are substantially free of nucleic acids and/or carbohydrates. For instance, in some embodiments, the vaccine or immunogenic composition contains less than 5%, less than 2%, less than 1%, less than 0.5%, less than 0.2%, or less than 0.1% host cell DNA and/or RNA. In certain embodiments, at least 80%, 90%, 95%, 99%, or 99.8% (by dry weight) of biological macromolecules of the same type are present in the preparation (but water, buffers, and other small molecules, especially molecules having a molecular weight of less than 5000, can be present).

[0134] It is preferred that the vaccine or immunogenic composition has low or no toxicity, within a reasonable risk-benefit ratio. For example, the compositions preferably have a low level of reactogenicity in animal toxicology studies. See, e.g., World Health Organization, "Procedure for assessing the acceptability, in principle, of vaccines for purchase by United Nations agencies" (WHO/IVB/05.19) published 2005; Dellepiane, N., et al., "New challenges in assuring vaccine quality," *Bulletin of the World Health Organization* 78(2):155-162 (2000), which are incorporated herein by reference.

[0135] The formulations suitable for introduction of the vaccine formulations or pharmaceutical composition vary according to route of administration. Formulations suitable for parenteral administration, such as, for example, by intraarticular (in the joints), intravenous, intramuscular, intradermal, intraperitoneal, intranasal, and subcutaneous routes, include aqueous and non-aqueous, isotonic sterile injection solutions, which can contain antioxidants, buffers, bacteriostats, and solutes that render the formulation isotonic with the blood of the intended recipient, and aqueous and non-aqueous sterile suspensions that can include suspending agents, solubilizers, thickening agents, stabilizers, and preservatives. The formulations can be presented in unit-dose or multi-dose sealed containers, such as ampoules and vials.

[0136] Injection solutions and suspensions can be prepared from sterile powders, granules, and tablets of the kind previously described. In the case of adoptive transfer of therapeutic T cells, the cells can be administered intravenously or parenterally.

[0137] Formulations suitable for oral administration can consist of (a) liquid solutions, such as an effective amount of the polypeptides suspended in diluents, such as water, saline or PEG 400; (b) capsules, sachets or tablets, each containing a predetermined amount of the active ingredient, as liquids, solids, granules or gelatin; (c) suspensions in an appropriate liquid; and (d) suitable emulsions. Tablet forms can include one or more of lactose, sucrose, mannitol, sorbitol, calcium phosphates, corn starch, potato starch, tragacanth, microcrystalline cellulose, acacia, gelatin, colloidal silicon dioxide, croscarmellose sodium, talc, magnesium stearate, stearic acid, and other excipients, colorants, fillers, binders, diluents, buffering agents, moistening agents, preservatives, flavoring agents, dyes, disintegrating agents, and pharmaceutically compatible carriers. Lozenge forms can comprise the active ingredient in a flavor, usually sucrose and acacia or tragacanth, as well as pastilles comprising the active ingredient in an inert base, such as gelatin and glycerin or sucrose and acacia emulsions, gels, and the like containing, in addition to the active ingredient, carriers known in the art. The pharmaceutical compositions can be encapsulated, e.g., in liposomes, or in a formulation that provides for slow release of the active ingredient.

[0138] The antigens, alone or in combination with other suitable components, can be made into aerosol formulations (e.g., they can be "nebulized") to be administered via inhalation. Aerosol formulations can be placed into pressurized acceptable propellants, such as dichlorodifluoromethane, propane, nitrogen, and the like. Aerosol formulations can be delivered orally or nasally.

[0139] Suitable formulations for vaginal or rectal administration include, for example, suppositories, which consist of the polypeptides with a suppository base. Suitable suppository bases include natural or synthetic triglycerides or paraffin hydrocarbons. In addition, it is also possible to use gelatin rectal capsules which consist of a combination of the polypeptides with a base, including, for example, liquid triglycerides, polyethylene glycols, and paraffin hydrocarbons.

F. Preparation and Storage

[0140] The *S. pneumoniae* vaccines and immunogenic compositions described herein, or the various subcomponents thereof, can be produced using a variety of techniques. For example, a polypeptide can be produced using recombinant DNA technology in a suitable host cell. A suitable host cell can be bacterial, yeast, mammalian, or other type of cell. The host cell can be modified to express an exogenous copy of one of the relevant polypeptide genes. Typically, the gene is operably linked to appropriate regulatory sequences such as a strong promoter and a polyadenylation sequence. In some embodiments, the promoter is inducible or repressible. Other regulatory sequences can provide for secretion or excretion of the polypeptide of interest or retention of the polypeptide of interest in the cytoplasm or in the membrane, depending on how one wishes to purify the polypeptide. The gene can be present on an extrachromosomal plasmid, or can be integrated into the host genome. One of skill in the art will recognize that it is not necessary to use a nucleic acid 100% identical to the naturally-occurring sequence. Rather, some alterations to these sequences are tolerated and can be desirable. For instance, the nucleic acid can be altered to take advantage of the degeneracy of the genetic code such that the encoded polypeptide remains the same. In some embodiments, the gene is codon-optimized to improve expression in a particular host. The nucleic acid can be produced, for example, by PCR or by chemical synthesis.

[0141] Once a recombinant cell line has been produced, a polypeptide can be isolated from it. The isolation can be accomplished, for example, by affinity purification techniques or by physical separation techniques (e.g., a size column).

[0142] In a further aspect of the present disclosure, there is provided a method of manufacture comprising mixing one or more polypeptides or an immunogenic fragment or variant thereof with a carrier and/or an adjuvant.

[0143] In some embodiments, antigens for inclusion the vaccine formulations and immunogenic compositions can be produced in cell culture. One method comprises providing one or more expression vectors and cloning nucleotides encoding one or more polypeptides described herein, then expressing and isolating the polypeptides.

[0144] The immunogenic polypeptides described herein and the polysaccharide antigens can be packaged in packs, dispenser devices, and kits for administering the compositions to a mammal. For example, packs or dispenser devices that contain one or more unit dosage forms are provided. Typically, instructions for administration of the compounds will be provided with the packaging, along with a suitable indication on the label that the compound is suitable for treatment of an indicated condition, such as those disclosed herein.

[0145] While various embodiments have been illustrated and described, it will be appreciated that various changes can be made therein without departing from the spirit and scope of the disclosure.

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Leu Gly Ala Gly Phe Val Ala Ser Ser Pro Thr Phe Val Arg Ala Glu
            20                  25                  30

Glu Ala Pro Val Ala Asn Gln Ser Lys Ala Glu Lys Asp Tyr Asp Ala
        35                  40                  45

Ala Val Lys Lys Ser Glu Ala Ala Lys Lys Asp Tyr Glu Thr Ala Lys
    50                  55                  60

Lys Lys Ala Glu Asp Ala Gln Lys Lys Tyr Asp Glu Asp Gln Lys Lys
65                  70                  75                  80

Thr Glu Ala Lys Ala Glu Lys Glu Arg Lys Ala Ser Glu Lys Ile Ala
                85                  90                  95

Glu Ala Thr Lys Glu Val Gln Gln Ala Tyr Leu Ala Tyr Leu Gln Ala
            100                 105                 110

Ser Asn Glu Ser Gln Arg Lys Glu Ala Asp Lys Lys Ile Lys Glu Ala
        115                 120                 125

Thr Gln Arg Lys Asp Glu Ala Glu Ala Ala Phe Ala Thr Ile Arg Thr
    130                 135                 140

Thr Ile Val Val Pro Glu Pro Ser Glu Leu Ala Glu Thr Lys Lys Lys
145                 150                 155                 160

Ala Glu Glu Ala Thr Lys Glu Ala Glu Val Ala Lys Lys Lys Ser Glu
                165                 170                 175

Glu Ala Ala Lys Glu Val Glu Val Glu Lys Asn Lys Ile Leu Glu Gln
            180                 185                 190

Asp Ala Glu Asn Glu Lys Lys Ile Asp Val Leu Gln Asn Lys Val Ala
        195                 200                 205

Asp Leu Glu Lys Gly Ile Ala Pro Tyr Gln Asn Glu Val Ala Glu Leu
    210                 215                 220

Asn Lys Glu Ile Ala Arg Leu Gln Ser Asp Leu Lys Asp Ala Glu Glu
225                 230                 235                 240

Asn Asn Val Glu Asp Tyr Ile Lys Glu Gly Leu Glu Gln Ala Ile Thr
                245                 250                 255

Asn Lys Lys Ala Glu Leu Ala Thr Thr Gln Gln Asn Ile Asp Lys Thr
            260                 265                 270

Gln Lys Asp Leu Glu Asp Ala Glu Leu Glu Leu Glu Lys Val Leu Ala
        275                 280                 285
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Thr Leu Asp Pro Glu Gly Lys Thr Gln Asp Glu Leu Asp Lys Glu Ala
    290                 295                 300

Ala Glu Ala Glu Leu Asn Glu Lys Val Glu Ala Leu Gln Asn Gln Val
305                 310                 315                 320

Ala Glu Leu Glu Glu Glu Leu Ser Lys Leu Glu Asp Asn Leu Lys Asp
                325                 330                 335

Ala Glu Thr Asn Asn Val Glu Asp Tyr Ile Lys Glu Gly Leu Glu Glu
            340                 345                 350

Ala Ile Ala Thr Lys Lys Ala Glu Leu Glu Lys Thr Gln Lys Glu Leu
        355                 360                 365

Asp Ala Ala Leu Asn Glu Leu Gly Pro Asp Gly Asp Glu Glu Glu Thr
    370                 375                 380

Pro Ala Pro Ala Pro Gln Pro Glu Lys Pro Ala Glu Glu Pro Glu Asn
385                 390                 395                 400

Pro Ala Pro Ala Pro Lys Pro Glu Lys Ser Ala Asp Gln Gln Ala Glu
                405                 410                 415

Glu Asp Tyr Ala Arg Arg Ser Glu Glu Glu Tyr Asn Arg Leu Thr Gln
            420                 425                 430

Gln Gln Pro Pro Lys Ala Glu Lys Pro Ala Pro Ala Pro Gln Pro Glu
        435                 440                 445

Gln Pro Ala Pro Ala Pro Lys Ile Gly Trp Lys Gln Glu Asn Gly Met
    450                 455                 460

Trp Tyr Phe Tyr Asn Thr Asp Gly Ser Met Ala Thr Gly Trp Leu Gln
465                 470                 475                 480

Asn Asn Gly Ser Trp Tyr Tyr Leu Asn Ser Asn Gly Ala Met Ala Thr
                485                 490                 495

Gly Trp Leu Gln Tyr Asn Gly Ser Trp Tyr Tyr Leu Asn Ala Asn Gly
            500                 505                 510

Ala Met Ala Thr Gly Trp Leu Gln Tyr Asn Gly Ser Trp Tyr Tyr Leu
        515                 520                 525

Asn Ala Asn Gly Ala Met Ala Thr Gly Trp Leu Gln Tyr Asn Gly Ser
    530                 535                 540

Trp Tyr Tyr Leu Asn Ala Asn Gly Asp Met Ala Thr Gly Trp Leu Gln
545                 550                 555                 560

Tyr Asn Gly Ser Trp Tyr Tyr Leu Asn Ala Asn Gly Asp Met Ala Thr
                565                 570                 575

Gly Trp Ala Lys Val His Gly Ser Trp Tyr Tyr Leu Asn Ala Asn Gly
            580                 585                 590

Ser Met Ala Thr Gly Trp Val Lys Asp Gly Glu Thr Trp Tyr Tyr Leu
        595                 600                 605

Glu Ala Ser Gly Ser Met Lys Ala Asn Gln Trp Phe Gln Val Ser Asp
    610                 615                 620

Lys Trp Tyr Tyr Val Asn Gly Leu Gly Ser Leu Ser Val Asn Thr Thr
625                 630                 635                 640

Val Asp Gly Tyr Lys Val Asn Ala Asn Gly Glu Trp Val
                645                 650


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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Synthetic

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1               5                   10                  15

Val Leu Lys Ala Asp Gly Ala Ile Leu Val Asp Phe Trp Ala Glu Trp
            20                  25                  30

Cys Gly Pro Cys Lys Met Ile Ala Pro Ile Leu Asp Glu Ile Ala Asp
        35                  40                  45

Glu Tyr Gln Gly Lys Leu Thr Val Ala Lys Leu Asn Ile Asp Gln Asn
    50                  55                  60

Pro Gly Thr Ala Pro Lys Tyr Gly Ile Arg Gly Ile Pro Thr Leu Leu
65                  70                  75                  80

Leu Phe Lys Asn Gly Glu Val Ala Ala Thr Lys Val Gly Ala Leu Ser
                85                  90                  95

Lys Gly Gln Leu Lys Glu Phe Leu Asp Ala Asn Leu Ala Gly Ser Gly
            100                 105                 110

Ser Gly His Met His His His His His His Ser Ser Gly Leu Val Pro
        115                 120                 125

Arg Gly Ser Gly Met Lys Glu Thr Ala Ala Ala Lys Phe Glu Arg Gln
    130                 135                 140

His Met Asp Ser Pro Asp Leu Gly Thr Asp Asp Asp Asp Lys Ala Met
145                 150                 155                 160

Ala Asp Leu Lys Lys Ala Val Asn Glu Pro Glu Lys Pro Ala Glu Glu
                165                 170                 175

Pro Glu Asn Pro Ala Pro Ala Pro Lys Pro Ala Pro Ala Pro Gln Pro
            180                 185                 190

Glu Lys Pro Ala Pro Ala Pro Ala Pro Lys Pro Glu Lys Ser Ala Asp
        195                 200                 205

Gln Gln Ala Glu Glu Asp Tyr Ala Arg Arg Ser Glu Glu Glu Tyr Asn
    210                 215                 220

Arg Leu Thr Gln Gln Gln Pro Pro Lys Ala Glu Lys Pro Ala Pro Ala
225                 230                 235                 240

Pro Val Pro Lys Pro Glu Gln Pro Ala Pro Ala Pro Lys Thr Gly Trp
                245                 250                 255

Gly Gln Glu Asn Gly Met Trp Cys Arg Gln Ala Cys Gly Arg Thr Arg
            260                 265                 270

Ala Pro Pro Pro Pro Pro Leu Arg Ser Gly Cys
        275                 280


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<212> TYPE: PRT
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<220> FEATURE:
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Ala Asp Leu Lys Lys Ala Val Asn Glu Pro Glu Lys Pro Ala Glu Glu
1               5                   10                  15

Pro Glu Asn Pro Ala Pro Ala Pro Lys Pro Ala Pro Ala Pro Gln Pro
            20                  25                  30

Glu Lys Pro Ala Pro Ala Pro Ala Pro Lys Pro Glu Lys Ser Ala Asp
        35                  40                  45
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Gln Gln Ala Glu Glu Asp Tyr Ala Arg Arg Ser Glu Glu Glu Tyr Asn
    50                  55                  60

Arg Leu Thr Gln Gln Gln Pro Pro Lys Ala Glu Lys Pro Ala Pro Ala
65                  70                  75                  80

Pro Val Pro Lys Pro Glu Gln Pro Ala Pro Ala Pro Lys Thr Gly Trp
                85                  90                  95

Gly Gln Glu Asn Gly Met Trp
            100


<210> SEQ ID NO 4
<211> LENGTH: 58
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 4

Met Ala Lys Lys Ala Glu Leu Glu Lys Thr Pro Glu Lys Pro Ala Glu
1               5                   10                  15

Glu Pro Glu Asn Pro Ala Pro Ala Pro Gln Pro Glu Lys Ser Ala Asp
            20                  25                  30

Gln Gln Ala Glu Glu Asp Tyr Ala Arg Arg Ser Glu Glu Glu Tyr Asn
        35                  40                  45

Arg Leu Thr Gln Gln Gln Pro Pro Lys Ala
    50                  55


<210> SEQ ID NO 5
<211> LENGTH: 286
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 5

Met Ser Asp Lys Ile Ile His Leu Thr Asp Asp Ser Phe Asp Thr Asp
1               5                   10                  15

Val Leu Lys Ala Asp Gly Ala Ile Leu Val Asp Phe Trp Ala Glu Trp
            20                  25                  30

Cys Gly Pro Cys Lys Met Ile Ala Pro Ile Leu Asp Glu Ile Ala Asp
        35                  40                  45

Glu Tyr Gln Gly Lys Leu Thr Val Ala Lys Leu Asn Ile Asp Gln Asn
    50                  55                  60

Pro Gly Thr Ala Pro Lys Tyr Gly Ile Arg Gly Ile Pro Thr Leu Leu
65                  70                  75                  80

Leu Phe Lys Asn Gly Glu Val Ala Ala Thr Lys Val Gly Ala Leu Ser
                85                  90                  95

Lys Gly Gln Leu Lys Glu Phe Leu Asp Ala Asn Leu Ala Gly Ser Gly
            100                 105                 110

Ser Gly His Met His His His His His His Ser Ser Gly Leu Val Pro
        115                 120                 125

Arg Gly Ser Gly Met Lys Glu Thr Ala Ala Ala Lys Phe Glu Arg Gln
    130                 135                 140

His Met Asp Ser Pro Asp Leu Gly Thr Asp Asp Asp Asp Lys Ala Met
145                 150                 155                 160

Ala Asp Leu Lys Lys Ala Val Asn Glu Pro Glu Thr Pro Ala Pro Ala
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                165                 170                 175

Pro Ala Pro Ala Pro Ala Pro Ala Pro Thr Pro Glu Ala Pro Ala Pro
            180                 185                 190

Ala Pro Ala Pro Ala Pro Lys Pro Ala Pro Ala Pro Lys Pro Ala Pro
        195                 200                 205

Ala Pro Lys Pro Ala Pro Ala Pro Lys Pro Ala Pro Ala Pro Lys Pro
    210                 215                 220

Ala Pro Ala Pro Lys Pro Ala Pro Ala Pro Ala Pro Ala Pro Lys Pro
225                 230                 235                 240

Glu Lys Pro Ala Glu Lys Pro Ala Pro Ala Pro Lys Pro Glu Thr Pro
                245                 250                 255

Lys Thr Gly Trp Lys Gln Glu Asn Gly Met Trp Cys Arg Gln Ala Cys
            260                 265                 270

Gly Arg Thr Arg Ala Pro Pro Pro Pro Pro Leu Arg Ser Gly
        275                 280                 285


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<211> LENGTH: 106
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 6

Asp Leu Lys Lys Ala Val Asn Glu Pro Glu Thr Pro Ala Pro Ala Pro
1               5                   10                  15

Ala Pro Ala Pro Ala Pro Ala Pro Thr Pro Glu Ala Pro Ala Pro Ala
            20                  25                  30

Pro Ala Pro Ala Pro Lys Pro Ala Pro Ala Pro Lys Pro Ala Pro Ala
        35                  40                  45

Pro Lys Pro Ala Pro Ala Pro Lys Pro Ala Pro Ala Pro Lys Pro Ala
    50                  55                  60

Pro Ala Pro Lys Pro Ala Pro Ala Pro Ala Pro Ala Pro Lys Pro Glu
65                  70                  75                  80

Lys Pro Ala Glu Lys Pro Ala Pro Ala Pro Lys Pro Glu Thr Pro Lys
                85                  90                  95

Thr Gly Trp Lys Gln Glu Asn Gly Met Trp
            100                 105


<210> SEQ ID NO 7
<211> LENGTH: 121
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 7

Tyr Phe Lys Glu Gly Leu Glu Lys Thr Ile Ala Ala Lys Lys Ala Glu
1               5                   10                  15

Leu Glu Lys Thr Glu Ala Asp Leu Lys Lys Ala Val Asn Glu Pro Glu
            20                  25                  30

Lys Pro Ala Pro Ala Pro Glu Thr Pro Ala Pro Glu Ala Pro Ala Glu
        35                  40                  45

Gln Pro Lys Pro Ala Pro Ala Pro Gln Pro Ala Pro Ala Pro Lys Pro
    50                  55                  60
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Glu Lys Pro Ala Glu Gln Pro Lys Pro Glu Lys Thr Asp Asp Gln Gln
65                  70                  75                  80

Ala Glu Glu Asp Tyr Ala Arg Arg Ser Glu Glu Glu Tyr Asn Arg Leu
                85                  90                  95

Thr Gln Gln Gln Pro Pro Lys Ala Glu Lys Pro Ala Pro Ala Pro Lys
            100                 105                 110

Thr Gly Trp Lys Gln Glu Asn Gly Met
        115                 120


<210> SEQ ID NO 8
<211> LENGTH: 27
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 8

Glu Lys Ser Ala Asp Gln Gln Ala Glu Glu Asp Tyr Ala Arg Arg Ser
1               5                   10                  15

Glu Glu Glu Tyr Asn Arg Leu Thr Gln Gln Gln
            20                  25


<210> SEQ ID NO 9
<211> LENGTH: 23
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 9

Asp Gln Gln Ala Glu Glu Asp Tyr Ala Arg Arg Ser Glu Glu Glu Tyr
1               5                   10                  15

Asn Arg Leu Thr Gln Gln Gln
            20


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<211> LENGTH: 28
<212> TYPE: PRT
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<400> SEQUENCE: 10

Met Glu Lys Ser Ala Asp Gln Gln Ala Glu Glu Asp Tyr Ala Arg Arg
1               5                   10                  15

Ser Glu Glu Glu Tyr Asn Arg Leu Thr Gln Gln Gln
            20                  25


<210> SEQ ID NO 11
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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<400> SEQUENCE: 11

Asp Leu Lys Lys Ala Val Asn Glu
1               5


<210> SEQ ID NO 12
<211> LENGTH: 13
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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
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<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 12

Lys Gly Thr Gly Trp Lys Gly Gln Glu Asn Gly Met Trp
1               5                   10


<210> SEQ ID NO 13
<211> LENGTH: 165
<212> TYPE: PRT
<213> ORGANISM: Streptococcus pneumoniae

<400> SEQUENCE: 13

Met Ser Tyr Phe Glu Gln Phe Met Gln Ala Asn Gln Ala Tyr Val Ala
1               5                   10                  15

Leu His Gly Gln Leu Asn Leu Pro Leu Lys Pro Lys Thr Arg Val Ala
            20                  25                  30

Ile Val Thr Cys Met Asp Ser Arg Leu His Val Ala Gln Ala Leu Gly
        35                  40                  45

Leu Ala Leu Gly Asp Ala His Ile Leu Arg Asn Ala Gly Gly Arg Val
    50                  55                  60

Thr Glu Asp Met Ile Arg Ser Leu Val Ile Ser Gln Gln Gln Met Gly
65                  70                  75                  80

Thr Arg Glu Ile Val Val Leu His His Thr Asp Cys Gly Ala Gln Thr
                85                  90                  95

Phe Glu Asn Glu Pro Phe Gln Glu Tyr Leu Lys Glu Glu Leu Gly Val
            100                 105                 110

Asp Val Ser Asp Gln Asp Phe Leu Pro Phe Gln Asp Ile Glu Glu Ser
        115                 120                 125

Val Arg Glu Asp Met Gln Leu Leu Ile Glu Ser Pro Leu Ile Pro Asp
    130                 135                 140

Asp Val Ile Ile Ser Gly Ala Ile Tyr Asn Val Asp Thr Gly Ser Met
145                 150                 155                 160

Thr Val Val Glu Leu
                165


<210> SEQ ID NO 14
<211> LENGTH: 274
<212> TYPE: PRT
<213> ORGANISM: Streptococcus pneumoniae

<400> SEQUENCE: 14

Met Asn Gln Ser Tyr Phe Tyr Leu Lys Met Lys Glu His Lys Leu Lys
1               5                   10                  15

Val Pro Tyr Thr Gly Lys Glu Arg Arg Val Arg Ile Leu Leu Pro Lys
            20                  25                  30

Asp Tyr Glu Lys Asp Thr Asp Arg Ser Tyr Pro Val Val Tyr Phe His
        35                  40                  45

Asp Gly Gln Asn Val Phe Asn Ser Lys Glu Ser Phe Ile Gly His Ser
    50                  55                  60

Trp Lys Ile Ile Pro Ala Ile Lys Arg Asn Pro Asp Ile Ser Arg Met
65                  70                  75                  80

Ile Val Val Ala Ile Asp Asn Asp Gly Met Gly Arg Met Asn Glu Tyr
                85                  90                  95
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Ala Ala Trp Lys Phe Gln Glu Ser Pro Ile Pro Gly Gln Gln Phe Gly
            100                 105                 110

Gly Lys Gly Val Glu Tyr Ala Glu Phe Val Met Glu Val Val Lys Pro
        115                 120                 125

Phe Ile Asp Glu Thr Tyr Arg Thr Lys Ala Asp Cys Gln His Thr Ala
    130                 135                 140

Met Ile Gly Ser Ser Leu Gly Gly Asn Ile Thr Gln Phe Ile Gly Leu
145                 150                 155                 160

Glu Tyr Gln Asp Gln Ile Gly Cys Leu Gly Val Phe Ser Ser Ala Asn
                165                 170                 175

Trp Leu His Gln Glu Ala Phe Asn Arg Tyr Phe Glu Cys Gln Lys Leu
            180                 185                 190

Ser Pro Asp Gln Arg Ile Phe Ile Tyr Val Gly Thr Glu Glu Ala Asp
        195                 200                 205

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

Asp Ser Ser Leu Cys Tyr Tyr His Asp Leu Ile Ala Gly Gly Val His
225                 230                 235                 240

Leu Asp Asn Leu Val Leu Lys Val Gln Ser Gly Ala Ile His Ser Glu
                245                 250                 255

Ile Pro Trp Ser Glu Asn Leu Pro Asp Cys Leu Arg Phe Phe Ala Glu
            260                 265                 270

Lys Trp


<210> SEQ ID NO 15
<211> LENGTH: 130
<212> TYPE: PRT
<213> ORGANISM: Streptococcus pneumoniae

<400> SEQUENCE: 15

Met Asn Gln Ser Tyr Phe Tyr Leu Lys Met Lys Glu His Lys Leu Lys
1               5                   10                  15

Val Pro Tyr Thr Gly Lys Glu Arg Arg Val Arg Ile Leu Leu Pro Lys
            20                  25                  30

Asp Tyr Glu Lys Asp Thr Asp Arg Ser Tyr Pro Val Val Tyr Phe His
        35                  40                  45

Asp Gly Gln Asn Val Phe Asn Ser Lys Glu Ser Phe Ile Gly His Ser
    50                  55                  60

Trp Lys Ile Ile Pro Ala Ile Lys Arg Asn Pro Asp Ile Ser Arg Met
65                  70                  75                  80

Ile Val Val Ala Ile Asp Asn Asp Gly Met Gly Arg Met Asn Glu Tyr
                85                  90                  95

Ala Ala Trp Lys Phe Gln Glu Ser Pro Ile Pro Gly Gln Gln Phe Gly
            100                 105                 110

Gly Lys Gly Val Glu Tyr Ala Glu Phe Val Met Glu Val Val Lys Pro
        115                 120                 125

Phe Ile
    130


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<211> LENGTH: 299
<212> TYPE: PRT
<213> ORGANISM: Streptococcus pneumoniae
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Met Ser Ser Lys Phe Met Lys Ser Ala Ala Val Leu Gly Thr Ala Thr
1               5                   10                  15

Leu Ala Ser Leu Leu Leu Val Ala Cys Met Asn Gln Ser Tyr Phe Tyr
            20                  25                  30

Leu Lys Met Lys Glu His Lys Leu Lys Val Pro Tyr Thr Gly Lys Glu
        35                  40                  45

Arg Arg Val Arg Ile Leu Leu Pro Lys Asp Tyr Glu Lys Asp Thr Asp
    50                  55                  60

Arg Ser Tyr Pro Val Val Tyr Phe His Asp Gly Gln Asn Val Phe Asn
65                  70                  75                  80

Ser Lys Glu Ser Phe Ile Gly His Ser Trp Lys Ile Ile Pro Ala Ile
                85                  90                  95

Lys Arg Asn Pro Asp Ile Ser Arg Met Ile Val Val Ala Ile Asp Asn
            100                 105                 110

Asp Gly Met Gly Arg Met Asn Glu Tyr Ala Ala Trp Lys Phe Gln Glu
        115                 120                 125

Ser Pro Ile Pro Gly Gln Gln Phe Gly Gly Lys Gly Val Glu Tyr Ala
    130                 135                 140

Glu Phe Val Met Glu Val Val Lys Pro Phe Ile Asp Glu Thr Tyr Arg
145                 150                 155                 160

Thr Lys Ala Asp Cys Gln His Thr Ala Met Ile Gly Ser Ser Leu Gly
                165                 170                 175

Gly Asn Ile Thr Gln Phe Ile Gly Leu Glu Tyr Gln Asp Gln Ile Gly
            180                 185                 190

Cys Leu Gly Val Phe Ser Ser Ala Asn Trp Leu His Gln Glu Ala Phe
        195                 200                 205

Asn Arg Tyr Phe Glu Cys Gln Lys Leu Ser Pro Asp Gln Arg Ile Phe
    210                 215                 220

Ile Tyr Val Gly Thr Glu Glu Ala Asp Asp Thr Asp Lys Thr Leu Met
225                 230                 235                 240

Asp Gly Asn Ile Lys Gln Ala Tyr Ile Asp Ser Ser Leu Cys Tyr Tyr
                245                 250                 255

His Asp Leu Ile Ala Gly Gly Val His Leu Asp Asn Leu Val Leu Lys
            260                 265                 270

Val Gln Ser Gly Ala Ile His Ser Glu Ile Pro Trp Ser Glu Asn Leu
        275                 280                 285

Pro Asp Cys Leu Arg Phe Phe Ala Glu Lys Trp
    290                 295


<210> SEQ ID NO 17
<211> LENGTH: 155
<212> TYPE: PRT
<213> ORGANISM: Streptococcus pneumoniae

<400> SEQUENCE: 17

Met Ser Ser Lys Phe Met Lys Ser Ala Ala Val Leu Gly Thr Ala Thr
1               5                   10                  15

Leu Ala Ser Leu Leu Leu Val Ala Cys Met Asn Gln Ser Tyr Phe Tyr
            20                  25                  30

Leu Lys Met Lys Glu His Lys Leu Lys Val Pro Tyr Thr Gly Lys Glu
        35                  40                  45
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Arg Arg Val Arg Ile Leu Leu Pro Lys Asp Tyr Glu Lys Asp Thr Asp
    50                  55                  60

Arg Ser Tyr Pro Val Val Tyr Phe His Asp Gly Gln Asn Val Phe Asn
65                  70                  75                  80

Ser Lys Glu Ser Phe Ile Gly His Ser Trp Lys Ile Ile Pro Ala Ile
                85                  90                  95

Lys Arg Asn Pro Asp Ile Ser Arg Met Ile Val Val Ala Ile Asp Asn
            100                 105                 110

Asp Gly Met Gly Arg Met Asn Glu Tyr Ala Ala Trp Lys Phe Gln Glu
        115                 120                 125

Ser Pro Ile Pro Gly Gln Gln Phe Gly Gly Lys Gly Val Glu Tyr Ala
    130                 135                 140

Glu Phe Val Met Glu Val Val Lys Pro Phe Ile
145                 150                 155


<210> SEQ ID NO 18
<211> LENGTH: 254
<212> TYPE: PRT
<213> ORGANISM: Streptococcus pneumoniae

<400> SEQUENCE: 18

Met Cys Ser Gly Gly Ala Lys Lys Glu Gly Glu Ala Ala Ser Lys Lys
1               5                   10                  15

Glu Ile Ile Val Ala Thr Asn Gly Ser Pro Lys Pro Phe Ile Tyr Glu
            20                  25                  30

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

Phe Lys Asp Ser Asp Lys Tyr Asp Val Lys Phe Glu Lys Thr Glu Trp
    50                  55                  60

Ser Gly Val Phe Ala Gly Leu Asp Ala Asp Arg Tyr Asn Met Ala Val
65                  70                  75                  80

Asn Asn Leu Ser Tyr Thr Lys Glu Arg Ala Glu Lys Tyr Leu Tyr Ala
                85                  90                  95

Ala Pro Ile Ala Gln Asn Pro Asn Val Leu Val Val Lys Lys Asp Asp
            100                 105                 110

Ser Ser Ile Lys Ser Leu Asp Asp Ile Gly Gly Lys Ser Thr Glu Val
        115                 120                 125

Val Gln Ala Thr Thr Ser Ala Lys Gln Leu Glu Ala Tyr Asn Ala Glu
    130                 135                 140

His Thr Asp Asn Pro Thr Ile Leu Asn Tyr Thr Lys Ala Asp Phe Gln
145                 150                 155                 160

Gln Ile Met Val Arg Leu Ser Asp Gly Gln Phe Asp Tyr Lys Ile Phe
                165                 170                 175

Asp Lys Ile Gly Val Glu Thr Val Ile Lys Asn Gln Gly Leu Asp Asn
            180                 185                 190

Leu Lys Val Ile Glu Leu Pro Ser Asp Gln Gln Pro Tyr Val Tyr Pro
        195                 200                 205

Leu Leu Ala Gln Gly Gln Asp Glu Leu Lys Ser Phe Val Asp Lys Arg
    210                 215                 220

Ile Lys Glu Leu Tyr Lys Asp Gly Thr Leu Glu Lys Leu Ser Lys Gln
225                 230                 235                 240

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


<210> SEQ ID NO 19
<211> LENGTH: 276
<212> TYPE: PRT
<213> ORGANISM: Streptococcus pneumoniae

<400> SEQUENCE: 19

Met Lys Lys Ile Val Lys Tyr Ser Ser Leu Ala Ala Leu Ala Leu Val
1               5                   10                  15

Ala Ala Gly Val Leu Ala Ala Cys Ser Gly Gly Ala Lys Lys Glu Gly
            20                  25                  30

Glu Ala Ala Ser Lys Lys Glu Ile Ile Val Ala Thr Asn Gly Ser Pro
        35                  40                  45

Lys Pro Phe Ile Tyr Glu Glu Asn Gly Glu Leu Thr Gly Tyr Glu Ile
    50                  55                  60

Glu Val Val Arg Ala Ile Phe Lys Asp Ser Asp Lys Tyr Asp Val Lys
65                  70                  75                  80

Phe Glu Lys Thr Glu Trp Ser Gly Val Phe Ala Gly Leu Asp Ala Asp
                85                  90                  95

Arg Tyr Asn Met Ala Val Asn Asn Leu Ser Tyr Thr Lys Glu Arg Ala
            100                 105                 110

Glu Lys Tyr Leu Tyr Ala Ala Pro Ile Ala Gln Asn Pro Asn Val Leu
        115                 120                 125

Val Val Lys Lys Asp Asp Ser Ser Ile Lys Ser Leu Asp Asp Ile Gly
    130                 135                 140

Gly Lys Ser Thr Glu Val Val Gln Ala Thr Thr Ser Ala Lys Gln Leu
145                 150                 155                 160

Glu Ala Tyr Asn Ala Glu His Thr Asp Asn Pro Thr Ile Leu Asn Tyr
                165                 170                 175

Thr Lys Ala Asp Phe Gln Gln Ile Met Val Arg Leu Ser Asp Gly Gln
            180                 185                 190

Phe Asp Tyr Lys Ile Phe Asp Lys Ile Gly Val Glu Thr Val Ile Lys
        195                 200                 205

Asn Gln Gly Leu Asp Asn Leu Lys Val Ile Glu Leu Pro Ser Asp Gln
    210                 215                 220

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

Ser Phe Val Asp Lys Arg Ile Lys Glu Leu Tyr Lys Asp Gly Thr Leu
                245                 250                 255

Glu Lys Leu Ser Lys Gln Phe Phe Gly Asp Thr Tyr Leu Pro Ala Glu
            260                 265                 270

Ala Asp Ile Lys
        275


<210> SEQ ID NO 20
<211> LENGTH: 586
<212> TYPE: PRT
<213> ORGANISM: Streptococcus pneumoniae

<400> SEQUENCE: 20

Met Val Asp Lys Gln Val Ile Glu Glu Ile Lys Asn Asn Ala Asn Ile
1               5                   10                  15

Val Glu Val Ile Gly Asp Val Ile Ser Leu Gln Lys Ala Gly Arg Asn
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            20                  25                  30

Tyr Leu Gly Leu Cys Pro Phe His Gly Glu Lys Thr Pro Ser Phe Asn
        35                  40                  45

Val Val Glu Asp Lys Gln Phe Tyr His Cys Phe Gly Cys Gly Arg Ser
    50                  55                  60

Gly Asp Val Phe Lys Phe Ile Glu Glu Tyr Gln Gly Val Pro Phe Ile
65                  70                  75                  80

Glu Ala Val Gln Ile Leu Gly Gln Arg Val Gly Ile Glu Val Glu Lys
                85                  90                  95

Pro Leu Tyr Ser Glu Gln Lys Ser Ala Ser Pro His Gln Ala Leu Tyr
            100                 105                 110

Asp Met His Glu Asp Ala Ala Lys Phe Tyr His Ala Ile Leu Met Thr
        115                 120                 125

Thr Thr Met Gly Glu Glu Ala Arg Asn Tyr Leu Tyr Gln Arg Gly Leu
    130                 135                 140

Thr Asp Glu Val Leu Lys His Phe Trp Ile Gly Leu Ala Pro Pro Glu
145                 150                 155                 160

Arg Asn Tyr Leu Tyr Gln Arg Leu Ser Asp Gln Tyr Arg Glu Glu Asp
                165                 170                 175

Leu Leu Asp Ser Gly Leu Phe Tyr Leu Ser Asp Ala Asn Gln Phe Val
            180                 185                 190

Asp Thr Phe His Asn Arg Ile Met Phe Pro Leu Thr Asn Asp Gln Gly
        195                 200                 205

Lys Val Ile Ala Phe Ser Gly Arg Ile Trp Gln Lys Thr Asp Ser Gln
    210                 215                 220

Thr Ser Lys Tyr Lys Asn Ser Arg Ser Thr Ala Ile Phe Asn Lys Ser
225                 230                 235                 240

Tyr Glu Leu Tyr His Met Asp Arg Ala Lys Arg Ser Ser Gly Lys Ala
                245                 250                 255

Ser Glu Ile Tyr Leu Met Glu Gly Phe Met Asp Val Ile Ala Ala Tyr
            260                 265                 270

Arg Ala Gly Ile Glu Asn Ala Val Ala Ser Met Gly Thr Ala Leu Ser
        275                 280                 285

Arg Glu His Val Glu His Leu Lys Arg Leu Thr Lys Lys Leu Val Leu
    290                 295                 300

Val Tyr Asp Gly Asp Lys Ala Gly Gln Ala Ala Thr Leu Lys Ala Leu
305                 310                 315                 320

Asp Glu Ile Gly Asp Met Pro Val Gln Ile Val Ser Met Pro Asp Asn
                325                 330                 335

Leu Asp Pro Asp Glu Tyr Leu Gln Lys Asn Gly Pro Glu Asp Leu Ala
            340                 345                 350

Tyr Leu Leu Thr Lys Thr Arg Ile Ser Pro Ile Glu Phe Tyr Ile His
        355                 360                 365

Gln Tyr Lys Pro Glu Asn Ser Glu Asn Leu Gln Ala Gln Ile Glu Phe
    370                 375                 380

Leu Glu Lys Ile Ala Pro Leu Ile Val Gln Glu Lys Ser Ile Ala Ala
385                 390                 395                 400

Gln Asn Ser Tyr Ile His Ile Leu Ala Asp Ser Leu Ala Ser Phe Asp
                405                 410                 415

Tyr Thr Gln Ile Glu Gln Ile Val Asn Glu Ser Arg Gln Val Gln Arg
            420                 425                 430
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Gln Asn Arg Met Glu Gly Ile Ser Arg Pro Thr Pro Ile Thr Met Pro
        435                 440                 445

Val Thr Lys Gln Leu Ser Ala Ile Met Arg Ala Glu Ala His Leu Leu
    450                 455                 460

Tyr Arg Met Met Glu Ser Pro Leu Val Leu Asn Asp Tyr Arg Leu Arg
465                 470                 475                 480

Glu Asp Phe Ala Phe Ala Thr Pro Glu Phe Gln Val Leu Tyr Asp Leu
                485                 490                 495

Leu Gly Gln Tyr Gly Asn Leu Pro Pro Glu Val Leu Ala Glu Gln Thr
            500                 505                 510

Glu Glu Val Glu Arg Ala Trp Tyr Gln Val Leu Ala Gln Asp Leu Pro
        515                 520                 525

Ala Glu Ile Ser Pro Gln Glu Leu Ser Glu Val Glu Met Thr Arg Asn
    530                 535                 540

Lys Ala Leu Leu Asn Gln Asp Asn Met Arg Ile Lys Lys Lys Val Gln
545                 550                 555                 560

Glu Ala Ser His Val Gly Asp Thr Asp Thr Ala Leu Glu Glu Leu Glu
                565                 570                 575

Arg Leu Ile Ser Gln Lys Arg Arg Met Glu
            580                 585


<210> SEQ ID NO 21
<211> LENGTH: 423
<212> TYPE: PRT
<213> ORGANISM: Streptococcus pneumoniae

<400> SEQUENCE: 21

Met Ser Ser Lys Phe Met Lys Ser Ala Ala Val Leu Gly Thr Ala Thr
1               5                   10                  15

Leu Ala Ser Leu Leu Leu Val Ala Cys Gly Ser Lys Thr Ala Asp Lys
            20                  25                  30

Pro Ala Asp Ser Gly Ser Ser Glu Val Lys Glu Leu Thr Val Tyr Val
        35                  40                  45

Asp Glu Gly Tyr Lys Ser Tyr Ile Glu Glu Val Ala Lys Ala Tyr Glu
    50                  55                  60

Lys Glu Ala Gly Val Lys Val Thr Leu Lys Thr Gly Asp Ala Leu Gly
65                  70                  75                  80

Gly Leu Asp Lys Leu Ser Leu Asp Asn Gln Ser Gly Asn Val Pro Asp
                85                  90                  95

Val Met Met Ala Pro Tyr Asp Arg Val Gly Ser Leu Gly Ser Asp Gly
            100                 105                 110

Gln Leu Ser Glu Val Lys Leu Ser Asp Gly Ala Lys Thr Asp Asp Thr
        115                 120                 125

Thr Lys Ser Leu Val Thr Ala Ala Asn Gly Lys Val Tyr Gly Ala Pro
    130                 135                 140

Ala Val Ile Glu Ser Leu Val Met Tyr Tyr Asn Lys Asp Leu Val Lys
145                 150                 155                 160

Asp Ala Pro Lys Thr Phe Ala Asp Leu Glu Asn Leu Ala Lys Asp Ser
                165                 170                 175

Lys Tyr Ala Phe Ala Gly Glu Asp Gly Lys Thr Thr Ala Phe Leu Ala
            180                 185                 190

Asp Trp Thr Asn Phe Tyr Tyr Thr Tyr Gly Leu Leu Ala Gly Asn Gly
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        195                 200                 205

Ala Tyr Val Phe Gly Gln Asn Gly Lys Asp Ala Lys Asp Ile Gly Leu
    210                 215                 220

Ala Asn Asp Gly Ser Ile Val Gly Ile Asn Tyr Ala Lys Ser Trp Tyr
225                 230                 235                 240

Glu Lys Trp Pro Lys Gly Met Gln Asp Thr Glu Gly Ala Gly Asn Leu
                245                 250                 255

Ile Gln Thr Gln Phe Gln Glu Gly Lys Thr Ala Ala Ile Ile Asp Gly
            260                 265                 270

Pro Trp Lys Ala Gln Ala Phe Lys Asp Ala Lys Val Asn Tyr Gly Val
        275                 280                 285

Ala Thr Ile Pro Thr Leu Pro Asn Gly Lys Glu Tyr Ala Ala Phe Gly
    290                 295                 300

Gly Gly Lys Ala Trp Val Ile Pro Gln Ala Val Lys Asn Leu Glu Ala
305                 310                 315                 320

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

Leu Tyr Asp Lys Thr Asn Glu Ile Pro Ala Asn Thr Glu Ala Arg Ser
            340                 345                 350

Tyr Ala Glu Gly Lys Asn Asp Glu Leu Thr Thr Ala Val Ile Lys Gln
        355                 360                 365

Phe Lys Asn Thr Gln Pro Leu Pro Asn Ile Ser Gln Met Ser Ala Val
    370                 375                 380

Trp Asp Pro Ala Lys Asn Met Leu Phe Asp Ala Val Ser Gly Gln Lys
385                 390                 395                 400

Asp Ala Lys Thr Ala Ala Asn Asp Ala Val Thr Leu Ile Lys Glu Thr
                405                 410                 415

Ile Lys Gln Lys Phe Gly Glu
            420


<210> SEQ ID NO 22
<211> LENGTH: 400
<212> TYPE: PRT
<213> ORGANISM: Streptococcus pneumoniae

<400> SEQUENCE: 22

Met Cys Gly Ser Lys Thr Ala Asp Lys Pro Ala Asp Ser Gly Ser Ser
1               5                   10                  15

Glu Val Lys Glu Leu Thr Val Tyr Val Asp Glu Gly Tyr Lys Ser Tyr
            20                  25                  30

Ile Glu Glu Val Ala Lys Ala Tyr Glu Lys Glu Ala Gly Val Lys Val
        35                  40                  45

Thr Leu Lys Thr Gly Asp Ala Leu Gly Gly Leu Asp Lys Leu Ser Leu
    50                  55                  60

Asp Asn Gln Ser Gly Asn Val Pro Asp Val Met Met Ala Pro Tyr Asp
65                  70                  75                  80

Arg Val Gly Ser Leu Gly Ser Asp Gly Gln Leu Ser Glu Val Lys Leu
                85                  90                  95

Ser Asp Gly Ala Lys Thr Asp Asp Thr Thr Lys Ser Leu Val Thr Ala
            100                 105                 110

Ala Asn Gly Lys Val Tyr Gly Ala Pro Ala Val Ile Glu Ser Leu Val
        115                 120                 125
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Met Tyr Tyr Asn Lys Asp Leu Val Lys Asp Ala Pro Lys Thr Phe Ala
    130                 135                 140

Asp Leu Glu Asn Leu Ala Lys Asp Ser Lys Tyr Ala Phe Ala Gly Glu
145                 150                 155                 160

Asp Gly Lys Thr Thr Ala Phe Leu Ala Asp Trp Thr Asn Phe Tyr Tyr
                165                 170                 175

Thr Tyr Gly Leu Leu Ala Gly Asn Gly Ala Tyr Val Phe Gly Gln Asn
            180                 185                 190

Gly Lys Asp Ala Lys Asp Ile Gly Leu Ala Asn Asp Gly Ser Ile Val
        195                 200                 205

Gly Ile Asn Tyr Ala Lys Ser Trp Tyr Glu Lys Trp Pro Lys Gly Met
    210                 215                 220

Gln Asp Thr Glu Gly Ala Gly Asn Leu Ile Gln Thr Gln Phe Gln Glu
225                 230                 235                 240

Gly Lys Thr Ala Ala Ile Ile Asp Gly Pro Trp Lys Ala Gln Ala Phe
                245                 250                 255

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

Asn Gly Lys Glu Tyr Ala Ala Phe Gly Gly Gly Lys Ala Trp Val Ile
        275                 280                 285

Pro Gln Ala Val Lys Asn Leu Glu Ala Ser Gln Lys Phe Val Asp Phe
    290                 295                 300

Leu Val Ala Thr Glu Gln Gln Lys Val Leu Tyr Asp Lys Thr Asn Glu
305                 310                 315                 320

Ile Pro Ala Asn Thr Glu Ala Arg Ser Tyr Ala Glu Gly Lys Asn Asp
                325                 330                 335

Glu Leu Thr Thr Ala Val Ile Lys Gln Phe Lys Asn Thr Gln Pro Leu
            340                 345                 350

Pro Asn Ile Ser Gln Met Ser Ala Val Trp Asp Pro Ala Lys Asn Met
        355                 360                 365

Leu Phe Asp Ala Val Ser Gly Gln Lys Asp Ala Lys Thr Ala Ala Asn
    370                 375                 380

Asp Ala Val Thr Leu Ile Lys Glu Thr Ile Lys Gln Lys Phe Gly Glu
385                 390                 395                 400


<210> SEQ ID NO 23
<211> LENGTH: 648
<212> TYPE: PRT
<213> ORGANISM: Streptococcus pneumoniae

<400> SEQUENCE: 23

Met Ser Gly Thr Ser Met Ala Thr Pro Ile Val Ala Ala Ser Thr Val
1               5                   10                  15

Leu Ile Arg Pro Lys Leu Lys Glu Met Leu Glu Arg Pro Val Leu Lys
            20                  25                  30

Asn Leu Lys Gly Asp Asp Lys Ile Asp Leu Thr Ser Leu Thr Lys Ile
        35                  40                  45

Ala Leu Gln Asn Thr Ala Arg Pro Met Met Asp Ala Thr Ser Trp Lys
    50                  55                  60

Glu Lys Ser Gln Tyr Phe Ala Ser Pro Arg Gln Gln Gly Ala Gly Leu
65                  70                  75                  80

Ile Asn Val Ala Asn Ala Leu Arg Asn Glu Val Val Ala Thr Phe Lys
                85                  90                  95
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Asn Thr Asp Ser Lys Gly Leu Val Asn Ser Tyr Gly Ser Ile Ser Leu
            100                 105                 110

Lys Glu Ile Lys Gly Asp Lys Lys Tyr Phe Thr Ile Lys Leu His Asn
        115                 120                 125

Thr Ser Asn Arg Pro Leu Thr Phe Lys Val Ser Ala Ser Ala Ile Thr
    130                 135                 140

Thr Asp Ser Leu Thr Asp Arg Leu Lys Leu Asp Glu Thr Tyr Lys Asp
145                 150                 155                 160

Glu Lys Ser Pro Asp Gly Lys Gln Ile Val Pro Glu Ile His Pro Glu
                165                 170                 175

Lys Val Lys Gly Ala Asn Ile Thr Phe Glu His Asp Thr Phe Thr Ile
            180                 185                 190

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

Ala Lys Asn Lys Asn Lys Phe Val Glu Ser Phe Ile His Phe Glu Ser
    210                 215                 220

Val Glu Glu Met Glu Ala Leu Asn Ser Asn Gly Lys Lys Ile Asn Phe
225                 230                 235                 240

Gln Pro Ser Leu Ser Met Pro Leu Met Gly Phe Ala Gly Asn Trp Asn
                245                 250                 255

His Glu Pro Ile Leu Asp Lys Trp Ala Trp Glu Glu Gly Ser Arg Ser
            260                 265                 270

Lys Thr Leu Gly Gly Tyr Asp Asp Asp Gly Lys Pro Lys Ile Pro Gly
        275                 280                 285

Thr Leu Asn Lys Gly Ile Gly Gly Glu His Gly Ile Asp Lys Phe Asn
    290                 295                 300

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

Asp Gln Asn Pro Glu Leu Phe Ala Phe Asn Asn Glu Gly Ile Asn Ala
                325                 330                 335

Pro Ser Ser Ser Gly Ser Lys Ile Ala Asn Ile Tyr Pro Leu Asp Ser
            340                 345                 350

Asn Gly Asn Pro Gln Asp Ala Gln Leu Glu Arg Gly Leu Thr Pro Ser
        355                 360                 365

Pro Leu Val Leu Arg Ser Ala Glu Glu Gly Leu Ile Ser Ile Val Asn
    370                 375                 380

Thr Asn Lys Glu Gly Glu Asn Gln Arg Asp Leu Lys Val Ile Ser Arg
385                 390                 395                 400

Glu His Phe Ile Arg Gly Ile Leu Asn Ser Lys Ser Asn Asp Ala Lys
                405                 410                 415

Gly Ile Lys Ser Ser Lys Leu Lys Val Trp Gly Asp Leu Lys Trp Asp
            420                 425                 430

Gly Leu Ile Tyr Asn Pro Arg Gly Arg Glu Glu Asn Ala Pro Glu Ser
        435                 440                 445

Lys Asp Asn Gln Asp Pro Ala Thr Lys Ile Arg Gly Gln Phe Glu Pro
    450                 455                 460

Ile Ala Glu Gly Gln Tyr Phe Tyr Lys Phe Lys Tyr Arg Leu Thr Lys
465                 470                 475                 480

Asp Tyr Pro Trp Gln Val Ser Tyr Ile Pro Val Lys Ile Asp Asn Thr
                485                 490                 495
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```
Ala Pro Lys Ile Val Ser Val Asp Phe Ser Asn Pro Glu Lys Ile Lys
            500                 505                 510

Leu Ile Thr Lys Asp Thr Tyr His Lys Val Lys Asp Gln Tyr Lys Asn
        515                 520                 525

Glu Thr Leu Phe Ala Arg Asp Gln Lys Glu His Pro Glu Lys Phe Asp
    530                 535                 540

Glu Ile Ala Asn Glu Val Trp Tyr Ala Gly Ala Ala Leu Val Asn Glu
545                 550                 555                 560

Asp Gly Glu Val Glu Lys Asn Leu Glu Val Thr Tyr Ala Gly Glu Gly
                565                 570                 575

Gln Gly Arg Asn Arg Lys Leu Asp Lys Asp Gly Asn Thr Ile Tyr Glu
            580                 585                 590

Ile Lys Gly Ala Gly Asp Leu Arg Gly Lys Ile Ile Glu Val Ile Ala
        595                 600                 605

Leu Asp Gly Ser Ser Asn Phe Thr Lys Ile His Arg Ile Lys Phe Ala
    610                 615                 620

Asn Gln Ala Asp Glu Lys Gly Met Ile Ser Tyr Tyr Leu Val Asp Pro
625                 630                 635                 640

Asp Gln Asp Ser Ser Lys Tyr Gln
                645


<210> SEQ ID NO 24
<211> LENGTH: 2140
<212> TYPE: PRT
<213> ORGANISM: Streptococcus pneumoniae

<400> SEQUENCE: 24

Met Lys Lys Ser Thr Val Leu Ser Leu Thr Thr Ala Ala Val Ile Leu
1               5                   10                  15

Ala Ala Tyr Ala Pro Asn Glu Val Val Leu Ala Asp Thr Ser Ser Ser
            20                  25                  30

Glu Asp Ala Leu Asn Ile Ser Asp Lys Glu Lys Val Ala Glu Asn Lys
        35                  40                  45

Glu Lys His Glu Asn Ile His Ser Ala Met Glu Thr Ser Gln Asp Phe
    50                  55                  60

Lys Glu Lys Lys Thr Ala Val Ile Lys Glu Lys Glu Val Val Ser Lys
65                  70                  75                  80

Asn Pro Val Ile Asp Asn Asn Thr Ser Asn Glu Glu Ala Lys Ile Lys
                85                  90                  95

Glu Glu Asn Ser Asn Lys Ser Gln Gly Asp Tyr Thr Asp Ser Phe Val
            100                 105                 110

Asn Lys Asn Thr Glu Asn Pro Lys Lys Glu Asp Lys Val Val Tyr Ile
        115                 120                 125

Ala Glu Phe Lys Asp Lys Glu Ser Gly Glu Lys Ala Ile Lys Glu Leu
    130                 135                 140

Ser Ser Leu Lys Asn Thr Lys Val Leu Tyr Thr Tyr Asp Arg Ile Phe
145                 150                 155                 160

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

Gln Ile Glu Gly Ile Ser Ser Val Glu Arg Ala Gln Lys Val Gln Pro
            180                 185                 190

Met Met Asn His Ala Arg Lys Glu Ile Gly Val Glu Glu Ala Ile Asp
        195                 200                 205
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```
Tyr Leu Lys Ser Ile Asn Ala Pro Phe Gly Lys Asn Phe Asp Gly Arg
    210                 215                 220

Gly Met Val Ile Ser Asn Ile Asp Thr Gly Thr Asp Tyr Arg His Lys
225                 230                 235                 240

Ala Met Arg Ile Asp Asp Asp Ala Lys Ala Ser Met Arg Phe Lys Lys
                245                 250                 255

Glu Asp Leu Lys Gly Thr Asp Lys Asn Tyr Trp Leu Ser Asp Lys Ile
            260                 265                 270

Pro His Ala Phe Asn Tyr Tyr Asn Gly Gly Lys Ile Thr Val Glu Lys
        275                 280                 285

Tyr Asp Asp Gly Arg Asp Tyr Phe Asp Pro His Gly Met His Ile Ala
    290                 295                 300

Gly Ile Leu Ala Gly Asn Asp Thr Glu Gln Asp Ile Lys Asn Phe Asn
305                 310                 315                 320

Gly Ile Asp Gly Ile Ala Pro Asn Ala Gln Ile Phe Ser Tyr Lys Met
                325                 330                 335

Tyr Ser Asp Ala Gly Ser Gly Phe Ala Gly Asp Glu Thr Met Phe His
            340                 345                 350

Ala Ile Glu Asp Ser Ile Lys His Asn Val Asp Val Val Ser Val Ser
        355                 360                 365

Ser Gly Phe Thr Gly Thr Gly Leu Val Gly Glu Lys Tyr Trp Gln Ala
    370                 375                 380

Ile Arg Ala Leu Arg Lys Ala Gly Ile Pro Met Val Val Ala Thr Gly
385                 390                 395                 400

Asn Tyr Ala Thr Ser Ala Ser Ser Ser Ser Trp Asp Leu Val Ala Asn
                405                 410                 415

Asn His Leu Lys Met Thr Asp Thr Gly Asn Val Thr Arg Thr Ala Ala
            420                 425                 430

His Glu Asp Ala Ile Ala Val Ala Ser Ala Lys Asn Gln Thr Val Glu
        435                 440                 445

Phe Asp Lys Val Asn Ile Gly Gly Glu Ser Phe Lys Tyr Arg Asn Ile
    450                 455                 460

Gly Ala Phe Phe Asp Lys Ser Lys Ile Thr Thr Asn Glu Asp Gly Thr
465                 470                 475                 480

Lys Ala Pro Ser Lys Leu Lys Phe Val Tyr Ile Gly Lys Gly Gln Asp
                485                 490                 495

Gln Asp Leu Ile Gly Leu Asp Leu Arg Gly Lys Ile Ala Val Met Asp
            500                 505                 510

Arg Ile Tyr Thr Lys Asp Leu Lys Asn Ala Phe Lys Lys Ala Met Asp
        515                 520                 525

Lys Gly Ala Arg Ala Ile Met Val Val Asn Thr Val Asn Tyr Tyr Asn
    530                 535                 540

Arg Asp Asn Trp Thr Glu Leu Pro Ala Met Gly Tyr Glu Ala Asp Glu
545                 550                 555                 560

Gly Thr Lys Ser Gln Val Phe Ser Ile Ser Gly Asp Asp Gly Val Lys
                565                 570                 575

Leu Trp Asn Met Ile Asn Pro Asp Lys Lys Thr Glu Val Lys Arg Asn
            580                 585                 590

Asn Lys Glu Asp Phe Lys Asp Lys Leu Glu Gln Tyr Tyr Pro Ile Asp
        595                 600                 605
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```
Met Glu Ser Phe Asn Ser Asn Lys Pro Asn Val Gly Asp Glu Lys Glu
    610                 615                 620

Ile Asp Phe Lys Phe Ala Pro Asp Thr Asp Lys Glu Leu Tyr Lys Glu
625                 630                 635                 640

Asp Ile Ile Val Pro Ala Gly Ser Thr Ser Trp Gly Pro Arg Ile Asp
                645                 650                 655

Leu Leu Leu Lys Pro Asp Val Ser Ala Pro Gly Lys Asn Ile Lys Ser
            660                 665                 670

Thr Leu Asn Val Ile Asn Gly Lys Ser Thr Tyr Gly Tyr Met Ser Gly
        675                 680                 685

Thr Ser Met Ala Thr Pro Ile Val Ala Ala Ser Thr Val Leu Ile Arg
    690                 695                 700

Pro Lys Leu Lys Glu Met Leu Glu Arg Pro Val Leu Lys Asn Leu Lys
705                 710                 715                 720

Gly Asp Asp Lys Ile Asp Leu Thr Ser Leu Thr Lys Ile Ala Leu Gln
                725                 730                 735

Asn Thr Ala Arg Pro Met Met Asp Ala Thr Ser Trp Lys Glu Lys Ser
            740                 745                 750

Gln Tyr Phe Ala Ser Pro Arg Gln Gln Gly Ala Gly Leu Ile Asn Val
        755                 760                 765

Ala Asn Ala Leu Arg Asn Glu Val Val Ala Thr Phe Lys Asn Thr Asp
    770                 775                 780

Ser Lys Gly Leu Val Asn Ser Tyr Gly Ser Ile Ser Leu Lys Glu Ile
785                 790                 795                 800

Lys Gly Asp Lys Lys Tyr Phe Thr Ile Lys Leu His Asn Thr Ser Asn
                805                 810                 815

Arg Pro Leu Thr Phe Lys Val Ser Ala Ser Ala Ile Thr Thr Asp Ser
            820                 825                 830

Leu Thr Asp Arg Leu Lys Leu Asp Glu Thr Tyr Lys Asp Glu Lys Ser
        835                 840                 845

Pro Asp Gly Lys Gln Ile Val Pro Glu Ile His Pro Glu Lys Val Lys
    850                 855                 860

Gly Ala Asn Ile Thr Phe Glu His Asp Thr Phe Thr Ile Gly Ala Asn
865                 870                 875                 880

Ser Ser Phe Asp Leu Asn Ala Val Ile Asn Val Gly Glu Ala Lys Asn
                885                 890                 895

Lys Asn Lys Phe Val Glu Ser Phe Ile His Phe Glu Ser Val Glu Glu
            900                 905                 910

Met Glu Ala Leu Asn Ser Asn Gly Lys Lys Ile Asn Phe Gln Pro Ser
        915                 920                 925

Leu Ser Met Pro Leu Met Gly Phe Ala Gly Asn Trp Asn His Glu Pro
    930                 935                 940

Ile Leu Asp Lys Trp Ala Trp Glu Glu Gly Ser Arg Ser Lys Thr Leu
945                 950                 955                 960

Gly Gly Tyr Asp Asp Asp Gly Lys Pro Lys Ile Pro Gly Thr Leu Asn
                965                 970                 975

Lys Gly Ile Gly Gly Glu His Gly Ile Asp Lys Phe Asn Pro Ala Gly
            980                 985                 990

Val Ile Gln Asn Arg Lys Asp Lys  Asn Thr Thr Ser Leu  Asp Gln Asn
        995                 1000                 1005

Pro Glu  Leu Phe Ala Phe Asn  Asn Glu Gly Ile Asn  Ala Pro Ser
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    1010                1015                1020

Ser Ser  Gly Ser Lys Ile Ala  Asn Ile Tyr Pro Leu  Asp Ser Asn
    1025                1030                1035

Gly Asn  Pro Gln Asp Ala Gln  Leu Glu Arg Gly Leu  Thr Pro Ser
    1040                1045                1050

Pro Leu  Val Leu Arg Ser Ala  Glu Glu Gly Leu Ile  Ser Ile Val
    1055                1060                1065

Asn Thr  Asn Lys Glu Gly Glu  Asn Gln Arg Asp Leu  Lys Val Ile
    1070                1075                1080

Ser Arg  Glu His Phe Ile Arg  Gly Ile Leu Asn Ser  Lys Ser Asn
    1085                1090                1095

Asp Ala  Lys Gly Ile Lys Ser  Ser Lys Leu Lys Val  Trp Gly Asp
    1100                1105                1110

Leu Lys  Trp Asp Gly Leu Ile  Tyr Asn Pro Arg Gly  Arg Glu Glu
    1115                1120                1125

Asn Ala  Pro Glu Ser Lys Asp  Asn Gln Asp Pro Ala  Thr Lys Ile
    1130                1135                1140

Arg Gly  Gln Phe Glu Pro Ile  Ala Glu Gly Gln Tyr  Phe Tyr Lys
    1145                1150                1155

Phe Lys  Tyr Arg Leu Thr Lys  Asp Tyr Pro Trp Gln  Val Ser Tyr
    1160                1165                1170

Ile Pro  Val Lys Ile Asp Asn  Thr Ala Pro Lys Ile  Val Ser Val
    1175                1180                1185

Asp Phe  Ser Asn Pro Glu Lys  Ile Lys Leu Ile Thr  Lys Asp Thr
    1190                1195                1200

Tyr His  Lys Val Lys Asp Gln  Tyr Lys Asn Glu Thr  Leu Phe Ala
    1205                1210                1215

Arg Asp  Gln Lys Glu His Pro  Glu Lys Phe Asp Glu  Ile Ala Asn
    1220                1225                1230

Glu Val  Trp Tyr Ala Gly Ala  Ala Leu Val Asn Glu  Asp Gly Glu
    1235                1240                1245

Val Glu  Lys Asn Leu Glu Val  Thr Tyr Ala Gly Glu  Gly Gln Gly
    1250                1255                1260

Arg Asn  Arg Lys Leu Asp Lys  Asp Gly Asn Thr Ile  Tyr Glu Ile
    1265                1270                1275

Lys Gly  Ala Gly Asp Leu Arg  Gly Lys Ile Ile Glu  Val Ile Ala
    1280                1285                1290

Leu Asp  Gly Ser Ser Asn Phe  Thr Lys Ile His Arg  Ile Lys Phe
    1295                1300                1305

Ala Asn  Gln Ala Asp Glu Lys  Gly Met Ile Ser Tyr  Tyr Leu Val
    1310                1315                1320

Asp Pro  Asp Gln Asp Ser Ser  Lys Tyr Gln Lys Leu  Gly Glu Ile
    1325                1330                1335

Ala Glu  Ser Lys Phe Lys Asn  Leu Gly Asn Gly Lys  Glu Gly Ser
    1340                1345                1350

Leu Lys  Lys Asp Thr Thr Gly  Val Glu His His His  Gln Glu Asn
    1355                1360                1365

Glu Glu  Ser Ile Lys Glu Lys  Ser Ser Phe Thr Ile  Asp Arg Asn
    1370                1375                1380

Ile Ser  Thr Ile Arg Asp Phe  Glu Asn Lys Asp Leu  Lys Lys Leu
    1385                1390                1395
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Ile Lys  Lys Lys Phe Arg Glu  Val Asp Asp Phe Thr  Ser Glu Thr
    1400                 1405                 1410

Gly Lys  Arg Met Glu Glu Tyr  Asp Tyr Lys Tyr Asp  Asp Lys Gly
    1415                 1420                 1425

Asn Ile  Ile Ala Tyr Asp Asp  Gly Thr Asp Leu Glu  Tyr Glu Thr
    1430                 1435                 1440

Glu Lys  Leu Asp Glu Ile Lys  Ser Lys Ile Tyr Gly  Val Leu Ser
    1445                 1450                 1455

Pro Ser  Lys Asp Gly His Phe  Glu Ile Leu Gly Lys  Ile Ser Asn
    1460                 1465                 1470

Val Ser  Lys Asn Ala Lys Val  Tyr Tyr Gly Asn Asn  Tyr Lys Ser
    1475                 1480                 1485

Ile Glu  Ile Lys Ala Thr Lys  Tyr Asp Phe His Ser  Lys Thr Met
    1490                 1495                 1500

Thr Phe  Asp Leu Tyr Ala Asn  Ile Asn Asp Ile Val  Asp Gly Leu
    1505                 1510                 1515

Ala Phe  Ala Gly Asp Met Arg  Leu Phe Val Lys Asp  Asn Asp Gln
    1520                 1525                 1530

Lys Lys  Ala Glu Ile Lys Ile  Arg Met Pro Glu Lys  Ile Lys Glu
    1535                 1540                 1545

Thr Lys  Ser Glu Tyr Pro Tyr  Val Ser Ser Tyr Gly  Asn Val Ile
    1550                 1555                 1560

Glu Leu  Gly Glu Gly Asp Leu  Ser Lys Asn Lys Pro  Asp Asn Leu
    1565                 1570                 1575

Thr Lys  Met Glu Ser Gly Lys  Ile Tyr Ser Asp Ser  Glu Lys Gln
    1580                 1585                 1590

Gln Tyr  Leu Leu Lys Asp Asn  Ile Ile Leu Arg Lys  Gly Tyr Ala
    1595                 1600                 1605

Leu Lys  Val Thr Thr Tyr Asn  Pro Gly Lys Thr Asp  Met Leu Glu
    1610                 1615                 1620

Gly Asn  Gly Val Tyr Ser Lys  Glu Asp Ile Ala Lys  Ile Gln Lys
    1625                 1630                 1635

Ala Asn  Pro Asn Leu Arg Ala  Leu Ser Glu Thr Thr  Ile Tyr Ala
    1640                 1645                 1650

Asp Ser  Arg Asn Val Glu Asp  Gly Arg Ser Thr Gln  Ser Val Leu
    1655                 1660                 1665

Met Ser  Ala Leu Asp Gly Phe  Asn Ile Ile Arg Tyr  Gln Val Phe
    1670                 1675                 1680

Thr Phe  Lys Met Asn Asp Lys  Gly Glu Ala Ile Asp  Lys Asp Gly
    1685                 1690                 1695

Asn Leu  Val Thr Asp Ser Ser  Lys Leu Val Leu Phe  Gly Lys Asp
    1700                 1705                 1710

Asp Lys  Glu Tyr Thr Gly Glu  Asp Lys Phe Asn Val  Glu Ala Ile
    1715                 1720                 1725

Lys Glu  Asp Gly Ser Met Leu  Phe Ile Asp Thr Lys  Pro Val Asn
    1730                 1735                 1740

Leu Ser  Met Asp Lys Asn Tyr  Phe Asn Pro Ser Lys  Ser Asn Lys
    1745                 1750                 1755

Ile Tyr  Val Arg Asn Pro Glu  Phe Tyr Leu Arg Gly  Lys Ile Ser
    1760                 1765                 1770
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Asp Lys  Gly Gly Phe Asn Trp  Glu Leu Arg Val Asn  Glu Ser Val
    1775                 1780                 1785

Val Asp  Asn Tyr Leu Ile Tyr  Gly Asp Leu His Ile  Asp Asn Thr
    1790                 1795                 1800

Arg Asp  Phe Asn Ile Lys Leu  Asn Val Lys Asp Gly  Asp Ile Met
    1805                 1810                 1815

Asp Trp  Gly Met Lys Asp Tyr  Lys Ala Asn Gly Phe  Pro Asp Lys
    1820                 1825                 1830

Val Thr  Asp Met Asp Gly Asn  Val Tyr Leu Gln Thr  Gly Tyr Ser
    1835                 1840                 1845

Asp Leu  Asn Ala Lys Ala Val  Gly Val His Tyr Gln  Phe Leu Tyr
    1850                 1855                 1860

Asp Asn  Val Lys Pro Glu Val  Asn Ile Asp Pro Lys  Gly Asn Thr
    1865                 1870                 1875

Ser Ile  Glu Tyr Ala Asp Gly  Lys Ser Val Val Phe  Asn Ile Asn
    1880                 1885                 1890

Asp Lys  Arg Asn Asn Gly Phe  Asp Gly Glu Ile Gln  Glu Gln His
    1895                 1900                 1905

Ile Tyr  Ile Asn Gly Lys Glu  Tyr Thr Ser Phe Asn  Asp Ile Lys
    1910                 1915                 1920

Gln Ile  Ile Asp Lys Thr Leu  Asn Ile Lys Ile Val  Val Lys Asp
    1925                 1930                 1935

Phe Ala  Arg Asn Thr Thr Val  Lys Glu Phe Ile Leu  Asn Lys Asp
    1940                 1945                 1950

Thr Gly  Glu Val Ser Glu Leu  Lys Pro His Arg Val  Thr Val Thr
    1955                 1960                 1965

Ile Gln  Asn Gly Lys Glu Met  Ser Ser Thr Ile Val  Ser Glu Glu
    1970                 1975                 1980

Asp Phe  Ile Leu Pro Val Tyr  Lys Gly Glu Leu Glu  Lys Gly Tyr
    1985                 1990                 1995

Gln Phe  Asp Gly Trp Glu Ile  Ser Gly Phe Glu Gly  Lys Lys Asp
    2000                 2005                 2010

Ala Gly  Tyr Val Ile Asn Leu  Ser Lys Asp Thr Phe  Ile Lys Pro
    2015                 2020                 2025

Val Phe  Lys Lys Ile Glu Glu  Lys Lys Glu Glu Glu  Asn Lys Pro
    2030                 2035                 2040

Thr Phe  Asp Val Ser Lys Lys  Lys Asp Asn Pro Gln  Val Asn His
    2045                 2050                 2055

Ser Gln  Leu Asn Glu Ser His  Arg Lys Glu Asp Leu  Gln Arg Glu
    2060                 2065                 2070

Glu His  Ser Gln Lys Ser Asp  Ser Thr Lys Asp Val  Thr Ala Thr
    2075                 2080                 2085

Val Leu  Asp Lys Asn Asn Ile  Ser Ser Lys Ser Thr  Thr Asn Asn
    2090                 2095                 2100

Pro Asn  Lys Leu Pro Lys Thr  Gly Thr Ala Ser Gly  Ala Gln Thr
    2105                 2110                 2115

Leu Leu  Ala Ala Gly Ile Met  Phe Ile Val Gly Ile  Phe Leu Gly
    2120                 2125                 2130

Leu Lys  Lys Lys Asn Gln Asp
    2135                 2140
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<210> SEQ ID NO 25
<211> LENGTH: 662
<212> TYPE: PRT
<213> ORGANISM: Streptococcus pneumoniae

<400> SEQUENCE: 25

Met Val Val Leu Ala Asp Thr Ser Ser Ser Glu Asp Ala Leu Asn Ile
1               5                   10                  15

Ser Asp Lys Glu Lys Val Ala Glu Asn Lys Glu Lys His Glu Asn Ile
            20                  25                  30

His Ser Ala Met Glu Thr Ser Gln Asp Phe Lys Glu Lys Lys Thr Ala
        35                  40                  45

Val Ile Lys Glu Lys Glu Val Val Ser Lys Asn Pro Val Ile Asp Asn
    50                  55                  60

Asn Thr Ser Asn Glu Glu Ala Lys Ile Lys Glu Glu Asn Ser Asn Lys
65                  70                  75                  80

Ser Gln Gly Asp Tyr Thr Asp Ser Phe Val Asn Lys Asn Thr Glu Asn
                85                  90                  95

Pro Lys Lys Glu Asp Lys Val Val Tyr Ile Ala Glu Phe Lys Asp Lys
            100                 105                 110

Glu Ser Gly Glu Lys Ala Ile Lys Glu Leu Ser Ser Leu Lys Asn Thr
        115                 120                 125

Lys Val Leu Tyr Thr Tyr Asp Arg Ile Phe Asn Gly Ser Ala Ile Glu
    130                 135                 140

Thr Thr Pro Asp Asn Leu Asp Lys Ile Lys Gln Ile Glu Gly Ile Ser
145                 150                 155                 160

Ser Val Glu Arg Ala Gln Lys Val Gln Pro Met Met Asn His Ala Arg
                165                 170                 175

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

Ala Pro Phe Gly Lys Asn Phe Asp Gly Arg Gly Met Val Ile Ser Asn
        195                 200                 205

Ile Asp Thr Gly Thr Asp Tyr Arg His Lys Ala Met Arg Ile Asp Asp
    210                 215                 220

Asp Ala Lys Ala Ser Met Arg Phe Lys Lys Glu Asp Leu Lys Gly Thr
225                 230                 235                 240

Asp Lys Asn Tyr Trp Leu Ser Asp Lys Ile Pro His Ala Phe Asn Tyr
                245                 250                 255

Tyr Asn Gly Gly Lys Ile Thr Val Glu Lys Tyr Asp Asp Gly Arg Asp
            260                 265                 270

Tyr Phe Asp Pro His Gly Met His Ile Ala Gly Ile Leu Ala Gly Asn
        275                 280                 285

Asp Thr Glu Gln Asp Ile Lys Asn Phe Asn Gly Ile Asp Gly Ile Ala
    290                 295                 300

Pro Asn Ala Gln Ile Phe Ser Tyr Lys Met Tyr Ser Asp Ala Gly Ser
305                 310                 315                 320

Gly Phe Ala Gly Asp Glu Thr Met Phe His Ala Ile Glu Asp Ser Ile
                325                 330                 335

Lys His Asn Val Asp Val Val Ser Val Ser Ser Gly Phe Thr Gly Thr
            340                 345                 350

Gly Leu Val Gly Glu Lys Tyr Trp Gln Ala Ile Arg Ala Leu Arg Lys
        355                 360                 365
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Ala Gly Ile Pro Met Val Val Ala Thr Gly Asn Tyr Ala Thr Ser Ala
    370                 375                 380

Ser Ser Ser Ser Trp Asp Leu Val Ala Asn Asn His Leu Lys Met Thr
385                 390                 395                 400

Asp Thr Gly Asn Val Thr Arg Thr Ala Ala His Glu Asp Ala Ile Ala
                405                 410                 415

Val Ala Ser Ala Lys Asn Gln Thr Val Glu Phe Asp Lys Val Asn Ile
            420                 425                 430

Gly Gly Glu Ser Phe Lys Tyr Arg Asn Ile Gly Ala Phe Phe Asp Lys
        435                 440                 445

Ser Lys Ile Thr Thr Asn Glu Asp Gly Thr Lys Ala Pro Ser Lys Leu
    450                 455                 460

Lys Phe Val Tyr Ile Gly Lys Gly Gln Asp Gln Asp Leu Ile Gly Leu
465                 470                 475                 480

Asp Leu Arg Gly Lys Ile Ala Val Met Asp Arg Ile Tyr Thr Lys Asp
                485                 490                 495

Leu Lys Asn Ala Phe Lys Lys Ala Met Asp Lys Gly Ala Arg Ala Ile
            500                 505                 510

Met Val Val Asn Thr Val Asn Tyr Tyr Asn Arg Asp Asn Trp Thr Glu
        515                 520                 525

Leu Pro Ala Met Gly Tyr Glu Ala Asp Glu Gly Thr Lys Ser Gln Val
    530                 535                 540

Phe Ser Ile Ser Gly Asp Asp Gly Val Lys Leu Trp Asn Met Ile Asn
545                 550                 555                 560

Pro Asp Lys Lys Thr Glu Val Lys Arg Asn Asn Lys Glu Asp Phe Lys
                565                 570                 575

Asp Lys Leu Glu Gln Tyr Tyr Pro Ile Asp Met Glu Ser Phe Asn Ser
            580                 585                 590

Asn Lys Pro Asn Val Gly Asp Glu Lys Glu Ile Asp Phe Lys Phe Ala
        595                 600                 605

Pro Asp Thr Asp Lys Glu Leu Tyr Lys Glu Asp Ile Ile Val Pro Ala
    610                 615                 620

Gly Ser Thr Ser Trp Gly Pro Arg Ile Asp Leu Leu Leu Lys Pro Asp
625                 630                 635                 640

Val Ser Ala Pro Gly Lys Asn Ile Lys Ser Thr Leu Asn Val Ile Asn
                645                 650                 655

Gly Lys Ser Thr Tyr Gly
            660
```

<210> SEQ ID NO 26
<211> LENGTH: 274
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (1)..(1)
<223> OTHER INFORMATION: Wherein the Xaa at position 1 is Met or Ile
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (55)..(55)
<223> OTHER INFORMATION: Wherein the Xaa at position 55 is Asn or Tyr
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (63)..(63)
<223> OTHER INFORMATION: Wherein the Xaa at position 63 is His or Tyr

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<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (79)..(79)
<223> OTHER INFORMATION: Wherein the Xaa at position 79 is Arg or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (97)..(97)
<223> OTHER INFORMATION: Wherein the Xaa at position 97 is Ala or Glu
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (108)..(108)
<223> OTHER INFORMATION: Wherein the Xaa at position 108 is Gly or Glu
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (164)..(164)
<223> OTHER INFORMATION: Wherein the Xaa at position 164 is Asp or Glu
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (165)..(165)
<223> OTHER INFORMATION: Wherein the Xaa at position 165 is Gln or Lys
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (187)..(187)
<223> OTHER INFORMATION: Wherein the Xaa at position 187 is Phe or Ile
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (197)..(197)
<223> OTHER INFORMATION: Wherein the Xaa at position 197 is Arg or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (238)..(238)
<223> OTHER INFORMATION: Wherein the Xaa at position 238 is Gly or Arg

<400> SEQUENCE: 26

Xaa Asn Gln Ser Tyr Phe Tyr Leu Lys Met Lys Glu His Lys Leu Lys
1               5                   10                  15

Val Pro Tyr Thr Gly Lys Glu Arg Arg Val Arg Ile Leu Leu Pro Lys
            20                  25                  30

Asp Tyr Glu Lys Asp Thr Asp Arg Ser Tyr Pro Val Val Tyr Phe His
        35                  40                  45

Asp Gly Gln Asn Val Phe Xaa Ser Lys Glu Ser Phe Ile Gly Xaa Ser
    50                  55                  60

Trp Lys Ile Ile Pro Ala Ile Lys Arg Asn Pro Asp Ile Ser Xaa Met
65                  70                  75                  80

Ile Val Val Ala Ile Asp Asn Asp Gly Met Gly Arg Met Asn Glu Tyr
                85                  90                  95

Xaa Ala Trp Lys Phe Gln Glu Ser Pro Ile Pro Xaa Gln Gln Phe Gly
            100                 105                 110

Gly Lys Gly Val Glu Tyr Ala Glu Phe Val Met Glu Val Val Lys Pro
        115                 120                 125

Phe Ile Asp Glu Thr Tyr Arg Thr Lys Ala Asp Cys Gln His Thr Ala
    130                 135                 140

Met Ile Gly Ser Ser Leu Gly Gly Asn Ile Thr Gln Phe Ile Gly Leu
145                 150                 155                 160

Glu Tyr Gln Xaa Xaa Ile Gly Cys Leu Gly Val Phe Ser Ser Ala Asn
                165                 170                 175

Trp Leu His Gln Glu Ala Phe Asn Arg Tyr Xaa Glu Cys Gln Lys Leu
            180                 185                 190

Ser Pro Asp Gln Xaa Ile Phe Ile Tyr Val Gly Thr Glu Glu Ala Asp
        195                 200                 205

Asp Thr Asp Lys Thr Leu Met Asp Gly Asn Ile Lys Gln Ala Tyr Ile
    210                 215                 220
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Asp Ser Ser Leu Cys Tyr Tyr His Asp Leu Ile Ala Gly Xaa Val His
225                 230                 235                 240

Leu Asp Asn Leu Val Leu Lys Val Gln Ser Gly Ala Ile His Ser Glu
                245                 250                 255

Ile Pro Trp Ser Glu Asn Leu Pro Asp Cys Leu Arg Phe Phe Ala Glu
            260                 265                 270

Lys Trp


<210> SEQ ID NO 27
<211> LENGTH: 130
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (1)..(1)
<223> OTHER INFORMATION: Wherein the Xaa at position 1 is Met or Ile
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (55)..(55)
<223> OTHER INFORMATION: Wherein the Xaa at position 55 is Asn or Tyr
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (63)..(63)
<223> OTHER INFORMATION: Wherein the Xaa at position 63 is His or Tyr
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (79)..(79)
<223> OTHER INFORMATION: Wherein the Xaa at position 79 is Arg or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (97)..(97)
<223> OTHER INFORMATION: Wherein the Xaa at position 97 is Ala or Glu
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (108)..(108)
<223> OTHER INFORMATION: Wherein the Xaa at position 108 is Gly or Glu

<400> SEQUENCE: 27

Xaa Asn Gln Ser Tyr Phe Tyr Leu Lys Met Lys Glu His Lys Leu Lys
1               5                   10                  15

Val Pro Tyr Thr Gly Lys Glu Arg Arg Val Arg Ile Leu Leu Pro Lys
            20                  25                  30

Asp Tyr Glu Lys Asp Thr Asp Arg Ser Tyr Pro Val Val Tyr Phe His
        35                  40                  45

Asp Gly Gln Asn Val Phe Xaa Ser Lys Glu Ser Phe Ile Gly Xaa Ser
    50                  55                  60

Trp Lys Ile Ile Pro Ala Ile Lys Arg Asn Pro Asp Ile Ser Xaa Met
65                  70                  75                  80

Ile Val Val Ala Ile Asp Asn Asp Gly Met Gly Arg Met Asn Glu Tyr
                85                  90                  95

Xaa Ala Trp Lys Phe Gln Glu Ser Pro Ile Pro Xaa Gln Gln Phe Gly
            100                 105                 110

Gly Lys Gly Val Glu Tyr Ala Glu Phe Val Met Glu Val Val Lys Pro
        115                 120                 125

Phe Ile
    130


<210> SEQ ID NO 28
<211> LENGTH: 299
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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (6)..(6)
<223> OTHER INFORMATION: Wherein the Xaa at position 6 is Met or Thr
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (9)..(9)
<223> OTHER INFORMATION: Wherein the Xaa at position 9 is Ala or Thr
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (15)..(15)
<223> OTHER INFORMATION: Wherein the Xaa at position 15 is Ala or Val
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (26)..(26)
<223> OTHER INFORMATION: Wherein the Xaa at position 26 is Met or Ile
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (80)..(80)
<223> OTHER INFORMATION: Wherein the Xaa at position 80 is Asn or Tyr
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (88)..(88)
<223> OTHER INFORMATION: Wherein the Xaa at position 88 is His or Tyr
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (104)..(104)
<223> OTHER INFORMATION: Wherein the Xaa at position 104 is Arg or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (122)..(122)
<223> OTHER INFORMATION: Wherein the Xaa at position 122 is Ala or Glu
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (133)..(133)
<223> OTHER INFORMATION: Wherein the Xaa at position 133 is Gly or Glu
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (189)..(189)
<223> OTHER INFORMATION: Wherein the Xaa at position 189 is Asp or Glu
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (190)..(190)
<223> OTHER INFORMATION: Wherein the Xaa at position 190 is Gln or Lys
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (212)..(212)
<223> OTHER INFORMATION: Wherein the Xaa at position 212 is Phe or Ile
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (222)..(222)
<223> OTHER INFORMATION: Wherein the Xaa at position 222 is Arg or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (263)..(263)
<223> OTHER INFORMATION: Wherein the Xaa at position 263 is Arg or His

<400> SEQUENCE: 28

Met Ser Ser Lys Phe Xaa Lys Ser Xaa Ala Val Leu Gly Thr Xaa Thr
1               5                   10                  15

Leu Ala Ser Leu Leu Leu Val Ala Cys Xaa Asn Gln Ser Tyr Phe Tyr
            20                  25                  30

Leu Lys Met Lys Glu His Lys Leu Lys Val Pro Tyr Thr Gly Lys Glu
        35                  40                  45

Arg Arg Val Arg Ile Leu Leu Pro Lys Asp Tyr Glu Lys Asp Thr Asp
    50                  55                  60

Arg Ser Tyr Pro Val Val Tyr Phe His Asp Gly Gln Asn Val Phe Xaa
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65                  70                  75                  80

Ser Lys Glu Ser Phe Ile Gly Xaa Ser Trp Lys Ile Ile Pro Ala Ile
                85                  90                  95

Lys Arg Asn Pro Asp Ile Ser Xaa Met Ile Val Val Ala Ile Asp Asn
            100                 105                 110

Asp Gly Met Gly Arg Met Asn Glu Tyr Xaa Ala Trp Lys Phe Gln Glu
        115                 120                 125

Ser Pro Ile Pro Xaa Gln Gln Phe Gly Gly Lys Gly Val Glu Tyr Ala
    130                 135                 140

Glu Phe Val Met Glu Val Val Lys Pro Phe Ile Asp Glu Thr Tyr Arg
145                 150                 155                 160

Thr Lys Ala Asp Cys Gln His Thr Ala Met Ile Gly Ser Ser Leu Gly
                165                 170                 175

Gly Asn Ile Thr Gln Phe Ile Gly Leu Glu Tyr Gln Xaa Xaa Ile Gly
            180                 185                 190

Cys Leu Gly Val Phe Ser Ser Ala Asn Trp Leu His Gln Glu Ala Phe
        195                 200                 205

Asn Arg Tyr Xaa Glu Cys Gln Lys Leu Ser Pro Asp Gln Xaa Ile Phe
    210                 215                 220

Ile Tyr Val Gly Thr Glu Glu Ala Asp Asp Thr Asp Lys Thr Leu Met
225                 230                 235                 240

Asp Gly Asn Ile Lys Gln Ala Tyr Ile Asp Ser Ser Leu Cys Tyr Tyr
                245                 250                 255

His Asp Leu Ile Ala Gly Xaa Val His Leu Asp Asn Leu Val Leu Lys
            260                 265                 270

Val Gln Ser Gly Ala Ile His Ser Glu Ile Pro Trp Ser Glu Asn Leu
        275                 280                 285

Pro Asp Cys Leu Arg Phe Phe Ala Glu Lys Trp
    290                 295


<210> SEQ ID NO 29
<211> LENGTH: 155
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (6)..(6)
<223> OTHER INFORMATION: Wherein the Xaa at position 6 is Met or Thr
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (9)..(9)
<223> OTHER INFORMATION: Wherein the Xaa at position 9 is Ala or Thr
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (15)..(15)
<223> OTHER INFORMATION: Wherein the Xaa at position 15 is Ala or Val
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (26)..(26)
<223> OTHER INFORMATION: Wherein the Xaa at position 26 is Met or Ile
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (80)..(80)
<223> OTHER INFORMATION: Wherein the Xaa at position 80 is Asn or Tyr
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (88)..(88)
<223> OTHER INFORMATION: Wherein the Xaa at position 88 is His or Tyr
<220> FEATURE:
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<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (104)..(104)
<223> OTHER INFORMATION: Wherein the Xaa at position 104 is Arg or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (122)..(122)
<223> OTHER INFORMATION: Wherein the Xaa at position 122 is Ala or Glu
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (133)..(133)
<223> OTHER INFORMATION: Wherein the Xaa at position 133 is Gly or Glu

<400> SEQUENCE: 29

Met Ser Ser Lys Phe Xaa Lys Ser Xaa Ala Val Leu Gly Thr Xaa Thr
1               5                   10                  15

Leu Ala Ser Leu Leu Leu Val Ala Cys Xaa Asn Gln Ser Tyr Phe Tyr
            20                  25                  30

Leu Lys Met Lys Glu His Lys Leu Lys Val Pro Tyr Thr Gly Lys Glu
        35                  40                  45

Arg Arg Val Arg Ile Leu Leu Pro Lys Asp Tyr Glu Lys Asp Thr Asp
    50                  55                  60

Arg Ser Tyr Pro Val Val Tyr Phe His Asp Gly Gln Asn Val Phe Xaa
65                  70                  75                  80

Ser Lys Glu Ser Phe Ile Gly Xaa Ser Trp Lys Ile Ile Pro Ala Ile
                85                  90                  95

Lys Arg Asn Pro Asp Ile Ser Xaa Met Ile Val Val Ala Ile Asp Asn
            100                 105                 110

Asp Gly Met Gly Arg Met Asn Glu Tyr Xaa Ala Trp Lys Phe Gln Glu
        115                 120                 125

Ser Pro Ile Pro Xaa Gln Gln Phe Gly Gly Lys Gly Val Glu Tyr Ala
    130                 135                 140

Glu Phe Val Met Glu Val Val Lys Pro Phe Ile
145                 150                 155


<210> SEQ ID NO 30
<211> LENGTH: 254
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (11)..(11)
<223> OTHER INFORMATION: Wherein the Xaa at position 11 is Gly or Glu
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (24)..(24)
<223> OTHER INFORMATION: Wherein the Xaa at position 24 is Gly or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (27)..(27)
<223> OTHER INFORMATION: Wherein the Xaa at position 27 is Lys or Arg
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (30)..(30)
<223> OTHER INFORMATION: Wherein the Xaa at position 30 is Ile or Asn
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (56)..(56)
<223> OTHER INFORMATION: Wherein the Xaa at position 56 is Asp or Asn
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (58)..(58)
<223> OTHER INFORMATION: Wherein the Xaa at position 58 is any amino acid
<220> FEATURE:
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<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (83)..(83)
<223> OTHER INFORMATION: Wherein the Xaa at position 83 is Leu or Ile
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (111)..(111)
<223> OTHER INFORMATION: Wherein the Xaa at position 111 is Asp or Glu
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (159)..(159)
<223> OTHER INFORMATION: Wherein the Xaa at position 159 is Leu or Phe
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (192)..(192)
<223> OTHER INFORMATION: Wherein the Xaa at position 192 is Asn or Tyr
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (199)..(199)
<223> OTHER INFORMATION: Wherein the Xaa at position 199 is Pro or Ser

<400> SEQUENCE: 30

Met Cys Ser Gly Gly Ala Lys Lys Glu Gly Xaa Ala Ala Ser Lys Lys
1               5                   10                  15

Glu Ile Ile Val Ala Thr Asn Xaa Ser Pro Xaa Pro Phe Xaa Tyr Glu
            20                  25                  30

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

Phe Lys Asp Ser Asp Lys Tyr Xaa Val Xaa Phe Glu Lys Thr Glu Trp
    50                  55                  60

Ser Gly Val Phe Ala Gly Leu Asp Ala Asp Arg Tyr Asn Met Ala Val
65                  70                  75                  80

Asn Asn Xaa Ser Tyr Thr Lys Glu Arg Ala Glu Lys Tyr Leu Tyr Ala
                85                  90                  95

Ala Pro Ile Ala Gln Asn Pro Asn Val Leu Val Val Lys Lys Xaa Asp
            100                 105                 110

Ser Ser Ile Lys Ser Leu Asp Asp Ile Gly Gly Lys Ser Thr Glu Val
        115                 120                 125

Val Gln Ala Thr Thr Ser Ala Lys Gln Leu Glu Ala Tyr Asn Ala Glu
    130                 135                 140

His Thr Asp Asn Pro Thr Ile Leu Asn Tyr Thr Lys Ala Asp Xaa Gln
145                 150                 155                 160

Gln Ile Met Val Arg Leu Ser Asp Gly Gln Phe Asp Tyr Lys Ile Phe
                165                 170                 175

Asp Lys Ile Gly Val Glu Thr Val Ile Lys Asn Gln Gly Leu Asp Xaa
            180                 185                 190

Leu Lys Val Ile Glu Leu Xaa Ser Asp Gln Gln Pro Tyr Val Tyr Pro
        195                 200                 205

Leu Leu Ala Gln Gly Gln Asp Glu Leu Lys Ser Phe Val Asp Lys Arg
    210                 215                 220

Ile Lys Glu Leu Tyr Lys Asp Gly Thr Leu Glu Lys Leu Ser Lys Gln
225                 230                 235                 240

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


<210> SEQ ID NO 31
<211> LENGTH: 276
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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<223> OTHER INFORMATION: Synthetic
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (14)..(14)
<223> OTHER INFORMATION: Wherein the Xaa at position 14 is Ala or Gly
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (20)..(20)
<223> OTHER INFORMATION: Wherein the Xaa at position 20 is Val or Leu
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (33)..(33)
<223> OTHER INFORMATION: Wherein the Xaa at position 33 is Glu or Gln
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (46)..(46)
<223> OTHER INFORMATION: Wherein the Xaa at position 46 is Gly or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (49)..(49)
<223> OTHER INFORMATION: Wherein the Xaa at position 49 is Lys or Arg
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (52)..(52)
<223> OTHER INFORMATION: Wherein the Xaa at position 52 is Ile or Asn
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (78)..(78)
<223> OTHER INFORMATION: Wherein the Xaa at position 78 is Asp or Asn
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (80)..(80)
<223> OTHER INFORMATION: Wherein the Xaa at position 80 is any amino acid
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (105)..(105)
<223> OTHER INFORMATION: Wherein the Xaa at position 105 is Leu or Ile
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (133)..(133)
<223> OTHER INFORMATION: Wherein the Xaa at position 133 is Asp or Glu
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (181)..(181)
<223> OTHER INFORMATION: Wherein the Xaa at position 181 is Asp or Glu
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (214)..(214)
<223> OTHER INFORMATION: Wherein the Xaa at position 214 is Asn or Tyr
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (221)..(221)
<223> OTHER INFORMATION: Wherein the Xaa at position 221 is Pro or Ser

<400> SEQUENCE: 31

Met Lys Lys Ile Val Lys Tyr Ser Ser Leu Ala Ala Leu Xaa Leu Val
1               5                   10                  15

Ala Ala Gly Xaa Leu Ala Ala Cys Ser Gly Gly Ala Lys Lys Glu Gly
            20                  25                  30

Xaa Ala Ala Ser Lys Lys Glu Ile Ile Val Ala Thr Asn Xaa Ser Pro
        35                  40                  45

Xaa Pro Phe Xaa Tyr Glu Glu Asn Gly Glu Leu Thr Gly Tyr Glu Ile
    50                  55                  60

Glu Val Val Arg Ala Ile Phe Lys Asp Ser Asp Lys Tyr Xaa Val Xaa
65                  70                  75                  80

Phe Glu Lys Thr Glu Trp Ser Gly Val Phe Ala Gly Leu Asp Ala Asp
                85                  90                  95

Arg Tyr Asn Met Ala Val Asn Asn Xaa Ser Tyr Thr Lys Glu Arg Ala
            100                 105                 110
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Glu Lys Tyr Leu Tyr Ala Ala Pro Ile Ala Gln Asn Pro Asn Val Leu
        115                 120                 125

Val Val Lys Lys Xaa Asp Ser Ser Ile Lys Ser Leu Asp Asp Ile Gly
    130                 135                 140

Gly Lys Ser Thr Glu Val Val Gln Ala Thr Thr Ser Ala Lys Gln Leu
145                 150                 155                 160

Glu Ala Tyr Asn Ala Glu His Thr Asp Asn Pro Thr Ile Leu Asn Tyr
                165                 170                 175

Thr Lys Ala Asp Xaa Gln Gln Ile Met Val Arg Leu Ser Asp Gly Gln
            180                 185                 190

Phe Asp Tyr Lys Ile Phe Asp Lys Ile Gly Val Glu Thr Val Ile Lys
        195                 200                 205

Asn Gln Gly Leu Asp Xaa Leu Lys Val Ile Glu Leu Xaa Ser Asp Gln
    210                 215                 220

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

Ser Phe Val Asp Lys Arg Ile Lys Glu Leu Tyr Lys Asp Gly Thr Leu
                245                 250                 255

Glu Lys Leu Ser Lys Gln Phe Phe Gly Asp Thr Tyr Leu Pro Ala Glu
            260                 265                 270

Ala Asp Ile Lys
        275


<210> SEQ ID NO 32
<211> LENGTH: 400
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (18)..(18)
<223> OTHER INFORMATION: Wherein the Xaa at position 18 is Val or Ala
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (48)..(48)
<223> OTHER INFORMATION: Wherein the Xaa at position 48 is Val or Ile
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (74)..(74)
<223> OTHER INFORMATION: Wherein the Xaa at position 74 is Val or Ile
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (83)..(83)
<223> OTHER INFORMATION: Wherein the Xaa at position 83 is any amino acid
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (100)..(100)
<223> OTHER INFORMATION: Wherein the Xaa at position 100 is Ala or Thr
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (177)..(177)
<223> OTHER INFORMATION: Wherein the Xaa at position 177 is Thr or Ala
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (186)..(186)
<223> OTHER INFORMATION: Wherein the Xaa at position 186 is Ala or Gly
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (196)..(196)
<223> OTHER INFORMATION: Wherein the Xaa at position 196 is Ala or Pro
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (208)..(208)
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<223> OTHER INFORMATION: Wherein the Xaa at position 208 is Val or Ala
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (214)..(214)
<223> OTHER INFORMATION: Wherein the Xaa at position 214 is any amino acid
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (237)..(237)
<223> OTHER INFORMATION: Wherein the Xaa at position 237 is Gln or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (298)..(298)
<223> OTHER INFORMATION: Wherein the Xaa at position 298 is Ser or Ala
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (307)..(307)
<223> OTHER INFORMATION: Wherein the Xaa at position 307 is Ala or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (313)..(313)
<223> OTHER INFORMATION: Wherein the Xaa at position 313 is Val or Ala
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (348)..(348)
<223> OTHER INFORMATION: Wherein the Xaa at position 348 is Asn or Ser

<400> SEQUENCE: 32

Met Cys Gly Ser Lys Thr Ala Asp Lys Pro Ala Asp Ser Gly Ser Ser
1               5                   10                  15

Glu Xaa Lys Glu Leu Thr Val Tyr Val Asp Glu Gly Tyr Lys Ser Tyr
            20                  25                  30

Ile Glu Glu Val Ala Lys Ala Tyr Glu Lys Glu Ala Gly Val Lys Xaa
        35                  40                  45

Thr Leu Lys Thr Gly Asp Ala Leu Gly Gly Leu Asp Lys Leu Ser Leu
    50                  55                  60

Asp Asn Gln Ser Gly Asn Val Pro Asp Xaa Met Met Ala Pro Tyr Asp
65                  70                  75                  80

Arg Val Xaa Ser Leu Gly Ser Asp Gly Gln Leu Ser Glu Val Lys Leu
                85                  90                  95

Ser Asp Gly Xaa Lys Thr Asp Asp Thr Thr Lys Ser Leu Val Thr Ala
            100                 105                 110

Ala Asn Gly Lys Val Tyr Gly Ala Pro Ala Val Ile Glu Ser Leu Val
        115                 120                 125

Met Tyr Tyr Asn Lys Asp Leu Val Lys Asp Ala Pro Lys Thr Phe Ala
    130                 135                 140

Asp Leu Glu Asn Leu Ala Lys Asp Ser Lys Tyr Ala Phe Ala Gly Glu
145                 150                 155                 160

Asp Gly Lys Thr Thr Ala Phe Leu Ala Asp Trp Thr Asn Phe Tyr Tyr
                165                 170                 175

Xaa Tyr Gly Leu Leu Ala Gly Asn Gly Xaa Tyr Val Phe Gly Gln Asn
            180                 185                 190

Gly Lys Asp Xaa Lys Asp Ile Gly Leu Ala Asn Asp Gly Ser Ile Xaa
        195                 200                 205

Gly Ile Asn Tyr Ala Xaa Ser Trp Tyr Glu Lys Trp Pro Lys Gly Met
    210                 215                 220

Gln Asp Thr Glu Gly Ala Gly Asn Leu Ile Gln Thr Xaa Phe Gln Glu
225                 230                 235                 240

Gly Lys Thr Ala Ala Ile Ile Asp Gly Pro Trp Lys Ala Gln Ala Phe
                245                 250                 255
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Lys Asp Ala Lys Val Asn Tyr Gly Val Ala Thr Ile Pro Thr Leu Pro
            260                 265                 270

Asn Gly Lys Glu Tyr Ala Ala Phe Gly Gly Gly Lys Ala Trp Val Ile
        275                 280                 285

Pro Gln Ala Val Lys Asn Leu Glu Ala Xaa Gln Lys Phe Val Asp Phe
    290                 295                 300

Leu Val Xaa Thr Glu Gln Gln Lys Xaa Leu Tyr Asp Lys Thr Asn Glu
305                 310                 315                 320

Ile Pro Ala Asn Thr Glu Ala Arg Ser Tyr Ala Glu Gly Lys Asn Asp
                325                 330                 335

Glu Leu Thr Thr Ala Val Ile Lys Gln Phe Lys Xaa Thr Gln Pro Leu
            340                 345                 350

Pro Asn Ile Ser Gln Met Ser Ala Val Trp Asp Pro Ala Lys Asn Met
        355                 360                 365

Leu Phe Asp Ala Val Ser Gly Gln Lys Asp Ala Lys Thr Ala Ala Asn
    370                 375                 380

Asp Ala Val Thr Leu Ile Lys Glu Thr Ile Lys Gln Lys Phe Gly Glu
385                 390                 395                 400


<210> SEQ ID NO 33
<211> LENGTH: 423
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (6)..(6)
<223> OTHER INFORMATION: Wherein the Xaa at position 6 is Met or Thr
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (9)..(9)
<223> OTHER INFORMATION: Wherein the Xaa at position 9 is Ala or Thr
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (15)..(15)
<223> OTHER INFORMATION: Wherein the Xaa at position 15 is Ala or Val
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (41)..(41)
<223> OTHER INFORMATION: Wherein the Xaa at position 41 is Val or Ala
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (71)..(71)
<223> OTHER INFORMATION: Wherein the Xaa at position 71 is Val or Ile
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (97)..(97)
<223> OTHER INFORMATION: Wherein the Xaa at position 97 is Val or Ile
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (106)..(106)
<223> OTHER INFORMATION: Wherein the Xaa at position 106 is any amino acid
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (123)..(123)
<223> OTHER INFORMATION: Wherein the Xaa at position 123 is Ala or Thr
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (200)..(200)
<223> OTHER INFORMATION: Wherein the Xaa at position 200 is Thr or Ala
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (209)..(209)
<223> OTHER INFORMATION: Wherein the Xaa at position 209 is Ala or Gly
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
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<222> LOCATION: (219)..(219)
<223> OTHER INFORMATION: Wherein the Xaa at position 219 is Ala or Pro
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (231)..(231)
<223> OTHER INFORMATION: Wherein the Xaa at position 231 is Val or Ala
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (237)..(237)
<223> OTHER INFORMATION: Wherein the Xaa at position 237 is any amino acid
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (260)..(260)
<223> OTHER INFORMATION: Wherein the Xaa at position 260 is Gln or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (321)..(321)
<223> OTHER INFORMATION: Wherein the Xaa at position 321 is Ser or Ala
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (330)..(330)
<223> OTHER INFORMATION: Wherein the Xaa at position 330 is Ala or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (336)..(336)
<223> OTHER INFORMATION: Wherein the Xaa at position 336 is Val or Ala
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (371)..(371)
<223> OTHER INFORMATION: Wherein the Xaa at position 371 is Asn or Ser

<400> SEQUENCE: 33

Met Ser Ser Lys Phe Xaa Lys Ser Xaa Ala Val Leu Gly Thr Xaa Thr
1               5                   10                  15

Leu Ala Ser Leu Leu Leu Val Ala Cys Gly Ser Lys Thr Ala Asp Lys
            20                  25                  30

Pro Ala Asp Ser Gly Ser Ser Glu Xaa Lys Glu Leu Thr Val Tyr Val
        35                  40                  45

Asp Glu Gly Tyr Lys Ser Tyr Ile Glu Glu Val Ala Lys Ala Tyr Glu
    50                  55                  60

Lys Glu Ala Gly Val Lys Xaa Thr Leu Lys Thr Gly Asp Ala Leu Gly
65                  70                  75                  80

Gly Leu Asp Lys Leu Ser Leu Asp Asn Gln Ser Gly Asn Val Pro Asp
                85                  90                  95

Xaa Met Met Ala Pro Tyr Asp Arg Val Xaa Ser Leu Gly Ser Asp Gly
            100                 105                 110

Gln Leu Ser Glu Val Lys Leu Ser Asp Gly Xaa Lys Thr Asp Asp Thr
        115                 120                 125

Thr Lys Ser Leu Val Thr Ala Ala Asn Gly Lys Val Tyr Gly Ala Pro
    130                 135                 140

Ala Val Ile Glu Ser Leu Val Met Tyr Tyr Asn Lys Asp Leu Val Lys
145                 150                 155                 160

Asp Ala Pro Lys Thr Phe Ala Asp Leu Glu Asn Leu Ala Lys Asp Ser
                165                 170                 175

Lys Tyr Ala Phe Ala Gly Glu Asp Gly Lys Thr Thr Ala Phe Leu Ala
            180                 185                 190

Asp Trp Thr Asn Phe Tyr Tyr Xaa Tyr Gly Leu Leu Ala Gly Asn Gly
        195                 200                 205

Xaa Tyr Val Phe Gly Gln Asn Gly Lys Asp Xaa Lys Asp Ile Gly Leu
    210                 215                 220

Ala Asn Asp Gly Ser Ile Xaa Gly Ile Asn Tyr Ala Xaa Ser Trp Tyr
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225                 230                 235                 240

Glu Lys Trp Pro Lys Gly Met Gln Asp Thr Glu Gly Ala Gly Asn Leu
                245                 250                 255

Ile Gln Thr Xaa Phe Gln Glu Gly Lys Thr Ala Ala Ile Ile Asp Gly
            260                 265                 270

Pro Trp Lys Ala Gln Ala Phe Lys Asp Ala Lys Val Asn Tyr Gly Val
        275                 280                 285

Ala Thr Ile Pro Thr Leu Pro Asn Gly Lys Glu Tyr Ala Ala Phe Gly
    290                 295                 300

Gly Gly Lys Ala Trp Val Ile Pro Gln Ala Val Lys Asn Leu Glu Ala
305                 310                 315                 320

Xaa Gln Lys Phe Val Asp Phe Leu Val Xaa Thr Glu Gln Gln Lys Xaa
                325                 330                 335

Leu Tyr Asp Lys Thr Asn Glu Ile Pro Ala Asn Thr Glu Ala Arg Ser
            340                 345                 350

Tyr Ala Glu Gly Lys Asn Asp Glu Leu Thr Thr Ala Val Ile Lys Gln
        355                 360                 365

Phe Lys Xaa Thr Gln Pro Leu Pro Asn Ile Ser Gln Met Ser Ala Val
    370                 375                 380

Trp Asp Pro Ala Lys Asn Met Leu Phe Asp Ala Val Ser Gly Gln Lys
385                 390                 395                 400

Asp Ala Lys Thr Ala Ala Asn Asp Ala Val Thr Leu Ile Lys Glu Thr
                405                 410                 415

Ile Lys Gln Lys Phe Gly Glu
            420


<210> SEQ ID NO 34
<211> LENGTH: 357
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 34

Met Ala Asn Ile Phe Asp Tyr Leu Lys Asp Val Ala Tyr Asp Ser Tyr
1               5                   10                  15

Tyr Asp Leu Pro Leu Asn Glu Leu Asp Ile Leu Thr Leu Ile Glu Ile
            20                  25                  30

Thr Tyr Leu Ser Phe Asp Asn Leu Val Ser Thr Leu Pro Gln Arg Leu
        35                  40                  45

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

Lys Asn Arg Leu Gln Leu Leu Asp Glu Leu Ala Gln His Lys Arg Phe
65                  70                  75                  80

Lys Asn Cys Lys Leu Ser His Phe Ile Asn Asp Ile Asp Pro Glu Leu
                85                  90                  95

Gln Lys Gln Phe Ala Ala Met Thr Tyr Arg Val Ser Leu Asp Thr Tyr
            100                 105                 110

Leu Ile Val Phe Arg Gly Thr Asp Asp Ser Ile Ile Gly Trp Lys Glu
        115                 120                 125

Asp Phe His Leu Thr Tyr Met Lys Glu Ile Pro Ala Gln Lys His Ala
    130                 135                 140

Leu Arg Tyr Leu Lys Asn Phe Phe Ala His His Pro Lys Gln Lys Val
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145                 150                 155                 160

Ile Leu Ala Gly His Ser Lys Gly Gly Asn Leu Ala Ile Tyr Ala Ala
                165                 170                 175

Ser Gln Ile Glu Gln Ser Leu Gln Asn Gln Ile Thr Ala Val Tyr Thr
            180                 185                 190

Phe Asp Ala Pro Gly Leu His Gln Glu Leu Thr Gln Thr Ala Gly Tyr
        195                 200                 205

Gln Arg Ile Met Asp Arg Ser Lys Ile Phe Ile Pro Gln Gly Ser Ile
    210                 215                 220

Ile Gly Met Met Leu Glu Ile Pro Ala His Gln Ile Ile Val Gln Ser
225                 230                 235                 240

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

Glu Asp Lys His Phe Val Gln Leu Asp Lys Thr Asn Ser Asp Ser Gln
            260                 265                 270

Gln Val Asp Thr Thr Phe Lys Glu Trp Val Ala Thr Val Pro Asp Glu
        275                 280                 285

Glu Leu Gln Leu Tyr Phe Asp Leu Phe Phe Gly Thr Ile Leu Asp Ala
    290                 295                 300

Gly Ile Ser Ser Ile Asn Asp Leu Ala Ser Leu Lys Ala Leu Glu Tyr
305                 310                 315                 320

Ile His His Leu Phe Val Gln Ala Gln Ser Leu Thr Pro Glu Glu Arg
                325                 330                 335

Glu Thr Leu Gly Arg Leu Thr Gln Leu Leu Ile Asp Thr Arg Tyr Gln
            340                 345                 350

Ala Trp Lys Asn Arg
        355


<210> SEQ ID NO 35
<211> LENGTH: 1066
<212> TYPE: PRT
<213> ORGANISM: Streptococcus pneumoniae

<400> SEQUENCE: 35

Met Gln Thr Lys Thr Lys Lys Leu Ile Val Ser Leu Ser Ser Leu Val
1               5                   10                  15

Leu Ser Gly Phe Leu Leu Asn His Tyr Met Thr Ile Gly Ala Glu Glu
            20                  25                  30

Thr Thr Thr Asn Thr Ile Gln Gln Ser Gln Lys Glu Val Gln Tyr Gln
        35                  40                  45

Gln Arg Asp Thr Lys Asn Leu Val Glu Asn Gly Asp Phe Gly Gln Thr
    50                  55                  60

Glu Asp Gly Ser Ser Pro Trp Thr Gly Ser Lys Ala Gln Gly Trp Ser
65                  70                  75                  80

Ala Trp Val Asp Gln Lys Asn Ser Ala Asp Ala Ser Thr Arg Val Ile
                85                  90                  95

Glu Ala Lys Asp Gly Ala Ile Thr Ile Ser Ser His Glu Lys Leu Arg
            100                 105                 110

Ala Ala Leu His Arg Met Val Pro Ile Glu Ala Lys Lys Lys Tyr Lys
        115                 120                 125

Leu Arg Phe Lys Ile Lys Thr Asp Asn Lys Ile Gly Ile Ala Lys Val
    130                 135                 140
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Arg Ile Ile Glu Glu Ser Gly Lys Asp Lys Arg Leu Trp Asn Ser Ala
145                 150                 155                 160

Thr Thr Ser Gly Thr Lys Asp Trp Gln Thr Ile Glu Ala Asp Tyr Ser
                165                 170                 175

Pro Thr Leu Asp Val Asp Lys Ile Lys Leu Glu Leu Phe Tyr Glu Thr
            180                 185                 190

Gly Thr Gly Thr Val Ser Phe Lys Asp Ile Glu Leu Val Glu Val Ala
        195                 200                 205

Asp Gln Leu Ser Glu Asp Ser Gln Thr Asp Lys Gln Leu Glu Glu Lys
    210                 215                 220

Ile Asp Leu Pro Ile Gly Lys Lys His Val Phe Ser Leu Ala Asp Tyr
225                 230                 235                 240

Thr Tyr Lys Val Glu Asn Pro Asp Val Ala Ser Val Lys Asn Gly Ile
                245                 250                 255

Leu Glu Pro Leu Lys Glu Gly Thr Thr Asn Val Ile Val Ser Lys Asp
            260                 265                 270

Gly Lys Glu Val Lys Lys Ile Pro Leu Lys Ile Leu Ala Ser Val Lys
        275                 280                 285

Asp Ala Tyr Thr Asp Arg Leu Asp Asp Trp Asn Gly Ile Ile Ala Gly
    290                 295                 300

Asn Gln Tyr Tyr Asp Ser Lys Asn Glu Gln Met Ala Lys Leu Asn Gln
305                 310                 315                 320

Glu Leu Glu Gly Lys Val Ala Asp Ser Leu Ser Ser Ile Ser Ser Gln
                325                 330                 335

Ala Asp Arg Thr Tyr Leu Trp Glu Lys Phe Ser Asn Tyr Lys Thr Ser
            340                 345                 350

Ala Asn Leu Thr Ala Thr Tyr Arg Lys Leu Glu Glu Met Ala Lys Gln
        355                 360                 365

Val Thr Asn Pro Ser Ser Arg Tyr Tyr Gln Asp Glu Thr Val Val Arg
    370                 375                 380

Thr Val Arg Asp Ser Met Glu Trp Met His Lys His Val Tyr Asn Ser
385                 390                 395                 400

Glu Lys Ser Ile Val Gly Asn Trp Trp Asp Tyr Glu Ile Gly Thr Pro
                405                 410                 415

Arg Ala Ile Asn Asn Thr Leu Ser Leu Met Lys Glu Tyr Phe Ser Asp
            420                 425                 430

Glu Glu Ile Lys Lys Tyr Thr Asp Val Ile Glu Lys Phe Val Pro Asp
        435                 440                 445

Pro Glu His Phe Arg Lys Thr Thr Asp Asn Pro Phe Lys Ala Leu Gly
    450                 455                 460

Gly Asn Leu Val Asp Met Gly Arg Val Lys Val Ile Ala Gly Leu Leu
465                 470                 475                 480

Arg Lys Asp Asp Gln Glu Ile Ser Ser Thr Ile Arg Ser Ile Glu Gln
                485                 490                 495

Val Phe Lys Leu Val Asp Gln Gly Glu Gly Phe Tyr Gln Asp Gly Ser
            500                 505                 510

Tyr Ile Asp His Thr Asn Val Ala Tyr Thr Gly Ala Tyr Gly Asn Val
        515                 520                 525

Leu Ile Asp Gly Leu Ser Gln Leu Leu Pro Val Ile Gln Lys Thr Lys
    530                 535                 540

Asn Pro Ile Asp Lys Asp Lys Met Gln Thr Met Tyr His Trp Ile Asp
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545                 550                 555                 560

Lys Ser Phe Ala Pro Leu Leu Val Asn Gly Glu Leu Met Asp Met Ser
                565                 570                 575

Arg Gly Arg Ser Ile Ser Arg Ala Asn Ser Glu Gly His Val Ala Ala
            580                 585                 590

Val Glu Val Leu Arg Gly Ile His Arg Ile Ala Asp Met Ser Glu Gly
        595                 600                 605

Glu Thr Lys Gln Cys Leu Gln Ser Leu Val Lys Thr Ile Val Gln Ser
    610                 615                 620

Asp Ser Tyr Tyr Asp Val Phe Lys Asn Leu Lys Thr Tyr Lys Asp Ile
625                 630                 635                 640

Ser Leu Met Gln Ser Leu Leu Ser Asp Ala Gly Val Ala Ser Val Pro
                645                 650                 655

Arg Pro Ser Tyr Leu Ser Ala Phe Asn Lys Met Asp Lys Thr Ala Met
            660                 665                 670

Tyr Asn Ala Glu Lys Gly Phe Gly Phe Gly Leu Ser Leu Phe Ser Ser
        675                 680                 685

Arg Thr Leu Asn Tyr Glu His Met Asn Lys Glu Asn Lys Arg Gly Trp
    690                 695                 700

Tyr Thr Ser Asp Gly Met Phe Tyr Leu Tyr Asn Gly Asp Leu Ser His
705                 710                 715                 720

Tyr Ser Asp Gly Tyr Trp Pro Thr Val Asn Pro Tyr Lys Met Pro Gly
                725                 730                 735

Thr Thr Glu Thr Asp Ala Lys Arg Ala Asp Ser Asp Thr Gly Lys Val
            740                 745                 750

Leu Pro Ser Ala Phe Val Gly Thr Ser Lys Leu Asp Asp Ala Asn Ala
        755                 760                 765

Thr Ala Thr Met Asp Phe Thr Asn Trp Asn Gln Thr Leu Thr Ala His
    770                 775                 780

Lys Ser Trp Phe Met Leu Lys Asp Lys Ile Ala Phe Leu Gly Ser Asn
785                 790                 795                 800

Ile Gln Asn Thr Ser Thr Asp Thr Ala Ala Thr Thr Ile Asp Gln Arg
                805                 810                 815

Lys Leu Glu Ser Gly Asn Pro Tyr Lys Val Tyr Val Asn Asp Lys Glu
            820                 825                 830

Ala Ser Leu Thr Glu Gln Glu Lys Asp Tyr Pro Glu Thr Gln Ser Val
        835                 840                 845

Phe Leu Glu Ser Phe Asp Ser Lys Lys Asn Ile Gly Tyr Phe Phe Phe
    850                 855                 860

Lys Lys Ser Ser Ile Ser Met Ser Lys Ala Leu Gln Lys Gly Ala Trp
865                 870                 875                 880

Lys Asp Ile Asn Glu Gly Gln Ser Asp Lys Glu Val Glu Asn Glu Phe
                885                 890                 895

Leu Thr Ile Ser Gln Ala His Lys Gln Asn Arg Asp Ser Tyr Gly Tyr
            900                 905                 910

Met Leu Ile Pro Asn Val Asp Arg Ala Thr Phe Asn Gln Met Ile Lys
        915                 920                 925

Glu Leu Glu Ser Ser Leu Ile Glu Asn Asn Glu Thr Leu Gln Ser Val
    930                 935                 940

Tyr Asp Ala Lys Gln Gly Val Trp Gly Ile Val Lys Tyr Asp Asp Ser
945                 950                 955                 960
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Val Ser Thr Ile Ser Asn Gln Phe Gln Val Leu Lys Arg Gly Val Tyr
                965                 970                 975

Thr Ile Arg Lys Glu Gly Asp Glu Tyr Lys Ile Ala Tyr Tyr Asn Pro
            980                 985                 990

Glu Thr Gln Glu Ser Ala Pro Asp  Gln Glu Val Phe Lys  Lys Leu Glu
        995                 1000                 1005

Gln Ala  Ala Gln Pro Gln Val  Gln Asn Ser Lys Glu  Lys Glu Lys
    1010                 1015                 1020

Ser Glu  Glu Glu Lys Asn His  Ser Asp Gln Lys Asn  Leu Pro Gln
    1025                 1030                 1035

Thr Gly  Glu Gly Gln Ser Ile  Leu Ala Ser Leu Gly  Phe Leu Leu
    1040                 1045                 1050

Leu Gly  Ala Phe Tyr Leu Phe  Arg Arg Gly Lys Asn  Asn
    1055                 1060                 1065


<210> SEQ ID NO 36
<211> LENGTH: 99
<212> TYPE: PRT
<213> ORGANISM: Streptococcus pneumoniae

<400> SEQUENCE: 36

Met Asn Gly Met Lys Ala Lys Lys Met Trp Met Ala Gly Leu Ala Leu
1               5                   10                  15

Leu Gly Ile Gly Ser Leu Ala Leu Ala Thr Lys Lys Val Ala Asp Asp
            20                  25                  30

Arg Lys Leu Met Lys Thr Gln Glu Glu Leu Thr Glu Ile Val Arg Asp
        35                  40                  45

His Phe Ser Asp Met Gly Glu Ile Ala Thr Leu Tyr Val Gln Val Tyr
    50                  55                  60

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

Arg His Tyr Thr Phe Val Tyr Glu Asn Glu Asp Leu Val Tyr Glu Glu
                85                  90                  95

Glu Val Leu


<210> SEQ ID NO 37
<211> LENGTH: 92
<212> TYPE: PRT
<213> ORGANISM: Streptococcus pneumoniae

<400> SEQUENCE: 37

Met Arg Tyr Leu Ala Thr Leu Leu Leu Ser Leu Ala Val Leu Ile Thr
1               5                   10                  15

Ala Gly Cys Lys Lys Val Ala Asp Asp Arg Lys Leu Met Lys Thr Gln
            20                  25                  30

Glu Glu Leu Thr Glu Ile Val Arg Asp His Phe Ser Asp Met Gly Glu
        35                  40                  45

Ile Ala Thr Leu Tyr Val Gln Val Tyr Glu Ser Ser Leu Glu Ser Leu
    50                  55                  60

Val Gly Gly Val Ile Phe Glu Asp Gly Arg His Tyr Thr Phe Val Tyr
65                  70                  75                  80

Glu Asn Glu Asp Leu Val Tyr Glu Glu Glu Val Leu
                85                  90
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<210> SEQ ID NO 38
<211> LENGTH: 978
<212> TYPE: PRT
<213> ORGANISM: Streptococcus pneumoniae

<400> SEQUENCE: 38

Asp Thr Ser Ser Ser Glu Asp Ala Leu Asn Ile Ser Asp Lys Glu Lys
1               5                   10                  15

Val Ala Glu Asn Lys Glu Lys His Glu Asn Ile His Ser Ala Met Glu
            20                  25                  30

Thr Ser Gln Asp Phe Lys Glu Lys Lys Thr Ala Val Ile Lys Glu Lys
        35                  40                  45

Glu Val Val Ser Lys Asn Pro Val Ile Asp Asn Asn Thr Ser Asn Glu
    50                  55                  60

Glu Ala Lys Ile Lys Glu Glu Asn Ser Asn Lys Ser Gln Gly Asp Tyr
65                  70                  75                  80

Thr Asp Ser Phe Val Asn Lys Asn Thr Glu Asn Pro Lys Lys Glu Asp
                85                  90                  95

Lys Val Val Tyr Ile Ala Glu Phe Lys Asp Lys Glu Ser Gly Glu Lys
            100                 105                 110

Ala Ile Lys Glu Leu Ser Ser Leu Lys Asn Thr Lys Val Leu Tyr Thr
        115                 120                 125

Tyr Asp Arg Ile Phe Asn Gly Ser Ala Ile Glu Thr Thr Pro Asp Asn
    130                 135                 140

Leu Asp Lys Ile Lys Gln Ile Glu Gly Ile Ser Ser Val Glu Arg Ala
145                 150                 155                 160

Gln Lys Val Gln Pro Met Met Asn His Ala Arg Lys Glu Ile Gly Val
                165                 170                 175

Glu Glu Ala Ile Asp Tyr Leu Lys Ser Ile Asn Ala Pro Phe Gly Lys
            180                 185                 190

Asn Phe Asp Gly Arg Gly Met Val Ile Ser Asn Ile Asp Thr Gly Thr
        195                 200                 205

Asp Tyr Arg His Lys Ala Met Arg Ile Asp Asp Asp Ala Lys Ala Ser
    210                 215                 220

Met Arg Phe Lys Lys Glu Asp Leu Lys Gly Thr Asp Lys Asn Tyr Trp
225                 230                 235                 240

Leu Ser Asp Lys Ile Pro His Ala Phe Asn Tyr Tyr Asn Gly Gly Lys
                245                 250                 255

Ile Thr Val Glu Lys Tyr Asp Asp Gly Arg Asp Tyr Phe Asp Pro His
            260                 265                 270

Gly Met His Ile Ala Gly Ile Leu Ala Gly Asn Asp Thr Glu Gln Asp
        275                 280                 285

Ile Lys Asn Phe Asn Gly Ile Asp Gly Ile Ala Pro Asn Ala Gln Ile
    290                 295                 300

Phe Ser Tyr Lys Met Tyr Ser Asp Ala Gly Ser Gly Phe Ala Gly Asp
305                 310                 315                 320

Glu Thr Met Phe His Ala Ile Glu Asp Ser Ile Lys His Asn Val Asp
                325                 330                 335

Val Val Ser Val Ser Ser Gly Phe Thr Gly Thr Gly Leu Val Gly Glu
            340                 345                 350

Lys Tyr Trp Gln Ala Ile Arg Ala Leu Arg Lys Ala Gly Ile Pro Met
        355                 360                 365
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Val Val Ala Thr Gly Asn Tyr Ala Thr Ser Ala Ser Ser Ser Ser Trp
    370                 375                 380

Asp Leu Val Ala Asn Asn His Leu Lys Met Thr Asp Thr Gly Asn Val
385                 390                 395                 400

Thr Arg Thr Ala Ala His Glu Asp Ala Ile Ala Val Ala Ser Ala Lys
                405                 410                 415

Asn Gln Thr Val Glu Phe Asp Lys Val Asn Ile Gly Gly Glu Ser Phe
            420                 425                 430

Lys Tyr Arg Asn Ile Gly Ala Phe Phe Asp Lys Ser Lys Ile Thr Thr
        435                 440                 445

Asn Glu Asp Gly Thr Lys Ala Pro Ser Lys Leu Lys Phe Val Tyr Ile
    450                 455                 460

Gly Lys Gly Gln Asp Gln Asp Leu Ile Gly Leu Asp Leu Arg Gly Lys
465                 470                 475                 480

Ile Ala Val Met Asp Arg Ile Tyr Thr Lys Asp Leu Lys Asn Ala Phe
                485                 490                 495

Lys Lys Ala Met Asp Lys Gly Ala Arg Ala Ile Met Val Val Asn Thr
            500                 505                 510

Val Asn Tyr Tyr Asn Arg Asp Asn Trp Thr Glu Leu Pro Ala Met Gly
        515                 520                 525

Tyr Glu Ala Asp Glu Gly Thr Lys Ser Gln Val Phe Ser Ile Ser Gly
    530                 535                 540

Asp Asp Gly Val Lys Leu Trp Asn Met Ile Asn Pro Asp Lys Lys Thr
545                 550                 555                 560

Glu Val Lys Arg Asn Asn Lys Glu Asp Phe Lys Asp Lys Leu Glu Gln
                565                 570                 575

Tyr Tyr Pro Ile Asp Met Glu Ser Phe Asn Ser Asn Lys Pro Asn Val
            580                 585                 590

Gly Asp Glu Lys Glu Ile Asp Phe Lys Phe Ala Pro Asp Thr Asp Lys
        595                 600                 605

Glu Leu Tyr Lys Glu Asp Ile Ile Val Pro Ala Gly Ser Thr Ser Trp
    610                 615                 620

Gly Pro Arg Ile Asp Leu Leu Leu Lys Pro Asp Val Ser Ala Pro Gly
625                 630                 635                 640

Lys Asn Ile Lys Ser Thr Leu Asn Val Ile Asn Gly Lys Ser Thr Tyr
                645                 650                 655

Gly Tyr Met Ser Gly Thr Ser Met Ala Thr Pro Ile Val Ala Ala Ser
            660                 665                 670

Thr Val Leu Ile Arg Pro Lys Leu Lys Glu Met Leu Glu Arg Pro Val
        675                 680                 685

Leu Lys Asn Leu Lys Gly Asp Asp Lys Ile Asp Leu Thr Ser Leu Thr
    690                 695                 700

Lys Ile Ala Leu Gln Asn Thr Ala Arg Pro Met Met Asp Ala Thr Ser
705                 710                 715                 720

Trp Lys Glu Lys Ser Gln Tyr Phe Ala Ser Pro Arg Gln Gln Gly Ala
                725                 730                 735

Gly Leu Ile Asn Val Ala Asn Ala Leu Arg Asn Glu Val Val Ala Thr
            740                 745                 750

Phe Lys Asn Thr Asp Ser Lys Gly Leu Val Asn Ser Tyr Gly Ser Ile
        755                 760                 765
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Ser Leu Lys Glu Ile Lys Gly Asp Lys Lys Tyr Phe Thr Ile Lys Leu
    770                 775                 780

His Asn Thr Ser Asn Arg Pro Leu Thr Phe Lys Val Ser Ala Ser Ala
785                 790                 795                 800

Ile Thr Thr Asp Ser Leu Thr Asp Arg Leu Lys Leu Asp Glu Thr Tyr
                805                 810                 815

Lys Asp Glu Lys Ser Pro Asp Gly Lys Gln Ile Val Pro Glu Ile His
            820                 825                 830

Pro Glu Lys Val Lys Gly Ala Asn Ile Thr Phe Glu His Asp Thr Phe
        835                 840                 845

Thr Ile Gly Ala Asn Ser Ser Phe Asp Leu Asn Ala Val Ile Asn Val
    850                 855                 860

Gly Glu Ala Lys Asn Lys Asn Lys Phe Val Glu Ser Phe Ile His Phe
865                 870                 875                 880

Glu Ser Val Glu Glu Met Glu Ala Leu Asn Ser Asn Gly Lys Lys Ile
                885                 890                 895

Asn Phe Gln Pro Ser Leu Ser Met Pro Leu Met Gly Phe Ala Gly Asn
            900                 905                 910

Trp Asn His Glu Pro Ile Leu Asp Lys Trp Ala Trp Glu Glu Gly Ser
        915                 920                 925

Arg Ser Lys Thr Leu Gly Gly Tyr Asp Asp Asp Gly Lys Pro Lys Ile
    930                 935                 940

Pro Gly Thr Leu Asn Lys Gly Ile Gly Gly Glu His Gly Ile Asp Lys
945                 950                 955                 960

Phe Asn Pro Ala Gly Val Ile Gln Asn Arg Lys Asp Lys Asn Thr Thr
                965                 970                 975

Ser Leu


<210> SEQ ID NO 39
<211> LENGTH: 99
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (33)..(33)
<223> OTHER INFORMATION: Wherein the Xaa at position 33 is Arg or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (44)..(44)
<223> OTHER INFORMATION: Wherein the Xaa at position 44 is Glu or Ala
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (49)..(49)
<223> OTHER INFORMATION: Wherein the Xaa at position 49 is His or Leu
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (61)..(61)
<223> OTHER INFORMATION: Wherein the Xaa at position 61 is Val or Ile
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (72)..(72)
<223> OTHER INFORMATION: Wherein the Xaa at position 72 is Val or Leu
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (74)..(74)
<223> OTHER INFORMATION: Wherein the Xaa at position 74 is Gly or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (86)..(86)
<223> OTHER INFORMATION: Wherein the Xaa at position 86 is Val or Ile
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<400> SEQUENCE: 39

Met Asn Gly Met Lys Ala Lys Lys Met Trp Met Ala Gly Leu Ala Leu
1               5                   10                  15

Leu Gly Ile Gly Ser Leu Ala Leu Ala Thr Lys Lys Val Ala Asp Asp
            20                  25                  30

Xaa Lys Leu Met Lys Thr Gln Glu Glu Leu Thr Xaa Ile Val Arg Asp
        35                  40                  45

Xaa Phe Ser Asp Met Gly Glu Ile Ala Thr Leu Tyr Xaa Gln Val Tyr
    50                  55                  60

Glu Ser Ser Leu Glu Ser Leu Xaa Gly Xaa Val Ile Phe Glu Asp Gly
65                  70                  75                  80

Arg His Tyr Thr Phe Xaa Tyr Glu Asn Glu Asp Leu Val Tyr Glu Glu
                85                  90                  95

Glu Val Leu


<210> SEQ ID NO 40
<211> LENGTH: 667
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (1)..(1)
<223> OTHER INFORMATION: Wherein the Xaa at position 1 is Met or absent
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (9)..(9)
<223> OTHER INFORMATION: Wherein the Xaa at position 9 is Ser or Asn
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (15)..(15)
<223> OTHER INFORMATION: Wherein the Xaa at position 15 is Asn or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (23)..(23)
<223> OTHER INFORMATION: Wherein the Xaa at position 23 is Ala or Val
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (24)..(24)
<223> OTHER INFORMATION: Wherein the Xaa at position 24 is absent or Val
      or Leu
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (25)..(25)
<223> OTHER INFORMATION: Wherein the Xaa at position 25 is absent or Asp
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (26)..(26)
<223> OTHER INFORMATION: Wherein the Xaa at position 26 is absent or Lys
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (27)..(27)
<223> OTHER INFORMATION: Wherein the Xaa at position 27 is absent or Glu
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (28)..(28)
<223> OTHER INFORMATION: Wherein the Xaa at position 28 is absent or Thr
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (35)..(35)
<223> OTHER INFORMATION: Wherein the Xaa at position 35 is Glu or Lys
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (36)..(36)
<223> OTHER INFORMATION: Wherein the Xaa at position 36 is Asn or Asp
<220> FEATURE:
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<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (39)..(39)
<223> OTHER INFORMATION: Wherein the Xaa at position 39 is Ser or Asn
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (41)..(41)
<223> OTHER INFORMATION: Wherein the Xaa at position 41 is Met or Ile
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (45)..(45)
<223> OTHER INFORMATION: Wherein the Xaa at position 45 is Gln or Lys
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (47)..(47)
<223> OTHER INFORMATION: Wherein the Xaa at position 47 is Phe or Thr
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (48)..(48)
<223> OTHER INFORMATION: Wherein the Xaa at position 48 is Lys and Glu
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (53)..(53)
<223> OTHER INFORMATION: Wherein the Xaa at position 53 is Ala or Thr
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (54)..(54)
<223> OTHER INFORMATION: Wherein the Xaa at position 54 is Val or Ile
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (56)..(56)
<223> OTHER INFORMATION: Wherein the Xaa at position 56 is Lys or Glu
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (57)..(57)
<223> OTHER INFORMATION: Wherein the Xaa at position 57 is Glu or Gly
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (59)..(59)
<223> OTHER INFORMATION: Wherein the Xaa at position 59 is Glu or Ala
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (67)..(67)
<223> OTHER INFORMATION: Wherein the Xaa at position 67 is Ile or Thr
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (69)..(69)
<223> OTHER INFORMATION: Wherein the Xaa at position 69 is Asn or Thr
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (70)..(70)
<223> OTHER INFORMATION: Wherein the Xaa at position 70 is Asn or Lys
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (77)..(77)
<223> OTHER INFORMATION: Wherein the Xaa at position 77 is Lys or Arg
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (81)..(81)
<223> OTHER INFORMATION: Wherein the Xaa at position 81 is Glu or Asp
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (82)..(82)
<223> OTHER INFORMATION: Wherein the Xaa at position 82 is Asn or absent
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (85)..(85)
<223> OTHER INFORMATION: Wherein the Xaa at position 85 is Lys or Gln
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (90)..(90)
<223> OTHER INFORMATION: Wherein the Xaa at position 90 is Tyr or His or
      Asn
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (91)..(91)
<223> OTHER INFORMATION: Wherein the Xaa at position 91 is Thr or Ala
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<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (92)..(92)
<223> OTHER INFORMATION: Wherein the Xaa at position 92 is Asp or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (94)..(94)
<223> OTHER INFORMATION: Wherein the Xaa at position 94 is Phe or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (95)..(95)
<223> OTHER INFORMATION: Wherein the Xaa at position 95 is Val or Ala
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (98)..(98)
<223> OTHER INFORMATION: Wherein the Xaa at position 98 is Asn or Gly
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (105)..(105)
<223> OTHER INFORMATION: Wherein the Xaa at position 105 is Glu or Gln
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (107)..(107)
<223> OTHER INFORMATION: Wherein the Xaa at position 107 is Lys or Arg
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (108)..(108)
<223> OTHER INFORMATION: Wherein the Xaa at position 108 is Val or Leu
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (121)..(121)
<223> OTHER INFORMATION: Wherein the Xaa at position 121 is Glu or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (126)..(126)
<223> OTHER INFORMATION: Wherein the Xaa at position 126 is Glu or Gln
      or Gly
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (129)..(129)
<223> OTHER INFORMATION: Wherein the Xaa at position 129 is Ser or Asn
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (146)..(146)
<223> OTHER INFORMATION: Wherein the Xaa at position 146 is Ser or Gly
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (152)..(152)
<223> OTHER INFORMATION: Wherein the Xaa at position 152 is Pro or Gln
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (165)..(165)
<223> OTHER INFORMATION: Wherein the Xaa at position 165 is Ser or Thr
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (167)..(167)
<223> OTHER INFORMATION: Wherein the Xaa at position 167 is Val or Ile
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (440)..(440)
<223> OTHER INFORMATION: Wherein the Xaa at position 440 is Glu or Gln
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (454)..(454)
<223> OTHER INFORMATION: Wherein the Xaa at position 454 is Ser or Asn
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (567)..(567)
<223> OTHER INFORMATION: Wherein the Xaa at position 567 is Asp or Asn

<400> SEQUENCE: 40

Xaa Val Val Leu Ala Asp Thr Ser Xaa Ser Glu Asp Ala Leu Xaa Ile
1               5                   10                  15

Ser Asp Lys Glu Lys Val Xaa Xaa Xaa Xaa Xaa Xaa Glu Asn Lys Glu
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            20                  25                  30

Lys His Xaa Xaa Ile His Xaa Ala Xaa Glu Thr Ser Xaa Asp Xaa Xaa
        35                  40                  45

Glu Lys Lys Thr Xaa Xaa Ile Xaa Xaa Lys Xaa Val Val Ser Lys Asn
    50                  55                  60

Pro Val Xaa Asp Xaa Xaa Thr Ser Asn Glu Glu Ala Xaa Ile Lys Glu
65                  70                  75                  80

Xaa Xaa Ser Asn Xaa Ser Gln Gly Asp Xaa Xaa Xaa Ser Xaa Xaa Asn
                85                  90                  95

Lys Xaa Thr Glu Asn Pro Lys Lys Xaa Asp Xaa Xaa Val Tyr Ile Ala
            100                 105                 110

Glu Phe Lys Asp Lys Glu Ser Gly Xaa Lys Ala Ile Lys Xaa Leu Ser
        115                 120                 125

Xaa Leu Lys Asn Thr Lys Val Leu Tyr Thr Tyr Asp Arg Ile Phe Asn
    130                 135                 140

Gly Xaa Ala Ile Glu Thr Thr Xaa Asp Asn Leu Asp Lys Ile Lys Gln
145                 150                 155                 160

Ile Glu Gly Ile Xaa Ser Xaa Glu Arg Ala Gln Lys Val Gln Pro Met
                165                 170                 175

Met Asn His Ala Arg Lys Glu Ile Gly Val Glu Glu Ala Ile Asp Tyr
            180                 185                 190

Leu Lys Ser Ile Asn Ala Pro Phe Gly Lys Asn Phe Asp Gly Arg Gly
        195                 200                 205

Met Val Ile Ser Asn Ile Asp Thr Gly Thr Asp Tyr Arg His Lys Ala
    210                 215                 220

Met Arg Ile Asp Asp Asp Ala Lys Ala Ser Met Arg Phe Lys Lys Glu
225                 230                 235                 240

Asp Leu Lys Gly Thr Asp Lys Asn Tyr Trp Leu Ser Asp Lys Ile Pro
                245                 250                 255

His Ala Phe Asn Tyr Tyr Asn Gly Gly Lys Ile Thr Val Glu Lys Tyr
            260                 265                 270

Asp Asp Gly Arg Asp Tyr Phe Asp Pro His Gly Met His Ile Ala Gly
        275                 280                 285

Ile Leu Ala Gly Asn Asp Thr Glu Gln Asp Ile Lys Asn Phe Asn Gly
    290                 295                 300

Ile Asp Gly Ile Ala Pro Asn Ala Gln Ile Phe Ser Tyr Lys Met Tyr
305                 310                 315                 320

Ser Asp Ala Gly Ser Gly Phe Ala Gly Asp Glu Thr Met Phe His Ala
                325                 330                 335

Ile Glu Asp Ser Ile Lys His Asn Val Asp Val Val Ser Val Ser Ser
            340                 345                 350

Gly Phe Thr Gly Thr Gly Leu Val Gly Glu Lys Tyr Trp Gln Ala Ile
        355                 360                 365

Arg Ala Leu Arg Lys Ala Gly Ile Pro Met Val Val Ala Thr Gly Asn
    370                 375                 380

Tyr Ala Thr Ser Ala Ser Ser Ser Ser Trp Asp Leu Val Ala Asn Asn
385                 390                 395                 400

His Leu Lys Met Thr Asp Thr Gly Asn Val Thr Arg Thr Ala Ala His
                405                 410                 415

Glu Asp Ala Ile Ala Val Ala Ser Ala Lys Asn Gln Thr Val Glu Phe
            420                 425                 430
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Asp Lys Val Asn Ile Gly Gly Xaa Ser Phe Lys Tyr Arg Asn Ile Gly
        435                 440                 445

Ala Phe Phe Asp Lys Xaa Lys Ile Thr Thr Asn Glu Asp Gly Thr Lys
    450                 455                 460

Ala Pro Ser Lys Leu Lys Phe Val Tyr Ile Gly Lys Gly Gln Asp Gln
465                 470                 475                 480

Asp Leu Ile Gly Leu Asp Leu Arg Gly Lys Ile Ala Val Met Asp Arg
                485                 490                 495

Ile Tyr Thr Lys Asp Leu Lys Asn Ala Phe Lys Lys Ala Met Asp Lys
            500                 505                 510

Gly Ala Arg Ala Ile Met Val Val Asn Thr Val Asn Tyr Tyr Asn Arg
        515                 520                 525

Asp Asn Trp Thr Glu Leu Pro Ala Met Gly Tyr Glu Ala Asp Glu Gly
    530                 535                 540

Thr Lys Ser Gln Val Phe Ser Ile Ser Gly Asp Asp Gly Val Lys Leu
545                 550                 555                 560

Trp Asn Met Ile Asn Pro Xaa Lys Lys Thr Glu Val Lys Arg Asn Asn
                565                 570                 575

Lys Glu Asp Phe Lys Asp Lys Leu Glu Gln Tyr Tyr Pro Ile Asp Met
            580                 585                 590

Glu Ser Phe Asn Ser Asn Lys Pro Asn Val Gly Asp Glu Lys Glu Ile
        595                 600                 605

Asp Phe Lys Phe Ala Pro Asp Thr Asp Lys Glu Leu Tyr Lys Glu Asp
    610                 615                 620

Ile Ile Val Pro Ala Gly Ser Thr Ser Trp Gly Pro Arg Ile Asp Leu
625                 630                 635                 640

Leu Leu Lys Pro Asp Val Ser Ala Pro Gly Lys Asn Ile Lys Ser Thr
                645                 650                 655

Leu Asn Val Ile Asn Gly Lys Ser Thr Tyr Gly
            660                 665


<210> SEQ ID NO 41
<211> LENGTH: 621
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (28)..(28)
<223> OTHER INFORMATION: Wherein the Xaa at position 28 is Arg or Lys
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (35)..(35)
<223> OTHER INFORMATION: Wherein the Xaa at position 35 is Lys or Thr
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (143)..(143)
<223> OTHER INFORMATION: Wherein the Xaa at position 143 is Ile or Val
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (165)..(165)
<223> OTHER INFORMATION: Wherein the Xaa at position 165 is Asp or Tyr
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (210)..(210)
<223> OTHER INFORMATION: Wherein the Xaa at position 210 is Lys or Arg
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (227)..(227)
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<223> OTHER INFORMATION: Wherein the Xaa at position 227 is Glu or Ala
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (232)..(232)
<223> OTHER INFORMATION: Wherein the Xaa at position 232 is Asn or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (238)..(238)
<223> OTHER INFORMATION: Wherein the Xaa at position 238 is Ile or Thr
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (239)..(239)
<223> OTHER INFORMATION: Wherein the Xaa at position 239 is Asn or Asp
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (271)..(271)
<223> OTHER INFORMATION: Wherein the Xaa at position 271 is Arg or Lys
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (275)..(275)
<223> OTHER INFORMATION: Wherein the Xaa at position 275 is Leu or Met
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (276)..(276)
<223> OTHER INFORMATION: Wherein the Xaa at position 276 is Gly or Glu
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (317)..(317)
<223> OTHER INFORMATION: Wherein the Xaa at position 317 is Thr or Arg
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (323)..(323)
<223> OTHER INFORMATION: Wherein the Xaa at position 323 is Asn or Asp
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (325)..(325)
<223> OTHER INFORMATION: Wherein the Xaa at position 325 is Glu or Asp
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (332)..(332)
<223> OTHER INFORMATION: Wherein the Xaa at position 332 is Glu or Gln
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (334)..(334)
<223> OTHER INFORMATION: Wherein the Xaa at position 334 is Ile or Val
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (335)..(335)
<223> OTHER INFORMATION: Wherein the Xaa at position 335 is Asn or His
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (337)..(337)
<223> OTHER INFORMATION: Wherein the Xaa at position 337 is Pro or Glu
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (339)..(339)
<223> OTHER INFORMATION: Wherein the Xaa at position 339 is Ser or Thr
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (393)..(393)
<223> OTHER INFORMATION: Wherein the Xaa at position 393 is Arg or Lys
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (398)..(398)
<223> OTHER INFORMATION: Wherein the Xaa at position 398 is Ile or Val
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (412)..(412)
<223> OTHER INFORMATION: Xaa can be any naturally occurring amino acid
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (421)..(421)
<223> OTHER INFORMATION: Wherein the Xaa at position 421 is Ser or Gly
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (594)..(594)
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<223> OTHER INFORMATION: Wherein the Xaa at position 594 is Lys or Ser
<220> FEATURE:
<221> NAME/KEY: MISC_FEATURE
<222> LOCATION: (612)..(612)
<223> OTHER INFORMATION: Wherein the Xaa at position 612 is Ser or Ala

<400> SEQUENCE: 41

Met Ser Gly Thr Ser Met Ala Thr Pro Ile Val Ala Ala Ser Thr Val
1               5                   10                  15

Leu Ile Arg Pro Lys Leu Lys Glu Met Leu Glu Xaa Pro Val Leu Lys
            20                  25                  30

Asn Leu Xaa Gly Asp Asp Lys Ile Asp Leu Thr Ser Leu Thr Lys Ile
        35                  40                  45

Ala Leu Gln Asn Thr Ala Arg Pro Met Met Asp Ala Thr Ser Trp Lys
    50                  55                  60

Glu Lys Ser Gln Tyr Phe Ala Ser Pro Arg Gln Gln Gly Ala Gly Leu
65                  70                  75                  80

Ile Asn Val Ala Asn Ala Leu Arg Asn Glu Val Val Ala Thr Phe Lys
                85                  90                  95

Asn Thr Asp Ser Lys Gly Leu Val Asn Ser Tyr Gly Ser Ile Ser Leu
            100                 105                 110

Lys Glu Ile Lys Gly Asp Lys Lys Tyr Phe Thr Ile Lys Leu His Asn
        115                 120                 125

Thr Ser Asn Arg Pro Leu Thr Phe Lys Val Ser Ala Ser Ala Xaa Thr
    130                 135                 140

Thr Asp Ser Leu Thr Asp Arg Leu Lys Leu Asp Glu Thr Tyr Lys Asp
145                 150                 155                 160

Glu Lys Ser Pro Xaa Gly Lys Gln Ile Val Pro Glu Ile His Pro Glu
                165                 170                 175

Lys Val Lys Gly Ala Asn Ile Thr Phe Glu His Asp Thr Phe Thr Ile
            180                 185                 190

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

Ala Xaa Asn Lys Asn Lys Phe Val Glu Ser Phe Ile His Phe Glu Ser
    210                 215                 220

Val Glu Xaa Met Glu Ala Leu Xaa Ser Asn Gly Lys Lys Xaa Xaa Phe
225                 230                 235                 240

Gln Pro Ser Leu Ser Met Pro Leu Met Gly Phe Ala Gly Asn Trp Asn
                245                 250                 255

His Glu Pro Ile Leu Asp Lys Trp Ala Trp Glu Glu Gly Ser Xaa Ser
            260                 265                 270

Lys Thr Xaa Xaa Gly Tyr Asp Asp Asp Gly Lys Pro Lys Ile Pro Gly
        275                 280                 285

Thr Leu Asn Lys Gly Ile Gly Gly Glu His Gly Ile Asp Lys Phe Asn
    290                 295                 300

Pro Ala Gly Val Ile Gln Asn Arg Lys Asp Lys Asn Xaa Thr Ser Leu
305                 310                 315                 320

Asp Gln Xaa Pro Xaa Leu Phe Ala Phe Asn Asn Xaa Gly Xaa Xaa Ala
                325                 330                 335

Xaa Ser Xaa Ser Gly Ser Lys Ile Ala Asn Ile Tyr Pro Leu Asp Ser
            340                 345                 350

Asn Gly Asn Pro Gln Asp Ala Gln Leu Glu Arg Gly Leu Thr Pro Ser
        355                 360                 365
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Pro Leu Val Leu Arg Ser Ala Glu Glu Gly Leu Ile Ser Ile Val Asn
    370                 375                 380

Thr Asn Lys Glu Gly Glu Asn Gln Xaa Asp Leu Lys Val Xaa Ser Arg
385                 390                 395                 400

Glu His Phe Ile Arg Gly Ile Leu Asn Ser Lys Xaa Asn Asp Ala Lys
                405                 410                 415

Gly Ile Lys Ser Ser Lys Leu Lys Val Trp Gly Asp Leu Lys Trp Asp
            420                 425                 430

Gly Leu Ile Tyr Asn Pro Arg Gly Arg Glu Glu Asn Ala Pro Glu Ser
        435                 440                 445

Lys Asp Asn Gln Asp Pro Ala Thr Lys Ile Arg Gly Gln Phe Glu Pro
    450                 455                 460

Ile Ala Glu Gly Gln Tyr Phe Tyr Lys Phe Lys Tyr Arg Leu Thr Lys
465                 470                 475                 480

Asp Tyr Pro Trp Gln Val Ser Tyr Ile Pro Val Lys Ile Asp Asn Thr
                485                 490                 495

Ala Pro Lys Ile Val Ser Val Asp Phe Ser Asn Pro Glu Lys Ile Lys
            500                 505                 510

Leu Ile Thr Lys Asp Thr Tyr His Lys Val Lys Asp Gln Tyr Lys Asn
        515                 520                 525

Glu Thr Leu Phe Ala Arg Asp Gln Lys Glu His Pro Glu Lys Phe Asp
    530                 535                 540

Glu Ile Ala Asn Glu Val Trp Tyr Ala Gly Ala Ala Leu Val Asn Glu
545                 550                 555                 560

Asp Gly Glu Val Glu Lys Asn Leu Glu Val Thr Tyr Ala Gly Glu Gly
                565                 570                 575

Gln Gly Arg Asn Arg Lys Leu Asp Lys Asp Gly Asn Thr Ile Tyr Glu
            580                 585                 590

Ile Xaa Gly Ala Gly Asp Leu Arg Gly Lys Ile Ile Glu Val Ile Ala
        595                 600                 605

Leu Asp Gly Xaa Ser Asn Phe Thr Asp His Lys Ala Glu
    610                 615                 620


<210> SEQ ID NO 42
<211> LENGTH: 19
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 42

Leu Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
1               5                   10                  15

Ala Ala Ala


<210> SEQ ID NO 43
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 43

Leu Ala Glu Ala Thr Ala Lys Glu Ala Thr Ala Lys Glu Ala Thr Ala
1               5                   10                  15
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Lys Ala Thr Ala
20

<210> SEQ ID NO 44
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 44

Gly Pro Lys Pro His Arg Ile Gln Ser Thr Pro Lys Gly Ser
1 5 10

<210> SEQ ID NO 45
<211> LENGTH: 2025
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 45

atgtcatcta aatttatgaa gagcgctgcg gtgcttggaa ctgctacact tgctagcttg 60

cttttggtag cttgcggaag caaaactgct gataagcctg ctgattctgg ttcatctgaa 120

gtcaaagaac tcactgtata tgtagacgag ggatataaga gctatattga agaggttgct 180

aaagcttatg aaaaagaagc tggagtaaaa gtcactctta aaactggtga tgctctagga 240

ggtcttgata aactttctct tgacaaccaa tctggtaatg tccctgatgt tatgatggct 300

ccatacgacc gtgtaggtag ccttggttct gacggacaac tttcagaagt gaaattgagc 360

gatggtgcta aaacagacga cacaactaaa tctcttgtaa cagctgctaa tggtaaagtt 420

tacggtgctc ctgccgttat cgagtcactt gttatgtact acaacaaaga cttggtgaaa 480

gatgctccaa aaacatttgc tgacttggaa aaccttgcta aagatagcaa atacgcattc 540

gctggtgaag atggtaaaac tactgccttc ctagctgact ggacaaactt ctactataca 600

tatggacttc ttgccggtaa cggtgcttac gtctttggcc aaaacggtaa agacgctaaa 660

gacatcggtc ttgcaaacga cggttctatc gtaggtatca actacgctaa atcttggtac 720

gaaaaatggc ctaaaggtat gcaagataca gaaggtgctg gaaacttaat ccaaactcaa 780

ttccaagaag gtaaaacagc tgctatcatc gacggacctt ggaaagctca agcctttaaa 840

gatgctaaag taaactacgg agttgcaact atcccaactc ttccaaatgg aaaagaatat 900

gctgcattcg gtggtggtaa agcttgggtc attcctcaag ccgttaagaa ccttgaagct 960

tctcaaaaat ttgtagactt ccttgttgca actgaacaac aaaaagtatt atatgataag 1020

actaacgaaa tcccagctaa tactgaggct cgttcatacg ctgaaggtaa aaacgatgag 1080

ttgacaacag ctgttatcaa acagttcaag aacactcaac cactgccaaa catctctcaa 1140

atgtctgcag tttgggatcc agcgaaaaat atgctctttg atgctgtaag tggtcaaaaa 1200

gatgctaaaa cagctgctaa cgatgctgta acattgatca aagaaacaat caaacaaaaa 1260

tttggtgaat caggggtgc taagaaagaa ggagaagcag ctagcaagaa agaaatcatc 1320

gttgcaacca atggatcacc aaagccattt atctatgaag aaaatggcga attgactggt 1380

tacgagattg aagtcgttcg cgctatcttt aaagattctg acaaatatga tgtcaagttt 1440

gaaaagacag aatggtcagg tgtctttgct ggtcttgacg ctgatcgtta caatatggct 1500

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gtcaacaatc ttagctacac taaagaacgt gcggagaaat acctctatgc cgcaccaatt   1560

gcccaaaatc ctaatgtcct tgtcgtgaag aaagatgact ctagtatcaa gtctctcgat   1620

gatatcggtg gaaaatcgac ggaagtcgtt caagccacta catcagctaa gcagttagaa   1680

gcatacaatg ctgaacacac ggacaaccca actatcctta actatactaa ggcagacttc   1740

caacaaatca tggtacgttt gagcgatgga caatttgact ataagatttt tgataaaatc   1800

ggtgttgaaa cagtgatcaa gaaccaaggt ttggacaact tgaaagttat cgaacttcca   1860

agcgaccaac aaccgtacgt ttacccactt cttgctcagg gtcaagatga gttgaaatcg   1920

tttgtagaca aacgcatcaa agaactttat aaagatggaa ctcttgaaaa attgtctaaa   1980

caattcttcg gagacactta tctaccggca gaagctgata ttaaa                   2025


<210> SEQ ID NO 46
<211> LENGTH: 675
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 46

Met Ser Ser Lys Phe Met Lys Ser Ala Ala Val Leu Gly Thr Ala Thr
1               5                   10                  15

Leu Ala Ser Leu Leu Leu Val Ala Cys Gly Ser Lys Thr Ala Asp Lys
            20                  25                  30

Pro Ala Asp Ser Gly Ser Ser Glu Val Lys Glu Leu Thr Val Tyr Val
        35                  40                  45

Asp Glu Gly Tyr Lys Ser Tyr Ile Glu Glu Val Ala Lys Ala Tyr Glu
    50                  55                  60

Lys Glu Ala Gly Val Lys Val Thr Leu Lys Thr Gly Asp Ala Leu Gly
65                  70                  75                  80

Gly Leu Asp Lys Leu Ser Leu Asp Asn Gln Ser Gly Asn Val Pro Asp
                85                  90                  95

Val Met Met Ala Pro Tyr Asp Arg Val Gly Ser Leu Gly Ser Asp Gly
            100                 105                 110

Gln Leu Ser Glu Val Lys Leu Ser Asp Gly Ala Lys Thr Asp Asp Thr
        115                 120                 125

Thr Lys Ser Leu Val Thr Ala Ala Asn Gly Lys Val Tyr Gly Ala Pro
    130                 135                 140

Ala Val Ile Glu Ser Leu Val Met Tyr Tyr Asn Lys Asp Leu Val Lys
145                 150                 155                 160

Asp Ala Pro Lys Thr Phe Ala Asp Leu Glu Asn Leu Ala Lys Asp Ser
                165                 170                 175

Lys Tyr Ala Phe Ala Gly Glu Asp Gly Lys Thr Thr Ala Phe Leu Ala
            180                 185                 190

Asp Trp Thr Asn Phe Tyr Tyr Thr Tyr Gly Leu Leu Ala Gly Asn Gly
        195                 200                 205

Ala Tyr Val Phe Gly Gln Asn Gly Lys Asp Ala Lys Asp Ile Gly Leu
    210                 215                 220

Ala Asn Asp Gly Ser Ile Val Gly Ile Asn Tyr Ala Lys Ser Trp Tyr
225                 230                 235                 240

Glu Lys Trp Pro Lys Gly Met Gln Asp Thr Glu Gly Ala Gly Asn Leu
                245                 250                 255
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Ile Gln Thr Gln Phe Gln Glu Gly Lys Thr Ala Ala Ile Ile Asp Gly
            260                 265                 270

Pro Trp Lys Ala Gln Ala Phe Lys Asp Ala Lys Val Asn Tyr Gly Val
        275                 280                 285

Ala Thr Ile Pro Thr Leu Pro Asn Gly Lys Glu Tyr Ala Ala Phe Gly
    290                 295                 300

Gly Gly Lys Ala Trp Val Ile Pro Gln Ala Val Lys Asn Leu Glu Ala
305                 310                 315                 320

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

Leu Tyr Asp Lys Thr Asn Glu Ile Pro Ala Asn Thr Glu Ala Arg Ser
            340                 345                 350

Tyr Ala Glu Gly Lys Asn Asp Glu Leu Thr Thr Ala Val Ile Lys Gln
        355                 360                 365

Phe Lys Asn Thr Gln Pro Leu Pro Asn Ile Ser Gln Met Ser Ala Val
    370                 375                 380

Trp Asp Pro Ala Lys Asn Met Leu Phe Asp Ala Val Ser Gly Gln Lys
385                 390                 395                 400

Asp Ala Lys Thr Ala Ala Asn Asp Ala Val Thr Leu Ile Lys Glu Thr
                405                 410                 415

Ile Lys Gln Lys Phe Gly Glu Ser Gly Gly Ala Lys Lys Glu Gly Glu
            420                 425                 430

Ala Ala Ser Lys Lys Glu Ile Ile Val Ala Thr Asn Gly Ser Pro Lys
        435                 440                 445

Pro Phe Ile Tyr Glu Glu Asn Gly Glu Leu Thr Gly Tyr Glu Ile Glu
    450                 455                 460

Val Val Arg Ala Ile Phe Lys Asp Ser Asp Lys Tyr Asp Val Lys Phe
465                 470                 475                 480

Glu Lys Thr Glu Trp Ser Gly Val Phe Ala Gly Leu Asp Ala Asp Arg
                485                 490                 495

Tyr Asn Met Ala Val Asn Asn Leu Ser Tyr Thr Lys Glu Arg Ala Glu
            500                 505                 510

Lys Tyr Leu Tyr Ala Ala Pro Ile Ala Gln Asn Pro Asn Val Leu Val
        515                 520                 525

Val Lys Lys Asp Asp Ser Ser Ile Lys Ser Leu Asp Asp Ile Gly Gly
    530                 535                 540

Lys Ser Thr Glu Val Val Gln Ala Thr Thr Ser Ala Lys Gln Leu Glu
545                 550                 555                 560

Ala Tyr Asn Ala Glu His Thr Asp Asn Pro Thr Ile Leu Asn Tyr Thr
                565                 570                 575

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

Asp Tyr Lys Ile Phe Asp Lys Ile Gly Val Glu Thr Val Ile Lys Asn
        595                 600                 605

Gln Gly Leu Asp Asn Leu Lys Val Ile Glu Leu Pro Ser Asp Gln Gln
    610                 615                 620

Pro Tyr Val Tyr Pro Leu Leu Ala Gln Gly Gln Asp Glu Leu Lys Ser
625                 630                 635                 640

Phe Val Asp Lys Arg Ile Lys Glu Leu Tyr Lys Asp Gly Thr Leu Glu
                645                 650                 655
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Lys Leu Ser Lys Gln Phe Phe Gly Asp Thr Tyr Leu Pro Ala Glu Ala
            660                 665                 670

Asp Ile Lys
        675
```

<210> SEQ ID NO 47
<211> LENGTH: 2022
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 47

atgaaaaaaa tcgttaaata ctcatctctt gcagcccttg ctcttgttgc tgcaggtgtg 60

cttgcggctt gctcaggggg tgctaagaaa gaaggagaag cagctagcaa gaaagaaatc 120

atcgttgcaa ccaatggatc accaaagcca tttatctatg aagaaaatgg cgaattgact 180

ggttacgaga ttgaagtcgt tcgcgctatc tttaaagatt ctgacaaata tgatgtcaag 240

tttgaaaaga cagaatggtc aggtgtcttt gctggtcttg acgctgatcg ttacaatatg 300

gctgtcaaca atcttagcta cactaaagaa cgtgcggaga aatacctcta tgccgcacca 360

attgcccaaa atcctaatgt ccttgtcgtg aagaaagatg actctagtat caagtctctc 420

gatgatatcg gtggaaaatc gacggaagtc gttcaagcca ctacatcagc taagcagtta 480

gaagcataca atgctgaaca cacggacaac ccaactatcc ttaactatac taaggcagac 540

ttscaacaaa tcatggtacg tttgagcgat ggacaatttg actataagat tttgataaa 600

atcggtgttg aaacagtgat caagaaccaa ggtttggaca acttgaaagt tatcgaactt 660

ccaagcgacc aacaaccgta cgtttaccca cttcttgctc agggtcaaga tgagttgaaa 720

tcgtttgtag acaaacgcat caaagaactt tataaagatg gaactcttga aaaattgtct 780

aaacaattct tcggagacac ttatctaccg gcagaagctg atattaaagg aagcaaaact 840

gctgataagc ctgctgattc tggttcatct gaagtcaaag aactcactgt atatgtagac 900

gagggatata agagctatat tgaagaggtt gctaaagctt atgaaaaaga agctggagta 960

aaagtcactc ttaaaactgg tgatgctcta ggaggtcttg ataaactttc tcttgacaac 1020

caatctggta atgtccctga tgttatgatg gctccatacg accgtgtagg tagccttggt 1080

tctgacggac aactttcaga agtgaaattg agcgatggtg ctaaaacaga cgacacaact 1140

aaatctcttg taacagctgc taatggtaaa gtttacggtg ctcctgccgt tatcgagtca 1200

cttgttatgt actacaacaa agacttggtg aaagatgctc caaaaacatt tgctgacttg 1260

gaaaaccttg ctaaagatag caaatacgca ttcgctggtg aagatggtaa aactactgcc 1320

ttcctagctg actggacaaa cttctactat acatatggac ttcttgccgg taacggtgct 1380

tacgtctttg gccaaaacgg taaagacgct aaagacatcg gtcttgcaaa cgacggttct 1440

atcgtaggta tcaactacgc taaatcttgg tacgaaaaat ggcctaaagg tatgcaagat 1500

acagaaggtg ctggaaactt aatccaaact caattccaag aaggtaaaac agctgctatc 1560

atcgacggac cttggaaagc tcaagccttt aaagatgcta aagtaaacta cggagttgca 1620

actatcccaa ctcttccaaa tggaaaagaa tatgctgcat tcggtggtgg taaagcttgg 1680

gtcattcctc aagccgttaa gaaccttgaa gcttctcaaa aatttgtaga cttccttgtt 1740

gcaactgaac aacaaaaagt attatatgat aagactaacg aaatcccagc taatactgag 1800

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gctcgttcat acgctgaagg taaaaacgat gagttgacaa cagctgttat caaacagttc   1860

aagaacactc aaccactgcc aaacatctct caaatgtctg cagtttggga tccagcgaaa   1920

aatatgctct ttgatgctgt aagtggtcaa aaagatgcta aaacagctgc taacgatgct   1980

gtaacattga tcaaagaaac aatcaaacaa aaatttggtg aa                      2022
```

<210> SEQ ID NO 48
<211> LENGTH: 674
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 48

```
Met Lys Lys Ile Val Lys Tyr Ser Ser Leu Ala Ala Leu Ala Leu Val
1               5                   10                  15

Ala Ala Gly Val Leu Ala Ala Cys Ser Gly Gly Ala Lys Lys Glu Gly
            20                  25                  30

Glu Ala Ala Ser Lys Lys Glu Ile Ile Val Ala Thr Asn Gly Ser Pro
        35                  40                  45

Lys Pro Phe Ile Tyr Glu Glu Asn Gly Glu Leu Thr Gly Tyr Glu Ile
    50                  55                  60

Glu Val Val Arg Ala Ile Phe Lys Asp Ser Asp Lys Tyr Asp Val Lys
65                  70                  75                  80

Phe Glu Lys Thr Glu Trp Ser Gly Val Phe Ala Gly Leu Asp Ala Asp
                85                  90                  95

Arg Tyr Asn Met Ala Val Asn Asn Leu Ser Tyr Thr Lys Glu Arg Ala
            100                 105                 110

Glu Lys Tyr Leu Tyr Ala Ala Pro Ile Ala Gln Asn Pro Asn Val Leu
        115                 120                 125

Val Val Lys Lys Asp Asp Ser Ser Ile Lys Ser Leu Asp Asp Ile Gly
    130                 135                 140

Gly Lys Ser Thr Glu Val Val Gln Ala Thr Thr Ser Ala Lys Gln Leu
145                 150                 155                 160

Glu Ala Tyr Asn Ala Glu His Thr Asp Asn Pro Thr Ile Leu Asn Tyr
                165                 170                 175

Thr Lys Ala Asp Phe Gln Gln Ile Met Val Arg Leu Ser Asp Gly Gln
            180                 185                 190

Phe Asp Tyr Lys Ile Phe Asp Lys Ile Gly Val Glu Thr Val Ile Lys
        195                 200                 205

Asn Gln Gly Leu Asp Asn Leu Lys Val Ile Glu Leu Pro Ser Asp Gln
    210                 215                 220

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

Ser Phe Val Asp Lys Arg Ile Lys Glu Leu Tyr Lys Asp Gly Thr Leu
                245                 250                 255

Glu Lys Leu Ser Lys Gln Phe Phe Gly Asp Thr Tyr Leu Pro Ala Glu
            260                 265                 270

Ala Asp Ile Lys Gly Ser Lys Thr Ala Asp Lys Pro Ala Asp Ser Gly
        275                 280                 285

Ser Ser Glu Val Lys Glu Leu Thr Val Tyr Val Asp Glu Gly Tyr Lys
    290                 295                 300

Ser Tyr Ile Glu Glu Val Ala Lys Ala Tyr Glu Lys Glu Ala Gly Val
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305                 310                 315                 320

Lys Val Thr Leu Lys Thr Gly Asp Ala Leu Gly Gly Leu Asp Lys Leu
                325                 330                 335

Ser Leu Asp Asn Gln Ser Gly Asn Val Pro Asp Val Met Met Ala Pro
            340                 345                 350

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

Lys Leu Ser Asp Gly Ala Lys Thr Asp Asp Thr Thr Lys Ser Leu Val
    370                 375                 380

Thr Ala Ala Asn Gly Lys Val Tyr Gly Ala Pro Ala Val Ile Glu Ser
385                 390                 395                 400

Leu Val Met Tyr Tyr Asn Lys Asp Leu Val Lys Asp Ala Pro Lys Thr
                405                 410                 415

Phe Ala Asp Leu Glu Asn Leu Ala Lys Asp Ser Lys Tyr Ala Phe Ala
            420                 425                 430

Gly Glu Asp Gly Lys Thr Thr Ala Phe Leu Ala Asp Trp Thr Asn Phe
        435                 440                 445

Tyr Tyr Thr Tyr Gly Leu Leu Ala Gly Asn Gly Ala Tyr Val Phe Gly
    450                 455                 460

Gln Asn Gly Lys Asp Ala Lys Asp Ile Gly Leu Ala Asn Asp Gly Ser
465                 470                 475                 480

Ile Val Gly Ile Asn Tyr Ala Lys Ser Trp Tyr Glu Lys Trp Pro Lys
                485                 490                 495

Gly Met Gln Asp Thr Glu Gly Ala Gly Asn Leu Ile Gln Thr Gln Phe
            500                 505                 510

Gln Glu Gly Lys Thr Ala Ala Ile Ile Asp Gly Pro Trp Lys Ala Gln
        515                 520                 525

Ala Phe Lys Asp Ala Lys Val Asn Tyr Gly Val Ala Thr Ile Pro Thr
    530                 535                 540

Leu Pro Asn Gly Lys Glu Tyr Ala Ala Phe Gly Gly Gly Lys Ala Trp
545                 550                 555                 560

Val Ile Pro Gln Ala Val Lys Asn Leu Glu Ala Ser Gln Lys Phe Val
                565                 570                 575

Asp Phe Leu Val Ala Thr Glu Gln Gln Lys Val Leu Tyr Asp Lys Thr
            580                 585                 590

Asn Glu Ile Pro Ala Asn Thr Glu Ala Arg Ser Tyr Ala Glu Gly Lys
        595                 600                 605

Asn Asp Glu Leu Thr Thr Ala Val Ile Lys Gln Phe Lys Asn Thr Gln
    610                 615                 620

Pro Leu Pro Asn Ile Ser Gln Met Ser Ala Val Trp Asp Pro Ala Lys
625                 630                 635                 640

Asn Met Leu Phe Asp Ala Val Ser Gly Gln Lys Asp Ala Lys Thr Ala
                645                 650                 655

Ala Asn Asp Ala Val Thr Leu Ile Lys Glu Thr Ile Lys Gln Lys Phe
            660                 665                 670

Gly Glu


<210> SEQ ID NO 49
<211> LENGTH: 1563
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 49

atgtcatcta aatttatgaa gagcgctgcg gtgcttggaa ctgctacact tgctagcttg 60

cttttggtag cttgcggaag caaaactgct gataagcctg ctgattctgg ttcatctgaa 120

gtcaaagaac tcactgtata tgtagacgag ggatataaga gctatattga agaggttgct 180

aaagcttatg aaaaagaagc tggagtaaaa gtcactctta aaactggtga tgctctagga 240

ggtcttgata aactttctct tgacaaccaa tctggtaatg tccctgatgt tatgatggct 300

ccatacgacc gtgtaggtag ccttggttct gacggacaac tttcagaagt gaaattgagc 360

gatggtgcta aaacagacga cacaactaaa tctcttgtaa cagctgctaa tggtaaagtt 420

tacggtgctc ctgccgttat cgagtcactt gttatgtact acaacaaaga cttggtgaaa 480

gatgctccaa aaacatttgc tgacttggaa aaccttgcta aagatagcaa atacgcattc 540

gctggtgaag atggtaaaac tactgccttc ctagctgact ggacaaactt ctactataca 600

tatggacttc ttgccggtaa cggtgcttac gtctttggcc aaaacggtaa agacgctaaa 660

gacatcggtc ttgcaaacga cggttctatc gtaggtatca actacgctaa atcttggtac 720

gaaaaatggc ctaaaggtat gcaagataca gaaggtgctg gaaacttaat ccaaactcaa 780

ttccaagaag gtaaaacagc tgctatcatc gacggacctt ggaaagctca agcctttaaa 840

gatgctaaag taaactacgg agttgcaact atcccaactc ttccaaatgg aaaagaatat 900

gctgcattcg gtggtggtaa agcttgggtc attcctcaag ccgttaagaa ccttgaagct 960

tctcaaaaat ttgtagactt ccttgttgca actgaacaac aaaaagtatt atatgataag 1020

actaacgaaa tcccagctaa tactgaggct cgttcatacg ctgaaggtaa aaacgatgag 1080

ttgacaacag ctgttatcaa acagttcaag aacactcaac cactgccaaa catctctcaa 1140

atgtctgcag tttgggatcc agcgaaaaat atgctctttg atgctgtaag tggtcaaaaa 1200

gatgctaaaa cagctgctaa cgatgctgta acattgatca aagaaacaat caaacaaaaa 1260

tttggtgaaa atggtatgaa agctaaaaaa atgtggatgg caggcttggc tctgctaggt 1320

atcggaagcc ttgctcttgc tacgaaaaaa gttgcagatg accgtaagct catgaagact 1380

caggaagagt tgacagagat tgtgcgagac catttttccg acatggggga aattgcgacc 1440

ctttatgttc aagtttacga aagcagtctg gagagcttgg ttggtggcgt catttttgag 1500

gatggccgtc attatacctt tgtctatgaa aatgaagacc tagtctatga ggaggaagtc 1560

tta 1563

<210> SEQ ID NO 50
<211> LENGTH: 521
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 50

Met Ser Ser Lys Phe Met Lys Ser Ala Ala Val Leu Gly Thr Ala Thr
1   5   10   15

Leu Ala Ser Leu Leu Leu Val Ala Cys Gly Ser Lys Thr Ala Asp Lys
            20   25   30

Pro Ala Asp Ser Gly Ser Ser Glu Val Lys Glu Leu Thr Val Tyr Val
        35   40   45

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Asp Glu Gly Tyr Lys Ser Tyr Ile Glu Glu Val Ala Lys Ala Tyr Glu
    50                  55                  60

Lys Glu Ala Gly Val Lys Val Thr Leu Lys Thr Gly Asp Ala Leu Gly
65                  70                  75                  80

Gly Leu Asp Lys Leu Ser Leu Asp Asn Gln Ser Gly Asn Val Pro Asp
                85                  90                  95

Val Met Met Ala Pro Tyr Asp Arg Val Gly Ser Leu Gly Ser Asp Gly
            100                 105                 110

Gln Leu Ser Glu Val Lys Leu Ser Asp Gly Ala Lys Thr Asp Asp Thr
        115                 120                 125

Thr Lys Ser Leu Val Thr Ala Ala Asn Gly Lys Val Tyr Gly Ala Pro
    130                 135                 140

Ala Val Ile Glu Ser Leu Val Met Tyr Tyr Asn Lys Asp Leu Val Lys
145                 150                 155                 160

Asp Ala Pro Lys Thr Phe Ala Asp Leu Glu Asn Leu Ala Lys Asp Ser
                165                 170                 175

Lys Tyr Ala Phe Ala Gly Glu Asp Gly Lys Thr Thr Ala Phe Leu Ala
            180                 185                 190

Asp Trp Thr Asn Phe Tyr Tyr Thr Tyr Gly Leu Leu Ala Gly Asn Gly
        195                 200                 205

Ala Tyr Val Phe Gly Gln Asn Gly Lys Asp Ala Lys Asp Ile Gly Leu
    210                 215                 220

Ala Asn Asp Gly Ser Ile Val Gly Ile Asn Tyr Ala Lys Ser Trp Tyr
225                 230                 235                 240

Glu Lys Trp Pro Lys Gly Met Gln Asp Thr Glu Gly Ala Gly Asn Leu
                245                 250                 255

Ile Gln Thr Gln Phe Gln Glu Gly Lys Thr Ala Ala Ile Ile Asp Gly
            260                 265                 270

Pro Trp Lys Ala Gln Ala Phe Lys Asp Ala Lys Val Asn Tyr Gly Val
        275                 280                 285

Ala Thr Ile Pro Thr Leu Pro Asn Gly Lys Glu Tyr Ala Ala Phe Gly
    290                 295                 300

Gly Gly Lys Ala Trp Val Ile Pro Gln Ala Val Lys Asn Leu Glu Ala
305                 310                 315                 320

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

Leu Tyr Asp Lys Thr Asn Glu Ile Pro Ala Asn Thr Glu Ala Arg Ser
            340                 345                 350

Tyr Ala Glu Gly Lys Asn Asp Glu Leu Thr Thr Ala Val Ile Lys Gln
        355                 360                 365

Phe Lys Asn Thr Gln Pro Leu Pro Asn Ile Ser Gln Met Ser Ala Val
    370                 375                 380

Trp Asp Pro Ala Lys Asn Met Leu Phe Asp Ala Val Ser Gly Gln Lys
385                 390                 395                 400

Asp Ala Lys Thr Ala Ala Asn Asp Ala Val Thr Leu Ile Lys Glu Thr
                405                 410                 415

Ile Lys Gln Lys Phe Gly Glu Asn Gly Met Lys Ala Lys Lys Met Trp
            420                 425                 430

Met Ala Gly Leu Ala Leu Leu Gly Ile Gly Ser Leu Ala Leu Ala Thr
        435                 440                 445
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Lys Lys Val Ala Asp Asp Arg Lys Leu Met Lys Thr Gln Glu Glu Leu
    450                 455                 460

Thr Glu Ile Val Arg Asp His Phe Ser Asp Met Gly Glu Ile Ala Thr
465                 470                 475                 480

Leu Tyr Val Gln Val Tyr Glu Ser Ser Leu Glu Ser Leu Val Gly Gly
                485                 490                 495

Val Ile Phe Glu Asp Gly Arg His Tyr Thr Phe Val Tyr Glu Asn Glu
            500                 505                 510

Asp Leu Val Tyr Glu Glu Glu Val Leu
        515                 520


<210> SEQ ID NO 51
<211> LENGTH: 1122
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 51

atgaaaaaaa tcgttaaata ctcatctctt gcagcccttg ctcttgttgc tgcaggtgtg      60

cttgcggctt gctcaggggg tgctaagaaa gaaggagaag cagctagcaa gaaagaaatc     120

atcgttgcaa ccaatggatc accaaagcca tttatctatg aagaaaatgg cgaattgact     180

ggttacgaga ttgaagtcgt tcgcgctatc tttaaagatt ctgacaaata tgatgtcaag     240

tttgaaaaga cagaatggtc aggtgtcttt gctggtcttg acgctgatcg ttacaatatg     300

gctgtcaaca atcttagcta cactaaagaa cgtgcggaga aatacctcta tgccgcacca     360

attgcccaaa atcctaatgt ccttgtcgtg aagaaagatg actctagtat caagtctctc     420

gatgatatcg gtggaaaatc gacggaagtc gttcaagcca ctacatcagc taagcagtta     480

gaagcataca atgctgaaca cacggacaac ccaactatcc ttaactatac taaggcagac     540

ttccaacaaa tcatggtacg tttgagcgat ggacaatttg actataagat tttgataaa     600

atcggtgttg aaacagtgat caagaaccaa ggtttggaca acttgaaagt tatcgaactt     660

ccaagcgacc aacaaccgta cgtttaccca cttcttgctc agggtcaaga tgagttgaaa     720

tcgtttgtag acaaacgcat caaagaactt tataaagatg gaactcttga aaaattgtct     780

aaacaattct tcggagacac ttatctaccg gcagaagctg atattaaaaa tggtatgaaa     840

gctaaaaaaa tgtggatggc aggcttggct ctgctaggta tcggaagcct tgctcttgct     900

acgaaaaaag ttgcagatga ccgtaagctc atgaagactc aggaagagtt gacagagatt     960

gtgcgagacc atttttccga catgggggaa attgcgaccc tttatgttca agtttacgaa    1020

agcagtctgg agagcttggt tggtggcgtc atttttgagg atggccgtca ttataccttt    1080

gtctatgaaa atgaagacct agtctatgag gaggaagtct ta                       1122


<210> SEQ ID NO 52
<211> LENGTH: 374
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 52

Met Lys Lys Ile Val Lys Tyr Ser Ser Leu Ala Ala Leu Ala Leu Val
1               5                   10                  15
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Ala Ala Gly Val Leu Ala Ala Cys Ser Gly Gly Ala Lys Lys Glu Gly
            20                  25                  30

Glu Ala Ala Ser Lys Lys Glu Ile Ile Val Ala Thr Asn Gly Ser Pro
        35                  40                  45

Lys Pro Phe Ile Tyr Glu Glu Asn Gly Glu Leu Thr Gly Tyr Glu Ile
    50                  55                  60

Glu Val Val Arg Ala Ile Phe Lys Asp Ser Asp Lys Tyr Asp Val Lys
65                  70                  75                  80

Phe Glu Lys Thr Glu Trp Ser Gly Val Phe Ala Gly Leu Asp Ala Asp
                85                  90                  95

Arg Tyr Asn Met Ala Val Asn Asn Leu Ser Tyr Thr Lys Glu Arg Ala
            100                 105                 110

Glu Lys Tyr Leu Tyr Ala Ala Pro Ile Ala Gln Asn Pro Asn Val Leu
        115                 120                 125

Val Val Lys Lys Asp Asp Ser Ser Ile Lys Ser Leu Asp Asp Ile Gly
    130                 135                 140

Gly Lys Ser Thr Glu Val Val Gln Ala Thr Thr Ser Ala Lys Gln Leu
145                 150                 155                 160

Glu Ala Tyr Asn Ala Glu His Thr Asp Asn Pro Thr Ile Leu Asn Tyr
                165                 170                 175

Thr Lys Ala Asp Phe Gln Gln Ile Met Val Arg Leu Ser Asp Gly Gln
            180                 185                 190

Phe Asp Tyr Lys Ile Phe Asp Lys Ile Gly Val Glu Thr Val Ile Lys
        195                 200                 205

Asn Gln Gly Leu Asp Asn Leu Lys Val Ile Glu Leu Pro Ser Asp Gln
    210                 215                 220

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

Ser Phe Val Asp Lys Arg Ile Lys Glu Leu Tyr Lys Asp Gly Thr Leu
                245                 250                 255

Glu Lys Leu Ser Lys Gln Phe Phe Gly Asp Thr Tyr Leu Pro Ala Glu
            260                 265                 270

Ala Asp Ile Lys Asn Gly Met Lys Ala Lys Lys Met Trp Met Ala Gly
        275                 280                 285

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

Ala Asp Asp Arg Lys Leu Met Lys Thr Gln Glu Glu Leu Thr Glu Ile
305                 310                 315                 320

Val Arg Asp His Phe Ser Asp Met Gly Glu Ile Ala Thr Leu Tyr Val
                325                 330                 335

Gln Val Tyr Glu Ser Ser Leu Glu Ser Leu Val Gly Gly Val Ile Phe
            340                 345                 350

Glu Asp Gly Arg His Tyr Thr Phe Val Tyr Glu Asn Glu Asp Leu Val
        355                 360                 365

Tyr Glu Glu Glu Val Leu
    370


<210> SEQ ID NO 53
<211> LENGTH: 2322
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic
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<400> SEQUENCE: 53

atgtcatcta aatttatgaa gagcgctgcg gtgcttggaa ctgctacact tgctagcttg 60

cttttggtag cttgcggaag caaaactgct gataagcctg ctgattctgg ttcatctgaa 120

gtcaaagaac tcactgtata tgtagacgag ggatataaga gctatattga agaggttgct 180

aaagcttatg aaaaagaagc tggagtaaaa gtcactctta aaactggtga tgctctagga 240

ggtcttgata aactttctct tgacaaccaa tctggtaatg tccctgatgt tatgatggct 300

ccatacgacc gtgtaggtag ccttggttct gacggacaac tttcagaagt gaaattgagc 360

gatggtgcta aaacagacga cacaactaaa tctcttgtaa cagctgctaa tggtaaagtt 420

tacggtgctc ctgccgttat cgagtcactt gttatgtact acaacaaaga cttggtgaaa 480

gatgctccaa aaacatttgc tgacttggaa aaccttgcta aagatagcaa atacgcattc 540

gctggtgaag atggtaaaac tactgccttc ctagctgact ggacaaactt ctactataca 600

tatggacttc ttgccggtaa cggtgcttac gtctttggcc aaaacggtaa agacgctaaa 660

gacatcggtc ttgcaaacga cggttctatc gtaggtatca actacgctaa atcttggtac 720

gaaaaatggc ctaaaggtat gcaagataca gaaggtgctg gaaacttaat ccaaactcaa 780

ttccaagaag gtaaaacagc tgctatcatc gacggacctt ggaaagctca agcctttaaa 840

gatgctaaag taaactacgg agttgcaact atcccaactc ttccaaatgg aaaagaatat 900

gctgcattcg gtggtggtaa agcttgggtc attcctcaag ccgttaagaa ccttgaagct 960

tctcaaaaat ttgtagactt ccttgttgca actgaacaac aaaaagtatt atatgataag 1020

actaacgaaa tcccagctaa tactgaggct cgttcatacg ctgaaggtaa aaacgatgag 1080

ttgacaacag ctgttatcaa acagttcaag aacactcaac cactgccaaa catctctcaa 1140

atgtctgcag tttgggatcc agcgaaaaat atgctctttg atgctgtaag tggtcaaaaa 1200

gatgctaaaa cagctgctaa cgatgctgta acattgatca aagaaacaat caaacaaaaa 1260

tttggtgaaa atggtatgaa agctaaaaaa atgtggatgg caggcttggc tctgctaggt 1320

atcggaagcc ttgctcttgc tacgaaaaaa gttgcagatg accgtaagct catgaagact 1380

caggaagagt tgacagagat tgtgcgagac catttttccg acatggggga aattgcgacc 1440

ctttatgttc aagtttacga aagcagtctg gagagcttgg ttggtggcgt catttttgag 1500

gatggccgtc attatacctt tgtctatgaa aatgaagacc tagtctatga ggaggaagtc 1560

ttatgctcag gggtgctaa gaaagaagga gaagcagcta gcaagaaaga aatcatcgtt 1620

gcaaccaatg gatcaccaaa gccatttatc tatgaagaaa atggcgaatt gactggttac 1680

gagattgaag tcgttcgcgc tatctttaaa gattctgaca aatatgatgt caagtttgaa 1740

aagacagaat ggtcaggtgt ctttgctggt cttgacgctg atcgttacaa tatggctgtc 1800

aacaatctta gctacactaa agaacgtgcg gagaaatacc tctatgccgc accaattgcc 1860

caaaatccta atgtccttgt cgtgaagaaa gatgactcta gtatcaagtc tctcgatgat 1920

atcggtggaa aatcgacgga agtcgttcaa gccactacat cagctaagca gttagaagca 1980

tacaatgctg aacacacgga caacccaact atccttaact atactaaggc agacttccaa 2040

caaatcatgg tacgtttgag cgatggacaa tttgactata agatttttga taaaatcggt 2100

gttgaaacag tgatcaagaa ccaaggtttg gacaacttga aagttatcga acttccaagc 2160

gaccaacaac cgtacgttta cccacttctt gctcagggtc aagatgagtt gaaatcgttt 2220

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gtagacaaac gcatcaaaga actttataaa gatggaactc ttgaaaaatt gtctaaacaa   2280

ttcttcggag acacttatct accggcagaa gctgatatta aa                       2322


<210> SEQ ID NO 54
<211> LENGTH: 773
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 54

Met Ser Ser Lys Phe Met Lys Ser Ala Ala Val Leu Gly Thr Ala Thr
1               5                   10                  15

Leu Ala Ser Leu Leu Leu Val Ala Cys Gly Ser Lys Thr Ala Asp Lys
            20                  25                  30

Pro Ala Asp Ser Gly Ser Ser Glu Val Lys Glu Leu Thr Val Tyr Val
        35                  40                  45

Asp Glu Gly Tyr Lys Ser Tyr Ile Glu Glu Val Ala Lys Ala Tyr Glu
    50                  55                  60

Lys Glu Ala Gly Val Lys Val Thr Leu Lys Thr Gly Asp Ala Leu Gly
65                  70                  75                  80

Gly Leu Asp Lys Leu Ser Leu Asp Asn Gln Ser Gly Asn Val Pro Asp
                85                  90                  95

Val Met Met Ala Pro Tyr Asp Arg Val Gly Ser Leu Gly Ser Asp Gly
            100                 105                 110

Gln Leu Ser Glu Val Lys Leu Ser Asp Gly Ala Lys Thr Asp Asp Thr
        115                 120                 125

Thr Lys Ser Leu Val Thr Ala Ala Asn Gly Lys Val Tyr Gly Ala Pro
    130                 135                 140

Ala Val Ile Glu Ser Leu Val Met Tyr Tyr Asn Lys Asp Leu Val Lys
145                 150                 155                 160

Asp Ala Pro Lys Thr Phe Ala Asp Leu Glu Asn Leu Ala Lys Asp Ser
                165                 170                 175

Lys Tyr Ala Phe Ala Gly Glu Asp Gly Lys Thr Thr Ala Phe Leu Ala
            180                 185                 190

Asp Trp Thr Asn Phe Tyr Tyr Thr Tyr Gly Leu Leu Ala Gly Asn Gly
        195                 200                 205

Ala Tyr Val Phe Gly Gln Asn Gly Lys Asp Ala Lys Asp Ile Gly Leu
    210                 215                 220

Ala Asn Asp Gly Ser Ile Val Gly Ile Asn Tyr Ala Lys Ser Trp Tyr
225                 230                 235                 240

Glu Lys Trp Pro Lys Gly Met Gln Asp Thr Glu Gly Ala Gly Asn Leu
                245                 250                 255

Ile Gln Thr Gln Phe Gln Glu Gly Lys Thr Ala Ala Ile Ile Asp Gly
            260                 265                 270

Pro Trp Lys Ala Gln Ala Phe Lys Asp Ala Lys Val Asn Tyr Gly Val
        275                 280                 285

Ala Thr Ile Pro Thr Leu Pro Asn Gly Lys Glu Tyr Ala Ala Phe Gly
    290                 295                 300

Gly Gly Lys Ala Trp Val Ile Pro Gln Ala Val Lys Asn Leu Glu Ala
305                 310                 315                 320

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

Leu Tyr Asp Lys Thr Asn Glu Ile Pro Ala Asn Thr Glu Ala Arg Ser
            340                 345                 350

Tyr Ala Glu Gly Lys Asn Asp Glu Leu Thr Thr Ala Val Ile Lys Gln
        355                 360                 365

Phe Lys Asn Thr Gln Pro Leu Pro Asn Ile Ser Gln Met Ser Ala Val
    370                 375                 380

Trp Asp Pro Ala Lys Asn Met Leu Phe Asp Ala Val Ser Gly Gln Lys
385                 390                 395                 400

Asp Ala Lys Thr Ala Ala Asn Asp Ala Val Thr Leu Ile Lys Glu Thr
                405                 410                 415

Ile Lys Gln Lys Phe Gly Glu Asn Gly Met Lys Ala Lys Lys Met Trp
            420                 425                 430

Met Ala Gly Leu Ala Leu Leu Gly Ile Gly Ser Leu Ala Leu Ala Thr
        435                 440                 445

Lys Lys Val Ala Asp Asp Arg Lys Leu Met Lys Thr Gln Glu Glu Leu
    450                 455                 460

Thr Glu Ile Val Arg Asp His Phe Ser Asp Met Gly Glu Ile Ala Thr
465                 470                 475                 480

Leu Tyr Val Gln Val Tyr Glu Ser Ser Leu Glu Ser Leu Val Gly Gly
                485                 490                 495

Val Ile Phe Glu Asp Gly Arg His Tyr Thr Phe Val Tyr Glu Asn Glu
            500                 505                 510

Asp Leu Val Tyr Glu Glu Glu Val Leu Ser Gly Gly Ala Lys Lys Glu
        515                 520                 525

Gly Glu Ala Ala Ser Lys Lys Glu Ile Ile Val Ala Thr Asn Gly Ser
    530                 535                 540

Pro Lys Pro Phe Ile Tyr Glu Glu Asn Gly Glu Leu Thr Gly Tyr Glu
545                 550                 555                 560

Ile Glu Val Val Arg Ala Ile Phe Lys Asp Ser Asp Lys Tyr Asp Val
                565                 570                 575

Lys Phe Glu Lys Thr Glu Trp Ser Gly Val Phe Ala Gly Leu Asp Ala
            580                 585                 590

Asp Arg Tyr Asn Met Ala Val Asn Asn Leu Ser Tyr Thr Lys Glu Arg
        595                 600                 605

Ala Glu Lys Tyr Leu Tyr Ala Ala Pro Ile Ala Gln Asn Pro Asn Val
    610                 615                 620

Leu Val Val Lys Lys Asp Asp Ser Ser Ile Lys Ser Leu Asp Asp Ile
625                 630                 635                 640

Gly Gly Lys Ser Thr Glu Val Val Gln Ala Thr Thr Ser Ala Lys Gln
                645                 650                 655

Leu Glu Ala Tyr Asn Ala Glu His Thr Asp Asn Pro Thr Ile Leu Asn
            660                 665                 670

Tyr Thr Lys Ala Asp Phe Gln Gln Ile Met Val Arg Leu Ser Asp Gly
        675                 680                 685

Gln Phe Asp Tyr Lys Ile Phe Asp Lys Ile Gly Val Glu Thr Val Ile
    690                 695                 700

Lys Asn Gln Gly Leu Asp Asn Leu Lys Val Ile Glu Leu Pro Ser Asp
705                 710                 715                 720

Gln Gln Pro Tyr Val Tyr Pro Leu Leu Ala Gln Gly Gln Asp Glu Leu
                725                 730                 735
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Lys Ser Phe Val Asp Lys Arg Ile Lys Glu Leu Tyr Lys Asp Gly Thr
740 745 750

Leu Glu Lys Leu Ser Lys Gln Phe Phe Gly Asp Thr Tyr Leu Pro Ala
755 760 765

Glu Ala Asp Ile Lys
770

<210> SEQ ID NO 55
<211> LENGTH: 2337
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 55

atgaaaaaaa tcgttaaata ctcatctctt gcagcccttg ctcttgttgc tgcaggtgtg 60

cttgcggctt gctcaggggg tgctaagaaa gaaggagaag cagctagcaa gaaagaaatc 120

atcgttgcaa ccaatggatc accaaagcca tttatctatg aagaaaatgg cgaattgact 180

ggttacgaga ttgaagtcgt tcgcgctatc tttaaagatt ctgacaaata tgatgtcaag 240

tttgaaaaga cagaatggtc aggtgtcttt gctggtcttg acgctgatcg ttacaatatg 300

gctgtcaaca atcttagcta cactaaagaa cgtgcggaga aatacctcta tgccgcacca 360

attgcccaaa atcctaatgt ccttgtcgtg aagaaagatg actctagtat caagtctctc 420

gatgatatcg gtggaaaatc gacggaagtc gttcaagcca ctacatcagc taagcagtta 480

gaagcataca atgctgaaca cacggacaac ccaactatcc ttaactatac taaggcagac 540

ttccaacaaa tcatggtacg tttgagcgat ggacaatttg actataagat tttgataaa 600

atcggtgttg aaacagtgat caagaaccaa ggtttggaca acttgaaagt tatcgaactt 660

ccaagcgacc aacaaccgta cgtttaccca cttcttgctc agggtcaaga tgagttgaaa 720

tcgtttgtag acaaacgcat caaagaactt tataaagatg gaactcttga aaaattgtct 780

aaacaattct tcggagacac ttatctaccg gcagaagctg atattaaaaa tggtatgaaa 840

gctaaaaaaa tgtggatggc aggcttggct ctgctaggta tcggaagcct tgctcttgct 900

acgaaaaaag ttgcagatga ccgtaagctc atgaagactc aggaagagtt gacagagatt 960

gtgcgagacc atttttccga catgggggaa attgcgaccc tttatgttca agtttacgaa 1020

agcagtctgg agagcttggt tggtggcgtc atttttgagg atggccgtca ttataccttt 1080

gtctatgaaa atgaagacct agtctatgag gaggaagtct taggaagcaa aactgctgat 1140

aagcctgctg attctggttc atctgaagtc aaagaactca ctgtatatgt agacgaggga 1200

tataagagct atattgaaga ggttgctaaa gcttatgaaa aagaagctgg agtaaaagtc 1260

actcttaaaa ctggtgatgc tctaggaggt cttgataaac tttctcttga caaccaatct 1320

ggtaatgtcc ctgatgttat gatggctcca tacgaccgtg taggtagcct tggttctgac 1380

ggacaacttt cagaagtgaa attgagcgat ggtgctaaaa cagacgacac aactaaatct 1440

cttgtaacag ctgctaatgg taaagtttac ggtgctcctg ccgttatcga gtcacttgtt 1500

atgtactaca acaaagactt ggtgaaagat gctccaaaaa catttgctga cttggaaaac 1560

cttgctaaag atagcaaata cgcattcgct ggtgaagatg gtaaaactac tgccttccta 1620

gctgactgga caaacttcta ctatacatat ggacttcttg ccggtaacgg tgcttacgtc 1680

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tttggccaaa acggtaaaga cgctaaagac atcggtcttg caaacgacgg ttctatcgta   1740

ggtatcaact acgctaaatc ttggtacgaa aaatggccta aaggtatgca agatacagaa   1800

ggtgctggaa acttaatcca aactcaattc caagaaggta aaacagctgc tatcatcgac   1860

ggaccttgga aagctcaagc ctttaaagat gctaaagtaa actacggagt tgcaactatc   1920

ccaactcttc caaatggaaa agaatatgct gcattcggtg gtggtaaagc ttgggtcatt   1980

cctcaagccg ttaagaacct tgaagcttct caaaaatttg tagacttcct tgttgcaact   2040

gaacaacaaa aagtattata tgataagact aacgaaatcc cagctaatac tgaggctcgt   2100

tcatacgctg aaggtaaaaa cgatgagttg acaacagctg ttatcaaaca gttcaagaac   2160

actcaaccac tgccaaacat ctctcaaatg tctgcagttt gggatccagc gaaaaatatg   2220

ctctttgatg ctgtaagtgg tcaaaaagat gctaaaacag ctgctaacga tgctgtaaca   2280

ttgatcaaag aaacaatcaa acaaaaattt ggtgaacacc accaccacca ccactga      2337
```

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<210> SEQ ID NO 56
<211> LENGTH: 772
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 56

Met Lys Lys Ile Val Lys Tyr Ser Ser Leu Ala Ala Leu Ala Leu Val
1               5                   10                  15

Ala Ala Gly Val Leu Ala Ala Cys Ser Gly Gly Ala Lys Lys Glu Gly
            20                  25                  30

Glu Ala Ala Ser Lys Lys Glu Ile Ile Val Ala Thr Asn Gly Ser Pro
        35                  40                  45

Lys Pro Phe Ile Tyr Glu Glu Asn Gly Glu Leu Thr Gly Tyr Glu Ile
    50                  55                  60

Glu Val Val Arg Ala Ile Phe Lys Asp Ser Asp Lys Tyr Asp Val Lys
65                  70                  75                  80

Phe Glu Lys Thr Glu Trp Ser Gly Val Phe Ala Gly Leu Asp Ala Asp
                85                  90                  95

Arg Tyr Asn Met Ala Val Asn Asn Leu Ser Tyr Thr Lys Glu Arg Ala
            100                 105                 110

Glu Lys Tyr Leu Tyr Ala Ala Pro Ile Ala Gln Asn Pro Asn Val Leu
        115                 120                 125

Val Val Lys Lys Asp Asp Ser Ser Ile Lys Ser Leu Asp Asp Ile Gly
    130                 135                 140

Gly Lys Ser Thr Glu Val Val Gln Ala Thr Thr Ser Ala Lys Gln Leu
145                 150                 155                 160

Glu Ala Tyr Asn Ala Glu His Thr Asp Asn Pro Thr Ile Leu Asn Tyr
                165                 170                 175

Thr Lys Ala Asp Phe Gln Gln Ile Met Val Arg Leu Ser Asp Gly Gln
            180                 185                 190

Phe Asp Tyr Lys Ile Phe Asp Lys Ile Gly Val Glu Thr Val Ile Lys
        195                 200                 205

Asn Gln Gly Leu Asp Asn Leu Lys Val Ile Glu Leu Pro Ser Asp Gln
    210                 215                 220

Gln Pro Tyr Val Tyr Pro Leu Leu Ala Gln Gly Gln Asp Glu Leu Lys
225                 230                 235                 240
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```
Ser Phe Val Asp Lys Arg Ile Lys Glu Leu Tyr Lys Asp Gly Thr Leu
                245                 250                 255

Glu Lys Leu Ser Lys Gln Phe Phe Gly Asp Thr Tyr Leu Pro Ala Glu
            260                 265                 270

Ala Asp Ile Lys Asn Gly Met Lys Ala Lys Lys Met Trp Met Ala Gly
        275                 280                 285

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

Ala Asp Asp Arg Lys Leu Met Lys Thr Gln Glu Glu Leu Thr Glu Ile
305                 310                 315                 320

Val Arg Asp His Phe Ser Asp Met Gly Glu Ile Ala Thr Leu Tyr Val
                325                 330                 335

Gln Val Tyr Glu Ser Ser Leu Glu Ser Leu Val Gly Gly Val Ile Phe
            340                 345                 350

Glu Asp Gly Arg His Tyr Thr Phe Val Tyr Glu Asn Glu Asp Leu Val
        355                 360                 365

Tyr Glu Glu Glu Val Leu Gly Ser Lys Thr Ala Asp Lys Pro Ala Asp
    370                 375                 380

Ser Gly Ser Ser Glu Val Lys Glu Leu Thr Val Tyr Val Asp Glu Gly
385                 390                 395                 400

Tyr Lys Ser Tyr Ile Glu Glu Val Ala Lys Ala Tyr Glu Lys Glu Ala
                405                 410                 415

Gly Val Lys Val Thr Leu Lys Thr Gly Asp Ala Leu Gly Gly Leu Asp
            420                 425                 430

Lys Leu Ser Leu Asp Asn Gln Ser Gly Asn Val Pro Asp Val Met Met
        435                 440                 445

Ala Pro Tyr Asp Arg Val Gly Ser Leu Gly Ser Asp Gly Gln Leu Ser
    450                 455                 460

Glu Val Lys Leu Ser Asp Gly Ala Lys Thr Asp Asp Thr Thr Lys Ser
465                 470                 475                 480

Leu Val Thr Ala Ala Asn Gly Lys Val Tyr Gly Ala Pro Ala Val Ile
                485                 490                 495

Glu Ser Leu Val Met Tyr Tyr Asn Lys Asp Leu Val Lys Asp Ala Pro
            500                 505                 510

Lys Thr Phe Ala Asp Leu Glu Asn Leu Ala Lys Asp Ser Lys Tyr Ala
        515                 520                 525

Phe Ala Gly Glu Asp Gly Lys Thr Thr Ala Phe Leu Ala Asp Trp Thr
    530                 535                 540

Asn Phe Tyr Tyr Thr Tyr Gly Leu Leu Ala Gly Asn Gly Ala Tyr Val
545                 550                 555                 560

Phe Gly Gln Asn Gly Lys Asp Ala Lys Asp Ile Gly Leu Ala Asn Asp
                565                 570                 575

Gly Ser Ile Val Gly Ile Asn Tyr Ala Lys Ser Trp Tyr Glu Lys Trp
            580                 585                 590

Pro Lys Gly Met Gln Asp Thr Glu Gly Ala Gly Asn Leu Ile Gln Thr
        595                 600                 605

Gln Phe Gln Glu Gly Lys Thr Ala Ala Ile Ile Asp Gly Pro Trp Lys
    610                 615                 620

Ala Gln Ala Phe Lys Asp Ala Lys Val Asn Tyr Gly Val Ala Thr Ile
625                 630                 635                 640
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Pro Thr Leu Pro Asn Gly Lys Glu Tyr Ala Ala Phe Gly Gly Gly Lys
                645                 650                 655

Ala Trp Val Ile Pro Gln Ala Val Lys Asn Leu Glu Ala Ser Gln Lys
            660                 665                 670

Phe Val Asp Phe Leu Val Ala Thr Glu Gln Gln Lys Val Leu Tyr Asp
        675                 680                 685

Lys Thr Asn Glu Ile Pro Ala Asn Thr Glu Ala Arg Ser Tyr Ala Glu
    690                 695                 700

Gly Lys Asn Asp Glu Leu Thr Thr Ala Val Ile Lys Gln Phe Lys Asn
705                 710                 715                 720

Thr Gln Pro Leu Pro Asn Ile Ser Gln Met Ser Ala Val Trp Asp Pro
                725                 730                 735

Ala Lys Asn Met Leu Phe Asp Ala Val Ser Gly Gln Lys Asp Ala Lys
            740                 745                 750

Thr Ala Ala Asn Asp Ala Val Thr Leu Ile Lys Glu Thr Ile Lys Gln
        755                 760                 765

Lys Phe Gly Glu
    770


<210> SEQ ID NO 57
<211> LENGTH: 2319
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 57

atgtcatcta aatttatgaa gagcgctgcg gtgcttggaa ctgctacact tgctagcttg     60

cttttggtag cttgcggaag caaaactgct gataagcctg ctgattctgg ttcatctgaa    120

gtcaaagaac tcactgtata tgtagacgag ggatataaga gctatattga agaggttgct    180

aaagcttatg aaaaagaagc tggagtaaaa gtcactctta aaactggtga tgctctagga    240

ggtcttgata aactttctct tgacaaccaa tctggtaatg tccctgatgt tatgatggct    300

ccatacgacc gtgtaggtag ccttggttct gacggacaac tttcagaagt gaaattgagc    360

gatggtgcta aaacagacga cacaactaaa tctcttgtaa cagctgctaa tggtaaagtt    420

tacggtgctc ctgccgttat cgagtcactt gttatgtact acaacaaaga cttggtgaaa    480

gatgctccaa aaacatttgc tgacttggaa aaccttgcta aagatagcaa atacgcattc    540

gctggtgaag atggtaaaac tactgccttc ctagctgact ggacaaactt ctactataca    600

tatggacttc ttgccggtaa cggtgcttac gtctttggcc aaaacggtaa agacgctaaa    660

gacatcggtc ttgcaaacga cggttctatc gtaggtatca actacgctaa atcttggtac    720

gaaaaatggc ctaaaggtat gcaagataca gaaggtgctg gaaacttaat ccaaactcaa    780

ttccaagaag gtaaaacagc tgctatcatc gacggacctt ggaaagctca agcctttaaa    840

gatgctaaag taaactacgg agttgcaact atcccaactc ttccaaatgg aaaagaatat    900

gctgcattcg gtggtggtaa agcttgggtc attcctcaag ccgttaagaa ccttgaagct    960

tctcaaaaat ttgtagactt ccttgttgca actgaacaac aaaaagtatt atatgataag   1020

actaacgaaa tcccagctaa tactgaggct cgttcatacg ctgaaggtaa aaacgatgag   1080

ttgacaacag ctgttatcaa acagttcaag aacactcaac cactgccaaa catctctcaa   1140

atgtctgcag tttgggatcc agcgaaaaat atgctctttg atgctgtaag tggtcaaaaa   1200
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gatgctaaaa cagctgctaa cgatgctgta acattgatca aagaaacaat caaacaaaaa   1260

tttggtgaat cagggggtgc taagaaagaa ggagaagcag ctagcaagaa agaaatcatc   1320

gttgcaacca atggatcacc aaagccattt atctatgaag aaaatggcga attgactggt   1380

tacgagattg aagtcgttcg cgctatcttt aaagattctg acaaatatga tgtcaagttt   1440

gaaaagacag aatggtcagg tgtctttgct ggtcttgacg ctgatcgtta caatatggct   1500

gtcaacaatc ttagctacac taaagaacgt gcggagaaat acctctatgc cgcaccaatt   1560

gcccaaaatc ctaatgtcct tgtcgtgaag aaagatgact ctagtatcaa gtctctcgat   1620

gatatcggtg gaaaatcgac ggaagtcgtt caagccacta catcagctaa gcagttagaa   1680

gcatacaatg ctgaacacac ggacaaccca actatcctta actatactaa ggcagacttc   1740

caacaaatca tggtacgttt gagcgatgga caatttgact ataagatttt tgataaaatc   1800

ggtgttgaaa cagtgatcaa gaaccaaggt ttggacaact tgaaagttat cgaacttcca   1860

agcgaccaac aaccgtacgt ttacccactt cttgctcagg gtcaagatga gttgaaatcg   1920

tttgtagaca aacgcatcaa agaactttat aaagatggaa ctcttgaaaa attgtctaaa   1980

caattcttcg gagacactta tctaccggca gaagctgata ttaaaaatgg tatgaaagct   2040

aaaaaaatgt ggatggcagg cttggctctg ctaggtatcg gaagccttgc tcttgctacg   2100

aaaaaagttg cagatgaccg taagctcatg aagactcagg aagagttgac agagattgtg   2160

cgagaccatt tttccgacat gggggaaatt gcgacccttt atgttcaagt ttacgaaagc   2220

agtctggaga gcttggttgg tggcgtcatt tttgaggatg gccgtcatta tacctttgtc   2280

tatgaaaatg aagacctagt ctatgaggag gaagtctta                          2319


<210> SEQ ID NO 58
<211> LENGTH: 773
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 58

Met Ser Ser Lys Phe Met Lys Ser Ala Ala Val Leu Gly Thr Ala Thr
1               5                   10                  15

Leu Ala Ser Leu Leu Leu Val Ala Cys Gly Ser Lys Thr Ala Asp Lys
            20                  25                  30

Pro Ala Asp Ser Gly Ser Ser Glu Val Lys Glu Leu Thr Val Tyr Val
        35                  40                  45

Asp Glu Gly Tyr Lys Ser Tyr Ile Glu Glu Val Ala Lys Ala Tyr Glu
    50                  55                  60

Lys Glu Ala Gly Val Lys Val Thr Leu Lys Thr Gly Asp Ala Leu Gly
65                  70                  75                  80

Gly Leu Asp Lys Leu Ser Leu Asp Asn Gln Ser Gly Asn Val Pro Asp
                85                  90                  95

Val Met Met Ala Pro Tyr Asp Arg Val Gly Ser Leu Gly Ser Asp Gly
            100                 105                 110

Gln Leu Ser Glu Val Lys Leu Ser Asp Gly Ala Lys Thr Asp Asp Thr
        115                 120                 125

Thr Lys Ser Leu Val Thr Ala Ala Asn Gly Lys Val Tyr Gly Ala Pro
    130                 135                 140
```

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```
Ala Val Ile Glu Ser Leu Val Met Tyr Tyr Asn Lys Asp Leu Val Lys
145                 150                 155                 160

Asp Ala Pro Lys Thr Phe Ala Asp Leu Glu Asn Leu Ala Lys Asp Ser
                165                 170                 175

Lys Tyr Ala Phe Ala Gly Glu Asp Gly Lys Thr Thr Ala Phe Leu Ala
            180                 185                 190

Asp Trp Thr Asn Phe Tyr Tyr Thr Tyr Gly Leu Leu Ala Gly Asn Gly
        195                 200                 205

Ala Tyr Val Phe Gly Gln Asn Gly Lys Asp Ala Lys Asp Ile Gly Leu
    210                 215                 220

Ala Asn Asp Gly Ser Ile Val Gly Ile Asn Tyr Ala Lys Ser Trp Tyr
225                 230                 235                 240

Glu Lys Trp Pro Lys Gly Met Gln Asp Thr Glu Gly Ala Gly Asn Leu
                245                 250                 255

Ile Gln Thr Gln Phe Gln Glu Gly Lys Thr Ala Ala Ile Ile Asp Gly
            260                 265                 270

Pro Trp Lys Ala Gln Ala Phe Lys Asp Ala Lys Val Asn Tyr Gly Val
        275                 280                 285

Ala Thr Ile Pro Thr Leu Pro Asn Gly Lys Glu Tyr Ala Ala Phe Gly
    290                 295                 300

Gly Gly Lys Ala Trp Val Ile Pro Gln Ala Val Lys Asn Leu Glu Ala
305                 310                 315                 320

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

Leu Tyr Asp Lys Thr Asn Glu Ile Pro Ala Asn Thr Glu Ala Arg Ser
            340                 345                 350

Tyr Ala Glu Gly Lys Asn Asp Glu Leu Thr Thr Ala Val Ile Lys Gln
        355                 360                 365

Phe Lys Asn Thr Gln Pro Leu Pro Asn Ile Ser Gln Met Ser Ala Val
    370                 375                 380

Trp Asp Pro Ala Lys Asn Met Leu Phe Asp Ala Val Ser Gly Gln Lys
385                 390                 395                 400

Asp Ala Lys Thr Ala Ala Asn Asp Ala Val Thr Leu Ile Lys Glu Thr
                405                 410                 415

Ile Lys Gln Lys Phe Gly Glu Ser Gly Gly Ala Lys Lys Glu Gly Glu
            420                 425                 430

Ala Ala Ser Lys Lys Glu Ile Ile Val Ala Thr Asn Gly Ser Pro Lys
        435                 440                 445

Pro Phe Ile Tyr Glu Glu Asn Gly Glu Leu Thr Gly Tyr Glu Ile Glu
    450                 455                 460

Val Val Arg Ala Ile Phe Lys Asp Ser Asp Lys Tyr Asp Val Lys Phe
465                 470                 475                 480

Glu Lys Thr Glu Trp Ser Gly Val Phe Ala Gly Leu Asp Ala Asp Arg
                485                 490                 495

Tyr Asn Met Ala Val Asn Asn Leu Ser Tyr Thr Lys Glu Arg Ala Glu
            500                 505                 510

Lys Tyr Leu Tyr Ala Ala Pro Ile Ala Gln Asn Pro Asn Val Leu Val
        515                 520                 525

Val Lys Lys Asp Asp Ser Ser Ile Lys Ser Leu Asp Asp Ile Gly Gly
    530                 535                 540

Lys Ser Thr Glu Val Val Gln Ala Thr Thr Ser Ala Lys Gln Leu Glu
```

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545                 550                 555                 560

Ala Tyr Asn Ala Glu His Thr Asp Asn Pro Thr Ile Leu Asn Tyr Thr
                565                 570                 575

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

Asp Tyr Lys Ile Phe Asp Lys Ile Gly Val Glu Thr Val Ile Lys Asn
        595                 600                 605

Gln Gly Leu Asp Asn Leu Lys Val Ile Glu Leu Pro Ser Asp Gln Gln
    610                 615                 620

Pro Tyr Val Tyr Pro Leu Leu Ala Gln Gly Gln Asp Glu Leu Lys Ser
625                 630                 635                 640

Phe Val Asp Lys Arg Ile Lys Glu Leu Tyr Lys Asp Gly Thr Leu Glu
                645                 650                 655

Lys Leu Ser Lys Gln Phe Phe Gly Asp Thr Tyr Leu Pro Ala Glu Ala
            660                 665                 670

Asp Ile Lys Asn Gly Met Lys Ala Lys Lys Met Trp Met Ala Gly Leu
        675                 680                 685

Ala Leu Leu Gly Ile Gly Ser Leu Ala Leu Ala Thr Lys Lys Val Ala
    690                 695                 700

Asp Asp Arg Lys Leu Met Lys Thr Gln Glu Glu Leu Thr Glu Ile Val
705                 710                 715                 720

Arg Asp His Phe Ser Asp Met Gly Glu Ile Ala Thr Leu Tyr Val Gln
                725                 730                 735

Val Tyr Glu Ser Ser Leu Glu Ser Leu Val Gly Gly Val Ile Phe Glu
            740                 745                 750

Asp Gly Arg His Tyr Thr Phe Val Tyr Glu Asn Glu Asp Leu Val Tyr
        755                 760                 765

Glu Glu Glu Val Leu
    770
```

<210> SEQ ID NO 59
<211> LENGTH: 2316
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 59

```
atgaaaaaaa tcgttaaata ctcatctctt gcagcccttg ctcttgttgc tgcaggtgtg     60

cttgcggctt gctcaggggg tgctaagaaa gaaggagaag cagctagcaa gaaagaaatc    120

atcgttgcaa ccaatggatc accaaagcca tttatctatg aagaaaatgg cgaattgact    180

ggttacgaga ttgaagtcgt tcgcgctatc tttaaagatt ctgacaaata tgatgtcaag    240

tttgaaaaga cagaatggtc aggtgtcttt gctggtcttg acgctgatcg ttacaatatg    300

gctgtcaaca atcttagcta cactaaagaa cgtgcggaga aatacctcta tgccgcacca    360

attgcccaaa atcctaatgt ccttgtcgtg aagaaagatg actctagtat caagtctctc    420

gatgatatcg gtggaaaatc gacggaagtc gttcaagcca ctacatcagc taagcagtta    480

gaagcataca atgctgaaca cacggacaac ccaactatcc ttaactatac taaggcagac    540

ttccaacaaa tcatggtacg tttgagcgat ggacaatttg actataagat tttgataaa    600

atcggtgttg aaacagtgat caagaaccaa ggtttggaca acttgaaagt tatcgaactt    660
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ccaagcgacc aacaaccgta cgtttaccca cttcttgctc agggtcaaga tgagttgaaa    720

tcgtttgtag acaaacgcat caaagaactt tataaagatg gaactcttga aaaattgtct    780

aaacaattct tcggagacac ttatctaccg gcagaagctg atattaaagg aagcaaaact    840

gctgataagc ctgctgattc tggttcatct gaagtcaaag aactcactgt atatgtagac    900

gagggatata agagctatat tgaagaggtt gctaaagctt atgaaaaaga agctggagta    960

aaagtcactc ttaaaactgg tgatgctcta ggaggtcttg ataaactttc tcttgacaac   1020

caatctggta atgtccctga tgttatgatg gctccatacg accgtgtagg tagccttggt   1080

tctgacggac aactttcaga agtgaaattg agcgatggtg ctaaaacaga cgacacaact   1140

aaatctcttg taacagctgc taatggtaaa gtttacggtg ctcctgccgt tatcgagtca   1200

cttgttatgt actacaacaa agacttggtg aaagatgctc caaaaacatt tgctgacttg   1260

gaaaaccttg ctaaagatag caaatacgca ttcgctggtg aagatggtaa aactactgcc   1320

ttcctagctg actggacaaa cttctactat acatatggac ttcttgccgg taacggtgct   1380

tacgtctttg gccaaaacgg taaagacgct aaagacatcg gtcttgcaaa cgacggttct   1440

atcgtaggta tcaactacgc taaatcttgg tacgaaaaat ggcctaaagg tatgcaagat   1500

acagaaggtg ctggaaactt aatccaaact caattccaag aaggtaaaac agctgctatc   1560

atcgacggac cttggaaagc tcaagccttt aaagatgcta aagtaaacta cggagttgca   1620

actatcccaa ctcttccaaa tggaaaagaa tatgctgcat tcggtggtgg taaagcttgg   1680

gtcattcctc aagccgttaa gaaccttgaa gcttctcaaa aatttgtaga cttccttgtt   1740

gcaactgaac aacaaaaagt attatatgat aagactaacg aaatcccagc taatactgag   1800

gctcgttcat acgctgaagg taaaaacgat gagttgacaa cagctgttat caaacagttc   1860

aagaacactc aaccactgcc aaacatctct caaatgtctg cagtttggga tccagcgaaa   1920

aatatgctct ttgatgctgt aagtggtcaa aaagatgcta aaacagctgc taacgatgct   1980

gtaacattga tcaaagaaac aatcaaacaa aaatttggtg aaaatggtat gaaagctaaa   2040

aaaatgtgga tggcaggctt ggctctgcta ggtatcggaa gccttgctct tgctacgaaa   2100

aaagttgcag atgaccgtaa gctcatgaag actcaggaag agttgacaga gattgtgcga   2160

gaccattttt ccgacatggg ggaaattgcg accctttatg ttcaagttta cgaaagcagt   2220

ctggagagct tggttggtgg cgtcattttt gaggatggcc gtcattatac ctttgtctat   2280

gaaaatgaag acctagtcta tgaggaggaa gtctta                             2316
```

<210> SEQ ID NO 60
<211> LENGTH: 772
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 60

```
Met Lys Lys Ile Val Lys Tyr Ser Ser Leu Ala Ala Leu Ala Leu Val
1               5                   10                  15

Ala Ala Gly Val Leu Ala Ala Cys Ser Gly Gly Ala Lys Lys Glu Gly
            20                  25                  30

Glu Ala Ala Ser Lys Lys Glu Ile Ile Val Ala Thr Asn Gly Ser Pro
        35                  40                  45

Lys Pro Phe Ile Tyr Glu Glu Asn Gly Glu Leu Thr Gly Tyr Glu Ile
```

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    50                  55                  60

Glu Val Val Arg Ala Ile Phe Lys Asp Ser Asp Lys Tyr Asp Val Lys
65                  70                  75                  80

Phe Glu Lys Thr Glu Trp Ser Gly Val Phe Ala Gly Leu Asp Ala Asp
                85                  90                  95

Arg Tyr Asn Met Ala Val Asn Asn Leu Ser Tyr Thr Lys Glu Arg Ala
            100                 105                 110

Glu Lys Tyr Leu Tyr Ala Ala Pro Ile Ala Gln Asn Pro Asn Val Leu
        115                 120                 125

Val Val Lys Lys Asp Asp Ser Ser Ile Lys Ser Leu Asp Asp Ile Gly
    130                 135                 140

Gly Lys Ser Thr Glu Val Val Gln Ala Thr Thr Ser Ala Lys Gln Leu
145                 150                 155                 160

Glu Ala Tyr Asn Ala Glu His Thr Asp Asn Pro Thr Ile Leu Asn Tyr
                165                 170                 175

Thr Lys Ala Asp Phe Gln Gln Ile Met Val Arg Leu Ser Asp Gly Gln
            180                 185                 190

Phe Asp Tyr Lys Ile Phe Asp Lys Ile Gly Val Glu Thr Val Ile Lys
        195                 200                 205

Asn Gln Gly Leu Asp Asn Leu Lys Val Ile Glu Leu Pro Ser Asp Gln
    210                 215                 220

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

Ser Phe Val Asp Lys Arg Ile Lys Glu Leu Tyr Lys Asp Gly Thr Leu
                245                 250                 255

Glu Lys Leu Ser Lys Gln Phe Phe Gly Asp Thr Tyr Leu Pro Ala Glu
            260                 265                 270

Ala Asp Ile Lys Gly Ser Lys Thr Ala Asp Lys Pro Ala Asp Ser Gly
        275                 280                 285

Ser Ser Glu Val Lys Glu Leu Thr Val Tyr Val Asp Glu Gly Tyr Lys
    290                 295                 300

Ser Tyr Ile Glu Glu Val Ala Lys Ala Tyr Glu Lys Glu Ala Gly Val
305                 310                 315                 320

Lys Val Thr Leu Lys Thr Gly Asp Ala Leu Gly Gly Leu Asp Lys Leu
                325                 330                 335

Ser Leu Asp Asn Gln Ser Gly Asn Val Pro Asp Val Met Met Ala Pro
            340                 345                 350

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

Lys Leu Ser Asp Gly Ala Lys Thr Asp Asp Thr Thr Lys Ser Leu Val
    370                 375                 380

Thr Ala Ala Asn Gly Lys Val Tyr Gly Ala Pro Ala Val Ile Glu Ser
385                 390                 395                 400

Leu Val Met Tyr Tyr Asn Lys Asp Leu Val Lys Asp Ala Pro Lys Thr
                405                 410                 415

Phe Ala Asp Leu Glu Asn Leu Ala Lys Asp Ser Lys Tyr Ala Phe Ala
            420                 425                 430

Gly Glu Asp Gly Lys Thr Thr Ala Phe Leu Ala Asp Trp Thr Asn Phe
        435                 440                 445

Tyr Tyr Thr Tyr Gly Leu Leu Ala Gly Asn Gly Ala Tyr Val Phe Gly
    450                 455                 460
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Gln Asn Gly Lys Asp Ala Lys Asp Ile Gly Leu Ala Asn Asp Gly Ser
465                 470                 475                 480

Ile Val Gly Ile Asn Tyr Ala Lys Ser Trp Tyr Glu Lys Trp Pro Lys
                485                 490                 495

Gly Met Gln Asp Thr Glu Gly Ala Gly Asn Leu Ile Gln Thr Gln Phe
            500                 505                 510

Gln Glu Gly Lys Thr Ala Ala Ile Ile Asp Gly Pro Trp Lys Ala Gln
        515                 520                 525

Ala Phe Lys Asp Ala Lys Val Asn Tyr Gly Val Ala Thr Ile Pro Thr
    530                 535                 540

Leu Pro Asn Gly Lys Glu Tyr Ala Ala Phe Gly Gly Gly Lys Ala Trp
545                 550                 555                 560

Val Ile Pro Gln Ala Val Lys Asn Leu Glu Ala Ser Gln Lys Phe Val
                565                 570                 575

Asp Phe Leu Val Ala Thr Glu Gln Gln Lys Val Leu Tyr Asp Lys Thr
            580                 585                 590

Asn Glu Ile Pro Ala Asn Thr Glu Ala Arg Ser Tyr Ala Glu Gly Lys
        595                 600                 605

Asn Asp Glu Leu Thr Thr Ala Val Ile Lys Gln Phe Lys Asn Thr Gln
    610                 615                 620

Pro Leu Pro Asn Ile Ser Gln Met Ser Ala Val Trp Asp Pro Ala Lys
625                 630                 635                 640

Asn Met Leu Phe Asp Ala Val Ser Gly Gln Lys Asp Ala Lys Thr Ala
                645                 650                 655

Ala Asn Asp Ala Val Thr Leu Ile Lys Glu Thr Ile Lys Gln Lys Phe
            660                 665                 670

Gly Glu Asn Gly Met Lys Ala Lys Lys Met Trp Met Ala Gly Leu Ala
        675                 680                 685

Leu Leu Gly Ile Gly Ser Leu Ala Leu Ala Thr Lys Lys Val Ala Asp
    690                 695                 700

Asp Arg Lys Leu Met Lys Thr Gln Glu Glu Leu Thr Glu Ile Val Arg
705                 710                 715                 720

Asp His Phe Ser Asp Met Gly Glu Ile Ala Thr Leu Tyr Val Gln Val
                725                 730                 735

Tyr Glu Ser Ser Leu Glu Ser Leu Val Gly Gly Val Ile Phe Glu Asp
            740                 745                 750

Gly Arg His Tyr Thr Phe Val Tyr Glu Asn Glu Asp Leu Val Tyr Glu
        755                 760                 765

Glu Glu Val Leu
    770


<210> SEQ ID NO 61
<211> LENGTH: 1170
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 61

atgaaaaaaa tcgttaaata ctcatctctt gcagcccttg ctcttgttgc tgcaggtgtg      60

cttgcggctt gctcaggggg tgctaagaaa gaaggagaag cagctagcaa gaaagaaatc     120

atcgttgcaa ccaatggatc accaaagcca tttatctatg aagaaaatgg cgaattgact     180
```

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```
ggttacgaga ttgaagtcgt tcgcgctatc tttaaagatt ctgacaaata tgatgtcaag     240

tttgaaaaga cagaatggtc aggtgtcttt gctggtcttg acgctgatcg ttacaatatg     300

gctgtcaaca atcttagcta cactaaagaa cgtgcggaga aatacctcta tgccgcacca     360

attgcccaaa atcctaatgt ccttgtcgtg aagaaagatg actctagtat caagtctctc     420

gatgatatcg gtggaaaatc gacggaagtc gttcaagcca ctacatcagc taagcagtta     480

gaagcataca atgctgaaca cacggacaac ccaactatcc ttaactatac taaggcagac     540

ttccaacaaa tcatggtacg tttgagcgat ggacaatttg actataagat ttttgataaa     600

atcggtgttg aaacagtgat caagaaccaa ggtttggaca acttgaaagt tatcgaactt     660

ccaagcgacc aacaaccgta cgtttaccca cttcttgctc agggtcaaga tgagttgaaa     720

tcgtttgtag acaaacgcat caaagaactt tataaagatg gaactcttga aaaattgtct     780

aaacaattct tcggagacac ttatctaccg gcagaagctg atattaaaat ggccatggcc     840

gacctgaaga aggccgtgaa cgagccggag aaaccggccg aagaggagcc ggagaacccg     900

gcaccggcac ctaaacctgc acctgcaccg cagcctgaga agcctgcccc tgcaccggca     960

ccgaaaccgg agaagagcgc cgaccagcag gcagaggaag actacgcccg ccgcagcgaa    1020

gaggagtaca atcgcctgac ccagcagcaa ccgccgaagg cagaaaagcc ggccccggcc    1080

ccggttccga aacctgaaca gccggcacct gcacctaaaa caggctggaa gcaggaaaac    1140

ggcatgtggc accaccacca ccaccactga                                     1170
```

<210> SEQ ID NO 62
<211> LENGTH: 389
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 62

```
Met Lys Lys Ile Val Lys Tyr Ser Ser Leu Ala Ala Leu Ala Leu Val
1               5                   10                  15

Ala Ala Gly Val Leu Ala Ala Cys Ser Gly Gly Ala Lys Lys Glu Gly
            20                  25                  30

Glu Ala Ala Ser Lys Lys Glu Ile Ile Val Ala Thr Asn Gly Ser Pro
        35                  40                  45

Lys Pro Phe Ile Tyr Glu Glu Asn Gly Glu Leu Thr Gly Tyr Glu Ile
    50                  55                  60

Glu Val Val Arg Ala Ile Phe Lys Asp Ser Asp Lys Tyr Asp Val Lys
65                  70                  75                  80

Phe Glu Lys Thr Glu Trp Ser Gly Val Phe Ala Gly Leu Asp Ala Asp
                85                  90                  95

Arg Tyr Asn Met Ala Val Asn Asn Leu Ser Tyr Thr Lys Glu Arg Ala
            100                 105                 110

Glu Lys Tyr Leu Tyr Ala Ala Pro Ile Ala Gln Asn Pro Asn Val Leu
        115                 120                 125

Val Val Lys Lys Asp Asp Ser Ser Ile Lys Ser Leu Asp Asp Ile Gly
    130                 135                 140

Gly Lys Ser Thr Glu Val Val Gln Ala Thr Thr Ser Ala Lys Gln Leu
145                 150                 155                 160

Glu Ala Tyr Asn Ala Glu His Thr Asp Asn Pro Thr Ile Leu Asn Tyr
```

-continued

```
                165                 170                 175

Thr Lys Ala Asp Phe Gln Gln Ile Met Val Arg Leu Ser Asp Gly Gln
            180                 185                 190

Phe Asp Tyr Lys Ile Phe Asp Lys Ile Gly Val Glu Thr Val Ile Lys
        195                 200                 205

Asn Gln Gly Leu Asp Asn Leu Lys Val Ile Glu Leu Pro Ser Asp Gln
    210                 215                 220

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

Ser Phe Val Asp Lys Arg Ile Lys Glu Leu Tyr Lys Asp Gly Thr Leu
                245                 250                 255

Glu Lys Leu Ser Lys Gln Phe Phe Gly Asp Thr Tyr Leu Pro Ala Glu
            260                 265                 270

Ala Asp Ile Lys Met Ala Met Ala Asp Leu Lys Lys Ala Val Asn Glu
        275                 280                 285

Pro Glu Lys Pro Ala Glu Glu Glu Pro Glu Asn Pro Ala Pro Ala Pro
    290                 295                 300

Lys Pro Ala Pro Ala Pro Gln Pro Glu Lys Pro Ala Pro Ala Pro Ala
305                 310                 315                 320

Pro Lys Pro Glu Lys Ser Ala Asp Gln Gln Ala Glu Glu Asp Tyr Ala
                325                 330                 335

Arg Arg Ser Glu Glu Glu Tyr Asn Arg Leu Thr Gln Gln Gln Pro Pro
            340                 345                 350

Lys Ala Glu Lys Pro Ala Pro Ala Pro Val Pro Lys Pro Glu Gln Pro
        355                 360                 365

Ala Pro Ala Pro Lys Thr Gly Trp Lys Gln Glu Asn Gly Met Trp His
    370                 375                 380

His His His His His
385
```

<210> SEQ ID NO 63
<211> LENGTH: 1215
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 63

```
atgaaaaaaa tcgttaaata ctcatctctt gcagcccttg ctcttgttgc tgcaggtgtg      60

cttgcggctt gctcaggggg tgctaagaaa gaaggagaag cagctagcaa gaaagaaatc     120

atcgttgcaa ccaatggatc accaaagcca tttatctatg aagaaaatgg cgaattgact     180

ggttacgaga ttgaagtcgt tcgcgctatc tttaaagatt ctgacaaata tgatgtcaag     240

tttgaaaaga cagaatggtc aggtgtcttt gctggtcttg acgctgatcg ttacaatatg     300

gctgtcaaca atcttagcta cactaaagaa cgtgcggaga aatacctcta tgccgcacca     360

attgcccaaa atcctaatgt ccttgtcgtg aagaaagatg actctagtat caagtctctc     420

gatgatatcg gtggaaaatc gacggaagtc gttcaagcca ctacatcagc taagcagtta     480

gaagcataca atgctgaaca cacggacaac ccaactatcc ttaactatac taaggcagac     540

ttccaacaaa tcatggtacg tttgagcgat ggacaatttg actataagat ttttgataaa     600

atcggtgttg aaacagtgat caagaaccaa ggtttggaca acttgaaagt tatcgaactt     660
```

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```
ccaagcgacc aacaaccgta cgtttaccca cttcttgctc agggtcaaga tgagttgaaa    720

tcgtttgtag acaaacgcat caaagaactt tataaagatg gaactcttga aaaattgtct    780

aaacaattct tcggagacac ttatctaccg gcagaagctg atattaaata cttcaaagag    840

ggcttagaga agaccatcgc cgccaagaag gccgagttag agaaaaccga ggccgacctg    900

aagaaagccg tgaacgagcc ggagaagcct gcacctgcac ctgaaacacc tgcccctgaa    960

gcaccggccg aacagcctaa gccggcaccg gcacctcaac ctgccccggc accgaagccg   1020

gaaaaaccgg ccgagcagcc gaaaccggag aaaaccgacg accagcaggc agaagaggac   1080

tatgcccgcc gcagcgagga agagtacaac cgcctgaccc agcagcagcc tccgaaagcc   1140

gagaaaccgg ccccggcccc gaaaaccggc tggaagcagg agaacggcat gtggcaccac   1200

caccaccacc actga                                                    1215


<210> SEQ ID NO 64
<211> LENGTH: 404
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 64

Met Lys Lys Ile Val Lys Tyr Ser Ser Leu Ala Ala Leu Ala Leu Val
1               5                   10                  15

Ala Ala Gly Val Leu Ala Ala Cys Ser Gly Gly Ala Lys Lys Glu Gly
            20                  25                  30

Glu Ala Ala Ser Lys Lys Glu Ile Ile Val Ala Thr Asn Gly Ser Pro
        35                  40                  45

Lys Pro Phe Ile Tyr Glu Glu Asn Gly Glu Leu Thr Gly Tyr Glu Ile
    50                  55                  60

Glu Val Val Arg Ala Ile Phe Lys Asp Ser Asp Lys Tyr Asp Val Lys
65                  70                  75                  80

Phe Glu Lys Thr Glu Trp Ser Gly Val Phe Ala Gly Leu Asp Ala Asp
                85                  90                  95

Arg Tyr Asn Met Ala Val Asn Asn Leu Ser Tyr Thr Lys Glu Arg Ala
            100                 105                 110

Glu Lys Tyr Leu Tyr Ala Ala Pro Ile Ala Gln Asn Pro Asn Val Leu
        115                 120                 125

Val Val Lys Lys Asp Asp Ser Ser Ile Lys Ser Leu Asp Asp Ile Gly
    130                 135                 140

Gly Lys Ser Thr Glu Val Val Gln Ala Thr Thr Ser Ala Lys Gln Leu
145                 150                 155                 160

Glu Ala Tyr Asn Ala Glu His Thr Asp Asn Pro Thr Ile Leu Asn Tyr
                165                 170                 175

Thr Lys Ala Asp Phe Gln Gln Ile Met Val Arg Leu Ser Asp Gly Gln
            180                 185                 190

Phe Asp Tyr Lys Ile Phe Asp Lys Ile Gly Val Glu Thr Val Ile Lys
        195                 200                 205

Asn Gln Gly Leu Asp Asn Leu Lys Val Ile Glu Leu Pro Ser Asp Gln
    210                 215                 220

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

Ser Phe Val Asp Lys Arg Ile Lys Glu Leu Tyr Lys Asp Gly Thr Leu
```

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245 250 255

Glu Lys Leu Ser Lys Gln Phe Phe Gly Asp Thr Tyr Leu Pro Ala Glu
260 265 270

Ala Asp Ile Lys Tyr Phe Lys Glu Gly Leu Glu Lys Thr Ile Ala Ala
275 280 285

Lys Lys Ala Glu Leu Glu Lys Thr Glu Ala Asp Leu Lys Lys Ala Val
290 295 300

Asn Glu Pro Glu Lys Pro Ala Pro Ala Pro Glu Thr Pro Ala Pro Glu
305 310 315 320

Ala Pro Ala Glu Gln Pro Lys Pro Ala Pro Ala Pro Gln Pro Ala Pro
325 330 335

Ala Pro Lys Pro Glu Lys Pro Ala Glu Gln Pro Lys Pro Glu Lys Thr
340 345 350

Asp Asp Gln Gln Ala Glu Glu Asp Tyr Ala Arg Arg Ser Glu Glu Glu
355 360 365

Tyr Asn Arg Leu Thr Gln Gln Gln Pro Pro Lys Ala Glu Lys Pro Ala
370 375 380

Pro Ala Pro Lys Thr Gly Trp Lys Gln Glu Asn Gly Met Trp His His
385 390 395 400

His His His His

<210> SEQ ID NO 65
<211> LENGTH: 1611
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 65

atgtcatcta aatttatgaa gagcgctgcg gtgcttggaa ctgctacact tgctagcttg 60

cttttggtag cttgcggaag caaaactgct gataagcctg ctgattctgg ttcatctgaa 120

gtcaaagaac tcactgtata tgtagacgag ggatataaga gctatattga agaggttgct 180

aaagcttatg aaaaagaagc tggagtaaaa gtcactctta aaactggtga tgctctagga 240

ggtcttgata aactttctct tgacaaccaa tctggtaatg tccctgatgt tatgatggct 300

ccatacgacc gtgtaggtag ccttggttct gacggacaac tttcagaagt gaaattgagc 360

gatggtgcta aaacagacga cacaactaaa tctcttgtaa cagctgctaa tggtaaagtt 420

tacggtgctc ctgccgttat cgagtcactt gttatgtact acaacaaaga cttggtgaaa 480

gatgctccaa aaacatttgc tgacttggaa aaccttgcta aagatagcaa atacgcattc 540

gctggtgaag atggtaaaac tactgccttc ctagctgact ggacaaactt ctactataca 600

tatggacttc ttgccggtaa cggtgcttac gtctttggcc aaaacggtaa agacgctaaa 660

gacatcggtc ttgcaaacga cggttctatc gtaggtatca actacgctaa atcttggtac 720

gaaaaatggc ctaaaggtat gcaagataca gaaggtgctg gaaacttaat ccaaactcaa 780

ttccaagaag gtaaaacagc tgctatcatc gacggacctt ggaaagctca agcctttaaa 840

gatgctaaag taaactacgg agttgcaact atcccaactc ttccaaatgg aaaagaatat 900

gctgcattcg gtggtggtaa agcttgggtc attcctcaag ccgttaagaa ccttgaagct 960

tctcaaaaat ttgtagactt ccttgttgca actgaacaac aaaaagtatt atatgataag 1020

actaacgaaa tcccagctaa tactgaggct cgttcatacg ctgaaggtaa aaacgatgag 1080

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ttgacaacag ctgttatcaa acagttcaag aacactcaac cactgccaaa catctctcaa 1140

atgtctgcag tttgggatcc agcgaaaaat atgctctttg atgctgtaag tggtcaaaaa 1200

gatgctaaaa cagctgctaa cgatgctgta acattgatca aagaaacaat caaacaaaaa 1260

tttggtgaaa tggccatggc cgacctgaag aaggccgtga acgagccgga gaaaccggcc 1320

gaagaggagc cggagaaccc ggcaccggca cctaaacctg cacctgcacc gcagcctgag 1380

aagcctgccc ctgcaccggc accgaaaccg gagaagagcg ccgaccagca ggcagaggaa 1440

gactacgccc gccgcagcga agaggagtac aatcgcctga cccagcagca accgccgaag 1500

gcagaaaagc cggccccggc cccggttccg aaacctgaac agccggcacc tgcacctaaa 1560

acaggctgga agcaggaaaa cggcatgtgg caccaccacc accaccactg a 1611

<210> SEQ ID NO 66
<211> LENGTH: 536
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 66

```
Met Ser Ser Lys Phe Met Lys Ser Ala Ala Val Leu Gly Thr Ala Thr
1               5                   10                  15

Leu Ala Ser Leu Leu Leu Val Ala Cys Gly Ser Lys Thr Ala Asp Lys
            20                  25                  30

Pro Ala Asp Ser Gly Ser Ser Glu Val Lys Glu Leu Thr Val Tyr Val
        35                  40                  45

Asp Glu Gly Tyr Lys Ser Tyr Ile Glu Glu Val Ala Lys Ala Tyr Glu
    50                  55                  60

Lys Glu Ala Gly Val Lys Val Thr Leu Lys Thr Gly Asp Ala Leu Gly
65                  70                  75                  80

Gly Leu Asp Lys Leu Ser Leu Asp Asn Gln Ser Gly Asn Val Pro Asp
                85                  90                  95

Val Met Met Ala Pro Tyr Asp Arg Val Gly Ser Leu Gly Ser Asp Gly
            100                 105                 110

Gln Leu Ser Glu Val Lys Leu Ser Asp Gly Ala Lys Thr Asp Asp Thr
        115                 120                 125

Thr Lys Ser Leu Val Thr Ala Ala Asn Gly Lys Val Tyr Gly Ala Pro
    130                 135                 140

Ala Val Ile Glu Ser Leu Val Met Tyr Tyr Asn Lys Asp Leu Val Lys
145                 150                 155                 160

Asp Ala Pro Lys Thr Phe Ala Asp Leu Glu Asn Leu Ala Lys Asp Ser
                165                 170                 175

Lys Tyr Ala Phe Ala Gly Glu Asp Gly Lys Thr Thr Ala Phe Leu Ala
            180                 185                 190

Asp Trp Thr Asn Phe Tyr Tyr Thr Tyr Gly Leu Leu Ala Gly Asn Gly
        195                 200                 205

Ala Tyr Val Phe Gly Gln Asn Gly Lys Asp Ala Lys Asp Ile Gly Leu
    210                 215                 220

Ala Asn Asp Gly Ser Ile Val Gly Ile Asn Tyr Ala Lys Ser Trp Tyr
225                 230                 235                 240

Glu Lys Trp Pro Lys Gly Met Gln Asp Thr Glu Gly Ala Gly Asn Leu
                245                 250                 255
```

```
Ile Gln Thr Gln Phe Gln Glu Gly Lys Thr Ala Ala Ile Ile Asp Gly
            260                 265                 270

Pro Trp Lys Ala Gln Ala Phe Lys Asp Ala Lys Val Asn Tyr Gly Val
        275                 280                 285

Ala Thr Ile Pro Thr Leu Pro Asn Gly Lys Glu Tyr Ala Ala Phe Gly
    290                 295                 300

Gly Gly Lys Ala Trp Val Ile Pro Gln Ala Val Lys Asn Leu Glu Ala
305                 310                 315                 320

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

Leu Tyr Asp Lys Thr Asn Glu Ile Pro Ala Asn Thr Glu Ala Arg Ser
            340                 345                 350

Tyr Ala Glu Gly Lys Asn Asp Glu Leu Thr Thr Ala Val Ile Lys Gln
        355                 360                 365

Phe Lys Asn Thr Gln Pro Leu Pro Asn Ile Ser Gln Met Ser Ala Val
    370                 375                 380

Trp Asp Pro Ala Lys Asn Met Leu Phe Asp Ala Val Ser Gly Gln Lys
385                 390                 395                 400

Asp Ala Lys Thr Ala Ala Asn Asp Ala Val Thr Leu Ile Lys Glu Thr
                405                 410                 415

Ile Lys Gln Lys Phe Gly Glu Met Ala Met Ala Asp Leu Lys Lys Ala
            420                 425                 430

Val Asn Glu Pro Glu Lys Pro Ala Glu Glu Glu Pro Glu Asn Pro Ala
        435                 440                 445

Pro Ala Pro Lys Pro Ala Pro Ala Pro Gln Pro Glu Lys Pro Ala Pro
    450                 455                 460

Ala Pro Ala Pro Lys Pro Glu Lys Ser Ala Asp Gln Gln Ala Glu Glu
465                 470                 475                 480

Asp Tyr Ala Arg Arg Ser Glu Glu Glu Tyr Asn Arg Leu Thr Gln Gln
                485                 490                 495

Gln Pro Pro Lys Ala Glu Lys Pro Ala Pro Ala Pro Val Pro Lys Pro
            500                 505                 510

Glu Gln Pro Ala Pro Ala Pro Lys Thr Gly Trp Lys Gln Glu Asn Gly
        515                 520                 525

Met Trp His His His His His His
    530                 535
```

```
<210> SEQ ID NO 67
<211> LENGTH: 1656
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 67

atgtcatcta aatttatgaa gagcgctgcg gtgcttggaa ctgctacact tgctagcttg      60

cttttggtag cttgcggaag caaaactgct gataagcctg ctgattctgg ttcatctgaa     120

gtcaaagaac tcactgtata tgtagacgag ggatataaga gctatattga agaggttgct     180

aaagcttatg aaaaagaagc tggagtaaaa gtcactctta aaactggtga tgctctagga     240

ggtcttgata aactttctct tgacaaccaa tctggtaatg tccctgatgt tatgatggct     300

ccatacgacc gtgtaggtag ccttggttct gacggacaac tttcagaagt gaaattgagc     360
```

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```
gatggtgcta aaacagacga cacaactaaa tctcttgtaa cagctgctaa tggtaaagtt     420

tacggtgctc ctgccgttat cgagtcactt gttatgtact acaacaaaga cttggtgaaa     480

gatgctccaa aaacatttgc tgacttggaa aaccttgcta aagatagcaa atacgcattc     540

gctggtgaag atggtaaaac tactgccttc ctagctgact ggacaaactt ctactataca     600

tatggacttc ttgccggtaa cggtgcttac gtctttggcc aaaacggtaa agacgctaaa     660

gacatcggtc ttgcaaacga cggttctatc gtaggtatca actacgctaa atcttggtac     720

gaaaaatggc ctaaaggtat gcaagataca gaaggtgctg gaaacttaat ccaaactcaa     780

ttccaagaag gtaaaacagc tgctatcatc gacggacctt ggaaagctca agcctttaaa     840

gatgctaaag taaactacgg agttgcaact atcccaactc ttccaaatgg aaaagaatat     900

gctgcattcg gtggtggtaa agcttgggtc attcctcaag ccgttaagaa ccttgaagct     960

tctcaaaaat ttgtagactt ccttgttgca actgaacaac aaaaagtatt atatgataag    1020

actaacgaaa tcccagctaa tactgaggct cgttcatacg ctgaaggtaa aaacgatgag    1080

ttgacaacag ctgttatcaa acagttcaag aacactcaac cactgccaaa catctctcaa    1140

atgtctgcag tttgggatcc agcgaaaaat atgctctttg atgctgtaag tggtcaaaaa    1200

gatgctaaaa cagctgctaa cgatgctgta acattgatca aagaaacaat caaacaaaaa    1260

tttggtgaat acttcaaaga gggcttagag aagaccatcg ccgccaagaa ggccgagtta    1320

gagaaaaccg aggccgacct gaagaaagcc gtgaacgagc cggagaagcc tgcacctgca    1380

cctgaaacac ctgcccctga agcaccggcc gaacagccta agccggcacc ggcacctcaa    1440

cctgccccgg caccgaagcc ggaaaaaccg gccgagcagc cgaaaccgga gaaaaccgac    1500

gaccagcagg cagaagagga ctatgcccgc cgcagcgagg aagagtacaa ccgcctgacc    1560

cagcagcagc ctccgaaagc cgagaaaccg gccccggccc cgaaaaccgg ctggaagcag    1620

gagaacggca tgtggcacca ccaccaccac cactga                              1656


<210> SEQ ID NO 68
<211> LENGTH: 551
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 68

Met Ser Ser Lys Phe Met Lys Ser Ala Ala Val Leu Gly Thr Ala Thr
1               5                   10                  15

Leu Ala Ser Leu Leu Leu Val Ala Cys Gly Ser Lys Thr Ala Asp Lys
            20                  25                  30

Pro Ala Asp Ser Gly Ser Ser Glu Val Lys Glu Leu Thr Val Tyr Val
        35                  40                  45

Asp Glu Gly Tyr Lys Ser Tyr Ile Glu Glu Val Ala Lys Ala Tyr Glu
    50                  55                  60

Lys Glu Ala Gly Val Lys Val Thr Leu Lys Thr Gly Asp Ala Leu Gly
65                  70                  75                  80

Gly Leu Asp Lys Leu Ser Leu Asp Asn Gln Ser Gly Asn Val Pro Asp
                85                  90                  95

Val Met Met Ala Pro Tyr Asp Arg Val Gly Ser Leu Gly Ser Asp Gly
            100                 105                 110
```

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```
Gln Leu Ser Glu Val Lys Leu Ser Asp Gly Ala Lys Thr Asp Asp Thr
        115                 120                 125

Thr Lys Ser Leu Val Thr Ala Ala Asn Gly Lys Val Tyr Gly Ala Pro
    130                 135                 140

Ala Val Ile Glu Ser Leu Val Met Tyr Tyr Asn Lys Asp Leu Val Lys
145                 150                 155                 160

Asp Ala Pro Lys Thr Phe Ala Asp Leu Glu Asn Leu Ala Lys Asp Ser
                165                 170                 175

Lys Tyr Ala Phe Ala Gly Glu Asp Gly Lys Thr Thr Ala Phe Leu Ala
            180                 185                 190

Asp Trp Thr Asn Phe Tyr Tyr Thr Tyr Gly Leu Leu Ala Gly Asn Gly
        195                 200                 205

Ala Tyr Val Phe Gly Gln Asn Gly Lys Asp Ala Lys Asp Ile Gly Leu
    210                 215                 220

Ala Asn Asp Gly Ser Ile Val Gly Ile Asn Tyr Ala Lys Ser Trp Tyr
225                 230                 235                 240

Glu Lys Trp Pro Lys Gly Met Gln Asp Thr Glu Gly Ala Gly Asn Leu
                245                 250                 255

Ile Gln Thr Gln Phe Gln Glu Gly Lys Thr Ala Ala Ile Ile Asp Gly
            260                 265                 270

Pro Trp Lys Ala Gln Ala Phe Lys Asp Ala Lys Val Asn Tyr Gly Val
        275                 280                 285

Ala Thr Ile Pro Thr Leu Pro Asn Gly Lys Glu Tyr Ala Ala Phe Gly
    290                 295                 300

Gly Gly Lys Ala Trp Val Ile Pro Gln Ala Val Lys Asn Leu Glu Ala
305                 310                 315                 320

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

Leu Tyr Asp Lys Thr Asn Glu Ile Pro Ala Asn Thr Glu Ala Arg Ser
            340                 345                 350

Tyr Ala Glu Gly Lys Asn Asp Glu Leu Thr Thr Ala Val Ile Lys Gln
        355                 360                 365

Phe Lys Asn Thr Gln Pro Leu Pro Asn Ile Ser Gln Met Ser Ala Val
    370                 375                 380

Trp Asp Pro Ala Lys Asn Met Leu Phe Asp Ala Val Ser Gly Gln Lys
385                 390                 395                 400

Asp Ala Lys Thr Ala Ala Asn Asp Ala Val Thr Leu Ile Lys Glu Thr
                405                 410                 415

Ile Lys Gln Lys Phe Gly Glu Tyr Phe Lys Glu Gly Leu Glu Lys Thr
            420                 425                 430

Ile Ala Ala Lys Lys Ala Glu Leu Glu Lys Thr Glu Ala Asp Leu Lys
        435                 440                 445

Lys Ala Val Asn Glu Pro Glu Lys Pro Ala Pro Ala Pro Glu Thr Pro
    450                 455                 460

Ala Pro Glu Ala Pro Ala Glu Gln Pro Lys Pro Ala Pro Ala Pro Gln
465                 470                 475                 480

Pro Ala Pro Ala Pro Lys Pro Glu Lys Pro Ala Glu Gln Pro Lys Pro
                485                 490                 495

Glu Lys Thr Asp Asp Gln Gln Ala Glu Glu Asp Tyr Ala Arg Arg Ser
            500                 505                 510

Glu Glu Glu Tyr Asn Arg Leu Thr Gln Gln Gln Pro Pro Lys Ala Glu
```

-continued

        515   520   525

Lys Pro Ala Pro Ala Pro Lys Thr Gly Trp Lys Gln Glu Asn Gly Met
    530   535   540

Trp His His His His His His
545   550

<210> SEQ ID NO 69
<211> LENGTH: 1212
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 69

atgaaaaaaa tcgttaaata ctcatctctt gcagcccttg ctcttgttgc tgcaggtgtg   60

cttgcggctt gctcaggggg tgctaagaaa gaaggagaag cagctagcaa gaaagaaatc   120

atcgttgcaa ccaatggatc accaaagcca tttatctatg aagaaaatgg cgaattgact   180

ggttacgaga ttgaagtcgt tcgcgctatc tttaaagatt ctgacaaata tgatgtcaag   240

tttgaaaaga cagaatggtc aggtgtcttt gctggtcttg acgctgatcg ttacaatatg   300

gctgtcaaca atcttagcta cactaaagaa cgtgcggaga aatacctcta tgccgcacca   360

attgcccaaa atcctaatgt ccttgtcgtg aagaaagatg actctagtat caagtctctc   420

gatgatatcg gtggaaaatc gacggaagtc gttcaagcca ctacatcagc taagcagtta   480

gaagcataca atgctgaaca cacggacaac ccaactatcc ttaactatac taaggcagac   540

ttccaacaaa tcatggtacg tttgagcgat ggacaatttg actataagat tttgataaa   600

atcggtgttg aaacagtgat caagaaccaa ggtttggaca acttgaaagt tatcgaactt   660

ccaagcgacc aacaaccgta cgtttaccca cttcttgctc agggtcaaga tgagttgaaa   720

tcgtttgtag acaaacgcat caaagaactt tataaagatg gaactcttga aaaattgtct   780

aaacaattct tcggagacac ttatctaccg gcagaagctg atattaaagg cccgaagccg   840

caccgtatcc agagcacccc gaagggcagc atggccatgg cagacctgaa gaaggccgtg   900

aacgagccgg aaaaacctgc cgaagaggag ccggaaaatc ctgcccctgc acctaaacct   960

gcacctgccc ctcagccgga gaaaccggca cctgcaccgg cacctaagcc ggagaagagc   1020

gccgatcagc aggccgagga ggactatgcc cgtcgcagcg aagaggagta caaccgcctg   1080

acccagcaac agcctccgaa ggccgaaaaa ccggcccctg caccggtgcc taagcctgag   1140

caacctgccc cggccccgaa aaccggctgg aagcaggaaa acggcatgtg gcaccaccac   1200

caccaccact ga   1212

<210> SEQ ID NO 70
<211> LENGTH: 403
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 70

Met Lys Lys Ile Val Lys Tyr Ser Ser Leu Ala Ala Leu Ala Leu Val
1   5   10   15

Ala Ala Gly Val Leu Ala Ala Cys Ser Gly Gly Ala Lys Lys Glu Gly
            20   25   30

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Glu Ala Ala Ser Lys Lys Glu Ile Ile Val Ala Thr Asn Gly Ser Pro
        35                  40                  45

Lys Pro Phe Ile Tyr Glu Glu Asn Gly Glu Leu Thr Gly Tyr Glu Ile
    50                  55                  60

Glu Val Val Arg Ala Ile Phe Lys Asp Ser Asp Lys Tyr Asp Val Lys
65                  70                  75                  80

Phe Glu Lys Thr Glu Trp Ser Gly Val Phe Ala Gly Leu Asp Ala Asp
                85                  90                  95

Arg Tyr Asn Met Ala Val Asn Asn Leu Ser Tyr Thr Lys Glu Arg Ala
            100                 105                 110

Glu Lys Tyr Leu Tyr Ala Ala Pro Ile Ala Gln Asn Pro Asn Val Leu
        115                 120                 125

Val Val Lys Lys Asp Asp Ser Ser Ile Lys Ser Leu Asp Asp Ile Gly
    130                 135                 140

Gly Lys Ser Thr Glu Val Val Gln Ala Thr Thr Ser Ala Lys Gln Leu
145                 150                 155                 160

Glu Ala Tyr Asn Ala Glu His Thr Asp Asn Pro Thr Ile Leu Asn Tyr
                165                 170                 175

Thr Lys Ala Asp Phe Gln Gln Ile Met Val Arg Leu Ser Asp Gly Gln
            180                 185                 190

Phe Asp Tyr Lys Ile Phe Asp Lys Ile Gly Val Glu Thr Val Ile Lys
        195                 200                 205

Asn Gln Gly Leu Asp Asn Leu Lys Val Ile Glu Leu Pro Ser Asp Gln
    210                 215                 220

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

Ser Phe Val Asp Lys Arg Ile Lys Glu Leu Tyr Lys Asp Gly Thr Leu
                245                 250                 255

Glu Lys Leu Ser Lys Gln Phe Phe Gly Asp Thr Tyr Leu Pro Ala Glu
            260                 265                 270

Ala Asp Ile Lys Gly Pro Lys Pro His Arg Ile Gln Ser Thr Pro Lys
        275                 280                 285

Gly Ser Met Ala Met Ala Asp Leu Lys Lys Ala Val Asn Glu Pro Glu
    290                 295                 300

Lys Pro Ala Glu Glu Glu Pro Glu Asn Pro Ala Pro Ala Pro Lys Pro
305                 310                 315                 320

Ala Pro Ala Pro Gln Pro Glu Lys Pro Ala Pro Ala Pro Ala Pro Lys
                325                 330                 335

Pro Glu Lys Ser Ala Asp Gln Gln Ala Glu Glu Asp Tyr Ala Arg Arg
            340                 345                 350

Ser Glu Glu Glu Tyr Asn Arg Leu Thr Gln Gln Gln Pro Pro Lys Ala
        355                 360                 365

Glu Lys Pro Ala Pro Ala Pro Val Pro Lys Pro Glu Gln Pro Ala Pro
    370                 375                 380

Ala Pro Lys Thr Gly Trp Lys Gln Glu Asn Gly Met Trp His His His
385                 390                 395                 400

His His His


<210> SEQ ID NO 71
<211> LENGTH: 1257
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
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<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 71

atgaaaaaaa tcgttaaata ctcatctctt gcagcccttg ctcttgttgc tgcaggtgtg      60

cttgcggctt gctcaggggg tgctaagaaa gaaggagaag cagctagcaa gaaagaaatc     120

atcgttgcaa ccaatggatc accaaagcca tttatctatg aagaaaatgg cgaattgact     180

ggttacgaga ttgaagtcgt tcgcgctatc tttaaagatt ctgacaaata tgatgtcaag     240

tttgaaaaga cagaatggtc aggtgtcttt gctggtcttg acgctgatcg ttacaatatg     300

gctgtcaaca atcttagcta cactaaagaa cgtgcggaga aatacctcta tgccgcacca     360

attgcccaaa atcctaatgt ccttgtcgtg aagaaagatg actctagtat caagtctctc     420

gatgatatcg gtggaaaatc gacggaagtc gttcaagcca ctacatcagc taagcagtta     480

gaagcataca atgctgaaca cacggacaac ccaactatcc ttaactatac taaggcagac     540

ttccaacaaa tcatggtacg tttgagcgat ggacaatttg actataagat ttttgataaa     600

atcggtgttg aaacagtgat caagaaccaa ggtttggaca acttgaaagt tatcgaactt     660

ccaagcgacc aacaaccgta cgtttaccca cttcttgctc agggtcaaga tgagttgaaa     720

tcgtttgtag acaaacgcat caaagaactt tataaagatg gaactcttga aaaattgtct     780

aaacaattct tcggagacac ttatctaccg gcagaagctg atattaaagg cccgaagccg     840

caccgyatcc agagcacacc gaaaggcagc tacttcaaag agggcttaga gaagaccatc     900

gccgccaaga aggccgagtt agagaaaacc gaggccgacc tgaagaaggc cgtgaacgag     960

ccggagaaac ctgcacctgc accggagaca ccggcacctg aagcccctgc agagcagcct    1020

aaacctgccc ctgcacctca accggcacct gcacctaagc cggaaaaacc tgccgagcag    1080

ccgaagccgg agaaaaccga cgaccagcag gccgaagagg actatgcacg ccgcagcgaa    1140

gaggagtaca accgcttaac ccaacagcag ccgccgaagg cagaaaaacc ggcccctgcc    1200

cctaagaccg gttggaagca ggagaacggc atgtggcacc accaccacca ccactga       1257


<210> SEQ ID NO 72
<211> LENGTH: 418
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 72

Met Lys Lys Ile Val Lys Tyr Ser Ser Leu Ala Ala Leu Ala Leu Val
1               5                   10                  15

Ala Ala Gly Val Leu Ala Ala Cys Ser Gly Gly Ala Lys Lys Glu Gly
            20                  25                  30

Glu Ala Ala Ser Lys Lys Glu Ile Ile Val Ala Thr Asn Gly Ser Pro
        35                  40                  45

Lys Pro Phe Ile Tyr Glu Glu Asn Gly Glu Leu Thr Gly Tyr Glu Ile
    50                  55                  60

Glu Val Val Arg Ala Ile Phe Lys Asp Ser Asp Lys Tyr Asp Val Lys
65                  70                  75                  80

Phe Glu Lys Thr Glu Trp Ser Gly Val Phe Ala Gly Leu Asp Ala Asp
                85                  90                  95

Arg Tyr Asn Met Ala Val Asn Asn Leu Ser Tyr Thr Lys Glu Arg Ala
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            100                 105                 110

Glu Lys Tyr Leu Tyr Ala Ala Pro Ile Ala Gln Asn Pro Asn Val Leu
        115                 120                 125

Val Val Lys Lys Asp Asp Ser Ser Ile Lys Ser Leu Asp Asp Ile Gly
    130                 135                 140

Gly Lys Ser Thr Glu Val Val Gln Ala Thr Thr Ser Ala Lys Gln Leu
145                 150                 155                 160

Glu Ala Tyr Asn Ala Glu His Thr Asp Asn Pro Thr Ile Leu Asn Tyr
                165                 170                 175

Thr Lys Ala Asp Phe Gln Gln Ile Met Val Arg Leu Ser Asp Gly Gln
            180                 185                 190

Phe Asp Tyr Lys Ile Phe Asp Lys Ile Gly Val Glu Thr Val Ile Lys
        195                 200                 205

Asn Gln Gly Leu Asp Asn Leu Lys Val Ile Glu Leu Pro Ser Asp Gln
    210                 215                 220

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

Ser Phe Val Asp Lys Arg Ile Lys Glu Leu Tyr Lys Asp Gly Thr Leu
                245                 250                 255

Glu Lys Leu Ser Lys Gln Phe Phe Gly Asp Thr Tyr Leu Pro Ala Glu
            260                 265                 270

Ala Asp Ile Lys Gly Pro Lys Pro His Arg Ile Gln Ser Thr Pro Lys
        275                 280                 285

Gly Ser Tyr Phe Lys Glu Gly Leu Glu Lys Thr Ile Ala Ala Lys Lys
    290                 295                 300

Ala Glu Leu Glu Lys Thr Glu Ala Asp Leu Lys Lys Ala Val Asn Glu
305                 310                 315                 320

Pro Glu Lys Pro Ala Pro Ala Pro Glu Thr Pro Ala Pro Glu Ala Pro
                325                 330                 335

Ala Glu Gln Pro Lys Pro Ala Pro Ala Pro Gln Pro Ala Pro Ala Pro
            340                 345                 350

Lys Pro Glu Lys Pro Ala Glu Gln Pro Lys Pro Glu Lys Thr Asp Asp
        355                 360                 365

Gln Gln Ala Glu Glu Asp Tyr Ala Arg Arg Ser Glu Glu Glu Tyr Asn
    370                 375                 380

Arg Leu Thr Gln Gln Gln Pro Pro Lys Ala Glu Lys Pro Ala Pro Ala
385                 390                 395                 400

Pro Lys Thr Gly Trp Lys Gln Glu Asn Gly Met Trp His His His His
                405                 410                 415

His His


<210> SEQ ID NO 73
<211> LENGTH: 1653
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 73

atgtcatcta aatttatgaa gagcgctgcg gtgcttggaa ctgctacact tgctagcttg     60

cttttggtag cttgcggaag caaaactgct gataagcctg ctgattctgg ttcatctgaa    120

gtcaaagaac tcactgtata tgtagacgag ggatataaga gctatattga agaggttgct    180
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aaagcttatg aaaaagaagc tggagtaaaa gtcactctta aaactggtga tgctctagga    240

ggtcttgata aactttctct tgacaaccaa tctggtaatg tccctgatgt tatgatggct    300

ccatacgacc gtgtaggtag ccttggttct gacggacaac tttcagaagt gaaattgagc    360

gatggtgcta aaacagacga cacaactaaa tctcttgtaa cagctgctaa tggtaaagtt    420

tacggtgctc ctgccgttat cgagtcactt gttatgtact acaacaaaga cttggtgaaa    480

gatgctccaa aaacatttgc tgacttggaa aaccttgcta aagatagcaa atacgcattc    540

gctggtgaag atggtaaaac tactgccttc ctagctgact ggacaaactt ctactataca    600

tatggacttc ttgccggtaa cggtgcttac gtctttggcc aaaacggtaa agacgctaaa    660

gacatcggtc ttgcaaacga cggttctatc gtaggtatca actacgctaa atcttggtac    720

gaaaaatggc ctaaaggtat gcaagataca gaaggtgctg gaaacttaat ccaaactcaa    780

ttccaagaag gtaaaacagc tgctatcatc gacggacctt ggaaagctca agcctttaaa    840

gatgctaaag taaactacgg agttgcaact atcccaactc ttccaaatgg aaaagaatat    900

gctgcattcg gtggtggtaa agcttgggtc attcctcaag ccgttaagaa ccttgaagct    960

tctcaaaaat ttgtagactt ccttgttgca actgaacaac aaaaagtatt atatgataag   1020

actaacgaaa tcccagctaa tactgaggct cgttcatacg ctgaaggtaa aaacgatgag   1080

ttgacaacag ctgttatcaa acagttcaag aacactcaac cactgccaaa catctctcaa   1140

atgtctgcag tttgggatcc agcgaaaaat atgctctttg atgctgtaag tggtcaaaaa   1200

gatgctaaaa cagctgctaa cgatgctgta acattgatca aagaaacaat caaacaaaaa   1260

tttggtgaag gcccgaagcc gcaccgtatc cagagcaccc cgaagggcag catggccatg   1320

gcagacctga agaaggccgt gaacgagccg gaaaaacctg ccgaagagga gccggaaaat   1380

cctgcccctg cacctaaacc tgcacctgcc cctcagccgg agaaaccggc acctgcaccg   1440

gcacctaagc cggagaagag cgccgatcag caggccgagg aggactatgc ccgtcgcagc   1500

gaagaggagt acaaccgcct gacccagcaa cagcctccga aggccgaaaa accggcccct   1560

gcaccggtgc ctaagcctga gcaacctgcc ccggccccga aaccggctg gaagcaggag   1620

aatggcatgt ggcaccacca ccaccaccac tga                                1653
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<210> SEQ ID NO 74
<211> LENGTH: 550
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 74

Met Ser Ser Lys Phe Met Lys Ser Ala Ala Val Leu Gly Thr Ala Thr
1               5                   10                  15

Leu Ala Ser Leu Leu Leu Val Ala Cys Gly Ser Lys Thr Ala Asp Lys
            20                  25                  30

Pro Ala Asp Ser Gly Ser Ser Glu Val Lys Glu Leu Thr Val Tyr Val
        35                  40                  45

Asp Glu Gly Tyr Lys Ser Tyr Ile Glu Glu Val Ala Lys Ala Tyr Glu
    50                  55                  60

Lys Glu Ala Gly Val Lys Val Thr Leu Lys Thr Gly Asp Ala Leu Gly
65                  70                  75                  80
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Gly Leu Asp Lys Leu Ser Leu Asp Asn Gln Ser Gly Asn Val Pro Asp
                85                  90                  95

Val Met Met Ala Pro Tyr Asp Arg Val Gly Ser Leu Gly Ser Asp Gly
            100                 105                 110

Gln Leu Ser Glu Val Lys Leu Ser Asp Gly Ala Lys Thr Asp Asp Thr
        115                 120                 125

Thr Lys Ser Leu Val Thr Ala Ala Asn Gly Lys Val Tyr Gly Ala Pro
    130                 135                 140

Ala Val Ile Glu Ser Leu Val Met Tyr Tyr Asn Lys Asp Leu Val Lys
145                 150                 155                 160

Asp Ala Pro Lys Thr Phe Ala Asp Leu Glu Asn Leu Ala Lys Asp Ser
                165                 170                 175

Lys Tyr Ala Phe Ala Gly Glu Asp Gly Lys Thr Thr Ala Phe Leu Ala
            180                 185                 190

Asp Trp Thr Asn Phe Tyr Tyr Thr Tyr Gly Leu Leu Ala Gly Asn Gly
        195                 200                 205

Ala Tyr Val Phe Gly Gln Asn Gly Lys Asp Ala Lys Asp Ile Gly Leu
    210                 215                 220

Ala Asn Asp Gly Ser Ile Val Gly Ile Asn Tyr Ala Lys Ser Trp Tyr
225                 230                 235                 240

Glu Lys Trp Pro Lys Gly Met Gln Asp Thr Glu Gly Ala Gly Asn Leu
                245                 250                 255

Ile Gln Thr Gln Phe Gln Glu Gly Lys Thr Ala Ala Ile Ile Asp Gly
            260                 265                 270

Pro Trp Lys Ala Gln Ala Phe Lys Asp Ala Lys Val Asn Tyr Gly Val
        275                 280                 285

Ala Thr Ile Pro Thr Leu Pro Asn Gly Lys Glu Tyr Ala Ala Phe Gly
    290                 295                 300

Gly Gly Lys Ala Trp Val Ile Pro Gln Ala Val Lys Asn Leu Glu Ala
305                 310                 315                 320

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

Leu Tyr Asp Lys Thr Asn Glu Ile Pro Ala Asn Thr Glu Ala Arg Ser
            340                 345                 350

Tyr Ala Glu Gly Lys Asn Asp Glu Leu Thr Thr Ala Val Ile Lys Gln
        355                 360                 365

Phe Lys Asn Thr Gln Pro Leu Pro Asn Ile Ser Gln Met Ser Ala Val
    370                 375                 380

Trp Asp Pro Ala Lys Asn Met Leu Phe Asp Ala Val Ser Gly Gln Lys
385                 390                 395                 400

Asp Ala Lys Thr Ala Ala Asn Asp Ala Val Thr Leu Ile Lys Glu Thr
                405                 410                 415

Ile Lys Gln Lys Phe Gly Glu Gly Pro Lys Pro His Arg Ile Gln Ser
            420                 425                 430

Thr Pro Lys Gly Ser Met Ala Met Ala Asp Leu Lys Lys Ala Val Asn
        435                 440                 445

Glu Pro Glu Lys Pro Ala Glu Glu Glu Pro Glu Asn Pro Ala Pro Ala
    450                 455                 460

Pro Lys Pro Ala Pro Ala Pro Gln Pro Glu Lys Pro Ala Pro Ala Pro
465                 470                 475                 480

Ala Pro Lys Pro Glu Lys Ser Ala Asp Gln Gln Ala Glu Glu Asp Tyr
```

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485 490 495

Ala Arg Arg Ser Glu Glu Glu Tyr Asn Arg Leu Thr Gln Gln Gln Pro
500 505 510

Pro Lys Ala Glu Lys Pro Ala Pro Ala Pro Val Pro Lys Pro Glu Gln
515 520 525

Pro Ala Pro Ala Pro Lys Thr Gly Trp Lys Gln Glu Asn Gly Met Trp
530 535 540

His His His His His His
545 550

<210> SEQ ID NO 75
<211> LENGTH: 1698
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 75

atgtcatcta aatttatgaa gagcgctgcg gtgcttggaa ctgctacact tgctagcttg 60

cttttggtag cttgcggaag caaaactgct gataagcctg ctgattctgg ttcatctgaa 120

gtcaaagaac tcactgtata tgtagacgag ggatataaga gctatattga agaggttgct 180

aaagcttatg aaaaagaagc tggagtaaaa gtcactctta aaactggtga tgctctagga 240

ggtcttgata aactttctct tgacaaccaa tctggtaatg tccctgatgt tatgatggct 300

ccatacgacc gtgtaggtag ccttggttct gacggacaac tttcagaagt gaaattgagc 360

gatggtgcta aaacagacga cacaactaaa tctcttgtaa cagctgctaa tggtaaagtt 420

tacggtgctc ctgccgttat cgagtcactt gttatgtact acaacaaaga cttggtgaaa 480

gatgctccaa aaacatttgc tgacttggaa aaccttgcta aagatagcaa atacgcattc 540

gctggtgaag atggtaaaac tactgccttc ctagctgact ggacaaactt ctactataca 600

tatggacttc ttgccggtaa cggtgcttac gtctttggcc aaaacggtaa agacgctaaa 660

gacatcggtc ttgcaaacga cggttctatc gtaggtatca actacgctaa atcttggtac 720

gaaaaatggc ctaaaggtat gcaagataca gaaggtgctg gaaacttaat ccaaactcaa 780

ttccaagaag gtaaaacagc tgctatcatc gacggacctt ggaaagctca agcctttaaa 840

gatgctaaag taaactacgg agttgcaact atcccaactc ttccaaatgg aaaagaatat 900

gctgcattcg gtggtggtaa agcttgggtc attcctcaag ccgttaagaa ccttgaagct 960

tctcaaaaat ttgtagactt ccttgttgca actgaacaac aaaaagtatt atatgataag 1020

actaacgaaa tcccagctaa tactgaggct cgttcatacg ctgaaggtaa aaacgatgag 1080

ttgacaacag ctgttatcaa acagttcaag aacactcaac cactgccaaa catctctcaa 1140

atgtctgcag tttgggatcc agcgaaaaat atgctctttg atgctgtaag tggtcaaaaa 1200

gatgctaaaa cagctgctaa cgatgctgta acattgatca aagaaacaat caaacaaaaa 1260

tttggtgaag gcccgaagcc gcaccgcatc cagagcacac cgaaaggcag ctacttcaaa 1320

gagggcttag agaagaccat cgccgccaag aaggccgagt tagagaaaac cgaggccgac 1380

ctgaagaagg ccgtgaacga gccggagaaa cctgcacctg caccggagac accggcacct 1440

gaagcccctg cagagcagcc taaacctgcc cctgcacctc aaccggcacc tgcacctaag 1500

ccggaaaaac ctgccgagca gccgaagccg gagaaaaccg acgaccagca ggccgaagag 1560

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gactatgcac gccgcagcga agaggagtac aaccgcttaa cccaacagca gccgccgaag   1620

gcagaaaaac cggcccctgc ccctaagacc ggttggaagc aggagaacgg catgtggcac   1680

caccaccacc accactga                                                 1698


<210> SEQ ID NO 76
<211> LENGTH: 565
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 76

Met Ser Ser Lys Phe Met Lys Ser Ala Ala Val Leu Gly Thr Ala Thr
1               5                   10                  15

Leu Ala Ser Leu Leu Leu Val Ala Cys Gly Ser Lys Thr Ala Asp Lys
            20                  25                  30

Pro Ala Asp Ser Gly Ser Ser Glu Val Lys Glu Leu Thr Val Tyr Val
        35                  40                  45

Asp Glu Gly Tyr Lys Ser Tyr Ile Glu Glu Val Ala Lys Ala Tyr Glu
    50                  55                  60

Lys Glu Ala Gly Val Lys Val Thr Leu Lys Thr Gly Asp Ala Leu Gly
65                  70                  75                  80

Gly Leu Asp Lys Leu Ser Leu Asp Asn Gln Ser Gly Asn Val Pro Asp
                85                  90                  95

Val Met Met Ala Pro Tyr Asp Arg Val Gly Ser Leu Gly Ser Asp Gly
            100                 105                 110

Gln Leu Ser Glu Val Lys Leu Ser Asp Gly Ala Lys Thr Asp Asp Thr
        115                 120                 125

Thr Lys Ser Leu Val Thr Ala Ala Asn Gly Lys Val Tyr Gly Ala Pro
    130                 135                 140

Ala Val Ile Glu Ser Leu Val Met Tyr Tyr Asn Lys Asp Leu Val Lys
145                 150                 155                 160

Asp Ala Pro Lys Thr Phe Ala Asp Leu Glu Asn Leu Ala Lys Asp Ser
                165                 170                 175

Lys Tyr Ala Phe Ala Gly Glu Asp Gly Lys Thr Thr Ala Phe Leu Ala
            180                 185                 190

Asp Trp Thr Asn Phe Tyr Tyr Thr Tyr Gly Leu Leu Ala Gly Asn Gly
        195                 200                 205

Ala Tyr Val Phe Gly Gln Asn Gly Lys Asp Ala Lys Asp Ile Gly Leu
    210                 215                 220

Ala Asn Asp Gly Ser Ile Val Gly Ile Asn Tyr Ala Lys Ser Trp Tyr
225                 230                 235                 240

Glu Lys Trp Pro Lys Gly Met Gln Asp Thr Glu Gly Ala Gly Asn Leu
                245                 250                 255

Ile Gln Thr Gln Phe Gln Glu Gly Lys Thr Ala Ala Ile Ile Asp Gly
            260                 265                 270

Pro Trp Lys Ala Gln Ala Phe Lys Asp Ala Lys Val Asn Tyr Gly Val
        275                 280                 285

Ala Thr Ile Pro Thr Leu Pro Asn Gly Lys Glu Tyr Ala Ala Phe Gly
    290                 295                 300

Gly Gly Lys Ala Trp Val Ile Pro Gln Ala Val Lys Asn Leu Glu Ala
305                 310                 315                 320
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Ser Gln Lys Phe Val Asp Phe Leu Val Ala Thr Glu Gln Gln Lys Val
                325                 330                 335

Leu Tyr Asp Lys Thr Asn Glu Ile Pro Ala Asn Thr Glu Ala Arg Ser
            340                 345                 350

Tyr Ala Glu Gly Lys Asn Asp Glu Leu Thr Thr Ala Val Ile Lys Gln
        355                 360                 365

Phe Lys Asn Thr Gln Pro Leu Pro Asn Ile Ser Gln Met Ser Ala Val
    370                 375                 380

Trp Asp Pro Ala Lys Asn Met Leu Phe Asp Ala Val Ser Gly Gln Lys
385                 390                 395                 400

Asp Ala Lys Thr Ala Ala Asn Asp Ala Val Thr Leu Ile Lys Glu Thr
                405                 410                 415

Ile Lys Gln Lys Phe Gly Glu Gly Pro Lys Pro His Arg Ile Gln Ser
            420                 425                 430

Thr Pro Lys Gly Ser Tyr Phe Lys Glu Gly Leu Glu Lys Thr Ile Ala
        435                 440                 445

Ala Lys Lys Ala Glu Leu Glu Lys Thr Glu Ala Asp Leu Lys Lys Ala
    450                 455                 460

Val Asn Glu Pro Glu Lys Pro Ala Pro Ala Pro Glu Thr Pro Ala Pro
465                 470                 475                 480

Glu Ala Pro Ala Glu Gln Pro Lys Pro Ala Pro Ala Pro Gln Pro Ala
                485                 490                 495

Pro Ala Pro Lys Pro Glu Lys Pro Ala Glu Gln Pro Lys Pro Glu Lys
            500                 505                 510

Thr Asp Asp Gln Gln Ala Glu Glu Asp Tyr Ala Arg Arg Ser Glu Glu
        515                 520                 525

Glu Tyr Asn Arg Leu Thr Gln Gln Gln Pro Pro Lys Ala Glu Lys Pro
    530                 535                 540

Ala Pro Ala Pro Lys Thr Gly Trp Lys Gln Glu Asn Gly Met Trp His
545                 550                 555                 560

His His His His His
                565
```

<210> SEQ ID NO 77
<211> LENGTH: 1230
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 77

```
atgaaaaaaa tcgttaaata ctcatctctt gcagcccttg ctcttgttgc tgcaggtgtg      60

cttgcggctt gctcaggggg tgctaagaaa gaaggagaag cagctagcaa gaaagaaatc     120

atcgttgcaa ccaatggatc accaaagcca tttatctatg aagaaaatgg cgaattgact     180

ggttacgaga ttgaagtcgt tcgcgctatc tttaaagatt ctgacaaata tgatgtcaag     240

tttgaaaaga cagaatggtc aggtgtcttt gctggtcttg acgctgatcg ttacaatatg     300

gctgtcaaca atcttagcta cactaaagaa cgtgcggaga aatacctcta tgccgcacca     360

attgcccaaa atcctaatgt ccttgtcgtg aagaaagatg actctagtat caagtctctc     420

gatgatatcg gtggaaaatc gacggaagtc gttcaagcca ctacatcagc taagcagtta     480

gaagcataca atgctgaaca cacggacaac ccaactatcc ttaactatac taaggcagac     540
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ttccaacaaa tcatggtacg tttgagcgat ggacaatttg actataagat ttttgataaa    600

atcggtgttg aaacagtgat caagaaccaa ggtttggaca acttgaaagt tatcgaactt    660

ccaagcgacc aacaaccgta cgtttaccca cttcttgctc agggtcaaga tgagttgaaa    720

tcgtttgtag acaaacgcat caaagaactt tataaagatg gaactcttga aaaattgtct    780

aaacaattct tcggagacac ttatctaccg gcagaagctg atattaaact ggccgaagca    840

accgccaaag aagccaccgc caaggaagcc acagccaagg ccaccgcaat ggccatggcc    900

gacctgaaga aggccgtgaa tgagccggag aagccggccg aagaagagcc ggagaatcct    960

gcaccggccc ctaagcctgc accggcacct cagcctgaaa aaccggcacc tgcacctgcc   1020

ccgaagcctg aaaagagcgc cgaccagcag gccgaagagg actatgcccg ccgcagcgaa   1080

gaggagtaca accgtctgac ccagcagcag ccgccgaaag ccgagaaacc tgccccggca   1140

ccggtgccta agccggaaca gcctgcccct gcaccgaaga ccggttggaa gcaggaaaac   1200

ggcatgtggc accaccacca ccaccactga                                    1230
```

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<210> SEQ ID NO 78
<211> LENGTH: 409
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 78

Met Lys Lys Ile Val Lys Tyr Ser Ser Leu Ala Ala Leu Ala Leu Val
1               5                   10                  15

Ala Ala Gly Val Leu Ala Ala Cys Ser Gly Gly Ala Lys Lys Glu Gly
            20                  25                  30

Glu Ala Ala Ser Lys Lys Glu Ile Ile Val Ala Thr Asn Gly Ser Pro
        35                  40                  45

Lys Pro Phe Ile Tyr Glu Glu Asn Gly Glu Leu Thr Gly Tyr Glu Ile
    50                  55                  60

Glu Val Val Arg Ala Ile Phe Lys Asp Ser Asp Lys Tyr Asp Val Lys
65                  70                  75                  80

Phe Glu Lys Thr Glu Trp Ser Gly Val Phe Ala Gly Leu Asp Ala Asp
                85                  90                  95

Arg Tyr Asn Met Ala Val Asn Asn Leu Ser Tyr Thr Lys Glu Arg Ala
            100                 105                 110

Glu Lys Tyr Leu Tyr Ala Ala Pro Ile Ala Gln Asn Pro Asn Val Leu
        115                 120                 125

Val Val Lys Lys Asp Asp Ser Ser Ile Lys Ser Leu Asp Asp Ile Gly
    130                 135                 140

Gly Lys Ser Thr Glu Val Val Gln Ala Thr Thr Ser Ala Lys Gln Leu
145                 150                 155                 160

Glu Ala Tyr Asn Ala Glu His Thr Asp Asn Pro Thr Ile Leu Asn Tyr
                165                 170                 175

Thr Lys Ala Asp Phe Gln Gln Ile Met Val Arg Leu Ser Asp Gly Gln
            180                 185                 190

Phe Asp Tyr Lys Ile Phe Asp Lys Ile Gly Val Glu Thr Val Ile Lys
        195                 200                 205

Asn Gln Gly Leu Asp Asn Leu Lys Val Ile Glu Leu Pro Ser Asp Gln
    210                 215                 220
```

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```
Gln Pro Tyr Val Tyr Pro Leu Leu Ala Gln Gly Gln Asp Glu Leu Lys
225                 230                 235                 240

Ser Phe Val Asp Lys Arg Ile Lys Glu Leu Tyr Lys Asp Gly Thr Leu
                245                 250                 255

Glu Lys Leu Ser Lys Gln Phe Phe Gly Asp Thr Tyr Leu Pro Ala Glu
            260                 265                 270

Ala Asp Ile Lys Leu Ala Glu Ala Thr Ala Lys Glu Ala Thr Ala Lys
        275                 280                 285

Glu Ala Thr Ala Lys Ala Thr Ala Met Ala Met Ala Asp Leu Lys Lys
    290                 295                 300

Ala Val Asn Glu Pro Glu Lys Pro Ala Glu Glu Glu Pro Glu Asn Pro
305                 310                 315                 320

Ala Pro Ala Pro Lys Pro Ala Pro Ala Pro Gln Pro Glu Lys Pro Ala
                325                 330                 335

Pro Ala Pro Ala Pro Lys Pro Glu Lys Ser Ala Asp Gln Gln Ala Glu
            340                 345                 350

Glu Asp Tyr Ala Arg Arg Ser Glu Glu Glu Tyr Asn Arg Leu Thr Gln
        355                 360                 365

Gln Gln Pro Pro Lys Ala Glu Lys Pro Ala Pro Ala Pro Val Pro Lys
    370                 375                 380

Pro Glu Gln Pro Ala Pro Ala Pro Lys Thr Gly Trp Lys Gln Glu Asn
385                 390                 395                 400

Gly Met Trp His His His His His His
                405
```

<210> SEQ ID NO 79
<211> LENGTH: 1275
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 79

```
atgaaaaaaa tcgttaaata ctcatctctt gcagcccttg ctcttgttgc tgcaggtgtg     60

cttgcggctt gctcaggggg tgctaagaaa gaaggagaag cagctagcaa gaaagaaatc    120

atcgttgcaa ccaatggatc accaaagcca tttatctatg aagaaaatgg cgaattgact    180

ggttacgaga ttgaagtcgt tcgcgctatc tttaaagatt ctgacaaata tgatgtcaag    240

tttgaaaaga cagaatggtc aggtgtcttt gctggtcttg acgctgatcg ttacaatatg    300

gctgtcaaca atcttagcta cactaaagaa cgtgcggaga aatacctcta tgccgcacca    360

attgcccaaa atcctaatgt ccttgtcgtg aagaaagatg actctagtat caagtctctc    420

gatgatatcg gtggaaaatc gacggaagtc gttcaagcca ctacatcagc taagcagtta    480

gaagcataca atgctgaaca cacggacaac ccaactatcc ttaactatac taaggcagac    540

ttccaacaaa tcatggtacg tttgagcgat ggacaatttg actataagat tttgataaa    600

atcggtgttg aaacagtgat caagaaccaa ggtttggaca acttgaaagt tatcgaactt    660

ccaagcgacc aacaaccgta cgtttaccca cttcttgctc agggtcaaga tgagttgaaa    720

tcgtttgtag acaaacgcat caaagaactt tataaagatg gaactcttga aaaattgtct    780

aaacaattct tcggagacac ttatctaccg gcagaagctg atattaaact ggccgaagca    840

accgccaaag aggccaccgc caaggaagcc accgccaaag ccaccgccta cttcaaagag    900
```

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```
ggcttagaga agaccatcgc cgccaagaag gccgagttag agaaaaccga ggccgacctg    960

aagaaggccg tgaacgagcc ggagaagcct gcacctgccc ctgaaacccc tgcaccggaa   1020

gcacctgcag agcagcctaa acctgcacct gcaccgcaac ctgcccctgc acctaaaccg   1080

gagaaaccgg cagagcagcc gaagccggag aaaaccgacg accagcaggc cgaggaagac   1140

tacgcccgtc gtagcgagga agagtacaac cgcctgaccc agcagcaacc gccgaaagcc   1200

gaaaagccgg cccctgcacc gaaaaccggc tggaagcagg agaacggcat gtggcaccac   1260

caccaccacc actga                                                     1275


<210> SEQ ID NO 80
<211> LENGTH: 424
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 80

Met Lys Lys Ile Val Lys Tyr Ser Ser Leu Ala Ala Leu Ala Leu Val
1               5                   10                  15

Ala Ala Gly Val Leu Ala Ala Cys Ser Gly Gly Ala Lys Lys Glu Gly
            20                  25                  30

Glu Ala Ala Ser Lys Lys Glu Ile Ile Val Ala Thr Asn Gly Ser Pro
        35                  40                  45

Lys Pro Phe Ile Tyr Glu Glu Asn Gly Glu Leu Thr Gly Tyr Glu Ile
    50                  55                  60

Glu Val Val Arg Ala Ile Phe Lys Asp Ser Asp Lys Tyr Asp Val Lys
65                  70                  75                  80

Phe Glu Lys Thr Glu Trp Ser Gly Val Phe Ala Gly Leu Asp Ala Asp
                85                  90                  95

Arg Tyr Asn Met Ala Val Asn Asn Leu Ser Tyr Thr Lys Glu Arg Ala
            100                 105                 110

Glu Lys Tyr Leu Tyr Ala Ala Pro Ile Ala Gln Asn Pro Asn Val Leu
        115                 120                 125

Val Val Lys Lys Asp Asp Ser Ser Ile Lys Ser Leu Asp Asp Ile Gly
    130                 135                 140

Gly Lys Ser Thr Glu Val Val Gln Ala Thr Thr Ser Ala Lys Gln Leu
145                 150                 155                 160

Glu Ala Tyr Asn Ala Glu His Thr Asp Asn Pro Thr Ile Leu Asn Tyr
                165                 170                 175

Thr Lys Ala Asp Phe Gln Gln Ile Met Val Arg Leu Ser Asp Gly Gln
            180                 185                 190

Phe Asp Tyr Lys Ile Phe Asp Lys Ile Gly Val Glu Thr Val Ile Lys
        195                 200                 205

Asn Gln Gly Leu Asp Asn Leu Lys Val Ile Glu Leu Pro Ser Asp Gln
    210                 215                 220

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

Ser Phe Val Asp Lys Arg Ile Lys Glu Leu Tyr Lys Asp Gly Thr Leu
                245                 250                 255

Glu Lys Leu Ser Lys Gln Phe Phe Gly Asp Thr Tyr Leu Pro Ala Glu
            260                 265                 270

Ala Asp Ile Lys Leu Ala Glu Ala Thr Ala Lys Glu Ala Thr Ala Lys
```

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```
        275                 280                 285

Glu Ala Thr Ala Lys Ala Thr Ala Tyr Phe Lys Glu Gly Leu Glu Lys
    290                 295                 300

Thr Ile Ala Ala Lys Lys Ala Glu Leu Glu Lys Thr Glu Ala Asp Leu
305                 310                 315                 320

Lys Lys Ala Val Asn Glu Pro Glu Lys Pro Ala Pro Ala Pro Glu Thr
                325                 330                 335

Pro Ala Pro Glu Ala Pro Ala Glu Gln Pro Lys Pro Ala Pro Ala Pro
            340                 345                 350

Gln Pro Ala Pro Ala Pro Lys Pro Glu Lys Pro Ala Glu Gln Pro Lys
        355                 360                 365

Pro Glu Lys Thr Asp Asp Gln Gln Ala Glu Glu Asp Tyr Ala Arg Arg
    370                 375                 380

Ser Glu Glu Glu Tyr Asn Arg Leu Thr Gln Gln Gln Pro Pro Lys Ala
385                 390                 395                 400

Glu Lys Pro Ala Pro Ala Pro Lys Thr Gly Trp Lys Gln Glu Asn Gly
                405                 410                 415

Met Trp His His His His His His
            420


<210> SEQ ID NO 81
<211> LENGTH: 1671
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 81

atgtcatcta aatttatgaa gagcgctgcg gtgcttggaa ctgctacact tgctagcttg     60

cttttggtag cttgcggaag caaaactgct gataagcctg ctgattctgg ttcatctgaa    120

gtcaaagaac tcactgtata tgtagacgag ggatataaga gctatattga agaggttgct    180

aaagcttatg aaaaagaagc tggagtaaaa gtcactctta aaactggtga tgctctagga    240

ggtcttgata aactttctct tgacaaccaa tctggtaatg tccctgatgt tatgatggct    300

ccatacgacc gtgtaggtag ccttggttct gacggacaac tttcagaagt gaaattgagc    360

gatggtgcta aaacagacga cacaactaaa tctcttgtaa cagctgctaa tggtaaagtt    420

tacggtgctc ctgccgttat cgagtcactt gttatgtact acaacaaaga cttggtgaaa    480

gatgctccaa aaacatttgc tgacttggaa aaccttgcta aagatagcaa atacgcattc    540

gctggtgaag atggtaaaac tactgccttc ctagctgact ggacaaactt ctactataca    600

tatggacttc ttgccggtaa cggtgcttac gtctttggcc aaaacggtaa agacgctaaa    660

gacatcggtc ttgcaaacga cggttctatc gtaggtatca actacgctaa atcttggtac    720

gaaaaatggc ctaaaggtat gcaagataca gaaggtgctg gaaacttaat ccaaactcaa    780

ttccaagaag gtaaaacagc tgctatcatc gacggacctt ggaaagctca agcctttaaa    840

gatgctaaag taaactacgg agttgcaact atcccaactc ttccaaatgg aaaagaatat    900

gctgcattcg gtggtggtaa agcttgggtc attcctcaag ccgttaagaa ccttgaagct    960

tctcaaaaat ttgtagactt ccttgttgca actgaacaac aaaaagtatt atatgataag   1020

actaacgaaa tcccagctaa tactgaggct cgttcatacg ctgaaggtaa aaacgatgag   1080

ttgacaacag ctgttatcaa acagttcaag aacactcaac cactgccaaa catctctcaa   1140
```

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```
atgtctgcag tttgggatcc agcgaaaaat atgctctttg atgctgtaag tggtcaaaaa   1200

gatgctaaaa cagctgctaa cgatgctgta acattgatca aagaaacaat caaacaaaaa   1260

tttggtgaac tggccgaggc aaccgccaaa gaagccaccg ccaaggaagc cacagccaag   1320

gccaccgcaa tggccatggc cgacctgaag aaggccgtga atgagccgga gaagccggcc   1380

gaagaagagc cggagaatcc tgcaccggcc cctaagcctg caccggcacc tcagcctgaa   1440

aaaccggcac ctgcacctgc cccgaagcct gaaaagagcg ccgaccagca ggccgaagag   1500

gactatgccc gccgcagcga agaggagtac aaccgtctga cccagcagca gccgccgaaa   1560

gccgagaaac ctgccccggc accggtgcct aagccggaac agcctgcccc tgcaccgaag   1620

accggttgga agcaggaraa cggcatgtgg caccaccacc accaccactg a            1671
```

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<210> SEQ ID NO 82
<211> LENGTH: 556
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 82

Met Ser Ser Lys Phe Met Lys Ser Ala Ala Val Leu Gly Thr Ala Thr
1               5                   10                  15

Leu Ala Ser Leu Leu Leu Val Ala Cys Gly Ser Lys Thr Ala Asp Lys
            20                  25                  30

Pro Ala Asp Ser Gly Ser Ser Glu Val Lys Glu Leu Thr Val Tyr Val
        35                  40                  45

Asp Glu Gly Tyr Lys Ser Tyr Ile Glu Glu Val Ala Lys Ala Tyr Glu
    50                  55                  60

Lys Glu Ala Gly Val Lys Val Thr Leu Lys Thr Gly Asp Ala Leu Gly
65                  70                  75                  80

Gly Leu Asp Lys Leu Ser Leu Asp Asn Gln Ser Gly Asn Val Pro Asp
                85                  90                  95

Val Met Met Ala Pro Tyr Asp Arg Val Gly Ser Leu Gly Ser Asp Gly
            100                 105                 110

Gln Leu Ser Glu Val Lys Leu Ser Asp Gly Ala Lys Thr Asp Asp Thr
        115                 120                 125

Thr Lys Ser Leu Val Thr Ala Ala Asn Gly Lys Val Tyr Gly Ala Pro
    130                 135                 140

Ala Val Ile Glu Ser Leu Val Met Tyr Tyr Asn Lys Asp Leu Val Lys
145                 150                 155                 160

Asp Ala Pro Lys Thr Phe Ala Asp Leu Glu Asn Leu Ala Lys Asp Ser
                165                 170                 175

Lys Tyr Ala Phe Ala Gly Glu Asp Gly Lys Thr Thr Ala Phe Leu Ala
            180                 185                 190

Asp Trp Thr Asn Phe Tyr Tyr Thr Tyr Gly Leu Leu Ala Gly Asn Gly
        195                 200                 205

Ala Tyr Val Phe Gly Gln Asn Gly Lys Asp Ala Lys Asp Ile Gly Leu
    210                 215                 220

Ala Asn Asp Gly Ser Ile Val Gly Ile Asn Tyr Ala Lys Ser Trp Tyr
225                 230                 235                 240

Glu Lys Trp Pro Lys Gly Met Gln Asp Thr Glu Gly Ala Gly Asn Leu
                245                 250                 255
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```
Ile Gln Thr Gln Phe Gln Glu Gly Lys Thr Ala Ala Ile Ile Asp Gly
            260                 265                 270

Pro Trp Lys Ala Gln Ala Phe Lys Asp Ala Lys Val Asn Tyr Gly Val
        275                 280                 285

Ala Thr Ile Pro Thr Leu Pro Asn Gly Lys Glu Tyr Ala Ala Phe Gly
    290                 295                 300

Gly Gly Lys Ala Trp Val Ile Pro Gln Ala Val Lys Asn Leu Glu Ala
305                 310                 315                 320

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

Leu Tyr Asp Lys Thr Asn Glu Ile Pro Ala Asn Thr Glu Ala Arg Ser
            340                 345                 350

Tyr Ala Glu Gly Lys Asn Asp Glu Leu Thr Thr Ala Val Ile Lys Gln
        355                 360                 365

Phe Lys Asn Thr Gln Pro Leu Pro Asn Ile Ser Gln Met Ser Ala Val
    370                 375                 380

Trp Asp Pro Ala Lys Asn Met Leu Phe Asp Ala Val Ser Gly Gln Lys
385                 390                 395                 400

Asp Ala Lys Thr Ala Ala Asn Asp Ala Val Thr Leu Ile Lys Glu Thr
                405                 410                 415

Ile Lys Gln Lys Phe Gly Glu Leu Ala Glu Ala Thr Ala Lys Glu Ala
            420                 425                 430

Thr Ala Lys Glu Ala Thr Ala Lys Ala Thr Ala Met Ala Met Ala Asp
        435                 440                 445

Leu Lys Lys Ala Val Asn Glu Pro Glu Lys Pro Ala Glu Glu Glu Pro
    450                 455                 460

Glu Asn Pro Ala Pro Ala Pro Lys Pro Ala Pro Ala Pro Gln Pro Glu
465                 470                 475                 480

Lys Pro Ala Pro Ala Pro Ala Pro Lys Pro Glu Lys Ser Ala Asp Gln
                485                 490                 495

Gln Ala Glu Glu Asp Tyr Ala Arg Arg Ser Glu Glu Glu Tyr Asn Arg
            500                 505                 510

Leu Thr Gln Gln Gln Pro Pro Lys Ala Glu Lys Pro Ala Pro Ala Pro
        515                 520                 525

Val Pro Lys Pro Glu Gln Pro Ala Pro Ala Pro Lys Thr Gly Trp Lys
    530                 535                 540

Gln Glu Asn Gly Met Trp His His His His His His
545                 550                 555


<210> SEQ ID NO 83
<211> LENGTH: 1716
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 83

atgtcatcta aatttatgaa gagcgctgcg gtgcttggaa ctgctacact tgctagcttg      60

cttttggtag cttgcggaag caaaactgct gataagcctg ctgattctgg ttcatctgaa     120

gtcaaagaac tcactgtata tgtagacgag ggatataaga gctatattga agaggttgct     180

aaagcttatg aaaaagaagc tggagtaaaa gtcactctta aaactggtga tgctctagga     240
```

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```
ggtcttgata aactttctct tgacaaccaa tctggtaatg tccctgatgt tatgatggct    300

ccatacgacc gtgtaggtag ccttggttct gacggacaac tttcagaagt gaaattgagc    360

gatggtgcta aaacagacga cacaactaaa tctcttgtaa cagctgctaa tggtaaagtt    420

tacggtgctc ctgccgttat cgagtcactt gttatgtact acaacaaaga cttggtgaaa    480

gatgctccaa aaacatttgc tgacttggaa aaccttgcta aagatagcaa atacgcattc    540

gctggtgaag atggtaaaac tactgccttc ctagctgact ggacaaactt ctactataca    600

tatggacttc ttgccggtaa cggtgcttac gtctttggcc aaaacggtaa agacgctaaa    660

gacatcggtc ttgcaaacga cggttctatc gtaggtatca actacgctaa atcttggtac    720

gaaaaatggc ctaaaggtat gcaagataca gaaggtgctg gaaacttaat ccaaactcaa    780

ttccaagaag gtaaaacagc tgctatcatc gacggacctt ggaaagctca agcctttaaa    840

gatgctaaag taaactacgg agttgcaact atcccaactc ttccaaatgg aaaagaatat    900

gctgcattcg gtggtggtaa agcttgggtc attcctcaag ccgttaagaa ccttgaagct    960

tctcaaaaat ttgtagactt ccttgttgca actgaacaac aaaaagtatt atatgataag   1020

actaacgaaa tcccagctaa tactgaggct cgttcatacg ctgaaggtaa aaacgatgag   1080

ttgacaacag ctgttatcaa acagttcaag aacactcaac cactgccaaa catctctcaa   1140

atgtctgcag tttgggatcc agcgaaaaat atgctctttg atgctgtaag tggtcaaaaa   1200

gatgctaaaa cagctgctaa cgatgctgta acattgatca aagaaacaat caaacaaaaa   1260

tttggtgaac tggccgaagc aaccgccaaa gaggccaccg ccaaggaagc caccgccaaa   1320

gccaccgcct acttcaaaga gggcttagag aagaccatcg ccgccaagaa ggccgagtta   1380

gagaaaaccg aggccgacct gaagaaggcc gtgaacgagc cggagaagcc tgcacctgcc   1440

cctgaaaccc ctgcaccgga agcacctgca gagcagccta aacctgcacc tgcaccgcaa   1500

cctgcccctg cacctaaacc ggagaaaccg gcagagcagc cgaagccgga gaaaaccgac   1560

gaccagcagg ccgaggaaga ctacgcccgt cgtagcgagg aagagtacaa ccgcctgacc   1620

cagcagcaac cgccgaaagc cgaaaagccg gcccctgcac cgaaaaccgg ctggaagcag   1680

gagaacggca tgtggcacca ccaccaccac cactga                             1716


<210> SEQ ID NO 84
<211> LENGTH: 571
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 84

Met Ser Ser Lys Phe Met Lys Ser Ala Ala Val Leu Gly Thr Ala Thr
1               5                   10                  15

Leu Ala Ser Leu Leu Leu Val Ala Cys Gly Ser Lys Thr Ala Asp Lys
            20                  25                  30

Pro Ala Asp Ser Gly Ser Ser Glu Val Lys Glu Leu Thr Val Tyr Val
        35                  40                  45

Asp Glu Gly Tyr Lys Ser Tyr Ile Glu Glu Val Ala Lys Ala Tyr Glu
    50                  55                  60

Lys Glu Ala Gly Val Lys Val Thr Leu Lys Thr Gly Asp Ala Leu Gly
65                  70                  75                  80

Gly Leu Asp Lys Leu Ser Leu Asp Asn Gln Ser Gly Asn Val Pro Asp
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                85                  90                  95

Val Met Met Ala Pro Tyr Asp Arg Val Gly Ser Leu Gly Ser Asp Gly
            100                 105                 110

Gln Leu Ser Glu Val Lys Leu Ser Asp Gly Ala Lys Thr Asp Asp Thr
        115                 120                 125

Thr Lys Ser Leu Val Thr Ala Ala Asn Gly Lys Val Tyr Gly Ala Pro
    130                 135                 140

Ala Val Ile Glu Ser Leu Val Met Tyr Tyr Asn Lys Asp Leu Val Lys
145                 150                 155                 160

Asp Ala Pro Lys Thr Phe Ala Asp Leu Glu Asn Leu Ala Lys Asp Ser
                165                 170                 175

Lys Tyr Ala Phe Ala Gly Glu Asp Gly Lys Thr Thr Ala Phe Leu Ala
            180                 185                 190

Asp Trp Thr Asn Phe Tyr Tyr Thr Tyr Gly Leu Leu Ala Gly Asn Gly
        195                 200                 205

Ala Tyr Val Phe Gly Gln Asn Gly Lys Asp Ala Lys Asp Ile Gly Leu
    210                 215                 220

Ala Asn Asp Gly Ser Ile Val Gly Ile Asn Tyr Ala Lys Ser Trp Tyr
225                 230                 235                 240

Glu Lys Trp Pro Lys Gly Met Gln Asp Thr Glu Gly Ala Gly Asn Leu
                245                 250                 255

Ile Gln Thr Gln Phe Gln Glu Gly Lys Thr Ala Ala Ile Ile Asp Gly
            260                 265                 270

Pro Trp Lys Ala Gln Ala Phe Lys Asp Ala Lys Val Asn Tyr Gly Val
        275                 280                 285

Ala Thr Ile Pro Thr Leu Pro Asn Gly Lys Glu Tyr Ala Ala Phe Gly
    290                 295                 300

Gly Gly Lys Ala Trp Val Ile Pro Gln Ala Val Lys Asn Leu Glu Ala
305                 310                 315                 320

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

Leu Tyr Asp Lys Thr Asn Glu Ile Pro Ala Asn Thr Glu Ala Arg Ser
            340                 345                 350

Tyr Ala Glu Gly Lys Asn Asp Glu Leu Thr Thr Ala Val Ile Lys Gln
        355                 360                 365

Phe Lys Asn Thr Gln Pro Leu Pro Asn Ile Ser Gln Met Ser Ala Val
    370                 375                 380

Trp Asp Pro Ala Lys Asn Met Leu Phe Asp Ala Val Ser Gly Gln Lys
385                 390                 395                 400

Asp Ala Lys Thr Ala Ala Asn Asp Ala Val Thr Leu Ile Lys Glu Thr
                405                 410                 415

Ile Lys Gln Lys Phe Gly Glu Leu Ala Glu Ala Thr Ala Lys Glu Ala
            420                 425                 430

Thr Ala Lys Glu Ala Thr Ala Lys Ala Thr Ala Tyr Phe Lys Glu Gly
        435                 440                 445

Leu Glu Lys Thr Ile Ala Ala Lys Lys Ala Glu Leu Glu Lys Thr Glu
    450                 455                 460

Ala Asp Leu Lys Lys Ala Val Asn Glu Pro Glu Lys Pro Ala Pro Ala
465                 470                 475                 480

Pro Glu Thr Pro Ala Pro Glu Ala Pro Ala Glu Gln Pro Lys Pro Ala
                485                 490                 495
```

```
Pro Ala Pro Gln Pro Ala Pro Ala Pro Lys Pro Glu Lys Pro Ala Glu
            500                 505                 510

Gln Pro Lys Pro Glu Lys Thr Asp Asp Gln Gln Ala Glu Glu Asp Tyr
        515                 520                 525

Ala Arg Arg Ser Glu Glu Glu Tyr Asn Arg Leu Thr Gln Gln Gln Pro
    530                 535                 540

Pro Lys Ala Glu Lys Pro Ala Pro Ala Pro Lys Thr Gly Trp Lys Gln
545                 550                 555                 560

Glu Asn Gly Met Trp His His His His His His
                565                 570


<210> SEQ ID NO 85
<211> LENGTH: 33
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 85

Leu Ile Val Met Phe Glu Ser Thr Ala Gly Pro Cys Leu Val Ile Ala
1               5                   10                  15

Met Phe Thr Gly Ile Val Met Ser Thr Ala Gly Cys Pro Ala Gly Ser
            20                  25                  30

Cys


<210> SEQ ID NO 86
<211> LENGTH: 25
<212> TYPE: PRT
<213> ORGANISM: Streptococcus pneumoniae

<400> SEQUENCE: 86

Met Ser Ser Lys Phe Met Lys Ser Ala Ala Val Leu Gly Thr Ala Thr
1               5                   10                  15

Leu Ala Ser Leu Leu Leu Val Ala Cys
            20                  25


<210> SEQ ID NO 87
<211> LENGTH: 19
<212> TYPE: PRT
<213> ORGANISM: E. coli

<400> SEQUENCE: 87

Met Arg Tyr Leu Ala Thr Leu Leu Leu Ser Leu Ala Val Leu Ile Thr
1               5                   10                  15

Ala Gly Cys


<210> SEQ ID NO 88
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 88

His His His His His His
1               5


<210> SEQ ID NO 89
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```
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Synthetic

<400> SEQUENCE: 89

Met Ser Tyr Tyr His His His His His His
1               5                   10


<210> SEQ ID NO 90
<211> LENGTH: 471
<212> TYPE: PRT
<213> ORGANISM: Streptococcus pneumoniae

<400> SEQUENCE: 90

Met Ala Asn Lys Ala Val Asn Asp Phe Ile Leu Ala Met Asn Tyr Asp
1               5                   10                  15

Lys Lys Lys Leu Leu Thr His Gln Gly Glu Ser Ile Glu Asn Arg Phe
            20                  25                  30

Ile Lys Glu Gly Asn Gln Leu Pro Asp Glu Phe Val Val Ile Glu Arg
        35                  40                  45

Lys Lys Arg Ser Leu Ser Thr Asn Thr Ser Asp Ile Ser Val Thr Ala
    50                  55                  60

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

Thr Leu Leu Glu Asn Asn Pro Thr Leu Leu Ala Val Asp Arg Ala Pro
                85                  90                  95

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

Leu Gln Val Glu Asp Pro Ser Asn Ser Ser Val Arg Gly Ala Val Asn
        115                 120                 125

Asp Leu Leu Ala Lys Trp His Gln Asp Tyr Gly Gln Val Asn Asn Val
    130                 135                 140

Pro Ala Arg Met Gln Tyr Glu Lys Ile Thr Ala His Ser Met Glu Gln
145                 150                 155                 160

Leu Lys Val Lys Phe Gly Ser Asp Phe Glu Lys Thr Gly Asn Ser Leu
                165                 170                 175

Asp Ile Asp Phe Asn Ser Val His Ser Gly Glu Lys Gln Ile Gln Ile
            180                 185                 190

Val Asn Phe Lys Gln Ile Tyr Tyr Thr Val Ser Val Asp Ala Val Lys
        195                 200                 205

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

Gln Arg Gly Ile Ser Ala Glu Arg Pro Leu Val Tyr Ile Ser Ser Val
225                 230                 235                 240

Ala Tyr Gly Arg Gln Val Tyr Leu Lys Leu Glu Thr Thr Ser Lys Ser
                245                 250                 255

Asp Glu Val Glu Ala Ala Phe Glu Ala Leu Ile Lys Gly Val Lys Val
            260                 265                 270

Ala Pro Gln Thr Glu Trp Lys Gln Ile Leu Asp Asn Thr Glu Val Lys
        275                 280                 285

Ala Val Ile Leu Gly Gly Asp Pro Ser Ser Gly Ala Arg Val Val Thr
    290                 295                 300
```

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```
Gly Lys Val Asp Met Val Glu Asp Leu Ile Gln Glu Gly Ser Arg Phe
305                 310                 315                 320

Thr Ala Asp His Pro Gly Leu Pro Ile Ser Tyr Thr Thr Ser Phe Leu
                325                 330                 335

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

Thr Lys Val Thr Ala Tyr Arg Asn Gly Asp Leu Leu Leu Asp His Ser
        355                 360                 365

Gly Ala Tyr Val Ala Gln Tyr Tyr Ile Thr Trp Asp Glu Leu Ser Tyr
    370                 375                 380

Asp His Gln Gly Lys Glu Val Leu Thr Pro Lys Ala Trp Asp Arg Asn
385                 390                 395                 400

Gly Gln Asp Leu Thr Ala His Phe Thr Thr Ser Ile Pro Leu Lys Gly
                405                 410                 415

Asn Val Arg Asn Leu Ser Val Lys Ile Arg Glu Cys Thr Gly Leu Ala
            420                 425                 430

Trp Glu Trp Trp Arg Thr Val Tyr Glu Lys Thr Asp Leu Pro Leu Val
        435                 440                 445

Arg Lys Arg Thr Ile Ser Ile Trp Gly Thr Thr Leu Tyr Pro Gln Val
    450                 455                 460

Glu Asp Lys Val Glu Asn Asp
465                 470


<210> SEQ ID NO 91
<211> LENGTH: 5
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<213> ORGANISM: Streptococcus pneumoniae

<400> SEQUENCE: 91

Pro Ala Pro Ala Pro
1               5


<210> SEQ ID NO 92
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<400> SEQUENCE: 92

Pro Lys Glu Pro Glu Gln
1               5
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The embodiments of the invention in which an exclusive property or privilege is claimed are defined as follows:

1. A method of generating an immune response against *Streptococcus pneumoniae*, comprising administering to a subject in need a therapeutically effective amount of an immunogenic composition, wherein the immunogenic composition comprises:

a plurality of different *S. pneumoniae* capsular polysaccharides (CPs) from *S. pneumoniae* serotypes 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19F, 19A, 20, 22F, 23F, or 33F;

a first polypeptide antigen with an amino acid sequence at least 90% identical to the polypeptide sequence of an antigen listed in Table 2, or an immunogenic fragment thereof; or

a second polypeptide antigen with an amino acid sequence at least 90% identical to the polypeptide sequence of an antigen listed in Table 1, or an immunogenic fragment thereof;

wherein the plurality of CPs are conjugated to the first polypeptide antigen.

2. The method of claim **1**, wherein the plurality of different CPs from *S. pneumoniae* serotypes is 1, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, or 23F.

3. The method of claim **2**, wherein the plurality of different CPs comprises at least one CP from each of the following serotypes 1, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F.

4. The method of claim **1**, wherein the first polypeptide antigen has an amino acid sequence with at least 90% identity to SEQ ID NO:22 or SEQ ID NO:36, or any immunogenic fragment thereof.

5. The method of claim **1**, wherein the second polypeptide antigen has an amino acid sequence with at least 90% identity to SEQ ID NO:90, or an antigenic fragment thereof, and comprises an L(Leu)460D(Asp) substitution.

6. The method of claim **1**, wherein the first and second polypeptide antigens are linked.

7. The method of claim **1**, wherein the immunogenic composition further comprises aluminum-based adjuvant.

8. The method of claim **1**, wherein the immunogenic compound is administered in a particle formulation.

9. The method of claim **1**, wherein the administration of the immunogenic composition reduces the mucosal carriage of *S. pneumoniae* in the subject.

10. The method of claim **1**, wherein the subject is a mammal.

11. The method of claim **1**, wherein the subject is a mouse or human.

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