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DESCRIPTION

BACKGROUND

Field of the Disclosure

[0001] This disclosure relates to the treatment and prevention of *Staphylococcus aureus* (*S. aureus*) infection. In particular, the disclosure provides compositions and methods for preventing *S. aureus* infection and treating a disease caused by a leukocidin, e.g., Pantone-Valentine leukocidin (PVL) or gamma-hemolysin expressing *S. aureus* infection.

Background of the Disclosure

[0002] *Staphylococcus aureus* (SA) is a gram positive human pathogen that is associated with or causes a wide range of pathologies ranging from skin and soft tissue infections to life-threatening systemic infections, e.g., minor skin infections such as pimples, impetigo, boils (furuncles), cellulitis folliculitis, carbuncles, scalded skin syndrome, and abscesses, to life-threatening deep infections such as pneumonia, sepsis, endocarditis, meningitis, post-operative wound infections, septicemia, and toxic shock syndrome (Nizet, V., J Allergy Clin Immunol, 2007. 120(1): p. 13-22; Kotzin, et al., Adv Immunol, 1993. 54: p. 99-166; Meyer et al., Int J Infect Dis, 2001. 5(3): p. 163-6; Schuberth et al., Vet Microbiol, 2001. 82(2): p. 187-99; and Silverstein et al., in Microbiology, Davis et al., eds. (Lippincott, Philadelphia, 1990), pp. 485-506).

[0003] Pneumonia is one of the most severe and prominent complications of *S. aureus* infection leading with 50,000 cases per year in the U.S. alone (Kuehnert, et al., Emerg. Infect. Dis. 11:868-872, 2005). *S. aureus* pneumonia has been traditionally ventilator associated but in recent years it has been recognized also as a major cause of community acquired pneumonia primarily in otherwise healthy children and young individuals.

[0004] The range of SA-associated pathologies reflects the diverse abilities of this microbe to escape the innate and adaptive immune response using multiple virulence factors including coagulase, capsular polysaccharides, adhesins, proteases, exoproteins that inactivate the complement system, pore-forming toxins, and other innate response mediators (Nizet, V., J Allergy Clin Immunol, 2007. 120(1): p. 13-22; Tristan et al., J Hosp Infect, 2007. 65 Suppl 2: p. 105-9). The rapid spread of methicillin resistant SA (MRSA) underscores the importance of developing vaccines for prevention or reduction of severity of MRSA infections. Most previous approaches for vaccine development have ignored the importance of including attenuated toxin components to disarm the immune evasion strategies of SA.

[0005] A significant increase in *S. aureus* isolates that exhibit resistance to most of the antibiotics currently available to treat infections has been observed in hospitals throughout the world. While MRSA strains were initially limited to health care settings, recent epidemics of community associated *S. aureus* (CA-MRSA) have been reported that cause severe disease in an otherwise healthy population. To date, five CA-MRSA clonal lineages are associated with these outbreaks: the Midwest clone (USA400, CC1), the European clone (CC80), the Southwest-Pacific Oceania clone (CC30), the Pacific clone (CC59), and the Pandemic clone (USA300, CC8). In addition to SCCmec IV, a characteristic feature of these major CA-MRSA lineages is that they have the *lukPV* operon encoding the Panton Valentine Leukocidin (PVL) (Diep, B.A. and M. Otto, Trends Microbiol, 2008. 16(8): p. 361-9), carried by the lysogenic phages ϕ SLT, ϕ PVL, ϕ SA2MW and ϕ SA2usa (Diep et al., Lancet, 2006. 367(9512): p. 731-9; Kaneko et al., Gene, 1998. 215(1): p. 57-67; Narita et al., Gene, 2001. 268(1-2): p. 195-206). The development of penicillin to combat *S. aureus* was a major advance in infection control and treatment. Unfortunately, penicillin-resistant organisms quickly emerged and the need for new antibiotics was paramount. With the introduction of every new antibiotic, *S. aureus* has been able to counter with β -lactamases, altered penicillin-binding proteins, and mutated cell membrane proteins allowing the bacterium to persist. Consequently, methicillin-resistant *S. aureus* (MRSA) and multidrug resistant organisms have emerged and established major footholds in hospitals and nursing homes around the world. (Chambers, H. F., Clin Microbiol Rev., 1:173, 1988; and Mulligan, M. E., et al., Am J Med., 94:313, 1993). Today, almost half of the Staphylococcal strains causing nosocomial infections are resistant to all antibiotics except vancomycin and linezolid. Since many vancomycin intermediate resistant *S. aureus* (VISA) among MRSA, and a few vancomycin resistant *S. aureus*, have been reported in the literature, it appears to be only a matter of time before vancomycin will become ineffective as well. (Appelbaum PC., Clin Microbiol Infect., 12 Suppl 1:16-23, 2006).

[0006] Natural immunity to *S. aureus* infections remains poorly understood. Typically, healthy humans and animals exhibit a high degree of innate resistance to *S. aureus* infections. Protection is attributed to intact epithelial and mucosal barriers and normal cellular and humoral responses. Titers of antibodies to *S. aureus* components are elevated after severe infections (Ryding et al., J Med Microbiol, 43(5):328-334, 1995), however to date there is no serological evidence of a correlation between these acquired antibody titers and human immunity.

[0007] Pore forming toxins that are secreted by *S. aureus* are crucial to its immune evasion. These toxins may create a survival advantage for the bacteria by forming pores into the membrane of target cells, inducing cell death and weakening the host during the first stages of infection. Because of the limited treatment modalities for *S. aureus* infection, the emergence of methicillin-resistant *S. aureus* poses a tremendous public health threat. While the molecular basis of the disease remains unclear, community-associated MRSA infection is closely linked to the presence of a Panton-Valentine leukocidin (PVL), a bipartite toxin consisting of the ~34 kDa LukF-PV and the ~32 kDa LukS-PV proteins (H. F. Chambers. The New England Journal of Medicine 352, 1485-1487, 2005). The function of the two PVL components (LukF-PV and LukS-PV) is synergistic and requires a sequence of events at the membrane surface of the

target cell (J. Kaneko and Y. Kamio. *Bioscience, Biotechnology, and Biochemistry* 68, 981-1003, 2004). In the first step, the secreted, water-soluble LukF-PV and LukS-PV monomers aggregate on the membrane surface, and subsequently assemble into heterodimers. In a stepwise fashion, these heterodimers further oligomerize into heterotetramers that are characterized by alternating LukF-PV and LukS-PV subunits. These heterotetramers further assemble into an octameric, disc-like structure that is comprised of alternating LukS-PV and LukF-PV subunits in a 1:1 stoichiometry (L. Jayasinghe and H. Bayley. *Protein Sci* 14, 2550-2561, 2005). At this stage, experimental data indicates that PVL exists as an octamer in pre-pore conformation that is not fully functional and not transversing the cell membrane. Subsequently, the pre-pore structure undergoes major conformational changes that result in the formation of a single transmembrane pore that allows the influx of calcium ions, leading to cell death (V. T. Nguyen, Y. Kamio, and H. Higuchi. *The EMBO Journal* 22, 4968-4979, 2003). PVL causes cytolysis resulting in loss of immune cells such as neutrophils and may also cause tissue damage promoting bacterial dissemination. PVL is believed to be involved in pathogenesis of invasive pneumonia and skin infections.

[0008] WO 2006/135912 and US 2009/0074755 disclose mutants of LukS-PV and LukF-PV with disrupted oligomerization. US 2010/0158871 discloses compositions and methods for targeted delivery of anti-tumor agents such as nucleic acids encoding PVL, using sickled erythrocytes, their nucleated precursors, and erythroleukemia cells.

[0009] Accordingly, there remains a need in the art for compositions and methods that can safely confer immunity to PVL-expressing *S. aureus*.

BRIEF SUMMARY

[0010] The present disclosure provides methods of inducing an immune response against a PVL-expressing *S. aureus*, methods of preventing or treating a PVL-expressing *S. aureus* infections, and compositions for preventing or treating a PVL-expressing *S. aureus* infections. In certain embodiments, the disclosure provides attenuated mutants of LukS-PV and LukF-PV as vaccines for *S. aureus* infections.

[0011] Some embodiments of the disclosure include an isolated mutant staphylococcal leukocidin subunit polypeptide comprising a wild-type staphylococcal leukocidin subunit except for one to five amino acid substitutions at conserved residues, which reduce toxicity of the mutant leukocidin subunit relative to the corresponding wild-type leukocidin subunit; where the wild-type leukocidin subunit comprises three consecutive regions designated A-B-C arranged from amino terminus to carboxy terminus, and wherein region B comprises the amino acid sequence of SEQ ID NO: 2.

[0012] Also disclosed is the mutant leukocidin subunit described herein, where region A of the wild-type leukocidin subunit comprises the amino acid sequence of SEQ ID NO: 1 and where region C of the wild-type leukocidin subunit comprises the amino acid sequence of SEQ ID NO:

3.

[0013] Also disclosed is the mutant leukocidin subunit as described herein, which comprises an amino acid substitution at position K24 of SEQ ID NO: 2. In certain embodiments of the disclosure, K24 is substituted with alanine.

[0014] Some embodiments of the disclosure include the mutant leukocidin subunit as described herein, which comprises an amino acid substitution at position S18 of SEQ ID NO: 3. In certain embodiments of the disclosure S18 is substituted with alanine.

[0015] Some embodiments of the disclosure include the mutant leukocidin as described herein, which comprises an amino acid substitution at position Y58 of SEQ ID NO: 2. In certain embodiments of the disclosure Y58 is substituted with alanine.

[0016] Some embodiments of the disclosure include the mutant leukocidin subunit as described herein, which comprises an amino acid substitution at position T11 of SEQ ID NO: 1. In certain embodiments of the disclosure T11 is substituted with phenylalanine.

[0017] Some embodiments of the disclosure include the mutant leukocidin subunit as described herein, which comprises an amino acid substitution at position D28 of SEQ ID NO: 2. In certain embodiments of the disclosure D28 is substituted with alanine.

[0018] In some embodiments of the disclosure the wild-type leukocidin subunit is a Pantone-Valentine leukocidin (PVL) LukS-PV. In certain embodiments of the disclosure, the wild-type leukocidin subunit comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 5, SEQ ID NO: 15, and SEQ ID NO: 16. In some embodiments of the disclosure the mutant LukS-PV subunit comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, and SEQ ID NO: 14. In certain embodiments of the disclosure the mutant leukocidin subunit as described herein, comprises the amino acid of SEQ ID NO: 14.

[0019] In some embodiments of the disclosure the mutant leukocidin subunit as described herein, comprises a calculated molecular energy between 600 kcal/mol and 7500 kcal/mol, or between 900 kcal/mol and 3900 kcal/mol, or between 2000 kcal/mol and 3650 kcal/mol in complex with a wild-type Pantone-Valentine leukocidin (PVL) LukF-PV subunit.

[0020] Some embodiments of the disclosure include an isolated mutant staphylococcal leukocidin subunit polypeptide comprising a wild-type staphylococcal leukocidin subunit except for one to five amino acid substitutions at conserved residues, which reduce toxicity of the mutant leukocidin subunit relative to the corresponding wild-type leukocidin subunit; wherein the wild-type leukocidin subunit comprises the amino acid sequence of SEQ ID NO: 4.

[0021] In some embodiments of the disclosure the mutant leukocidin subunit as described

herein, comprises an amino acid substitution at position K8. In certain embodiments of the disclosure K8 is substituted with alanine.

[0022] In some embodiments of the disclosure the mutant leukocidin subunit as described herein, comprises an amino acid substitution at position D28. In certain embodiments of the disclosure D28 is substituted with alanine.

[0023] In some embodiments of the disclosure the mutant leukocidin subunit as described herein, comprises an amino acid substitution at position E53. In certain embodiments of the disclosure E53 is substituted with alanine.

[0024] In some embodiments of the disclosure the wild-type leukocidin subunit is a Pantone-Valentine leukocidin (PVL) LukF-PV. In certain embodiments of the disclosure the wild-type leukocidin subunit comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 16, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 26, and SEQ ID NO: 27. In some embodiments of the disclosure, the mutant LukF-PV subunit comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 18, SEQ ID NO: 19, and SEQ ID NO: 20. In one embodiment of the disclosure, the mutant LukF-PV subunit comprises an amino acid sequence of SEQ ID NO: 18.

[0025] In some embodiments of the disclosure the mutant leukocidin subunit as described herein, comprises a calculated molecular energy between 900 kcal/mol and 1500 kcal/mol in complex with a wild-type Pantone-Valentine leukocidin (PVL) LukS-PV.

[0026] Some embodiments of the disclosure include the mutant leukocidin subunit as described herein, which is less toxic in a neutrophil toxicity assay compared to the corresponding wild-type leukocidin subunit.

[0027] Some embodiments of the disclosure include the mutant leukocidin subunit as described herein, which does not oligomerize with a wild-type leukocidin component. In certain embodiments of the disclosure, the wild-type leukocidin component is selected from the group consisting of a LukS-PV subunit, a LukF-PV subunit, Gamma hemolysin A, Gamma hemolysin B, Gamma hemolysin C, LukE and LukD subunit, or any combination thereof.

[0028] Also disclosed is a polypeptide complex comprising the mutant leukocidin subunits as described herein.

[0029] Also disclosed is an isolated polynucleotide comprising a nucleic acid which encodes the mutant leukocidin subunit described herein. In some embodiments of the disclosure, the polynucleotide further comprises a heterologous nucleic acid. In some embodiments of the disclosure, the heterologous nucleic acid comprises a promoter operably associated with the nucleic acid encoding the polypeptide described herein.

[0030] Also included is a vector comprising the polynucleotide described herein, or a host cell

comprising the vector. In some embodiments of the disclosure, the vector is a plasmid. In some embodiments of the disclosure, the host cell is a bacterium, an insect cell, a mammalian cell, yeast or a plant cell. In certain embodiments of the disclosure, the bacterium is *Escherichia coli*.

[0031] Also disclosed is a method of producing a mutant staphylococcal leukocidin subunit polypeptide, comprising culturing the host cell described herein and recovering the polypeptide.

[0032] Further disclosed is a composition comprising the mutant leukocidin subunit or the polypeptide complex, as described herein, and a carrier. The composition can further comprise an adjuvant. Further disclosed is a composition comprising an additional staphylococcal antigen. In certain embodiments of the disclosure, the additional staphylococcal antigen is an alpha-hemolysin subunit polypeptide.

[0033] Also disclosed is a method of inducing a host immune response against a *Staphylococcus aureus* strain, comprising administering to a subject in need of the immune response an effective amount of the composition described herein. In certain embodiments of the disclosure the immune response is an antibody response. In some embodiments of the disclosure the the immune response selected from the group consisting of an innate response, a humoral response, an antibody response a T cell response, and a combination of two or more of said immune responses.

[0034] Also disclosed is a method of preventing or treating a Staphylococcal disease or infection in a subject comprising administering to a subject in need thereof the composition described herein. The infection can be localized or systemic infection of skin, soft tissue, blood, or an organ, or is auto-immune in nature, and disease can be a respiratory disease, such as pneumonia. The subject can be an animal, a vertebrate, a mammal, or a human. The composition described herein can be administered via intramuscular injection, intradermal injection, intraperitoneal injection, subcutaneous injection, intravenous injection, oral administration, mucosal administration, intranasal administration, or pulmonary administration.

[0035] Also included is a method of producing a vaccine against *S. aureus* infection comprising isolating the mutant leukocidin subunit or the polypeptide complex, as described herein, and combining the mutant leukocidin subunit or polypeptide complex with an adjuvant. In certain embodiments of the disclosure, the method discloses further comprising combining the mutant leukocidin subunit or polypeptide complex with an additional staphylococcal antigen.

BRIEF DESCRIPTION OF THE DRAWING

[0036]

Figure 1-Interface interactions between Thr28 of LukS-PV and Asn158 and Phe159 of LukF-

PV.

Figure 2-Interface interaction between Ser209 of LukS-PV and Lys102 of LukF-PV.

Figure 3-Percent (%) survival of HL-60 derived neutrophils in the presence of 3000 or 300 ng/ml of LukS-PV mutants (K97A, D101A, S209A, T28F, T28F/Y131A, T28F/S209A, or T28F/K97A/S209A) or the wild-type LukS-PV along with the same concentrations of the wild-type LukF-PV. Cells only bar represents the control with no toxin added. Data are shown as average of 3-5 experiments with standard deviation shown as error bars.

Figure 4-Percent (%) survival of HL-60 derived neutrophils in the presence of 3000 or 300 ng/ml of LukF-PV mutants (K102A, D121A, or E147A) or the wild-type LukF-PV along with the same concentrations of the wild-type LukS-PV or triple mutant of LukS-PV as defined in Figure 3. Cells only bar represents the control with no toxin added.

Figure 5-Alignment of S subunits of leukocidins amino acid sequences.

Figure 6-Percent (%) survival of polymorphonuclear neutrophils (PMN) in supernatants of PVL positive (USA300&400) and PVL negative (Newman, 8325-4) SA strains treated with anti-LukS-PV or control (rabbit total IgG). PVL: purified PVL; BHI: medium control; and Cells only: control with no toxin added.

Figure 7-(**A**) SDS-PAGE and (**B**) Western blot analysis of mutant PVL subunits. M: MW marker; Lane 1: LukS-PV Mut9; Lane 2: LukF-PV Mut1. (**C**) SDS-PAGE (Lane 1) and Western blot (Lane 2) analysis of LukF-PV triple mutant (K102A/D121A/E147A); M: MW marker.

Figure 8-(**A**) Percent (%) survival of HL-60 derived neutrophils treated with increasing concentrations of wild-type or mutant LukS in combination with wild-type LukF. Results are from 5 independent experiments. STDV is shown only for wild-type and triple mutant. (**B**) % survival of HL-60 derived neutrophils treated with increasing concentrations of wild-type or mutant LukF in combination with wild-type LukS or LukS Triple mutant (Mut9). (**C**) % survival of HL-60 with increasing concentrations of wild-type or triple mutant LukF or LukF mutant 1 in combination with wild-type LukS or LukS Triple mutant (Mut9).

Figure 9-Thermal unfolding of LukS-PV and LukF-PV proteins as monitored by thermofluor assay using Sypro Orange dye. (**A**) Plot of fluorescence intensity of PVL proteins (wild-type LukS-PV, LukS-PV Mut 8, LukS-PV Mut 9, wild-type LukF-PV, and LukF-PV Mut 1) at 588 nm against temperature. Data was collected for every 5°C. (**B**) Plot of unfolded fraction calculated from the thermal denaturation curve for PVL proteins (wild-type LukS-PV, LukS-PV Mut 8, LukS-PV Mut 9, wild-type LukF-PV, and LukF-PV Mut 1).

Figure 10-Immunogenicity of LukS-Mut9, wild-type LukS-PV, and control (STEBVax) in mice with different adjuvants. Doses used: antigens: 10 ug; Al(OH)₃: 34 ug, AlPO₄: 70 ug, IDC-1001: 20 ug, and CpG: 10 ug/mouse. (**A**) Total antibody titers determined by ELISA for individual mouse sera (EC₅₀; i.e. dilution of serum with 50% maximal signal on ELISA plates coated with wild type LukS-PV). (**B**) Neutralization determined in HL-60 toxin neutralization assay using wild type LukS-PV and LukF-PV toxins. Percent neutralization of wild type toxin is

shown at 1:100 dilution of serum from vaccinated mice (sera pooled from 5 mice in each group).

Figure 11-Bacterial CFU in blood and organs (liver, spleen, lung, and kidneys) after treatment of mice with 2 mg naive IgG (N), 2 mg AT62-IgG (AT) or the combination of 2mg AT62-IgG and 0.25 mg of LukS-PV IgG (AT+S).

Figure 12-Survival curves showing protection against (A) bacteremia/sepsis and (B) pneumonia with Luk (LukS Mut 9, LukF Mut1, and LukS Mut 9 + LukF Mut1) and Hla (AT-62aa) vaccine candidates as well as the combination of LukS Mut 9 + LukF Mut1 + AT-62aa and BSA control. No further lethality was observed after the time points shown.

Figure 13-(A) Specificity of LukS-PV mutant-9 mouse sera to homologous antigen, (B) Cross-reactivity of LukS-PV mutant-9 mouse sera to HlgB antigen, (C) Cross-reactivity of LukS-PV mutant-9 mouse sera to HlgC antigen. (D) Neutralization efficacy of LukS-PV mutant-9 mouse sera against 200 ng/ml of PVL and or gamma-hemolysin toxins in invitro XTT cytotoxicity assay based on human neutrophil cell line HL-60.

Figure 14-(A) MPD based oligomerization assay. Lane 1: Molecular weight marker; Lane 2: LukS wt+LukFwt; Lane 3: LukS wt +Lukf mut1; Lane 4: LukS wt+ Gamma B; Lane 5: LukF wt+ LukS mut9; Lane 6: LukS mut9 + LukF mut1; Lane 7: LukS mut9 + Gamma B. (B) Inhibition of oligomeric band by anti LukS specific polyclonal antibody. Lane 1: Marker; Lanes 2-8: LukS+LukF + anti-LukS pAbs at 2-fold decreasing concentrations (5.5mg/ml to 0.85mg/ml); Lane 9: LukS+LukF without pAbs; Lane 10: LukS+LukF+ pAbs without MPD; Lane 11: pAbs + MPD only. (C) Inhibition of oligomeric band formed by LukS-PV + hlgB by anti LukS specific polyclonal antibody. Lane 1: Marker; Lanes 2-8: LukS-PV + hlgB (940 ng each) + anti-LukS pAbs at 2-fold decreasing concentrations (34.5 ug/ml to 0.5mg/ml); Lane 9: LukS-PV + hlgB without pAbs; Lane 10: LukS-PV + hlgB + pAbs without MPD; Lanes 11-14 Naive Rabbit pAbs (34.5 ug/ml to 4.3 mg/ml) + LukS-PV + hlgB (940 ng each) and Lane 15: Naive Rabbit pAbs+ MPD only.

DETAILED DESCRIPTION

[0037] The invention is defined by the appended claims. Any embodiment not falling under the scope of the appended claims does not form part of the invention.

[0038] Disclosed herein are mutant staphylococcal leukocidin subunit polypeptides, *e.g.*, a mutant LukS-PV subunit polypeptide or a mutant LukF-PV subunit polypeptide, compositions comprising one or more mutant leukocidin subunits as disclosed herein, and methods of eliciting an immune response against staphylococci, *e.g.* *S. aureus*, or treating or preventing a staphylococcal infection in a subject, comprising administering to a subject an effective amount of a mutant staphylococcal leukocidin subunit polypeptide as disclosed herein.

[0039] It is to be noted that the term "a" or "an" entity refers to one or more of that entity; for example, "a polynucleotide," is understood to represent one or more polynucleotides. As such, the terms "a" (or "an"), "one or more," and "at least one" can be used interchangeably herein.

[0040] The terms "nucleic acid" or "nucleic acid fragment" refers to any one or more nucleic acid segments, *e.g.*, DNA or RNA fragments, present in a polynucleotide or construct. Two or more nucleic acids of the disclosure can be present in a single polynucleotide construct, *e.g.*, on a single plasmid, or in separate (non-identical) polynucleotide constructs, *e.g.*, on separate plasmids. Furthermore, any nucleic acid or nucleic acid fragment can encode a single polypeptide, *e.g.*, a single antigen, cytokine, or regulatory polypeptide, or can encode more than one polypeptide, *e.g.*, a nucleic acid can encode two or more polypeptides. In addition, a nucleic acid can encode a regulatory element such as a promoter or a transcription terminator, or can encode a specialized element or motif of a polypeptide or protein, such as a secretory signal peptide or a functional domain.

[0041] The term "polynucleotide" is intended to encompass a singular nucleic acid or nucleic acid fragment as well as plural nucleic acids or nucleic acid fragments, and refers to an isolated molecule or construct, *e.g.*, a virus genome (*e.g.*, a non-infectious viral genome), messenger RNA (mRNA), plasmid DNA (pDNA), or derivatives of pDNA (*e.g.*, minicircles as described in (Darquet, A-M et al., Gene Therapy 4:1341-1349, 1997) comprising a polynucleotide. A polynucleotide can be provided in linear (*e.g.*, mRNA), circular (*e.g.*, plasmid), or branched form as well as double-stranded or single-stranded forms. A polynucleotide can comprise a conventional phosphodiester bond or a non-conventional bond (*e.g.*, an amide bond, such as found in peptide nucleic acids (PNA)).

[0042] As used herein, the term "polypeptide" is intended to encompass a singular "polypeptide" as well as plural "polypeptides," and comprises any chain or chains of two or more amino acids. Thus, as used herein, a "peptide," an "oligopeptide," a "dipeptide," a "tripeptide," a "protein," an "amino acid chain," an "amino acid sequence," or any other term used to refer to a chain or chains of two or more amino acids, are included in the definition of a "polypeptide," (even though each of these terms can have a more specific meaning) and the term "polypeptide" can be used instead of, or interchangeably with any of these terms. The term further includes polypeptides which have undergone post-translational modifications, for example, glycosylation, acetylation, phosphorylation, amidation, derivatization by known protecting/blocking groups, proteolytic cleavage, or modification by non-naturally occurring amino acids.

[0043] The terms "staphylococcal leukocidin subunit," "LukS-PV polypeptide," and "LukF-PV polypeptide," as used herein, encompass mature or full length staphylococcal leukocidin subunits (*e.g.*, LukS-PV or LukF-PV), and fragments, variants or derivatives of mature or full length staphylococcal leukocidin subunits (*e.g.*, LukS-PV and LukF-PV), and chimeric and fusion polypeptides comprising mature or full length staphylococcal leukocidin subunits (*e.g.*, LukS-PV and LukF-PV) or one or more fragments of mature or full length staphylococcal leukocidin subunits (*e.g.*, LukS-PV and LukF-PV). In certain embodiments of the disclosure,

staphylococcal leukocidin subunits as disclosed herein are mutant staphylococcal leukocidin subunits, which are reduced in toxicity relative to a corresponding wild-type leukocidin subunit. By "corresponding wild-type leukocidin subunit" is meant the native leukocidin subunit from which the mutant leukocidin subunit was derived.

[0044] Pore forming toxins, e.g., single-component alpha-hemolysin and the bi-component hemolysins and leukotoxins, play an important role in staphylococcal immune evasion. These toxins kill key immune cells and cause tissue destruction, thereby often weakening the host during the first stage of infection and promoting bacterial dissemination and metastatic growth. The two PVL components, LukS-PV and LukF-PV, are secreted separately and form the pore-forming octameric complex upon binding of LukS-PV to its receptor and subsequent binding of LukF-PV to LukS-PV (Miles et al., Protein Sci, 2002. 11(4): p. 894-902; Pedelacq et al., Int J Med Microbiol, 2000. 290(4-5): p. 395-401). Targets of PVL include, e.g., polymorphonuclear neutrophils (PMN), monocytes, and macrophages.

[0045] Other bi-component toxins have been characterized in *S. aureus*: S components HlgA and HlgC and the F component HlgB for γ -hemolysin; lukE (S) and lukD (F); and lukM (S) and lukF-PV-like (F). Due to their close similarity, these S components can combine with a F component and form an active toxin with different target specificity (Ferrerias et al., Biochim Biophys Acta, 1998. 1414(1-2): p. 108-26; Prevost et al., Infect Immun, 1995. 63(10): p. 4121-9). γ -Hemolysin is strongly hemolytic and 90% less leukotoxic than PVL, while PVL is non-hemolytic. However, HlgA or HlgC paired with lukF-PV promotes leukotoxic activity (Prevost et al., Infect Immun, 1995. 63(10): p. 4121-9). Luk and PVL lyse neutrophils, and Hlg is hemolytic (Kaneko et al., Biosci Biotechnol Biochem, 2004. 68(5): p. 981-1003) and was also reported to lyse neutrophils (Malachowa et al., PLoS One, 2011. 6(4): p. e18617). While PVL subunits are phage derived (the F&S leukocidin), Hlg proteins are derived from Hlg locus (*hlg*) and found in 99% of clinical isolates (Kaleko et al.). Hlg subunits are strongly upregulated during *S. aureus* growth in blood (Malachowa et al.), and Hlg was shown to be involved in survival of *S. aureus* in blood (Malachowa et al., Virulence, 2011. 2(6)). The mutant USA300 Δ -hlgABC has reduced capacity to cause mortality in a mouse bacteremia model (Malachowa et al., PLoS One, 2011. 6(4): p. e18617). Alonzo et al. have shown that LukED toxin is critical for bloodstream infections in mice (Alonzo et al., Mol Microbiol, 2012. 83(2): p. 423-35). Another novel *S. aureus* leukotoxin, LukGH, has also been described, which synergizes with PVL to enhance human PMN lysis (Ventura et al., PLoS One, 2010. 5(7): p. e11634).

[0046] The terms "fragment," "analog," "derivative," or "variant" when referring to a staphylococcal leukocidin subunit (e.g., LukS-PV or LukF-PV) of the present disclosure include any polypeptide which retains at least some of the immunogenicity or antigenicity of the source protein. Fragments of staphylococcal leukocidin subunits (e.g., LukS-PV or LukF-PV) as described herein include proteolytic fragments, deletion fragments and in particular, fragments of staphylococcal leukocidin subunits (e.g., LukS-PV or LukF-PV) which exhibit increased solubility during expression, purification, or administration to an animal. Fragments of staphylococcal leukocidin subunits (e.g., LukS-PV or LukF-PV) as described herein further include proteolytic fragments or deletion fragments which exhibit reduced pathogenicity or

toxicity when delivered to a subject. Polypeptide fragments further include any portion of the polypeptide which comprises an antigenic or immunogenic epitope of the source polypeptide, including linear as well as three-dimensional epitopes.

[0047] An "epitopic fragment" of a polypeptide antigen is a portion of the antigen that contains an epitope. An "epitopic fragment" can, but need not, contain amino acid sequence in addition to one or more epitopes.

[0048] The term "variant," as used herein, refers to a polypeptide that differs from the recited polypeptide due to amino acid substitutions, deletions, insertions, and/or modifications. Non-naturally occurring variants can be produced using art-known mutagenesis techniques. In some embodiments of the disclosure, variant polypeptides differ from an identified sequence by substitution, deletion or addition of three amino acids or fewer. Such variants can generally be identified by modifying a polypeptide sequence, and evaluating the antigenic or pathogenic properties of the modified polypeptide using, for example, the representative procedures described herein. In some embodiments of the disclosure, variants of a wild-type staphylococcal leukocidin subunit (e.g., LukS-PV, or LukF-PV, or both) form a protein complex which is less toxic than the wild-type complex.

[0049] Polypeptide variants disclosed herein exhibit at least about 85%, 90%, 94%, 95%, 96%, 97%, 98%, 99% or 99.9% sequence identity with identified polypeptide. Variant polypeptides can comprise conservative or non-conservative amino acid substitutions, deletions or insertions. Variants can comprise staphylococcal leukocidin subunits (e.g., LukS-PV or LukF-PV, or both) identical to a wild-type leukocidin subunit except for at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, or more amino acid substitutions, where the substitutions render a leukocidin complex comprising the variant leukocidin subunit less toxic than a corresponding wild-type protein complex. Derivatives of staphylococcal leukocidin subunits (e.g., LukS-PV and LukF-PV) as described herein are polypeptides which have been altered so as to exhibit additional features not found on the native polypeptide. Examples include fusion proteins. An analog is another form of a staphylococcal leukocidin subunit (e.g., LukS-PV and LukF-PV) described herein. An example is a proprotein which can be activated by cleavage of the proprotein to produce an active mature polypeptide.

[0050] Variants can also, or alternatively, contain other modifications, whereby, for example, a polypeptide can be conjugated or coupled, e.g., fused to a heterologous amino acid sequence, e.g., a signal (or leader) sequence at the N-terminal end of the protein which co-translationally or post-translationally directs transfer of the protein. The polypeptide can also be conjugated or produced coupled to a linker or other sequence for ease of synthesis, purification or identification of the polypeptide (e.g., 6-His), or to enhance binding of the polypeptide to a solid support. For example, the polypeptide can be conjugated or coupled to an immunoglobulin Fc region. The polypeptide can also be conjugated or coupled to a sequence that imparts or modulates the immune response to the polypeptide (e.g., a T-cell epitope, B-cell epitope, cytokine, chemokine, etc.) and/or enhances uptake and/or processing of the polypeptide by antigen presenting cells or other immune system cells. The polypeptide can also be conjugated

or coupled to other polypeptides/epitopes from *Staphylococcus sp.* and/or from other bacteria and/or other viruses to generate a hybrid immunogenic protein that alone or in combination with various adjuvants can elicit protective immunity to other pathogenic organisms. The polypeptide can also be conjugated or coupled to moieties which confer greater stability or improve half life such as, but not limited to albumin, an immunoglobulin Fc region, polyethylene glycol (PEG), and the like. The polypeptide can also be conjugated or coupled to moieties (e.g., immunogenic carbohydrates, e.g., a capsular polysaccharide or a surface polysaccharide) from *Staphylococcus sp.* and/or from other bacteria and/or other viruses to generate a modified immunogenic protein that alone or in combination with one or more adjuvants can enhance and/or synergize protective immunity. In certain embodiments of the disclosure, the polypeptide described herein further comprises an immunogenic carbohydrate. In one embodiment of the disclosure, the immunogenic carbohydrate is a saccharide.

[0051] The term "saccharide" throughout this specification may indicate polysaccharide or oligosaccharide and includes both. Polysaccharides of the present disclosure may be isolated from bacteria and may be sized by known methods. For example, full length polysaccharides may be "sized" (e.g., their size may be reduced by various methods such as acid hydrolysis treatment, hydrogen peroxide treatment, sizing by EMULSIFLEX® followed by a hydrogen peroxide treatment to generate oligosaccharide fragments or microfluidization). Polysaccharides can be sized in order to reduce viscosity in polysaccharide samples and/or to improve filterability for conjugated products. Oligosaccharides have a low number of repeat units (e.g., 5-30 repeat units) and are typically hydrolysed polysaccharides. Polysaccharides of the present disclosure may be produced recombinantly.

[0052] *S. aureus* capsular antigens are surface associated, limited in antigenic specificity, and highly conserved among clinical isolates. In one embodiment of the disclosure, the immunogenic carbohydrate of the present disclosure is a capsular polysaccharide (CP) of *S. aureus*. In one embodiment of the disclosure, a capsular saccharide may be a full length polysaccharide, however in other embodiments it may be one oligosaccharide unit, or a shorter than native length saccharide chain of repeating oligosaccharide units. Serotyping studies of staphylococcal isolates have revealed several putative capsular serotypes, with types 5 and 8 (CP5 and CP8) being the most prevalent among isolates from clinical infections, accounting for about 25% and 50% of isolates recovered from humans, respectively (O'Riordan and Lee, Clinical Microbiology Reviews, January 2004, p. 218-234, Vol. 17, No. 1; Poutrel and Sutra, J Clin Microbiol. 1993 Feb;31(2):467-9). The same isolates were also recovered from poultry, cows, horses and pigs (Tollersrud et al., J Clin Microbiol. 2000 Aug;38(8):2998-3003; Cunnion KM et al., Infect Immun. 2001 Nov;69(11):6796-803). Type 5 and 8 capsular polysaccharides purified from the prototype strains Reynolds and Becker, respectively, are structurally very similar to each other and to the capsule made by strain T, described previously by Wu and Park (Wu and Park. 1971. J. Bacteriol. 108:874-884). Type 5 has the structure $(\rightarrow 4)\text{-}3\text{-O-Ac-}\beta\text{-D-MaaNAcA-(1}\rightarrow 4)\text{-}\alpha\text{-L-FucNAc-(1}\rightarrow 3)\text{-}\beta\text{-D-FucNAc-(1}\rightarrow)_n$ (Fournier, J. M., et al., 1987. Ann. Inst. Pasteur Microbiol. 138:561-567; Moreau, M., et al., 1990. Carbohydr. Res. 201:285-297), and type 8 has the structure $(\rightarrow 3)\text{-}4\text{-O-Ac-}\beta\text{-D-ManNAcA-(1}\rightarrow 3)\text{-}\alpha\text{-L-FucNAc-(1}\rightarrow 3)\text{-}\beta\text{-D-FucNAc-(1}\rightarrow)_n$ (Fournier, J. M., et al., 1984. Infect. Immun. 45:87-93). Type 5 and 8

polysaccharides differ only in the linkages between the sugars and in the sites of O-acetylation of the mannosaminuronic acid residues, yet they are serologically distinct.

[0053] Type 5 and 8 CP conjugated to a detoxified recombinant *Pseudomonas aeruginosa* exotoxin A carrier were shown to be highly immunogenic and protective in a mouse model (A Fattom et al., Infect Immun. 1993 March; 61(3): 1023-1032; A Fattom et al., Infect Immun. 1996 May; 64(5): 1659-1665) and passive transfer of the CP5-specific antibodies from the immunized animals induced protection against systemic infection in mice (Lee et al., Infect Immun. 1997 October; 65(10): 4146-4151) and against endocarditis in rats challenged with a serotype 5 *S. aureus* (Shinefield H et al., N Engl J Med. 2002 Feb 14;346(7):491-6). A bivalent CP5 and CP8 conjugate vaccine (StaphVAX®, Nabi Biopharmaceutical) was developed that provided 75% protection in mice against *S. aureus* challenge. The vaccine has been tested on humans (Fattom Al et al., Vaccine. 2004 Feb 17;22(7):880-7; Maira-Litrán T et al., Infect Immun. 2005 Oct;73(10):6752-62). In certain embodiments of the disclosure, the oligopeptide of the present disclosure is combined with or conjugated to an immunogenic carbohydrate (e.g., CP5, CP8, a CP fragment or a combination thereof).

[0054] Immunization with poly-N-acetylglucosamine (PNAG) (McKenney D. et al., Science. 1999 May 28;284(5419):1523-7) or poly-N-succinyl glucosamine (PNSG) (Tuchscher LP. et al., Infect Immun. 2008 Dec;76(12):5738-44. Epub 2008 Sep 22), both *S. aureus* surface carbohydrates, has been shown to generate at least partial protection against *S. aureus* challenge in experimental animal models. PNSG was identified as the chemical form of the *S. epidermidis* capsular polysaccharide/adhesin (PS/A) which mediates adherence of coagulase-negative staphylococci (CoNS) to biomaterials, serves as the capsule for strains of CoNS that express PS/A, and is a target for protective antibodies. PNSG is also made by *S. aureus*, where it is an environmentally regulated, *in vivo*-expressed surface polysaccharide and similarly serves as a target for protective immunity (McKenney D. et al., J. Biotechnol. 2000 Sept 29;83(1-2): 37-44). In certain embodiments of the present disclosure, the immunogenic carbohydrate is a surface polysaccharide, e.g., poly-N-acetylglucosamine (PNAG), poly-N-succinyl glucosamine (PNSG), a surface polysaccharide fragment or a combination thereof.

[0055] Wall Teichoic Acid (WTA) is a prominent polysaccharide widely expressed on *S. aureus* strains (Neuhaus, F.C. and J. Baddiley, Microbiol Mol Biol Rev, 2003. 67(4):686-723) and antisera to WTA have been shown to induce opsonophagocytic killing alone and in presence of complement ((Thakker, M., et al., Infect Immun, 1998. 66(11):5183-9), and Fattom et al, US Patent 7,754,225). WTA is linked to peptidoglycans and protrudes through the cell wall becoming prominently exposed on non-encapsulated strains such as USA300 responsible for most cases of community acquired MRSA (CA MRSA) in the US (Hidron, A.I., et al., Lancet Infect Dis, 2009. 9(6):384-92).

[0056] Lipoteichoic acid (LTA) is a constituent of the cell wall of Gram-positive bacteria, e.g., *Staphylococcus aureus*. LTA may bind to target cells non-specifically through membrane phospholipids, or specifically to CD14 and to Toll-like receptors. Target-bound LTA can interact with circulating antibodies and activate the complement cascade to induce a passive immune

kill phenomenon. It also triggers the release from neutrophils and macrophages of reactive oxygen and nitrogen species, acid hydrolases, highly cationic proteinases, bactericidal cationic peptides, growth factors, and cytotoxic cytokines, which may act in synergy to amplify cell damage.

[0057] In certain embodiments of the disclosure, a surface polysaccharide is combined with or conjugated to a polypeptide of the disclosure. In certain embodiments of the disclosure the surface polysaccharide is, e.g., poly-N-acetylglucosamine (PNAG), poly-N-succinyl glucosamine (PNSG), Wall Teichoic Acid (WTA), Lipoteichoic acid (LPA), a fragment of any of said surface polysaccharides, or a combination of two or more of said surface polysaccharides.

[0058] The term "sequence identity" as used herein refers to a relationship between two or more polynucleotide sequences or between two or more polypeptide sequences. When a position in one sequence is occupied by the same nucleic acid base or amino acid in the corresponding position of the comparator sequence, the sequences are said to be "identical" at that position. The percentage "sequence identity" is calculated by determining the number of positions at which the identical nucleic acid base or amino acid occurs in both sequences to yield the number of "identical" positions. The number of "identical" positions is then divided by the total number of positions in the comparison window and multiplied by 100 to yield the percentage of "sequence identity." Percentage of "sequence identity" is determined by comparing two optimally aligned sequences over a comparison window and a homologous polypeptide from another isolate. In order to optimally align sequences for comparison, the portion of a polynucleotide or polypeptide sequence in the comparison window can comprise additions or deletions termed gaps while the reference sequence is kept constant. An optimal alignment is that alignment which, even with gaps, produces the greatest possible number of "identical" positions between the reference and comparator sequences. Percentage "sequence identity" between two sequences can be determined using the version of the program "BLAST 2 Sequences" which is available from the National Center for Biotechnology Information as of September 1, 2004, which program incorporates the programs BLASTN (for nucleotide sequence comparison) and BLASTP (for polypeptide sequence comparison), which programs are based on the algorithm of Karlin and Altschul (Proc. Natl. Acad. Sci. USA 90(12):5873-5877, 1993). When utilizing "BLAST 2 Sequences," parameters that were default parameters as of September 1, 2004, can be used for word size (3), open gap penalty (11), extension gap penalty (1), gap drop-off (50), expect value (10) and any other required parameter including but not limited to matrix option.

[0059] The term "epitope," as used herein, refers to portions of a polypeptide having antigenic or immunogenic activity in an animal, for example a mammal, for example, a human. An "immunogenic epitope," as used herein, is defined as a portion of a protein that elicits an immune response in an animal, as determined by any method known in the art. The term "antigenic epitope," as used herein, is defined as a portion of a protein to which an antibody or T-cell receptor can immunospecifically bind its antigen as determined by any method well known in the art. Immunospecific binding excludes non-specific binding but does not necessarily exclude cross-reactivity with other antigens. Whereas all immunogenic epitopes

are antigenic, antigenic epitopes need not be immunogenic.

[0060] As used herein, a "coding region" is a portion of nucleic acid which consists of codons translated into amino acids. Although a "stop codon" (TAG, TGA, or TAA) is not translated into an amino acid, it can be considered to be part of a coding region, but any flanking sequences, for example promoters, ribosome binding sites, transcriptional terminators, and the like, are outside the coding region.

[0061] The term "codon optimization" is defined herein as modifying a nucleic acid sequence for enhanced expression in the cells of the host of interest by replacing at least one, more than one, or a significant number, of codons of the native sequence with codons that are more frequently or most frequently used in the genes of that host. Various species exhibit particular bias for certain codons of a particular amino acid.

[0062] The term "composition," or "pharmaceutical composition" can include compositions containing immunogenic polypeptides of the disclosure along with *e.g.*, adjuvants or pharmaceutically acceptable carriers, excipients, or diluents, which are administered to an individual already suffering from *S. aureus* infection or an individual in need of immunization against *S. aureus* infection.

[0063] The term "pharmaceutically acceptable" refers to compositions that are, within the scope of sound medical judgment, suitable for contact with the tissues of human beings and animals without excessive toxicity or other complications commensurate with a reasonable benefit/risk ratio. In some embodiments of the disclosure, the polypeptides, polynucleotides, compositions, and vaccines described herein are pharmaceutically acceptable.

[0064] An "effective amount" is that amount the administration of which to an individual, either in a single dose or as part of a series, is effective for treatment or prevention. An amount is effective, for example, when its administration results in a reduced incidence of *S. aureus* infection relative to an untreated individual, as determined, *e.g.*, after infection or challenge with infectious *S. aureus*, including, but is not limited to reduced bacteremia, reduced toxemia, reduced sepsis, reduced symptoms, increased immune response, modulated immune response, or reduced time required for recovery. This amount varies depending upon the health and physical condition of the individual to be treated, the taxonomic group of individual to be treated (*e.g.*, human, nonhuman primate, primate, etc.), the responsive capacity of the individual's immune system, the extent of treatment or protection desired, the formulation of the vaccine, a professional assessment of the medical situation, and other relevant factors. It is expected that the effective amount will fall in a relatively broad range that can be determined through routine trials. Typically a single dose is from about 10 µg to 10 mg/kg body weight of purified polypeptide or an amount of a modified carrier organism or virus, or a fragment or remnant thereof, sufficient to provide a comparable quantity of recombinantly expressed mutant staphylococcal leukocidin subunit (*e.g.*, LukS-PV or LukF-PV, or both), as described herein. The term "peptide vaccine" or "subunit vaccine" refers to a composition comprising one or more polypeptides described herein, which when administered to an animal are useful in

stimulating an immune response against staphylococcal (*e.g.*, *S. aureus*) infection.

[0065] The term "subject" is meant any subject, particularly a mammalian subject, for whom diagnosis, prognosis, immunization, or therapy is desired. Mammalian subjects include, but are not limited to, humans, domestic animals, farm animals, zoo animals such as bears, sport animals, pet animals such as dogs, cats, guinea pigs, rabbits, rats, mice, horses, cattle, bears, cows; primates such as apes, monkeys, orangutans, and chimpanzees; canids such as dogs and wolves; felids such as cats, lions, and tigers; equids such as horses, donkeys, and zebras; food animals such as cows, pigs, and sheep; ungulates such as deer and giraffes; rodents such as mice, rats, hamsters and guinea pigs; and so on. In one embodiment of the disclosure, the subject is a human subject.

[0066] As used herein, a "subject in need thereof" refers to an individual for whom it is desirable to treat, *i.e.*, to prevent, cure, retard, or reduce the severity of staphylococcal (*e.g.*, *S. aureus*) disease symptoms, or result in no worsening of disease cause by *S. aureus* over a specified period of time, or both.

[0067] The terms "priming" or "primary" and "boost" or "boosting" as used herein to refer to the initial and subsequent immunizations, respectively, *i.e.*, in accordance with the definitions these terms normally have in immunology. However, in certain embodiments of the disclosure, *e.g.*, where the priming component and boosting component are in a single formulation, initial and subsequent immunizations may not be necessary as both the "prime" and the "boost" compositions are administered simultaneously.

Polypeptides

[0068] Disclosed is an isolated mutant staphylococcal leukocidin subunit polypeptide comprising, consisting of, or consisting essentially of a wild-type staphylococcal leukocidin subunit except for 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20 or more amino acid substitutions at conserved residues, which reduce toxicity of the mutant leukocidin subunit relative to the corresponding wild-type leukocidin subunit; where the wild-type leukocidin subunit comprises, consists of, or consists essentially of three consecutive regions designated A-B-C arranged from amino terminus to carboxy terminus, and where region B comprises the amino acid consensus sequence presented here as SEQ ID NO: 2: FQYNIX1LX2X3X4DX5X6X7X8LINX9X10X11LPKX12KIX13X14X15X16VX17QX18LGYNX19GX20X21X22X23X24X25X26X27X28X29GX30GX31FX32YSK; where

X1=Glycine(G), Serine(S) or Alanine(A)

X2=Lysine(K), Threonine(T), Serine(S) or Methionine(M)

X3=Threonine(T) or Serine(S)

X4=Asparagine(N) or Lysine(K)

X5=Proline(P), Lysine(K), Serine(S) or Glutamine(Q)

X6=Asparagine(N) or Tyrosine(Y)

X7=Valine(V), Threonine(T) or Isoleucine(I)

X8=Aspartic acid(D),Serine(S) or Phenylalanine(F)

X9=Serine(S) or no amino acid

X10=Isoleucine(I) or no amino acid

X11=Tyrosine(Y), Histidine(H) or Threonine(T)

X12=Asparagine(N) or Threonine(T)

X13=Aspartic acid(D) or Glutamic acid (E)

X14=Serine(S) or Threonine(T)

X15=Valine(V), Threonine(T), Alanine(A) or Isoleucine(I)

X16=Asparagine(N) or Aspartic acid(D)

X17=Serine(S) or Glycine(G)

X18=Threonine(T) or Lysine(K)

X19=Isoleucine(I) orValine(V)

X20= Glycine(G)or no amino acid

X21= Asparagine(N), Lysine(K) or no amino acid

X22= Phenylalanine(F) or no amino acid

X23= Asparagine(N), Glutamine(Q) or no amino acid

X24=Serine(S), Threonine(T) or no amino acid

X25=Glycine(G), Alanine(A), Valine(V) or no amino acid

X26=Proline(P) or no amino acid

X27=Serine(S), Leucine(L) or no amino acid

X28=Threonine(T), Leucine(L), Isoleucine(I) or no amino acid

X29=Glycine(G), Alanine(A) or no amino acid

X30=Asparagine(N), Serine(S) or Lysine(K)

X31=Serine(S), Alanine(A) or Glutamic acid (E); and

X32=Asparagine(N) or Serine(S).

[0069] In some embodiments of the disclosure, region A of the wild-type leukocidin subunit comprises the amino acid consensus sequence presented here as SEQ ID NO: 1:

X1X2X3X4SX5X6X7X8X9TQNX10QFX11FX12KDX13KYNKX14ALX15X16KMQ
GFIX17SX18TX19X20X21X22X23KX24X25X26X27X28X29X30KX31X32X33WP;
 where

X1=Glutamic acid (E), Glutamine(Q) or no amino acid

X2=Aspartic acid(D), Glycine(G) or no amino acid

X3=Threonine(T), Lysine(K), Isoleucine(I), Valine(V) or no amino acid

X4=Serine(S), Threonine(T), Alanine(A) or no amino acid

X5=Aspartic acid(D), Lysine(K), Asparagine(N), Arginine(R) or no amino acid

X6=Lysine(K), Arginine(R) or no amino acid

X7=Tryptophan(W), Leucine(L) or no amino acid

X8=Glycine(G), Alanine(A) or no amino acid

X9=Valine(V), Isoleucine(I) or no amino acid

X10=Isoleucine(I), Valine(V) or no amino acid

X11=Aspartic acid(D), Glycine(G) or no amino acid

X12=Valine(V) or Methionine(M)

X13=Lysine(K), Threonine(T) or Proline(P)

X14=Aspartic acid(D), Asparagine(N) or Valine(V)

X15=Isoleucine(I) or Valine(V)

X16=Leucine(L), Valine(V) or Isoleucine(I)

X17=Asparagine(N), Serine(S) or Lysine(K)

X18=Lysine(K) or Arginine(R)

X19=Threonine(T), Serine(S) or Alanine(A)

X20=Tyrosine(Y) or Phenylalanine(F)

X21=Tyrosine(Y), Serine(S), Asparagine(N) or Threonine(T)

X22=Asparagine(N) or Aspartic acid(D)

X23=Tyrosine(Y),Valine(V), Leucine(L),Phenylalanine(F) or Serine(S)

X24=Asparagine(N), Lysine(K), Glycine(G) or Glutamine(Q)

X25=Threonine(T), Tyrosine(Y), Serine(S), Asparagine(N), Lysine(K) or Arginine(R)

X26=Glycine(G) or no amino acid

X27=Tyrosine(Y) or no amino acid

X28=Aspartic acid(D), Asparagine(N), Glutamic acid (E), Proline(P) orArginine(R)

X29=Histidine(H), Tyrosine(Y), Leucine(L) or Alanine(A)

X30=Isoleucine(I), Threonine(T),Valine(V) or Asparagine(N)

X31=Alanine(A), Arginine(R) or Serine(S)

X32=Methionine(M), Isoleucine(I) or Leucine(L); and

X33=Arginine(R), Isoleucine(I), Valine(V) or Leucine(L).

[0070] In some embodiments of the disclosure, region C of the wild-type leukocidin subunit comprises the amino acid consensus sequence presented here as SEQ ID NO: 3:

FX1X2X3X4X5LPPLX6X7SGFNPSFIX8TX9SHEX10X11X12X13X14X15X16X17X1

8X19X20X21X22YGRNX23DX24TX25AX26X27X28X29X30X31X32X33X34X35X36; where

X1=Valine(V) or Alanine(A)

X2=Proline(P) or Aspartic acid(D)

X3=Aspartic acid(D) or Asparagine(N)

X4=Asparagine(N), Serine(S) or Aspartic acid(D)

X5=Glutamic acid (E) or Glutamine(Q)

X6=Valine(V) or Isoleucine(I)

X7=Histidine(H), Glutamine(Q) or Threonine(T)

X8=Alanine(A) or Threonine(T)

X9=Valine(V) or Leucine(L)

X10=Lysine(K) or Arginine(R)

X11=Glycine(G) or Aspartic acid(D)

X12=Serine(S), Lysine(K) or Threonine(T)

X13=Glycine(G), Serine(S) or Lysine(K)

X14=Aspartic acid(D), Glutamic acid (E) or Leucine(L)

X15=Threonine(T), Lysine(K) or Isoleucine(I)

X16=Arginine(R) or no amino acid

X17=Serine(S) or Valine(V)

X18=Glutamic acid (E), Aspartic acid(D) or Asparagine(N)

X19=Phenylalanine(F) or Leucine(L)

X20=Glutamic acid (E) or Lysine(K)

X21=Isoleucine(I) or Phenylalanine(F)

X22=Threonine(T), Serine(S) or Alanine(A)

X23=Methionine(M) or Leucine(L)

X24=Valine(V), Alanine(A), Isoleucine(I) or Threonine(T)

X25=Histidine(H) or Tyrosine(Y)

X26=Threonine(T), Isoleucine(I) or Tyrosine(Y)

X27=Arginine(R), Lysine(K), Valine(V), Leucine(L) or Phenylalanine(F)

X28=Arginine(R), Threonine(T), Phenylalanine(F) or Leucine(L)

X29=Threonine(T), Serine(S), Arginine(R) or Proline(P)

X30=Threonine(T), Histidine(H), Arginine(R), Lysine(K) or Proline(P)

X31=Histidine(H), Arginine(R), Threonine(T), Leucine(L) or Glutamine(Q)

X32=Tyrosine(Y) or no amino acid

X33=Glycine(G) or no amino acid

X34=Asparagine(N) or no amino acid

X35=Serine(S) or no amino acid; and

X36=Tyrosine(Y) or Glycine(G).

[0071] In some embodiments of the disclosure the mutant leukocidin subunit comprises amino acid substitutions at positions T11, K24, D28, Y58, S18, or any combination thereof. In certain embodiments, the substitutions can be with any amino acid which maintains the antigenicity of the mutant staphylococcal leukocidin subunit. In certain embodiments of the disclosure T11, K24, D28, Y58, or S18 is substituted with alanine or phenylalanine.

[0072] Also disclosed is the mutant leukocidin subunit, as described herein, which comprises an amino acid substitution at position K24 of SEQ ID NO: 2. The substitution can be with any amino acid which maintains the antigenicity of the mutant staphylococcal leukocidin subunit. In certain embodiments of the disclosure K24 is substituted with alanine.

[0073] Also disclosed is the mutant leukocidin subunit, as described herein, which comprises an amino acid substitution at position S18 of SEQ ID NO: 3. The substitution can be with any amino acid which maintains the antigenicity of the mutant staphylococcal leukocidin subunit. In certain embodiments of the disclosure S18 is substituted with alanine.

[0074] Some embodiments include the mutant leukocidin subunit, as described herein, which comprises an amino acid substitution at position Y58 of SEQ ID NO:2. The substitution can be with any amino acid which maintains the antigenicity of the mutant staphylococcal leukocidin subunit. In certain embodiments of the disclosure Y58 is substituted with alanine.

[0075] Some embodiments of the disclosure include the mutant leukocidin subunit, as described herein, which comprises an amino acid substitution at position T11 of SEQ ID NO: 1. The substitution can be with any amino acid which maintains the antigenicity of the mutant staphylococcal leukocidin subunit. In certain embodiments of the disclosure T11 is substituted with phenylalanine.

[0076] Some embodiments of the disclosure include the mutant leukocidin subunit, as described herein, which comprises amino acid substitutions at positions T11 and Y58. The substitutions can be with any amino acid which maintains the antigenicity of the mutant staphylococcal leukocidin subunit. In certain embodiments of the disclosure T11 and Y58 are substituted with phenylalanine and alanine, respectively.

[0077] Some embodiments of the disclosure include the mutant leukocidin subunit, as described herein, which comprises amino acid substitutions at positions T11 and S18. The substitutions can be with any amino acid which maintains the antigenicity of the mutant staphylococcal leukocidin subunit. In certain embodiments of the disclosure T11 and S18 are substituted with phenylalanine and alanine, respectively.

[0078] Some embodiments of the disclosure include the mutant leukocidin subunit, as described herein, which comprises amino acid substitutions at positions T11, K24, and S18. The substitutions can be with any amino acid which maintains the antigenicity of the mutant

staphylococcal leukocidin subunit. In certain embodiments of the disclosure T11 is substituted with phenylalanine, and K24 and S18 are substituted with alanine.

[0079] Also disclosed is the mutant leukocidin subunit, as described herein, which comprises an amino acid substitution at position D28 of SEQ ID NO: 2. The substitution can be with any amino acid which maintains the antigenicity of the mutant staphylococcal leukocidin subunit. In certain embodiments of the disclosure D28 is substituted with alanine.

[0080] Also disclosed is an isolated mutant staphylococcal leukocidin subunit polypeptide comprising, consisting of, or consisting essentially of a wild-type staphylococcal leukocidin subunit except for 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, or more amino acid substitutions at conserved residues, which reduce toxicity of the mutant leukocidin subunit relative to the corresponding wild-type leukocidin subunit; where the wild-type leukocidin is a Pantone-Valentine leukocidin (PVL) LukS-PV. In some embodiments of the disclosure, the wild-type LukS-PV comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 5, SEQ ID NO: 15, and SEQ ID NO: 16. In certain embodiments of the disclosure the wild-type LukS-PV comprises an amino acid sequence of SEQ ID NO: 5:

mvkkrlaat lsliitpia tsfhskadn nienigdgae vvkrtedtss dkwgvtqniq
fdvfkdkkyn kdaliikmqg finsktttyn ykntdhikam rwpfqynigl ktndpnvdl
nylpknkids vnvsqtlgyn iggnfnsgps tggngsfyns ktisynqqny isevehqnsk
svqwgikans fitslgkmsg hdpnlfvgyk pysqnprdyf vpdnelpllv hsgfnpsfia
tvshekgsgd tsefeitygr nmdvthatrr tthygnsyle gsrihnaavn mytvkyevn
wktheikvkg hn

(precursor protein sequence for LukS-PV. GenBank accession number: NP_058465.1; 28 amino acid signal peptide (amino acids 1-28) is underlined).

[0081] In some embodiments of the disclosure the mutant LukS-PV subunit comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, and SEQ ID NO: 14. In certain embodiments of the disclosure the mutant leukocidin subunit as described herein, comprises the amino acid of SEQ ID NO: 14.

[0082] Also disclosed is an isolated mutant staphylococcal leukocidin subunit polypeptide comprising, consisting of, or consisting essentially of a wild-type staphylococcal leukocidin subunit except for 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, or more amino acid substitutions at conserved residues, which reduce toxicity of the mutant leukocidin subunit relative to the corresponding wild-type leukocidin subunit; where the wild-type leukocidin subunit comprises, consists of, or consists essentially of the amino acid consensus sequence presented here as SEQ ID NO: 4:

**NX1VX2YAPKNQNEEFQVQX3TX4GYX5X6GGDIX7IX8X9GLX10GGX11NGX12
X13X14FSETINYKQESYRX15X16X17X18;** where

X1=Valine(V), Isoleucine(I) or Alanine(A)

X2=Aspartic acid(D) or Histidine(H)

X3=Asparagine(N) or Glutamine(Q)

X4=Leucine(L) or Valine(V)

X5=Serine(S) or Threonine(T)

X6=Phenylalanine(F) or Tyrosine(Y)

X7=Serine(S) or Asparagine(N)

X8=Serine(S), Isoleucine(I), Asparagine(N) or Threonine(T)

X9=Lysine(K) or Asparagine(N)

X10=Serine(S) or Threonine(T)

X11=Leucine(L) or Glycine(G)

X12=Serine(S) or Asparagine(N)

X13=Glutamic acid (E), Threonine(T) or Lysine(K)

X14=Serine(S) or Alanine(A)

X15=Threonine(T) or no amino acid

X16=Threonine(T) or Serine(S)

X17=Isoleucine(I) or Leucine(L); and

X18=Aspartic acid(D) or Serine(S).

[0083] In some embodiments of the disclosure the mutant leukocidin subunit comprises amino acid substitutions at positions K8, D28, E53, or any combination thereof. In certain embodiments of the disclosure, the substitutions can be with any amino acid which maintains the antigenicity of the mutant staphylococcal leukocidin subunit. In certain embodiments of the disclosure K8, D28, or E53 is substituted with alanine.

[0084] Also disclosed is an isolated mutant staphylococcal leukocidin subunit polypeptide comprising, consisting of, or consisting essentially of a wild-type staphylococcal leukocidin subunit except for 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, or more amino acid substitutions at conserved residues, which reduce toxicity of the mutant leukocidin subunit relative to the corresponding wild-type leukocidin subunit; where the wild-type leukocidin is a Pantone-Valentine leukocidin (PVL) LukF-PV. In some embodiments of the disclosure the wild-type LukF-PV comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 16, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID

NO: 26, and SEQ ID NO: 27. In certain embodiments of the disclosure the wild-type LukF-PV comprises an amino acid sequence of SEQ ID NO: 16:

mkkivkssvv tsialllsn tydaaqhitp vsekkvddki tlykttatsd sdklkisqil
tfnfikdkxy dkdtilkkaa gniysgytkp npkdtissqf ywgsdynisi nsdsndsvnv
vdyapknqne efqvqqtvgy syggdinisn glsgggngsk sfsetinykq esyrtsldkr
tnfkkgwdv eahkimnngw gpygrdsyhs tygnemflgs rqslnagqn fleyhkmpvl
srgnfnpefi gvlsrkqnaa kkskitvtyq remdrytnfw nqlhwignny kdenrathts
iyevdwenht vklidtske knpms

(precursor protein sequence for LukF-PV. GenBank accession number: NP_058466.1; 24 amino acid signal peptide (amino acids 1-24) is underlined).

[0085] In some embodiments of the disclosure, the mutant LukF-PV subunit comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 20, and SEQ ID NO: 136. In certain embodiments of the disclosure the mutant LukF-PV subunit comprises an amino acid sequence of SEQ ID NO: 18. In certain embodiments of the disclosure the mutant LukF-PV subunit comprises an amino acid sequence of SEQ ID NO: 136.

[0086] Also disclosed is a polypeptide complex comprising the mutant leukocidin subunits as described herein. The substitution can be any amino acid that maintains structure and conformation of the the mutant leukocidin subunit complex.

[0087] In another embodiment of the disclosure, the mutant staphylococcal leukocidin subunit (e.g., LukS-PV or LukF-PV, or both), as described herein, can be attached to a heterologous polypeptide. Various heterologous polypeptides can be used, including, but not limited to an N- or C-terminal peptide imparting stabilization, secretion, or simplified purification, such as a hexa-Histidine-tag, a ubiquitin tag, a NusA tag, a chitin binding domain, ompT, ompA, pelB, DsbA, DsbC, c-myc, KSI, polyaspartic acid, (Ala-Trp-Trp-Pro)_n, polyphenylalanine, polycysteine, polyarginine, a B-tag, a HSB-tag, green fluorescent protein (GFP), influenza virus hemagglutinin (HA), a calmodulin binding protein (CBP), a galactose-binding protein, a maltose binding protein (MBP), a cellulose binding domains (CBD's), dihydrofolate reductase (DHFR), glutathione-S-transferase (GST), streptococcal protein G, staphylococcal protein A, T7gene10, an avidin/streptavidin/Strep-tag complex, trpE, chloramphenicol acetyltransferase, lacZ (β -Galactosidase), His-patch thioredoxin, thioredoxin, a FLAG[™] peptide (Sigma-Aldrich), an S-tag, or a T7-tag. See, e.g., Stevens, R.C., Structure, 8:R177-R185 (2000). Heterologous polypeptides can also include any pre- and/or pro- sequences that facilitate the transport, translocations, processing and/or purification of LukS-PV and/or LukF-PV polypeptide as described herein from a host cell or any useful immunogenic sequence, including but not limited to sequences that encode a T-cell epitope of a microbial pathogen, or other immunogenic proteins and/or epitopes.

[0088] In some embodiments of the disclosure, the mutant staphylococcal leukocidin subunit (e.g., LukS-PV or LukF-PV, or both), attached to a heterologous polypeptide, as described

herein, can include a peptide linker sequence joining sequences that comprise two or more peptide regions. Suitable peptide linker sequences can be chosen based on their ability to adopt a flexible, extended conformation, or a secondary structure that could interact with joined epitopes, or based on their ability to increase overall solubility of the fusion polypeptide, or based on their lack of electrostatic or water-interaction effects that influence joined peptide regions.

[0089] In some embodiments of the disclosure, the mutant staphylococcal leukocidin subunit (e.g., LukS-PV or LukF-PV, or both), as described herein, is isolated. An "isolated" polypeptide is one that has been removed from its natural milieu. The term "isolated" does not connote any particular level of purification. Recombinantly produced mutant staphylococcal leukocidin subunit (e.g., LukS-PV or LukF-PV, or both), as described herein, expressed in non-native host cells is considered isolated for purposes of the disclosure, as is the polypeptide which have been separated, fractionated, or partially or substantially purified by any suitable technique, including by filtration, chromatography, centrifugation, and the like.

[0090] Production of the mutant staphylococcal leukocidin subunit (e.g., LukS-PV or LukF-PV, or both), as described herein, can be achieved by culturing a host cell comprising a polynucleotide which operably encodes the polypeptide of the disclosure, and recovering the polypeptide. Determining conditions for culturing such a host cell and expressing the polynucleotide are generally specific to the host cell and the expression system and are within the knowledge of one of skill in the art. Likewise, appropriate methods for recovering the polypeptide of the disclosure are known to those in the art, and include, but are not limited to, chromatography, filtration, precipitation, or centrifugation.

[0091] In certain embodiments of the disclosure, the mutant staphylococcal leukocidin subunit, as described herein, comprises a calculated molecular energy of less than 7000 kcal/mol, or less than 4000 kcal/mol, or less than 2000 kcal/mol, or between 600 kcal/mol and 7500 kcal/mol, or between 900 kcal/mol and 3900 kcal/mol, or between 900 kcal/mol and 1500 kcal/mol, or between 2000 kcal/mol and 3650 kcal/mol. Specific calculated molecular energies for the heterodimer complex structure for LukS-PV and LukF-PV mutants are represented in Table 1. These measurements are explained in detail in the examples section.

Table 1: Calculated molecular energies for the heterodimer complex structure for LukS-PV and LukF-PV mutants

LukS-PV Mutants (numbering according to mature (<i>i.e.</i> , without signal peptide) wild-type LukS-PV sequence of SEQ ID NO: 6)	Energy (kcal/mol)	LukS-PV Mutants (corresponding numbers according to consensus wild-type LukS-PV sequences of SEQ ID NO: 1, SEQ ID NO: 2 or SEQ ID NO: 3)
T28F	2535	T11F of SEQ ID NO: 1
K97A	655	K24A of SEQ ID NO: 2
D101A	3200	D28A of SEQ ID NO: 2
Y131A	1027	Y58A of SEQ ID NO: 2

LukS-PV Mutants (numbering according to mature (<i>i.e.</i> , without signal peptide) wild-type LukS-PV sequence of SEQ ID NO: 6)	Energy (kcal/mol)	LukS-PV Mutants (corresponding numbers according to consensus wild-type LukS-PV sequences of SEQ ID NO: 1, SEQ ID NO: 2 or SEQ ID NO: 3)
S209A	7399	S18A of SEQ ID NO: 3
T28F/Y131A	2032	T11F/Y58A
T28F/S209A	3187	T11F/S18A
T28F/K97A/S209A	3595	T11F/K24A/S18A
LukF-PV Mutants (numbering according to mature (<i>i.e.</i> , without signal peptide) wild-type LukF-PV sequence of SEQ ID NO: 17)	Energy (kcal/mol)	LukF-PV Mutants (corresponding numbers according to consensus wild-type LukF-PV sequence of SEQ ID NO: 4)
K102A	1209	K8A
D121A	989	D28A
E147A	1384	E53A
K102A/D121A/E147A	n/a	K8A/D28A/E53A

Polynucleotides

[0092] The disclosure is further directed to an isolated polynucleotide comprising a nucleic acid encoding an isolated mutant staphylococcal leukocidin subunit polypeptide comprising, consisting of, or consisting essentially of a wild-type staphylococcal leukocidin subunit except for 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, or more amino acid substitutions at conserved residues, which reduce toxicity of the mutant leukocidin subunit relative to the corresponding wild-type leukocidin subunit; where the wild-type leukocidin subunit comprises, consists of, or consists essentially of three consecutive regions designated A-B-C arranged from amino terminus to carboxy terminus, and where region B comprises the amino acid consensus sequence of SEQ ID NO: 2.

[0093] Also disclosed is an isolated polynucleotide comprising a nucleic acid encoding an isolated mutant staphylococcal leukocidin subunit polypeptide comprising, consisting of, or consisting essentially of a wild-type staphylococcal leukocidin subunit except for 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, or more amino acid substitutions at conserved residues, which reduce toxicity of the mutant leukocidin subunit relative to the corresponding wild-type leukocidin subunit; where the wild-type leukocidin subunit comprises, consists of, or consists essentially of the amino acid consensus sequence presented here as SEQ ID NO: 4.

[0094] In certain embodiments of the disclosure, the isolated polynucleotide as described herein further comprises non-coding regions such as promoters, operators, or transcription

terminators as described elsewhere herein. In some embodiments of the disclosure, the disclosure is directed to the polynucleotide as described herein, and further comprising a heterologous nucleic acid. The heterologous nucleic acid can, in some embodiments of the disclosure, encode a heterologous polypeptide fused to the polypeptide as described herein. For example, the isolated polynucleotide as described herein can comprise additional coding regions encoding, *e.g.*, a heterologous polypeptide fused to the polypeptide as described herein, or coding regions encoding heterologous polypeptides separate from the polypeptide as described herein such as, but not limited to, selectable markers, additional immunogens, immune enhancers, and the like.

[0095] Also provided are expression constructs, vectors, and/or host cells comprising the polynucleotides described herein.

[0096] An example of an isolated polynucleotide is a recombinant polynucleotide contained in a vector. Further examples of an isolated polynucleotide include recombinant polynucleotides maintained in heterologous host cells or purified (partially or substantially) polynucleotides in solution. In certain embodiments of the disclosure a polynucleotide is "recombinant." Isolated polynucleotides or nucleic acids according to the disclosure further include such molecules produced synthetically. The relative degree of purity of a polynucleotide or polypeptide described herein is easily determined by well-known methods.

Codon Optimization

[0097] Also included within the scope of the disclosure are genetically engineered polynucleotides encoding the mutant staphylococcal leukocidin subunit (*e.g.*, LukS-PV or LukF-PV, or both), as described herein. Modifications of nucleic acids encoding the mutant staphylococcal leukocidin subunit *e.g.*, (LukS-PV or LukF-PV, or both), as described herein, can readily be accomplished by those skilled in the art, for example, by oligonucleotide-directed site-specific mutagenesis or de novo nucleic acid synthesis.

[0098] Some embodiments of the disclosure disclose an isolated polynucleotide comprising a nucleic acid fragment, which encodes the mutant staphylococcal leukocidin subunit (*e.g.*, LukS-PV or LukF-PV, or both), as described herein, where the coding region encoding the polypeptide has been codon-optimized. As appreciated by one of ordinary skill in the art, various nucleic acid coding regions will encode the same polypeptide due to the redundancy of the genetic code. Deviations in the nucleotide sequence that comprise the codons encoding the amino acids of any polypeptide chain allow for variations in the sequence of the coding region. Since each codon consists of three nucleotides, and the nucleotides comprising DNA are restricted to four specific bases, there are 64 possible combinations of nucleotides, 61 of which encode amino acids (the remaining three codons encode signals ending translation). The "genetic code" which shows which codons encode which amino acids is reproduced herein as Table 2. As a result, many amino acids are designated by more than one codon. For example, the amino acids alanine and proline are coded for by four triplets, serine and arginine

by six, whereas tryptophan and methionine are coded by just one triplet. This degeneracy allows for DNA base composition to vary over a wide range without altering the amino acid sequence of the polypeptides encoded by the DNA.

TABLE 2: The Standard Genetic Code

	T	C	A	G
T	TTT Phe (F)	TCT Ser (S)	TAT Tyr (Y)	TGT Cys (C)
	TTC "	TCC "	TAC "	TGC "
	TTA Leu (L)	TCA "	TAA Ter	TGA Ter
	TTG "	TCG "	TAG Ter	TGG Trp (W)
C	CTT Leu (L)	CCT Pro (P)	CAT His (H)	CGT Arg (R)
	CTC "	CCC "	CAC "	CGC "
	CTA "	CCA "	CAA Gln (Q)	CGA "
	CTG "	CCG "	CAG "	CGG "
A	ATT Ile (I)	ACT Thr (T)	AAT Asn (N)	AGT Ser (S)
	ATC "	ACC "	AAC "	AGC "
	ATA "	ACA "	AAA Lys (K)	AGA Arg (R)
	ATG Met (M)	ACG "	AAG "	AGG "
G	GTT Val (V)	GCT Ala (A)	GAT Asp (D)	GGT Gly (G)
	GTC "	GCC "	GAC "	GGC "
	GTA "	GCA "	GAA Glu (E)	GGA "
	GTG "	GCG "	GAG "	GGG "

[0099] It is to be appreciated that any polynucleotide that encodes a polypeptide in accordance with the disclosure falls within the scope of this disclosure, regardless of the codons used.

[0100] Many organisms display a bias for use of particular codons to code for insertion of a particular amino acid in a growing polypeptide chain. Codon preference or codon bias, differences in codon usage between organisms, is afforded by degeneracy of the genetic code, and is well documented among many organisms.

[0101] Different factors have been proposed to contribute to codon usage preference, including translational selection, GC composition, strand-specific mutational bias, amino acid conservation, protein hydrophathy, transcriptional selection and even RNA stability. One factor that determines codon usage is mutational bias that shapes genome GC composition. This factor is most significant in genomes with extreme base composition: species with high GC content (e.g., gram positive bacteria). Mutational bias is responsible not only for intergenetic difference in codon usage but also for codon usage bias within the same genome (Ermolaeva M, Curr. Issues Mol. Biol. 3(4):91-97, 2001).

[0102] Codon bias often correlates with the efficiency of translation of messenger RNA (mRNA), which is in turn believed to be dependent on, *inter alia*, the properties of the codons being translated and the availability of particular transfer RNA (tRNA) molecules. The predominance of selected tRNAs in a cell is generally a reflection of the codons used most frequently in peptide synthesis. Accordingly, genes can be tailored for optimal gene expression in a given organism based on codon optimization.

[0103] The present disclosure relates to a polynucleotide comprising a codon-optimized coding region which encodes the mutant staphylococcal leukocidin subunit polypeptide (e.g., LukS-PV or LukF-PV, or both), as described herein. The codon usage is adapted for optimized expression in a given prokaryotic or eukaryotic host cell.

[0104] Codon-optimized polynucleotides are prepared by incorporating codons preferred for use in the genes of a given species into the DNA sequence. Also provided are polynucleotide expression constructs, vectors, host cells comprising polynucleotides comprising codon-optimized coding regions which encode the mutant staphylococcal leukocidin subunit polypeptide (e.g., LukS-PV or LukF-PV, or both), as described herein.

[0105] Given the large number of gene sequences available for a wide variety of animal, plant and microbial species, it is possible to calculate the relative frequencies of codon usage. Codon usage tables are readily available, for example, at the "Codon Usage Database" available at <http://www.kazusa.or.jp/codon/> (visited October 12, 2011), and these tables can be adapted in a number of ways. (Nakamura, Y., et al., "Codon usage tabulated from the international DNA sequence databases: status for the year 2000" Nucl. Acids Res. 28:292, 2000).

[0106] By utilizing available tables, one of ordinary skill in the art can apply the frequencies to any given polypeptide sequence, and produce a nucleic acid fragment of a codon-optimized coding region which encodes a desired polypeptide, but which uses codons optimal for a given species. For example, in some embodiments of the disclosure, the coding region is codon-optimized for expression in *E. coli*.

DNA Synthesis

[0107] A number of options are available for synthesizing codon optimized coding regions designed by any of the methods described above, using standard and routine molecular biological manipulations well known to those of ordinary skill in the art. In addition, gene synthesis is readily available commercially.

Vectors and Expression Systems

[0108] Further disclosed is a vector comprising the polynucleotide as described herein. The term "vector," as used herein, refers to *e.g.*, any of a number of nucleic acids into which a desired sequence can be inserted, *e.g.*, by restriction and ligation, for transport between different genetic environments or for expression in a host cell. Nucleic acid vectors can be DNA or RNA. Vectors include, but are not limited to, plasmids, phage, phagemids, bacterial genomes, and virus genomes. A cloning vector is one which is able to replicate in a host cell, and which is further characterized by one or more endonuclease restriction sites at which the vector can be cut in a determinable fashion and into which a desired DNA sequence can be ligated such that the new recombinant vector retains its ability to replicate in the host cell. In the case of plasmids, replication of the desired sequence can occur many times as the plasmid increases in copy number within the host bacterium or just a single time per host before the host reproduces by mitosis. In the case of phage, replication can occur actively during a lytic phase or passively during a lysogenic phase. Certain vectors are capable of autonomous replication in a host cell into which they are introduced. Other vectors are integrated into the genome of a host cell upon introduction into the host cell, and thereby are replicated along with the host genome.

[0109] Any of a wide variety of suitable cloning vectors are known in the art and commercially available which can be used with appropriate hosts. As used herein, the term "plasmid" refers to a circular, double-stranded construct made up of genetic material (*i.e.*, nucleic acids), in which the genetic material is extrachromosomal and in some instances, replicates autonomously. A polynucleotide described herein can be in a circular or linearized plasmid or in any other sort of vector. Procedures for inserting a nucleotide sequence into a vector, *e.g.*, an expression vector, and transforming or transfecting into an appropriate host cell and cultivating under conditions suitable for expression are generally known in the art.

[0110] In accordance with one aspect of the disclosure, provided is a vector comprising a nucleic acid sequence encoding the mutant staphylococcal leukocidin subunit (*e.g.*, LukS-PV or LukF-PV, or both), as described herein. In certain embodiments of the disclosure the vector is an expression vector capable of expressing the mutant staphylococcal leukocidin subunit (*e.g.*, LukS-PV or LukF-PV, or both), as described herein in a suitable host cell. The term "expression vector" refers to a vector that is capable of expressing the polypeptide described herein, *i.e.*, the vector sequence contains the regulatory sequences required for transcription and translation of a polypeptide, including, but not limited to promoters, operators, transcription termination sites, ribosome binding sites, and the like. The term "expression" refers to the biological production of a product encoded by a coding sequence. In most cases a DNA sequence, including the coding sequence, is transcribed to form a messenger-RNA (mRNA). The messenger-RNA is then translated to form a polypeptide product which has a relevant biological activity. Also, the process of expression can involve further processing steps to the RNA product of transcription, such as splicing to remove introns, and/or post-translational processing of a polypeptide product.

[0111] Vector-host systems include, but are not limited to, systems such as bacterial, mammalian, yeast, insect or plant cell systems, either *in vivo*, *e.g.*, in an animal or *in vitro*, *e.g.*,

in bacteria or in cell cultures. The selection of an appropriate host is deemed to be within the scope of those skilled in the art from the teachings herein. In certain embodiments of the disclosure, the host cell is a bacterium, *e.g.*, *E. coli*.

[0112] Host cells are genetically engineered (infected, transduced, transformed, or transfected) with vectors of the disclosure. Thus, one aspect of the disclosure is directed to a host cell comprising a vector which contains the polynucleotide as describe herein. The engineered host cell can be cultured in conventional nutrient media modified as appropriate for activating promoters, selecting transformants or amplifying the polynucleotides. The culture conditions, such as temperature, pH and the like, are those previously used with the host cell selected for expression, and will be apparent to the ordinarily skilled artisan. The term "transfect," as used herein, refers to any procedure whereby eukaryotic cells are induced to accept and incorporate into their genome isolated DNA, including but not limited to DNA in the form of a plasmid. The term "transform," as used herein, refers to any procedure whereby bacterial cells are induced to accept and incorporate into their genome isolated DNA, including but not limited to DNA in the form of a plasmid.

[0113] Bacterial host-expression vector systems include, but are not limited to, a prokaryote (*e.g.*, *E. coli*), transformed with recombinant bacteriophage DNA, plasmid DNA or cosmid DNA. In some embodiments of the disclosure, the plasmids used with *E. coli* use the T7 promoter-driven system regulated by the LacI protein *via* IPTG induction. A large number of suitable vectors are known to those of skill in the art, and are commercially available. The following bacterial vectors are provided by way of example: pET (Novagen), pET28, pBAD, pTrcHIS, pBR322, pQE70, pQE60, pQE-9 (Qiagen), phagescript, psiX174, pBluescript SK, pbsks, pNH8A, pNH16a, pNH18A, pNH46A (Stratagene), ptrc99a, pKK223-3, pKK243-3, pDR540, pBR322, pPS10, RSF1010, pRIT5 (Pharmacia); pCR (Invitrogen); pLex (Invitrogen), and pUC plasmid derivatives.

[0114] A suitable expression vector contains regulatory sequences which can be operably joined to an inserted nucleotide sequence encoding the mutant staphylococcal leukocidin subunit (*e.g.*, LukS-PV or LukF-PV, or both), as described herein. As used herein, the term "regulatory sequences" means nucleotide sequences which are necessary for or conducive to the transcription of an inserted sequence coding the mutant staphylococcal leukocidin subunit (*e.g.*, LukS-PV or LukF-PV, or both), as described herein by a host cell and/or which are necessary for or conducive to the translation by a host cell of the resulting transcript into the desired mutant leukocidin subunit (*e.g.*, LukS-PV or LukF-PV, or both). Regulatory sequences include, but are not limited to, 5' sequences such as operators, promoters and ribosome binding sequences, and 3' sequences such as polyadenylation signals or transcription terminators. Regulatory sequences can also include enhancer sequences or upstream activator sequences.

[0115] Generally, bacterial vectors will include origins of replication and selectable markers, *e.g.*, the ampicillin, tetracycline, kanamycin, resistance genes of *E. coli*, permitting transformation of the host cell and a promoter derived from a highly-expressed gene to direct

transcription of a downstream structural sequence. Suitable promoters include, but are not limited to, the T7 promoter, lambda (λ) promoter, T5 promoter, and lac promoter, or promoters derived from operons encoding glycolytic enzymes such as 3-phosphoglycerate kinase (PGK), acid phosphatase, or heat shock proteins, or inducible promoters like cadmium (pcad), and beta-lactamase (pbla).

[0116] Once an expression vector is selected, the polynucleotide as described herein can be cloned downstream of the promoter, for example, in a polylinker region. The vector is transformed into an appropriate bacterial strain, and DNA is prepared using standard techniques. The orientation and DNA sequence of the polynucleotide as well as all other elements included in the vector, are confirmed using restriction mapping, DNA sequence analysis, and/or PCR analysis. Bacterial cells harboring the correct plasmid can be stored as cell banks.

Immunogenic and Pharmaceutical Compositions

[0117] Further disclosed are compositions, e.g., immunogenic or pharmaceutical compositions, that contain an effective amount of the mutant staphylococcal leukocidin subunit (e.g., LukS-PV or LukF-PV, or both), as described herein, or a polynucleotide encoding the polypeptide of the disclosure. Compositions as described herein can further comprise additional immunogenic components, e.g., as a multivalent vaccine, as well as carriers, excipients or adjuvants.

[0118] Compositions as described herein can be formulated according to known methods. Suitable preparation methods are described, for example, in Remington's Pharmaceutical Sciences, 19th Edition, A.R. Gennaro, ed., Mack Publishing Co., Easton, PA (1995), which is incorporated herein by reference in its entirety. Composition can be in a variety of forms, including, but not limited to an aqueous solution, an emulsion, a gel, a suspension, lyophilized form, or any other form known in the art. In addition, the composition can contain pharmaceutically acceptable additives including, for example, diluents, binders, stabilizers, and preservatives. Once formulated, compositions of the disclosure can be administered directly to the subject. The subjects to be treated can be animals; in particular, human subjects can be treated.

[0119] Carriers that can be used with compositions of the disclosure are well known in the art, and include, without limitation, e.g., thyroglobulin, albumins such as human serum albumin, tetanus toxoid, and polyamino acids such as poly L-lysine, poly L-glutamic acid, influenza, hepatitis B virus core protein, and the like. A variety of aqueous carriers can be used, e.g., water, buffered water, 0.8% saline, 0.3% glycine, hyaluronic acid and the like. Compositions can be sterilized by conventional, well known sterilization techniques, or can be sterile filtered. A resulting composition can be packaged for use as is, or lyophilized, the lyophilized preparation being combined with a sterile solution prior to administration. Compositions can contain pharmaceutically acceptable auxiliary substances as required to approximate

physiological conditions, such as pH adjusting and buffering agents, tonicity adjusting agents, wetting agents and the like, for example, sodium acetate, sodium lactate, sodium chloride, potassium chloride, calcium chloride, sorbitan monolaurate, triethanolamineoleate, etc.

[0120] Certain compositions as described herein further include one or more adjuvants, a substance added to an immunogenic composition to, for example, enhance, sustain, localize, or modulate an immune response to an immunogen. The term "adjuvant" refers to any material having the ability to (1) alter or increase the immune response to a particular antigen or (2) increase or aid an effect of a pharmacological agent. Any compound which can increase the expression, antigenicity or immunogenicity of the polypeptide is a potential adjuvant. The term "immunogenic carrier" as used herein refers to a first moiety, *e.g.*, a polypeptide or fragment, variant, or derivative thereof which enhances the immunogenicity of a second polypeptide or fragment, variant, or derivative thereof.

[0121] A great variety of materials have been shown to have adjuvant activity through a variety of mechanisms. For example, an increase in humoral immunity is typically manifested by a significant increase in the titer of antibodies raised to the antigen, and an increase in T-cell activity is typically manifested in increased cell proliferation, or cellular cytotoxicity, or cytokine secretion. An adjuvant can also alter or modulate an immune response, for example, by changing a primarily humoral or Th₂ response into a primarily cellular, or Th₁ response. Immune responses to a given antigen can be tested by various immunoassays well known to those of ordinary skill in the art, and/or described elsewhere herein.

[0122] A wide number of adjuvants are familiar to persons of ordinary skill in the art, and are described in numerous references. Adjuvants which can be used in compositions described herein include, but are not limited to: inert carriers, such as alum, bentonite, latex, and acrylic particles; incomplete Freund's adjuvant, complete Freund's adjuvant; aluminum-based salts such as aluminum hydroxide; Alhydrogel (Al(OH)₃); aluminum phosphate (AlPO₄); calcium-based salts; silica; any TLR biological ligand(s); IDC-1001 (also known as GLA-SE; glucopyranosyl lipid adjuvant stable emulsion) (Coler et al., PLoS One, 2010. 5(10): p. e13677; Coler et al., PLoS One, 2011. 6(1): p. e16333); CpG (Mullen et al., PLoS One, 2008. 3(8): p. e2940), or any combination thereof. The amount of adjuvant, how it is formulated, and how it is administered all parameters which are well within the purview of a person of ordinary skill in the art.

[0123] In some embodiments of the disclosure, a composition of the disclosure further comprises a liposome or other particulate carrier, which can serve, *e.g.*, to stabilize a formulation, to target the formulation to a particular tissue, such as lymphoid tissue, or to increase the half-life of the polypeptide composition. Such particulate carriers include emulsions, foams, micelles, insoluble monolayers, liquid crystals, phospholipid dispersions, lamellar layers, iscoms, and the like. In these preparations, the polypeptide described herein can be incorporated as part of a liposome or other particle, or can be delivered in conjunction with a liposome. Liposomes for use in accordance with the disclosure can be formed from standard vesicle-forming lipids, which generally include neutral and negatively charged

phospholipids and a sterol, such as cholesterol. A composition comprising a liposome or other particulate suspension as well as the polypeptide as described herein can be administered intravenously, locally, topically, *etc.* in a dose which varies according to, *inter alia*, the manner of administration, the polypeptide being delivered, and the stage of the disease being treated.

[0124] For solid compositions, conventional nontoxic solid carriers can be used which include, for example, pharmaceutical grades of mannitol, lactose, starch, magnesium stearate, sodium saccharin, talcum, cellulose, glucose, sucrose, magnesium carbonate, and the like. For oral administration, a pharmaceutically acceptable nontoxic composition is formed by incorporating any of the normally employed excipients, such as those carriers previously listed, and generally 10-95% of active ingredient, that is, the polypeptide as described herein, often at a concentration of 25%-75%.

[0125] For aerosol or mucosal administration, the polypeptide as described herein can be supplied in finely divided form, optionally along with a surfactant and, propellant and/or a mucoadhesive, *e.g.*, chitosan. The surfactant must, of course, be pharmaceutically acceptable, and in some embodiments of the disclosure soluble in the propellant. Representative of such agents are the esters or partial esters of fatty acids containing from 6 to 22 carbon atoms, such as caproic, octanoic, lauric, palmitic, stearic, linoleic, linolenic, olesteric and oleic acids with an aliphatic polyhydric alcohol or its cyclic anhydride. Mixed esters, such as mixed or natural glycerides can be employed. The surfactant can constitute 0.1%-20% by weight of the composition, in some embodiments of the disclosure 0.25-5% by weight. The balance of the composition is ordinarily propellant, although an atomizer can be used in which no propellant is necessary and other percentages are adjusted accordingly. In some embodiments of the disclosure, the immunogenic polypeptides can be incorporated within an aerodynamically light particle, such as those particles described in U.S. Pat. No. 6,942,868 or U.S. Pat. Pub. No. 2005/0008633. A carrier can also be included, *e.g.*, lecithin for intranasal delivery.

[0126] The disclosure is also directed to a method of producing the composition according to the disclosure. In some embodiments of the disclosure, the method of producing the composition comprises (a) isolating a polypeptide according to the disclosure; and (b) adding an adjuvant, carrier and/or excipient to the isolated polypeptide. Some embodiments of the disclosure disclose further combining the polypeptide with other staphylococcal antigens.

[0127] Some embodiments of the disclosure include a multivalent vaccine. A multivalent vaccine of the present disclosure comprises the mutant staphylococcal leukocidin subunit (*e.g.*, LukS-PV or LukF-PV, or both), as described herein, or a polynucleotide encoding one or both subunits, and one or more additional immunogenic components. Such components can be additional immunogens of the same infectious agent, *e.g.*, *S. aureus*, or from other staphylococci, or can be immunogens derived from other infectious agents which can be effectively, conveniently, or economically administered together. In certain embodiments of the disclosure, the mutant staphylococcal leukocidin subunit (*e.g.*, LukS-PV or LukF-PV, or both), as described herein, can be combined with other toxins or other virulent component-based

vaccines to make a broad toxin-based multivalent vaccine capable of targeting multiple bacterial virulence determinants. In other embodiments of the disclosure, the mutant staphylococcal leukocidin subunit (e.g., LukS-PV or LukF-PV, or both), as described herein, can be fused to other immunogenic, biologically significant, or protective epitope containing polypeptides to generate a multivalent vaccine in a single chain and induce an immune response against multiple antigens. In yet another embodiment of the disclosure, the mutant staphylococcal leukocidin subunit (e.g., LukS-PV or LukF-PV, or both), as described herein, can be fused to one or more T cell epitopes to induce T cell immunity along with anti PVL antibodies.

Methods of Treatment/Prevention and Regimens

[0128] Also provided is a method of treating or preventing *Staphylococcus* infection, e.g., *S. aureus* infection or treating or preventing a disease caused by *Staphylococcus*, e.g., *S. aureus* in a subject, comprising administering to a subject in need thereof a composition as described herein comprising the mutant staphylococcal leukocidin subunit (e.g., LukS-PV or LukF-PV, or both), as described herein, or polynucleotides, vectors, or host cells encoding same. In certain embodiments of the disclosure, the subject is an animal, e.g., a vertebrate, e.g., a mammal, e.g., a human. Some embodiments of the disclosure include a method of inducing an immune response against a *S. aureus* strain, comprising administering to a subject in need of said immune response an effective amount of a composition as described herein comprising the mutant staphylococcal leukocidin subunit (e.g., LukS-PV or LukF-PV, or both), as described herein, or polynucleotides, vectors, or host cells encoding same.

[0129] In some embodiments of the disclosure, a subject is administered a composition as described herein comprising the mutant staphylococcal leukocidin subunit (e.g., LukS-PV or LukF-PV, or both), as described herein, or polynucleotides, vectors, or host cells encoding same prophylactically, e.g., as a prophylactic vaccine, to establish or enhance immunity to *Staphylococcus*, e.g., *S. aureus*, in a healthy animal prior to potential or actual exposure to *Staphylococcus*, e.g., *S. aureus* or contraction of a *Staphylococcus*-related symptom, thus preventing disease, alleviating symptoms, reducing symptoms, or reducing the severity of disease symptoms. In one embodiment of the disclosure the disease is a respiratory disease, e.g., pneumonia. Other diseases or conditions to be treated or prevented include, but are not limited to, bacteremia, sepsis, skin infections, wound infections, endocarditis, bone and joint infections, osteomyelitis, and/or meningitis. One or more compositions, polypeptides, polynucleotides, vectors, or host cells as described herein can also be used to treat a subject already exposed to *Staphylococcus*, e.g., *S. aureus*, or already suffering from a *Staphylococcus* related symptom to further stimulate the immune system of the animal, thus reducing or eliminating the symptoms associated with that exposure. As defined herein, "treatment of an animal" refers to the use of one or more compositions, polypeptides, polynucleotides, vectors, or host cells of the disclosure to prevent, cure, retard, or reduce the severity of *S. aureus* symptoms in an animal, and/or result in no worsening of *S. aureus* symptoms over a specified period of time. It is not required that any composition, polypeptide,

polynucleotide, a vector, or a host cell as described herein provides total protection against a staphylococcal infection or totally cure or eliminate all *Staphylococcus* related symptoms.

[0130] As used herein, "a subject in need of therapeutic and/or preventative immunity" refers to a subject in which it is desirable to treat, *i.e.*, to prevent, cure, retard, or reduce the severity of *Staphylococcus* related symptoms, or result in no worsening of *Staphylococcus* related symptoms over a specified period of time. As used herein, "a subject in need of the immune response" refers to a subject for which an immune response(s) against any of PVL expressing *Staphylococcus* strains is desired.

[0131] Treatment with pharmaceutical compositions comprising an immunogenic composition, polypeptide or polynucleotide as described herein can occur separately or in conjunction with other treatments, as appropriate.

[0132] In therapeutic applications, a composition, polypeptide or polynucleotide of the disclosure is administered to a patient in an amount sufficient to elicit an effective innate, humoral or cellular response, or both, to the *S. aureus* PVL derived polypeptide to cure or at least partially arrest symptoms or complications.

[0133] An amount adequate to accomplish this is defined as "therapeutically effective dose" or "unit dose." Amounts effective for this use will depend on, *e.g.*, the polypeptide or polynucleotide composition, the manner of administration, the stage and severity of the disease being treated, the weight and general state of health of the patient, and the judgment of the prescribing physician, but generally range for the initial immunization for polypeptide vaccines is (that is for therapeutic or prophylactic administration) from about *e.g.*, 0.1 μg to about 5000 μg of polypeptide, depending upon the patient's response and condition by measuring, for example, antibody levels in the patient's blood. In some embodiments of the disclosure, a priming dose is followed by a boosting dose over a period of time.

[0134] In non-limiting embodiments of the disclosure, an effective amount of a composition as disclosed herein produces an elevation of antibody titer to at least 2, 5, 10, 50, 100, 500, 1000, 5000, 10^4 , 5×10^4 , or 10^5 times the antibody titer prior to administration.

[0135] In alternative embodiments of the disclosure, generally for humans an initial immunization (that is for therapeutic or prophylactic administration) is administered followed by boosting dosages in the same dose range pursuant to a boosting regimen over weeks to months depending upon the patient's response and condition by measuring the antibody or T lymphocyte response in the patient's blood.

[0136] It must be kept in mind that the polypeptides and compositions as described herein can generally be employed in serious disease states, that is, life-threatening or potentially life threatening situations. In such cases, in view of the minimization of extraneous substances and the relative nontoxic nature of the polypeptides, it is possible and can be felt desirable by the treating physician to administer substantial excesses of these polypeptide compositions.

[0137] For therapeutic use, administration should begin at the first sign of *S. aureus* infection or risk factors. In certain embodiments of the disclosure, the initial dose is followed by boosting doses until, e.g., symptoms are substantially abated and for a period thereafter. In frequent infection, loading doses followed by boosting doses can be required.

[0138] In certain embodiments of the disclosure, the composition as described herein is delivered to a subject by methods described herein, thereby achieving an effective immune response, and/or an effective therapeutic or preventative immune response. Any mode of administration can be used so long as the mode results in the delivery and/or expression of the desired polypeptide in the desired tissue, in an amount sufficient to generate an immune response to *Staphylococcus*, e.g., *S. aureus*, and/or to generate a prophylactically or therapeutically effective immune response to *Staphylococcus*, e.g., to *S. aureus*, in an animal in need of such response. According to the disclosed methods, a composition described herein can be administered by mucosal delivery, transdermal delivery, subcutaneous injection, intravenous injection, oral administration, pulmonary administration, intramuscular (i.m.) administration, or via intraperitoneal injection. Other suitable routes of administration include, but not limited to intratracheal, transdermal, intraocular, intranasal, inhalation, intracavity, intraductal (e.g., into the pancreas) and intraparenchymal (i.e., into any tissue) administration. Transdermal delivery includes, but not limited to intradermal (e.g., into the dermis or epidermis), transdermal (e.g., percutaneous) and transmucosal administration (i.e., into or through skin or mucosal tissue). Intracavity administration includes, but not limited to administration into oral, vaginal, rectal, nasal, peritoneal, or intestinal cavities as well as, intrathecal (i.e., into spinal canal), intraventricular (i.e., into the brain ventricles or the heart ventricles), intra-arterial (i.e., into the heart atrium) and sub arachnoidal (i.e., into the sub arachnoid spaces of the brain) administration.

[0139] Any mode of administration can be used so long as the mode results in the delivery and/or expression of the desired polypeptide in an amount sufficient to generate an immune response to *Staphylococcus*, e.g., *S. aureus*, and/or to generate a prophylactically or therapeutically effective immune response to *Staphylococcus*, e.g., *S. aureus*, in an animal in need of such response. Administration as described herein can be by e.g., needle injection, or other delivery or devices known in the art.

[0140] In some embodiments of the disclosure, a composition comprising the mutant staphylococcal leukocidin subunit (e.g., LukS-PV or LukF-PV, or both), as described herein, or polynucleotides, vectors, or host cells encoding same, stimulate an antibody response or a cell-mediated immune response sufficient for protection of an animal against *Staphylococcus*, e.g., *S. aureus* infection. In other embodiments of the disclosure, a composition comprising the mutant staphylococcal leukocidin subunit (e.g., LukS-PV or LukF-PV, or both), as described herein, or polynucleotides, vectors, or host cells encoding same, stimulate both a humoral and a cell-mediated response, the combination of which is sufficient for protection of an animal against *Staphylococcus*, e.g., *S. aureus* infection. In some embodiments of the disclosure, a composition comprising the mutant staphylococcal leukocidin subunit (e.g., LukS-PV or LukF-

PV, or both), as described herein, or polynucleotides, vectors, or host cells encoding same, further stimulates an innate, an antibody, and/or a cellular immune response.

[0141] In some embodiments of the disclosure, a composition comprising the mutant staphylococcal leukocidin subunit (e.g., LukS-PV or LukF-PV, or both), as described herein, or polynucleotides, vectors, or host cells encoding same, induce antibody responses to *S. aureus* PVL. In certain embodiments of the disclosure, components that induce T cell responses (e.g., T cell epitopes) are combined with components such as the polypeptides as described herein that primarily induce an antibody response.

[0142] Further disclosed is a method for generating, enhancing, or modulating a protective and/or therapeutic immune response to *S. aureus* infection in a subject, comprising administering to a subject in need of therapeutic and/or preventative immunity one or more of the compositions as described herein.

[0143] The compositions as described herein can be administered to an animal at any time during the lifecycle of the animal to which it is being administered. In humans, administration of the composition as described herein can, and often advantageously occurs while other vaccines are being administered, e.g., as a multivalent vaccine as described elsewhere herein.

[0144] Furthermore, the composition as described herein can be used in any desired immunization or administration regimen; e.g., in a single administration or alternatively as part of periodic vaccination regimes such as annual vaccinations, or as in a prime-boost regime in which composition or polypeptide or polynucleotide of the disclosure is administered either before or after the administration of the same or of a different polypeptide or polynucleotide. Recent studies have indicated that a prime-boost protocol is often a suitable method of administering vaccines. In a prime-boost protocol, one or more compositions as described herein can be utilized in a "prime boost" regimen. An example of a "prime boost" regimen can be found in Yang, Z. et al. J. Virol. 77:799-803, 2002, which is incorporated herein by reference in its entirety.

[0145] Infections to be treated include, but are not limited to a localized or systemic infection of skin, soft tissue, blood, or an organ or an auto-immune disease. Specific diseases or conditions to be treated or prevented include, but are not limited to, respiratory diseases, e.g., pneumonia, sepsis, skin infections, wound infections, endocarditis, bone and joint infections, osteomyelitis, and/or meningitis.

Immune correlates

[0146] A number of animal models for *S. aureus* infection are known in the art, and can be used with the methods disclosed herein without undue experimentation. For example, a hamster model of methicillin-resistant *Staphylococcus aureus* (MRSA) pneumonia has been described for the testing of antimicrobials. (Verghese A. et al., Chemotherapy. 34:497-503

(1988), Kephart PA. et al. J Antimicrob Chemother. 21:33-9, (1988)). Further, a model of *S. aureus*-induced pneumonia in adult, immunocompetent C57BL/6J mice is described, which closely mimics the clinical and pathological features of pneumonia in human patients. (Bubeck-Wardenburg J. et al., Infect Immun. 75:1040-4 (2007)). Additionally, virulence has been tested in a rat model of *S. aureus* pneumonia as described in McElroy *et al.* (McElroy MC. et al., Infect Immun. 67:5541-4 (1999)). Finally, a standardized and reproducible model of MRSA-induced septic pneumonia to evaluate new therapies was established in sheep. (Enkhbaatar P. et al., Shock. 29(5):642-9 (2008)).

[0147] The practice of the disclosure will employ, unless otherwise indicated, conventional techniques of cell biology, cell culture, molecular biology, transgenic biology, microbiology, recombinant DNA, and immunology, which are within the skill of the art. Such techniques are explained fully in the literature. See, for example, Molecular Cloning A Laboratory Manual, 2nd Ed., Sambrook et al., ed., Cold Spring Harbor Laboratory Press: (1989); Molecular Cloning: A Laboratory Manual, Sambrook et al., ed., Cold Springs Harbor Laboratory, New York (1992), DNA Cloning, D. N. Glover ed., Volumes I and II (1985); Oligonucleotide Synthesis, M. J. Gait ed., (1984); Mullis et al. U.S. Pat. No: 4,683,195; Nucleic Acid Hybridization, B. D. Hames & S. J. Higgins eds. (1984); Transcription And Translation, B. D. Hames & S. J. Higgins eds. (1984); Culture Of Animal Cells, R. I. Freshney, Alan R. Liss, Inc., (1987); Immobilized Cells And Enzymes, IRL Press, (1986); B. Perbal, A Practical Guide To Molecular Cloning (1984); the treatise, Methods In Enzymology, Academic Press, Inc., N.Y.; Gene Transfer Vectors For Mammalian Cells, J. H. Miller and M. P. Calos eds., Cold Spring Harbor Laboratory (1987); Methods In Enzymology, Vols. 154 and 155 (Wu et al. eds.); Immunochemical Methods In Cell And Molecular Biology, Mayer and Walker, eds., Academic Press, London (1987); Handbook Of Experimental Immunology, Volumes I-IV, D. M. Weir and C. C. Blackwell, eds., (1986); Manipulating the Mouse Embryo, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., (1986); and in Ausubel et al., Current Protocols in Molecular Biology, John Wiley and Sons, Baltimore, Maryland (1989).

[0148] Standard reference works setting forth general principles of immunology include Current Protocols in Immunology, John Wiley & Sons, New York; Klein, J., Immunology: The Science of Self-Nonself Discrimination, John Wiley & Sons, New York (1982); Roitt, I., Brostoff, J. and Male D., Immunology, 6th ed. London: Mosby (2001); Abbas A., Abul, A. and Lichtman, A., Cellular and Molecular Immunology, Ed. 5, Elsevier Health Sciences Division (2005); and Harlow and Lane, Antibodies: A Laboratory Manual, Cold Spring Harbor Press (1988).

EXAMPLES

[0149] Examples not falling under the scope of the appended claims do not form part of the invention.

Example 1: Molecular modeling and design of vaccine candidates

[0150] This example describes molecular modeling (computer based) techniques for deriving, analyzing and manipulating the structure of Pantone-Valentine leukocidin (PVL) LukF-PV and LukS-PV subunits in order to design vaccine candidates.

[0151] To develop a vaccine that is composed of attenuated forms of LukF-PV and/or LukS-PV, the subunits were modified to avoid *in vivo* pore assembly and the cytolytic and inflammatory effects that occur upon pore formation. To identify regions on the LukF-PV and LukS-PV protein surfaces that may be amenable to mutations that abolish pore-formation without disrupting the structural integrity of each subunit, the structure of the LukF-PV/LukS-PV heterodimer and octamer was modeled as described in Aman et al. J Biomol Struct Dyn 28, 1-12, 2010. Briefly, LukF-PV and LukS-PV monomers were extracted from the 1PVL and 1T5R crystal structures, respectively. Missing residues in each structure were modeled into the polypeptide. The resulting structures were energy refined using tethered minimization. Since each subunit possesses two interacting faces in the octamer ring-like structure, it was necessary to construct two different LukF-PV/LukS-PV heterodimer models to fully elucidate the binding interactions on each subunit. These two molecular models were identified as F_R-S_L and S_L-F_R . This nomenclature is based on the side-by-side relationship of the LukF-PV and LukS-PV constituents in the octameric ring-like structure. F and S represent the two classes, and subscript R and L denote right and left faces, respectively. If one views the two subunits from inside the channel lumen, in the F_R-S_L model, the right side of LukF-PV (F_R) is bound with the left side of LukS-PV (S_L) and alternatively, in the S_L-F_R model, the right side of LukS-PV (S_L) is bound with the left side of LukF-PV (F_R). The Discovery Studio 2.1 (Accelrys, Inc) program running on a Dell Precision 690 with Red Hat Enterprise Linux 4 was used to build, visualize, and analyze the protein models. Simulations were performed *in vacuo* using a distance-dependent dielectric of 1 and nonbonded interactions limited to within 14 Å in a CHARMM force-field. The template in the model building is disclosed in Aman *et al.*

[0152] The F_R-S_L model shows that the Thr28 side chain is tightly packed against the polypeptide backbone of residues Asn158 and Phe159 in the neighboring LukF-PV subunit (**Figure 1**).

[0153] To identify other interaction sites that may be crucial to oligomerization, molecular modeling as described above was used to scan the F_R-S_L and S_R-F_L interfaces in the PVL octamer model for hotspots that, if mutated, would significantly shift the monomer-dimer equilibrium constant in favor of monomer. In mature LukS-PV, these sites were Tyr131 and Ser209, which were identified from the F_R-S_L interface model and Lys97 and Asp101 from the S_R-F_L model. The corresponding sites in mature LukF-PV were Lys102 and Asp121 in the F_R-S_L model and Glu147 and Asn220 in the S_R-F_L model.

[0154] As one of the metrics used to determine the effect of each mutant on dimerization, the positions were mutated to alanine *in silico* for residues outside of Thr28 and to phenylalanine

for Thr28. The single- and double-point mutant complexes were energy minimized, and their molecular energies were calculated relative to wild-type. Similar alanine mutations of Lys97, Asp101 and Tyr131 in LukS-PV and of Lys102, Asp121, and Glu147 in LukF-PV in the molecular models resulted in significant increases in the calculated energy of the complex relative to wild-type (see **Table 1** above). The most dramatic increase in destabilization energy was observed for the Ser209Ala mutant of LukS-PV. Ser209 connects loop and strand structures in LukS-PV and is buried near the middle of the dimer interface between Ser209 of LukS-PV and Lys 102 of LukF-PV (**Figure 2**).

[0155] Single point mutations at the above-described sites were predicted to shift the monomer-heterodimer equilibrium of PVL in favor of monomers, and these mutants were selected as candidates for vaccine development.

[0156] Thr28 on LukS-PV has been reported in the literature to play a role in dimerization (V. Guillet et al., The Journal of Biological Chemistry 279: 41028-41037 (2004)). The potential utility of Thr28 in double mutants was examined. In this preliminary analysis, the double mutants Thr28Phe/Tyr131Ala and Thr28Phe/Ser209Ala as well as a triple mutant Thr28Phe/Tyr131Ala/Ser209Ala was investigated *in silico*. Based on energy calculations, the Thr28Phe/Ser209Ala mutant followed by the triple mutant had the most significant effect. **Table 1** also lists the calculated energy increase in the heterodimer complex structure as a result of the different proposed single and double mutations of LukS-PV.

Example 2: Generation of LukS-PV and LukF-PV mutants

[0157] Mutations were designed based on the octameric model and were introduced into cDNA constructs for LukS-PV and LukF-PV that carried a N-Terminal 6xHis tag for purification purposes. Wild-type LukS-PV and LukF-PV DNA fragments encoding the respective mature protein sequences were synthesized by PCR, treated by BamHI and KpnI restriction enzymes to create cohesive ends, and cloned into pQE30 vector (Qiagen) digested by BamHI and KpnI restriction enzymes. Mutations were introduced into DNA by using the QuickChange[®] II Site-Directed Mutagenesis Kit (Stratagene). The nucleotide sequence of the plasmid construct encoding the wild-type LukS-PV is presented as SEQ ID NO: 123. The nucleotide sequence of the plasmid construct encoding the mutant (K97A) LukS-PV is presented as SEQ ID NO: 124. The nucleotide sequence of the plasmid construct encoding the mutant (D102A) LukS-PV is presented as SEQ ID NO: 125. The nucleotide sequence of the plasmid construct encoding the mutant (Y131A) LukS-PV is presented as SEQ ID NO: 126. The nucleotide sequence of the plasmid construct encoding the mutant (S209A) LukS-PV is presented as SEQ ID NO: 127. The nucleotide sequence of the plasmid construct encoding the mutant (T28F) LukS-PV is presented as SEQ ID NO: 128. The nucleotide sequence of the plasmid construct encoding the mutant (T28F/Y131A) LukS-PV is presented as SEQ ID NO: 129. The nucleotide sequence of the plasmid construct encoding the mutant (T28F/S209A) LukS-PV is presented as SEQ ID NO: 130. The nucleotide sequence of the plasmid construct encoding the mutant

(T28F/K97A/S209A) LukS-PV is presented as SEQ ID NO: 131. The nucleotide sequence of the plasmid construct encoding the wild-type LukF-PV is presented as SEQ ID NO: 132. The nucleotide sequence of the plasmid construct encoding the mutant (K102A) LukF-PV is presented as SEQ ID NO: 133. The nucleotide sequence of the plasmid construct encoding the mutant (D121A) LukF-PV is presented as SEQ ID NO: 134. The nucleotide sequence of the plasmid construct encoding the mutant (E147A) LukF-PV is presented as SEQ ID NO: 135.

[0158] A plasmid construct encoding the LukF-PV triple mutant (K102A/D121A/E147A) listed in **Table 1** was also generated as described above. The mature protein sequence of the LukF-PV Triple Mutant (Lys102Ala (K102A)/Asp121Ala (D121A)/Glu147Ala (E147A)) is shown below with the mutated amino acids underlined and presented as SEQ ID NO: 136:

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1      aqhithpvsek kvddkitlyk ttatsdsdkl kisqiltfnf ikdktsydkdt lilkaagniy
61     sgytkpnpkd tissqfywgs kynisinsds ndsvnvvdya panqneefqv qqtvgysygg
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301    s

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[0159] The nucleotide sequence of the plasmid construct encoding the triple mutant (K102A/D121A/E147A) LukF-PV is shown below (cloning sites BamHI and KpnI are underlined, the mutations are double underlined, and the termination codon is in italics) and presented as SEQ ID NO: 137:

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```

[0160] The mutants, which were selected based on structural analysis described above, included five single, two double and one triple mutants of LukS-PV as well as four single and one triple mutants of LukF-PV (Table 1). The mutant proteins along with the His-tagged wild-type subunits were produced in *E.coli* strain XL1-Blue [*recA1 endA1 gyrA96 thi-1 hsdR17 supE44 relA1 lac* [F' *proAB LacIqΔM15 Tn10* (Tetr)]] and purified on a HisTrap™ HP column

(GE Healthcare Cat#17-5248-02) used according to the manufacturer's instructions. All proteins were quality controlled by SDS-PAGE (Sodium Dodecyl Sulfate-Polyacrylamide Gel Electrophoresis) using common techniques and western blotting with respective antibodies (LukS-PV: V5184 rabbit polyclonal Ab (Genscript), LukF-PV: 1A11 mAb (IBT)).

[0161] SDS-PAGE and Western blot analysis of LukS-PV Mut9, LukF-PV Mut1 and LukF-PV triple mutant (K102A/D121A/E147A) are shown in **Figure 7A-C**.

Example 3: Attenuation of LukS-PV and LukF-PV Mutants

[0162] Each of the LukS-PV and LukF-PV mutants were tested in a neutrophil toxicity assay in combination with the wild-type LukF-PV, or LukS-PV, respectively. Using a 96-well round bottom tissue culture plate, the wild-type or mutant LukS-PV or LukF-PV proteins were semi-log diluted in duplicates down the plate in assay media (RPMI, 2% FBS, 5mM glutamine) followed by addition of 5×10^5 DMSO induced HL-60 cells. HL-60 cells were differentiated into neutrophils by treatment with DMSO. The suspension was gently tapped and plates incubated for 48 hours at 37°C with 5% CO₂ and 95% humidity. To determine cellular viability, 20 µL of 2mg/mL diluted XTT (Sigma-Aldrich, St. Louis, MO) was added to each well, incubated for 6 hours at 37°C with 5% CO₂ and 95% humidity, centrifuged and supernatant transferred to an ELISA plate and read to 470nm. The percent (%) viability was determined as follows: % Viability = (OD value of Experimental Sample Well / OD value of HL-60 cells without PVL Toxin) x 100. The data are presented as % cell survival in **Figures 3 and 4**.

[0163] Mutant LukS-PV data showed that while each of the single mutants or double mutants slightly reduced the toxicity of LukS-PV in complex with the wild-type LukF-PV, a triple mutant combining the mutations T28F, K97A, and S209A led to nearly complete attenuation. In the presence of the triple mutant combined with the wild-type LukF-PV, over 90% of cells remained viable (**Figure 3**).

[0164] Mutant LukF-PV proteins were tested in a neutrophil toxicity assay as described above, in combination with the wild-type LukS-PV or LukS-PV triple mutant (T28F, K97A, and S209A). As shown in **Figure 4**, each of the single mutations reduced the toxicity of LukF-PV when combined with the wild-type LukS-PV. Of the three LukF-PV mutants tested, the K102A mutant showed the highest degree of attenuation with complete loss of toxicity at 300 ng/ml and about 50% reduced toxicity at 3000 ng/ml. When combined with the LukS-PV triple mutant all three LukF-PV mutants (LukF K102A, LukF D121A and LukF E147A) showed complete inactivation.

Example 4: Polyclonal antibodies to PVL protect mice from lethal challenge with community acquired *S. aureus* strain USA300 (LAC)

[0165] The ability of anti-PVL polyclonal antibodies to protect against bacteremia caused by *S.*

aureus USA300 in mice was tested. For this study polyclonal antibodies were generated in rabbits by immunizing with His-tagged protein containing the wild-type sequence of LukS-PV presented by SEQ ID NO: 6 and an N-terminal 6xHis tag. Polyclonal antibodies (total IgG) were purified from hyperimmune serum over a protein G column. Furthermore, specific anti-LukS-PV antibodies were purified from total IgG using AminoLink® Plus Immobilization Kit (Thermoscientific). The Kit included reagents, column and buffers needed to make the affinity column packed with beads. Beads coupled with LukS-PV protein and affinity purification of polyclonal anti-LukS-PV antibody was carried out according to the manufacturer's protocol. Furthermore, to test the ability of anti-LukS-PV antibodies to synergize with anti- α -hemolysin antibodies (Hla), combinations of anti-LukS-PV and anti-Hla polyclonal antibodies were examined. A model as disclosed in Fattom et al., Infect Immun 64, 1659-1665, 1996, in which BALB/c mice were challenged via intraperitoneal route with *S. aureus* mixed with Hog-Mucin was applied. Mice were pre-treated with the indicated antibodies 24 hour prior to challenge. Naive mouse IgG was used as control. After challenge with 5×10^4 USA300 and 3% Hog-Mucin (Sigma-Aldrich, St. Louis, MO), mice were monitored for morbidity and mortality for 5 days. As shown in Table 3, all mice treated with naive mouse IgG succumbed to death within 16-20 hours post challenge. In contrast, 3 out of 5 mice who received 50 ug of purified anti-LukS-PV and 2 out of 5 mice who received 2 mg of anti-Hla total IgG survived suggesting that each component contributes to protection. When 2 mg of anti-Hla IgG was combined with 50 or 25 μ g of purified anti LukS-PV antibodies, 100% survival was observed. Lower dose of purified anti-LukS-PV (12.5 μ g) when added to anti-Hla lead to 80% survival which was higher than the survival achieved by either component alone. These data suggest that vaccination with a combination of LukS-PV or Hla vaccines may lead to additive or synergistic protective effect against *S. aureus* bacteremia.

Table 3: Protection against USA300 bacteremia by antibodies to LukS-PV and Hla

Group#	N	Anti-LukS (affinity Purified)	Anti-Hla (Total IgG)	Naive mouse IgG	% Survival				
					16h	20h	36h	48h	120h
1	5	50 ug	2 mg	0	100%	100%	100%	100%	100%
2	5	25 ug	2 mg	0	100%	100%	100%	100%	100%
3	5	12.5 ug	2 mg	0	80%	80%	80%	80%	80%
4	5	50 ug	0	0	100%	60%	60%	60%	60%
5	5	0	2 mg	0	60%	40%	40%	40%	40%
6	5	0	0	2 mg	60%	0%	0%	0%	0%

Example 5: Sequence identity for staphylococcal two component pore-forming toxins

[0166] The sequence identity between LukS, LukM, LukE, and HlgA/S was compared. *S. aureus* γ -hemolysin (Hlg), leukocidin (Luk) and PVL are related two-component pore-forming toxins (Kaneko et al., Biosci Biotechnol Biochem, 2004. 68(5): p. 981-1003).

[0167] LukS-PV has high sequence identity with LukS, LukM, LukE, and HlgA/C ranging from 65% to 81% as shown in **Figure 5**. All three sites mutagenized in the attenuated triple mutant LukS-PV vaccine candidate tested herein were shown to be conserved throughout the family (shown in box with * in **Figure 5**). Similarly, LukF-PV was shown to be highly homologous to LukF, LukD, LukDv, and HlgB, and the sites mutated in the LukS-PV vaccines tested herein were conserved. Consistent with this homology, it was shown that LukS-PV polyclonal antibodies inhibited cytotoxic activity towards PMNs in the supernatants of not only PVL-positive strains (USA300&400) but also in PVL deficient strains such as Newman and 8325-4 (**Figure 6**). These data showed that antibodies elicited against PVL subunits showed broader reactivity and neutralized non-PVL leukocidins.

Example 6: *In vitro* structural and functional characterization of mutant proteins

[0168] Functional activity of LukS-PV and LukF-PV mutants disclosed herein was tested in a cytotoxicity assay using HL-60 cells differentiated to neutrophils (Romero-Steiner et al., Clin Diagn Lab Immunol, 1997. 4(4): p. 415-22). To ensure the structural integrity of the mutants, these proteins along with wild-type counterparts were analyzed by circular dichroism (CD) spectrometry. Furthermore, the thermal stability of the proteins was determined using Differential Scanning Fluorimetry (DSF).

[0169] Analysis of cytotoxicity: Cellular cytotoxicity was tested using a combination of each mutant subunit with the wild-type form of the other subunit using HL-60 cells (ATCC, Catalog Number CCL-240) differentiated *in vitro* into neutrophils (Romero-Steiner et al.). The HL-60 cells were propagated in RPMI/15% FBS and 1.6% dimethylsulfoxide (DMSO) for 6 days. The differentiated neutrophil-like cells were harvested and transferred to 96 well plates for PVL toxicity assay at a final density of 5×10^5 cells/well. Each PVL subunit (mutant or wild-type) was used at 200 ng/ml. Cells were incubated for 48 hours at 37°C and cellular viability was evaluated after 16 hours of further incubation with 100 µg/ml of XTT (Sigma-Aldrich) and colorimetric measurement at OD470 nm. Percent viability of the cells was then calculated in comparison to the wells without toxin.

[0170] As shown in **Figure 8A**, single mutants of LukS-PV did not have a significant impact on toxicity of PVL when the mutant was combined with wild-type LukF, and double mutants slightly reduced the PVL toxicity. However, the triple mutant LukS-PV_T28F/K97A/S209A (denoted as Mut9) was completely attenuated despite combining with wild-type LukF (**Figure 8A**). All three single mutants of LukF caused a right shift in dose response curve with the highest attenuation achieved with LukF_K102A (denoted as Mut1) (**Figure 8B**). When this mutant was combined with LukS Mut9 no toxicity was observed (**Figure 8B**). Low toxicity was observed with LukF mut1 when combined with wild-type LukS toward high concentration. A triple LukF mutant (K102A/D121A/E147A) was constructed and tested. As shown in **Figure 8C**, the triple LukF mutant was completely attenuated when combined with wild-type LukS and also with LukS mut9.

[0171] *Thermal Stability analysis:* Thermal stability of LukS-PV and LukF-PV mutant proteins was assessed by Thermofluor (Differential Scanning Fluorimetry) using Sypro Orange as the external fluorescent probe, which binds to hydrophobic residues detecting their exposure during protein unfolding. When heated above critical temperature ($>70^{\circ}\text{C}$ for LukS and LukF-PV), proteins tend to unfold. This results in increased fluorescence, but if unfolding leads to aggregation the result is a decreased fluorescence. This increase and decrease of the fluorescent signal is a means to monitor protein unfolding, calculate the melting temperatures, and compare the thermal stabilities of different proteins under different experimental conditions (Ericsson et al., *Anal Biochem*, 2006. 357(2): p. 289-98; He et al., *J Pharm Sci*, 2010. 99(4): p. 1707-20). The results are shown in **Figure 9**.

[0172] **Figure 9A** shows the changes in fluorescent signal of the proteins during thermal unfolding in the presence of dye while **Figure 9B** shows the plot of the fraction of unfolded protein based on fitting each protein melting curve using two-state equations as described in Devi et al., *Biochemistry*, 2006. 45(6): p. 1599-607. Wild-type and mutant proteins of both subunits showed very low background fluorescence when properly folded at 25°C and retain intensity until 55°C showing that the proteins were stable. Melting above 55°C caused an increase in the fluorescent signal, which was due to protein unfolding. This steep increase also supported a highly co-operative unfolding process. LukS-PV wild-type curve was slightly shifted to the right indicating its higher stability. The maximum fluorescence intensity was observed at 75°C for the LukS-PV wild-type while it was at 70°C for other mutants. When heated above these temperatures, the fluorescent intensity dropped down for all the proteins indicating an aggregation event was taking place. Therefore, intensity values only up to 75°C were considered for creating the fraction unfolded protein plot (**Figure 9B**). Apparent T_m values from Boltzmann Sigmoid fitting of the data showed that the T_m for all the tested mutants ranged from 62.6 to 63.6, which was similar to wild-type LukS (64.8) and wild-type LukF (62.9) and suggested that the mutations did not affect the thermal stability of the proteins.

Example 7: Immunogenicity study in mice using different clinically relevant adjuvants

[0173] *Immunogenicity and adjuvant studies:* An immunogenicity study was performed in mice using different clinically relevant adjuvants including two forms of alum-based adjuvants, Alhydrogel ($\text{Al}(\text{OH})_3$) and aluminum phosphate (AlPO_4), as well as two novel adjuvants currently in clinical trials IDC-1001 (also known as GLA-SE; glucopyranosyl lipid adjuvant stable emulsion) (Coler et al., *PLoS One*, 2010. 5(10): p. e13677; Coler et al., *PLoS One*, 2011. 6(1): p. e16333) and CpG (Mullen et al., *PLoS One*, 2008. 3(8): p. e2940).

[0174] Groups of 5 female BALB/c mice were vaccinated intramuscularly (IM) three times with $5\text{ }\mu\text{g}$ of LukS-PV T28F/K97A/S209A (LukS-Mut9) with each of the adjuvants at 2 week intervals. As controls, the wild-type (wt) LukS-PV as well as an irrelevant antigen (STEBVax; staph enterotoxin B vaccine) were combined with Alhydrogel. Mice were bled on days 21 and 35. All tested adjuvants induced robust total antibody response over one log higher than

without adjuvant (**Figure 10A**). Neutralizing antibody titer was determined using HL-60 derived neutrophils as described above. As shown in **Figure 10B**, the highest neutralizing titer was achieved after three vaccinations using the alum-based adjuvants and IDC-1001. The antibody response to LukS-Mut9 was compared to the response to wild-type LukS-PV, and the results supported the conservation of immunological epitopes in the mutant.

Example 8: Efficacy of PVL vaccine candidates in murine pneumonia and intraperitoneal sepsis models

[0175] Efficacy studies were performed in murine pneumonia and intraperitoneal sepsis models. Studies were performed to evaluate the efficacy of PVL vaccine candidates alone and in combination with a subunit vaccine for α -hemolysin, AT-62 (Adhikari et al., PLoS One, 2012. 7(6): p. e38567). Initially, passive immunization studies were performed with lethality and bacterial burden as endpoints using the bacteremia model in mice. Thereafter, proof of concept active immunization studies in both bacteremia/sepsis as well as pneumonia models were performed.

[0176] *Description of animal models:* In the mouse pneumonia model, female BALB/c mice were anesthetized with isoflurane and inoculated intranasally (IN) with a lethal dose ($\sim 2 \times 10^8$) of USA300 in 50 μ l PBS and placed into the cages in a prone position and monitored for morbidity (weight, hunched posture, labored breathing, ruffled fur, impaired mobility) and mortality 4 times a day within the first 48 hours and then once a day until termination of the study. In the bacteremia model, female BALB/c mice were challenged via intra-peritoneal (IP) injection with USA300 in 3% mucin solution as previously described in Fattom et al., Infect Immun, 1996. 64(5): p. 1659-65. Briefly, lyophilized hog mucin type III was solubilized to 6% in PBS, sterilized by autoclaving and rapidly cooled on ice. PBS washed, overnight grown bacteria were suspended in PBS at 2×10^5 CFU/ml. Bacteria and mucin solution were mixed to achieve the intended challenge dose (see **Table 4** below) in 0.5ml of 3% hog mucin. Mice were monitored for morbidity and mortality twice a day for 7-14 days. Mice were 6 weeks of age for active and 10 weeks for passive immunogenicity studies. To determine bacterial dissemination to organs, mice were euthanized at 12h after challenge and blood and organs (liver, combined kidneys, lungs and spleen) were aseptically removed, homogenized and taken up in 500 μ l PBS. Blood samples and organ homogenates were streaked in different dilutions on BHI agar plates and CFU was enumerated after ON incubation at 37°C.

[0177] *Passive immunization studies:* The efficacy of rabbit polyclonal antibodies to LukS-PV (LukS-IgG) and Hla (AT62-IgG) alone and in combination was explored in the bacteremia model. Groups of 5 mice were injected IP with different doses of the antibodies, challenged 24 hours later, and monitored for 7 days. As shown in **Table 4** (Exp.1), as low as 0.25 mg of LukS-IgG provided full protection. In contrast, 4 mg of AT62-IgG was needed to provide 100% protection with partial efficacy at 2.5 mg (see **Table 4** (Exp. 2)).

Table 4: Efficacy of passive immunization with rabbit polyclonal antibodies against LukS and

Alpha toxin in USA300 bacteremia model

Exp. 1	Survivor/Total
4 mg LukS-IgG	5/5
1 mg LukS-IgG	5/5
0.25 mg LukS-IgG	5/5
4 mg naive IgG	0/5
Exp. 2	Survivor/Total
5 mg AT62-IgG	5/5
2.5 mg AT62-IgG	2/5
1.25 mg AT62-IgG	1/5
0.62 mg AT62-IgG	0/5
5 mg naive IgG	1/5

[0178] Next, the affinity purified LukS-IgG was combined with a suboptimal dose (2 mg) of AT62-IgG. As shown in **Table 5**, 50µg of affinity purified LukS-IgG or 2 mg of AT62-IgG provided partial protection while the combination of the two antibodies at these doses fully protected mice. Full protection was also observed with 2 mg of AT62-IgG and 25 µg of affinity purified LukS-IgG, and 4 out of 5 mice survived with 12.5 µg LukS antibody in the combination with 2 mg of AT62-IgG.

Table 5: Combination passive immunization study of rabbit pAb against LukS and Alpha toxin in USA300 bacteremia model

AT62-IgG	Affinity Pur. LukS-IgG	Naive IgG	Survivor Total
2 mg	-	-	2/5
-	50 ug	2 mg	3/5
2 mg	50 ug	-	5/5
2 mg	25 ug	-	5/5
2 mg	12.5 ug	-	4/5
-	-	2 mg	0/5

[0179] In a set of similar studies, the synergistic effect of pretreatment (24 hours before challenge) with AT62-IgG and LukS-IgG on bacterial dissemination determined 12 hours after USA 300 challenge was tested. As shown in **Figure 11**, the two antibodies strongly synergized the reduction of bacterial burden in blood and organs. These data strongly supported that antibodies to LukS and alpha toxin act synergistically in protecting from lethal bacteremia and sepsis.

[0180] The efficacy of LukS-PV mut9 and LukF-PV mut1 in combination with alpha toxin

vaccine AT-62 was tested in BALB/c mice. Groups of 10 mice were immunized three times IM with 10µg of each vaccine or BSA (as control) individually or in double or triple combinations at two weeks intervals with AIPO₄ in a 1:8 ratio. For the bacteremia/sepsis model, mice were challenged IP on day 42 with 1xLD₉₀ of USA300 (5x10⁴ CFU) in 3% mucin and monitored for 7 days. As shown in **Figure 12A**, the S and F mutants provided 60% and 40% protection, respectively, and the combination of the two mutant subunits increased protection to 80%, which was similar to AT-62 alone. Full protection was observed when the three antigens were combined together. A similar study was performed in a pneumonia model with a high challenge dose (2x10⁸ CFU) of USA300. While none of the individual components provided significant protection, a combination of the two leukocidins with AT-62 led to 50% protection (P=0.0021) (**Figure 12B**).

Example 9: Cross-reactive and cross-neutralizing antibody generated by LukS-PV mut9 *in vivo*

[0181] An immunogenicity assay was carried out by immunizing the LukS-PV mutant 9 (LukS-PV T28F/K97A/S209A) in a group of 4 mice. Serum samples were collected after the fourth immunization and the antibody titer against wild-type LukS-PV (**Figure 13A**), HlgC (**Figure 13B**) and HlgB (**Figure 13C**) were determined. These results clearly show the presence of cross reactive antibodies for both HlgB and C induced by immunization with LukS-PV mut9. Based on HL-60 cell based neutralization assay, polyclonal anti-LukS-PV mut9 antibody was shown to neutralize both PVL (wild-type LukS-PV + LukF-PV) and Gamma hemolysin (wild type HlgB + HlgC) leukotoxins (**Figure 13D**). These experiments further confirmed the induction of cross protective anti-leukotoxin antibodies by immunization with LukS-PV mut9 and supporting the broad spectrum application of this mutant vaccine.

Example 10: Leukocidin oligomerization and inhibition of oligomerization by antibodies to LukS-PV

[0182] Oligomerization of the leukocidin components is a required step for cytotoxicity of these toxins. In studies described herein, it was explored whether (i) mutations in LukS-PV or LukF-PV interfere with homologous and/or heterologous oligomerization of the leukocidin components, and (ii) whether antibodies to LukS inhibit homologous and/or heterologous oligomerization. An oligomerization assay for Leukocidin components (PVL and gamma hemolysins) was performed using a 2-methyl-2,4-pentenediol (MPD) based assay as described in Yamashita et al., Proc Natl Acad Sci U S A, 2011. 108(42): p. 17314-9. Briefly, equal amounts of both components were incubated together in the presence of 40% MPD for 24 hours at room temperature. Samples were run in a SDS PAGE without boiling and gels were stained with Gel Code Blue™ reagent. For the inhibition of PVL oligomerization, LukS-PV was pre-incubated with rabbit anti-LukS-PV polyclonal antibodies (pAbs) at decreasing concentration for 30 minutes. An equal amount of LukF-PV was added to the mix and

incubated at room temperature in the presence of 40% MPD for 24 hours. Samples were analyzed in a SDS PAGE without boiling and gels were stained with Gel Code Blue™ reagent.

[0183] As shown in **Figure 14A (Lane 2)**, wild-type (wt) forms of LukS-PV and LukF-PV formed an oligomeric band of >160 kd. A similar oligomeric band was seen with LukF-PV mutant 1 in combination with wild-type LukS-PV (**Figure 14A, Lane 3**). Cross oligomerization between wild-type LukS-PV and gamma hemolysin component B was shown (**Figure 14A, Lane 4**). However, LukS-PV mutant 9 did not oligomerize with either wild-type LukF-PV or with LukF-PV mutant 1 (**Figure 14A, Lanes 5 and 6**), which is consistent with the attenuated toxicity observed for LukS-PV mutant 9. This mutant also did not oligomerize with wild-type gamma hemolysin B subunit (**Figure 14A, Lane 7**), further confirming its safety to use as a vaccine candidate. **Figure 14B**, shows the inhibition of oligomerization of wild-type LukS-PV/LukF-PV with rabbit polyclonal anti-LukS antibody in a dose dependent manner. **Figure 14C**, showed that rabbit polyclonal anti-LukS antibody was also able to cross inhibit the heterologous oligomerization of LukS-PV + hlgB.

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Met	Gln	Gly	Phe	Ile	Xaa	Ser	Xaa	Thr	Xaa	Xaa	Xaa	Xaa	Xaa	Lys	Xaa
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Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Lys	Xaa	Xaa	Xaa	Trp	Pro
	50					55					60

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<212> PRT

<213> Artificial Sequence

<220>

<223> wild-type LukS-PV amino acid consensus sequence B

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<222> (6)..(6)

<223> X can be Gly, Ser, or Ala

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<222> (8)..(8)
<223> X can be Lys, Thr, Ser, or Met

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<223> X can be Thr or Ser

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<223> X can be Asn or Lys

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<222> (12)..(12)
<223> X can be Pro, Lys, Ser, or Gln

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<222> (13)..(13)
<223> X can be Asn or Tyr

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<222> (14)..(14)
<223> X can be Val, Thr, or Ile

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<222> (15)..(15)
<223> X can be Asp, Ser, or Phe

<220>
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<223> X can be Ser or may be missing

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<222> (20)..(20)
<223> X can be Ile or may be missing

<220>
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<222> (21)..(21)

<223> X can be Tyr, His, or Thr

<220>

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<222> (25)..(25)

<223> X can be Asn or Thr

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<222> (28)..(28)

<223> X can be Asp or Glu

<220>

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<222> (29)..(29)

<223> X can be Ser or Thr

<220>

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<222> (30)..(30)

<223> X can be Val, Thr, Ala, or Ile

<220>

<221> misc_feature

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<223> X can be Asn or Asp

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<222> (33)..(33)

<223> X can be Ser or Gly

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<222> (35)..(35)

<223> X can be Thr or Lys

<220>

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<222> (40)..(40)

<223> X can be Ile or Val

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<223> X can be Gly or may be missing

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<221> misc_feature

<222> (43)..(43)

<223> X can be Asn, Lys, or may be missing

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<221> misc_feature

<222> (44)..(44)

<223> X can be Phe or may be missing

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<221> misc_feature

<222> (45)..(45)

<223> X can be Asn, Gln, or may be missing

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<221> misc_feature

<222> (46)..(46)

<223> X can be Ser, Thr, or may be missing

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<222> (47)..(47)

<223> X can be Gly, Ala, Val, or may be missing

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<223> X can be Pro or may be missing

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<221> misc_feature

<222> (49)..(49)

<223> X can be Ser, Leu, or may be missing

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<221> misc_feature

<222> (50)..(50)

<223> X can be Thr, Leu, Ile, or may be missing

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<221> misc_feature

<222> (51)..(51)

<223> X can be Gly, Ala, or may be missing

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<221> misc_feature

<222> (53)..(53)

<223> X can be Asn, Ser, or Lys

<220>

<221> misc_feature

<222> (55)..(55)

<223> X can be Ser, Ala, or Glu

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<222> (57)..(57)

<223> X can be Asn or Ser

<400> 2

Phe Gln Tyr Asn Ile Xaa Leu Xaa Xaa Xaa Asp Xaa Xaa Xaa Xaa Leu
1 5 10 15

Ile Asn Xaa Xaa Xaa Leu Pro Lys Xaa Lys Ile Xaa Xaa Xaa Xaa Val
20 25 30

Xaa Gln Xaa Leu Gly Tyr Asn Xaa Gly Xaa Xaa Xaa Xaa Xaa Xaa Xaa
35 40 45

Xaa Xaa Xaa Gly Xaa Gly Xaa Phe Xaa Tyr Ser Lys
50 55 60

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<211> 60

<212> PRT

<213> Artificial Sequence

<220>

<223> wild-type LukS-PV amino acid consensus sequence C

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<222> (2)..(2)

<223> X can be Val or Ala

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<222> (3)..(3)

<223> X can be Pro or Asp

<220>

<221> misc_feature

<222> (4)..(4)

<223> X can be Asp or Asn

<220>

<221> misc_feature
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<223> X can be Asn, Ser, or Asp

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<222> (6)..(6)
<223> X can be Glu or Gln

<220>
<221> misc_feature
<222> (11)..(11)
<223> X can be Val or Ile

<220>
<221> misc_feature
<222> (12)..(12)
<223> X can be His, Gln, or Thr

<220>
<221> misc_feature
<222> (21)..(21)
<223> X can be Ala or Thr

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<223> X can be Val or Leu

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<222> (27)..(27)
<223> X can be Lys or Arg

<220>
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<222> (28)..(28)
<223> X can be Gly or Asp

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<222> (29)..(29)
<223> X can be Ser, Lys, or Thr

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<222> (30)..(30)

<223> X can be Gly, Ser, or Lys

<220>

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<222> (31)..(31)

<223> X can be Asp, Glu, or Leu

<220>

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<222> (32)..(32)

<223> X can be Thr, Lys, or Ile

<220>

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<223> X can be Arg or may be missing

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<222> (34)..(34)

<223> X can be Ser or Val

<220>

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<222> (35)..(35)

<223> X can be Glu, Asp, or Asn

<220>

<221> misc_feature

<222> (36)..(36)

<223> X can be Phe or Leu

<220>

<221> misc_feature

<222> (37)..(37)

<223> X can be Glu or Lys

<220>

<221> misc_feature

<222> (38)..(38)

<223> X can be Ile or Phe

<220>

<221> misc_feature

<222> (39)..(39)

<223> X can be Thr, Ser, or Ala

<220>

<221> misc_feature

<222> (44)..(44)

<223> X can be Met or Leu

<220>

<221> misc_feature

<222> (46)..(46)

<223> X can be Val, Ala, Ile, or Thr

<220>

<221> misc_feature

<222> (48)..(48)

<223> X can be His or Tyr

<220>

<221> misc_feature

<222> (50)..(50)

<223> X can be Thr, Ile, or Tyr

<220>

<221> misc_feature

<222> (51)..(51)

<223> X can be Arg, Lys, Val, Leu, or Phe

<220>

<221> misc_feature

<222> (52)..(52)

<223> X can be Arg, Thr, Phe, or Leu

<220>

<221> misc_feature

<222> (53)..(53)

<223> X can be Thr, Ser, Arg, or Pro

<220>

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<222> (54)..(54)

<223> X can be Thr, His, Arg, Lys, or Pro

<220>

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<222> (55)..(55)

<223> X can be His, Arg, Thr, Leu, or Gln

<220>

<221> misc_feature

<222> (56)..(56)

<223> X can be Tyr or may be missing

<220>

<221> misc_feature

<222> (57)..(57)

<223> X can be Gly or may be missing

<220>

<221> misc_feature

<222> (58)..(58)

<223> X can be Asn or may be missing

<220>

<221> misc_feature

<222> (59)..(59)

<223> X can be Ser or may be missing

<220>

<221> misc_feature

<222> (60)..(60)

<223> X can be Tyr or Gly

<400> 3

Phe	Xaa	Xaa	Xaa	Xaa	Xaa	Leu	Pro	Pro	Leu	Xaa	Xaa	Ser	Gly	Phe	Asn
1				5					10					15	

Pro	Ser	Phe	Ile	Xaa	Thr	Xaa	Ser	His	Glu	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa
		20					25					30			

Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Tyr	Gly	Arg	Asn	Xaa	Asp	Xaa	Thr	Xaa
		35					40					45			

Ala	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa
	50					55					60

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<212> PRT

<213> Artificial Sequence

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<223> wild-type LukF-PV amino acid consensus sequence

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<222> (2)..(2)

<223> X can be Val, Ile, or Ala

<220>

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<222> (4)..(4)
<223> X can be Asp or His

<220>
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<222> (18)..(18)
<223> X can be Asn or Gln

<220>
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<222> (20)..(20)
<223> X can be Leu or Val

<220>
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<222> (23)..(23)
<223> X can be Ser or Thr

<220>
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<222> (24)..(24)
<223> X can be Phe or Tyr

<220>
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<222> (29)..(29)
<223> X can be Ser or Asn

<220>
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<223> X can be Ser, Ile, Asn, or Thr

<220>
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<223> X can be Lys or Asn

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<222> (35)..(35)
<223> X can be Ser or Thr

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<223> X can be Leu or Gly

<220>

<221> misc_feature

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<223> X can be Ser or Asn

<220>

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<222> (42)..(42)

<223> X can be Glu, Thr, or Lys

<220>

<221> misc_feature

<222> (43)..(43)

<223> X can be Ser or Ala

<220>

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<222> (57)..(57)

<223> X can be Thr or may be missing

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<222> (58)..(58)

<223> X can be Thr or Ser

<220>

<221> misc_feature

<222> (59)..(59)

<223> X can be Ile or Leu

<220>

<221> misc_feature

<222> (60)..(60)

<223> X can be Asp or Ser

<400> 4

Asn	Xaa	Val	Xaa	Tyr	Ala	Pro	Lys	Asn	Gln	Asn	Glu	Glu	Phe	Gln	Val
1				5					10					15	

Gln	Xaa	Thr	Xaa	Gly	Tyr	Xaa	Xaa	Gly	Gly	Asp	Ile	Xaa	Ile	Xaa	Xaa
		20						25					30		

Gly	Leu	Xaa	Gly	Gly	Xaa	Asn	Gly	Xaa	Xaa	Xaa	Phe	Ser	Glu	Thr	Ile
		35					40					45			

Asn	Tyr	Lys	Gln	Glu	Ser	Tyr	Arg	Xaa	Xaa	Xaa	Xaa
	50					55					60

$\langle 210 \rangle$ 5

$\langle 211 \rangle$ 312

<212> PRT

<213> Artificial Sequence

$\langle 220 \rangle$

<223> wild-type LukS-PV amino acid sequence (with signal peptide)

$\langle 400 \rangle$ 5

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

Thr Pro Ile Ala Thr Ser Phe His Glu Ser Lys Ala Asp Asn Asn Ile
20 25 30

Glu Asn Ile Gly Asp Gly Ala Glu Val Val Lys Arg Thr Glu Asp Thr
35 40 45

Ser Ser Asp Lys Trp Gly Val Thr Gln Asn Ile Gln Phe Asp Phe Val
50 55 60

Lys Asp Lys Lys Tyr Asn Lys Asp Ala Leu Ile Leu Lys Met Gln Gly
65 70 75 80

Phe Ile Asn Ser Lys Thr Thr Tyr Tyr Asn Tyr Lys Asn Thr Asp His
85 90 95

Ile Lys Ala Met Arg Trp Pro Phe Gln Tyr Asn Ile Gly Leu Lys Thr
100 105 110

Asn Asp Pro Asn Val Asp Leu Ile Asn Tyr Leu Pro Lys Asn Lys Ile
115 120 125

Asp Ser Val Asn Val Ser Gln Thr Leu Gly Tyr Asn Ile Gly Gly Asn
130 135 140

Phe Asn Ser Gly Pro Ser Thr Gly Gly Asn Gly Ser Phe Asn Tyr Ser
145 150 155 160

Lys Thr Ile Ser Tyr Asn Gln Gln Asn Tyr Ile Ser Glu Val Glu His
165 170 175

Gln Asn Ser Lys Ser Val Gln Trp Gly Ile Lys Ala Asn Ser Phe Ile
180 185 190

Thr Ser Leu Gly Lys Met Ser Gly His Asp Pro Asn Leu Phe Val Gly
195 200 205

Tyr Lys Pro Tyr Ser Gln Asn Pro Arg Asp Tyr Phe Val Pro Asp Asn
210 215 220

Glu Leu Pro Pro Leu Val His Ser Gly Phe Asn Pro Ser Phe Ile Ala
225 230 235 240

[illegible]

Thr Val Ser His Glu Lys Gly Ser Gly Asp Thr Ser Glu Phe Glu Ile
245 250 255

Thr Tyr Gly Arg Asn Met Asp Val Thr His Ala Thr Arg Arg Thr Thr
260 265 270

His Tyr Gly Asn Ser Tyr Leu Glu Gly Ser Arg Ile His Asn Ala Phe
275 280 285

Val Asn Arg Asn Tyr Thr Val Lys Tyr Glu Val Asn Trp Lys Thr His
290 295 300

Glu Ile Lys Val Lys Gly His Asn
305 310

<210> 6

<211> 284

<212> PRT

<213> Artificial Sequence

<220>

<223> wild-type LukS-PV amino acid sequence (without signal peptide)

<400> 6

Asp Asn Asn Ile Glu Asn Ile Gly Asp Gly Ala Glu Val Val Lys Arg
1 5 10 15

Thr Glu Asp Thr Ser Ser Asp Lys Trp Gly Val Thr Gln Asn Ile Gln
20 25 30

Phe Asp Phe Val Lys Asp Lys Lys Tyr Asn Lys Asp Ala Leu Ile Leu
35 40 45

Lys Met Gln Gly Phe Ile Asn Ser Lys Thr Thr Tyr Tyr Asn Tyr Lys
50 55 60

Asn Thr Asp His Ile Lys Ala Met Arg Trp Pro Phe Gln Tyr Asn Ile
65 70 75 80

Gly Leu Lys Thr Asn Asp Pro Asn Val Asp Leu Ile Asn Tyr Leu Pro
85 90 95

Lys Asn Lys Ile Asp Ser Val Asn Val Ser Gln Thr Leu Gly Tyr Asn
100 105 110

Ile Gly Gly Asn Phe Asn Ser Gly Pro Ser Thr Gly Gly Asn Gly Ser
115 120 125

Phe Asn Tyr Ser Lys Thr Ile Ser Tyr Asn Gln Gln Asn Tyr Ile Ser
130 135 140

Glu Val Glu His Gln Asn Ser Lys Ser Val Gln Trp Gly Ile Lys Ala
145 150 155 160

Asn Ser Phe Ile Thr Ser Leu Gly Lys Met Ser Gly His Asp Pro Asn

165 170 175
 Leu Phe Val Gly Tyr Lys Pro Tyr Ser Gln Asn Pro Arg Asp Tyr Phe
 180 185 190
 Val Pro Asp Asn Glu Leu Pro Pro Leu Val His Ser Gly Phe Asn Pro
 195 200 205
 Ser Phe Ile Ala Thr Val Ser His Glu Lys Gly Ser Gly Asp Thr Ser
 210 215 220
 Glu Phe Glu Ile Thr Tyr Gly Arg Asn Met Asp Val Thr His Ala Thr
 225 230 235 240
 Arg Arg Thr Thr His Tyr Gly Asn Ser Tyr Leu Glu Gly Ser Arg Ile
 245 250 255
 His Asn Ala Phe Val Asn Arg Asn Tyr Thr Val Lys Tyr Glu Val Asn
 260 265 270
 Trp Lys Thr His Glu Ile Lys Val Lys Gly His Asn
 275 280
 <210> 7
 <211> 284
 <212> PRT
 <213> Artificial Sequence
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 <223> mutant LukS-PV amino acid sequence-Lys97Ala (K97A)
 <400> 7
 Asp Asn Asn Ile Glu Asn Ile Gly Asp Gly Ala Glu Val Val Lys Arg
 1 5 10 15
 Thr Glu Asp Thr Ser Ser Asp Lys Trp Gly Val Thr Gln Asn Ile Gln
 20 25 30
 Phe Asp Phe Val Lys Asp Lys Lys Tyr Asn Lys Asp Ala Leu Ile Leu
 35 40 45
 Lys Met Gln Gly Phe Ile Asn Ser Lys Thr Thr Tyr Tyr Asn Tyr Lys
 50 55 60
 Asn Thr Asp His Ile Lys Ala Met Arg Trp Pro Phe Gln Tyr Asn Ile
 65 70 75 80
 Gly Leu Lys Thr Asn Asp Pro Asn Val Asp Leu Ile Asn Tyr Leu Pro
 85 90 95
 Ala Asn Lys Ile Asp Ser Val Asn Val Ser Gln Thr Leu Gly Tyr Asn
 100 105 110
 Ile Gly Gly Asn Phe Asn Ser Gly Pro Ser Thr Gly Gly Asn Gly Ser
 115 120 125

Phe Asn Tyr Ser Lys Thr Ile Ser Tyr Asn Gln Gln Asn Tyr Ile Ser
130 135 140

Glu Val Glu His Gln Asn Ser Lys Ser Val Gln Trp Gly Ile Lys Ala
145 150 155 160

Asn Ser Phe Ile Thr Ser Leu Gly Lys Met Ser Gly His Asp Pro Asn
165 170 175

Leu Phe Val Gly Tyr Lys Pro Tyr Ser Gln Asn Pro Arg Asp Tyr Phe
180 185 190

Val Pro Asp Asn Glu Leu Pro Pro Leu Val His Ser Gly Phe Asn Pro
195 200 205

Ser Phe Ile Ala Thr Val Ser His Glu Lys Gly Ser Gly Asp Thr Ser
210 215 220

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

Arg Arg Thr Thr His Tyr Gly Asn Ser Tyr Leu Glu Gly Ser Arg Ile
245 250 255

His Asn Ala Phe Val Asn Arg Asn Tyr Thr Val Lys Tyr Glu Val Asn
260 265 270

Trp Lys Thr His Glu Ile Lys Val Lys Gly His Asn
275 280

<210> 8

<211> 284

<212> PRT

<213> Artificial Sequence

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<223> mutant LukS-PV amino acid sequence-Asp101Ala (D101A)

<400> 8

Asp Asn Asn Ile Glu Asn Ile Gly Asp Gly Ala Glu Val Val Lys Arg
1 5 10 15

Thr Glu Asp Thr Ser Ser Asp Lys Trp Gly Val Thr Gln Asn Ile Gln
20 25 30

Phe Asp Phe Val Lys Asp Lys Lys Tyr Asn Lys Asp Ala Leu Ile Leu
35 40 45

Lys Met Gln Gly Phe Ile Asn Ser Lys Thr Thr Tyr Tyr Asn Tyr Lys
50 55 60

Asn Thr Asp His Ile Lys Ala Met Arg Trp Pro Phe Gln Tyr Asn Ile

65					70					75					80
Gly	Leu	Lys	Thr	Asn	Asp	Pro	Asn	Val	Asp	Leu	Ile	Asn	Tyr	Leu	Pro
				85					90					95	
Lys	Asn	Lys	Ile	Ala	Ser	Val	Asn	Val	Ser	Gln	Thr	Leu	Gly	Tyr	Asn
			100					105					110		
Ile	Gly	Gly	Asn	Phe	Asn	Ser	Gly	Pro	Ser	Thr	Gly	Gly	Asn	Gly	Ser
		115					120					125			
Phe	Asn	Tyr	Ser	Lys	Thr	Ile	Ser	Tyr	Asn	Gln	Gln	Asn	Tyr	Ile	Ser
	130					135					140				
Glu	Val	Glu	His	Gln	Asn	Ser	Lys	Ser	Val	Gln	Trp	Gly	Ile	Lys	Ala
145					150					155					160
Asn	Ser	Phe	Ile	Thr	Ser	Leu	Gly	Lys	Met	Ser	Gly	His	Asp	Pro	Asn
				165					170					175	
Leu	Phe	Val	Gly	Tyr	Lys	Pro	Tyr	Ser	Gln	Asn	Pro	Arg	Asp	Tyr	Phe
			180					185					190		
Val	Pro	Asp	Asn	Glu	Leu	Pro	Pro	Leu	Val	His	Ser	Gly	Phe	Asn	Pro
		195					200					205			
Ser	Phe	Ile	Ala	Thr	Val	Ser	His	Glu	Lys	Gly	Ser	Gly	Asp	Thr	Ser
	210					215					220				
Glu	Phe	Glu	Ile	Thr	Tyr	Gly	Arg	Asn	Met	Asp	Val	Thr	His	Ala	Thr
225					230					235					240
Arg	Arg	Thr	Thr	His	Tyr	Gly	Asn	Ser	Tyr	Leu	Glu	Gly	Ser	Arg	Ile
				245					250					255	
His	Asn	Ala	Phe	Val	Asn	Arg	Asn	Tyr	Thr	Val	Lys	Tyr	Glu	Val	Asn
			260					265					270		
Trp	Lys	Thr	His	Glu	Ile	Lys	Val	Lys	Gly	His	Asn				
		275					280								
<210>	9														
<211>	284														
<212>	PRT														
<213>	Artificial Sequence														
<220>															
<223>	mutant LukS-PV amino acid sequence-Tyr131Ala (Y131A)														
<400>	9														
Asp	Asn	Asn	Ile	Glu	Asn	Ile	Gly	Asp	Gly	Ala	Glu	Val	Val	Lys	Arg
1				5					10					15	
Thr	Glu	Asp	Thr	Ser	Ser	Asp	Lys	Trp	Gly	Val	Thr	Gln	Asn	Ile	Gln
			20					25					30		

Phe Asp Phe Val Lys Asp Lys Lys Tyr Asn Lys Asp Ala Leu Ile Leu
 35 40 45
 Lys Met Gln Gly Phe Ile Asn Ser Lys Thr Thr Tyr Tyr Asn Tyr Lys
 50 55 60
 Asn Thr Asp His Ile Lys Ala Met Arg Trp Pro Phe Gln Tyr Asn Ile
 65 70 75 80
 Gly Leu Lys Thr Asn Asp Pro Asn Val Asp Leu Ile Asn Tyr Leu Pro
 85 90 95
 Lys Asn Lys Ile Asp Ser Val Asn Val Ser Gln Thr Leu Gly Tyr Asn
 100 105 110
 Ile Gly Gly Asn Phe Asn Ser Gly Pro Ser Thr Gly Gly Asn Gly Ser
 115 120 125
 Phe Asn Ala Ser Lys Thr Ile Ser Tyr Asn Gln Gln Asn Tyr Ile Ser
 130 135 140
 Glu Val Glu His Gln Asn Ser Lys Ser Val Gln Trp Gly Ile Lys Ala
 145 150 155 160
 Asn Ser Phe Ile Thr Ser Leu Gly Lys Met Ser Gly His Asp Pro Asn
 165 170 175
 Leu Phe Val Gly Tyr Lys Pro Tyr Ser Gln Asn Pro Arg Asp Tyr Phe
 180 185 190
 Val Pro Asp Asn Glu Leu Pro Pro Leu Val His Ser Gly Phe Asn Pro
 195 200 205
 Ser Phe Ile Ala Thr Val Ser His Glu Lys Gly Ser Gly Asp Thr Ser
 210 215 220
 Glu Phe Glu Ile Thr Tyr Gly Arg Asn Met Asp Val Thr His Ala Thr
 225 230 235 240
 Arg Arg Thr Thr His Tyr Gly Asn Ser Tyr Leu Glu Gly Ser Arg Ile
 245 250 255
 His Asn Ala Phe Val Asn Arg Asn Tyr Thr Val Lys Tyr Glu Val Asn
 260 265 270
 Trp Lys Thr His Glu Ile Lys Val Lys Gly His Asn
 275 280

<210> 10

<211> 284

<212> PRT

<213> Artificial Sequence

<220>

<223> mutant LukS-PV amino acid sequence-Ser209Ala (S209A)

<400> 10

Asp Asn Asn Ile Glu Asn Ile Gly Asp Gly Ala Glu Val Val Lys Arg
 1 5 10 15

Thr Glu Asp Thr Ser Ser Asp Lys Trp Gly Val Thr Gln Asn Ile Gln
 20 25 30

Phe Asp Phe Val Lys Asp Lys Lys Tyr Asn Lys Asp Ala Leu Ile Leu
 35 40 45

Lys Met Gln Gly Phe Ile Asn Ser Lys Thr Thr Tyr Tyr Asn Tyr Lys
 50 55 60

Asn Thr Asp His Ile Lys Ala Met Arg Trp Pro Phe Gln Tyr Asn Ile
 65 70 75 80

Gly Leu Lys Thr Asn Asp Pro Asn Val Asp Leu Ile Asn Tyr Leu Pro
 85 90 95

Lys Asn Lys Ile Asp Ser Val Asn Val Ser Gln Thr Leu Gly Tyr Asn
 100 105 110

Ile Gly Gly Asn Phe Asn Ser Gly Pro Ser Thr Gly Gly Asn Gly Ser
 115 120 125

Phe Asn Tyr Ser Lys Thr Ile Ser Tyr Asn Gln Gln Asn Tyr Ile Ser
 130 135 140

Glu Val Glu His Gln Asn Ser Lys Ser Val Gln Trp Gly Ile Lys Ala
 145 150 155 160

Asn Ser Phe Ile Thr Ser Leu Gly Lys Met Ser Gly His Asp Pro Asn
 165 170 175

Leu Phe Val Gly Tyr Lys Pro Tyr Ser Gln Asn Pro Arg Asp Tyr Phe
 180 185 190

Val Pro Asp Asn Glu Leu Pro Pro Leu Val His Ser Gly Phe Asn Pro
 195 200 205

Ala Phe Ile Ala Thr Val Ser His Glu Lys Gly Ser Gly Asp Thr Ser
 210 215 220

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

Arg Arg Thr Thr His Tyr Gly Asn Ser Tyr Leu Glu Gly Ser Arg Ile
 245 250 255

His Asn Ala Phe Val Asn Arg Asn Tyr Thr Val Lys Tyr Glu Val Asn
 260 265 270

Trp Lys Thr His Glu Ile Lys Val Lys Gly His Asn
 275 280

<210> 11

<211> 284

<212> PRT

<213> Artificial Sequence

<220>

<223> mutant LukS-PV amino acid sequence-Thr28Phe (T28F)

<400> 11

Asp	Asn	Asn	Ile	Glu	Asn	Ile	Gly	Asp	Gly	Ala	Glu	Val	Val	Lys	Arg
1				5					10					15	

Thr	Glu	Asp	Thr	Ser	Ser	Asp	Lys	Trp	Gly	Val	Phe	Gln	Asn	Ile	Gln
		20						25					30		

Phe	Asp	Phe	Val	Lys	Asp	Lys	Lys	Tyr	Asn	Lys	Asp	Ala	Leu	Ile	Leu
	35					40					45				

Lys	Met	Gln	Gly	Phe	Ile	Asn	Ser	Lys	Thr	Thr	Tyr	Tyr	Asn	Tyr	Lys
	50					55					60				

Asn	Thr	Asp	His	Ile	Lys	Ala	Met	Arg	Trp	Pro	Phe	Gln	Tyr	Asn	Ile
65					70					75					80

Gly	Leu	Lys	Thr	Asn	Asp	Pro	Asn	Val	Asp	Leu	Ile	Asn	Tyr	Leu	Pro
				85					90					95	

Lys	Asn	Lys	Ile	Asp	Ser	Val	Asn	Val	Ser	Gln	Thr	Leu	Gly	Tyr	Asn
			100					105					110		

Ile	Gly	Gly	Asn	Phe	Asn	Ser	Gly	Pro	Ser	Thr	Gly	Gly	Asn	Gly	Ser
		115					120					125			

Phe	Asn	Tyr	Ser	Lys	Thr	Ile	Ser	Tyr	Asn	Gln	Gln	Asn	Tyr	Ile	Ser
	130					135					140				

Glu	Val	Glu	His	Gln	Asn	Ser	Lys	Ser	Val	Gln	Trp	Gly	Ile	Lys	Ala
145					150					155					160

Asn	Ser	Phe	Ile	Thr	Ser	Leu	Gly	Lys	Met	Ser	Gly	His	Asp	Pro	Asn
			165						170					175	

Leu	Phe	Val	Gly	Tyr	Lys	Pro	Tyr	Ser	Gln	Asn	Pro	Arg	Asp	Tyr	Phe
		180						185					190		

Val	Pro	Asp	Asn	Glu	Leu	Pro	Pro	Leu	Val	His	Ser	Gly	Phe	Asn	Pro
		195					200					205			

Ser	Phe	Ile	Ala	Thr	Val	Ser	His	Glu	Lys	Gly	Ser	Gly	Asp	Thr	Ser
	210					215					220				

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

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Arg Arg Thr Thr His Tyr Gly Asn Ser Tyr Leu Glu Gly Ser Arg Ile
245 250 255

His Asn Ala Phe Val Asn Arg Asn Tyr Thr Val Lys Tyr Glu Val Asn
260 265 270

Trp Lys Thr His Glu Ile Lys Val Lys Gly His Asn
275 280

<210> 12

<211> 284

<212> PRT

<213> Artificial Sequence

<220>

<223> LukS-PV amino acid sequence-Thr28Phe/Tyr131Ala (T28F/Y131A)

<400> 12

Asp Asn Asn Ile Glu Asn Ile Gly Asp Gly Ala Glu Val Val Lys Arg
1 5 10 15

Thr Glu Asp Thr Ser Ser Asp Lys Trp Gly Val Phe Gln Asn Ile Gln
20 25 30

Phe Asp Phe Val Lys Asp Lys Lys Tyr Asn Lys Asp Ala Leu Ile Leu
35 40 45

Lys Met Gln Gly Phe Ile Asn Ser Lys Thr Thr Tyr Tyr Asn Tyr Lys
50 55 60

Asn Thr Asp His Ile Lys Ala Met Arg Trp Pro Phe Gln Tyr Asn Ile
65 70 75 80

Gly Leu Lys Thr Asn Asp Pro Asn Val Asp Leu Ile Asn Tyr Leu Pro
85 90 95

Lys Asn Lys Ile Asp Ser Val Asn Val Ser Gln Thr Leu Gly Tyr Asn
100 105 110

Ile Gly Gly Asn Phe Asn Ser Gly Pro Ser Thr Gly Gly Asn Gly Ser
115 120 125

Phe Asn Ala Ser Lys Thr Ile Ser Tyr Asn Gln Gln Asn Tyr Ile Ser
130 135 140

Glu Val Glu His Gln Asn Ser Lys Ser Val Gln Trp Gly Ile Lys Ala
145 150 155 160

Asn Ser Phe Ile Thr Ser Leu Gly Lys Met Ser Gly His Asp Pro Asn
165 170 175

Leu Phe Val Gly Tyr Lys Pro Tyr Ser Gln Asn Pro Arg Asp Tyr Phe
180 185 190

Val Pro Asp Asn Glu Leu Pro Pro Leu Val His Ser Gly Phe Asn Pro
195 200 205

Ser Phe Ile Ala Thr Val Ser His Glu Lys Gly Ser Gly Asp Thr Ser
210 215 220

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

Arg Arg Thr Thr His Tyr Gly Asn Ser Tyr Leu Glu Gly Ser Arg Ile
245 250 255

His Asn Ala Phe Val Asn Arg Asn Tyr Thr Val Lys Tyr Glu Val Asn
260 265 270

Trp Lys Thr His Glu Ile Lys Val Lys Gly His Asn
275 280

<210> 13

<211> 284

<212> PRT

<213> Artificial Sequence

<220>

<223> mutant LukS-PV amino acid sequence-Thr28Phe/Ser209Ala (T28F/S209A)

<400> 13

Asp Asn Asn Ile Glu Asn Ile Gly Asp Gly Ala Glu Val Val Lys Arg
1 5 10 15

Thr Glu Asp Thr Ser Ser Asp Lys Trp Gly Val Phe Gln Asn Ile Gln
20 25 30

Phe Asp Phe Val Lys Asp Lys Lys Tyr Asn Lys Asp Ala Leu Ile Leu
35 40 45

Lys Met Gln Gly Phe Ile Asn Ser Lys Thr Thr Tyr Tyr Asn Tyr Lys
50 55 60

Asn Thr Asp His Ile Lys Ala Met Arg Trp Pro Phe Gln Tyr Asn Ile
65 70 75 80

Gly Leu Lys Thr Asn Asp Pro Asn Val Asp Leu Ile Asn Tyr Leu Pro
85 90 95

Lys Asn Lys Ile Asp Ser Val Asn Val Ser Gln Thr Leu Gly Tyr Asn
100 105 110

Ile Gly Gly Asn Phe Asn Ser Gly Pro Ser Thr Gly Gly Asn Gly Ser
115 120 125

Phe Asn Tyr Ser Lys Thr Ile Ser Tyr Asn Gln Gln Asn Tyr Ile Ser
130 135 140

Glu Val Glu His Gln Asn Ser Lys Ser Val Gln Trp Gly Ile Lys Ala

145 150 155 160
 Asn Ser Phe Ile Thr Ser Leu Gly Lys Met Ser Gly His Asp Pro Asn
 165 170 175
 Leu Phe Val Gly Tyr Lys Pro Tyr Ser Gln Asn Pro Arg Asp Tyr Phe
 180 185 190
 Val Pro Asp Asn Glu Leu Pro Pro Leu Val His Ser Gly Phe Asn Pro
 195 200 205
 Ala Phe Ile Ala Thr Val Ser His Glu Lys Gly Ser Gly Asp Thr Ser
 210 215 220
 Glu Phe Glu Ile Thr Tyr Gly Arg Asn Met Asp Val Thr His Ala Thr
 225 230 235 240
 Arg Arg Thr Thr His Tyr Gly Asn Ser Tyr Leu Glu Gly Ser Arg Ile
 245 250 255
 His Asn Ala Phe Val Asn Arg Asn Tyr Thr Val Lys Tyr Glu Val Asn
 260 265 270
 Trp Lys Thr His Glu Ile Lys Val Lys Gly His Asn
 275 280
 <210> 14
 <211> 284
 <212> PRT
 <213> Artificial Sequence
 <220>
 <223> mutant LukS-PV amino acid sequence-Thr28Phe/Lys97Ala/Ser209Ala
 (T28F/K97A/S209A)
 <400> 14
 Asp Asn Asn Ile Glu Asn Ile Gly Asp Gly Ala Glu Val Val Lys Arg
 1 5 10 15
 Thr Glu Asp Thr Ser Ser Asp Lys Trp Gly Val Phe Gln Asn Ile Gln
 20 25 30
 Phe Asp Phe Val Lys Asp Lys Lys Tyr Asn Lys Asp Ala Leu Ile Leu
 35 40 45
 Lys Met Gln Gly Phe Ile Asn Ser Lys Thr Thr Tyr Tyr Asn Tyr Lys
 50 55 60
 Asn Thr Asp His Ile Lys Ala Met Arg Trp Pro Phe Gln Tyr Asn Ile
 65 70 75 80
 Gly Leu Lys Thr Asn Asp Pro Asn Val Asp Leu Ile Asn Tyr Leu Pro
 85 90 95
 Val Ser Thr Phe Ser Ser Val Ser Val Ser Glu Thr Tyr Glu Thr Ser

Ala Asn Lys Ile Asp Ser Val Asn Val Ser Gln Thr Leu Gly Tyr Asn
100 105 110

Ile Gly Gly Asn Phe Asn Ser Gly Pro Ser Thr Gly Gly Asn Gly Ser
115 120 125

Phe Asn Tyr Ser Lys Thr Ile Ser Tyr Asn Gln Gln Asn Tyr Ile Ser
130 135 140

Glu Val Glu His Gln Asn Ser Lys Ser Val Gln Trp Gly Ile Lys Ala
145 150 155 160

Asn Ser Phe Ile Thr Ser Leu Gly Lys Met Ser Gly His Asp Pro Asn
165 170 175

Leu Phe Val Gly Tyr Lys Pro Tyr Ser Gln Asn Pro Arg Asp Tyr Phe
180 185 190

Val Pro Asp Asn Glu Leu Pro Pro Leu Val His Ser Gly Phe Asn Pro
195 200 205

Ala Phe Ile Ala Thr Val Ser His Glu Lys Gly Ser Gly Asp Thr Ser
210 215 220

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

Arg Arg Thr Thr His Tyr Gly Asn Ser Tyr Leu Glu Gly Ser Arg Ile
245 250 255

His Asn Ala Phe Val Asn Arg Asn Tyr Thr Val Lys Tyr Glu Val Asn
260 265 270

Trp Lys Thr His Glu Ile Lys Val Lys Gly His Asn
275 280

<210> 15

<211> 311

<212> PRT

<213> Artificial Sequence

<220>

<223> wild-type LukS-PV amino acid sequence

<400> 15

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

Thr Pro Ile Ala Thr Ser Phe His Glu Ser Lys Ala Asp Asn Asn Ile
20 25 30

Glu Asn Ile Gly Asp Gly Ala Glu Val Val Lys Arg Thr Glu Asp Thr
35 40 45

Ser Ser Asp Lys Trp Gly Val Thr Gln Asn Ile Gln Phe Asp Phe Val

50	55	60
Lys Asp Lys Lys Tyr Asn Lys Asp Ala Leu Ile Leu Lys Met Gln Gly 65 70 75 80		
Phe Ile Asn Ser Lys Thr Thr Tyr Tyr Asn Tyr Lys Asn Thr Asp His 85 90 95		
Ile Lys Ala Met Arg Trp Pro Phe Gln Tyr Asn Ile Gly Leu Lys Thr 100 105 110		
Asn Asp Pro Asn Val Asp Leu Ile Asn Tyr Leu Pro Lys Asn Lys Ile 115 120 125		
Asp Ser Val Asn Val Ser Gln Thr Leu Gly Tyr Asn Ile Gly Gly Asn 130 135 140		
Phe Asn Ser Gly Pro Ser Thr Gly Gly Asn Gly Ser Phe Asn Tyr Ser 145 150 155 160		
Lys Thr Ile Ser Tyr Asn Gln Gln Asn Tyr Ile Ser Glu Val Glu Arg 165 170 175		
Gln Asn Ser Lys Ser Val Gln Trp Gly Ile Lys Ala Asn Ser Phe Ile 180 185 190		
Thr Ser Leu Gly Lys Met Ser Gly His Asp Pro Asn Leu Phe Val Gly 195 200 205		
Tyr Lys Pro Tyr Ser Gln Asn Pro Arg Asp Tyr Phe Val Pro Asp Asn 210 215 220		
Glu Leu Pro Pro Leu Val His Ser Gly Phe Asn Pro Ser Phe Ile Ala 225 230 235 240		
Val Ser His Glu Lys Gly Ser Gly Asp Thr Ser Glu Phe Glu Ile Thr 245 250 255		
Tyr Gly Arg Asn Met Asp Val Thr His Ala Thr Arg Arg Thr Thr His 260 265 270		
Tyr Gly Asn Ser Tyr Leu Glu Gly Ser Arg Ile His Asn Ala Phe Val 275 280 285		
Asn Arg Asn Tyr Thr Val Lys Tyr Glu Val Asn Trp Lys Thr His Glu 290 295 300		
Ile Lys Val Lys Gly His Asn 305 310		

<210> 16

<211> 325

<212> PRT

<213> Artificial Sequence

<220>

<223> wild-type LukF-PV amino acid sequence (with signal peptide)

<400> 16

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

Leu Leu Ser Asn Thr Val Asp Ala Ala Gln His Ile Thr Pro Val Ser
          20           25           30

Glu Lys Lys Val Asp Asp Lys Ile Thr Leu Tyr Lys Thr Thr Ala Thr
 35           40           45

Ser Asp Ser Asp Lys Leu Lys Ile Ser Gln Ile Leu Thr Phe Asn Phe
 50           55           60

Ile Lys Asp Lys Ser Tyr Asp Lys Asp Thr Leu Ile Leu Lys Ala Ala
 65           70           75           80

Gly Asn Ile Tyr Ser Gly Tyr Thr Lys Pro Asn Pro Lys Asp Thr Ile
          85           90           95

Ser Ser Gln Phe Tyr Trp Gly Ser Lys Tyr Asn Ile Ser Ile Asn Ser
          100          105          110

Asp Ser Asn Asp Ser Val Asn Val Val Asp Tyr Ala Pro Lys Asn Gln
          115          120          125

Asn Glu Glu Phe Gln Val Gln Gln Thr Val Gly Tyr Ser Tyr Gly Gly
          130          135          140

Asp Ile Asn Ile Ser Asn Gly Leu Ser Gly Gly Gly Asn Gly Ser Lys
          145          150          155          160

Ser Phe Ser Glu Thr Ile Asn Tyr Lys Gln Glu Ser Tyr Arg Thr Ser
          165          170          175

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

His Lys Ile Met Asn Asn Gly Trp Gly Pro Tyr Gly Arg Asp Ser Tyr
          195          200          205

His Ser Thr Tyr Gly Asn Glu Met Phe Leu Gly Ser Arg Gln Ser Asn
          210          215          220

Leu Asn Ala Gly Gln Asn Phe Leu Glu Tyr His Lys Met Pro Val Leu
          225          230          235          240

Ser Arg Gly Asn Phe Asn Pro Glu Phe Ile Gly Val Leu Ser Arg Lys
          245          250          255

Gln Asn Ala Ala Lys Lys Ser Lys Ile Thr Val Thr Tyr Gln Arg Glu
          260          265          270

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Met Asp Arg Tyr Thr Asn Phe Trp Asn Gln Leu His Trp Ile Gly Asn
 275 280 285

Asn Tyr Lys Asp Glu Asn Arg Ala Thr His Thr Ser Ile Tyr Glu Val
 290 295 300

Asp Trp Glu Asn His Thr Val Lys Leu Ile Asp Thr Gln Ser Lys Glu
 305 310 315 320

Lys Asn Pro Met Ser
 325

<210> 17

<211> 301

<212> PRT

<213> Artificial Sequence

<220>

<223> wild-type LukF-PV amino acid sequence (without signal peptide)

<400> 17

Ala Gln His Ile Thr Pro Val Ser Glu Lys Lys Val Asp Asp Lys Ile
 1 5 10 15

Thr Leu Tyr Lys Thr Thr Ala Thr Ser Asp Ser Asp Lys Leu Lys Ile
 20 25 30

Ser Gln Ile Leu Thr Phe Asn Phe Ile Lys Asp Lys Ser Tyr Asp Lys
 35 40 45

Asp Thr Leu Ile Leu Lys Ala Ala Gly Asn Ile Tyr Ser Gly Tyr Thr
 50 55 60

Lys Pro Asn Pro Lys Asp Thr Ile Ser Ser Gln Phe Tyr Trp Gly Ser
 65 70 75 80

Lys Tyr Asn Ile Ser Ile Asn Ser Asp Ser Asn Asp Ser Val Asn Val
 85 90 95

Val Asp Tyr Ala Pro Lys Asn Gln Asn Glu Glu Phe Gln Val Gln Gln
 100 105 110

Thr Val Gly Tyr Ser Tyr Gly Gly Asp Ile Asn Ile Ser Asn Gly Leu
 115 120 125

Ser Gly Gly Gly Asn Gly Ser Lys Ser Phe Ser Glu Thr Ile Asn Tyr
 130 135 140

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

Lys Ile Gly Trp Asp Val Glu Ala His Lys Ile Met Asn Asn Gly Trp
 165 170 175

Gly Pro Tyr Gly Arg Asp Ser Tyr His Ser Thr Tyr Gly Asn Glu Met
180 185 190

Phe Leu Gly Ser Arg Gln Ser Asn Leu Asn Ala Gly Gln Asn Phe Leu
195 200 205

Glu Tyr His Lys Met Pro Val Leu Ser Arg Gly Asn Phe Asn Pro Glu
210 215 220

Phe Ile Gly Val Leu Ser Arg Lys Gln Asn Ala Ala Lys Lys Ser Lys
225 230 235 240

Ile Thr Val Thr Tyr Gln Arg Glu Met Asp Arg Tyr Thr Asn Phe Trp
245 250 255

Asn Gln Leu His Trp Ile Gly Asn Asn Tyr Lys Asp Glu Asn Arg Ala
260 265 270

Thr His Thr Ser Ile Tyr Glu Val Asp Trp Glu Asn His Thr Val Lys
275 280 285

Leu Ile Asp Thr Gln Ser Lys Glu Lys Asn Pro Met Ser
290 295 300

<210> 18

<211> 301

<212> PRT

<213> Artificial Sequence

<220>

<223> mutant LukF-PV amino acid sequence-Lys102Ala (K102A)

<400> 18

Ala Gln His Ile Thr Pro Val Ser Glu Lys Lys Val Asp Asp Lys Ile
1 5 10 15

Thr Leu Tyr Lys Thr Thr Ala Thr Ser Asp Ser Asp Lys Leu Lys Ile
20 25 30

Ser Gln Ile Leu Thr Phe Asn Phe Ile Lys Asp Lys Ser Tyr Asp Lys
35 40 45

Asp Thr Leu Ile Leu Lys Ala Ala Gly Asn Ile Tyr Ser Gly Tyr Thr
50 55 60

Lys Pro Asn Pro Lys Asp Thr Ile Ser Ser Gln Phe Tyr Trp Gly Ser
65 70 75 80

Lys Tyr Asn Ile Ser Ile Asn Ser Asp Ser Asn Asp Ser Val Asn Val
85 90 95

Val Asp Tyr Ala Pro Ala Asn Gln Asn Glu Glu Phe Gln Val Gln Gln
100 105 110

Thr Val Gly Tyr Ser Tyr Gly Gly Asp Ile Asn Ile Ser Asn Gly Leu
115 120 125

Ser Gly Gly Gly Asn Gly Ser Lys Ser Phe Ser Glu Thr Ile Asn Tyr
130 135 140

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

Lys Ile Gly Trp Asp Val Glu Ala His Lys Ile Met Asn Asn Gly Trp
165 170 175

Gly Pro Tyr Gly Arg Asp Ser Tyr His Ser Thr Tyr Gly Asn Glu Met
180 185 190

Phe Leu Gly Ser Arg Gln Ser Asn Leu Asn Ala Gly Gln Asn Phe Leu
195 200 205

Glu Tyr His Lys Met Pro Val Leu Ser Arg Gly Asn Phe Asn Pro Glu
210 215 220

Phe Ile Gly Val Leu Ser Arg Lys Gln Asn Ala Ala Lys Lys Ser Lys
225 230 235 240

Ile Thr Val Thr Tyr Gln Arg Glu Met Asp Arg Tyr Thr Asn Phe Trp
245 250 255

Asn Gln Leu His Trp Ile Gly Asn Asn Tyr Lys Asp Glu Asn Arg Ala
260 265 270

Thr His Thr Ser Ile Tyr Glu Val Asp Trp Glu Asn His Thr Val Lys
275 280 285

Leu Ile Asp Thr Gln Ser Lys Glu Lys Asn Pro Met Ser
290 295 300

<210> 19

<211> 301

<212> PRT

<213> Artificial Sequence

<220>

<223> mutant LukF-PV amino acid sequence-Asp121Ala (D121A)

<400> 19

Ala Gln His Ile Thr Pro Val Ser Glu Lys Lys Val Asp Asp Lys Ile
1 5 10 15

Thr Leu Tyr Lys Thr Thr Ala Thr Ser Asp Ser Asp Lys Leu Lys Ile
20 25 30

Ser Gln Ile Leu Thr Phe Asn Phe Ile Lys Asp Lys Ser Tyr Asp Lys
35 40 45

Asp Thr Leu Ile Leu Lys Ala Ala Gly Asn Ile Tyr Ser Gly Tyr Thr

50 55 60
 Lys Pro Asn Pro Lys Asp Thr Ile Ser Ser Gln Phe Tyr Trp Gly Ser
 65 70 75 80
 Lys Tyr Asn Ile Ser Ile Asn Ser Asp Ser Asn Asp Ser Val Asn Val
 85 90 95
 Val Asp Tyr Ala Pro Lys Asn Gln Asn Glu Glu Phe Gln Val Gln Gln
 100 105 110
 Thr Val Gly Tyr Ser Tyr Gly Gly Ala Ile Asn Ile Ser Asn Gly Leu
 115 120 125
 Ser Gly Gly Gly Asn Gly Ser Lys Ser Phe Ser Glu Thr Ile Asn Tyr
 130 135 140
 Lys Gln Glu Ser Tyr Arg Thr Ser Leu Asp Lys Arg Thr Asn Phe Lys
 145 150 155 160
 Lys Ile Gly Trp Asp Val Glu Ala His Lys Ile Met Asn Asn Gly Trp
 165 170 175
 Gly Pro Tyr Gly Arg Asp Ser Tyr His Ser Thr Tyr Gly Asn Glu Met
 180 185 190
 Phe Leu Gly Ser Arg Gln Ser Asn Leu Asn Ala Gly Gln Asn Phe Leu
 195 200 205
 Glu Tyr His Lys Met Pro Val Leu Ser Arg Gly Asn Phe Asn Pro Glu
 210 215 220
 Phe Ile Gly Val Leu Ser Arg Lys Gln Asn Ala Ala Lys Lys Ser Lys
 225 230 235 240
 Ile Thr Val Thr Tyr Gln Arg Glu Met Asp Arg Tyr Thr Asn Phe Trp
 245 250 255
 Asn Gln Leu His Trp Ile Gly Asn Asn Tyr Lys Asp Glu Asn Arg Ala
 260 265 270
 Thr His Thr Ser Ile Tyr Glu Val Asp Trp Glu Asn His Thr Val Lys
 275 280 285
 Leu Ile Asp Thr Gln Ser Lys Glu Lys Asn Pro Met Ser
 290 295 300

<210> 20

<211> 301

<212> PRT

<213> Artificial Sequence

<220>

<223> mutant LukF-PV amino acid sequence-Glu147Ala (E147A)

<400> 20

Ala Gln His Ile Thr Pro Val Ser Glu Lys Lys Val Asp Asp Lys Ile
1 5 10 15

Thr Leu Tyr Lys Thr Thr Ala Thr Ser Asp Ser Asp Lys Leu Lys Ile
20 25 30

Ser Gln Ile Leu Thr Phe Asn Phe Ile Lys Asp Lys Ser Tyr Asp Lys
35 40 45

Asp Thr Leu Ile Leu Lys Ala Ala Gly Asn Ile Tyr Ser Gly Tyr Thr
50 55 60

Lys Pro Asn Pro Lys Asp Thr Ile Ser Ser Gln Phe Tyr Trp Gly Ser
65 70 75 80

Lys Tyr Asn Ile Ser Ile Asn Ser Asp Ser Asn Asp Ser Val Asn Val
85 90 95

Val Asp Tyr Ala Pro Lys Asn Gln Asn Glu Glu Phe Gln Val Gln Gln
100 105 110

Thr Val Gly Tyr Ser Tyr Gly Gly Asp Ile Asn Ile Ser Asn Gly Leu
115 120 125

Ser Gly Gly Gly Asn Gly Ser Lys Ser Phe Ser Glu Thr Ile Asn Tyr
130 135 140

Lys Gln Ala Ser Tyr Arg Thr Ser Leu Asp Lys Arg Thr Asn Phe Lys
145 150 155 160

Lys Ile Gly Trp Asp Val Glu Ala His Lys Ile Met Asn Asn Gly Trp
165 170 175

Gly Pro Tyr Gly Arg Asp Ser Tyr His Ser Thr Tyr Gly Asn Glu Met
180 185 190

Phe Leu Gly Ser Arg Gln Ser Asn Leu Asn Ala Gly Gln Asn Phe Leu
195 200 205

Glu Tyr His Lys Met Pro Val Leu Ser Arg Gly Asn Phe Asn Pro Glu
210 215 220

Phe Ile Gly Val Leu Ser Arg Lys Gln Asn Ala Ala Lys Lys Ser Lys
225 230 235 240

Ile Thr Val Thr Tyr Gln Arg Glu Met Asp Arg Tyr Thr Asn Phe Trp
245 250 255

Asn Gln Leu His Trp Ile Gly Asn Asn Tyr Lys Asp Glu Asn Arg Ala
260 265 270

Thr His Thr Ser Ile Tyr Glu Val Asp Trp Glu Asn His Thr Val Lys
275 280 285

Leu Ile Asp Thr Gln Ser Lys Glu Lys Asn Pro Met Ser
290 295 300

<210> 21

<211> 323

<212> PRT

<213> Artificial Sequence

<220>

<223> wild-type LukF-PV amino acid sequence

<400> 21

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

Leu	Leu	Ser	Asn	Thr	Val	Asp	Ala	Ala	Gln	His	Ile	Thr	Pro	Val	Ser
			20					25					30		

Glu	Lys	Lys	Val	Asp	Asp	Lys	Ile	Thr	Leu	Tyr	Lys	Thr	Thr	Ala	Thr
		35					40					45			

Ser	Asp	Ser	Asp	Lys	Leu	Lys	Ile	Ser	Gln	Ile	Leu	Thr	Phe	Asn	Phe
	50					55					60				

Ile	Lys	Asp	Lys	Ser	Tyr	Asp	Lys	Asp	Thr	Leu	Ile	Leu	Lys	Ala	Ala
65					70					75					80

Gly	Asn	Ile	Tyr	Ser	Gly	Tyr	Thr	Lys	Pro	Asn	Pro	Lys	Asp	Thr	Ile
				85					90					95	

Ser	Ser	Gln	Phe	Tyr	Trp	Gly	Ser	Lys	Tyr	Asn	Ile	Ser	Ile	Asn	Ser
			100					105					110		

Asp	Ser	Asn	Asp	Ser	Val	Asn	Val	Val	Asp	Tyr	Ala	Pro	Lys	Asn	Gln
		115					120					125			

Asn	Glu	Glu	Phe	Gln	Val	Gln	Gln	Thr	Val	Gly	Tyr	Ser	Tyr	Gly	Gly
	130					135					140				

Asp	Ile	Asn	Ile	Ser	Asn	Gly	Leu	Ser	Gly	Gly	Gly	Asn	Gly	Ser	Lys
145					150					155					160

Ser	Phe	Ser	Glu	Thr	Ile	Asn	Tyr	Lys	Gln	Glu	Ser	Tyr	Arg	Thr	Ser
				165					170					175	

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

His	Lys	Ile	Met	Asn	Asn	Gly	Trp	Gly	Pro	Tyr	Gly	Arg	Asp	Ser	Tyr
		195					200					205			

His	Ser	Thr	Tyr	Gly	Asn	Glu	Met	Phe	Leu	Gly	Ser	Arg	Gln	Ser	Asn
		210				215					220				

Leu	Asn	Ala	Gly	Gln	Asn	Phe	Leu	Glu	Tyr	His	Lys	Met	Pro	Val	Leu
225					230					235					240

Ser Arg Gly Asn Phe Asn Pro Glu Phe Ile Gly Val Leu Ser Arg Lys
245 250 255

Gln Asn Ala Ala Lys Lys Ser Lys Ile Thr Val Thr Tyr Gln Arg Glu
260 265 270

Met Asp Arg Tyr Thr Asn Phe Trp Asn Gln Leu His Trp Ile Gly Asn
275 280 285

Asn Tyr Lys Asp Glu Asn Arg Ala Thr His Thr Ser Ile Tyr Glu Val
290 295 300

Asp Trp Glu Asn His Thr Val Lys Leu Ile Asp Thr Gln Ser Lys Glu
305 310 315 320

Lys Asn Pro

<210> 22

<211> 328

<212> PRT

<213> Artificial Sequence

<220>

<223> wild-type LukF-PV amino acid sequence

<400> 22

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

Leu Leu Ser Asn Thr Val Asp Ala Ala Gln His Ile Thr Pro Val Ser
20 25 30

Glu Lys Lys Val Asp Asp Lys Ile Thr Leu Tyr Lys Thr Thr Ala Thr
35 40 45

Ser Asp Ser Asp Lys Leu Lys Ile Ser Gln Ile Leu Thr Phe Asn Phe
50 55 60

Ile Lys Asp Lys Ser Tyr Asp Lys Asp Thr Leu Ile Leu Lys Ala Ala
65 70 75 80

Gly Asn Ile Tyr Ser Gly Tyr Thr Lys Pro Asn Pro Lys Asp Thr Ile
85 90 95

Ser Ser Gln Phe Tyr Trp Gly Ser Lys Tyr Asn Ile Ser Ile Asn Ser
100 105 110

Asp Ser Asn Asp Ser Val Asn Val Val Asp Tyr Ala Pro Lys Asn Gln
115 120 125

Asn Glu Glu Phe Gln Val Gln Gln Thr Val Gly Tyr Ser Tyr Gly Gly
130 135 140

Asp Ile Asn Ile Ser Asn Gly Leu Ser Gly Gly Gly Asn Gly Ser Lys
145 150 155 160

Ser Phe Ser Glu Thr Ile Asn Tyr Lys Gln Glu Ser Tyr Arg Thr Ser
165 170 175

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

His Lys Ile Met Asn Asn Gly Trp Gly Pro Tyr Gly Arg Asp Ser Tyr
195 200 205

His Ser Thr Tyr Gly Asn Glu Met Phe Leu Gly Ser Arg Gln Ser Asn
210 215 220

Leu Asn Ala Gly Gln Asn Phe Leu Glu Tyr His Lys Met Pro Val Leu
225 230 235 240

Ser Arg Gly Asn Phe Asn Pro Glu Phe Ile Gly Val Leu Ser Arg Lys
245 250 255

Gln Asn Ala Ala Lys Lys Ser Lys Ile Thr Val Thr Tyr Gln Arg Glu
260 265 270

Met Asp Arg Tyr Thr Asn Phe Trp Asn Gln Leu His Trp Ile Gly Asn
275 280 285

Asn Tyr Lys Asp Glu Asn Arg Ala Thr His Thr Ser Ile Tyr Glu Val
290 295 300

Asp Trp Glu Asn His Thr Val Lys Leu Ile Asp Thr Gln Ser Lys Glu
305 310 315 320

Lys Lys Ser Tyr Glu Leu Asn Arg
325

<210> 23

<211> 324

<212> PRT

<213> Artificial Sequence

<220>

<223> wild-type LukF-PV amino acid sequence

<400> 23

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

Leu Leu Ser Asn Thr Val Asp Ala Ala Gln His Ile Thr Pro Val Ser
20 25 30

Glu Lys Lys Val Asp Asp Lys Ile Thr Leu Tyr Lys Thr Thr Ala Thr
35 40 45

Ser Asn Ser Asn Lys Leu Lys Ile Ser Gln Ile Leu Thr Phe Asn Phe

Ser Asp Ser Asp Lys Ser Tyr Asp Lys Asp Thr Leu Ile Leu Lys Ala Ala
 50 55 60
 Ile Lys Asp Lys Ser Tyr Asp Lys Asp Thr Leu Ile Leu Lys Ala Ala
 65 70 75 80
 Gly Asn Ile Tyr Ser Gly Tyr Thr Lys Pro Asn Pro Lys Asp Thr Ile
 85 90 95
 Ser Ser Gln Phe Tyr Trp Gly Ser Lys Tyr Asn Ile Ser Ile Asn Ser
 100 105 110
 Asp Ser Asn Asp Ser Val Asn Val Val Asp Tyr Ala Pro Lys Asn Gln
 115 120 125
 Asn Glu Glu Phe Gln Val Gln Gln Thr Val Gly Tyr Ser Tyr Gly Gly
 130 135 140
 Asp Ile Asn Ile Ser Asn Gly Leu Ser Gly Gly Gly Asn Gly Ser Lys
 145 150 155 160
 Ser Phe Ser Glu Thr Ile Asn Tyr Lys Gln Glu Ser Tyr Arg Thr Ser
 165 170 175
 Leu Asp Lys Arg Thr Asn Phe Lys Lys Ile Gly Trp Asp Val Glu Ala
 180 185 190
 His Lys Ile Met Asn Asn Gly Trp Gly Pro Tyr Gly Arg Asp Ser Tyr
 195 200 205
 His Ser Thr Tyr Gly Asn Glu Met Phe Leu Gly Ser Arg Gln Ser Asn
 210 215 220
 Leu Asn Ala Gly Gln Asn Phe Leu Glu Tyr His Lys Met Pro Val Leu
 225 230 235 240
 Ser Arg Gly Asn Phe Asn Pro Glu Phe Ile Gly Val Leu Ser Arg Lys
 245 250 255
 Gln Asn Ala Ala Lys Lys Ser Lys Ile Thr Val Thr Tyr Gln Arg Glu
 260 265 270
 Met Asp Arg Tyr Thr Asn Phe Trp Ile Asn Phe Asn Trp Ile Gly Asn
 275 280 285
 Asn Tyr Lys Asp Glu Asn Arg Ala Thr His Thr Ser Ile Tyr Glu Val
 290 295 300
 Asp Trp Glu Asn His Thr Val Lys Leu Ile Asp Thr Gln Ser Lys Glu
 305 310 315 320
 Lys Asn Pro Met

<210> 24

<211> 327

<212> PRT

<213> Artificial Sequence

<220>

<223> wild-type LukF-PV amino acid sequence

<400> 24

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

Leu Leu Leu Leu Ser Asn Thr Val Asp Ala Ala Gln His Ile Thr Pro
 20 25 30

Val Ser Glu Lys Lys Val Asp Asp Lys Ile Thr Leu Tyr Lys Thr Thr
 35 40 45

Ala Thr Ser Asp Asn Asp Lys Leu Asn Ile Ser Gln Ile Leu Thr Phe
 50 55 60

Asn Phe Ile Lys Asp Lys Ser Tyr Asp Lys Asp Thr Leu Val Leu Lys
 65 70 75 80

Ala Ala Gly Asn Ile Asn Ser Gly Tyr Lys Lys Pro Asn Pro Lys Asp
 85 90 95

Tyr Asn Tyr Ser Gln Phe Tyr Trp Gly Gly Lys Tyr Asn Val Ser Val
 100 105 110

Ser Ser Glu Ser Asn Asp Ala Val Asn Val Val Asp Tyr Ala Pro Lys
 115 120 125

Asn Gln Asn Glu Glu Phe Gln Val Gln Gln Thr Leu Gly Tyr Ser Tyr
 130 135 140

Gly Gly Asp Ile Asn Ile Ser Asn Gly Leu Ser Gly Gly Leu Asn Gly
 145 150 155 160

Ser Lys Ser Phe Ser Glu Thr Ile Asn Tyr Lys Gln Glu Ser Tyr Arg
 165 170 175

Thr Thr Ile Asp Arg Lys Thr Asn His Lys Ser Ile Gly Trp Gly Val
 180 185 190

Glu Ala His Lys Ile Met Asn Asn Gly Trp Gly Pro Tyr Gly Arg Asp
 195 200 205

Ser Tyr Asp Pro Thr Tyr Gly Asn Glu Leu Phe Leu Gly Gly Arg Gln
 210 215 220

Ser Ser Ser Asn Ala Gly Gln Asn Phe Leu Pro Thr His Gln Met Pro
 225 230 235 240

Leu Leu Ala Arg Gly Asn Phe Asn Pro Glu Phe Ile Ser Val Leu Ser
 245 250 255

His Lys Gln Asn Asp Thr Lys Lys Ser Lys Ile Lys Val Thr Tyr Gln
260 265 270

Arg Glu Leu Asp Arg Tyr Thr Asn Gln Trp Asn Arg Leu His Trp Ile
275 280 285

Gly Asn Asn Tyr Lys Asn Gln Asn Thr Val Thr Phe Thr Ser Thr Tyr
290 295 300

Glu Val Asp Trp Gln Asn His Thr Val Lys Leu Ile Gly Thr Asp Ser
305 310 315 320

Lys Glu Thr Asn Pro Gly Val
325

<210> 25

<211> 322

<212> PRT

<213> Artificial Sequence

<220>

<223> wild-type LukF-PV amino acid sequence

<400> 25

Met Lys Phe Lys Asn Ile Val Lys Ser Ser Val Ala Thr Ser Ile Thr
1 5 10 15

Leu Ile Met Leu Ser Asn Thr Val Asp Ala Ala Gln His Ile Thr Pro
20 25 30

Val Ser Glu Lys Lys Val Asp Asp Lys Ile Thr Leu Tyr Lys Thr Thr
35 40 45

Ala Thr Ser Asp Ser Asp Lys Leu Lys Ile Ser Gln Ile Leu Thr Phe
50 55 60

Asn Phe Ile Lys Asp Lys Ser Tyr Asp Lys Asp Thr Leu Ile Leu Lys
65 70 75 80

Ala Ala Gly Asn Ile Tyr Ser Gly Tyr Thr Gln Pro Thr Ser Asp Ser
85 90 95

Ser Ile Asn Ser Gln Phe Tyr Trp Gly Ala Lys Tyr Asn Val Phe Val
100 105 110

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

Asn Gln Asn Glu Glu Phe Gln Val Gln Gln Thr Leu Gly Tyr Ser Tyr
130 135 140

Gly Gly Asp Ile Asn Ile Ile Asn Gly Leu Thr Gly Gly Leu Asn Gly
145 150 155 160

Ser Lys Ser Phe Ser Glu Thr Ile Asn Tyr Lys Gln Glu Ser Tyr Arg
 165 170 175

Thr Thr Ile Asp Arg Lys Thr Asn His Lys Ser Ile Gly Trp Gly Val
 180 185 190

Glu Ala His Lys Ile Met Asn Asn Gly Trp Gly Pro Tyr Gly Arg Asp
 195 200 205

Ser Ser Asp Ser Leu Tyr Gly Asn Glu Leu Phe Leu Gly Gly Arg Gln
 210 215 220

Ser Ser Ser Asn Ala Asn Gln Asn Phe Leu Pro Thr His Gln Met Pro
 225 230 235 240

Ile Leu Ala Arg Gly Asn Phe Asn Pro Glu Phe Ile Ser Val Leu Ser
 245 250 255

His Lys Gln Lys Asp Val Lys Lys Ser Lys Ile Lys Val Thr Tyr Gln
 260 265 270

Arg Glu Met Asp Arg Tyr Glu Asn Phe Trp Asn Asn Leu His Trp Ile
 275 280 285

Gly Tyr Asn Phe Lys Asn Gln Lys Arg Ala Thr His Thr Ser Ile Tyr
 290 295 300

Glu Ile Asp Trp Glu Lys His Thr Val Lys Leu Val Ala Ser Gln Ser
 305 310 315 320

Ser Glu

<210> 26

<211> 322

<212> PRT

<213> Artificial Sequence

<220>

<223> wild-type LukF-PV amino acid sequence

<400> 26

Met Lys Phe Lys Asn Ile Val Lys Ser Ser Val Ala Thr Ser Ile Thr
 1 5 10 15

Leu Ile Met Leu Ser Asn Thr Val Asp Ala Ala Gln His Ile Thr Pro
 20 25 30

Val Ser Glu Lys Lys Val Asp Asp Lys Ile Thr Leu Tyr Lys Thr Thr
 35 40 45

Ala Thr Ser Asp Ser Asp Lys Leu Lys Ile Ser Gln Ile Leu Thr Phe
 50 55 60

Asn Phe Ile Lys Asp Lys Ser Tyr Asp Lys Asp Thr Leu Ile Leu Lys

65						70						75						80
Ala	Ala	Gly	Asn	Ile	Tyr	Ser	Gly	Tyr	Thr	Gln	Pro	Thr	Ser	Asp	Ser			
			85					90						95				
Ser	Ile	Asn	Ser	Gln	Phe	Tyr	Trp	Gly	Ala	Lys	Tyr	Asn	Val	Phe	Val			
			100					105						110				
Ser	Ser	Glu	Ser	Lys	Asp	Ser	Val	Asn	Ile	Val	Asp	Tyr	Ala	Pro	Lys			
			115					120						125				
Asn	Gln	Asn	Glu	Glu	Phe	Gln	Val	Gln	Gln	Thr	Leu	Gly	Tyr	Ser	Tyr			
			130					135						140				
Gly	Gly	Asp	Ile	Asn	Ile	Ile	Asn	Gly	Leu	Thr	Gly	Gly	Leu	Asn	Gly			
			145					150						155				
Ser	Lys	Ser	Phe	Ser	Glu	Thr	Ile	Asn	Tyr	Lys	Gln	Glu	Ser	Tyr	Arg			
			165					170						175				
Thr	Thr	Ile	Asp	Arg	Lys	Thr	Asn	His	Lys	Ser	Ile	Gly	Trp	Gly	Val			
			180					185						190				
Glu	Ala	His	Lys	Ile	Met	Asn	Asn	Gly	Trp	Gly	Pro	Tyr	Gly	Arg	Asp			
			195					200						205				
Ser	Ser	Asp	Ser	Leu	Tyr	Gly	Asn	Glu	Leu	Phe	Leu	Gly	Gly	Arg	Gln			
			210					215						220				
Ser	Ser	Ser	Asn	Ala	Asn	Gln	Asn	Phe	Leu	Pro	Thr	His	Gln	Met	Pro			
			225					230						235				
Ile	Leu	Ala	Arg	Gly	Asn	Phe	Asn	Pro	Glu	Phe	Ile	Ser	Val	Leu	Ser			
			245					250						255				
His	Lys	Gln	Lys	Asp	Val	Lys	Lys	Ser	Lys	Ile	Lys	Val	Thr	Tyr	Gln			
			260					265						270				
Arg	Glu	Met	Asp	Arg	Tyr	Glu	Asn	Phe	Trp	Asn	Asn	Leu	His	Trp	Ile			
			275					280						285				
Gly	Tyr	Asn	Ile	Lys	Asn	Gln	Lys	Arg	Ala	Thr	His	Thr	Ser	Ile	Tyr			
			290					295						300				
Glu	Ile	Asp	Trp	Glu	Lys	His	Thr	Val	Lys	Leu	Val	Ala	Ser	Gln	Ser			
			305					310						315				

Ser Glu

<210> 27

<211> 322

<212> PRT

<213> Artificial Sequence

 $\langle 220 \rangle$

<223> wild-type LukF-PV amino acid sequence

<400> 27

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

Phe Ile Met Leu Ser Asn Thr Val Asp Ala Ala Gln His Ile Thr Pro
      20      25      30

Val Ser Glu Lys Lys Val Asp Asp Lys Ile Thr Leu Tyr Lys Thr Thr
      35      40      45

Ala Thr Ser Asp Ser Asp Lys Leu Lys Ile Ser Gln Ile Leu Thr Phe
      50      55      60

Asn Phe Ile Lys Asp Lys Ser Tyr Asp Lys Asp Thr Leu Ile Leu Lys
65      70      75      80

Ala Ala Gly Asn Ile Tyr Ser Gly Tyr Thr Gln Pro Thr Ser Asp Ser
      85      90      95

Ser Ile Asn Ser Gln Phe Tyr Trp Gly Ala Lys Tyr Asn Val Phe Val
      100      105      110

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

Asn Gln Asn Glu Glu Phe Gln Val Gln Gln Thr Leu Gly Tyr Ser Tyr
      130      135      140

Gly Gly Asp Ile Asn Ile Ile Asn Gly Leu Thr Gly Gly Leu Asn Gly
145      150      155      160

Ser Lys Ser Phe Ser Glu Thr Ile Asn Tyr Lys Gln Glu Ser Tyr Arg
      165      170      175

Thr Thr Ile Asp Arg Lys Ile Asn His Lys Leu Ile Gly Trp Gly Val
      180      185      190

Glu Ala His Lys Ile Met Asn Asn Gly Trp Gly Pro Tyr Gly Arg Asp
      195      200      205

Ser Ser Asp Ser Leu Tyr Gly Asn Glu Leu Phe Leu Gly Gly Arg Gln
      210      215      220

Ser Ser Ser Asn Ala Asn Gln Asn Phe Leu Pro Thr His Gln Met Pro
225      230      235      240

Ile Leu Ala Arg Gly Asn Phe Asn Pro Glu Phe Ile Ser Val Leu Ser
      245      250      255

His Lys Gln Lys Asp Val Lys Lys Ser Lys Ile Lys Val Thr Tyr Gln
      260      265      270

Arg Gln Met Asp Arg Tyr Glu Asn Phe Trp Asn Asn Leu His Trp Ile
      275      280      285

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 Gly Tyr Asn Ile Lys Asn Gln Lys Arg Ala Thr His Thr Ser Ile Tyr
 290 295 300

Glu Ile Asp Trp Glu Lys His Thr Val Lys Leu Val Ala Ser Gln Ser
 305 310 315 320

Ser Glu

<210> 28

<211> 315

<212> PRT

<213> Artificial Sequence

<220>

<223> Panton-Valentine leukocidin chain S precursor amino acid sequence

<400> 28

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

Gly Ile Ile Thr Pro Ile Ala Thr Ser Phe His Glu Ser Lys Ala Asp
 20 25 30

Asn Asn Ile Glu Asn Ile Gly Asp Gly Ala Glu Val Val Lys Arg Thr
 35 40 45

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

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

Met Gln Gly Phe Ile Asn Ser Lys Thr Thr Tyr Tyr Asn Tyr Lys Asn
 85 90 95

Thr Asp His Ile Lys Ala Met Arg Trp Pro Phe Gln Tyr Asn Ile Gly
 100 105 110

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

Asn Lys Ile Asp Ser Val Asn Val Ser Gln Thr Leu Gly Tyr Asn Ile
 130 135 140

Gly Gly Asn Phe Asn Ser Gly Pro Ser Thr Gly Gly Asn Gly Ser Phe
 145 150 155 160

Asn Tyr Ser Lys Thr Ile Ser Tyr Asn Gln Gln Asn Tyr Ile Ser Glu
 165 170 175

Val Glu His Gln Asn Ser Lys Ser Val Gln Trp Gly Ile Lys Ala Asn
 180 185 190

Ser Phe Ile Thr Ser Leu Gly Lys Met Ser Gly His Asp Pro Asn Leu
195 200 205

Phe Val Gly Tyr Lys Pro Tyr Ser Gln Asn Pro Arg Asp Tyr Phe Val
210 215 220

Pro Asp Asn Glu Leu Pro Pro Leu Val His Ser Gly Phe Asn Pro Ser
225 230 235 240

Phe Ile Ala Thr Val Ser His Glu Lys Gly Ser Gly Asp Thr Ser Glu
245 250 255

Phe Glu Ile Thr Tyr Gly Arg Asn Met Asp Val Thr His Ala Thr Arg
260 265 270

Arg Thr Thr His Tyr Gly Asn Ser Tyr Leu Glu Gly Ser Arg Ile His
275 280 285

Asn Ala Phe Val Asn Arg Asn Tyr Thr Val Lys Tyr Glu Val Asn Trp
290 295 300

Lys Thr His Glu Ile Lys Val Lys Gly His Asn
305 310 315

<210> 29

<211> 315

<212> PRT

<213> Artificial Sequence

<220>

<223> gamma-hemolysin component C precursor amino acid sequence

<400> 29

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

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

Thr Glu Asp Ile Gly Lys Gly Ser Asp Val Glu Ile Ile Lys Arg Thr
35 40 45

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

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

Met Gln Gly Phe Ile Ser Ser Arg Thr Ala Tyr Tyr Asn Tyr Lys Lys
85 90 95

Ser Asn His Val Lys Ala Met Arg Trp Pro Phe Gln Tyr Asn Ile Gly
100 105 110

Leu Lys Thr Asn Asp Pro Asn Val Ser Leu Ile Asn Tyr Leu Pro Lys

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      115              120              125
Asn Lys Ile Glu Ser Thr Asn Val Ser Gln Thr Leu Gly Tyr Asn Ile
130              135              140

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

Asn Tyr Ser Lys Ser Ile Ser Tyr Thr Gln Gln Asn Tyr Val Ser Glu
165              170              175

Val Glu Gln Gln Asn Ser Lys Gly Val Leu Trp Gly Val Lys Ala Asn
180              185              190

Ser Phe Ala Thr Glu Ser Gly Gln Lys Ser Ala Phe Asp Ser Asp Leu
195              200              205

Phe Val Gly Tyr Lys Pro His Ser Lys Asp Pro Arg Asp Tyr Phe Val
210              215              220

Pro Asp Ser Glu Leu Pro Pro Leu Val Gln Ser Gly Phe Asn Pro Ser
225              230              235              240

Phe Ile Ala Thr Val Ser His Glu Lys Gly Ser Gly Asp Thr Ser Glu
245              250              255

Phe Glu Ile Thr Tyr Gly Arg Asn Met Asp Val Thr His Ala Ile Lys
260              265              270

Arg Ser Thr His Tyr Gly Asn Ser Tyr Leu Asp Gly His Arg Val His
275              280              285

Asn Ala Phe Val Asn Arg Asn Tyr Thr Val Lys Tyr Glu Val Asn Trp
290              295              300

Lys Thr His Glu Ile Lys Val Lys Gly Gln Asn
305              310              315

<210> 30
<211> 315
<212> PRT
<213> Artificial Sequence

<220>
<223> Leukocidin S subunit amino acid sequence

<400> 30
Met Leu Lys Asn Lys Ile Leu Ala Thr Thr Leu Ser Val Ser Leu Leu
1              5              10              15

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

Thr Glu Asp Ile Gly Lys Gly Asn Asp Val Glu Ile Ile Lys Arg Thr
35              40              45

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Glu Asp Lys Thr Ser Asn Lys Trp Gly Val Thr Gln Asn Ile Gln Phe
 50 55 60
 Asp Phe Val Lys Asp Lys Lys Tyr Asn Lys Asp Ala Leu Ile Leu Lys
 65 70 75 80
 Met Gln Gly Phe Ile Ser Ser Arg Thr Thr Tyr Tyr Asn Tyr Lys Asn
 85 90 95
 Thr Asn His Ile Lys Ser Met Arg Trp Pro Phe Gln Tyr Asn Ile Gly
 100 105 110
 Leu Lys Thr Asn Asp Pro Asn Val Ser Leu Ile Asn Tyr Leu Pro Lys
 115 120 125
 Asn Lys Ile Glu Ser Thr Asn Val Ser Gln Thr Leu Gly Tyr Asn Ile
 130 135 140
 Gly Gly Asn Phe Gln Ser Ala Pro Ser Leu Gly Gly Asn Gly Ser Phe
 145 150 155 160
 Asn Tyr Ser Lys Ser Ile Ser Tyr Thr Gln Gln Asn Tyr Val Ser Glu
 165 170 175
 Val Glu Gln Gln Asn Ser Lys Ser Val Leu Trp Gly Val Lys Ala Asn
 180 185 190
 Ser Phe Val Thr Ala Ser Gly Gln Lys Ser Ala Phe Asp Ser Asp Leu
 195 200 205
 Phe Val Gly Tyr Lys Pro His Ser Lys Asp Pro Arg Asp Tyr Phe Val
 210 215 220
 Pro Asp Ser Glu Leu Pro Pro Leu Val Gln Ser Gly Phe Asn Pro Ser
 225 230 235 240
 Phe Ile Ala Thr Val Ser His Glu Lys Gly Ser Gly Asp Thr Ser Glu
 245 250 255
 Phe Glu Ile Thr Tyr Gly Arg Asn Met Asp Val Thr His Ala Ile Lys
 260 265 270
 Arg Ser Thr His Tyr Gly Asn Ser Tyr Leu Asp Gly His Arg Ile His
 275 280 285
 Asn Ala Phe Lys Asn Arg Asn Tyr Thr Val Lys Tyr Glu Val Asn Trp
 290 295 300
 Lys Thr His Glu Ile Lys Val Lys Gly Gln Asn
 305 310 315

<211> 318

<212> PRT

<213> Artificial Sequence

<220>

<223> Panton-Valentine leukocidin subunit S amino acid sequence

<400> 31

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

Ser Leu Leu Ala Pro Leu Ala Asn Pro Leu Leu Glu Asn Ala Lys Ala
 20 25 30

Ala Asn Asp Thr Glu Asp Ile Gly Lys Gly Ser Asp Ile Glu Ile Ile
 35 40 45

Lys Arg Thr Glu Asp Lys Thr Ser Asn Lys Trp Gly Val Thr Gln Asn
 50 55 60

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

Ile Leu Lys Met Gln Gly Phe Ile Ser Ser Arg Thr Thr Tyr Tyr Asn
 85 90 95

Tyr Lys Asn Thr Asn His Ile Lys Ser Met Arg Trp Pro Phe Gln Tyr
 100 105 110

Asn Ile Gly Leu Lys Thr Asn Asp Ser Asn Val Ser Leu Ile Asn Tyr
 115 120 125

Leu Pro Lys Asn Lys Ile Glu Ser Thr Asn Val Ser Gln Thr Leu Gly
 130 135 140

Tyr Asn Ile Gly Gly Asn Phe Gln Ser Ala Pro Ser Leu Gly Gly Asn
 145 150 155 160

Gly Ser Phe Asn Tyr Ser Lys Ser Ile Ser Tyr Thr Gln Gln Asn Tyr
 165 170 175

Val Ser Glu Val Glu Gln Gln Asn Ser Lys Ser Val Leu Trp Gly Val
 180 185 190

Lys Ala Asn Ser Phe Val Thr Ala Ser Gly Gln Lys Ser Ala Phe Asp
 195 200 205

Ser Asp Leu Phe Val Gly Tyr Lys Pro Asn Ser Lys Asp Pro Arg Asp
 210 215 220

Tyr Phe Val Pro Asp Ser Glu Leu Pro Pro Leu Val Gln Ser Gly Phe
 225 230 235 240

Asn Pro Ser Phe Ile Ala Thr Val Ser His Glu Lys Gly Ser Gly Asp
 245 250 255

Thr Ser Glu Phe Glu Ile Thr Tyr Gly Arg Asn Met Asp Val Thr His
 260 265 270

Ala Ile Lys Arg Ser Thr His Tyr Gly Asn Ser Tyr Leu Asp Gly His
 275 280 285

Arg Val His Asn Ala Phe Val Asn Arg Asn Tyr Thr Val Lys Tyr Glu
 290 295 300

Val Asn Trp Lys Thr His Glu Ile Lys Val Lys Gly Gln Asn
 305 310 315

<210> 32

<211> 315

<212> PRT

<213> Artificial Sequence

<220>

<223> gamma-hemolysin component C amino acid sequence

<400> 32

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

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

Thr Glu Asp Ile Gly Lys Gly Ser Asp Ile Glu Ile Ile Lys Arg Thr
 35 40 45

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

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

Met Gln Gly Phe Ile Ser Ser Arg Thr Thr Tyr Tyr Asn Tyr Lys Lys
 85 90 95

Thr Asn His Val Lys Ala Met Arg Trp Pro Phe Gln Tyr Asn Ile Gly
 100 105 110

Leu Lys Thr Asn Asp Pro Asn Ile Ser Leu Ile Asn Tyr Leu Pro Lys
 115 120 125

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

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

Asn Tyr Ser Lys Ser Ile Ser Tyr Thr Gln Gln Asn Tyr Val Ser Glu
 165 170 175

Val Glu Gln Gln Asn Ser Lys Ser Val Leu Trp Gly Val Lys Ala Asn
180 185 190

Ser Phe Ala Thr Glu Ser Gly Gln Lys Ser Ala Phe Asp Ser Asp Leu
195 200 205

Phe Val Gly Tyr Lys Pro His Ser Lys Asp Pro Arg Asp Tyr Phe Val
210 215 220

Pro Asp Ser Glu Leu Pro Pro Leu Val Gln Ser Gly Phe Asn Pro Ser
225 230 235 240

Phe Ile Ala Thr Val Ser His Glu Lys Gly Ser Ser Asp Thr Ser Glu
245 250 255

Phe Glu Ile Thr Tyr Gly Arg Asn Met Asp Val Thr His Ala Ile Lys
260 265 270

Arg Ser Thr His Tyr Gly Asn Ser Tyr Leu Asp Gly His Arg Val His
275 280 285

Asn Ala Phe Val Asn Arg Asn Tyr Thr Val Lys Tyr Glu Val Asn Trp
290 295 300

Lys Thr His Glu Ile Lys Val Lys Gly Gln Asn
305 310 315

<210> 33

<211> 315

<212> PRT

<213> Artificial Sequence

<220>

<223> Leukocidin S subunit amino acid sequence

<400> 33

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

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

Thr Glu Asp Ile Gly Lys Gly Asn Asp Val Glu Ile Ile Lys Arg Thr
35 40 45

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

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

Met Gln Gly Phe Ile Ser Ser Arg Thr Thr Tyr Tyr Asn Tyr Lys Asn
85 90 95

Thr Asn His Ile Lys Ser Met Arg Trp Pro Phe Gln Tyr Asn Ile Gly
100 105 110

Leu Lys Thr Asn Asp Pro Asn Val Ser Leu Ile Asn Tyr Leu Pro Lys
115 120 125

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

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

Asn Tyr Ser Lys Ser Ile Ser Tyr Thr Gln Gln Asn Tyr Val Ser Glu
165 170 175

Val Glu Gln Gln Asn Ser Lys Ser Val Leu Trp Gly Val Lys Ala Asn
180 185 190

Ser Phe Val Thr Ala Ser Gly Gln Lys Ser Ala Phe Asp Ser Asp Leu
195 200 205

Phe Val Gly Tyr Lys Pro Asn Ser Lys Asp Pro Arg Asp Tyr Phe Val
210 215 220

Pro Asp Ser Glu Leu Pro Pro Leu Val Gln Ser Gly Phe Asn Pro Ser
225 230 235 240

Phe Ile Ala Thr Val Ser His Glu Lys Gly Ser Gly Asp Thr Ser Glu
245 250 255

Phe Glu Ile Thr Tyr Gly Arg Asn Met Asp Val Thr His Ala Ile Lys
260 265 270

Arg Ser Thr His Tyr Gly Asn Ser Tyr Leu Asp Gly His Arg Val His
275 280 285

Asn Ala Phe Lys Asn Arg Asn Tyr Thr Val Lys Tyr Glu Val Asn Trp
290 295 300

Lys Thr His Glu Ile Lys Val Lys Gly Gln Asn
305 310 315

<210> 34

<211> 315

<212> PRT

<213> Artificial Sequence

<220>

<223> gamma-hemolysin component C amino acid sequence

<400> 34

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

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

Thr Glu Asp Ile Gly Lys Gly Ser Asp Ile Glu Ile Ile Lys Arg Thr
 35 40 45
 Glu Asp Lys Thr Ser Asn Lys Trp Gly Val Thr Gln Asn Ile Gln Phe
 50 55 60
 Asp Phe Val Lys Asp Lys Lys Tyr Asn Lys Asp Ala Leu Ile Leu Lys
 65 70 75 80
 Met Gln Gly Phe Ile Ser Ser Arg Thr Thr Tyr Tyr Asn Tyr Lys Lys
 85 90 95
 Thr Asn His Val Lys Ala Met Arg Trp Pro Phe Gln Tyr Asn Ile Gly
 100 105 110
 Leu Lys Thr Asn Asp Lys Tyr Val Ser Leu Ile Asn Tyr Leu Pro Lys
 115 120 125
 Asn Lys Ile Glu Ser Thr Asn Val Ser Gln Thr Leu Gly Tyr Asn Ile
 130 135 140
 Gly Gly Asn Phe Gln Ser Ala Pro Ser Leu Gly Gly Asn Gly Ser Phe
 145 150 155 160
 Asn Tyr Ser Lys Ser Ile Ser Tyr Thr Gln Gln Asn Tyr Val Ser Glu
 165 170 175
 Val Glu Gln Gln Asn Ser Lys Ser Val Leu Trp Gly Val Lys Ala Asn
 180 185 190
 Ser Phe Ala Thr Glu Ser Gly Gln Lys Ser Ala Phe Asp Ser Asp Leu
 195 200 205
 Phe Val Gly Tyr Lys Pro His Ser Lys Asp Pro Arg Asp Tyr Phe Val
 210 215 220
 Pro Asp Ser Glu Leu Pro Pro Leu Val Gln Ser Gly Phe Asn Pro Ser
 225 230 235 240
 Phe Ile Ala Thr Val Ser His Glu Lys Gly Ser Ser Asp Thr Ser Glu
 245 250 255
 Phe Glu Ile Thr Tyr Gly Arg Asn Met Asp Val Thr His Ala Ile Lys
 260 265 270
 Arg Ser Thr His Tyr Gly Asn Ser Tyr Leu Asp Gly His Arg Val His
 275 280 285
 Asn Ala Phe Val Asn Arg Asn Tyr Thr Val Lys Tyr Glu Val Asn Trp
 290 295 300
 Lys Thr His Glu Ile Lys Val Lys Gly Gln Asn
 305 310 315

<210> 35

<211> 315

<212> PRT

<213> Artificial Sequence

<220>

<223> gamma-hemolysin component C precursor amino acid sequence

<400> 35

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

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

Thr	Glu	Glu	Ile	Gly	Lys	Gly	Ser	Asp	Ile	Glu	Ile	Ile	Lys	Arg	Thr
		35					40					45			

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

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

Met	Gln	Gly	Phe	Ile	Ser	Ser	Arg	Thr	Thr	Tyr	Tyr	Asn	Tyr	Lys	Lys
				85					90					95	

Thr	Asn	His	Val	Lys	Ala	Met	Arg	Trp	Pro	Phe	Gln	Tyr	Asn	Ile	Gly
			100					105						110	

Leu	Lys	Thr	Asn	Asp	Lys	Tyr	Val	Ser	Leu	Ile	Asn	Tyr	Leu	Pro	Lys
		115					120					125			

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

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

Asn	Tyr	Ser	Lys	Ser	Ile	Ser	Tyr	Thr	Gln	Gln	Asn	Tyr	Val	Ser	Glu
			165						170					175	

Val	Glu	Gln	Gln	Asn	Ser	Lys	Ser	Val	Leu	Trp	Gly	Val	Lys	Ala	Asn
			180					185					190		

Ser	Phe	Ala	Thr	Glu	Ser	Gly	Gln	Lys	Ser	Ala	Phe	Asp	Ser	Asp	Leu
		195					200					205			

Phe	Val	Gly	Tyr	Lys	Pro	His	Ser	Lys	Asp	Pro	Arg	Asp	Tyr	Phe	Val
	210					215					220				

Pro	Asp	Ser	Glu	Leu	Pro	Pro	Leu	Val	Gln	Ser	Gly	Phe	Asn	Pro	Ser
225					230					235					240

Phe	Ile	Ala	Thr	Val	Ser	His	Glu	Lys	Glu	Ser	Ser	Asn	Thr	Ser	Glu
-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----

Phe Ile Ala Thr Val Ser His Glu Lys Gly Ser Ser Asp Thr Ser Glu
245 250 255

Phe Glu Ile Thr Tyr Gly Arg Asn Met Asp Val Thr His Ala Ile Lys
260 265 270

Arg Ser Thr His Tyr Gly Asn Ser Tyr Leu Asp Gly His Arg Val His
275 280 285

Asn Ala Phe Val Asn Arg Asn Tyr Thr Val Lys Tyr Glu Val Asn Trp
290 295 300

Lys Thr His Glu Ile Lys Val Lys Gly Gln Asn
305 310 315

<210> 36

<211> 315

<212> PRT

<213> Artificial Sequence

<220>

<223> Leukocidin S subunit amino acid sequence

<400> 36

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

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

Thr Glu Asp Ile Gly Lys Gly Ser Asp Ile Glu Ile Ile Lys Arg Thr
35 40 45

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

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

Met Gln Gly Phe Ile Ser Ser Arg Thr Thr Tyr Tyr Asn Tyr Lys Lys
85 90 95

Thr Asn His Val Lys Ala Met Arg Trp Pro Phe Gln Tyr Asn Ile Ala
100 105 110

Leu Lys Thr Asn Asp Lys Tyr Val Ser Leu Ile Asn Tyr Leu Pro Lys
115 120 125

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

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

Asn Tyr Ser Lys Ser Ile Ser Tyr Thr Gln Gln Asn Tyr Val Ser Glu
165 170 175 180 185 190 195

165

170

175

Val Glu Gln Gln Asn Ser Lys Ser Val Leu Trp Gly Val Lys Ala Asn
180 185 190

Ser Phe Ala Thr Glu Ser Gly Gln Lys Ser Ala Phe Asp Ser Asp Leu
195 200 205

Phe Val Gly Tyr Lys Pro His Ser Lys Asp Pro Arg Asp Tyr Phe Val
210 215 220

Pro Asp Ser Glu Leu Pro Pro Leu Val Gln Ser Gly Phe Asn Pro Ser
225 230 235 240

Phe Ile Ala Thr Val Ser His Glu Lys Gly Ser Ser Asp Thr Ser Glu
245 250 255

Phe Glu Ile Thr Tyr Gly Arg Asn Met Asp Val Thr His Ala Ile Lys
260 265 270

Arg Ser Thr His Tyr Gly Asn Ser Tyr Leu Asp Gly His Arg Val His
275 280 285

Asn Ala Phe Val Asn Arg Asn Tyr Thr Val Lys Tyr Glu Val Asn Trp
290 295 300

Lys Thr His Glu Ile Lys Val Lys Gly Gln Asn
305 310 315

<210> 37

<211> 315

<212> PRT

<213> Artificial Sequence

<220>

<223> gamma-hemolysin component C precursor amino acid sequence

<400> 37

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

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

Thr Glu Asp Ile Gly Lys Gly Ser Asp Ile Glu Ile Ile Lys Arg Thr
35 40 45

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

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

Met Gln Gly Phe Ile Ser Ser Arg Thr Thr Tyr Tyr Asn Tyr Lys Lys
85 90 95

Thr Asn His Ile Lys Ala Met Arg Trp Pro Phe Gln Tyr Asn Ile Ser
100 105 110

Leu Lys Thr Asn Asp Lys Tyr Val Ser Leu Ile Asn Tyr Leu Pro Lys
115 120 125

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

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

Asn Tyr Ser Lys Ser Ile Ser Tyr Thr Gln Gln Asn Tyr Val Ser Glu
165 170 175

Val Glu Gln Gln Asn Ser Lys Ser Val Leu Trp Gly Val Lys Ala Asn
180 185 190

Ser Phe Ala Thr Glu Ser Gly Gln Lys Ser Ala Phe Asp Ser Asp Leu
195 200 205

Phe Val Gly Tyr Lys Pro His Ser Lys Asp Pro Arg Asp Tyr Phe Val
210 215 220

Pro Asp Ser Glu Leu Pro Pro Leu Val Gln Ser Gly Phe Asn Pro Ser
225 230 235 240

Phe Ile Ala Thr Val Ser His Glu Lys Gly Ser Ser Asp Thr Ser Glu
245 250 255

Phe Glu Ile Thr Tyr Gly Arg Asn Met Asp Val Thr His Ala Ile Lys
260 265 270

Arg Ser Thr His Tyr Gly Asn Ser Tyr Leu Asp Gly His Arg Val His
275 280 285

Asn Ala Phe Val Asn Arg Asn Tyr Thr Val Lys Tyr Glu Val Asn Trp
290 295 300

Lys Thr His Glu Ile Lys Val Lys Gly Gln Asn
305 310 315

<210> 38

<211> 318

<212> PRT

<213> Artificial Sequence

<220>

<223> gamma-hemolysin component C precursor amino acid sequence

<400> 38

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

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1           5           10           15

Ser Leu Leu Ala Pro Leu Ala Asn Pro Leu Leu Glu Asn Ala Lys Ala
    20                25                30

Ala Asn Asp Thr Glu Asp Ile Gly Lys Gly Ser Asp Ile Glu Ile Ile
    35                40                45

Lys Arg Thr Glu Asp Lys Thr Ser Asn Lys Trp Gly Val Thr Gln Asn
    50                55                60

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

Ile Leu Lys Met Gln Gly Phe Ile Ser Ser Arg Thr Thr Tyr Tyr Asn
    85                90                95

Tyr Lys Lys Thr Asn His Val Lys Ala Met Arg Trp Pro Phe Gln Tyr
   100                105                110

Asn Ile Gly Leu Lys Thr Asn Asp Lys Tyr Val Ser Leu Ile Asn Tyr
   115                120                125

Leu Pro Lys Asn Lys Ile Glu Ser Thr Asn Val Ser Gln Thr Leu Gly
   130                135                140

Tyr Asn Ile Gly Gly Asn Phe Gln Ser Ala Pro Ser Leu Gly Gly Asn
   145                150                155                160

Gly Ser Phe Asn Tyr Ser Lys Ser Ile Ser Tyr Thr Gln Gln Asn Tyr
   165                170                175

Val Ser Glu Val Glu Gln Gln Asn Ser Lys Ser Val Leu Trp Gly Val
   180                185                190

Lys Ala Asn Ser Phe Ala Thr Glu Ser Gly Gln Lys Ser Ala Phe Asp
   195                200                205

Ser Asp Leu Phe Val Gly Tyr Lys Pro His Ser Lys Asp Pro Arg Asp
   210                215                220

Tyr Phe Val Pro Asp Ser Glu Leu Pro Pro Leu Val Gln Ser Gly Phe
   225                230                235                240

Asn Pro Ser Phe Ile Ala Thr Val Ser His Glu Lys Gly Ser Ser Asp
   245                250                255

Thr Ser Glu Phe Glu Ile Thr Tyr Gly Arg Asn Met Asp Val Thr His
   260                265                270

Ala Ile Lys Arg Ser Thr His Tyr Gly Asn Ser Tyr Leu Asp Gly His
   275                280                285

Arg Val His Asn Ala Phe Val Asn Arg Asn Tyr Thr Val Lys Tyr Glu
   290                295                300

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Val Asn Trp Lys Thr His Glu Ile Lys Val Lys Gly Gln Asn
 305 310 315

<210> 39

<211> 315

<212> PRT

<213> Artificial Sequence

<220>

<223> gamma-hemolysin component C precursor amino acid sequence

<400> 39

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

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

Thr Glu Asp Ile Gly Lys Gly Ser Asp Ile Glu Ile Ile Lys Arg Thr
 35 40 45

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

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

Met Gln Gly Phe Ile Ser Ser Arg Thr Thr Tyr Tyr Asn Tyr Lys Lys
 85 90 95

Thr Asn His Val Lys Ala Met Arg Trp Pro Phe Gln Tyr Asn Ile Gly
 100 105 110

Leu Lys Thr Asn Asp Lys Tyr Val Ser Leu Ile Asn His Leu Pro Lys
 115 120 125

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

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

Asn Tyr Ser Lys Ser Ile Ser Tyr Thr Gln Gln Asn Tyr Val Ser Glu
 165 170 175

Val Glu Gln Gln Asn Ser Lys Ser Val Leu Trp Gly Val Lys Ala Asn
 180 185 190

Ser Phe Ala Thr Glu Ser Gly Gln Lys Ser Ala Phe Asp Ser Asp Leu
 195 200 205

Phe Val Gly Tyr Lys Pro His Ser Lys Asp Pro Arg Asp Tyr Phe Val
 210 215 220

Pro Asp Ser Glu Leu Pro Pro Leu Val Gln Ser Gly Phe Asn Pro Ser
225 230 235 240

Phe Ile Ala Thr Val Ser His Glu Lys Gly Ser Ser Asp Thr Ser Glu
245 250 255

Phe Glu Ile Thr Tyr Gly Arg Asn Met Asp Val Thr His Ala Ile Lys
260 265 270

Arg Ser Thr His Tyr Gly Asn Ser Tyr Leu Asp Gly His Arg Val His
275 280 285

Asn Ala Phe Val Asn Arg Asn Tyr Thr Val Lys Tyr Glu Val Asn Trp
290 295 300

Lys Thr His Glu Ile Lys Val Lys Gly Gln Asn
305 310 315

<210> 40

<211> 318

<212> PRT

<213> Artificial Sequence

<220>

<223> gamma-hemolysin component C precursor amino acid sequence

<400> 40

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

Ser Leu Leu Ala Pro Leu Ala Asn Pro Leu Leu Glu Asn Ala Lys Ala
20 25 30

Ala Asn Asp Thr Glu Asp Ile Gly Lys Gly Asn Asp Val Glu Ile Ile
35 40 45

Lys Arg Thr Glu Asp Lys Thr Ser Asn Lys Trp Gly Val Thr Gln Asn
50 55 60

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

Ile Leu Lys Met Gln Gly Phe Ile Ser Ser Arg Thr Thr Tyr Tyr Asn
85 90 95

Tyr Lys Asn Thr Asn His Ile Lys Ser Met Arg Trp Pro Phe Gln Tyr
100 105 110

Asn Ile Gly Leu Lys Thr Asn Asp Lys Tyr Val Ser Leu Ile Asn Tyr
115 120 125

Leu Pro Lys Asn Lys Ile Glu Ser Thr Asn Val Ser Gln Thr Leu Gly
130 135 140

Tyr Asn Ile Gly Gly Asn Phe Gln Ser Ala Pro Ser Leu Gly Gly Asn
145 150 155 160

Gly Ser Phe Asn Tyr Ser Lys Ser Ile Ser Tyr Thr Gln Gln Asn Tyr
165 170 175

Val	Ser	Glu	Val	Glu	Gln	Gln	Asn	Ser	Lys	Ser	Val	Leu	Trp	Gly	Val
			180					185					190		

Lys Ala Asn Ser Phe Ala Thr Glu Ser Gly Gln Lys Ser Ala Phe Asp
195 200 205

Ser Asp Leu Phe Val Gly Tyr Lys Pro His Ser Lys Asp Pro Arg Asp
210 215 220

Tyr Phe Val Pro Asp Ser Glu Leu Pro Pro Leu Val Gln Ser Gly Phe
225 230 235 240

Asn Pro Ser Phe Ile Ala Thr Val Ser His Glu Lys Gly Ser Ser Asp
245 250 255

Thr Ser Glu Phe Glu Ile Thr Tyr Gly Arg Asn Met Asp Val Thr His
260 265 270

Ala Ile Lys Arg Ser Thr His Tyr Gly Asn Ser Tyr Leu Asp Gly His
275 280 285

Arg Val His Asn Ala Phe Lys Asn Arg Asn Tyr Thr Val Lys Tyr Glu
290 295 300

Val Asn Trp Lys Thr His Glu Ile Lys Val Lys Gly Gln Asn
305 310 315

<210> 41

$\langle 211 \rangle$ 315

<212> PRT

<213> Artificial Sequence

<220>

<223> gamma-hemolysin component C precursor amino acid sequence

<400> 41

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

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

Thr Glu Asp Ile Gly Lys Gly Ser Asp Ile Glu Ile Ile Lys Arg Thr
35 40 45

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

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

Met Gln Gly Phe Ile Ser Ser Arg Thr Thr Tyr Tyr Asn Tyr Lys Lys
85 90 95

Thr Asn His Val Lys Ala Met Arg Trp Pro Phe Gln Tyr Asn Ile Gly
100 105 110

Leu Lys Thr Asn Asp Lys Tyr Val Ser Leu Ile Asn Tyr Leu Pro Lys
115 120 125

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

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

Asn Tyr Ser Lys Ser Ile Ser Tyr Thr Gln Gln Asn Tyr Val Ser Glu
165 170 175

Val Glu Gln Gln Asn Ser Lys Ser Val Leu Trp Gly Val Lys Ala Asn
180 185 190

Ser Phe Ala Thr Glu Ser Gly Gln Lys Ser Ala Phe Asp Ser Asp Leu
195 200 205

Phe Val Gly Tyr Lys Pro His Ser Lys Asp Pro Arg Asp Tyr Phe Val
210 215 220

Pro Asp Ser Glu Leu Pro Pro Leu Val Gln Ser Gly Phe Asn Pro Ser
225 230 235 240

Phe Ile Ala Thr Val Ser His Glu Lys Gly Ser Ser Asp Thr Ser Glu
245 250 255

Phe Glu Ile Thr Tyr Gly Arg Asn Met Asp Val Thr His Ala Ile Lys
260 265 270

Arg Ser Thr His Tyr Gly Asn Ser Tyr Leu Asp Gly His Arg Val His
275 280 285

Asn Ala Phe Val Asn Arg Asn Tyr Thr Val Lys Tyr Glu Val Asn Trp
290 295 300

Lys Thr His Glu Ile Lys Val Lys Gly Gln Asn
305 310 315

<210> 42

<211> 315

<212> PRT

<213> Artificial Sequence

<220>

<223> Leukocidin S subunit amino acid sequence

<400> 42

Met Leu Lys Asn Lys Ile Leu Ala Thr Thr Leu Ser Val Ser Leu Leu

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1           5           10           15
Ala Pro Leu Ala Asn Pro Leu Leu Glu Asn Ala Lys Ala Ala Asn Asp
      20                25                30
Thr Glu Asp Ile Gly Lys Gly Ser Asp Ile Glu Ile Ile Lys Arg Thr
      35                40                45
Glu Asp Lys Thr Ser Asn Lys Trp Gly Val Thr Gln Asn Ile Gln Phe
      50                55                60
Asp Phe Val Lys Asp Thr Lys Tyr Asn Lys Asp Ala Leu Ile Leu Lys
      65                70                75                80
Met Gln Gly Phe Ile Ser Ser Arg Thr Thr Tyr Tyr Asn Tyr Lys Lys
      85                90                95
Thr Asn His Val Lys Ala Met Arg Trp Pro Phe Gln Tyr Asn Ile Gly
      100               105               110
Leu Lys Thr Asn Asp Lys Tyr Val Ser Leu Ile Asn Tyr Leu Pro Lys
      115               120               125
Asn Lys Ile Glu Ser Thr Asn Val Ser Gln Thr Leu Gly Tyr Asn Ile
      130               135               140
Gly Gly Asn Phe Gln Ser Ala Pro Ser Leu Gly Gly Asn Gly Ser Phe
      145               150               155               160
Asn Tyr Ser Lys Ser Ile Ser Tyr Thr Gln Gln Asn Tyr Val Ser Glu
      165               170               175
Val Glu Gln Gln Asn Ser Lys Ser Val Leu Trp Gly Val Lys Ala Asn
      180               185               190
Ser Phe Ala Thr Glu Ser Gly Gln Lys Ser Ala Phe Asp Ser Asp Leu
      195               200               205
Phe Val Gly Tyr Lys Pro His Ser Lys Asp Pro Arg Asp Tyr Phe Val
      210               215               220
Pro Asp Ser Glu Leu Pro Pro Leu Val Gln Ser Gly Phe Asn Pro Ser
      225               230               235               240
Phe Ile Ala Thr Val Ser His Glu Lys Gly Ser Ser Asp Thr Ser Glu
      245               250               255
Phe Glu Ile Thr Tyr Gly Arg Asn Met Asp Val Thr His Ala Ile Lys
      260               265               270
Arg Ser Thr His Tyr Gly Asn Ser Tyr Leu Asp Gly His Arg Val His
      275               280               285
Asn Ala Phe Val Asn Arg Asn Tyr Thr Val Lys Tyr Glu Val Asn Trp
      290               295               300

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Lys Thr His Glu Ile Lys Val Lys Gly Gln Asn
 305 310 315

<210> 43

<211> 315

<212> PRT

<213> Artificial Sequence

<220>

<223> gamma-hemolysin component C precursor amino acid sequence

<400> 43

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

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

Thr Glu Asp Ile Gly Lys Gly Asn Asp Val Glu Ile Ile Lys Arg Thr
 35 40 45

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

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

Met Gln Gly Phe Ile Ser Ser Arg Thr Thr Tyr Tyr Asn Tyr Lys Asn
 85 90 95

Thr Asn His Ile Lys Ser Met Arg Trp Pro Phe Gln Tyr Asn Ile Gly
 100 105 110

Leu Lys Thr Asn Asp Lys Tyr Val Ser Leu Ile Asn Tyr Leu Pro Lys
 115 120 125

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

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

Asn Tyr Ser Lys Ser Ile Ser Tyr Thr Gln Gln Asn Tyr Val Ser Glu
 165 170 175

Val Glu Gln Gln Asn Ser Lys Ser Val Leu Trp Gly Val Lys Ala Asn
 180 185 190

Ser Phe Ala Thr Glu Ser Gly Gln Lys Ser Ala Phe Asp Ser Asp Leu
 195 200 205

Phe Val Gly Tyr Lys Pro His Ser Lys Asp Pro Arg Asp Tyr Phe Val
 210 215 220

Pro Asp Ser Glu Leu Pro Pro Leu Val Gln Ser Gly Phe Asn Pro Ser
225 230 235 240

Phe Ile Ala Thr Val Ser His Glu Lys Gly Ser Ser Asp Thr Ser Glu
245 250 255

Phe Glu Ile Thr Tyr Gly Arg Asn Met Asp Val Thr His Ala Ile Lys
260 265 270

Arg Ser Thr His Tyr Gly Asn Ser Tyr Leu Asp Gly His Arg Val His
275 280 285

Asn Ala Phe Lys Asn Arg Asn Tyr Thr Val Lys Tyr Glu Val Asn Trp
290 295 300

Lys Thr His Glu Ile Lys Val Lys Gly Gln Asn
305 310 315

<210> 44

<211> 315

<212> PRT

<213> Artificial Sequence

<220>

<223> gamma-hemolysin component C precursor amino acid sequence

<400> 44

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

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

Thr Glu Asp Ile Gly Lys Gly Ser Asp Ile Glu Ile Ile Lys Arg Thr
35 40 45

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

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

Met Gln Gly Phe Ile Ser Ser Arg Thr Thr Tyr Tyr Asn Tyr Lys Lys
85 90 95

Thr Asn His Ile Lys Ala Met Arg Trp Pro Phe Gln Tyr Asn Ile Gly
100 105 110

Leu Lys Thr Asn Asp Lys Tyr Val Ser Leu Ile Asn Tyr Leu Pro Lys
115 120 125

Asn Lys Ile Glu Ser Thr Asn Val Ser Gln Thr Leu Gly Tyr Asn Ile

130

135

140

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

Ser Tyr Ser Lys Ser Ile Ser Tyr Thr Gln Gln Asn Tyr Val Ser Glu
165 170 175

Val Glu Gln Gln Asn Ser Lys Ser Val Leu Trp Gly Val Lys Ala Asn
180 185 190

Ser Phe Ala Thr Glu Ser Gly Gln Lys Ser Ala Phe Asp Ser Asp Leu
195 200 205

Phe Val Gly Tyr Lys Pro His Ser Lys Asp Pro Arg Asp Tyr Phe Val
210 215 220

Pro Asp Ser Glu Leu Pro Pro Leu Val Gln Ser Gly Phe Asn Pro Ser
225 230 235 240

Phe Ile Ala Thr Val Ser His Glu Lys Gly Ser Ser Asp Thr Ser Glu
245 250 255

Phe Glu Ile Thr Tyr Gly Arg Asn Met Asp Val Thr His Ala Ile Lys
260 265 270

Arg Ser Thr His Tyr Gly Asn Ser Tyr Leu Asp Gly His Arg Val His
275 280 285

Asn Ala Phe Val Asn Arg Asn Tyr Thr Val Lys Tyr Glu Val Asn Trp
290 295 300

Lys Thr His Glu Ile Lys Val Lys Gly Gln Asn
305 310 315

<210> 45

<211> 315

<212> PRT

<213> Artificial Sequence

<220>

<223> gamma-hemolysin component C precursor amino acid sequence

<400> 45

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

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

Thr Glu Asp Ile Gly Lys Gly Ser Asp Ile Glu Ile Ile Lys Arg Thr
35 40 45

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

Asn Phe Val Lys Asn Lys Lys Thr Asn Lys Asn Ala Leu Ile Leu Lys

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Asp Phe Val Lys Asp Lys Lys Lys Asn Lys Asp Ala Leu Ile Leu Lys
65                               70                               75                               80

Met Gln Gly Phe Ile Ser Ser Arg Thr Thr Tyr Tyr Asn Tyr Lys Lys
85                               90                               95

Thr Asn His Val Lys Ala Met Arg Trp Pro Phe Gln Tyr Asn Ile Gly
100                            105                            110

Leu Lys Thr Asn Asp Lys Tyr Val Ser Leu Ile Asn Tyr Leu Pro Lys
115                            120                            125

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

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

Asn Tyr Ser Lys Ser Ile Ser Tyr Thr Gln Gln Asn Tyr Val Ser Glu
165                            170                            175

Val Glu Gln Gln Asn Ser Lys Ser Val Leu Trp Gly Val Lys Ala Asn
180                            185                            190

Ser Phe Ala Thr Glu Ser Gly Gln Lys Ser Ala Phe Asp Ser Asp Leu
195                            200                            205

Phe Val Gly Tyr Lys Pro His Ser Lys Asp Pro Arg Asp Tyr Phe Val
210                            215                            220

Pro Asp Ser Glu Leu Pro Pro Leu Val Gln Ser Gly Phe Asn Pro Ser
225                            230                            235                            240

Phe Ile Ala Thr Val Ser His Glu Lys Gly Ser Ser Asp Thr Ser Glu
245                            250                            255

Phe Glu Ile Thr Tyr Gly Arg Asn Met Asp Val Thr His Ala Ile Lys
260                            265                            270

Arg Ser Thr His Tyr Gly Asn Ser Tyr Leu Asp Gly His Arg Val His
275                            280                            285

Asn Ala Phe Val Asn Arg Asn Tyr Thr Val Lys Tyr Glu Val Asn Trp
290                            295                            300

Lys Thr His Glu Ile Lys Val Lys Gly Gln Asn
305                            310                            315

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<210> 46

<211> 315

<212> PRT

<213> Artificial Sequence

<220>

<223> S component of leucocodin R amino acid sequence

<400> 46

Met	Leu	Lys	Asn	Lys	Ile	Leu	Ala	Thr	Thr	Leu	Ser	Val	Ser	Leu	Leu	1	5	10	15
Ala	Pro	Leu	Ala	Asn	Pro	Leu	Leu	Glu	Asn	Ala	Lys	Ala	Ala	Asn	Asp	20	25	30	
Thr	Glu	Asp	Ile	Gly	Lys	Gly	Asn	Asp	Val	Glu	Ile	Ile	Lys	Arg	Thr	35	40	45	
Glu	Asp	Lys	Thr	Ser	Asn	Lys	Trp	Gly	Val	Thr	Gln	Asn	Ile	Gln	Phe	50	55	60	
Asp	Phe	Val	Lys	Asp	Lys	Lys	Tyr	Asn	Lys	Asp	Ala	Leu	Ile	Leu	Lys	65	70	75	80
Met	Gln	Gly	Phe	Ile	Ser	Ser	Arg	Thr	Thr	Tyr	Tyr	Asn	Ser	Lys	Asn	85	90	95	
Thr	Asn	His	Ile	Lys	Ser	Met	Arg	Trp	Pro	Phe	Gln	Tyr	Asn	Ile	Gly	100	105	110	
Leu	Lys	Thr	Asn	Asp	Lys	Tyr	Val	Ser	Leu	Ile	Asn	Tyr	Leu	Pro	Lys	115	120	125	
Asn	Lys	Ile	Glu	Ser	Thr	Asn	Val	Ser	Gln	Thr	Leu	Gly	Tyr	Asn	Ile	130	135	140	
Gly	Gly	Asn	Phe	Gln	Ser	Ala	Pro	Ser	Leu	Gly	Gly	Asn	Gly	Ser	Phe	145	150	155	160
Asn	Tyr	Ser	Lys	Ser	Ile	Ser	Tyr	Thr	Gln	Gln	Asn	Tyr	Val	Ser	Glu	165	170	175	
Val	Glu	Gln	Gln	Asn	Ser	Lys	Ser	Val	Leu	Trp	Gly	Val	Lys	Ala	Asn	180	185	190	
Ser	Phe	Ala	Thr	Glu	Ser	Gly	Gln	Lys	Ser	Ala	Phe	Asp	Ser	Asp	Leu	195	200	205	
Phe	Val	Gly	Tyr	Lys	Pro	His	Ser	Lys	Asp	Pro	Arg	Asp	Tyr	Phe	Val	210	215	220	
Pro	Asp	Ser	Glu	Leu	Pro	Pro	Leu	Val	Gln	Ser	Gly	Phe	Asn	Pro	Ser	225	230	235	240
Phe	Ile	Ala	Thr	Val	Ser	His	Glu	Lys	Gly	Ser	Ser	Asp	Thr	Ser	Glu	245	250	255	
Phe	Glu	Ile	Thr	Tyr	Gly	Arg	Asn	Met	Asp	Val	Thr	His	Ala	Ile	Lys	260	265	270	
Arg	Ser	Thr	His	Tyr	Gly	Asn	Ser	Tyr	Leu	Asp	Gly	His	Arg	Val	His	275	280	285	

Asn Ala Phe Lys Asn Arg Asn Tyr Thr Val Lys Tyr Glu Val Asn Trp
 290 295 300

Lys Thr His Glu Ile Lys Val Lys Gly Gln Asn
 305 310 315

<210> 47

<211> 315

<212> PRT

<213> Artificial Sequence

<220>

<223> hlgC-like ORFamino acid sequence

<400> 47

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

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

Thr Glu Asp Ile Gly Lys Gly Asn Asp Val Glu Ile Ile Lys Arg Thr
 35 40 45

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

Gly Phe Val Lys Asp Lys Lys Tyr Asn Lys Val Ala Leu Ile Leu Lys
 65 70 75 80

Met Gln Gly Phe Ile Ser Ser Arg Thr Thr Tyr Tyr Asn Tyr Lys Asn
 85 90 95

Thr Asn His Ile Lys Ser Met Arg Trp Pro Phe Gln Tyr Asn Ile Gly
 100 105 110

Leu Lys Thr Asn Asp Lys Tyr Val Ser Leu Ile Asn Tyr Leu Pro Lys
 115 120 125

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

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

Asn Tyr Ser Lys Ser Ile Ser Tyr Thr Gln Gln Asn Tyr Val Ser Glu
 165 170 175

Val Glu Gln Gln Asn Ser Lys Ser Val Leu Trp Gly Val Lys Ala Asn
 180 185 190

Ser Phe Ala Thr Glu Ser Gly Gln Lys Ser Ala Phe Asp Ser Asp Leu
 195 200 205

Phe Val Gly Tyr Lys Pro His Ser Lys Asp Pro Arg Asp Tyr Phe Val
210 215 220

Pro Asp Ser Glu Leu Pro Pro Leu Val Gln Ser Gly Phe Asn Pro Ser
225 230 235 240

Phe Ile Ala Thr Val Ser His Glu Lys Gly Ser Ser Asp Thr Ser Glu
245 250 255

Phe Glu Ile Thr Tyr Gly Arg Asn Met Asp Val Thr His Ala Ile Lys
260 265 270

Arg Ser Thr His Tyr Gly Asn Ser Tyr Leu Asp Gly His Arg Val His
275 280 285

Asn Ala Phe Lys Asn Arg Asn Tyr Thr Val Lys Tyr Glu Val Asn Trp
290 295 300

Lys Thr His Glu Ile Lys Val Lys Gly Gln Asn
305 310 315

<210> 48

<211> 286

<212> PRT

<213> Artificial Sequence

<220>

<223> Leukocidin LukS component amino acid sequence

<400> 48

Ala Asn Asp Thr Glu Asp Ile Gly Lys Gly Ser Asp Ile Glu Ile Ile
1 5 10 15

Lys Arg Thr Glu Asp Lys Thr Ser Asn Lys Trp Gly Val Thr Gln Asn
20 25 30

Ile Gln Phe Asp Phe Val Lys Asp Lys Lys Tyr Asn Lys Asp Ala Leu
35 40 45

Ile Leu Lys Met Gln Gly Phe Ile Ser Ser Arg Thr Thr Tyr Tyr Asn
50 55 60

Tyr Lys Lys Thr Asn His Val Lys Ala Met Arg Trp Pro Phe Gln Tyr
65 70 75 80

Asn Ile Gly Leu Lys Thr Asn Asp Lys Tyr Val Ser Leu Ile Asn Tyr
85 90 95

Leu Pro Lys Asn Lys Ile Glu Ser Thr Asn Val Ser Gln Thr Leu Gly
100 105 110

Tyr Asn Ile Gly Gly Asn Phe Gln Ser Ala Pro Ser Leu Gly Gly Asn
115 120 125

Gly Ser Phe Asn Tyr Ser Lys Ser Ile Ser Tyr Thr Gln Gln Asn Tyr
130 135 140

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130          135          140
Val Ser Glu Val Glu Gln Gln Asn Ser Lys Ser Val Leu Trp Gly Val
145          150          155          160

Lys Ala Asn Ser Phe Ala Thr Glu Ser Gly Gln Lys Ser Ala Phe Asp
165          170          175

Ser Asp Leu Phe Val Gly Tyr Lys Pro His Ser Lys Asp Pro Arg Asp
180          185          190

Tyr Phe Val Pro Asp Ser Glu Leu Pro Pro Leu Val Gln Ser Gly Phe
195          200          205

Asn Pro Ser Phe Ile Ala Thr Val Ser His Glu Lys Gly Ser Ser Asp
210          215          220

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

Ala Ile Lys Arg Ser Thr His Tyr Gly Asn Ser Tyr Leu Asp Gly His
245          250          255

Arg Val His Asn Ala Phe Val Asn Arg Asn Tyr Thr Val Lys Tyr Glu
260          265          270

Val Asn Trp Lys Thr His Glu Ile Lys Glu Lys Gly Gln Asn
275          280          285

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<210> 49

<211> 305

<212> PRT

<213> Artificial Sequence

<220>

<223> gamma-hemolysin component C amino acid sequence

<400> 49

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

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

Thr Glu Asp Ile Gly Lys Gly Asn Asp Val Glu Ile Ile Lys Arg Thr
35      40      45

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

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

Met Gln Gly Phe Ile Ser Ser Arg Thr Thr Tyr Tyr Asn Tyr Lys Asn
85      90      95

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Thr Asn His Ile Lys Ser Met Arg Trp Pro Phe Gln Tyr Asn Ile Gly
 100 105 110

Leu Lys Thr Asn Asp Lys Tyr Val Ser Leu Ile Asn Tyr Leu Pro Lys
 115 120 125

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

Gly Gly Asn Gly Ser Phe Asn Tyr Ser Lys Ser Ile Ser Tyr Thr Gln
 145 150 155 160

Gln Asn Tyr Val Ser Glu Val Glu Gln Gln Asn Ser Lys Ser Val Leu
 165 170 175

Trp Gly Val Lys Ala Asn Ser Phe Ala Thr Glu Ser Gly Gln Lys Ser
 180 185 190

Ala Phe Asp Ser Asp Leu Phe Val Gly Tyr Lys Pro His Ser Lys Asp
 195 200 205

Pro Arg Asp Tyr Phe Val Pro Asp Ser Glu Leu Pro Pro Leu Val Gln
 210 215 220

Ser Gly Phe Asn Pro Ser Phe Ile Ala Thr Val Ser His Glu Lys Gly
 225 230 235 240

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

Val Thr His Ala Ile Lys Arg Ser Thr His Tyr Gly Asn Ser Tyr Leu
 260 265 270

Asp Gly His Arg Val His Asn Ala Phe Lys Asn Arg Asn Tyr Thr Val
 275 280 285

Lys Tyr Glu Val Asn Trp Lys Thr His Glu Ile Lys Val Lys Gly Gln
 290 295 300

Asn
 305

<210> 50

<211> 311

<212> PRT

<213> Artificial Sequence

<220>

<223> gamma-hemolysin component A amino acid sequence

<400> 50

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

Ala Pro Leu Ala Ser Pro Ile Gln Glu Ser Arg Ala Asn Thr Asn Ile
20 25 30

Glu Asn Ile Gly Asp Gly Ala Glu Val Ile Lys Arg Thr Glu Asp Val
35 40 45

Ser Ser Lys Lys Trp Gly Val Thr Gln Asn Val Gln Phe Asp Phe Val
50 55 60

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

Phe Ile Asn Ser Arg Thr Ser Phe Ser Asp Val Lys Gly Ser Gly Tyr
85 90 95

Glu Leu Thr Lys Arg Met Ile Trp Pro Phe Gln Tyr Asn Ile Gly Leu
100 105 110

Thr Thr Lys Asp Pro Asn Val Ser Leu Ile Asn Tyr Leu Pro Lys Asn
115 120 125

Lys Ile Glu Thr Thr Asp Val Gly Gln Thr Leu Gly Tyr Asn Ile Gly
130 135 140

Gly Asn Phe Gln Ser Ala Pro Ser Ile Gly Gly Asn Gly Ser Phe Asn
145 150 155 160

Tyr Ser Lys Thr Ile Ser Tyr Thr Gln Lys Ser Tyr Val Ser Glu Val
165 170 175

Asp Lys Gln Asn Ser Lys Ser Val Lys Trp Gly Val Lys Ala Asn Glu
180 185 190

Phe Val Thr Pro Asp Gly Lys Lys Ser Ala His Asp Arg Tyr Leu Phe
195 200 205

Val Gln Ser Pro Asn Gly Pro Ser Gly Ser Ala Arg Glu Tyr Phe Val
210 215 220

Pro Asp Asn Gln Leu Pro Pro Leu Val Gln Ser Gly Phe Asn Pro Ser
225 230 235 240

Phe Ile Thr Thr Leu Ser His Glu Lys Gly Ser Ser Asp Thr Ser Glu
245 250 255

Phe Glu Ile Ser Tyr Gly Arg Asn Leu Asp Ile Thr Tyr Ala Thr Leu
260 265 270

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

Asn Arg Asn Phe Val Val Arg Tyr Glu Val Asn Trp Lys Thr His Glu
290 295 300

Ile Lys Val Lys Gly His Asn

305 310

<210> 51

<211> 314

<212> PRT

<213> Artificial Sequence

<220>

<223> Leukotoxin S-subunit amino acid sequence

<400> 51

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

Gly Leu Ile Ala Pro Leu Ala Ser Pro Ile Gln Glu Ser Arg Ala Asn
20 25 30

Thr Asn Ile Glu Asn Ile Gly Asp Gly Ala Glu Val Ile Lys Arg Thr
35 40 45

Glu Asp Val Ser Ser Lys Lys Trp Gly Val Thr Gln Asn Val Gln Phe
50 55 60

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

Met Gln Gly Phe Ile Asn Ser Arg Thr Ser Phe Ser Asp Val Lys Gly
85 90 95

Ser Gly Tyr Glu Leu Thr Lys Arg Met Ile Trp Pro Phe Gln Tyr Asn
100 105 110

Ile Gly Leu Thr Thr Lys Asp Pro Asn Val Ser Leu Ile Asn Tyr Leu
115 120 125

Pro Lys Asn Lys Ile Glu Thr Thr Asp Val Gly Gln Thr Leu Gly Tyr
130 135 140

Asn Ile Gly Gly Asn Phe Gln Ser Ala Pro Ser Ile Gly Gly Asn Gly
145 150 155 160

Ser Phe Asn Tyr Ser Lys Thr Ile Ser Tyr Thr Gln Lys Ser Tyr Val
165 170 175

Ser Glu Val Asp Lys Gln Asn Ser Lys Ser Val Lys Trp Gly Val Lys
180 185 190

Ala Asn Glu Phe Val Thr Pro Asp Gly Lys Lys Ser Ala His Asp Arg
195 200 205

Tyr Leu Phe Val Gln Ser Pro Asn Gly Pro Thr Gly Ser Ala Arg Glu
210 215 220

Tyr Phe Ala Pro Asp Asn Gln Leu Pro Pro Leu Val Gln Ser Gly Phe
225 230 235 240

Asn Pro Ser Phe Ile Thr Thr Leu Ser His Glu Lys Gly Ser Ser Asp
245 250 255

Thr Ser Glu Phe Glu Ile Ser Tyr Gly Arg Asn Leu Asp Ile Thr Tyr
260 265 270

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

Ala Phe Val Asn Arg Asn Phe Val Val Arg Tyr Glu Val Asn Trp Lys
290 295 300

Thr His Glu Ile Lys Val Lys Gly His Asn
305 310

<210> 52

<211> 311

<212> PRT

<213> Artificial Sequence

<220>

<223> Leukotoxin S-subunit amino acid sequence

<400> 52

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

Ala Pro Leu Ala Ser Pro Ile Gln Glu Ser Arg Ala Asn Thr Asn Ile
20 25 30

Glu Asn Ile Gly Asp Gly Ala Glu Val Ile Lys Arg Thr Glu Asp Val
35 40 45

Ser Ser Lys Lys Trp Gly Val Thr Gln Asn Val Gln Phe Asp Phe Val
50 55 60

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

Phe Ile Asn Ser Arg Thr Ser Phe Ser Asp Val Lys Gly Ser Gly Tyr
85 90 95

Glu Leu Thr Lys Arg Met Ile Trp Pro Phe Gln Tyr Asn Ile Gly Leu
100 105 110

Thr Thr Lys Asp Pro Asn Val Ser Leu Ile Asn Tyr Leu Pro Lys Asn
115 120 125

Lys Ile Glu Thr Thr Asp Val Gly Gln Thr Leu Gly Tyr Asn Ile Gly
130 135 140

Gly Asn Phe Gln Ser Ala Pro Ser Ile Gly Gly Asn Gly Ser Phe Asn
145 150 155 160

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170          180          190          200

Tyr Ser Lys Thr Ile Ser Tyr Thr Gln Lys Ser Tyr Val Ser Glu Val
      165          170          175

Asp Lys Gln Asn Ser Lys Ser Val Lys Trp Gly Val Lys Ala Asn Glu
      180          185          190

Phe Val Thr Pro Asp Gly Lys Lys Ser Ala His Asp Arg Tyr Leu Phe
      195          200          205

Val Gln Ser Pro Asn Gly Pro Thr Gly Ser Ala Arg Glu Tyr Phe Ala
      210          215          220

Pro Asp Asn Gln Leu Pro Pro Leu Val Gln Ser Gly Phe Asn Pro Ser
      225          230          235          240

Phe Ile Thr Thr Leu Ser His Glu Lys Gly Ser Ser Asp Thr Ser Glu
      245          250          255

Phe Glu Ile Ser Tyr Gly Arg Asn Leu Asp Ile Thr Tyr Ala Thr Leu
      260          265          270

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

Asn Arg Asn Phe Val Val Arg Tyr Glu Val Asn Trp Lys Thr His Glu
      290          295          300

Ile Lys Val Lys Gly His Asn

305          310

<210> 53
<211> 311
<212> PRT
<213> Artificial Sequence

<220>
<223> Leukocidin LukE precursor amino acid sequence

<400> 53
Met Phe Lys Lys Lys Met Leu Ala Ala Thr Leu Ser Val Gly Leu Ile
1          5          10          15

Ala Pro Leu Ala Ser Pro Ile His Glu Ser Arg Ala Asn Thr Asn Ile
      20          25          30

Glu Asn Ile Gly Asp Gly Ala Glu Val Ile Lys Arg Thr Glu Asp Val
      35          40          45

Ser Ser Lys Lys Trp Gly Val Thr Gln Asn Val Gln Phe Asp Phe Val
      50          55          60

Lys Asp Lys Lys Tyr Asn Lys Asp Ala Leu Ile Val Lys Met Gln Gly

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65		70		75		80									
Phe	Ile	Asn	Ser	Arg	Thr	Ser	Phe	Ser	Asp	Val	Lys	Gly	Ser	Gly	Tyr
				85					90					95	
Glu	Leu	Thr	Lys	Arg	Met	Ile	Trp	Pro	Phe	Gln	Tyr	Asn	Ile	Gly	Leu
			100					105					110		
Met	Thr	Lys	Asp	Pro	Asn	Val	Ser	Leu	Ile	Asn	Tyr	Leu	Pro	Lys	Asn
		115					120					125			
Lys	Ile	Glu	Thr	Thr	Asp	Val	Gly	Gln	Thr	Leu	Gly	Tyr	Asn	Ile	Gly
	130					135					140				
Gly	Asn	Phe	Gln	Ser	Ala	Pro	Ser	Ile	Gly	Gly	Asn	Gly	Ser	Phe	Asn
145					150					155					160
Tyr	Ser	Lys	Thr	Ile	Ser	Tyr	Thr	Gln	Lys	Ser	Tyr	Val	Ser	Glu	Val
				165					170					175	
Asp	Lys	Gln	Asn	Ser	Lys	Ser	Val	Lys	Trp	Gly	Val	Lys	Ala	Asn	Glu
			180					185					190		
Phe	Val	Thr	Pro	Asp	Gly	Lys	Lys	Ser	Ala	His	Asp	Arg	Tyr	Leu	Phe
		195					200					205			
Val	Gln	Ser	Pro	Asn	Gly	Pro	Ser	Gly	Ser	Ala	Arg	Glu	Tyr	Phe	Ala
	210					215					220				
Pro	Asp	Asn	Gln	Leu	Pro	Pro	Leu	Ile	Gln	Ser	Gly	Phe	Asn	Pro	Ser
225					230					235					240
Phe	Ile	Thr	Thr	Ile	Ser	His	Glu	Lys	Gly	Thr	Ser	Glu	Thr	Ser	Glu
				245					250					255	
Phe	Glu	Ile	Ser	Tyr	Gly	Arg	Asn	Leu	Asp	Ile	Thr	Tyr	Ala	Thr	Leu
			260					265					270		
Phe	Pro	Arg	Thr	Gly	Ile	Tyr	Ala	Glu	Arg	Lys	His	Asn	Ala	Phe	Val
		275					280					285			
Asn	Arg	Asn	Phe	Val	Val	Arg	Tyr	Glu	Val	Asn	Trp	Lys	Thr	His	Glu
	290					295					300				
Ile	Lys	Val	Lys	Gly	His	Asn									
305					310										

<210> 54

<211> 311

<212> PRT

<213> Artificial Sequence

<220>

<223> LukNS amino acid sequence

<400> 54

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

Ala Pro Leu Ala Ser Pro Ile Gln Glu Ser Arg Ala Asn Thr Asn Ile
 20 25 30

Glu Asn Ile Gly Asp Gly Ala Glu Val Ile Lys Arg Thr Glu Asp Val
 35 40 45

Ser Ser Lys Lys Trp Gly Val Thr Gln Asn Val Gln Phe Asp Phe Val
 50 55 60

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

Phe Ile Asn Ser Arg Thr Ser Phe Ser Asp Val Lys Gly Ser Gly Tyr
 85 90 95

Glu Leu Thr Lys Arg Met Ile Trp Pro Phe Gln Tyr Asn Ile Gly Leu
 100 105 110

Thr Thr Lys Asp Pro Asn Val Ser Leu Ile Asn Tyr Leu Pro Lys Asn
 115 120 125

Lys Ile Glu Thr Thr Asp Val Gly Gln Thr Leu Gly Tyr Asn Ile Gly
 130 135 140

Gly Asn Phe Gln Ser Ala Pro Ser Ile Gly Gly Asn Gly Ser Phe Asn
 145 150 155 160

Tyr Ser Lys Thr Ile Ser Tyr Thr Gln Lys Ser Tyr Val Ser Glu Val
 165 170 175

Asp Lys Gln Asn Ser Lys Ser Val Lys Trp Gly Val Lys Ala Asn Glu
 180 185 190

Phe Val Thr Pro Asp Gly Lys Lys Ser Ala His Asp Arg Tyr Leu Phe
 195 200 205

Val Gln Ser Pro Asn Gly Pro Thr Gly Ser Ala Arg Glu Tyr Phe Ala
 210 215 220

Pro Asp Asn Gln Leu Pro Pro Leu Val Gln Ser Gly Phe Asn Pro Ser
 225 230 235 240

Phe Ile Thr Thr Leu Ser His Glu Lys Gly Ser Ser Asp Thr Ser Glu
 245 250 255

Phe Glu Ile Ser Tyr Gly Arg Asn Leu Asp Ile Thr Tyr Ala Thr Leu
 260 265 270

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

Asn Asp Asn Phe Val Val Asn Thr Gln Val Asn Thr Lys Thr His Glu

Asn Arg Asn Phe Val Val Arg Tyr Glu Val Asn Leu Lys Thr His Glu
290 295 300

Ile Lys Val Lys Gly His Asn
305 310

<210> 55

<211> 311

<212> PRT

<213> Artificial Sequence

<220>

<223> Leukocidin/Hemolysin toxin family protein amino acid sequence

<400> 55

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

Ala Pro Leu Ala Ser Pro Ile Gln Glu Ser Arg Ala Asn Thr Asn Ile
20 25 30

Glu Asn Ile Gly Asp Gly Ala Glu Val Ile Lys Arg Thr Glu Asp Val
35 40 45

Ser Ser Lys Lys Trp Gly Val Thr Gln Asn Val Gln Phe Asp Phe Val
50 55 60

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

Phe Ile Asn Ser Arg Thr Ser Phe Ser Asp Val Lys Gly Ser Gly Tyr
85 90 95

Glu Leu Thr Lys Arg Met Ile Trp Pro Phe Gln Tyr Asn Ile Gly Leu
100 105 110

Thr Thr Lys Asp Pro Asn Val Ser Leu Ile Asn Tyr Leu Pro Lys Asn
115 120 125

Lys Ile Glu Thr Thr Asp Val Gly Gln Thr Leu Gly Tyr Asn Ile Gly
130 135 140

Gly Asn Phe Gln Ser Ala Pro Ser Ile Gly Gly Asn Gly Ala Phe Asn
145 150 155 160

Tyr Ser Lys Thr Ile Ser Tyr Thr Gln Lys Ser Tyr Val Ser Glu Val
165 170 175

Asp Lys Gln Asn Ser Lys Ser Val Lys Trp Gly Val Lys Ala Asn Glu
180 185 190

Phe Val Thr Pro Asp Gly Lys Lys Ser Ala His Asp Arg Tyr Leu Phe
195 200 205

Val Gln Ser Pro Asn Gly Pro Ser Gly Ser Ala Arg Glu Tyr Phe Ala
210 215 220

210 215 220
 Pro Asp Asn Gln Leu Pro Pro Leu Val Gln Ser Gly Phe Asn Pro Ser
 225 230 235 240
 Phe Ile Thr Thr Leu Ser His Glu Lys Gly Ser Ser Asp Thr Ser Glu
 245 250 255
 Phe Glu Ile Ser Tyr Gly Arg Asn Leu Asp Ile Thr Tyr Ala Thr Leu
 260 265 270
 Phe Pro Arg Thr Gly Ile Tyr Ala Glu Arg Lys His Asn Ala Phe Val
 275 280 285
 Asn Arg Asn Phe Val Val Arg Tyr Glu Val Asn Trp Lys Thr His Glu
 290 295 300
 Ile Lys Val Lys Gly His Asn
 305 310
 <210> 56
 <211> 311
 <212> PRT
 <213> Artificial Sequence
 <220>
 <223> Leukotoxin E-subunit amino acid sequence
 <400> 56
 Met Phe Lys Lys Lys Met Leu Ala Ala Thr Leu Ser Val Gly Leu Ile
 1 5 10 15
 Ala Pro Leu Ala Ser Pro Ile Gln Glu Ser Arg Ala Asn Thr Asn Ile
 20 25 30
 Glu Asn Ile Gly Asp Gly Ala Glu Val Ile Lys Arg Thr Glu Asp Val
 35 40 45
 Ser Ser Lys Lys Trp Gly Val Thr Gln Asn Val Gln Phe Asp Phe Val
 50 55 60
 Lys Asp Lys Lys Tyr Asn Lys Asp Ala Leu Ile Val Lys Met Gln Gly
 65 70 75 80
 Phe Ile Asn Ser Arg Thr Ser Phe Ser Asp Val Lys Gly Ser Gly Tyr
 85 90 95
 Glu Leu Thr Lys Arg Met Ile Trp Pro Phe Gln Tyr Asn Ile Gly Leu
 100 105 110
 Ser Thr Lys Asp Pro Tyr Val Ser Leu Ile Asn Tyr Leu Pro Lys Asn
 115 120 125
 Lys Ile Glu Thr Thr Asp Val Gly Gln Thr Leu Gly Tyr Asn Ile Gly
 130 135 140

Gly Asn Phe Gln Ser Ala Pro Ser Ile Gly Gly Asn Gly Ser Phe Asn
 145 150 155 160

Tyr Ser Lys Thr Ile Ser Tyr Thr Gln Lys Ser Tyr Val Ser Glu Val
 165 170 175

Asp Lys Gln Asn Ser Lys Ser Val Lys Trp Gly Val Lys Ala Asn Ala
 180 185 190

Phe Val Thr Pro Asp Gly Lys Lys Ser Ala His Asp Arg Tyr Leu Phe
 195 200 205

Val Gln Ser Pro Asn Gly Pro Ser Gly Ser Ala Arg Glu Tyr Phe Val
 210 215 220

Pro Asp Asn Gln Leu Pro Pro Leu Val Gln Ser Gly Phe Asn Pro Ser
 225 230 235 240

Phe Ile Thr Thr Leu Ser His Glu Lys Gly Ser Ser Asp Thr Ser Glu
 245 250 255

Phe Glu Ile Ser Tyr Gly Arg Asn Leu Asp Ile Thr Tyr Ala Thr Leu
 260 265 270

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

Asn Arg Asn Phe Val Val Arg Tyr Glu Val Asn Trp Lys Thr His Glu
 290 295 300

Ile Lys Val Lys Gly His Asn
 305 310

<210> 57

<211> 311

<212> PRT

<213> Artificial Sequence

<220>

<223> Leukotoxin S-subunit amino acid sequence

<400> 57

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

Ala Pro Leu Ala Ser Pro Ile Gln Glu Ser Arg Ala Asn Thr Asn Ile
 20 25 30

Glu Asn Ile Gly Asp Gly Ala Glu Val Ile Lys Arg Thr Glu Asp Val
 35 40 45

Ser Ser Lys Lys Trp Gly Val Thr Gln Asn Val Gln Phe Asp Phe Val
 50 55 60

Lys Asp Lys Lys Tyr Asn Lys Asp Ala Leu Ile Val Lys Met Gln Gly
 65 70 75 80
 Phe Ile Asn Ser Arg Thr Ser Phe Ser Asp Val Lys Gly Ser Gly Tyr
 85 90 95
 Glu Leu Thr Lys Arg Met Ile Trp Pro Phe Gln Tyr Asn Ile Gly Leu
 100 105 110
 Thr Thr Lys Asp Pro Asn Val Ser Leu Ile Asn Tyr Leu Pro Lys Asn
 115 120 125
 Lys Ile Glu Thr Thr Asp Val Gly Gln Thr Leu Gly Tyr Asn Ile Gly
 130 135 140
 Gly Asn Phe Gln Ser Ala Pro Ser Ile Gly Gly Asn Gly Ser Phe Asn
 145 150 155 160
 Tyr Ser Lys Thr Ile Ser Tyr Thr Gln Lys Ser Tyr Val Ser Glu Val
 165 170 175
 Asp Lys Gln Asn Ser Lys Ser Val Lys Trp Gly Val Lys Ala Asn Glu
 180 185 190
 Phe Val Thr Pro Asp Gly Lys Lys Ser Ala His Asp Arg Tyr Leu Phe
 195 200 205
 Val Gln Ser Pro Asn Gly Pro Thr Gly Ser Ala Arg Glu Tyr Phe Ala
 210 215 220
 Pro Asp Asn Gln Leu Pro Pro Leu Val Gln Ser Gly Phe Asn Pro Ser
 225 230 235 240
 Phe Ile Thr Thr Leu Ser His Glu Arg Gly Ser Ser Asp Thr Ser Glu
 245 250 255
 Phe Glu Ile Ser Tyr Gly Arg Asn Leu Asp Ile Thr Tyr Ala Thr Leu
 260 265 270
 Phe Pro Arg Thr Gly Ile Tyr Ala Glu Arg Lys His Asn Ala Phe Val
 275 280 285
 Asn Arg Asn Phe Val Val Arg Tyr Glu Val Asn Trp Lys Thr His Glu
 290 295 300
 Ile Lys Val Lys Gly His Asn
 305 310

<210> 58

<211> 311

<212> PRT

<213> Artificial Sequence

<220>

<223> Beta-channel forming cytolysin amino acid sequence

<400> 58

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

Ala Pro Leu Ala Ser Pro Ile Gln Glu Ser Arg Ala Asn Thr Asn Ile
      20           25           30

Glu Asn Ile Gly Asp Gly Ala Glu Val Ile Lys Arg Thr Glu Asp Val
      35           40           45

Ser Ser Lys Lys Trp Gly Val Thr Gln Asn Val Gln Phe Asp Phe Val
 50           55           60

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

Phe Ile Asn Ser Arg Thr Ser Phe Ser Asp Val Lys Gly Ser Gly Tyr
      85           90           95

Glu Leu Thr Lys Arg Met Ile Trp Pro Phe Gln Tyr Asn Ile Gly Leu
      100          105          110

Thr Thr Lys Asp Pro Asn Val Ser Leu Ile Asn Tyr Leu Pro Lys Asn
115           120           125

Lys Ile Glu Thr Thr Asp Val Gly Gln Thr Leu Gly Tyr Asn Ile Gly
130           135          140

Gly Asn Phe Gln Ser Ala Pro Ser Ile Gly Gly Asn Gly Ser Phe Asn
145           150          155          160

Tyr Ser Lys Thr Ile Ser Tyr Thr Gln Lys Ser Tyr Val Ser Glu Val
      165           170           175

Asp Lys Gln Asn Ser Lys Ser Val Lys Trp Gly Ala Lys Ala Asn Glu
180           185          190

Phe Val Thr Pro Asp Gly Lys Lys Ser Ala His Asp Arg Tyr Leu Phe
195           200          205

Val Gln Ser Pro Asn Gly Pro Thr Gly Ser Ala Arg Glu Tyr Phe Ala
210           215          220

Pro Asp Asn Gln Leu Pro Pro Leu Val Gln Ser Gly Phe Asn Pro Ser
225           230          235          240

Phe Ile Thr Thr Leu Ser His Glu Lys Gly Ser Ser Asp Thr Ser Glu
245           250          255

Phe Glu Ile Ser Tyr Gly Arg Asn Leu Asp Ile Thr Tyr Ala Thr Leu
260           265          270

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

Asn Arg Asn Phe Val Val Arg Tyr Glu Val Asn Trp Lys Thr His Glu
 290 295 300

Ile Lys Val Lys Gly His Asn
 305 310

<210> 59

<211> 311

<212> PRT

<213> Artificial Sequence

<220>

<223> Gamma-hemolysin component A amino acid sequence

<400> 59

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

Ala Pro Leu Ala Ser Pro Ile Gln Glu Ser Arg Ala Asn Thr Asn Ile
 20 25 30

Glu Asn Ile Gly Asp Gly Ala Glu Val Ile Lys Arg Thr Glu Asp Val
 35 40 45

Ser Ser Lys Lys Trp Gly Val Thr Gln Asn Val Gln Phe Asp Phe Val
 50 55 60

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

Phe Ile Asn Ser Arg Thr Ser Phe Ser Asp Val Lys Gly Ser Gly Tyr
 85 90 95

Glu Leu Thr Lys Arg Met Ile Trp Pro Phe Gln Tyr Asn Ile Gly Leu
 100 105 110

Thr Thr Lys Asp Pro Asn Val Ser Leu Ile Asn Tyr Leu Pro Lys Asn
 115 120 125

Lys Ile Glu Thr Thr Asp Val Gly Gln Thr Leu Gly Tyr Asn Ile Gly
 130 135 140

Gly Asn Phe Gln Ser Ala Pro Ser Ile Ala Gly Asn Gly Ser Phe Asn
 145 150 155 160

Tyr Ser Lys Thr Ile Ser Tyr Thr Gln Lys Ser Tyr Val Ser Glu Val
 165 170 175

Asp Lys Gln Asn Ser Lys Ser Val Lys Trp Gly Val Lys Ala Asn Glu
 180 185 190

Phe Val Thr Pro Asp Gly Lys Lys Ser Ala His Asp Arg Tyr Leu Phe
 195 200 205 210 215

195 200 205
 Val Gln Ser Pro Asn Gly Pro Thr Gly Ser Ala Arg Glu Tyr Phe Ala
 210 215 220

 Pro Asp Asn Gln Leu Pro Pro Leu Val Gln Ser Gly Phe Asn Pro Ser
 225 230 235 240

 Phe Ile Thr Thr Leu Ser His Glu Lys Gly Ser Ser Asp Thr Ser Glu
 245 250 255

 Phe Glu Ile Ser Tyr Gly Arg Asn Leu Asp Ile Thr Tyr Ala Thr Leu
 260 265 270

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

 Asn Arg Asn Phe Val Val Arg Tyr Glu Val Asn Trp Lys Thr His Glu
 290 295 300

 Ile Lys Val Lys Gly His Asn

 305 310

 <210> 60
 <211> 311
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> Leukotoxin E-subunit amino acid sequence

 <400> 60
 Met Phe Lys Lys Lys Met Leu Ala Ala Thr Leu Ser Val Gly Leu Ile
 1 5 10 15

 Ala Pro Leu Ala Ser Pro Ile Gln Glu Ser Arg Ala Asn Thr Asn Ile
 20 25 30

 Glu Asn Ile Gly Asp Gly Ala Glu Val Ile Lys Arg Thr Glu Gly Val
 35 40 45

 Ser Ser Lys Lys Trp Gly Val Thr Gln Asn Val Gln Phe Asp Phe Val
 50 55 60

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

 Phe Ile Asn Ser Arg Thr Ser Phe Ser Asp Val Lys Gly Ser Gly Tyr
 85 90 95

 Glu Leu Thr Lys Arg Met Ile Trp Pro Phe Gln Tyr Asn Ile Gly Leu
 100 105 110

 Thr Thr Lys Asp Pro Asn Val Ser Leu Ile Asn Trp Leu Pro Lys Asn

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115          120          125

Lys Ile Glu Thr Thr Asp Val Gly Gln Thr Leu Gly Tyr Asn Ile Gly
130          135          140

Gly Asn Phe Gln Ser Ala Pro Ser Ile Gly Gly Asn Gly Ser Phe Asn
145          150          155          160

Tyr Ser Lys Thr Ile Ser Tyr Thr Gln Lys Ser Tyr Val Ser Glu Val
165          170          175

Asp Lys Gln Asn Ser Lys Ser Val Lys Trp Gly Val Lys Ala Asn Glu
180          185          190

Phe Val Thr Pro Asp Gly Lys Lys Ser Ala His Asp Arg Tyr Leu Phe
195          200          205

Val Gln Ser Pro Asn Gly Pro Ser Gly Ser Ala Arg Glu Tyr Phe Ala
210          215          220

Pro Asp Asn Gln Leu Pro Pro Leu Val Gln Ser Gly Phe Asn Pro Ser
225          230          235          240

Phe Ile Thr Thr Leu Ser His Glu Lys Gly Ser Ser Asp Thr Ser Glu
245          250          255

Phe Glu Ile Ser Tyr Gly Arg Asn Leu Asp Ile Thr Tyr Ala Thr Leu
260          265          270

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

Asn Arg Asn Phe Val Val Arg Tyr Glu Val Asn Trp Lys Thr His Glu
290          295          300

Ile Lys Val Lys Gly His Asn
305          310

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<210> 61

<211> 249

<212> PRT

<213> Artificial Sequence

<220>

<223> Leukotoxin S-subunit amino acid sequence

<400> 61

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Met Lys Asp Lys Lys Tyr Asn Lys Asp Ala Leu Ile Leu Lys Met Gln
1          5          10          15

Gly Phe Ile Ser Ser Arg Thr Thr Tyr Tyr Asn Tyr Lys Lys Thr Asn
20          25          30

His Val Lys Ala Met Arg Trp Pro Phe Gln Tyr Asn Ile Gly Leu Lys
35          40          45

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Thr Asn Asp Lys Tyr Val Ser Leu Ile Asn Tyr Leu Pro Lys Asn Lys
50 55 60

Ile Glu Ser Thr Asn Val Ser Gln Thr Leu Gly Tyr Asn Ile Gly Gly
65 70 75 80

Asn Phe Gln Ser Ala Pro Ser Leu Gly Gly Asn Gly Ser Phe Asn Tyr
85 90 95

Ser Lys Ser Ile Ser Tyr Thr Gln Gln Asn Tyr Val Ser Glu Val Glu
100 105 110

Gln Gln Asn Ser Lys Ser Val Leu Trp Gly Val Lys Ala Asn Ser Phe
115 120 125

Ala Thr Glu Ser Gly Gln Lys Ser Ala Phe Asp Ser Asp Leu Phe Val
130 135 140

Gly Tyr Lys Pro His Ser Lys Asp Pro Arg Asp Tyr Phe Val Pro Asp
145 150 155 160

Ser Glu Leu Pro Pro Leu Val Gln Ser Gly Phe Asn Pro Ser Phe Ile
165 170 175

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

Ile Thr Tyr Gly Arg Asn Met Asp Val Thr His Ala Ile Lys Arg Ser
195 200 205

Thr His Tyr Gly Asn Ser Tyr Leu Asp Gly His Arg Val His Asn Ala
210 215 220

Phe Val Asn Arg Asn Tyr Thr Val Lys Tyr Glu Val Asn Trp Lys Thr
225 230 235 240

His Glu Ile Lys Val Lys Gly Gln Asn
245

<210> 62

<211> 306

<212> PRT

<213> Artificial Sequence

<220>

<223> Leukotoxin S-subunit amino acid sequence

<400> 62

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

Pro Ile Gln Glu Ser Arg Ala Asn Thr Asn Ile Glu Asn Ile Gly Asp
20 25 30

Gly Ala Glu Val Ile Lys Arg Thr Glu Asp Val Ser Ser Lys Lys Trp
 35 40 45
 Gly Val Thr Gln Asn Val Gln Phe Asp Phe Val Lys Asp Lys Lys Tyr
 50 55 60
 Asn Lys Asp Ala Leu Ile Val Lys Met Gln Gly Phe Ile Asn Ser Arg
 65 70 75 80
 Thr Ser Phe Ser Asp Val Lys Gly Ser Gly Tyr Glu Leu Thr Lys Arg
 85 90 95
 Met Ile Trp Pro Phe Gln Tyr Asn Ile Gly Leu Thr Thr Lys Asp Pro
 100 105 110
 Asn Val Ser Leu Ile Asn Tyr Leu Pro Lys Asn Lys Ile Glu Thr Thr
 115 120 125
 Asp Val Gly Gln Thr Leu Gly Tyr Asn Ile Gly Gly Asn Phe Gln Ser
 130 135 140
 Ala Pro Ser Ile Gly Gly Asn Gly Ser Phe Asn Tyr Ser Lys Thr Ile
 145 150 155 160
 Ser Tyr Thr Gln Lys Ser Tyr Val Ser Glu Val Asp Lys Gln Asn Ser
 165 170 175
 Lys Ser Val Lys Trp Gly Val Lys Ala Asn Glu Phe Val Thr Pro Asp
 180 185 190
 Gly Lys Lys Ser Ala His Asp Arg Tyr Leu Phe Val Gln Ser Pro Asn
 195 200 205
 Gly Pro Thr Gly Ser Ala Arg Glu Tyr Phe Ala Pro Asp Asn Gln Leu
 210 215 220
 Pro Pro Leu Val Gln Ser Gly Phe Asn Pro Ser Phe Ile Thr Thr Leu
 225 230 235 240
 Ser His Glu Lys Gly Ser Ser Asp Thr Ser Glu Phe Glu Ile Ser Tyr
 245 250 255
 Gly Arg Asn Leu Asp Ile Thr Tyr Ala Thr Leu Phe Pro Arg Thr Gly
 260 265 270
 Ile Tyr Ala Glu Arg Lys His Asn Ala Phe Val Asn Arg Asn Phe Val
 275 280 285
 Val Arg Tyr Glu Val Asn Trp Lys Thr His Glu Ile Lys Val Lys Gly
 290 295 300
 His Asn
 305

<211> 306

<212> PRT

<213> Artificial Sequence

<220>

<223> Leukotoxin E-subunit amino acid sequence

<400> 63

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

Pro Ile Gln Glu Ser Arg Ala Asn Thr Asn Ile Glu Asn Ile Gly Asp
 20 25 30

Gly Ala Glu Val Ile Lys Arg Thr Glu Asp Val Ser Ser Lys Lys Trp
 35 40 45

Gly Val Thr Gln Asn Val Gln Phe Asp Phe Val Lys Asp Lys Lys Tyr
 50 55 60

Asn Lys Asp Ala Leu Ile Val Lys Met Gln Gly Phe Ile Asn Ser Arg
 65 70 75 80

Thr Ser Phe Ser Asp Val Lys Gly Ser Gly Tyr Glu Leu Thr Lys Arg
 85 90 95

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

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

Asp Val Gly Gln Thr Leu Gly Tyr Asn Ile Gly Gly Asn Phe Gln Ser
 130 135 140

Ala Pro Ser Ile Gly Gly Asn Gly Ser Phe Asn Tyr Ser Lys Thr Ile
 145 150 155 160

Ser Tyr Thr Gln Lys Ser Tyr Val Ser Glu Val Asp Lys Gln Asn Ser
 165 170 175

Lys Ser Val Lys Trp Gly Val Lys Ala Asn Ala Phe Val Thr Pro Asp
 180 185 190

Gly Lys Lys Ser Ala His Asp Arg Tyr Leu Phe Val Gln Ser Pro Asn
 195 200 205

Gly Pro Ser Gly Ser Ala Arg Glu Tyr Phe Val Pro Asp Asn Gln Leu
 210 215 220

Pro Pro Leu Val Gln Ser Gly Phe Asn Pro Ser Phe Ile Thr Thr Leu
 225 230 235 240

Ser His Glu Lys Gly Ser Ser Asp Thr Ser Glu Phe Glu Ile Ser Tyr
 245 250 255

Gly Arg Asn Leu Asp Ile Thr Tyr Ala Thr Leu Phe Pro Arg Thr Gly
 260 265 270

Ile Tyr Ala Glu Arg Lys His Asn Ala Phe Val Asn Arg Asn Phe Val
 275 280 285

Val Arg Tyr Glu Val Asn Trp Lys Thr His Glu Ile Lys Val Lys Gly
 290 295 300

His Asn
 305

<210> 64

<211> 306

<212> PRT

<213> Artificial Sequence

<220>

<223> Gamma-hemolysin component A amino acid sequence

<400> 64

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

Pro Ile Gln Glu Ser Arg Ala Asn Thr Asn Ile Glu Asn Ile Gly Asp
 20 25 30

Gly Ala Glu Val Ile Lys Arg Met Glu Asp Val Ser Ser Lys Lys Trp
 35 40 45

Gly Val Thr Gln Asn Val Gln Phe Asp Phe Val Lys Asp Lys Lys Tyr
 50 55 60

Asn Lys Asp Ala Leu Ile Val Lys Met Gln Gly Phe Ile Asn Ser Arg
 65 70 75 80

Thr Ser Phe Ser Asp Val Lys Gly Ser Gly Tyr Glu Leu Thr Lys Arg
 85 90 95

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

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

Asp Val Gly Gln Thr Leu Gly Tyr Asn Ile Gly Gly Asn Phe Gln Ser
 130 135 140

Ala Pro Ser Ile Gly Gly Asn Gly Ser Phe Asn Tyr Ser Lys Thr Ile
 145 150 155 160

Ser Tyr Thr Gln Lys Ser Tyr Val Ser Glu Val Asp Lys Gln Asn Ser

165 170 175
 Lys Ser Val Lys Trp Gly Val Lys Ala Asn Glu Phe Val Thr Pro Asp
 180 185 190
 Gly Lys Lys Ser Ala His Asp Arg Tyr Leu Phe Val Gln Ser Pro Asn
 195 200 205
 Gly Pro Ser Gly Ser Ala Arg Glu Tyr Phe Ala Pro Asp Asn Gln Leu
 210 215 220
 Pro Pro Leu Val Gln Ser Gly Phe Asn Pro Ser Phe Ile Thr Thr Leu
 225 230 235 240
 Ser His Glu Lys Gly Ser Ser Asp Thr Ser Glu Phe Glu Ile Ser Tyr
 245 250 255
 Gly Arg Asn Leu Asp Ile Thr Tyr Ala Thr Leu Phe Pro Arg Thr Gly
 260 265 270
 Ile Tyr Ala Glu Arg Lys His Asn Ala Phe Val Asn Arg Asn Phe Val
 275 280 285
 Val Arg Tyr Glu Val Asn Trp Lys Thr His Glu Ile Lys Val Lys Gly
 290 295 300

His Asn
305

<210> 65

<211> 306

<212> PRT

<213> Artificial Sequence

<220>

<223> Gamma-hemolysin component A amino acid sequence

<400> 65

Met Leu Ala Ala Thr Leu Ser Val Gly Leu Ile Ala Pro Leu Ala Ser
 1 5 10 15
 Pro Ile His Glu Ser Arg Ala Asn Thr Asn Ile Glu Asn Ile Gly Asp
 20 25 30
 Gly Ala Glu Val Ile Lys Arg Thr Glu Asp Val Ser Ser Lys Lys Trp
 35 40 45
 Gly Val Thr Gln Asn Val Gln Phe Asp Phe Val Lys Asp Lys Lys Tyr
 50 55 60
 Asn Lys Asp Ala Leu Ile Val Lys Met Gln Gly Phe Ile Asn Ser Arg
 65 70 75 80
 Thr Ser Phe Ser Asp Val Lys Gly Ser Gly Tyr Glu Leu Thr Lys Arg
 85 90 95

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

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

Asp Val Gly Gln Thr Leu Gly Tyr Asn Ile Gly Gly Asn Phe Gln Ser
 130 135 140

Ala Pro Ser Ile Gly Gly Asn Gly Ser Phe Asn Tyr Ser Lys Thr Ile
 145 150 155 160

Ser Tyr Thr Gln Lys Ser Tyr Val Ser Glu Val Asp Lys Gln Asn Ser
 165 170 175

Lys Ser Val Lys Trp Gly Val Lys Ala Asn Glu Phe Val Thr Pro Asp
 180 185 190

Gly Lys Lys Ser Ala Gln Asp Arg Tyr Leu Phe Val Gln Ser Pro Asn
 195 200 205

Gly Pro Ser Gly Ser Ala Arg Glu Tyr Phe Ala Pro Asp Asn Gln Leu
 210 215 220

Pro Pro Leu Val Gln Ser Gly Phe Asn Pro Ser Phe Ile Thr Thr Leu
 225 230 235 240

Ser His Glu Lys Gly Ser Ser Asp Thr Ser Glu Phe Glu Ile Ser Tyr
 245 250 255

Gly Arg Asn Leu Asp Ile Thr Tyr Ala Thr Leu Phe Pro Arg Thr Gly
 260 265 270

Ile Tyr Ala Glu Arg Lys His Asn Ala Phe Val Asn Arg Asn Phe Val
 275 280 285

Val Arg Tyr Glu Val Asn Trp Lys Thr His Glu Ile Lys Val Lys Gly
 290 295 300

His Asn
 305

<210> 66

<211> 308

<212> PRT

<213> Artificial Sequence

<220>

<223> Leukocidin chain lukM precursor amino acid sequence

<400> 66

Met Phe Lys Arg Lys Leu Leu Val Thr Thr Leu Ser Leu Gly Leu Ile

1	5	10	15
Val Pro Ile Ala Thr Pro Phe Gln Gly Ser Lys Ala Thr Thr Asn Ala	20	25	30
Glu Asp Ile Gly Asp Asp Ala Glu Val Ile Lys Arg Thr Glu Asp Val	35	40	45
Ser Ser Arg Lys Trp Gly Val Thr Gln Asn Val Gln Phe Asp Phe Val	50	55	60
Lys Asp Lys Lys Tyr Asn Lys Asp Ala Leu Ile Ile Lys Met Gln Gly	65	70	75
Phe Ile Asn Ser Arg Thr Thr Phe Asn Asp Val Lys Gln Asn Arg Ala	85	90	95
Asn Lys Arg Met Val Trp Pro Phe Gln Tyr Asn Ile Gly Leu Thr Ser	100	105	110
Lys Asp Gln Asn Thr Ser Leu Ile Asn Tyr Leu Pro Lys Asn Lys Ile	115	120	125
Glu Thr Val Asp Val Gly Gln Thr Leu Gly Tyr Asn Ile Gly Gly Lys	130	135	140
Phe Gln Ser Ala Pro Ser Ile Gly Gly Asn Gly Ser Phe Asn Tyr Ser	145	150	155
Lys Ser Ile Lys Tyr Ser Gln Lys Ser Tyr Val Ser Glu Val Glu Gln	165	170	175
Gln Ser Ser Lys Thr Ile Lys Trp Gly Val Lys Ala Asn Ser Phe Val	180	185	190
Ile Ala Gly His Arg Trp Ser Ala Tyr Asp Glu Leu Leu Phe Ile Arg	195	200	205
Asn Thr Thr Arg Gly Pro Asn Ala Arg Asp Tyr Phe Val Asp Asp Asn	210	215	220
Glu Leu Pro Pro Leu Ile Thr Ser Gly Phe Asn Pro Ser Phe Ile Ala	225	230	235
Thr Val Ser His Glu Lys Asp Ser Gly Asp Thr Ser Glu Phe Glu Ile	245	250	255
Thr Tyr Gly Arg Asn Met Asp Val Thr Tyr Ala Thr Tyr Leu Pro Lys	260	265	270
Gln Gly Leu Tyr Pro Glu Arg Lys His Asn Glu Phe Val Asn Arg Asn	275	280	285
Phe Val Val Lys Tyr Glu Val Asn Trp Lys Thr His Glu Ile Lys Val	290	295	300

Lys Gly His Asn
305

<210> 67

<211> 308

<212> PRT

<213> Artificial Sequence

<220>

<223> Leukocidin chain lukM precursor amino acid sequence

<400> 67

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

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

Glu Asp Ile Gly Asp Asp Ala Glu Val Ile Lys Arg Thr Glu Asp Val
35 40 45

Ser Ser Arg Lys Trp Gly Val Thr Gln Asn Val Gln Phe Asp Phe Val
50 55 60

Lys Asp Lys Lys Tyr Asn Lys Asp Ala Leu Ile Ile Lys Met Gln Gly
65 70 75 80

Phe Ile Asn Ser Arg Thr Thr Phe Asn Asp Val Lys Gln Asn Arg Ala
85 90 95

Asn Lys Arg Met Val Trp Pro Phe Gln Tyr Asn Ile Gly Leu Thr Ser
100 105 110

Lys Asp Gln Asn Thr Ser Leu Ile Asn Tyr Leu Pro Lys Asn Lys Ile
115 120 125

Glu Thr Val Asp Val Gly Gln Thr Leu Gly Tyr Asn Ile Gly Gly Lys
130 135 140

Phe Gln Ser Ala Pro Ser Ile Gly Gly Asn Gly Ser Phe Asn Tyr Ser
145 150 155 160

Lys Ser Ile Lys Tyr Ser Gln Lys Ser Tyr Val Ser Glu Val Glu Gln
165 170 175

Gln Ser Ser Lys Thr Ile Lys Trp Gly Val Lys Ala Asn Ser Phe Val
180 185 190

Ile Ala Gly His Arg Trp Ser Ala Tyr Asp Glu Leu Leu Phe Ile Arg
195 200 205

Asn Thr Thr Arg Gly Pro Asn Ala Arg Asp Tyr Phe Val Asp Asp Asn
210 215 220

Glu Leu Pro Pro Leu Ile Thr Ser Gly Phe Asn Pro Ser Phe Ile Ala
225 230 235 240

Thr Val Ser His Glu Lys Asp Ser Gly Asp Thr Ser Glu Phe Glu Ile
 245 250 255

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

Leu Gly Leu Tyr Pro Glu Arg Lys His Asn Glu Phe Val Asn Arg Asn
 275 280 285

Phe Val Val Lys Tyr Glu Val Asn Trp Lys Thr Tyr Glu Ile Lys Val
 290 295 300

Lys Gly His Asn
 305

<210> 68

<211> 308

<212> PRT

<213> Artificial Sequence

<220>

<223> LukM precursor amino acid sequence

<400> 68

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

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

Glu Asp Ile Gly Asp Asp Ala Glu Val Ile Lys Arg Thr Glu Asp Val
 35 40 45

Ser Ser Arg Lys Trp Gly Val Thr Gln Asn Val Gln Phe Asp Phe Val
 50 55 60

Lys Asp Lys Lys Tyr Asn Lys Asp Ala Leu Ile Ile Lys Met Gln Gly
 65 70 75 80

Phe Ile Asn Ser Arg Thr Thr Phe Asn Asp Val Lys Gln Asn Arg Ala
 85 90 95

Asn Lys Arg Met Val Trp Pro Phe Gln Tyr Asn Ile Gly Leu Thr Ser
 100 105 110

Lys Asp Gln Asn Thr Ser Leu Ile Asn Tyr Leu Pro Lys Asn Lys Ile
 115 120 125

Glu Thr Val Asp Val Gly Gln Thr Leu Gly Tyr Asn Ile Gly Gly Lys
 130 135 140

Phe Gln Ser Val Pro Ser Ile Gly Gly Asn Gly Ser Phe Asn Tyr Ser
 145 150 155 160

Lys Ser Ile Lys Tyr Ser Gln Lys Ser Tyr Val Ser Glu Val Glu Gln
 165 170 175

Gln Ser Ser Lys Thr Ile Lys Trp Gly Val Lys Ala Asn Ser Phe Val
 180 185 190

Ile Ala Gly His Arg Trp Ser Ala Tyr Asp Glu Leu Leu Phe Ile Arg
 195 200 205

Asn Thr Thr Arg Gly Pro Asn Ala Arg Asp Tyr Phe Val Asp Asp Asn
 210 215 220

Glu Leu Pro Pro Leu Ile Thr Ser Gly Phe Asn Pro Ser Phe Ile Ala
 225 230 235 240

Thr Val Ser His Glu Lys Asp Ser Gly Asp Thr Ser Glu Phe Glu Ile
 245 250 255

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

Leu Gly Leu Tyr Pro Glu Arg Lys His Asn Glu Phe Val Asn Arg Asn
 275 280 285

Phe Val Val Lys Tyr Glu Val Asn Trp Lys Thr Tyr Glu Ile Lys Val
 290 295 300

Lys Gly His Asn
 305

<210> 69

<211> 309

<212> PRT

<213> Artificial Sequence

<220>

<223> gamma-hemolysin component A precursor amino acid sequence

<400> 69

Met Ile Lys Asn Lys Ile Leu Thr Ala Thr Leu Ala Val Gly Leu Ile
 1 5 10 15

Ala Pro Leu Ala Asn Pro Phe Ile Glu Ile Ser Lys Ala Glu Asn Lys
 20 25 30

Ile Glu Asp Ile Gly Gln Gly Ala Glu Ile Ile Lys Arg Thr Gln Asp
 35 40 45

Ile Thr Ser Lys Arg Leu Ala Ile Thr Gln Asn Ile Gln Phe Asp Phe
 50 55 60

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

Gly Phe Ile Ser Ser Arg Thr Thr Tyr Ser Asp Leu Lys Lys Tyr Pro

				85					90					95			
Tyr	Ile	Lys	Arg	Met	Ile	Trp	Pro	Phe	Gln	Tyr	Asn	Ile	Ser	Leu	Lys		
			100					105					110				
Thr	Lys	Asp	Pro	Asn	Val	Asp	Leu	Ile	Asn	Tyr	Leu	Pro	Lys	Asn	Lys		
		115					120					125					
Ile	Asp	Ser	Ala	Asp	Val	Ser	Gln	Lys	Leu	Gly	Tyr	Asn	Ile	Gly	Gly		
	130					135					140						
Asn	Phe	Gln	Thr	Ala	Pro	Ser	Ile	Gly	Gly	Ser	Gly	Ser	Phe	Asn	Tyr		
145					150					155					160		
Ser	Lys	Thr	Ile	Ser	Tyr	Asn	Gln	Lys	Asn	Tyr	Val	Thr	Glu	Val	Glu		
				165					170					175			
Ser	Gln	Asn	Ser	Lys	Gly	Val	Lys	Trp	Gly	Ile	Lys	Ala	Asn	Ser	Phe		
			180					185					190				
Val	Thr	Pro	Asn	Gly	Gln	Val	Ser	Ala	Tyr	Asp	Gln	Tyr	Leu	Phe	Ala		
		195					200					205					
Gln	Asp	Pro	Thr	Gly	Pro	Ala	Ala	Arg	Asp	Tyr	Phe	Val	Pro	Asp	Asn		
	210					215					220						
Gln	Leu	Pro	Pro	Leu	Ile	Gln	Ser	Gly	Phe	Asn	Pro	Ser	Phe	Ile	Thr		
225					230					235					240		
Thr	Leu	Ser	His	Glu	Arg	Gly	Lys	Gly	Asp	Lys	Ser	Glu	Phe	Glu	Ile		
				245					250					255			
Thr	Tyr	Gly	Arg	Asn	Met	Asp	Ala	Thr	Tyr	Ala	Tyr	Val	Thr	Arg	His		
			260					265					270				
Arg	Leu	Ala	Val	Asp	Arg	Lys	His	Asp	Ala	Phe	Lys	Asn	Arg	Asn	Val		
		275					280					285					
Thr	Val	Lys	Tyr	Glu	Val	Asn	Trp	Lys	Thr	His	Glu	Val	Lys	Ile	Lys		
	290					295					300						

$\langle 210 \rangle$ 70

$\langle 211 \rangle$ 321

<212> PRT

<213> Artificial Sequence

<220>

<223> gamma-hemolysin component A precursor amino acid sequence

<400> 70

Met Asn Leu Lys Leu Asn Arg Lys Lys Val Ile Ser Met Ile Lys Asn
1 5 10 15

Lys Ile Leu Thr Ala Thr Leu Ala Val Gly Leu Ile Ala Pro Leu Ala
 20 25 30

Asn Pro Phe Ile Glu Ile Ser Lys Ala Glu Asn Lys Ile Glu Asp Ile
 35 40 45

Gly Gln Gly Ala Glu Ile Ile Lys Arg Thr Gln Asp Ile Thr Ser Lys
 50 55 60

Arg Leu Ala Ile Thr Gln Asn Ile Gln Phe Asp Phe Val Lys Asp Lys
 65 70 75 80

Lys Tyr Asn Lys Asp Ala Leu Val Val Lys Met Gln Gly Phe Ile Ser
 85 90 95

Ser Arg Thr Thr Tyr Ser Asp Phe Lys Lys Tyr Pro Tyr Ile Lys Arg
 100 105 110

Met Ile Trp Pro Phe Gln Tyr Asn Ile Ser Leu Lys Thr Lys Asp Ser
 115 120 125

Asn Val Asp Leu Ile Asn Tyr Leu Pro Lys Asn Lys Ile Asp Ser Ala
 130 135 140

Asp Val Ser Gln Lys Leu Gly Tyr Asn Ile Gly Gly Asn Phe Gln Ser
 145 150 155 160

Ala Pro Ser Ile Gly Gly Ser Gly Ser Phe Asn Tyr Ser Lys Thr Ile
 165 170 175

Ser Tyr Asn Gln Lys Asn Tyr Val Thr Glu Val Glu Ser Gln Asn Ser
 180 185 190

Lys Gly Val Lys Trp Gly Val Lys Ala Asn Ser Phe Val Thr Pro Asn
 195 200 205

Gly Gln Val Ser Ala Tyr Asp Gln Tyr Leu Phe Ala Gln Asp Pro Thr
 210 215 220

Gly Pro Ala Ala Arg Asp Tyr Phe Val Pro Asp Asn Gln Leu Pro Pro
 225 230 235 240

Leu Ile Gln Ser Gly Phe Asn Pro Ser Phe Ile Thr Thr Leu Ser His
 245 250 255

Glu Arg Gly Lys Gly Asp Lys Ser Glu Phe Glu Ile Thr Tyr Gly Arg
 260 265 270

Asn Met Asp Ala Thr Tyr Ala Tyr Val Thr Arg His Arg Leu Ala Val
 275 280 285

Asp Arg Lys His Asp Ala Phe Lys Asn Arg Asn Val Thr Val Lys Tyr
 290 295 300

Glu Val Asn Trp Lys Thr His Glu Val Lys Ile Lys Ser Ile Thr Pro
 305 310 315 320

Lys

<210> 71

<211> 321

<212> PRT

<213> Artificial Sequence

<220>

<223> beta-channel forming cytolysin amino acid sequence

<400> 71

Met Asn Leu Lys Leu Asn Arg Lys Lys Val Ile Ser Met Ile Lys Asn
1 5 10 15

Lys Ile Leu Thr Ala Thr Leu Ala Val Gly Leu Ile Ala Pro Leu Ala
20 25 30

Asn Pro Phe Thr Glu Ile Ser Lys Ala Glu Asn Lys Ile Glu Asp Ile
35 40 45

Gly Gln Gly Ala Glu Ile Ile Lys Arg Thr Gln Asp Ile Thr Ser Lys
50 55 60

Arg Leu Ala Ile Thr Gln Asn Ile Gln Phe Asp Phe Val Lys Asp Lys

65 70 75 80

Lys Tyr Asn Lys Asp Ala Leu Val Val Lys Met Gln Gly Phe Ile Ser
85 90 95

Ser Arg Thr Thr Tyr Ser Asp Leu Lys Lys Tyr Pro Tyr Ile Lys Arg
100 105 110

Met Ile Trp Pro Phe Gln Tyr Asn Ile Ser Leu Lys Thr Lys Asp Ser
115 120 125

Asn Val Asp Leu Ile Asn Tyr Leu Pro Lys Asn Lys Ile Asp Ser Ala
130 135 140

Asp Val Ser Gln Lys Leu Gly Tyr Asn Ile Gly Gly Asn Phe Gln Ser
145 150 155 160

Ala Pro Ser Ile Gly Gly Ser Gly Ser Phe Asn Tyr Ser Lys Thr Ile
165 170 175

Ser Tyr Asn Gln Lys Asn Tyr Val Thr Glu Val Glu Ser Gln Asn Ser
180 185 190

Lys Gly Val Lys Trp Gly Val Lys Ala Asn Ser Phe Val Thr Pro Asn
195 200 205

Gly Gln Val Ser Ala Tyr Asp Gln Tyr Leu Phe Ala Gln Asp Pro Thr
210 215 220

Gly Pro Ala Ala Arg Asp Tyr Phe Val Pro Asp Asn Gln Leu Pro Pro
225 230 235 240

Leu Ile Gln Ser Gly Phe Asn Pro Ser Phe Ile Thr Thr Leu Ser His
245 250 255

Glu Lys Gly Lys Gly Asp Lys Ser Glu Phe Glu Ile Thr Tyr Gly Arg
260 265 270

Asn Met Asp Ala Thr Tyr Ala Tyr Val Thr Arg His Arg Leu Ala Val
275 280 285

Asp Arg Lys His Asp Ala Phe Lys Asn Arg Asn Val Thr Val Lys Tyr
290 295 300

Glu Val Asn Trp Lys Thr His Glu Val Lys Ile Lys Ser Ile Thr Pro
305 310 315 320

Lys

<210> 72

<211> 309

<212> PRT

<213> Artificial Sequence

<220>

<223> gamma hemolysin amino acid sequence

<400> 72

Met Ile Lys Asn Lys Ile Leu Thr Ala Thr Leu Ala Val Gly Leu Ile
1 5 10 15

Ala Pro Leu Ala Asn Pro Phe Ile Glu Ile Ser Lys Ala Glu Asn Lys
20 25 30

Ile Glu Asp Ile Gly Gln Gly Ala Glu Ile Ile Lys Arg Thr Gln Asp
35 40 45

Ile Thr Ser Lys Arg Leu Ala Ile Thr Gln Asn Ile Gln Phe Asp Phe
50 55 60

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

Gly Phe Ile Ser Ser Arg Thr Thr Tyr Ser Asp Leu Lys Lys Tyr Pro
85 90 95

Tyr Ile Lys Arg Met Ile Trp Pro Phe Gln Tyr Asn Ile Ser Leu Lys
100 105 110

Thr Lys Asp Ser Asn Val Asp Leu Ile Asn Tyr Leu Pro Lys Asn Lys
115 120 125

Ile Asp Ser Ala Asp Val Ser Gln Lys Leu Gly Tyr Asn Ile Gly Gly
130 135 140

Asn Phe Gln Ser Ala Pro Ser Ile Gly Gly Ser Gly Ser Phe Asn Tyr
145 150 155 160

Ser Lys Thr Ile Ser Tyr Asn Gln Lys Asn Tyr Val Thr Glu Val Glu
165 170 175

Ser Gln Asn Ser Lys Gly Val Lys Trp Gly Val Lys Ala Asn Ser Phe
180 185 190

Val Thr Pro Asn Gly Gln Val Ser Ala Tyr Asp Gln Tyr Leu Phe Ala
195 200 205

Gln Asp Pro Thr Gly Pro Ala Ala Arg Asp Tyr Phe Val Pro Asp Asn
210 215 220

Gln Leu Pro Pro Leu Ile Gln Ser Gly Phe Asn Pro Ser Phe Ile Thr
225 230 235 240

Thr Leu Ser His Glu Lys Gly Lys Gly Asp Lys Ser Glu Phe Glu Ile
245 250 255

Thr Tyr Gly Arg Asn Met Asp Ala Thr Tyr Ala Tyr Val Thr Arg His
260 265 270

Arg Leu Ala Val Asp Arg Lys His Asp Ala Phe Lys Asn Arg Asn Val
275 280 285

Thr Val Lys Tyr Glu Val Asn Trp Lys Thr His Glu Val Lys Ile Lys
290 295 300

Ser Ile Thr Pro Lys
305

<210> 73

<211> 309

<212> PRT

<213> Artificial Sequence

<220>

<223> gamma-hemolysin component A precursor amino acid sequence

<400> 73

Met Ile Lys Asn Lys Ile Leu Thr Ala Thr Leu Ala Val Gly Leu Ile
1 5 10 15

Ala Pro Leu Ala Asn Pro Phe Ile Glu Ile Ser Lys Ala Glu Asn Lys
20 25 30

Ile Glu Asp Ile Gly Gln Gly Ala Glu Ile Ile Lys Arg Thr Gln Asp
35 40 45

Ile Thr Ser Lys Arg Leu Ala Ile Thr Gln Asn Ile Gln Phe Asp Phe
 50 55 60
 Val Lys Asp Lys Lys Tyr Asn Lys Asp Ala Leu Val Val Lys Met Gln
 65 70 75 80
 Gly Phe Ile Ser Ser Arg Thr Thr Tyr Ser Asp Leu Lys Lys Tyr Pro
 85 90 95
 Tyr Ile Lys Arg Met Ile Trp Pro Phe Gln Tyr Asn Ile Ser Leu Lys
 100 105 110
 Thr Lys Asp Ser Asn Val Asp Leu Ile Asn Tyr Leu Pro Lys Asn Lys
 115 120 125
 Ile Asp Ser Ala Asp Val Ser Gln Lys Leu Gly Tyr Asn Ile Gly Gly
 130 135 140
 Asn Phe Gln Ser Ala Pro Ser Ile Gly Gly Ser Gly Ser Phe Asn Tyr
 145 150 155 160
 Ser Lys Thr Ile Ser Tyr Asn Gln Lys Asn Tyr Val Thr Glu Val Glu
 165 170 175
 Ser Gln Asn Ser Lys Gly Val Lys Trp Gly Val Lys Ala Asn Ser Phe
 180 185 190
 Val Thr Pro Asn Gly Gln Val Ser Ala Tyr Asp Gln Tyr Leu Phe Ala
 195 200 205
 Gln Asp Pro Thr Gly Pro Ala Ala Arg Asp Tyr Phe Val Pro Asp Asn
 210 215 220
 Gln Leu Pro Pro Leu Ile Gln Ser Gly Phe Asn Pro Ser Phe Ile Thr
 225 230 235 240
 Thr Leu Ser His Glu Lys Gly Lys Gly Asp Lys Ser Glu Phe Glu Ile
 245 250 255
 Thr Tyr Gly Arg Asn Met Asp Thr Thr Tyr Ala Tyr Val Thr Arg His
 260 265 270
 Arg Leu Ala Val Asp Arg Lys His Asp Ala Phe Lys Asn Arg Asn Val
 275 280 285
 Thr Val Lys Tyr Glu Val Asn Trp Lys Thr His Glu Val Lys Ile Lys
 290 295 300
 Ser Ile Thr Pro Lys
 305

<210> 74

<211> 321

<212> PRT

<213> Artificial Sequence

<220>

<223> gamma-hemolysin component A precursor amino acid sequence

<400> 74

Met Asn Leu Lys Leu Asn Arg Lys Lys Val Ile Ser Met Ile Lys Asn
1 5 10 15

Lys Ile Leu Thr Ala Thr Leu Ala Val Gly Leu Ile Ala Pro Leu Ala
20 25 30

Asn Pro Phe Ile Glu Ile Ser Lys Ala Glu Asn Lys Ile Glu Asp Ile
35 40 45

Gly Gln Gly Ala Glu Ile Ile Lys Arg Thr Gln Asp Ile Thr Ser Lys
50 55 60

Arg Leu Ala Ile Thr Gln Asn Ile Gln Phe Asp Phe Val Lys Asp Lys
65 70 75 80

Lys Tyr Asn Lys Asp Ala Leu Val Val Lys Met Gln Gly Phe Ile Ser
85 90 95

Ser Arg Thr Thr Tyr Ser Asp Leu Lys Lys Tyr Pro Tyr Ile Lys Arg
100 105 110

Met Ile Trp Pro Phe Gln Tyr Asn Ile Ser Leu Lys Thr Lys Asp Ser
115 120 125

Asn Val Asp Leu Ile Asn Tyr Leu Pro Lys Asn Lys Ile Asp Ser Ala
130 135 140

Asp Val Ser Gln Lys Leu Gly Tyr Asn Ile Gly Gly Asn Phe Gln Ser
145 150 155 160

Ala Pro Ser Ile Gly Gly Ser Gly Ser Phe Asn Tyr Ser Lys Thr Ile
165 170 175

Ser Tyr Asn Gln Lys Asn Tyr Val Thr Glu Val Glu Ser Gln Asn Ser
180 185 190

Lys Gly Val Lys Trp Gly Val Lys Ala Asn Ser Phe Val Thr Pro Asn
195 200 205

Gly Gln Val Ser Ala Tyr Asp Gln Tyr Leu Phe Ala Gln Asp Pro Thr
210 215 220

Gly Pro Ala Ala Arg Asp Tyr Phe Val Pro Asp Asn Gln Leu Pro Pro
225 230 235 240

Leu Ile Gln Ser Gly Phe Asn Pro Ser Phe Ile Thr Thr Leu Ser His
245 250 255

Glu Lys Gly Lys Gly Asp Lys Ser Glu Phe Glu Ile Thr Tyr Gly Arg
260 265 270

260 265 270
 Asn Met Asp Ala Thr Tyr Ala Tyr Val Thr Arg His Arg Leu Ala Val
 275 280 285

Asp Arg Lys His Asp Ala Phe Lys Asn Arg Asn Val Thr Val Lys Tyr
 290 295 300

Glu Val Asn Trp Lys Thr His Glu Val Lys Ile Lys Ser Ile Thr Pro
 305 310 315 320

Lys

<210> 75

<211> 309

<212> PRT

<213> Artificial Sequence

<220>

<223> gamma-hemolysin component A precursor amino acid sequence

<400> 75

Met Ile Lys Asn Lys Ile Leu Thr Ala Thr Leu Ala Val Gly Leu Ile
 1 5 10 15

Ala Pro Leu Ala Asn Pro Phe Ile Glu Ile Ser Lys Ala Glu Asn Lys
 20 25 30

Ile Glu Asp Ile Gly Gln Gly Ala Glu Ile Ile Lys Arg Thr Gln Asp
 35 40 45

Ile Ala Ser Lys Arg Leu Ala Ile Thr Gln Asn Ile Gln Phe Asp Phe
 50 55 60

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

Gly Phe Ile Ser Ser Arg Thr Thr Tyr Ser Asp Leu Lys Lys Tyr Pro
 85 90 95

Tyr Ile Lys Arg Met Ile Trp Pro Phe Gln Tyr Asn Ile Ser Leu Lys
 100 105 110

Thr Lys Asp Ser Asn Val Asp Leu Ile Asn Tyr Leu Pro Lys Asn Lys
 115 120 125

Ile Asp Ser Ala Asp Val Ser Gln Lys Leu Gly Tyr Asn Ile Gly Gly
 130 135 140

Asn Phe Gln Ser Ala Pro Ser Ile Gly Gly Ser Gly Ser Phe Asn Tyr
 145 150 155 160

Ser Lys Thr Ile Ser Tyr Asn Gln Lys Asn Tyr Val Thr Glu Val Glu
 165 170 175

Ser Gln Asn Ser Lys Gly Val Lys Trp Gly Val Lys Ala Asn Ser Phe
 180 185 190

Val Thr Pro Asn Gly Gln Val Ser Ala Tyr Asp Gln Tyr Leu Phe Ala
 195 200 205

Gln Asp Pro Thr Gly Pro Ala Ala Arg Asp Tyr Phe Val Pro Asp Asn
 210 215 220

Gln Leu Pro Pro Leu Ile Gln Ser Gly Phe Asn Pro Ser Phe Ile Thr
 225 230 235 240

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

Thr Tyr Gly Arg Asn Met Asp Ala Thr Tyr Ala Tyr Val Thr Arg His
 260 265 270

Arg Leu Ala Val Asp Arg Lys His Asp Ala Phe Lys Asn Arg Asn Val
 275 280 285

Thr Val Lys Tyr Glu Val Asn Trp Lys Thr His Glu Val Lys Ile Lys
 290 295 300

Ser Ile Thr Pro Lys
 305

<210> 76

<211> 309

<212> PRT

<213> Artificial Sequence

<220>

<223> gamma-hemolysin chain II precursor amino acid sequence

<400> 76

Met Ile Lys Asn Lys Ile Leu Thr Ala Thr Leu Ala Val Gly Leu Ile
 1 5 10 15

Ala Pro Leu Ala Asn Pro Phe Ile Glu Ile Ser Lys Ala Glu Asn Lys
 20 25 30

Ile Glu Asp Ile Gly Gln Gly Ala Glu Ile Ile Lys Arg Thr Gln Asp
 35 40 45

Ile Thr Ser Lys Arg Leu Ala Ile Thr Gln Asn Ile Gln Phe Asp Phe
 50 55 60

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

Gly Phe Ile Ser Ser Arg Thr Thr Tyr Ser Asp Leu Lys Lys Tyr Pro
 85 90 95

Tyr Ile Lys Arg Met Ile Trp Pro Phe Gln Tyr Asn Ile Ser Leu Lys

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      100      105      110
Thr Lys Asp Ser Asn Val Asp Leu Ile Asn Tyr Leu Pro Lys Asn Lys
    115      120      125

Ile Asp Ser Ala Asp Val Ser Gln Lys Leu Gly Tyr Asn Ile Gly Gly
    130      135      140

Asn Phe Gln Ser Ala Pro Ser Ile Gly Gly Ser Gly Ser Phe Asn Tyr
    145      150      155      160

Ser Lys Thr Ile Ser Tyr Asn Gln Lys Asn Tyr Val Thr Glu Val Glu
    165      170      175

Ser Gln Asn Ser Lys Gly Val Lys Trp Gly Val Lys Ala Asn Ser Phe
    180      185      190

Val Thr Pro Asn Gly Gln Val Ser Ala Tyr Asp Gln Tyr Leu Phe Ala
    195      200      205

Gln Asp Pro Thr Gly Pro Ala Ala Arg Asp Tyr Phe Val Pro Asp Asn
    210      215      220

Gln Leu Pro Pro Leu Ile Gln Ser Gly Phe Asn Pro Ser Phe Ile Thr
    225      230      235      240

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

Thr Tyr Gly Arg Asn Met Asp Ala Thr Tyr Ala Tyr Val Thr Arg His
    260      265      270

Arg Leu Ala Val Asp Arg Lys His Asp Ala Phe Lys Asn Arg Asn Val
    275      280      285

Thr Val Lys Tyr Glu Val Asn Trp Lys Thr His Glu Val Lys Ile Lys
    290      295      300

Ser Ile Thr Pro Lys
    305

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<210> 77

<211> 321

<212> PRT

<213> Artificial Sequence

<220>

<223> beta-channel forming cytolysin amino acid sequence

<400> 77

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Met Asn Leu Lys Leu Asn Arg Lys Lys Val Ile Ser Met Ile Lys Asn
 1          5          10          15

Lys Ile Leu Thr Ala Thr Leu Ala Val Gly Leu Ile Ala Pro Leu Ala
 20          25          30

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Asn Pro Phe Ile Glu Ile Ser Lys Ala Glu Asn Lys Ile Glu Asp Ile
 35 40 45
 Gly Gln Gly Ala Glu Ile Ile Lys Arg Thr Gln Asp Ile Thr Ser Lys
 50 55 60
 Arg Leu Ala Ile Thr Gln Asn Ile Gln Phe Asp Phe Val Lys Asp Lys
 65 70 75 80
 Lys Tyr Asn Lys Asp Ala Leu Val Val Lys Met Gln Gly Phe Ile Ser
 85 90 95
 Ser Arg Thr Thr Tyr Ser Asp Leu Lys Lys Tyr Pro Tyr Ile Lys Arg
 100 105 110
 Met Ile Trp Pro Phe Gln Tyr Asn Ile Ser Leu Lys Thr Lys Asp Ser
 115 120 125
 Asn Val Asp Leu Ile Asn Tyr Leu Pro Lys Asn Lys Ile Asp Ser Ala
 130 135 140
 Asp Val Ser Gln Lys Leu Gly Tyr Asn Ile Gly Gly Asn Phe Gln Ser
 145 150 155 160
 Ala Pro Ser Ile Gly Gly Ser Gly Ser Phe Asn Tyr Ser Lys Thr Ile
 165 170 175
 Ser Tyr Asn Gln Lys Asn Tyr Val Thr Glu Val Glu Ser Gln Asn Ser
 180 185 190
 Lys Gly Val Lys Trp Gly Val Lys Ala Asn Ser Phe Val Thr Pro Asn
 195 200 205
 Gly Gln Val Ser Ala Tyr Asp Gln Tyr Leu Phe Ala Gln Asp Pro Thr
 210 215 220
 Gly Pro Ala Ala Arg Asp Tyr Phe Val Pro Asp Asn Gln Leu Pro Pro
 225 230 235 240
 Leu Ile Gln Ser Gly Phe Asn Pro Ser Phe Ile Thr Thr Leu Ser His
 245 250 255
 Glu Arg Gly Lys Gly Asp Lys Ser Glu Phe Glu Ile Thr Tyr Gly Arg
 260 265 270
 Asn Met Asp Ala Thr Tyr Ala Tyr Val Thr Arg His Arg Leu Ala Val
 275 280 285
 Asp Arg Lys His Asp Ala Phe Lys Asn Arg Asn Val Thr Val Lys Tyr
 290 295 300
 Glu Val Asn Trp Lys Thr His Glu Val Lys Ile Lys Ser Ile Thr Pro
 305 310 315 320
 Lys

<210> 78

<211> 321

<212> PRT

<213> Artificial Sequence

<220>

<223> beta-channel forming cytolysin amino acid sequence

<400> 78

Met	Asn	Leu	Lys	Leu	Asn	Arg	Lys	Lys	Val	Ile	Ser	Met	Ile	Lys	Asn
1				5					10					15	

Lys	Ile	Leu	Thr	Ala	Thr	Leu	Ala	Val	Gly	Leu	Ile	Ala	Pro	Leu	Ala
-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----

20

25

30

Asn	Pro	Phe	Ile	Glu	Ile	Ser	Lys	Ala	Glu	Asn	Lys	Ile	Glu	Asp	Ile
		35					40					45			

Gly	Gln	Gly	Ala	Glu	Ile	Ile	Lys	Arg	Thr	Gln	Asp	Ile	Thr	Ser	Lys
	50					55					60				

Arg	Leu	Ala	Ile	Thr	Gln	Asn	Ile	Gln	Phe	Asp	Phe	Val	Lys	Asp	Lys
65					70					75					80

Lys	Tyr	Asn	Lys	Asp	Ala	Leu	Val	Val	Lys	Met	Gln	Gly	Phe	Ile	Ser
				85					90					95	

Ser	Arg	Thr	Thr	Tyr	Ser	Asp	Leu	Lys	Lys	Tyr	Leu	Tyr	Ile	Lys	Arg
			100					105					110		

Met	Ile	Trp	Pro	Phe	Gln	Tyr	Asn	Ile	Ser	Leu	Lys	Thr	Lys	Asp	Ser
		115					120					125			

Asn	Val	Asp	Leu	Ile	Asn	Tyr	Leu	Pro	Lys	Asn	Lys	Ile	Asp	Ser	Ala
	130					135					140				

Asp	Val	Ser	Gln	Lys	Leu	Gly	Tyr	Asn	Ile	Gly	Gly	Asn	Phe	Gln	Ser
145					150					155					160

Ala	Pro	Ser	Ile	Gly	Gly	Ser	Gly	Ser	Phe	Asn	Tyr	Ser	Lys	Thr	Ile
				165					170					175	

Ser	Tyr	Asn	Gln	Lys	Asn	Tyr	Val	Thr	Glu	Val	Glu	Ser	Gln	Asn	Ser
		180						185					190		

Lys	Gly	Val	Lys	Trp	Gly	Val	Lys	Ala	Asn	Ser	Phe	Val	Thr	Pro	Asn
	195						200					205			

Gly	Gln	Val	Ser	Ala	Tyr	Asp	Gln	Tyr	Leu	Phe	Ala	Gln	Asp	Pro	Thr
	210					215					220				

Gly	Pro	Ala	Ala	Arg	Asp	Tyr	Phe	Val	Pro	Asp	Asn	Gln	Leu	Pro	Pro
225					230					235				240	

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Leu Ile Gln Ser Gly Phe Asn Pro Ser Phe Ile Thr Thr Leu Ser His
      245                      250                      255

Glu Arg Gly Lys Gly Asp Lys Ser Glu Phe Glu Ile Thr Tyr Gly Arg
      260                      265                      270

Asn Met Asp Ala Thr Tyr Ala Tyr Val Thr Arg His Arg Leu Ala Val
      275                      280                      285

Asp Arg Lys His Asp Ala Phe Lys Asn Arg Asn Val Thr Val Lys Tyr
      290                      295                      300

Glu Val Asn Trp Lys Thr His Glu Val Lys Ile Lys Ser Ile Thr Pro
      305                      310                      315                      320

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Lys

<210> 79

<211> 308

<212> PRT

<213> Artificial Sequence

<220>

<223> preLukM amino acid sequence

<400> 79

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Met Phe Asn Arg Lys Leu Leu Val Thr Thr Leu Ser Leu Gly Leu Ile
 1           5           10           15

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

Glu Asp Ile Gly Asp Asp Ala Glu Val Ile Lys Arg Thr Glu Asp Val
      35           40           45

Ser Ser Arg Lys Trp Gly Val Thr Gln Asn Val Gln Phe Asp Phe Val
      50           55           60

Lys Asp Lys Lys Tyr Asn Lys Asp Ala Leu Ile Ile Lys Met Gln Gly
      65           70           75           80

Phe Ile Asn Ser Arg Thr Thr Phe Asn Asp Val Lys Gln Asn Arg Ala
      85           90           95

Asn Lys Arg Met Val Trp Pro Phe Gln Tyr Asn Ile Gly Leu Thr Ser
      100          105          110

Lys Asp Gln Asn Thr Ser Leu Ile Asn Tyr Leu Pro Lys Asn Lys Ile
      115          120          125

Glu Thr Val Asp Val Gly Gln Thr Leu Gly Tyr Asn Ile Gly Gly Lys
      130          135          140

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Phe Gln Ser Val Pro Ser Ile Gly Gly Asn Gly Ser Phe Asn Tyr Ser

145 150 155 160

Lys Ser Ile Lys Tyr Ser Gln Lys Ser Tyr Val Ser Glu Val Glu Gln
165 170 175

Gln Ser Ser Lys Thr Ile Lys Trp Gly Val Lys Ala Asn Ser Phe Val
180 185 190

Ile Ala Gly His Arg Trp Ser Ala Tyr Asp Glu Leu Leu Phe Ile Arg
195 200 205

Asn Thr Thr Arg Gly Pro Asn Ala Arg Asp Tyr Phe Val Asp Asp Asn
210 215 220

Glu Leu Pro Pro Leu Ile Thr Ser Gly Phe Asn Pro Ser Phe Ile Ala
225 230 235 240

Thr Val Ser His Glu Lys Asp Ser Gly Asp Thr Ser Glu Phe Glu Ile
245 250 255

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

Leu Gly Leu Tyr Pro Glu Arg Lys His Asn Glu Phe Val Asn Arg Asn
275 280 285

Leu Val Val Lys Tyr Glu Val Asn Trp Lys Thr Ser Glu Leu Lys Val
290 295 300

Arg Gly His Asn
305

<210> 80

<211> 309

<212> PRT

<213> Artificial Sequence

<220>

<223> gamma-hemolysin component A precursor amino acid sequence

<400> 80

Met Ile Lys Asn Lys Ile Leu Thr Ala Thr Leu Ala Val Gly Leu Met
1 5 10 15

Ala Pro Leu Ala Asn Pro Phe Ile Glu Ile Ser Lys Ala Glu Asn Lys
20 25 30

Ile Glu Asp Ile Gly Gln Gly Ala Glu Ile Ile Lys Arg Thr Gln Asp
35 40 45

Ile Thr Ser Lys Arg Leu Ala Ile Thr Gln Asn Ile Gln Phe Asp Phe
50 55 60

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

Gly Phe Ile Ser Ser Arg Thr Thr Tyr Ser Asp Leu Lys Lys Tyr Pro
85 90 95

Tyr Ile Lys Arg Met Ile Trp Pro Phe Gln Tyr Asn Ile Ser Leu Lys
100 105 110

Thr Lys Asp Ser Asn Val Asp Leu Ile Asn Tyr Leu Pro Lys Asn Lys
115 120 125

Ile Asp Ser Ala Asp Val Ser Gln Lys Leu Gly Tyr Asn Ile Gly Gly
130 135 140

Asn Phe Gln Ser Ala Pro Ser Ile Gly Gly Ser Gly Ser Phe Asn Tyr
145 150 155 160

Ser Lys Thr Ile Ser Tyr Asn Gln Lys Asn Tyr Val Thr Glu Val Glu
165 170 175

Ser Gln Asn Ser Lys Gly Val Lys Trp Gly Val Lys Ala Asn Ser Phe
180 185 190

Val Thr Pro Asn Gly Gln Val Ser Ala Tyr Asp Gln Tyr Leu Phe Ala
195 200 205

Gln Asp Pro Thr Gly Pro Ala Thr Arg Asp Tyr Phe Val Pro Asp Asn
210 215 220

Gln Leu Pro Pro Leu Ile Gln Ser Gly Phe Asn Pro Ser Phe Ile Thr
225 230 235 240

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

Thr Tyr Gly Arg Asn Met Asp Ala Thr Tyr Ala Tyr Val Thr Arg His
260 265 270

Arg Leu Ala Val Asp Arg Lys His Asp Ala Phe Lys Asn Arg Asn Val
275 280 285

Thr Val Lys Tyr Glu Val Asn Trp Lys Thr His Glu Val Lys Ile Lys
290 295 300

Ser Ile Thr Pro Lys
305

<210> 81

<211> 309

<212> PRT

<213> Artificial Sequence

<220>

<223> Leukocidin-S subunit amino acid sequence

<400> 81

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Met Ile Lys Asn Lys Ile Leu Thr Ala Thr Leu Ala Val Gly Leu Ile
1           5           10           15

Ala Pro Leu Ala Asn Pro Phe Ile Glu Ile Ser Lys Ala Glu Asn Lys
20           25           30

Ile Glu Asp Ile Gly Gln Gly Ala Glu Ile Ile Lys Arg Thr Gln Asp
35           40           45

Ile Thr Ser Lys Arg Leu Ala Ile Thr Gln Asn Ile Gln Phe Asp Phe
50           55           60

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

Gly Phe Ile Ser Ser Arg Thr Thr Tyr Ser Asp Leu Lys Lys Tyr Pro
85           90           95

Tyr Ile Lys Arg Met Ile Trp Pro Phe Gln Tyr Asn Ile Ser Leu Lys
100          105          110

Thr Lys Asp Ser Asn Val Asp Leu Ile Asn Tyr Leu Pro Lys Asn Lys
115          120          125

Ile Asp Ser Ala Asp Val Ser Gln Lys Leu Gly Tyr Asn Ile Gly Gly
130          135          140

Asn Phe Gln Ser Ala Pro Ser Ile Gly Gly Ser Gly Ser Phe Asn Tyr
145          150          155          160

Ser Lys Thr Ile Ser Tyr Asn Gln Lys Asn Tyr Val Thr Glu Val Glu
165          170          175

Ser Gln Asn Ser Lys Gly Val Lys Trp Gly Val Lys Ala Asn Ser Phe
180          185          190

Val Thr Pro Asn Gly Gln Val Ser Ala Tyr Asp Gln Tyr Leu Phe Ala
195          200          205

Gln Asp Pro Thr Gly Pro Ala Ala Arg Asp Tyr Phe Val Pro Asp Asn
210          215          220

Gln Leu Pro Pro Leu Ile Gln Ser Gly Phe Asn Pro Ser Phe Ile Thr
225          230          235          240

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

Thr Tyr Gly Arg Asn Met Asp Ala Thr Tyr Ala Tyr Val Thr Arg His
260          265          270

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Arg Phe Ala Val Asp Arg Lys His Asp Ala Phe Lys Asn Arg Asn Val
 275 280 285

Thr Val Lys Tyr Glu Val Asn Trp Lys Thr His Glu Val Lys Ile Lys
 290 295 300

Ser Ile Thr Pro Lys
 305

<210> 82

<211> 321

<212> PRT

<213> Artificial Sequence

<220>

<223> hlgA-like ORF amino acid sequence

<400> 82

Met Asn Leu Lys Leu Asn Arg Lys Lys Val Ile Ser Met Ile Lys Asn
 1 5 10 15

Lys Ile Leu Thr Ala Thr Leu Ala Val Gly Leu Ile Ala Pro Leu Ala
 20 25 30

Asn Pro Phe Ile Glu Ile Ser Lys Ala Glu Asn Lys Ile Glu Asp Ile
 35 40 45

Gly Gln Gly Ala Glu Ile Ile Lys Arg Thr Gln Asp Ile Thr Ser Lys
 50 55 60

Arg Leu Ala Ile Thr Gln Asn Ile Gln Phe Asp Phe Val Lys Asp Lys
 65 70 75 80

Lys Tyr Asn Lys Asp Ala Leu Val Val Lys Met Gln Gly Phe Ile Ser
 85 90 95

Ser Arg Thr Thr Tyr Ser Asp Leu Lys Lys Tyr Pro Tyr Ile Lys Arg
 100 105 110

Met Ile Trp Pro Phe Gln Tyr Asn Ile Ser Leu Lys Thr Lys Asp Ser
 115 120 125

Asn Val Asp Leu Ile Asn Tyr Leu Pro Lys Asn Lys Ile Asp Ser Ala
 130 135 140

Asp Val Ser Gln Lys Leu Gly Tyr Asn Ile Gly Gly Asn Phe Gln Ser
 145 150 155 160

Ala Pro Ser Ile Gly Gly Ser Gly Ser Phe Asn Tyr Ser Lys Thr Ile
 165 170 175

Ser Tyr Asn Gln Lys Asn Tyr Val Thr Glu Val Glu Ser Gln Asn Ser
 180 185 190

Lys Gly Gly Lys Trp Gly Val Lys Ala Asn Ser Phe Val Thr Pro Asn
 195 200 205

Gly Gln Val Ser Ala Tyr Asp Gln Tyr Leu Phe Ala Gln Asp Pro Thr
 210 215 220

Gly Pro Ala Ala Arg Asp Tyr Phe Val Pro Asp Asn Gln Leu Pro Pro
 225 230 235 240

Leu Ile Gln Ser Gly Phe Asn Pro Ser Phe Ile Thr Thr Leu Ser His
 245 250 255

Glu Lys Gly Lys Gly Asp Lys Ser Glu Phe Glu Ile Thr Tyr Gly Arg
 260 265 270

Asn Met Asp Ala Thr Tyr Ala Tyr Val Thr Arg Pro Arg Leu Ala Val
 275 280 285

Asp Arg Lys His Asp Ala Phe Lys Asn Arg Asn Val Thr Val Lys Tyr
 290 295 300

Glu Val Asn Trp Lys Thr His Glu Val Lys Ile Lys Ser Ile Thr Pro
 305 310 315 320

Lys

<210> 83

<211> 321

<212> PRT

<213> Artificial Sequence

<220>

<223> gamma-hemolysin component A precursor amino acid sequence

<400> 83

Met Asn Leu Lys Leu Asn Arg Lys Lys Val Ile Ser Met Ile Lys Asn
 1 5 10 15

Lys Ile Leu Thr Ala Thr Leu Ala Val Gly Leu Ile Ala Pro Leu Ala
 20 25 30

Asn Pro Phe Ile Glu Ile Ser Arg Ala Glu Asn Lys Ile Glu Asp Ile
 35 40 45

Gly Gln Gly Ala Glu Ile Ile Lys Arg Thr Gln Asp Ile Thr Ser Lys
 50 55 60

Arg Leu Ala Ile Thr Gln Asn Ile Gln Phe Asp Phe Val Lys Asp Lys
 65 70 75 80

Lys Tyr Asn Lys Asp Ala Leu Val Val Lys Met Gln Gly Phe Ile Ser
 85 90 95

Ser Arg Thr Thr Tyr Ser Asp Leu Lys Lys Tyr Pro Tyr Ile Lys Arg
 100 105 110

Met Ile Trp Pro Phe Gln Tyr Asn Ile Ser Leu Lys Thr Lys Asp Ser
115 120 125

Asn Val Asp Leu Ile Asn Tyr Leu Pro Lys Asn Lys Ile Asp Ser Ala
130 135 140

Asp Val Ser Gln Lys Leu Gly Tyr Asn Ile Gly Gly Asn Phe Gln Ser
145 150 155 160

Ala Pro Ser Ile Gly Gly Ser Gly Ser Phe Asn Tyr Ser Lys Thr Ile
165 170 175

Ser Tyr Asn Gln Lys Asn Tyr Val Thr Glu Val Glu Ser Gln Asn Ser
180 185 190

Lys Gly Val Lys Trp Gly Val Lys Ala Asn Ser Phe Val Thr Pro Asn
195 200 205

Gly Gln Val Ser Ala Tyr Asp Gln Tyr Leu Phe Ala Gln Asp Pro Thr
210 215 220

Gly Pro Ala Ala Arg Asp Tyr Phe Val Pro Asp Asn Gln Leu Pro Pro
225 230 235 240

Leu Ile Gln Ser Gly Phe Asn Pro Ser Phe Ile Thr Thr Leu Ser His
245 250 255

Glu Arg Gly Lys Gly Asp Lys Ser Asp Phe Glu Ile Thr Tyr Gly Arg
260 265 270

Asn Met Asp Ala Thr Tyr Ala Tyr Val Thr Arg His Arg Leu Ala Val
275 280 285

Asp Arg Lys His Asp Ala Phe Lys Asn Arg Asn Val Thr Val Lys Tyr
290 295 300

Glu Val Asn Trp Lys Thr His Glu Val Lys Ile Lys Ser Ile Thr Pro
305 310 315 320

Lys

<210> 84

<211> 321

<212> PRT

<213> Artificial Sequence

<220>

<223> gamma-hemolysin component A precursor amino acid sequence

<400> 84

Met Asn Leu Lys Leu Asn Arg Lys Lys Val Ile Ser Met Ile Lys Asn
1 5 10 15

Lys Ile Leu Thr Ala Thr Leu Ala Val Gly Leu Ile Ala Pro Leu Ala
20 25 30

Asn Pro Phe Ile Glu Ile Ser Lys Ala Glu Asn Lys Ile Glu Asp Ile
 35 40 45

Gly Gln Gly Ala Glu Ile Ile Lys Arg Thr Gln Asp Ile Thr Ser Lys
 50 55 60

Arg Leu Ala Ile Thr Gln Asn Ile Gln Phe Asp Phe Val Lys Asp Lys
 65 70 75 80

Lys Tyr Asn Lys Asp Ala Leu Val Val Lys Met Gln Gly Phe Ile Ser
 85 90 95

Ser Arg Thr Thr Tyr Ser Asp Leu Lys Lys Tyr Pro Tyr Ile Lys Arg
 100 105 110

Met Ile Trp Pro Phe Gln Tyr Asn Ile Ser Leu Lys Thr Lys Asp Ser
 115 120 125

Asn Val Asp Leu Ile Asn Tyr Leu Pro Lys Asn Lys Ile Asp Ser Ala
 130 135 140

Asp Val Ser Gln Lys Leu Gly Tyr Asn Ile Gly Gly Asn Phe Gln Ser
 145 150 155 160

Ala Pro Ser Ile Gly Gly Ser Gly Ser Phe Asn Tyr Ser Lys Thr Ile
 165 170 175

Ser Tyr Asn Gln Lys Asn Tyr Val Thr Glu Val Glu Ser Gln Asn Ser
 180 185 190

Lys Gly Val Lys Arg Gly Val Lys Ala Asn Ser Phe Val Thr Pro Asn
 195 200 205

Gly Gln Val Ser Ala Tyr Asp Gln Tyr Leu Phe Ala Gln Asp Pro Thr
 210 215 220

Gly Pro Ala Ala Arg Asp Tyr Phe Val Pro Asp Asn Gln Leu Pro Pro
 225 230 235 240

Leu Ile Gln Ser Gly Phe Asn Pro Ser Phe Ile Thr Thr Leu Ser His
 245 250 255

Glu Lys Gly Lys Gly Asp Lys Ser Glu Phe Glu Ile Thr Tyr Gly Arg
 260 265 270

Asn Met Asp Ala Thr Tyr Ala Tyr Val Thr Arg His Arg Leu Ala Val
 275 280 285

Asp Arg Lys His Asp Ala Phe Lys Asn Arg Asn Val Thr Val Lys Tyr
 290 295 300

Glu Val Asn Trp Lys Thr His Glu Val Lys Ile Lys Ser Ile Thr Pro
 305 310 315 320

Lys

<210> 85

<211> 321

<212> PRT

<213> Artificial Sequence

<220>

<223> gamma-hemolysin component A precursor amino acid sequence

<400> 85

Met	Asn	Leu	Lys	Leu	Asn	Arg	Lys	Lys	Val	Ile	Ser	Met	Ile	Lys	Asn
1				5					10					15	

Lys	Ile	Leu	Thr	Ala	Thr	Leu	Ala	Val	Gly	Leu	Ile	Ala	Pro	Leu	Ala
		20						25					30		

Asn	Pro	Phe	Ile	Glu	Ile	Ser	Arg	Ala	Glu	Asn	Lys	Ile	Glu	Asp	Ile
		35					40					45			

Gly	Gln	Gly	Ala	Glu	Ile	Ile	Lys	Arg	Thr	Gln	Asp	Ile	Thr	Ser	Lys
	50					55					60				

Arg	Leu	Ala	Ile	Thr	Gln	Asn	Ile	Gln	Phe	Asp	Phe	Val	Lys	Asp	Lys
65					70					75					80

Lys	Tyr	Asn	Lys	Asp	Ala	Leu	Val	Val	Lys	Met	Gln	Gly	Phe	Ile	Ser
			85						90					95	

Ser	Arg	Thr	Thr	Tyr	Ser	Asp	Leu	Lys	Lys	Tyr	Pro	Tyr	Ile	Lys	Arg
			100					105						110	

Met	Ile	Trp	Pro	Phe	Gln	Tyr	Asn	Ile	Ser	Leu	Lys	Thr	Lys	Asp	Ser
		115					120					125			

Asn	Val	Asp	Leu	Ile	Asn	Tyr	Leu	Pro	Lys	Asn	Lys	Ile	Asp	Ser	Ala
	130					135					140				

Asp	Val	Ser	Gln	Lys	Leu	Gly	Tyr	Asn	Ile	Gly	Gly	Asn	Phe	Gln	Ser
145					150					155					160

Ala	Pro	Ser	Ile	Gly	Gly	Ser	Gly	Ser	Phe	Asn	Tyr	Ser	Lys	Thr	Ile
				165					170					175	

Ser	Tyr	Asn	Gln	Lys	Asn	Tyr	Val	Thr	Glu	Val	Glu	Ser	Gln	Asn	Ser
			180					185					190		

Lys	Gly	Val	Lys	Trp	Gly	Val	Lys	Ala	Asn	Ser	Phe	Val	Thr	Pro	Asn
		195					200					205			

Gly	Gln	Val	Ser	Ala	Tyr	Asp	Gln	Tyr	Leu	Phe	Ala	Gln	Asp	Gln	Thr
	210					215					220				

Gly	Pro	Ala	Ala	Arg	Asp	Tyr	Phe	Val	Pro	Asp	Asn	Gln	Leu	Pro	Pro
225					230					235					240

Leu Ile Gln Ser Gly Phe Asn Pro Ser Phe Ile Thr Thr Leu Ser His
245 250 255

Glu Arg Gly Lys Gly Asp Lys Ser Glu Phe Glu Ile Thr Tyr Gly Arg
260 265 270

Asn Met Asp Ala Thr Tyr Ala Tyr Val Thr Arg His Arg Leu Ala Val
275 280 285

Asp Arg Lys His Asp Ala Phe Lys Asn Arg Asn Val Thr Val Lys Tyr
290 295 300

Glu Val Asn Trp Lys Thr His Glu Val Lys Ile Lys Ser Ile Thr Pro
305 310 315 320

Lys

<210> 86

<211> 310

<212> PRT

<213> Artificial Sequence

<220>

<223> Synergohymenotropic toxin amino acid sequenceSynergohymenotropic toxin amino acid sequence

<400> 86

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

Leu Pro Leu Ile Thr Pro Tyr Ser Glu Glu Ala Lys Ala Ala Asn Thr
20 25 30

Ile Glu Glu Ile Gly Glu Gly Ala Gln Ile Ile Lys Arg Thr Glu Asp
35 40 45

Val Ser Ser Arg Lys Trp Gly Val Thr Gln Asn Ile Gln Phe Asp Phe
50 55 60

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

Gly Phe Ile Lys Ser Arg Thr Ser Phe Thr Asp Val Lys Gly Lys Gly
85 90 95

Tyr Glu Ser Thr Lys Arg Ile Leu Trp Pro Phe Gln Tyr Asn Ile Ala
100 105 110

Leu Lys Thr Asn Asp Pro Asn Val Phe Leu Ile Asn Tyr Leu Pro Lys
115 120 125

Asn Lys Ile Glu Ser Ile Asp Val Ser Gln Thr Leu Gly Tyr Asn Val
130 135 140

Gly Gly Asn Phe Gln Ser Ala Pro Leu Leu Gly Gly Lys Gly Glu Phe
145 150 155 160

Asn Tyr Ser Lys Lys Ile Ser Tyr Thr Gln Lys Asn Tyr Ile Ser Glu
165 170 175

Val Ala Gln Gln Asn Ser Lys Asn Ile Arg Trp Glu Val Lys Ala Asn
180 185 190

Ser Phe Asn Thr Glu Asn Gly Gln Val Ser Ala Tyr Asp Arg His Leu
195 200 205

Phe Val Arg Ser Pro Ile Gly Pro Asn Ala Arg Asp Phe Phe Val Pro
210 215 220

Asn Asp Glu Leu Pro Pro Leu Ile Gln Ser Gly Phe Asn Pro Ser Phe
225 230 235 240

Ile Ala Thr Val Ser His Glu Lys Asp Lys Gly Asp Thr Ser Glu Phe
245 250 255

Glu Ile Ala Tyr Gly Arg Asn Leu Asp Ile Thr Tyr Ala Thr Phe Phe
260 265 270

Pro Arg Thr Gly Ile Phe Ala Glu Arg Arg His Asn Ala Leu Met Asn
275 280 285

Arg Asn Leu Val Thr Lys Tyr Glu Val Asn Trp Lys Thr His Glu Ile
290 295 300

Lys Val Lys Gly His Asn
305 310

<210> 87

<211> 314

<212> PRT

<213> Artificial Sequence

<220>

<223> Leukotoxin LukEamino acid sequence

<400> 87

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

Ala Pro Leu Ala Ser Pro Ile Gln Glu Ser Arg Ala Asn Thr Asn Ile
20 25 30

Glu Asn Ile Gly Asp Gly Ala Glu Val Ile Lys Arg Thr Glu Asp Val
35 40 45

Ser Ser Lys Lys Trp Gly Val Thr Gln Asn Val Gln Phe Asp Phe Val
50 55 60

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

Phe Ile Asn Ser Arg Thr Ser Phe Ser Asp Val Lys Gly Arg Gly Tyr
85 90 95

Glu Leu Thr Lys Arg Leu Ile Trp Pro Phe Gln Tyr Asn Ile Gly Leu
100 105 110

Thr Thr Lys Asp Pro Asn Val Ser Leu Ile Asn Ser Ile Thr Leu Pro
115 120 125

Lys Thr Lys Ile Glu Thr Thr Asp Val Gly Gln Thr Leu Gly Tyr Asn
130 135 140

Ile Gly Gly Asn Phe Gln Ser Ala Pro Ser Ile Gly Gly Asn Gly Ser
145 150 155 160

Phe Asn Tyr Ser Lys Thr Ile Ser Tyr Thr Gln Lys Ser Tyr Val Ser
165 170 175

Glu Val Asp Lys Gln Asn Ser Lys Ser Val Lys Trp Gly Val Lys Ala
180 185 190

Asn Lys Phe Val Thr Pro Asp Gly Lys Lys Phe Ala His Asp Arg Tyr
195 200 205

Leu Phe Val Gln Ser Pro Asn Gly Pro Thr Gly Ser Ala Arg Glu Tyr
210 215 220

Phe Ala Pro Asp Asn Gln Leu Pro Pro Leu Val Gln Ser Gly Phe Asn
225 230 235 240

Pro Ser Phe Ile Thr Thr Leu Ser His Glu Lys Gly Ser Lys Leu Ile
245 250 255

Arg Val Asn Leu Lys Phe Ser Tyr Gly Arg Asn Leu Asp Ile Thr Tyr
260 265 270

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

Ala Phe Val Asn Arg Asn Phe Val Val Arg Tyr Lys Val Asn Trp Lys
290 295 300

Thr His Glu Ile Lys Val Lys Gly His Asn
305 310

<210> 88

<211> 290

<212> PRT

<213> Artificial Sequence

<220>

<223> Chain B, crystal structure of octameric pore form of gamma-hemolysin amino acid

sequence

<400> 88

Met Gly His His His His His His Ala Met Glu Asn Lys Ile Glu Asp
 1 5 10 15

Ile Gly Gln Gly Ala Glu Ile Ile Lys Arg Thr Gln Asp Ile Thr Ser
 20 25 30

Lys Arg Leu Ala Ile Thr Gln Asn Ile Gln Phe Asp Phe Val Lys Asp
 35 40 45

Lys Lys Tyr Asn Lys Asp Ala Leu Val Val Lys Met Gln Gly Phe Ile
 50 55 60

Ser Ser Arg Thr Thr Tyr Ser Asp Leu Lys Lys Tyr Pro Tyr Ile Lys
 65 70 75 80

Arg Met Ile Trp Pro Phe Gln Tyr Asn Ile Ser Leu Lys Thr Lys Asp
 85 90 95

Ser Asn Val Asp Leu Ile Asn Tyr Leu Pro Lys Asn Lys Ile Asp Ser
 100 105 110

Ala Asp Val Ser Gln Lys Leu Gly Tyr Asn Ile Gly Gly Asn Phe Gln
 115 120 125

Ser Ala Pro Ser Ile Gly Gly Ser Gly Ser Phe Asn Tyr Ser Lys Thr
 130 135 140

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

Ser Lys Gly Val Lys Trp Gly Val Lys Ala Asn Ser Phe Val Thr Pro
 165 170 175

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

Thr Gly Pro Ala Ala Arg Asp Tyr Phe Val Pro Asp Asn Gln Leu Pro
 195 200 205

Pro Leu Ile Gln Ser Gly Phe Asn Pro Ser Phe Ile Thr Thr Leu Ser
 210 215 220

His Glu Arg Gly Lys Gly Asp Lys Ser Glu Phe Glu Ile Thr Tyr Gly
 225 230 235 240

Arg Asn Met Asp Ala Thr Tyr Ala Tyr Val Thr Arg His Arg Leu Ala
 245 250 255

Val Asp Arg Lys His Asp Ala Phe Lys Asn Arg Asn Val Thr Val Lys
 260 265 270

Tyr Glu Val Asn Trp Lys Thr His Glu Val Lys Ile Lys Ser Ile Thr
 275 280 285

Pro Lys
290

<210> 89

<211> 203

<212> PRT

<213> Artificial Sequence

<220>

<223> gamma-hemolysin component C amino acid sequence

<400> 89

Leu Lys Thr Asn Asp Lys Tyr Val Ser Leu Ile Asn Tyr Leu Pro Lys
1 5 10 15

Asn Lys Ile Glu Ser Thr Asn Val Ser Gln Thr Leu Gly Tyr Asn Ile

20

25

30

Gly Gly Asn Phe Gln Ser Ala Pro Ser Leu Gly Gly Asn Gly Ser Phe
35 40 45

Asn Tyr Ser Lys Ser Ile Ser Tyr Thr Gln Gln Asn Tyr Val Ser Glu
50 55 60

Val Glu Gln Gln Asn Ser Lys Ser Val Leu Trp Gly Val Lys Ala Asn
65 70 75 80

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

Phe Val Gly Tyr Lys Pro His Ser Lys Asp Pro Arg Asp Tyr Phe Val
100 105 110

Pro Asp Ser Glu Leu Pro Pro Leu Val Gln Ser Gly Phe Asn Pro Ser
115 120 125

Phe Ile Ala Thr Val Ser His Glu Lys Gly Ser Ser Asp Thr Ser Glu
130 135 140

Phe Glu Ile Thr Tyr Gly Arg Asn Met Asp Val Thr His Ala Ile Lys
145 150 155 160

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

Asn Ala Phe Val Asn Arg Asn Tyr Thr Val Lys Tyr Glu Val Asn Trp
180 185 190

Lys Thr His Glu Ile Lys Val Lys Gly Gln Asn
195 200

<210> 90

<211> 325

<212> PRT

<213> Artificial Sequence

<220>

<223> Leucocidin F amino acid sequence

<400> 90

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

Leu Leu Ser Asn Thr Leu Asp Ala Ala Gln His Ile Thr Pro Val Ser
 20 25 30

Glu Lys Lys Val Asp Asp Lys Ile Thr Leu Tyr Lys Thr Thr Ala Thr
 35 40 45

Ser Asp Ser Asp Lys Leu Lys Ile Ser Gln Ile Leu Thr Phe Asn Phe
 50 55 60

Ile Lys Asp Lys Ser Tyr Asp Lys Asp Thr Leu Ile Leu Lys Ala Ala
 65 70 75 80

Gly Asn Ile Tyr Ser Gly Tyr Thr Lys Pro Asn Pro Lys Asp Thr Ile
 85 90 95

Ser Ser Gln Phe Tyr Trp Gly Ser Lys Tyr Asn Ile Ser Ile Asn Ser
 100 105 110

Asp Ser Asn Asp Ser Val Asn Val Val Asp Tyr Ala Pro Lys Asn Gln
 115 120 125

Asn Glu Glu Phe Gln Val Gln Gln Thr Val Gly Tyr Ser Tyr Gly Gly
 130 135 140

Asp Ile Asn Ile Ser Asn Gly Leu Ser Gly Gly Gly Asn Gly Ser Lys
 145 150 155 160

Ser Phe Ser Glu Thr Ile Asn Tyr Lys Gln Glu Ser Tyr Arg Thr Ser
 165 170 175

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

His Lys Ile Met Asn Asn Gly Trp Gly Pro Tyr Gly Arg Asp Ser Tyr
 195 200 205

His Ser Thr Tyr Gly Asn Glu Met Phe Leu Gly Ser Arg Gln Ser Asn
 210 215 220

Leu Asn Ala Gly Gln Asn Phe Leu Glu Tyr His Lys Met Pro Val Leu
 225 230 235 240

Ser Arg Gly Asn Phe Asn Pro Glu Phe Ile Gly Val Leu Ser Arg Lys
 245 250 255

Gln Asn Ala Ala Lys Lys Ser Lys Ile Thr Val Thr Tyr Gln Ser Glu
 260 265 270

Met Asp Arg Tyr Thr Asn Phe Trp Ile Asn Phe Asn Trp Ile Gly Asn
 275 280 285

Asn Tyr Lys Asp His Ile Arg Ala Thr His Thr Ser Ile Tyr Glu Val
 290 295 300

Asp Trp Glu Asn His Thr Val Lys Leu Ile Asp Thr Gln Ser Lys Glu
 305 310 315 320

Lys Asn Pro Met Ser
 325

<210> 91

<211> 327

<212> PRT

<213> Artificial Sequence

<220>

<223> gamma-hemolysin component B amino acid sequence

<400> 91

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

Leu Leu Leu Leu Ser Asn Thr Val Asp Ala Ala Gln His Ile Thr Pro
 20 25 30

Val Ser Glu Lys Lys Val Asp Asp Lys Ile Thr Leu Tyr Lys Thr Thr
 35 40 45

Ala Thr Ser Asp Asn Asp Lys Leu Asn Ile Ser Gln Ile Leu Thr Phe
 50 55 60

Asn Phe Ile Lys Asp Lys Ser Tyr Asp Lys Asp Thr Leu Val Leu Lys
 65 70 75 80

Ala Ala Gly Asn Ile Asn Ser Gly Tyr Lys Lys Pro Asn Pro Lys Asp
 85 90 95

Tyr Asn Tyr Ser Gln Phe Tyr Trp Gly Gly Lys Tyr Asn Val Ser Val
 100 105 110

Ser Ser Glu Ser Asn Asp Ala Val Asn Val Val Asp Tyr Ala Pro Lys
 115 120 125

Asn Gln Asn Glu Glu Phe Gln Val Gln Gln Thr Leu Gly Tyr Ser Tyr
 130 135 140

Gly Gly Asp Ile Asn Ile Ser Asn Gly Leu Ser Gly Gly Leu Asn Gly
 145 150 155 160

Ser Lys Ser Phe Ser Glu Thr Ile Asn Tyr Lys Gln Glu Ser Tyr Arg
165 170 175

Thr Thr Ile Asp Arg Lys Thr Asn His Lys Ser Ile Gly Trp Gly Val
180 185 190

Glu Ala His Lys Ile Met Asn Asn Gly Trp Gly Pro Tyr Gly Arg Asp
195 200 205

Ser Tyr Asp Pro Thr Tyr Gly Asn Glu Leu Phe Leu Gly Gly Arg Gln
210 215 220

Ser Ser Leu Asn Ala Gly Gln Asn Phe Leu Pro Thr His Gln Met Pro
225 230 235 240

Leu Leu Ala Arg Gly Asn Phe Asn Pro Glu Phe Ile Ser Val Leu Ser
245 250 255

His Lys Gln Asn Asp Thr Lys Lys Ser Lys Ile Lys Val Thr Tyr Gln
260 265 270

Arg Glu Met Asp Arg Tyr Thr Asn Gln Trp Asn Arg Leu His Trp Ile
275 280 285

Gly Asn Asn Tyr Lys Asn Gln Asn Thr Val Thr Phe Thr Ser Thr Tyr
290 295 300

Glu Val Asp Trp Gln Asn His Thr Val Lys Leu Ile Gly Thr Asp Ser
305 310 315 320

Lys Glu Thr Asn Pro Gly Val
325

<210> 92

<211> 327

<212> PRT

<213> Artificial Sequence

<220>

<223> gamma-hemolysin component B amino acid sequence

<400> 92

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

Leu Leu Leu Leu Ser Asn Thr Val Asp Ala Ala Gln His Ile Thr Pro
20 25 30

Val Ser Glu Lys Lys Val Asp Asp Lys Ile Thr Leu Tyr Lys Thr Thr
35 40 45

Ala Thr Ser Asp Asn Asp Lys Leu Asn Ile Ser Gln Ile Leu Thr Phe
50 55 60

Asn Phe Ile Lys Asp Lys Ser Tyr Asp Lys Asp Thr Leu Val Leu Lys
 65 70 75 80
 Ala Ala Gly Asn Ile Asn Ser Gly Tyr Lys Lys Pro Asn Pro Lys Asp
 85 90 95
 Tyr Asn Tyr Ser Gln Phe Tyr Trp Gly Gly Lys Tyr Asn Val Ser Val
 100 105 110
 Ser Ser Glu Ser Asn Asp Ala Val Asn Val Val Asp Tyr Ala Pro Lys
 115 120 125
 Asn Gln Asn Glu Glu Phe Gln Val Gln Gln Thr Leu Gly Tyr Ser Tyr
 130 135 140
 Gly Gly Asp Ile Asn Ile Ser Asn Gly Leu Ser Gly Gly Leu Asn Gly
 145 150 155 160
 Ser Lys Ser Phe Ser Glu Thr Ile Asn Tyr Lys Gln Glu Ser Tyr Arg
 165 170 175
 Thr Thr Ile Asp Arg Lys Thr Asn His Lys Ser Ile Gly Trp Gly Val
 180 185 190
 Glu Ala His Lys Ile Met Asn Asn Gly Trp Gly Pro Tyr Gly Arg Asp
 195 200 205
 Ser Tyr Asp Pro Thr Tyr Gly Asn Glu Leu Phe Leu Gly Gly Arg Gln
 210 215 220
 Ser Ser Ser Asn Ala Gly Gln Asn Phe Leu Pro Thr His Gln Met Pro
 225 230 235 240
 Leu Leu Ala Arg Gly Asn Phe Asn Pro Glu Phe Ile Ser Val Leu Ser
 245 250 255
 His Lys Gln Asn Asp Thr Lys Lys Ser Lys Ile Lys Val Thr Tyr Gln
 260 265 270
 Arg Glu Met Asp Arg Tyr Thr Asn Gln Trp Asn Arg Leu His Trp Ile
 275 280 285
 Gly Asn Asn Tyr Lys Asn Gln Asn Thr Ala Thr Phe Thr Ser Thr Tyr
 290 295 300
 Glu Val Asp Trp Gln Asn His Thr Val Lys Leu Ile Ser Thr Asp Ser
 305 310 315 320
 Lys Glu Thr Asn Pro Gly Val
 325

<210> 93

<211> 327

<212> PRT

<213> Artificial Sequence

<220>

<223> Leukocidin/Hemolysin toxin family protein amino acid sequence

<400> 93

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

Leu Ile Met Leu Ser Asn Thr Val Asp Ala Ala Gln His Ile Thr Pro
 20 25 30

Val Ser Glu Lys Lys Val Asp Asp Lys Ile Thr Leu Tyr Lys Thr Thr
 35 40 45

Ala Thr Ser Asp Asn Asp Lys Leu Asn Ile Ser Gln Ile Leu Thr Phe
 50 55 60

Asn Phe Ile Lys Asp Lys Ser Tyr Asp Lys Asp Thr Leu Val Leu Lys
 65 70 75 80

Ala Ala Gly Asn Ile Asn Ser Gly Tyr Lys Lys Pro Asn Pro Lys Asp
 85 90 95

Tyr Asn Tyr Ser Tyr Phe Tyr Trp Gly Ala Lys Tyr Asn Val Ser Val
 100 105 110

Ser Ser Glu Ser Asn Asp Ser Val Asn Val Val Asp Tyr Ala Pro Lys
 115 120 125

Asn Gln Asn Glu Glu Phe Gln Val Gln Gln Thr Leu Gly Tyr Ser Tyr
 130 135 140

Gly Gly Asp Ile Asn Ile Thr Asn Gly Leu Ser Gly Gly Leu Asn Gly
 145 150 155 160

Ser Lys Ser Phe Ser Glu Thr Ile Asn Tyr Lys Gln Glu Ser Tyr Arg
 165 170 175

Thr Thr Ile Asp Arg Lys Thr Asn His Lys Ser Ile Gly Trp Gly Val
 180 185 190

Glu Ala His Lys Ile Met Asn Asn Gly Trp Gly Pro Tyr Gly Arg Asp
 195 200 205

Ser Tyr Asp Pro Thr Tyr Gly Asn Glu Leu Phe Leu Gly Gly Arg Gln
 210 215 220

Ser Ser Ser Asn Ala Gly Gln Asn Phe Leu Pro Thr His Gln Met Pro
 225 230 235 240

Leu Leu Ala Arg Gly Asn Phe Asn Pro Glu Phe Ile Ser Val Leu Ser
 245 250 255

His Lys Gln Asn Glu Ala Lys Lys Ser Lys Ile Lys Val Thr Tyr Gln
 260 265 270

Arg Glu Met Asp Arg Tyr Thr Asn Tyr Trp Asn Arg Leu His Trp Ile
 275 280 285

Gly Asn Asn His Lys Asn Gln Asn Thr Val Thr Phe Thr Ser Thr Tyr
 290 295 300

Glu Val Asp Trp His Asn His Thr Val Lys Leu Ile Asp Thr Asn Ser
 305 310 315 320

Lys Glu Thr Asn Pro Gly Val
 325

<210> 94

<211> 327

<212> PRT

<213> Artificial Sequence

<220>

<223> Leukotoxin, LukD amino acid sequence

<400> 94

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

Leu Leu Met Leu Ser Asn Thr Val Asp Ala Ala Gln His Ile Thr Pro
 20 25 30

Val Ser Glu Lys Lys Val Asp Asp Lys Ile Thr Leu Tyr Lys Thr Thr
 35 40 45

Ala Thr Ser Asp Asn Asp Lys Leu Asn Ile Ser Gln Ile Leu Thr Phe
 50 55 60

Asn Phe Ile Lys Asp Lys Ser Tyr Asp Lys Asp Thr Leu Val Leu Lys
 65 70 75 80

Ala Ala Gly Asn Ile Asn Ser Gly Tyr Lys Lys Pro Asn Pro Lys Asp
 85 90 95

Tyr Asn Tyr Ser Gln Phe Tyr Trp Gly Gly Lys Tyr Asn Val Ser Val
 100 105 110

Ser Ser Glu Ser Asn Asp Ala Val Asn Val Val Asp Tyr Ala Pro Lys
 115 120 125

Asn Gln Asn Glu Glu Phe Gln Val Gln Gln Thr Leu Gly Tyr Ser Tyr
 130 135 140

Gly Gly Asp Ile Asn Ile Ser Asn Gly Leu Ser Gly Gly Leu Asn Gly
 145 150 155 160

Ser Lys Ser Phe Ser Glu Thr Ile Asn Tyr Lys Gln Glu Ser Tyr Arg
 165 170 175

Thr Thr Ile Asp Arg Lys Thr Asn His Lys Ser Ile Gly Trp Gly Val
 180 185 190

Glu Ala His Lys Ile Met Asn Asn Gly Trp Gly Pro Tyr Gly Arg Asp
 195 200 205

Ser Tyr Asp Pro Thr Tyr Gly Asn Glu Leu Phe Leu Gly Gly Arg Gln
 210 215 220

Ser Ser Ser Asn Ala Gly Gln Asn Phe Leu Pro Thr His Gln Met Pro
 225 230 235 240

Leu Leu Ala Arg Gly Asn Phe Asn Pro Glu Phe Ile Ser Val Leu Ser
 245 250 255

His Lys Gln Asn Asp Thr Lys Lys Ser Lys Ile Lys Val Thr Tyr Gln
 260 265 270

Arg Glu Met Asp Arg Tyr Thr Asn Gln Trp Asn Arg Leu His Trp Ile
 275 280 285

Gly Asn Asn Tyr Lys Asn Gln Asn Thr Val Thr Phe Thr Ser Thr Tyr
 290 295 300

Glu Val Asp Trp Gln Asn His Thr Val Lys Leu Ile Gly Thr Asp Ser
 305 310 315 320

Lys Glu Thr Asn Pro Gly Val
 325

<210> 95

<211> 327

<212> PRT

<213> Artificial Sequence

<220>

<223> Leukotoxin, LukD amino acid sequence

<400> 95

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

Leu Leu Met Leu Ser Asn Thr Val Asp Ala Ala Gln His Ile Thr Pro
 20 25 30

Val Ser Glu Lys Lys Val Asp Asp Lys Ile Thr Leu Tyr Lys Thr Thr
 35 40 45

Ala Thr Ser Asp Asn Asp Lys Leu Asn Ile Ser Gln Ile Leu Thr Phe
 50 55 60

Asn Phe Ile Lys Asp Lys Ser Tyr Asp Lys Asp Thr Leu Val Leu Lys
 65 70 75 80

Ala Ala Gly Asn Val Asn Ser Gly Tyr Lys Lys Pro Asn Pro Lys Asp
 85 90 95

- - - - -

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

Ser Ser Glu Ser Asn Asp Ala Val Asn Val Val Asp Tyr Ala Pro Lys
 115 120 125

Asn Gln Asn Glu Glu Phe Gln Val Gln Gln Thr Leu Gly Tyr Ser Tyr
 130 135 140

Gly Gly Asp Ile Asn Ile Ser Asn Gly Leu Ser Gly Gly Leu Asn Gly
 145 150 155 160

Ser Lys Ser Phe Ser Glu Thr Ile Asn Tyr Lys Gln Glu Ser Tyr Arg
 165 170 175

Thr Thr Ile Asp Arg Lys Thr Asn His Lys Ser Ile Gly Trp Gly Val
 180 185 190

Glu Ala His Lys Ile Met Asn Asn Gly Trp Gly Pro Tyr Gly Arg Asp
 195 200 205

Ser Tyr Asp Pro Thr Tyr Gly Asn Glu Leu Phe Leu Gly Gly Arg Gln
 210 215 220

Ser Ser Ser Asn Ala Gly Gln Asn Phe Leu Pro Thr His Gln Met Pro
 225 230 235 240

Leu Leu Ala Arg Gly Asn Phe Asn Pro Glu Phe Ile Ser Val Leu Ser
 245 250 255

His Lys Gln Asn Asp Thr Lys Lys Ser Lys Ile Lys Val Thr Tyr Gln
 260 265 270

Arg Glu Met Asp Arg Tyr Thr Asn Gln Trp Asn Arg Leu His Trp Ile
 275 280 285

Gly Asn Asn Tyr Lys Asn Gln Asn Thr Val Thr Phe Thr Ser Thr Tyr
 290 295 300

Glu Val Asp Trp Gln Asn His Thr Val Lys Leu Ile Gly Thr Asp Ser
 305 310 315 320

Lys Glu Thr Asn Pro Gly Val
 325

<210> 96

<211> 327

<212> PRT

<213> Artificial Sequence

<220>

<223> Leukotoxin, LukD amino acid sequence

<400> 96

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

```

Leu Leu Leu Leu Ser Asn Thr Val Asp Ala Ala Gln His Ile Thr Pro
    20                      25                      30

Val Ser Glu Lys Lys Val Asp Asp Lys Ile Thr Leu Tyr Lys Thr Thr
    35                      40                      45

Ala Thr Ser Asp Asn Asp Lys Leu Asn Ile Ser Gln Ile Leu Thr Phe
    50                      55                      60

Asn Phe Ile Lys Asp Lys Ser Tyr Asp Lys Asp Thr Leu Val Leu Lys
    65                      70                      75                      80

Ala Ala Gly Asn Ile Asn Ser Gly Tyr Lys Lys Pro Asn Pro Lys Asp
    85                      90                      95

Tyr Asn Tyr Ser Gln Phe Tyr Trp Gly Gly Lys Tyr Asn Val Ser Val
    100                     105                     110

Ser Ser Glu Ser Asn Asp Ala Val Asn Val Val Asp Tyr Ala Pro Lys
    115                     120                     125

Asn Gln Asn Glu Glu Phe Gln Val Gln Gln Thr Leu Gly Tyr Ser Tyr
    130                     135                     140

Gly Gly Asp Ile Asn Ile Ser Asn Gly Leu Ser Gly Gly Leu Asn Gly
    145                     150                     155                     160

Ser Lys Ser Phe Ser Glu Thr Ile Asn Tyr Lys Gln Glu Ser Tyr Arg
    165                     170                     175

Thr Thr Ile Asp Arg Lys Thr Asn His Lys Ser Ile Gly Trp Gly Val
    180                     185                     190

Glu Ala His Lys Ile Met Asn Asn Gly Trp Gly Pro Tyr Gly Arg Asp
    195                     200                     205

Ser Tyr Asp Pro Thr Tyr Gly Asn Glu Leu Phe Leu Gly Gly Arg Gln
    210                     215                     220

Ser Ser Ser Asn Ala Gly Gln Asn Phe Leu Pro Thr His Gln Met Pro
    225                     230                     235                     240

Leu Leu Ala Arg Gly Asn Phe Asn Pro Glu Phe Ile Ser Val Leu Ser
    245                     250                     255

His Lys Gln Asn Asp Thr Lys Lys Ser Lys Ile Lys Val Thr Tyr Gln
    260                     265                     270

Arg Glu Met Asp Arg Tyr Thr Asn Gln Trp Asn Arg Leu His Trp Ile
    275                     280                     285

Gly Asn Asn Tyr Lys Asn Gln Asn Thr Val Thr Phe Thr Ser Thr Tyr
    290                     295                     300

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Glu Val Asp Trp Gln Asn His Thr Val Lys Leu Ile Gly Thr Asp Ser
 305 310 315 320

Lys Glu Thr Asn Pro Gly Val
 325

<210> 97

<211> 327

<212> PRT

<213> Artificial Sequence

<220>

<223> Leukotoxin amino acid sequence

<400> 97

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

Leu Leu Leu Leu Ser Asn Thr Val Asp Ala Ala Gln His Ile Thr Pro
 20 25 30

Val Ser Glu Lys Lys Val Asp Asp Lys Ile Thr Leu Tyr Lys Thr Thr
 35 40 45

Ala Thr Ser Asp Asn Asp Lys Leu Asn Ile Ser Gln Ile Leu Thr Phe
 50 55 60

Asn Phe Ile Lys Asp Lys Ser Tyr Asp Lys Asp Thr Leu Val Leu Lys
 65 70 75 80

Ala Ala Gly Asn Ile Asn Ser Gly Tyr Lys Lys Pro Asn Pro Lys Asp
 85 90 95

Tyr Asn Tyr Ser Gln Phe Tyr Trp Gly Gly Lys Tyr Asn Val Ser Val
 100 105 110

Ser Ser Glu Ser Asn Asp Ala Val Asn Val Val Asp Tyr Ala Pro Lys
 115 120 125

Asn Gln Asn Glu Glu Phe Gln Val Gln Gln Thr Leu Gly Tyr Ser Tyr
 130 135 140

Gly Gly Asp Ile Asn Ile Ser Asn Gly Leu Ser Gly Gly Leu Asn Gly
 145 150 155 160

Ser Lys Ser Phe Ser Glu Thr Ile Asn Tyr Lys Gln Glu Ser Tyr Arg
 165 170 175

Thr Thr Ile Asp Arg Lys Thr Asn His Lys Ser Ile Gly Trp Gly Val
 180 185 190

Glu Ala His Lys Ile Met Asn Asn Gly Trp Gly Pro Tyr Gly Arg Asp
 195 200 205

Ser Tyr Asp Pro Thr Tyr Gly Asn Glu Leu Phe Leu Gly Gly Arg Gln
 210 215 220

Ser Ser Ser Asn Ala Gly Gln Asn Phe Leu Pro Thr His Gln Met Pro
 225 230 235 240

Leu Leu Ala Arg Gly Asn Phe Asn Pro Glu Phe Ile Ser Val Leu Ser
 245 250 255

His Lys Gln Asn Asp Thr Lys Lys Ser Lys Ile Lys Val Thr Tyr Gln
 260 265 270

Arg Glu Met Asp Arg Tyr Thr Asn Gln Trp Asn Arg Leu His Trp Val
 275 280 285

Gly Asn Asn Tyr Lys Asn Gln Asn Thr Val Thr Phe Thr Ser Thr Tyr
 290 295 300

Glu Val Asp Trp Gln Asn His Thr Val Lys Leu Ile Gly Thr Asp Ser
 305 310 315 320

Lys Glu Thr Asn Pro Gly Val
 325

<210> 98

<211> 327

<212> PRT

<213> Artificial Sequence

<220>

<223> gamma-hemolysin component C precursor amino acid sequence

<400> 98

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

Leu Leu Leu Leu Ser Asn Thr Val Asp Ala Ala Gln His Ile Thr Pro
 20 25 30

Val Ser Glu Lys Lys Val Asp Asp Lys Ile Thr Leu Tyr Lys Thr Thr
 35 40 45

Ala Thr Ser Asp Asn Asp Lys Leu Asn Ile Ser Gln Ile Leu Thr Phe
 50 55 60

Asn Phe Ile Lys Asp Lys Ser Tyr Asp Lys Asp Thr Leu Val Leu Lys
 65 70 75 80

Ala Ala Gly Asn Ile Asn Ser Gly Tyr Lys Lys Pro Asn Pro Lys Asp
 85 90 95

Tyr Asn Tyr Ser Gln Phe Tyr Trp Gly Gly Lys Tyr Asn Val Ser Val
 100 105 110

Ser Ser Glu Ser Asn Asp Ala Val Asn Val Val Asp Tyr Ala Pro Lys
 115 120 125

Asn Gln Asn Glu Glu Phe Gln Val Gln Gln Thr Leu Gly Tyr Ser Tyr
 130 135 140

Gly Gly Asp Ile Asn Ile Ser Asn Gly Leu Ser Gly Gly Leu Asn Gly
 145 150 155 160

Ser Lys Ser Phe Ser Glu Thr Ile Asn Tyr Lys Gln Glu Ser Tyr Arg
 165 170 175

Thr Thr Ile Asp Arg Lys Thr Asn His Lys Ser Ile Gly Trp Gly Val
 180 185 190

Glu Ala His Lys Ile Met Asn Asn Gly Trp Gly Pro Tyr Gly Arg Asp
 195 200 205

Ser Tyr Asp Pro Thr Tyr Gly Asn Glu Leu Phe Leu Gly Gly Arg Gln
 210 215 220

Ser Ser Ser Asn Ala Gly Gln Asn Phe Leu Pro Thr His Gln Met Pro
 225 230 235 240

Leu Leu Ala Arg Gly Asn Phe Asn Pro Glu Phe Ile Ser Val Leu Ser
 245 250 255

His Lys Gln Asn Asp Thr Lys Lys Ser Lys Ile Lys Val Thr Tyr Gln
 260 265 270

Arg Glu Met Asp Arg Tyr Thr Asn Gln Trp Asn Arg Leu His Trp Ile
 275 280 285

Gly Asn Asn Tyr Lys Asn Gln Asn Thr Val Thr Phe Thr Ser Thr Tyr
 290 295 300

Glu Val Asp Trp Gln Asn His Thr Val Lys Leu Ile Gly Thr Asp Ser
 305 310 315 320

Lys Glu Thr Asn Pro Gly Val
 325

<210> 99

<211> 327

<212> PRT

<213> Artificial Sequence

<220>

<223> gamma-hemolysin component B amino acid sequence

<400> 99

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

Leu Leu Leu Leu Ser Asn Thr Val Asp Ala Ala Gln His Ile Thr Pro
 20 25 30

Val Ser Glu Lys Lys Val Asp Asp Lys Ile Thr Leu Tyr Lys Thr Thr
 35 40 45

Ala Thr Ser Asp Asn Asp Lys Leu Asn Ile Ser Gln Ile Leu Thr Phe
 50 55 60

Asn Phe Ile Lys Asp Lys Ser Tyr Asp Lys Asp Thr Leu Val Leu Lys
 65 70 75 80

Ala Ala Gly Asn Ile Asn Ser Gly Tyr Lys Lys Pro Asn Pro Arg Asp
 85 90 95

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

Ser Ser Glu Ser Asn Asp Ala Val Asn Val Val Asp Tyr Ala Pro Lys
 115 120 125

Asn Gln Asn Glu Glu Phe Gln Val Gln Gln Thr Leu Gly Tyr Ser Tyr
 130 135 140

Gly Gly Asp Ile Asn Ile Ser Asn Gly Leu Ser Gly Gly Leu Asn Gly
 145 150 155 160

Ser Lys Ser Phe Ser Glu Thr Ile Asn Tyr Lys Gln Glu Ser Tyr Arg
 165 170 175

Thr Thr Ile Asp Arg Lys Thr Asn His Lys Ser Ile Gly Trp Gly Val
 180 185 190

Glu Ala His Lys Ile Met Asn Asn Gly Trp Gly Pro Tyr Gly Arg Asp
 195 200 205

Ser Tyr Asp Pro Thr Tyr Gly Asn Glu Leu Phe Leu Gly Gly Arg Gln
 210 215 220

Ser Ser Ser Asn Ala Gly Gln Asn Phe Leu Pro Thr His Gln Met Pro
 225 230 235 240

Leu Leu Ala Arg Gly Asn Phe Asn Pro Glu Phe Ile Ser Val Leu Ser
 245 250 255

His Lys Gln Asn Asp Thr Lys Lys Ser Lys Ile Lys Val Thr Tyr Gln
 260 265 270

Arg Glu Met Asp Arg Tyr Thr Asn Gln Trp Asn Arg Leu His Trp Ile
 275 280 285

Gly Asn Asn Tyr Lys Asn Gln Asn Thr Val Thr Phe Thr Ser Thr Tyr
 290 295 300

Glu Val Asp Trp Gln Asn His Thr Val Lys Leu Ile Ser Thr Asp Ser

305 310 315 320

Lys Glu Thr Asn Pro Gly Val
325

<210> 100

<211> 327

<212> PRT

<213> Artificial Sequence

<220>

<223> Leukotoxin D subunit amino acid sequence

<400> 100

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

Leu Leu Leu Leu Ser Asn Thr Val Asp Ala Ala Gln His Ile Thr Pro
20 25 30

Val Ser Glu Lys Lys Val Asp Asp Lys Ile Thr Leu Tyr Lys Thr Thr
35 40 45

Ala Thr Ser Asp Asn Asp Lys Leu Asn Ile Ser Gln Ile Leu Thr Phe
50 55 60

Asn Phe Ile Lys Asp Lys Ser Tyr Asp Lys Asp Thr Leu Val Leu Lys
65 70 75 80

Ala Ala Gly Asn Ile Asn Ser Gly Tyr Lys Lys Pro Asn Pro Arg Asp
85 90 95

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

Ser Ser Glu Ser Asn Asp Ala Val Asn Val Val Asp Tyr Ala Pro Lys
115 120 125

Asn Gln Asn Glu Glu Phe Gln Val Gln Gln Thr Leu Gly Tyr Ser Tyr
130 135 140

Gly Gly Asp Ile Asn Ile Ser Asn Gly Leu Ser Gly Gly Leu Asn Gly
145 150 155 160

Ser Lys Ser Phe Ser Glu Thr Ile Asn Tyr Lys Gln Glu Ser Tyr Arg
165 170 175

Thr Thr Ile Asp Arg Lys Thr Asn His Lys Ser Ile Gly Trp Gly Val
180 185 190

Glu Ala His Lys Ile Met Asn Asn Gly Trp Gly Pro Tyr Gly Arg Asp
195 200 205

Ser Tyr Asp Pro Thr Tyr Gly Asn Glu Leu Phe Leu Gly Gly Arg Gln
210 215 220

Ser Ser Ser Asn Ala Gly Gln Asn Phe Leu Pro Thr His Gln Met Pro
225 230 235 240

Leu Leu Ala Arg Gly Asn Phe Asn Pro Glu Phe Ile Ser Val Leu Ser
245 250 255

His Lys Gln Asn Asp Thr Lys Lys Ser Lys Ile Lys Val Thr Tyr Gln
260 265 270

Arg Glu Met Asp Arg Tyr Thr Asn Gln Trp Asn Arg Leu His Trp Ile
275 280 285

Gly Asn Asn Tyr Lys Asn Gln Asn Thr Val Thr Phe Thr Ser Thr Tyr
290 295 300

Glu Val Asp Trp Gln Asn His Thr Val Lys Leu Ile Gly Thr Asp Ser
305 310 315 320

Lys Glu Thr Asn Pro Gly Val
325

<210> 101

<211> 327

<212> PRT

<213> Artificial Sequence

<220>

<223> Leukotoxin D subunit amino acid sequence

<400> 101

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

Leu Leu Leu Leu Ser Asn Thr Val Asp Ala Ala Gln His Ile Thr Pro
20 25 30

Val Asn Glu Lys Lys Val Asp Asp Lys Ile Thr Leu Tyr Lys Thr Thr
35 40 45

Ala Thr Ser Asp Asn Asp Lys Leu Asn Ile Ser Gln Ile Leu Thr Phe
50 55 60

Asn Phe Ile Lys Asp Lys Ser Tyr Asp Lys Asp Thr Leu Val Leu Lys
65 70 75 80

Ala Ala Gly Asn Ile Asn Ser Gly Tyr Lys Lys Pro Asn Pro Arg Asp
85 90 95

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

Ser Ser Glu Ser Asn Asp Ala Val Asn Val Val Asp Tyr Ala Pro Lys
115 120 125

Asn Gln Asn Glu Glu Phe Gln Val Gln Gln Thr Leu Gly Tyr Ser Tyr

[illegible]

<210> 102

<211> 327

<212> PRT

<213> Artificial Sequence

<220>

<223> gamma-hemolysin component B amino acid sequence

<400> 102

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

Leu Leu Leu Leu Ser Asn Thr Val Asp Ala Ala Gln His Ile Thr Pro
20 25 30

Val Ser Glu Lys Lys Val Asp Asp Lys Ile Thr Leu Tyr Lys Thr Thr
35 40 45

Ala Thr Ser Asp Asn Asp Lys Leu Asn Ile Ser Gln Ile Leu Thr Phe
 50 55 60
 Asn Phe Ile Lys Asp Lys Ser Tyr Asp Lys Asp Thr Leu Val Leu Lys
 65 70 75 80
 Ala Ala Gly Asn Ile Asn Ser Gly Tyr Lys Lys Pro Asn Pro Lys Asp
 85 90 95
 Tyr Asn Tyr Ser Gln Phe Tyr Trp Gly Gly Lys Tyr Asn Val Ser Val
 100 105 110
 Ser Ser Glu Ser Asn Asp Ala Val Asn Val Val His Tyr Ala Pro Lys
 115 120 125
 Asn Gln Asn Glu Glu Phe Gln Val Gln Gln Thr Leu Gly Tyr Ser Tyr
 130 135 140
 Gly Gly Asp Ile Asn Ile Ser Asn Gly Leu Ser Gly Gly Leu Asn Gly
 145 150 155 160
 Ser Lys Ser Phe Ser Glu Thr Ile Asn Tyr Lys Gln Glu Ser Tyr Arg
 165 170 175
 Thr Thr Ile Asp Arg Lys Thr Asn His Lys Ser Ile Gly Trp Gly Val
 180 185 190
 Glu Ala His Lys Ile Met Asn Asn Gly Trp Gly Pro Tyr Gly Arg Asp
 195 200 205
 Ser Tyr Asp Pro Thr Tyr Gly Asn Glu Leu Phe Leu Gly Gly Arg Gln
 210 215 220
 Ser Ser Ser Asn Ala Gly Gln Asn Phe Leu Pro Thr His Gln Met Pro
 225 230 235 240
 Leu Leu Ala Arg Gly Asn Phe Asn Pro Glu Phe Ile Ser Val Leu Ser
 245 250 255
 His Lys Gln Asn Asp Thr Lys Lys Ser Lys Ile Lys Val Thr Tyr Gln
 260 265 270
 Arg Glu Met Asp Arg Tyr Thr Asn Gln Trp Asn Arg Leu His Trp Ile
 275 280 285
 Gly Asn Asn Tyr Lys Asn Gln Asn Thr Val Thr Phe Thr Ser Thr Tyr
 290 295 300
 Glu Val Asp Trp Gln Asn His Thr Val Lys Leu Ile Gly Thr Asp Ser
 305 310 315 320
 Lys Glu Thr Asn Pro Gly Val
 325

<210> 103

<211> 327

<212> PRT

<213> Artificial Sequence

<220>

<223> Leukotoxin LukD amino acid sequence

<400> 103

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

Leu Leu Leu Leu Ser Asn Thr Val Asp Ala Ala Gln His Ile Thr Pro
 20          25          30

Val Ser Glu Lys Lys Val Asp Asp Lys Ile Thr Leu Tyr Lys Thr Thr
 35          40          45

Ala Thr Ser Asp Asn Asp Lys Leu Asn Ile Ser Gln Ile Leu Thr Phe
 50          55          60

Asn Phe Ile Lys Asp Lys Ser Tyr Asp Lys Asp Thr Leu Val Leu Lys
 65          70          75          80

Ala Ala Gly Asn Ile Asn Ser Gly Tyr Lys Lys Pro Asn Pro Lys Asp
 85          90          95

Tyr Asn Tyr Ser Gln Phe Tyr Trp Ser Gly Lys Tyr Asn Val Ser Val
100          105          110

Ser Ser Glu Ser Asn Asp Ala Val Asn Val Val Asp Tyr Ala Pro Lys
115          120          125

Asn Gln Asn Glu Glu Phe Gln Val Gln Gln Thr Leu Gly Tyr Ser Tyr
130          135          140

Gly Gly Asp Ile Asn Ile Ser Asn Gly Leu Ser Gly Gly Leu Asn Gly
145          150          155          160

Ser Lys Ser Phe Ser Glu Thr Ile Asn Tyr Lys Gln Glu Ser Tyr Arg
165          170          175

Thr Thr Ile Asp Arg Lys Thr Asn His Lys Ser Ile Gly Trp Gly Val
180          185          190

Glu Ala His Lys Ile Met Asn Asn Gly Trp Gly Pro Tyr Gly Arg Asp
195          200          205

Ser Tyr Asp Pro Thr Tyr Gly Asn Glu Leu Phe Leu Gly Gly Arg Gln
210          215          220

Ser Ser Ser Asn Ala Gly Gln Asn Phe Leu Pro Thr His Gln Met Pro
225          230          235          240

Leu Leu Ala Arg Gly Asn Phe Asn Pro Glu Phe Ile Ser Val Leu Ser
245          250          255

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His Lys Gln Asn Asp Thr Lys Lys Ser Lys Ile Lys Val Thr Tyr Gln
260 265 270

Arg Glu Met Asp Arg Tyr Thr Asn Gln Trp Asn Arg Leu His Trp Val
275 280 285

Gly Asn Asn Tyr Lys Asn Gln Asn Thr Val Thr Phe Thr Ser Thr Tyr
290 295 300

Glu Val Asp Trp Gln Asn His Thr Val Lys Leu Ile Gly Thr Asp Ser
305 310 315 320

Lys Glu Thr Asn Pro Gly Val
325

<210> 104

<211> 327

<212> PRT

<213> Artificial Sequence

<220>

<223> Leukotoxin LukD amino acid sequence

<400> 104

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

Leu Leu Leu Leu Ser Asn Thr Val Asp Ala Ala Gln His Ile Thr Pro
20 25 30

Val Ser Glu Lys Lys Val Asp Asp Lys Ile Thr Leu Tyr Lys Thr Thr
35 40 45

Ala Thr Phe Asp Asn Asp Lys Leu Asn Ile Ser Gln Ile Leu Thr Phe

50

55

60

Asn Phe Ile Lys Asp Lys Ser Tyr Asp Lys Asp Thr Leu Val Leu Lys
65 70 75 80

Ala Ala Gly Asn Ile Asn Ser Gly Tyr Lys Lys Pro Asn Pro Lys Asp
85 90 95

Tyr Asn Tyr Ser Gln Phe Tyr Trp Gly Gly Lys Tyr Asn Val Ser Val
100 105 110

Ser Ser Glu Ser Asn Asp Ala Val Asn Val Val Asp Tyr Ala Pro Lys
115 120 125

Asn Gln Asn Glu Glu Phe Gln Val Gln Gln Thr Leu Gly Tyr Ser Tyr
130 135 140

Gly Gly Asp Ile Asn Ile Ser Asn Gly Leu Ser Gly Gly Leu Asn Gly
145 150 155 160

Ser Lys Ser Phe Ser Glu Thr Ile Asn Tyr Lys Gln Glu Ser Tyr Arg
165 170 175

Thr Thr Ile Asp Arg Lys Thr Asn His Lys Ser Ile Gly Trp Gly Val
180 185 190

Glu Ala His Lys Ile Met Asn Asn Gly Trp Gly Pro Tyr Gly Arg Asp
195 200 205

Ser Tyr Asp Pro Thr Tyr Gly Asn Glu Leu Phe Leu Gly Gly Arg Gln
210 215 220

Ser Ser Ser Asn Ala Gly Gln Asn Phe Leu Pro Thr His Gln Met Pro
225 230 235 240

Leu Leu Ala Arg Gly Asn Phe Asn Pro Glu Phe Ile Ser Val Leu Ser
245 250 255

His Lys Gln Asn Asp Thr Lys Lys Ser Lys Ile Lys Val Thr Tyr Gln
260 265 270

Arg Glu Met Asp Arg Tyr Thr Asn Gln Trp Asn Arg Leu His Trp Val
275 280 285

Gly Asn Asn Tyr Lys Asn Gln Asn Thr Val Thr Phe Thr Ser Thr Tyr
290 295 300

Glu Val Asp Trp Gln Asn His Thr Val Lys Leu Ile Gly Thr Asp Ser
305 310 315 320

Lys Glu Thr Asn Pro Gly Val
325

<210> 105

<211> 326

<212> PRT

<213> Artificial Sequence

<220>

<223> Leukocidin/hemolysin toxin family protein amino acid sequence

<400> 105

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

Leu Ile Met Leu Ser Asn Thr Val Asp Ala Ala Gln His Ile Thr Pro
20 25 30

Val Ser Glu Lys Lys Val Asp Asp Lys Ile Thr Leu Tyr Lys Thr Thr
35 40 45

Ala Thr Ser Asp Asn Asp Lys Leu Asn Ile Ser Gln Ile Leu Thr Phe
50 55 60

Asn Phe Ile Lys Asp Lys Ser Tyr Asp Lys Asp Thr Leu Val Leu Lys

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65              70              75              80
Ala Ala Gly Asn Ile Asn Ser Gly Tyr Lys Lys Pro Asn Pro Lys Asp
      85              90              95
Tyr Asn Tyr Ser Tyr Phe Tyr Trp Gly Ala Lys Tyr Asn Val Ser Val
      100             105             110
Ser Ser Glu Ser Asn Asp Ser Val Asn Val Val Asp Tyr Ala Pro Lys
      115             120             125
Asn Gln Asn Glu Glu Phe Gln Val Gln Gln Thr Leu Gly Tyr Ser Tyr
      130             135             140
Gly Gly Asp Ile Asn Ile Asn Gly Leu Ser Gly Gly Leu Asn Gly Ser
      145             150             155             160
Lys Ser Phe Ser Glu Thr Ile Asn Tyr Lys Gln Glu Ser Tyr Arg Thr
      165             170             175
Thr Ile Asp Arg Lys Thr Asn His Lys Ser Ile Gly Trp Gly Val Glu
      180             185             190
Ala His Lys Ile Met Asn Asn Gly Trp Gly Pro Tyr Gly Arg Asp Ser
      195             200             205
Tyr Asp Pro Thr Tyr Gly Asn Glu Leu Phe Leu Gly Gly Arg Gln Ser
      210             215             220
Ser Ser Asn Ala Gly Gln Asn Phe Leu Pro Thr His Gln Met Pro Leu
      225             230             235             240
Leu Ala Arg Gly Asn Phe Asn Pro Glu Phe Ile Ser Val Leu Ser His
      245             250             255
Lys Gln Asn Glu Ala Lys Lys Ser Lys Ile Lys Val Thr Tyr Gln Arg
      260             265             270
Glu Met Asp Arg Tyr Thr Asn Tyr Trp Asn Arg Leu His Trp Ile Gly
      275             280             285
Asn Asn His Lys Asn Gln Asn Thr Val Thr Phe Thr Ser Thr Tyr Glu
      290             295             300
Val Asp Trp His Asn His Thr Val Lys Leu Ile Asp Thr Asn Ser Lys
      305             310             315             320
Glu Thr Asn Pro Gly Val
      325

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<210> 106

<211> 327

<212> PRT

<213> Artificial Sequence

<220>

<223> Leukotoxin, LukD amino acid sequence

<400> 106

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Met Lys Ile Glu Lys Leu Gly Lys Ser Ser Val Ala Ser Ser Ile Ala
1           5           10           15

Leu Leu Leu Leu Ser Asn Thr Val Asp Ala Ala Gln Asn Ile Thr Pro
20           25           30

Lys Arg Glu Lys Lys Val Asp Asp Lys Ile Thr Leu Tyr Lys Thr Thr
35           40           45

Ala Thr Ser Asp Asn Asp Lys Leu Asn Ile Phe Gln Ile Leu Thr Phe
50           55           60

Asn Phe Ile Lys Asp Lys Ser Tyr Asp Lys Asp Thr Leu Val Leu Lys
65           70           75           80

Ala Ala Gly Asn Ile Asn Ser Gly Tyr Lys Asn Ser Asn Pro Lys Asp
85           90           95

Tyr Asn Tyr Ser Gln Phe Tyr Trp Gly Gly Lys Tyr Asn Val Ser Val
100          105          110

Ser Ser Glu Ser Asn Asp Ala Val Asn Val Val Asp Tyr Ala Pro Lys
115          120          125

Asn Gln Asn Glu Glu Phe Gln Val Gln Gln Thr Leu Gly Tyr Ser Tyr
130          135          140

Gly Gly Asp Ile Asn Ile Ser Asn Gly Leu Ser Gly Gly Leu Asn Gly
145          150          155          160

Ser Lys Ser Phe Ser Glu Thr Ile Asn Tyr Lys Gln Glu Ser Tyr Arg
165          170          175

Thr Thr Ile Asp Arg Lys Thr Asn His Lys Ser Ile Gly Trp Gly Val
180          185          190

Glu Ala His Lys Ile Met Asn Asn Gly Trp Gly Pro Tyr Gly Arg Asp
195          200          205

Ser Tyr Asp Pro Thr Tyr Gly Asn Glu Leu Phe Leu Gly Gly Asp Lys
210          215          220

Ser Ser Ser Asn Ala Gly Gln Asn Phe Leu Pro Thr His Gln Ile Pro
225          230          235          240

Leu Leu Ala Arg Gly Asn Phe Asn Pro Glu Phe Ile Ser Val Leu Ser
245          250          255

His Lys Leu Phe Asp Thr Lys Lys Ser Lys Ile Lys Val Thr Tyr Gln
260          265          270

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Arg Glu Met Asp Arg Tyr Thr Asn Gln Trp Asn Arg Ser His Trp Val
 275 280 285

Gly Asn Asn Tyr Lys Asn Gln Asn Thr Val Thr Phe Thr Ser Thr Tyr
 290 295 300

Glu Val Asp Trp Gln Asn Ile Leu Leu Lys Leu Ile Gly Thr Asp Ser
 305 310 315 320

Lys Glu Thr Asn Pro Gly Val
 325

<210> 107

<211> 326

<212> PRT

<213> Artificial Sequence

<220>

<223> Gamma-hemolysin component B amino acid sequence

<400> 107

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

Leu Met Leu Phe Ser Asn Pro Val Tyr Ala Ala Asn Gln Ile Thr Pro
 20 25 30

Val Ser Glu Lys Lys Val Asp Asp Lys Ile Thr Leu Tyr Lys Thr Thr
 35 40 45

Ala Thr Ala Asp Ser Asp Lys Leu Asn Ile Ser Gln Leu Leu Thr Phe
 50 55 60

Asn Phe Ile Lys Asp Lys Ser Tyr Asp Lys Asp Thr Leu Val Leu Lys
 65 70 75 80

Ala Ala Gly Asn Ile Asn Ser Gly Tyr Lys Ser Pro Asn Pro Asn Asp
 85 90 95

Tyr Ile Tyr Ser Ser Phe Tyr Trp Gly Ala Lys Tyr Asn Val Ser Ile
 100 105 110

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

Asn Gln Asn Glu Glu Phe Gln Val Gln Asn Thr Leu Gly Tyr Ser Phe
 130 135 140

Gly Gly Asp Ile Ser Ile Ser Lys Gly Leu Ser Gly Gly Leu Asn Gly
 145 150 155 160

Ser Glu Ser Phe Ser Glu Thr Ile Asn Tyr Lys Gln Glu Ser Tyr Arg

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165              170              175
Thr Thr Ile Asp Lys His Thr Asp Asn Lys Thr Ile Gly Trp Gly Val
180              185              190
Glu Ala His Lys Ile Met Asn Ala Gly Trp Gly Pro Tyr Gly Arg Asp
195              200              205
Ser Phe His Asp Leu Tyr Gly Asn Glu Leu Phe Leu Gly Gly Arg Gln
210              215              220
Ser Lys Leu Asn Ala Gly Gln Asn Phe Leu Pro Thr Ser Gln Met Pro
225              230              235              240
Leu Leu Ala Arg Gly Asn Phe Asn Pro Glu Phe Leu Ser Val Leu Ser
245              250              255
His Lys Pro Asn Gly Ala Lys Thr Ser Lys Ile Lys Val Thr Tyr Gln
260              265              270
Arg Glu Met Asp Glu Tyr Thr Asn Tyr Trp Asn Gly Phe His Trp Met
275              280              285
Gly Thr Asn Tyr Lys Asn Gln Asn Asn Ala Thr Phe Thr Ser Phe Tyr
290              295              300
Glu Ile Asp Trp Asp Gln His Thr Val Lys Leu Ile Lys Thr His Ser
305              310              315              320
Asp Glu Lys Asn Pro Ser
325

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<210> 108

<211> 326

<212> PRT

<213> Artificial Sequence

<220>

<223> Synergohymenotropic toxin amino acid sequence

<400> 108

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Met Lys Ile Ser Lys Val Ile Lys Ala Ala Thr Ala Thr Ser Val Ala
1      5      10      15
Leu Met Leu Phe Ser Asn Pro Val Tyr Ala Ala Asn Gln Ile Thr Pro
20     25     30
Val Ser Glu Lys Lys Val Asp Asp Lys Ile Thr Leu Tyr Lys Thr Thr
35     40     45
Ala Thr Ala Asp Ser Asp Asn Leu Asn Ile Ser Gln Leu Leu Thr Phe
50     55     60
Asn Phe Ile Lys Asp Lys Ser Tyr Asp Lys Asp Thr Leu Val Leu Lys
65     70     75     80

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Ala Ala Gly Asn Ile Asn Ser Gly Tyr Lys Ser Pro Asn Pro Asn Asp
 85 90 95

Tyr Ile Tyr Ser Ser Phe Tyr Trp Gly Ala Lys Tyr Asn Val Ser Ile
 100 105 110

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

Asn Gln Asn Glu Glu Phe Gln Val Gln Asn Thr Leu Gly Tyr Ser Phe
 130 135 140

Gly Gly Asp Ile Ser Ile Ser Lys Gly Leu Ser Gly Gly Leu Asn Gly
 145 150 155 160

Ser Glu Ser Phe Ser Glu Thr Ile Asn Tyr Lys Gln Glu Ser Tyr Arg
 165 170 175

Thr Thr Ile Asp Lys His Thr Asp Asn Lys Thr Ile Gly Trp Gly Val
 180 185 190

Glu Ala His Lys Ile Met Asn Ala Gly Trp Gly Pro Tyr Gly Arg Asp
 195 200 205

Ser Phe His Asp Leu Tyr Gly Asn Glu Leu Phe Leu Gly Gly Arg Gln
 210 215 220

Ser Lys Leu Asn Ala Gly Gln Asn Phe Leu Pro Thr Arg Gln Met Pro
 225 230 235 240

Leu Leu Ala Arg Gly Asn Phe Asn Pro Glu Phe Leu Ser Val Leu Ser
 245 250 255

His Lys Pro Asn Gly Ala Lys Thr Ser Lys Ile Lys Val Thr Tyr Gln
 260 265 270

Arg Glu Met Asp Glu Tyr Thr Asn Tyr Trp Asn Gly Phe His Trp Met
 275 280 285

Gly Thr Asn Tyr Lys Asn Gln Asn Asn Ala Thr Phe Thr Ser Phe Tyr
 290 295 300

Glu Ile Asp Trp Asp Gln His Thr Val Lys Leu Ile Lys Thr His Ser
 305 310 315 320

Asp Glu Lys Asn Pro Ser
 325

<210> 109

<211> 325

<212> PRT

<213> Artificial Sequence

<220>

<223> gamma-hemolysin component C precursor amino acid sequence

<400> 109

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

Leu Leu Leu Leu Ser Asn Thr Ala Asn Ala Glu Gly Lys Ile Thr Pro
20      25      30

Val Ser Val Lys Lys Val Asp Asp Lys Val Thr Leu Tyr Lys Thr Thr
35      40      45

Ala Thr Ala Asp Ser Asp Lys Phe Lys Ile Ser Gln Ile Leu Thr Phe
50      55      60

Asn Phe Ile Lys Asp Lys Ser Tyr Asp Lys Asp Thr Leu Val Leu Lys
65      70      75      80

Ala Ala Gly Asn Ile Asn Ser Gly Tyr Glu Lys Pro Asn Pro Lys Asp
85      90      95

Tyr Asp Phe Ser Lys Leu Tyr Trp Gly Ala Lys Tyr Asn Val Ser Ile
100     105     110

Ser Ser Gln Ser Asn Asp Ser Val Asn Val Val Asp Tyr Ala Pro Lys
115     120     125

Asn Gln Asn Glu Glu Phe Gln Val Gln Asn Thr Leu Gly Tyr Thr Phe
130     135     140

Gly Gly Asp Ile Ser Ile Ser Asn Gly Leu Ser Gly Gly Leu Asn Gly
145     150     155     160

Asn Thr Ala Phe Ser Glu Thr Ile Asn Tyr Lys Gln Glu Ser Tyr Arg
165     170     175

Thr Thr Leu Ser Arg Asn Thr Asn Tyr Lys Asn Val Gly Trp Gly Val
180     185     190

Glu Ala His Lys Ile Met Asn Asn Gly Trp Gly Pro Tyr Gly Arg Asp
195     200     205

Ser Phe His Pro Thr Tyr Gly Asn Glu Leu Phe Leu Ala Gly Arg Gln
210     215     220

Ser Ser Ser Tyr Ala Gly Gln Asn Phe Ile Ala Gln His Gln Met Pro
225     230     235     240

Leu Leu Ser Arg Ser Asn Phe Asn Pro Glu Phe Leu Ser Val Leu Ser
245     250     255

His Lys Gln Asn Gly Ala Lys Lys Ser Lys Ile Thr Val Thr Tyr Gln
260     265     270

Arg Glu Met Asp Leu Tyr Gln Ile Arg Trp Asn Gly Phe Tyr Trp Ala
275     280     285

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Gly Ala Asn Tyr Lys Asn Phe Lys Thr Arg Thr Phe Lys Ser Thr Tyr
 290 295 300

Glu Ile Asp Trp Glu Asn His Lys Val Lys Leu Leu Asp Thr Lys Glu
 305 310 315 320

Thr Glu Ile Asn Lys
 325

<210> 110

<211> 325

<212> PRT

<213> Artificial Sequence

<220>

<223> gamma-hemolysin component C precursor amino acid sequence

<400> 110

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

Leu Leu Leu Leu Ser Asn Thr Ala Asn Ala Glu Gly Lys Ile Thr Pro
 20 25 30

Val Ser Val Lys Lys Val Asp Asp Lys Val Thr Leu Tyr Lys Thr Thr
 35 40 45

Ala Thr Ala Asp Ser Asp Lys Phe Lys Ile Ser Gln Ile Leu Thr Phe
 50 55 60

Asn Phe Ile Lys Asp Lys Ser Tyr Asp Lys Asp Thr Leu Val Leu Lys
 65 70 75 80

Ala Ala Gly Asn Ile Asn Ser Gly Tyr Glu Arg Pro Asn Pro Lys Asp
 85 90 95

Tyr Asp Phe Ser Lys Ile Tyr Trp Gly Ala Lys Tyr Asn Val Ser Ile
 100 105 110

Ser Ser Gln Ser Asn Asp Ser Val Asn Val Val Asp Tyr Ala Pro Lys
 115 120 125

Asn Gln Asn Glu Glu Phe Gln Val Gln Asn Thr Leu Gly Tyr Thr Phe
 130 135 140

Gly Gly Asp Ile Ser Ile Ser Asn Gly Leu Ser Gly Gly Leu Asn Gly
 145 150 155 160

Asn Thr Ala Phe Ser Glu Thr Ile Asn Tyr Lys Gln Glu Ser Tyr Arg
 165 170 175

Thr Thr Leu Ser Arg Asn Thr Asn Tyr Lys Asn Val Gly Trp Gly Val
 180 185 190

Glu Ala His Lys Ile Met Asn Asn Gly Trp Gly Pro Tyr Gly Arg Asp
 195 200 205

Ser Phe His Pro Thr Tyr Gly Asn Glu Leu Phe Leu Ala Gly Arg Gln
 210 215 220

Ser Ser Ala Tyr Ala Gly Gln Asn Phe Ile Ala Gln His Gln Met Pro
 225 230 235 240

Leu Leu Ser Arg Ser Asn Phe Asn Pro Glu Phe Leu Ser Val Leu Ser
 245 250 255

His Arg Gln Asp Gly Ala Lys Lys Ser Lys Ile Thr Val Thr Tyr Gln
 260 265 270

Arg Glu Met Asp Leu Tyr Gln Ile Arg Trp Asn Gly Phe Tyr Trp Ala
 275 280 285

Gly Ala Asn Tyr Lys Asn Tyr Lys Thr Arg Thr Phe Lys Ser Thr Tyr
 290 295 300

Glu Ile Asp Trp Glu Asn His Lys Val Lys Leu Leu Asp Thr Lys Glu
 305 310 315 320

Thr Glu Ile Asn Lys
 325

<210> 111

<211> 325

<212> PRT

<213> Artificial Sequence

<220>

<223> gamma-hemolysin component C precursor amino acid sequence

<400> 111

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

Leu Leu Leu Leu Ser Asn Thr Ala Asn Ala Glu Gly Lys Ile Thr Pro
 20 25 30

Val Ser Val Lys Lys Val Asp Asp Lys Val Thr Leu Tyr Lys Thr Thr
 35 40 45

Ala Thr Ala Asp Ser Asp Lys Phe Lys Ile Ser Gln Ile Leu Thr Phe
 50 55 60

Asn Phe Ile Lys Asp Lys Ser Tyr Asp Lys Asp Thr Leu Val Leu Lys
 65 70 75 80

Ala Ala Gly Asn Ile Asn Ser Gly Tyr Glu Arg Pro Asn Pro Lys Asp
 85 90 95

Tyr Asp Phe Ser Lys Ile Tyr Trp Gly Ala Lys Tyr Asn Val Ser Ile
 100 105 110

Ser Ser Gln Ser Asn Asp Ser Val Asn Val Val Asp Tyr Ala Pro Lys
 115 120 125

Asn Gln Asn Glu Glu Phe Gln Val Gln Asn Thr Leu Gly Tyr Thr Phe
 130 135 140

Gly Gly Asp Ile Ser Ile Ser Asn Gly Leu Ser Gly Gly Leu Asn Gly
 145 150 155 160

Asn Thr Ala Phe Ser Glu Thr Ile Asn Tyr Lys Gln Glu Ser Tyr Arg
 165 170 175

Thr Thr Leu Ser Arg Asn Thr Asn Tyr Lys Asn Val Gly Trp Gly Val
 180 185 190

Glu Ala His Lys Ile Met Asn Asn Gly Trp Gly Pro Tyr Gly Arg Asp
 195 200 205

Ser Phe His Pro Thr Tyr Gly Asn Glu Leu Phe Leu Ala Gly Arg Gln
 210 215 220

Ser Ser Ala Tyr Ala Gly Gln Asn Phe Ile Ala Gln His Gln Met Pro
 225 230 235 240

Leu Leu Ser Arg Ser Asn Phe Asn Pro Glu Phe Leu Ser Val Leu Ser
 245 250 255

His Arg Gln Asp Gly Ala Lys Lys Ser Lys Ile Thr Val Thr Tyr Gln
 260 265 270

Arg Glu Met Asp Leu Tyr Gln Ile Arg Trp Asn Gly Phe Tyr Trp Ala
 275 280 285

Gly Ala Asn Tyr Lys Asn Phe Lys Thr Arg Thr Phe Lys Ser Thr Tyr
 290 295 300

Glu Ile Asp Trp Glu Asn His Lys Val Lys Leu Leu Asp Thr Lys Glu
 305 310 315 320

Thr Glu Asn Asn Lys
 325

<210> 112

<211> 281

<212> PRT

<213> Artificial Sequence

<220>

<223> gamma-hemolysin component B amino acid sequence

<400> 112

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

Leu Leu Leu Leu Ser Asn Thr Val Asp Ala Ala Gln His Ile Thr Pro
 20 25 30

20					25					30					
Val	Ser	Glu	Lys	Lys	Val	Asp	Asp	Lys	Ile	Thr	Leu	Tyr	Lys	Thr	Thr
		35					40					45			
Ala	Thr	Ser	Asp	Asn	Asp	Lys	Leu	Asn	Ile	Ser	Gln	Ile	Leu	Thr	Phe
	50					55					60				
Asn	Phe	Ile	Lys	Asp	Lys	Ser	Tyr	Asp	Lys	Asp	Thr	Leu	Val	Leu	Lys
65					70					75					80
Ala	Ala	Gly	Asn	Ile	Asn	Ser	Gly	Tyr	Lys	Lys	Pro	Asn	Pro	Lys	Asp
				85					90					95	
Tyr	Asn	Tyr	Ser	Gln	Phe	Tyr	Trp	Gly	Gly	Lys	Tyr	Asn	Val	Ser	Val
			100					105					110		
Ser	Ser	Glu	Ser	Asn	Asp	Ala	Val	Asn	Val	Val	Asp	Tyr	Ala	Pro	Lys
		115					120					125			
Asn	Gln	Asn	Glu	Glu	Phe	Gln	Val	Gln	Gln	Thr	Leu	Gly	Tyr	Ser	Tyr
	130					135					140				
Gly	Gly	Asp	Ile	Asn	Ile	Ser	Asn	Gly	Leu	Ser	Gly	Gly	Leu	Asn	Gly
145					150					155					160
Ser	Lys	Ser	Phe	Ser	Glu	Thr	Ile	Asn	Tyr	Lys	Gln	Glu	Ser	Tyr	Arg
				165					170					175	
Thr	Thr	Ile	Asp	Arg	Lys	Thr	Asn	His	Lys	Ser	Ile	Gly	Trp	Gly	Val
			180					185					190		
Glu	Ala	His	Lys	Ile	Met	Asn	Asn	Gly	Trp	Gly	Pro	Tyr	Gly	Arg	Asp
		195					200					205			
Ser	Tyr	Asp	Pro	Thr	Tyr	Gly	Asn	Glu	Leu	Phe	Leu	Gly	Gly	Arg	Gln
	210					215					220				
Ser	Ser	Ser	Asn	Ala	Gly	Gln	Asn	Phe	Leu	Pro	Thr	His	Gln	Met	Pro
225					230					235				240	
Leu	Leu	Ala	Arg	Gly	Asn	Phe	Asn	Pro	Glu	Phe	Ile	Ser	Val	Leu	Ser
				245					250					255	
His	Lys	Gln	Asn	Asp	Thr	Lys	Lys	Ser	Lys	Ile	Lys	Val	Thr	Tyr	Gln
			260					265					270		
Arg	Glu	Met	Asp	Arg	Tyr	Thr	Asn	Gln							
	275						280								

<210> 113

<211> 325

<212> PRT

His Arg Gln Asp Gly Ala Lys Lys Ser Lys Ile Thr Val Thr Tyr Gln
260 265 270

Arg Glu Met Asp Leu Tyr Gln Ile Arg Trp Asn Gly Phe Tyr Trp Ala
275 280 285

Gly Ala Asn Tyr Lys Asn Phe Lys Thr Arg Thr Phe Lys Ser Thr Tyr
290 295 300

Glu Ile Asp Trp Glu Asn His Lys Val Lys Leu Leu Asp Thr Lys Glu
305 310 315 320

Thr Glu Asn Asn Lys
325

<210> 114

<211> 325

<212> PRT

<213> Artificial Sequence

<220>

<223> gamma-hemolysin component B amino acid sequence

<400> 114

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

Leu Leu Leu Leu Ser Asn Thr Ala Asn Ala Glu Gly Lys Ile Thr Pro
20 25 30

Val Ser Val Lys Lys Val Asp Asp Lys Val Thr Leu Tyr Lys Thr Thr
35 40 45

Ala Thr Ala Asp Ser Asp Lys Phe Lys Ile Ser Gln Ile Leu Thr Phe
50 55 60

Asn Phe Ile Lys Asp Lys Ser Tyr Asp Lys Asp Thr Leu Val Leu Lys
65 70 75 80

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

Tyr Asp Phe Ser Lys Leu Tyr Trp Gly Ala Lys Tyr Asn Val Ser Ile
100 105 110

Ser Ser Gln Ser Asn Asp Ser Val Asn Val Val Asp Tyr Ala Pro Lys
115 120 125

Asn Gln Asn Glu Glu Phe Gln Val Gln Asn Thr Leu Gly Tyr Thr Phe
130 135 140

Gly Gly Asp Ile Ser Ile Ser Asn Gly Leu Ser Gly Gly Leu Asn Gly
145 150 155 160

Asn Thr Ala Phe Ser Glu Thr Ile Asn Tyr Lys Gln Glu Ser Tyr Arg
165 170 175

Thr Thr Leu Ser Arg Asn Thr Asn Tyr Lys Asn Val Gly Trp Gly Val
180 185 190

Glu Ala His Lys Ile Met Asn Asn Gly Trp Gly Pro Tyr Gly Arg Asp
195 200 205

Ser Phe His Pro Thr Tyr Gly Asn Glu Leu Phe Leu Ala Gly Arg Gln
210 215 220

Ser Ser Ala Tyr Ala Gly Gln Asn Phe Ile Ala Gln His Gln Met Pro
225 230 235 240

Leu Leu Ser Arg Ser Asn Phe Asn Pro Glu Phe Leu Ser Val Leu Ser
245 250 255

His Arg Gln Asp Gly Ala Lys Lys Ser Lys Ile Thr Val Thr Tyr Gln
260 265 270

Arg Glu Met Asp Leu Tyr Gln Ile Arg Trp Asn Gly Phe Tyr Trp Ala
275 280 285

Gly Ala Asn Tyr Lys Asn Phe Lys Thr Arg Thr Phe Lys Ser Thr Tyr
290 295 300

Glu Ile Asp Trp Glu Asn His Lys Val Lys Leu Leu Asp Thr Lys Glu
305 310 315 320

Thr Glu Asn Asn Lys
325

<210> 115

<211> 325

<212> PRT

<213> Artificial Sequence

<220>

<223> gamma-hemolysin component B amino acid sequence

<400> 115

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

Leu Leu Leu Leu Ser Gly Thr Ala Asn Ala Glu Gly Lys Ile Thr Pro
20 25 30

Val Ser Val Lys Lys Val Asp Asp Lys Val Thr Leu Tyr Lys Thr Thr
35 40 45

Ala Thr Ala Asp Ser Asp Lys Phe Lys Ile Ser Gln Ile Leu Thr Phe
50 55 60

Asn Phe Ile Lys Asp Lys Ser Tyr Asp Lys Asp Thr Leu Val Leu Lys
65 70 75 80

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

Tyr Asp Phe Ser Lys Leu Tyr Trp Gly Ala Lys Tyr Asn Val Ser Ile
 100 105 110

Ser Ser Gln Ser Asn Asp Ser Val Asn Val Val Asp Tyr Ala Pro Lys
 115 120 125

Asn Gln Asn Glu Glu Phe Gln Val Gln Asn Thr Leu Gly Tyr Thr Phe
 130 135 140

Gly Gly Asp Ile Ser Ile Ser Asn Gly Leu Ser Gly Gly Leu Asn Gly
 145 150 155 160

Asn Thr Ala Phe Ser Glu Thr Ile Asn Tyr Lys Gln Glu Ser Tyr Arg
 165 170 175

Thr Thr Leu Ser Arg Asn Thr Asn Tyr Lys Asn Val Gly Trp Gly Val
 180 185 190

Glu Ala His Lys Ile Met Asn Asn Gly Trp Gly Pro Tyr Gly Arg Asp
 195 200 205

Ser Phe His Pro Thr Tyr Gly Asn Glu Leu Phe Leu Ala Gly Arg Gln
 210 215 220

Ser Ser Ala Tyr Ala Gly Gln Asn Phe Ile Ala Gln His Gln Met Pro
 225 230 235 240

Leu Leu Ser Arg Ser Asn Phe Asn Pro Glu Phe Leu Ser Val Leu Ser
 245 250 255

His Arg Gln Asp Gly Ala Lys Lys Ser Lys Ile Thr Val Thr Tyr Gln
 260 265 270

Arg Glu Met Asp Leu Tyr Gln Ile Cys Trp Asn Gly Phe Tyr Trp Ala
 275 280 285

Gly Ala Asn Tyr Lys Asn Phe Lys Thr Arg Thr Phe Lys Ser Thr Tyr
 290 295 300

Glu Ile Asp Trp Glu Asn His Lys Val Lys Leu Leu Asp Thr Lys Glu
 305 310 315 320

Thr Glu Asn Asn Lys
 325

<210> 116

<211> 325

<212> PRT

<213> Artificial Sequence

<220>

<223> gamma-hemolysin component B amino acid sequence

<400> 116

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

Leu Leu Leu Leu Ser Gly Thr Ala Asn Ala Glu Gly Lys Ile Thr Pro
 20 25 30

Val Ser Val Lys Lys Val Asp Asp Lys Val Thr Leu Tyr Lys Thr Thr
 35 40 45

Ala Thr Ala Asp Ser Asp Lys Phe Lys Ile Ser Gln Ile Leu Thr Phe
 50 55 60

Asn Phe Ile Lys Asp Lys Ser Tyr Asp Lys Asp Thr Leu Val Leu Lys
 65 70 75 80

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

Tyr Asp Phe Ser Lys Leu Tyr Trp Gly Ala Lys Tyr Asn Val Ser Ile
 100 105 110

Ser Ser Gln Ser Asn Asp Ser Val Asn Val Val Asp Tyr Ala Pro Lys
 115 120 125

Asn Gln Asn Glu Glu Phe Gln Val Gln Asn Thr Leu Gly Tyr Thr Phe
 130 135 140

Gly Gly Asp Ile Ser Ile Ser Asn Gly Leu Ser Gly Gly Leu Asn Gly
 145 150 155 160

Asn Thr Ala Phe Ser Glu Thr Ile Asn Tyr Lys Gln Glu Ser Tyr Arg
 165 170 175

Thr Thr Leu Ser Arg Asn Thr Asn Tyr Lys Asn Val Gly Trp Arg Val
 180 185 190

Glu Ala His Lys Ile Met Asn Asn Gly Trp Gly Pro Tyr Gly Arg Asp
 195 200 205

Ser Phe His Pro Thr Tyr Gly Asn Glu Leu Phe Leu Ala Gly Arg Gln
 210 215 220

Ser Ser Ala Tyr Ala Gly Gln Asn Phe Ile Ala Gln His Gln Met Pro
 225 230 235 240

Leu Leu Ser Arg Ser Asn Phe Asn Pro Glu Phe Leu Ser Val Leu Ser
 245 250 255

His Arg Gln Asp Gly Ala Lys Lys Ser Lys Ile Thr Val Thr Tyr Gln
 260 265 270

Arg Glu Met Asp Leu Tyr Gln Ile Arg Trp Asn Gly Phe Tyr Trp Ala
 275 280 285

Gly Ala Asn Tyr Lys Asn Phe Lys Thr Arg Thr Phe Lys Ser Thr Tyr
 290 295 300

Glu Ile Asp Trp Glu Asn His Lys Val Lys Leu Leu Asp Thr Lys Glu
 305 310 315 320

Thr Glu Asn Asn Lys
 325

<210> 117

<211> 325

<212> PRT

<213> Artificial Sequence

<220>

<223> gamma-hemolysin component B amino acid sequence

<400> 117

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

Leu Leu Leu Leu Ser Gly Thr Ala Asn Ala Glu Gly Lys Ile Thr Pro
 20 25 30

Val Ser Val Lys Lys Val Asp Asp Lys Val Thr Leu Tyr Lys Thr Thr
 35 40 45

Ala Thr Ala Asp Ser Asp Lys Phe Lys Ile Ser Gln Ile Leu Thr Phe
 50 55 60

Asn Phe Ile Lys Asp Lys Ser Tyr Asp Lys Asp Thr Leu Val Leu Lys
 65 70 75 80

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

Tyr Asp Phe Ser Lys Leu Tyr Trp Gly Ala Lys Tyr Asn Val Ser Ile
 100 105 110

Ser Ser Gln Ser Asn Asp Ser Val Asn Val Val Asp Tyr Ala Pro Lys
 115 120 125

Asn Gln Asn Glu Glu Phe Gln Val Gln Asn Thr Leu Gly Tyr Thr Phe
 130 135 140

Gly Gly Asp Ile Ser Ile Ser Asn Gly Leu Ser Gly Gly Leu Asn Gly
 145 150 155 160

Asn Thr Ala Phe Ser Glu Thr Ile Asn Tyr Lys Gln Glu Ser Tyr Arg
 165 170 175

Thr Thr Leu Ser Arg Asn Thr Asn Tyr Lys Asn Val Gly Trp Gly Val
 180 185 190

Glu Ala His Lys Ile Met Asn Asn Gly Trp Gly Pro Tyr Gly Arg Asp
 195 200 205

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Ser Phe His Pro Thr Tyr Gly Asn Glu Leu Phe Leu Ala Gly Arg Gln
210                215                220

Ser Ser Ala Tyr Ala Gly Gln Asn Phe Ile Ala Gln His Gln Met Pro
225                230                235                240

Leu Leu Ser Arg Ser Asn Phe Asn Pro Glu Phe Leu Ser Val Leu Ser
                245                250                255

His Arg Gln Asp Gly Ala Lys Lys Ser Lys Ile Thr Val Thr Tyr Gln
                260                265                270

Arg Glu Met Asp Leu Tyr Gln Ile Arg Trp Asn Gly Phe Tyr Trp Ala
275                280                285

Gly Ala Asn Tyr Lys Asn Phe Lys Thr Arg Thr Phe Lys Ser Thr Tyr
290                295                300

Glu Ile Asp Trp Glu Asn His Lys Val Lys Leu Leu Asp Thr Lys Glu
305                310                315                320

Thr Glu Asn Asn Lys
                325

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<210> 118

<211> 325

<212> PRT

<213> Artificial Sequence

<220>

<223> gamma-hemolysin component C precursor amino acid sequence

<400> 118

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

Leu Leu Leu Leu Ser Gly Thr Ala Asn Ala Glu Gly Lys Ile Thr Pro
20                25                30

Val Ser Val Lys Lys Val Asp Asp Lys Val Thr Leu Tyr Lys Thr Thr
35                40                45

Ala Thr Ala Asp Ser Asp Lys Phe Lys Ile Ser Gln Ile Leu Thr Phe
50                55                60

Asn Phe Ile Lys Asp Lys Ser Tyr Asp Lys Asp Thr Leu Val Leu Lys
65                70                75                80

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

Tyr Asp Phe Ser Lys Leu Tyr Trp Gly Ala Lys Tyr Asn Val Ser Ile
100               105               110

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Ser Ser Gln Ser Asn Asp Ser Val Asn Val Val Asp Tyr Ala Pro Lys
 115 120 125
 Asn Gln Asn Glu Glu Phe Gln Val Gln Asn Thr Leu Gly Tyr Thr Phe
 130 135 140
 Gly Gly Asp Ile Ser Ile Ser Asn Gly Leu Ser Gly Gly Leu Asn Gly
 145 150 155 160
 Asn Thr Ala Phe Ser Glu Thr Ile Asn Tyr Lys Gln Glu Ser Tyr Arg
 165 170 175
 Thr Thr Leu Ser Arg Asn Thr Asn Tyr Lys Asn Val Gly Trp Gly Val
 180 185 190
 Glu Ala His Lys Ile Met Asn Asn Gly Trp Gly Pro Tyr Gly Arg Asp
 195 200 205
 Ser Phe His Pro Thr Tyr Gly Asn Glu Leu Phe Leu Ala Gly Arg Gln
 210 215 220
 Ser Ser Ala Tyr Ala Gly Gln Asn Phe Ile Ala Gln His Gln Met Pro
 225 230 235 240
 Leu Leu Ser Arg Ser Asn Phe Asn Pro Glu Phe Leu Ser Val Leu Ser
 245 250 255
 His Arg Gln Asp Gly Ala Lys Lys Ser Lys Ile Thr Val Thr Tyr Gln
 260 265 270
 Arg Glu Met Asp Leu Tyr Gln Ile Arg Trp Asn Gly Phe Tyr Trp Ala
 275 280 285
 Gly Ala Asn Tyr Lys Asn Phe Lys Thr Arg Thr Phe Lys Ser Thr Tyr
 290 295 300
 Glu Ile Asp Trp Glu Asn His Lys Val Lys Leu Leu Asp Thr Lys Glu
 305 310 315 320
 Thr Glu Asn Asn Lys
 325

<210> 119

<211> 325

<212> PRT

<213> Artificial Sequence

<220>

<223> gamma-hemolysin component B amino acid sequence

<400> 119

Met Asn Met Asn Lys Leu Val Lys Ser Ser Val Ala Thr Ser Met Ala

Leu Leu Leu Leu Ser Gly Thr Ala Asn Ala Glu Gly Lys Ile Thr Pro
 20 25 30
 Val Ser Val Lys Lys Val Asp Asp Lys Val Thr Leu Tyr Lys Thr Thr
 35 40 45
 Ala Thr Ala Asp Ser Asp Lys Phe Lys Ile Ser Gln Ile Leu Thr Phe
 50 55 60
 Asn Phe Ile Lys Asp Lys Ser Tyr Asp Lys Asp Thr Leu Val Leu Lys
 65 70 75 80
 Ala Ala Gly Asn Ile Asn Ser Gly Tyr Glu Arg Pro Asn Pro Lys Asp
 85 90 95
 Tyr Asp Phe Ser Lys Ile Tyr Trp Gly Ala Lys Tyr Asn Val Ser Ile
 100 105 110
 Ser Ser Gln Ser Asn Asp Ser Val Asn Val Val Asp Tyr Ala Pro Lys
 115 120 125
 Asn Gln Asn Glu Glu Phe Gln Val Gln Asn Thr Leu Gly Tyr Thr Phe
 130 135 140
 Gly Gly Asp Ile Ser Ile Ser Asn Gly Leu Ser Gly Gly Leu Asn Gly
 145 150 155 160
 Asn Thr Ala Phe Ser Glu Thr Ile Asn Tyr Lys Gln Glu Ser Tyr Arg
 165 170 175
 Thr Thr Leu Ser Arg Asn Thr Asn Tyr Lys Asn Val Gly Trp Gly Val
 180 185 190
 Glu Ala His Lys Ile Met Asn Asn Gly Trp Gly Pro Tyr Gly Arg Asp
 195 200 205
 Ser Phe His Pro Thr Tyr Gly Asn Glu Ile Phe Leu Ala Gly Arg Gln
 210 215 220
 Ser Ser Ser Tyr Ala Gly Gln Asn Phe Ile Ala Gln His Gln Met Pro
 225 230 235 240
 Leu Leu Ser Arg Ser Asn Phe Asn Pro Glu Phe Leu Ser Val Leu Ser
 245 250 255
 His Arg Gln Asp Gly Ala Lys Lys Ser Lys Ile Thr Val Thr Tyr Gln
 260 265 270
 Arg Glu Met Asp Leu Tyr Gln Ile Arg Trp Asn Gly Phe Tyr Trp Ala
 275 280 285
 Gly Ala Asn Tyr Lys Asn Phe Lys Thr Arg Thr Phe Lys Ser Thr Tyr
 290 295 300
 Glu Ile Asp Trp Glu Asn His Lys Val Lys Leu Leu Gly Thr Lys Glu
 305 310 315 320

Thr Glu Asn Asn Lys
325

<210> 120

<211> 323

<212> PRT

<213> Artificial Sequence

<220>

<223> Leukocidin-F subunit amino acid sequence

<400> 120

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

Leu Leu Leu Leu Ser Gly Thr Ala Asn Ala Glu Gly Lys Ile Thr Pro
20 25 30

Val Ser Val Lys Lys Val Asp Asp Lys Val Thr Leu Tyr Lys Thr Thr
35 40 45

Ala Thr Ala Asp Ser Asp Lys Phe Lys Ile Ser Gln Ile Leu Thr Phe
50 55 60

Asn Phe Ile Lys Asp Lys Ser Tyr Asp Lys Asp Thr Leu Val Leu Lys
65 70 75 80

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

Tyr Asp Phe Ser Lys Leu Tyr Trp Gly Ala Lys Tyr Asn Val Ser Ile
100 105 110

Ser Ser Gln Ser Asn Asp Ser Val Asn Ala Val Asp Tyr Ala Pro Lys
115 120 125

Asn Gln Asn Glu Glu Phe Gln Val Gln Asn Thr Leu Gly Tyr Thr Phe

130

135

140

Gly Gly Asp Ile Ser Ile Ser Asn Gly Leu Ser Gly Gly Leu Asn Gly
145 150 155 160

Asn Thr Ala Phe Ser Glu Thr Ile Asn Tyr Lys Gln Glu Ser Tyr Arg
165 170 175

Thr Leu Ser Arg Asn Thr Asn Tyr Lys Asn Val Gly Trp Gly Val Glu
180 185 190

Ala His Lys Ile Met Asn Gly Trp Gly Pro Tyr Gly Arg Asp Ser Phe
195 200 205

Wia Daa Mha Maa Glu Asp Glu Tyr Phe Tyr Ala Glu Asp Glu Ser Ser

His Pro Thr Tyr Gly Asn Glu Leu Phe Leu Ala Gly Arg Gln Ser Ser
210 215 220

Ala Tyr Ala Gly Gln Asn Phe Ile Ala Gln His Gln Met Pro Leu Leu
225 230 235 240

Ser Arg Ser Asn Phe Asn Pro Glu Phe Leu Ser Val Leu Ser His Arg
245 250 255

Gln Asp Arg Ala Lys Lys Ser Lys Ile Thr Val Thr Tyr Gln Arg Glu
260 265 270

Met Asp Leu Tyr Gln Ile Arg Trp Asn Gly Phe Tyr Trp Ala Gly Ala
275 280 285

Asn Tyr Lys Asn Phe Lys Thr Arg Thr Phe Lys Ser Thr Tyr Glu Ile
290 295 300

Asp Trp Glu Asn His Lys Val Lys Leu Leu Asp Thr Lys Glu Thr Glu
305 310 315 320

Asn Asn Lys

<210> 121

<211> 268

<212> PRT

<213> Artificial Sequence

<220>

<223> gamma-hemolysin component B amino acid sequence

<400> 121

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

Leu Leu Leu Leu Ser Ser Thr Ala Asn Ala Glu Gly Lys Ile Thr Pro
20 25 30

Val Ser Val Lys Lys Val Asp Asp Lys Val Thr Leu Tyr Lys Thr Thr
35 40 45

Ala Thr Ala Asp Ser Asp Lys Phe Lys Ile Ser Gln Ile Leu Thr Phe
50 55 60

Asn Phe Ile Lys Asp Lys Ser Tyr Asp Lys Asp Thr Leu Val Leu Lys
65 70 75 80

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

Tyr Asp Phe Ser Lys Leu Tyr Trp Gly Ala Lys Tyr Asn Val Ser Ile
100 105 110

Ser Ser Gln Ser Asn Asp Ser Val Asn Val Val Asp Tyr Ala Pro Lys
115 120 125

Asn Gln Asn Glu Glu Phe Gln Val Gln Asn Thr Leu Gly Tyr Thr Phe
 130 135 140

Gly Gly Asp Ile Ser Ile Ser Asn Gly Leu Ser Gly Gly Leu Asn Gly
 145 150 155 160

Asn Thr Ala Phe Ser Glu Thr Ile Asn Tyr Lys Gln Glu Ser Tyr Arg
 165 170 175

Thr Thr Leu Ser Arg Asn Thr Asn Tyr Lys Asn Val Gly Trp Gly Val
 180 185 190

Glu Ala His Lys Ile Met Asn Asn Gly Trp Gly Pro Tyr Gly Arg Asp
 195 200 205

Ser Phe His Pro Thr Tyr Gly Asn Glu Leu Phe Leu Ala Gly Arg Gln
 210 215 220

Ser Ile Ala Tyr Ala Gly Gln Asn Phe Ile Ala Gln His Gln Met Pro
 225 230 235 240

Leu Leu Ser Arg Ser Asn Phe Asn Pro Glu Phe Leu Ser Val Leu Ser
 245 250 255

His Arg Gln Asp Gly Ala Lys Asn Leu Lys Leu Gln

260 265

<210> 122

<211> 236

<212> PRT

<213> Artificial Sequence

<220>

<223> gamma-hemolysin component B amino acid sequence

<400> 122

Met Lys Pro Asn Pro Asn Asp Tyr Asp Phe Ser Lys Leu Tyr Trp Gly
 1 5 10 15

Ala Lys Tyr Asn Val Ser Ile Ser Ser Gln Ser Asn Asp Ser Val Asn
 20 25 30

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

Asn Thr Leu Gly Tyr Thr Phe Gly Gly Asp Ile Ser Ile Ser Asn Gly
 50 55 60

Leu Ser Gly Gly Leu Asn Gly Asn Thr Ala Phe Ser Glu Thr Ile Asn
 65 70 75 80

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

Lys Asn Val Gly Trp Gly Val Glu Ala His Lys Ile Met Asn Asn Gly
 100 105 110

Trp Gly Pro Tyr Gly Arg Asp Ser Phe His Pro Thr Tyr Gly Asn Glu
 115 120 125

Leu Phe Leu Ala Gly Arg Gln Ser Ser Ala Tyr Ala Gly Gln Asn Phe
 130 135 140

Ile Ala Gln His Gln Met Pro Leu Leu Ser Arg Ser Asn Phe Asn Pro
 145 150 155 160

Glu Phe Leu Ser Val Leu Ser His Arg Gln Asp Gly Ala Lys Lys Ser
 165 170 175

Lys Ile Thr Val Thr Tyr Gln Arg Glu Met Asp Leu Tyr Gln Ile Arg
 180 185 190

Trp Asn Gly Phe Tyr Trp Ala Gly Ala Asn Tyr Lys Asn Phe Lys Thr
 195 200 205

Arg Thr Phe Lys Ser Thr Tyr Glu Ile Asp Trp Glu Asn His Lys Val
 210 215 220

Lys Leu Leu Asp Thr Lys Glu Thr Glu Asn Asn Lys
 225 230 235

<210> 123

<211> 4304

<212> DNA

<213> Artificial Sequence

<220>

<223> plasmid construct encoding the wild-type LukS-PV

<400> 123

ctcgagaaat cataaaaaat ttatttgctt tgtgagcgga taacaattat aatagattca	60
attgtgagcg gataacaatt tcacacagaa ttcattaaag aggagaaatt aactatgaga	120
ggatcgcatc accatcacca tcacggatcc gataacaata ttgagaatat tggatgatggc	180
gctgaggtag tcaaaagaac agaagataca agtagcgata agtgggggggt cacacaaaat	240
attcagtttg attttggtta agataaaaag tataacaaag acgctttgat tttaaaaatg	300
caaggtttta tcaattcaaa gactacttat tacaattaca aaaacacaga tcatataaaa	360
gcaatgaggt ggcctttcca atacaatatt ggtctcaaaa caaatgaccc caatgtagat	420
ttaataaatt atctacctaa aaataaaata gattcagtaa atgttagtca aacattaggt	480
tataacatag gtggttaatt taatagtggg ccatcaacag gaggtaatgg ttcatttaat	540
tattcaaaaa caattagtta taatcaacaa aactatatca gtgaagtaga acatcaaaat	600
tcaaaaagtg ttcaatgggg aataaaagct aattcattta tcacatcatt aggtaaaatg	660
tctggacatg atccaaattt atttggttga tataaaccat atagtcaaaa tccgagagac	720

tattttgtgc cagacaatga attaccccca ttagtacaca gtggtttcaa tccttcattt	780
attgcaactg tttctcatga aaaaggctca ggagatacaa gtgaatttga aataacgtat	840
ggcagaaata tggatgttac tcatgctact agaagaacaa cacactatgg caatagttat	900
ttagaaggat ctagaatata caacgcattt gtaaacagaa attacacagt taaatatgaa	960
gtgaactgga aaactcatga aattaaagtg aaaggacata attgaggtac cccgggtcga	1020
cctgcagcca agcttaatta gctgagcttg gactcctgtt gatagatcca gtaatgacct	1080
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<211> 4304

<212> DNA

<213> Artificial Sequence

<220>

<223> plasmid construct encoding the mutant (K97A) LukS-PV

<400> 124

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<210> 125

<211> 4304

<212> DNA

<213> Artificial Sequence

<220>

<223> plasmid construct encoding the mutant (D102A) LukS-PV

<400> 125

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<210> 126

<211> 4304

<212> DNA

<213> Artificial Sequence

<220>

<223> plasmid construct encoding the mutant (Y131A) LukS-PV

<400> 126

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<211> 4304

<212> DNA

<213> Artificial Sequence

<220>

<223> plasmid construct encoding the mutant (S209A) LukS-PV

<400> 127

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<210> 128

<211> 4184

<212> DNA

<213> Artificial Sequence

<220>

<223> plasmid construct encoding the mutant (T28F) LukS-PV

<400> 128

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<211> 4304

<212> DNA

<213> Artificial Sequence

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<223> plasmid construct encoding the mutant (T28F/Y131A) LukS-PV

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<210> 130

<211> 4304

<212> DNA

<213> Artificial Sequence

<220>

<223> plasmid construct encoding the mutant (T28F/S209A) LukS-PV

<400> 130

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<210> 131

<211> 4304

<212> DNA

<213> Artificial Sequence

<220>

<223> plasmid construct encoding the mutant (T28F/K97A/Y131A) LukS-PV

<400> 131

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<210> 132

<211> 2375

<212> DNA

<213> Artificial Sequence

<220>

<223> plasmid construct encoding the wild-type LukF-PV

<400> 132

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<210> 133

<211> 4355

<212> DNA

<213> Artificial Sequence

<220>

<223> plasmid construct encoding the mutant (K102A) LukF-PV

<400> 133

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<210> 134

<211> 4354

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<213> Artificial Sequence

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<400> 134

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<223> plasmid construct encoding the mutant (E147A) LukF-PV

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tgagcggata cataatttgaa tgtatttaga aaaataaaca aataggggtt ccgcgcacat 4260
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35          40          45

Asp Thr Leu Ile Leu Lys Ala Ala Gly Asn Ile Tyr Ser Gly Tyr Thr
50          55          60

Lys Pro Asn Pro Lys Asp Thr Ile Ser Ser Glu Phe Tyr Trp Gly Ser
65          70          75          80

Lys Tyr Asn Ile Ser Ile Asn Ser Asp Ser Asn Asp Ser Val Asn Val
85          90          95

Val Asp Tyr Ala Pro Ala Asn Gln Asn Glu Glu Phe Gln Val Gln Gln
100         105         110

Thr Val Gly Tyr Ser Tyr Gly Gly Ala Ile Asn Ile Ser Asn Gly Leu
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Lys Gln Ala Ser Tyr Arg Thr Ser Leu Asp Lys Arg Thr Asn Phe Lys
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Lys Ile Gly Trp Asp Val Glu Ala His Lys Ile Met Asn Asn Gly Trp
165 170 175

Gly Pro Tyr Gly Arg Asp Ser Tyr His Ser Thr Tyr Gly Asn Glu Met
180 185 190

Phe Leu Gly Ser Arg Gln Ser Asn Leu Asn Ala Gly Gln Asn Phe Leu
195 200 205

Glu Tyr His Lys Met Pro Val Leu Ser Arg Gly Asn Phe Asn Pro Glu
210 215 220

Phe Ile Gly Val Leu Ser Arg Lys Gln Asn Ala Ala Lys Lys Ser Lys
225 230 235 240

Ile Thr Val Thr Tyr Gln Arg Glu Met Asp Arg Tyr Thr Asn Phe Trp
245 250 255

Asn Gln Leu His Trp Ile Gly Asn Asn Tyr Lys Asp Glu Asn Arg Ala
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Thr His Thr Ser Ile Tyr Glu Val Asp Trp Glu Asn His Thr Val Lys
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aaagacacta ttagttctca attttattgg ggttctaagt acaacatttc aattaattca	300
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caagtacaac aaacggtagg ttattcttat ggtggagcta ttaatatctc taacggctta	420
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ttaatagata ctcaatctaa ggaaaaaaat cctatgagct aaggtacc	948

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Patentkrav

1. Isoleret mutant af et vildtypestafylokok-leukocidin-subunitpolypeptid, der omfatter SEQ ID NO: 5, 6 eller 15,
5 hvor det mutante stafylokok-leukocidin-subunitpolypeptid omfatter en aminosyresubstitution i en position, der svarer til K97 af SEQ ID NO: 6, som reducerer toksiciteten af den mutante leukocidin-subunit i forhold til den tilsvarende vildtype-leukocidin-subunit;
10 eller
isoleret mutant af et vildtypestafylokok-leukocidin-subunitpolypeptid, der omfatter SEQ ID NO: 16, 17, 21, 22, 23, 24, 25 eller 26,
hvor det mutante stafylokok-leukocidin-subunitpolypeptid
15 omfatter en aminosyresubstitution i en position, der svarer til K102 af SEQ ID NO: 17,
som reducerer toksiciteten af den mutante leukocidin-subunit i forhold til den tilsvarende vildtype-leukocidin-subunit.
- 20 2. Mutant leukocidin-subunit ifølge krav 1, hvor positionen, der svarer til K97 af SEQ ID NO: 6 eller K102 af SEQ ID NO: 17, er substitueret med alanin.
3. Mutant leukocidin-subunit ifølge krav 1 eller 2, hvor den
25 mutante leukocidin-subunit er en Panton-Valentine-leukocidin (PVL)-LukS-PV, der omfatter aminosyresekvensen SEQ ID NO: 7 eller 14, eller hvor den mutante leukocidin-subunit er en Panton-Valentine-leukocidin (PVL)-LukF-PV, der omfatter aminosyresekvensen SEQ ID NO: 18 eller 136.
- 30 4. Polypeptidkompleks, der omfatter en mutant leukocidin-subunit ifølge et hvilket som helst af kravene 1 til 3 eller en kombination deraf.
- 35 5. Mutant leukocidin-subunit ifølge et hvilket som helst af kravene 1 til 3, der yderligere omfatter en heterolog aminosyresekvens.

6. Mutant leukocidin-subunit ifølge krav 5, hvor den heterologe aminosyresekvens koder for:

- (a) et peptid valgt fra en gruppe, der består af et His-tag, et ubikvitin-tag, et NusA-tag, et chitinbindende domæne, et B-tag, et HSB-tag, grønt fluorescerende protein (GFP), et calmodulinbindende protein (CBP), et galactosebindende protein, et maltosebindende protein (MBP), cellulosebindende domæner (CBD'er), et avidin/streptavidin/Strep-tag, trpE, chloramphenicol-acetyltransferase, lacZ(β -galactosidase), et FLAGTM-peptid, et S-tag, et T7-tag, et fragment af et hvilket som helst af de heterologe peptider og en kombination af to eller flere af de heterologe peptider; eller
- (b) hvor den heterologe aminosyresekvens koder for et immunogen, en T-celleepitop, en B-celleepitop, et fragment af et hvilket som helst af de heterologe peptider og en kombination af to eller flere af de heterologe peptider.

7. Isoleret polynukleotid, der omfatter en nukleinsyre, der koder for den mutante leukocidin-subunit ifølge et hvilket som helst af kravene 1-3 eller 5-6.

8. Vektor, der omfatter polynukleotidet ifølge krav 7.

9. Værtscelle, der omfatter polynukleotidet ifølge krav 7 eller vektoren ifølge krav 8.

10. Fremgangsmåde til fremstilling af et mutant stafylokok-leukocidin-subunitpolypeptid, som omfatter dyrkning af værtscellen ifølge krav 9 og indvinding af polypeptidet.

11. Sammensætning, der omfatter den mutante leukocidin-subunit ifølge et hvilket som helst af kravene 1-3 eller 5-6 eller polypeptidkomplekset ifølge krav 4 og et bæremateriale.

12. Sammensætning ifølge krav 11 til anvendelse i en fremgangsmåde til inducering af et værtsimmunrespons mod en Staphylococcus aureus-stamme, som omfatter administrering til et individ, der har brug for immunresponsen, af en effektiv

mængde af sammensætningen.

13. Sammensætning, der omfatter den mutante leukocidin-subunit ifølge et hvilket som helst af kravene 1 til 3 eller 5
5 til 6 eller polypeptidkomplekset ifølge krav 4, til anvendelse i en fremgangsmåde til forebyggelse eller behandling af en stafylokoksygdom eller -infektion hos et individ, som omfatter administrering af sammensætningen til et individ, der har brug for det.

10

14. Fremgangsmåde til fremstilling af en vaccine mod S. aureus-infektion, som omfatter:

(a) isolering af den mutante leukocidin-subunit ifølge et hvilket som helst af kravene 1-3 eller 5-6 eller
15 polypeptidkomplekset ifølge krav 4; og

(b) kombinerings af den mutante leukocidin-subunit eller polypeptidkomplekset med et adjuvans.

DRAWINGS

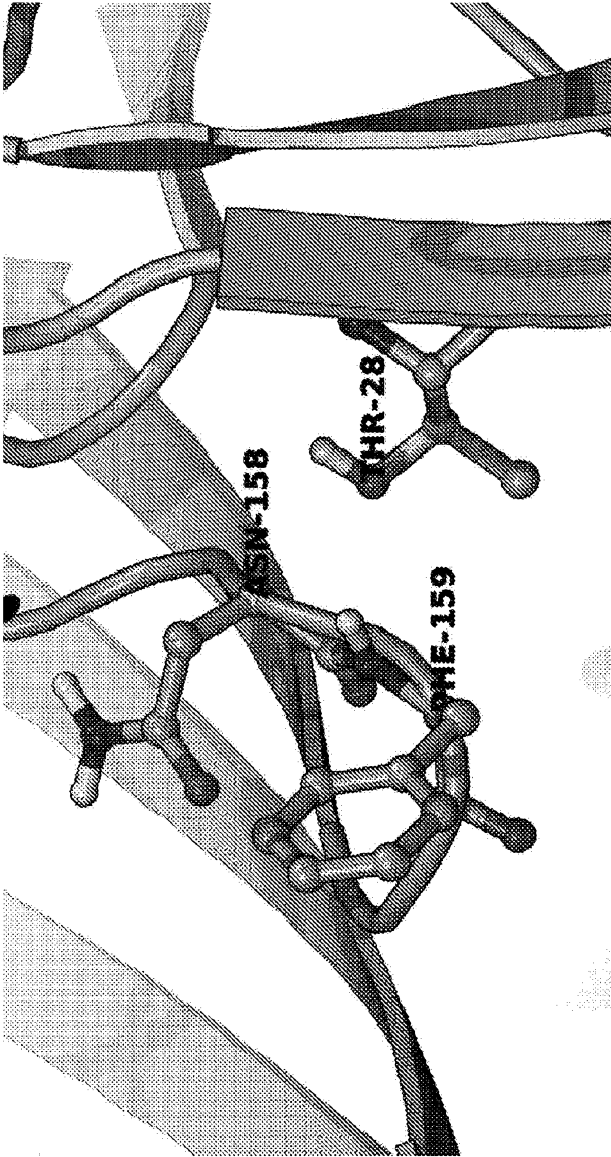


FIG. 1

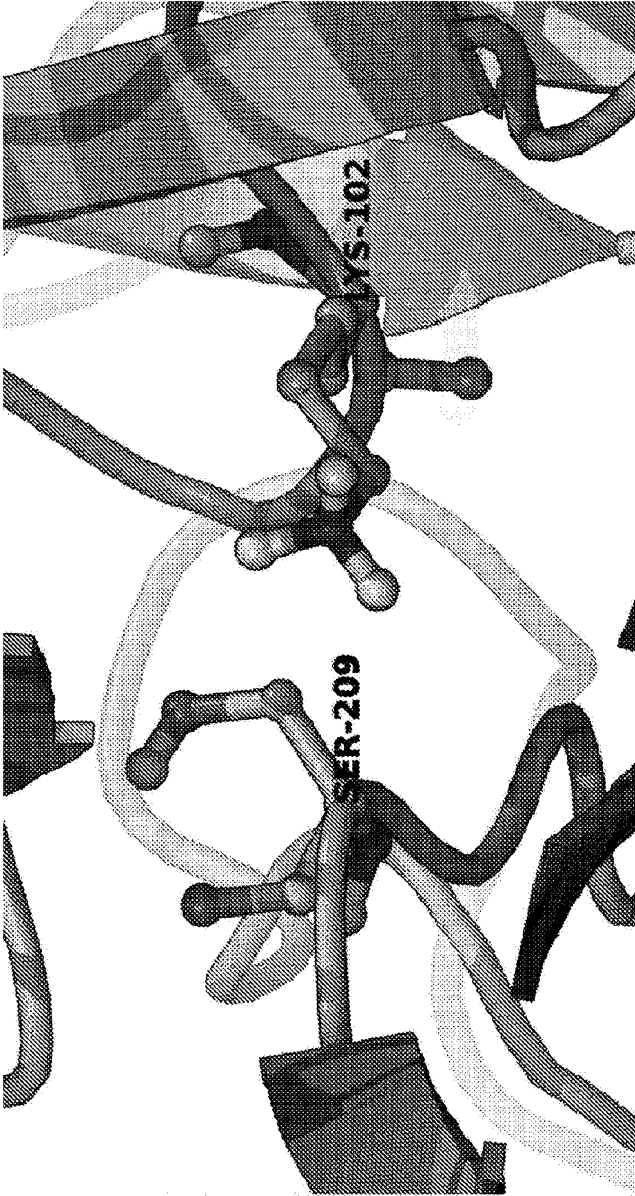


FIG. 2

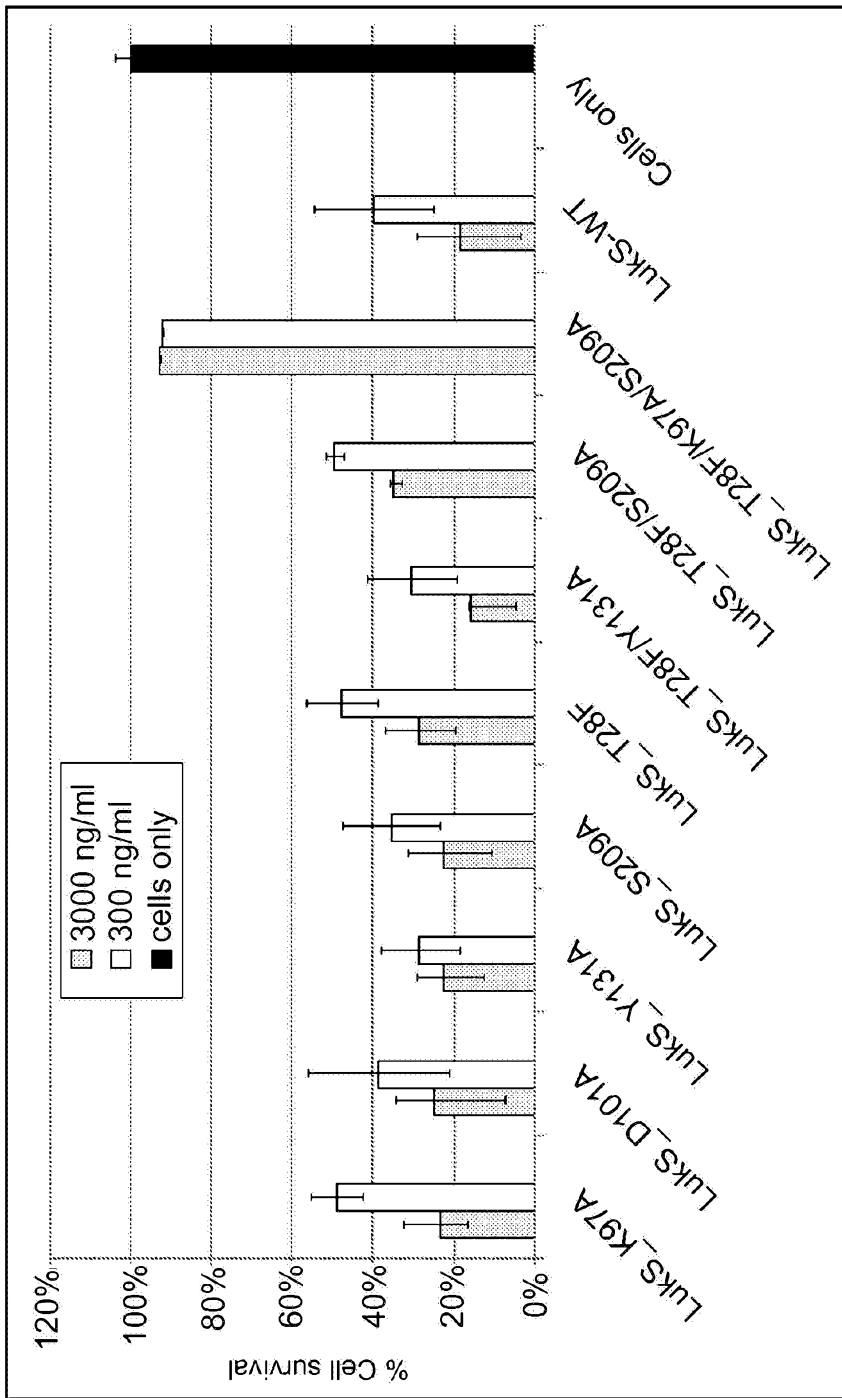


FIG. 3

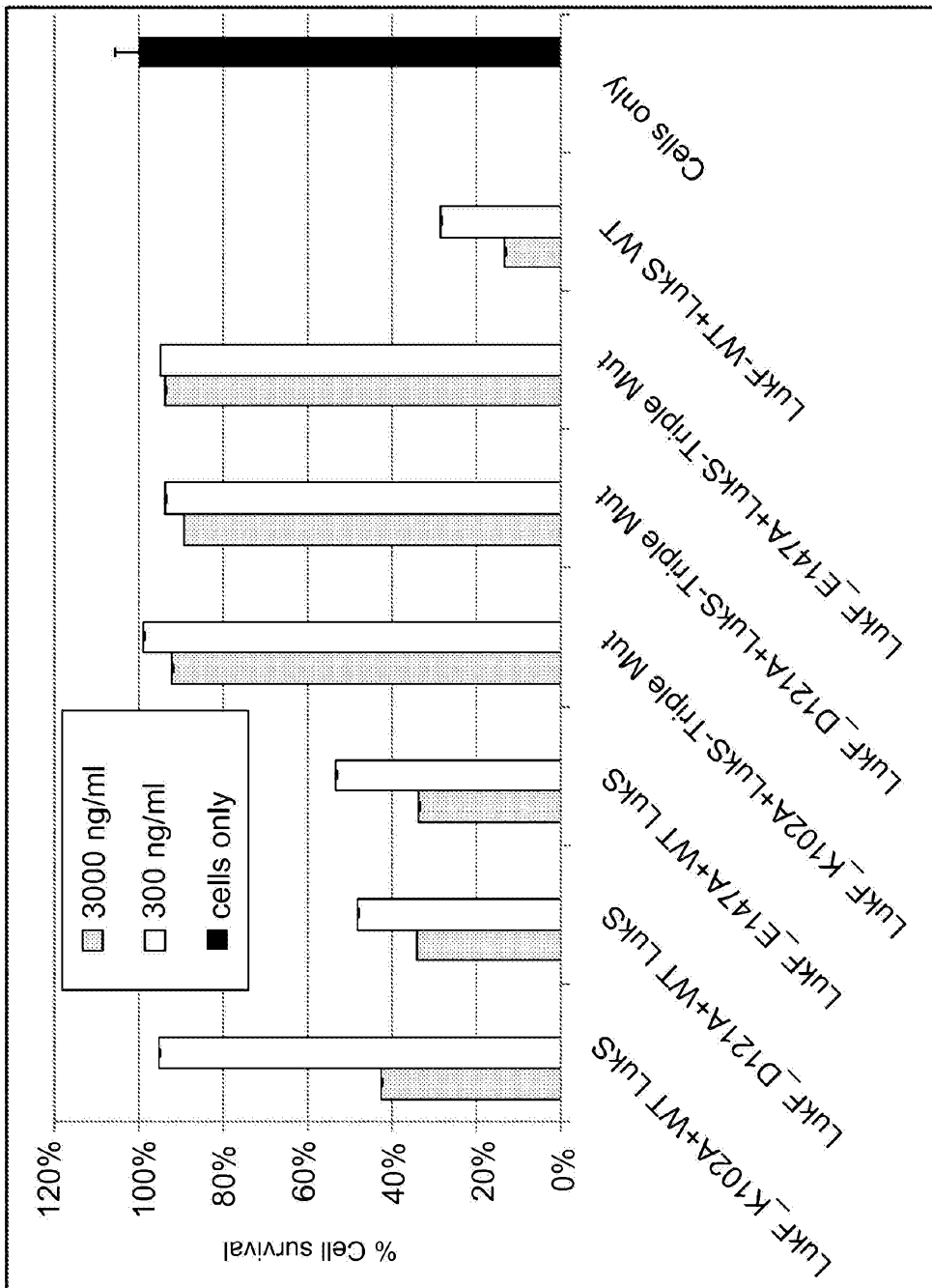


FIG. 4

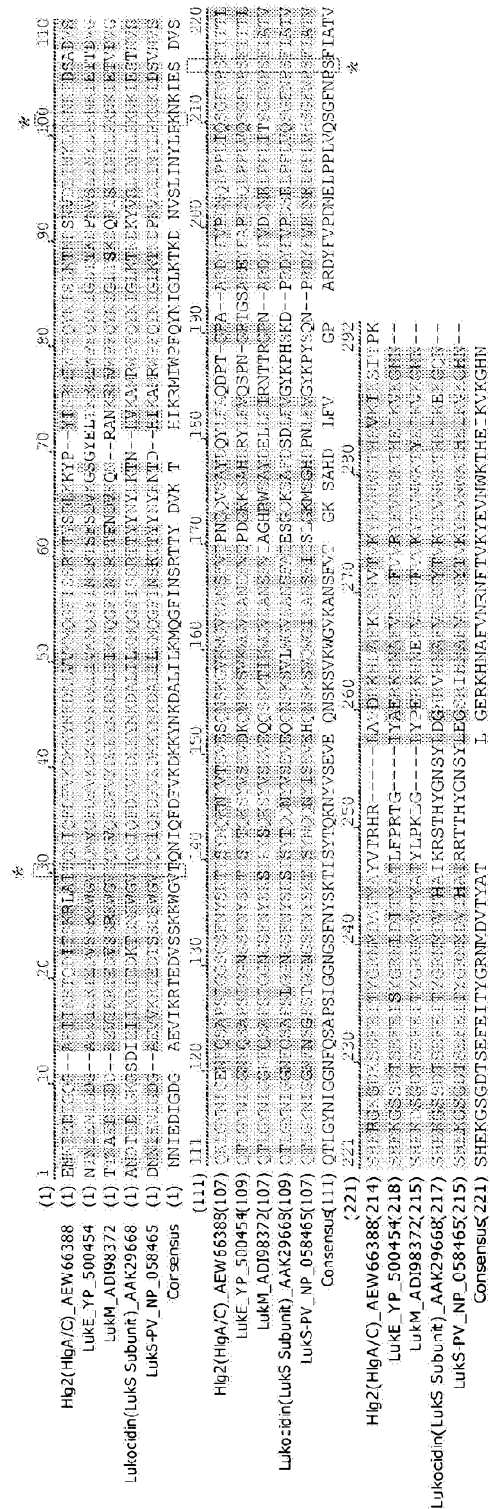


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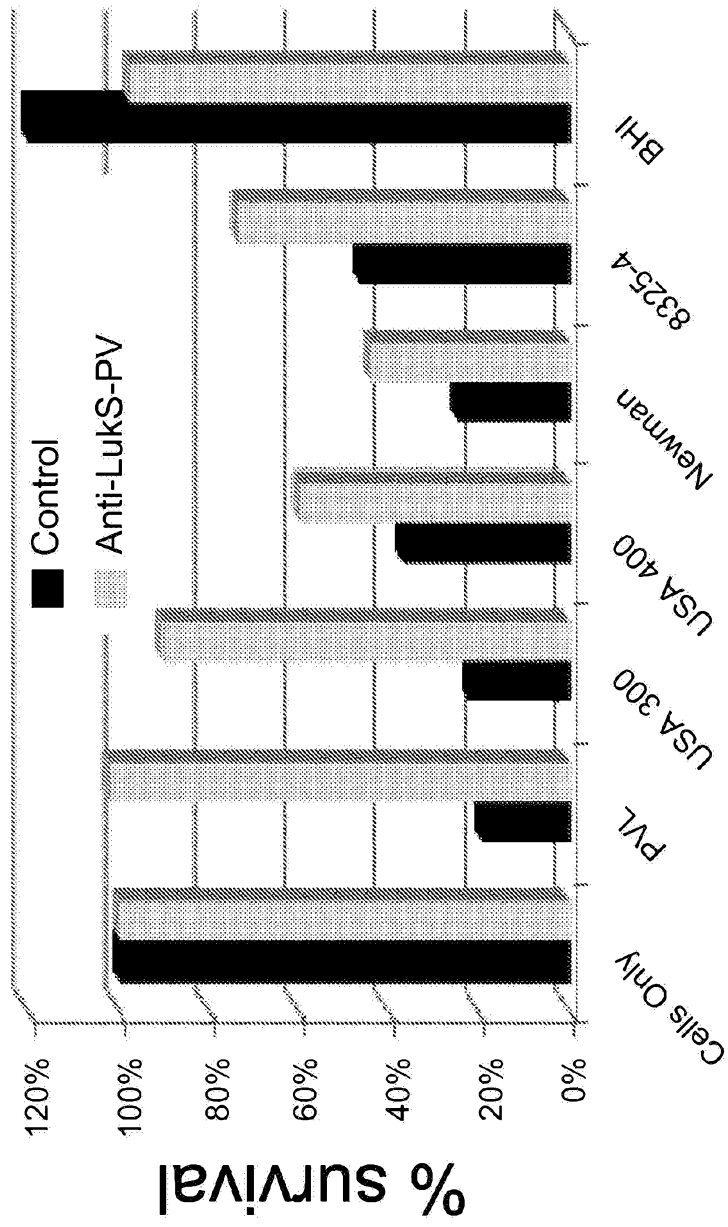


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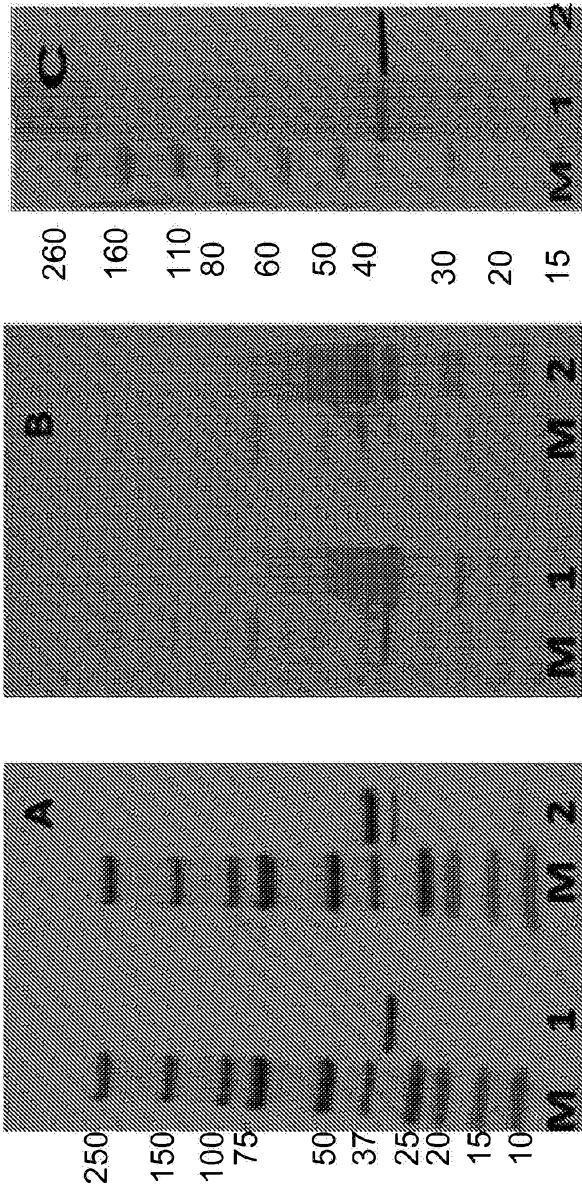


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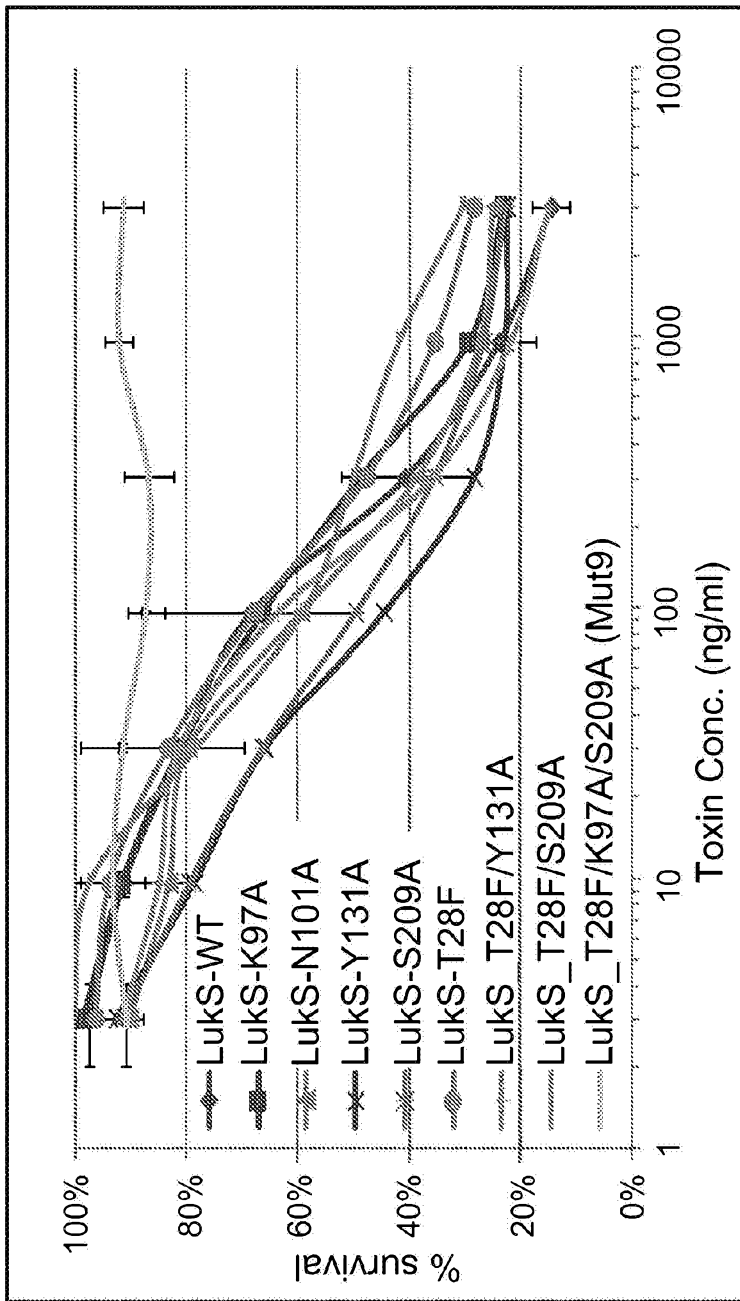


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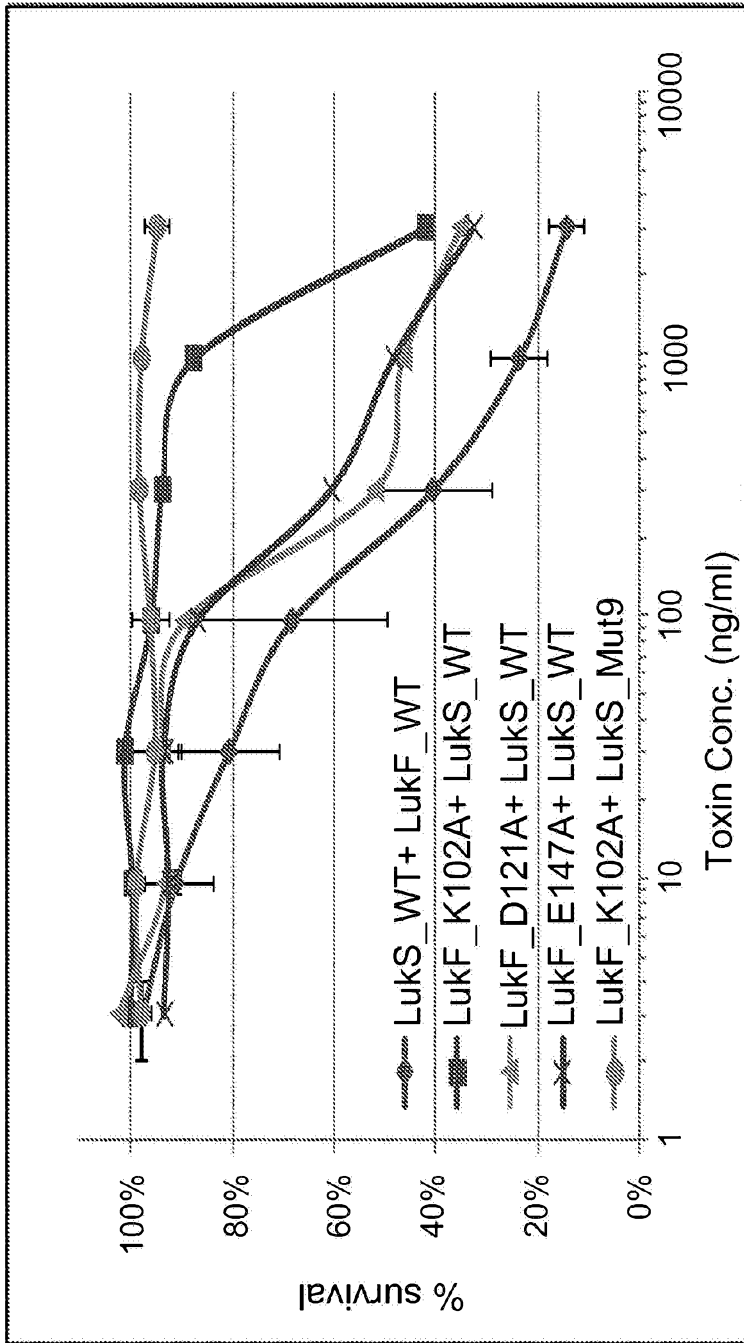


FIG. 8B

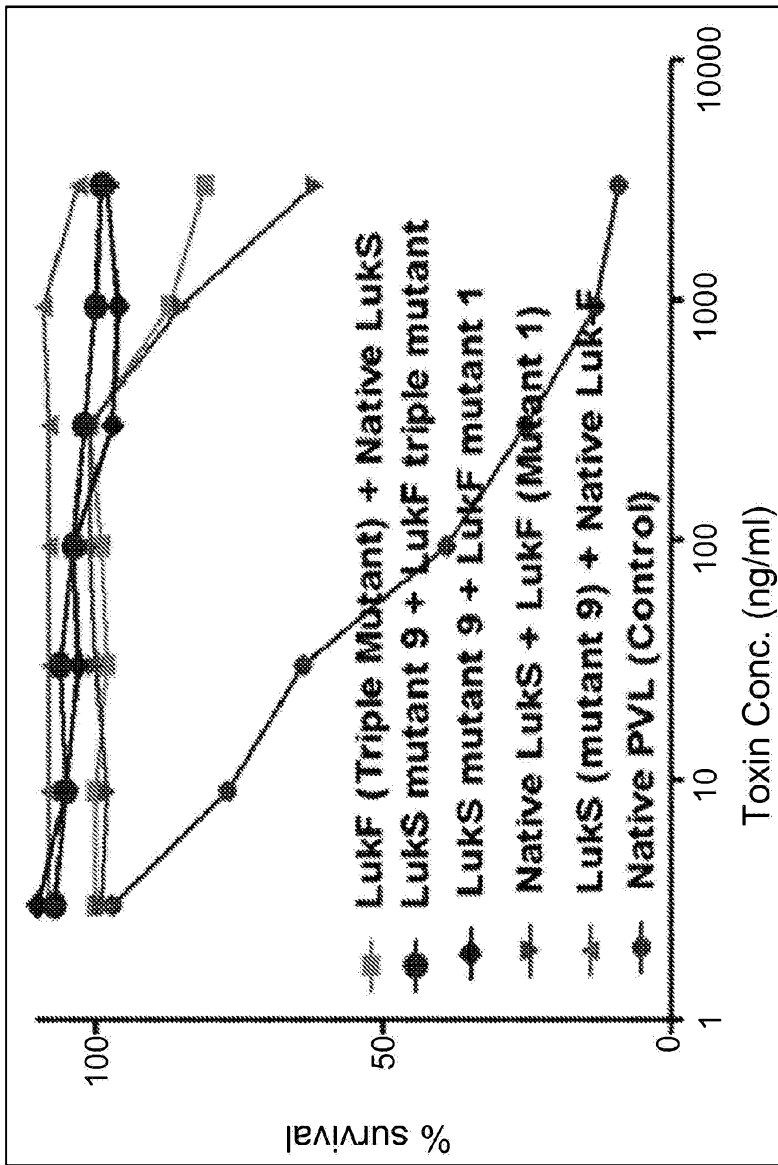


FIG. 8C

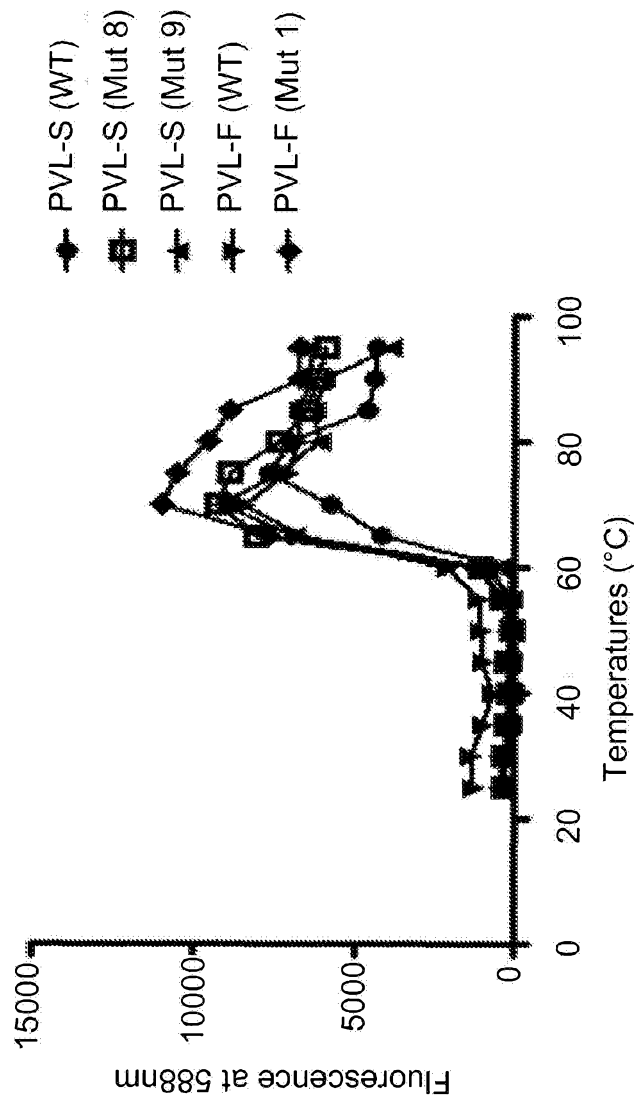


FIG. 9A

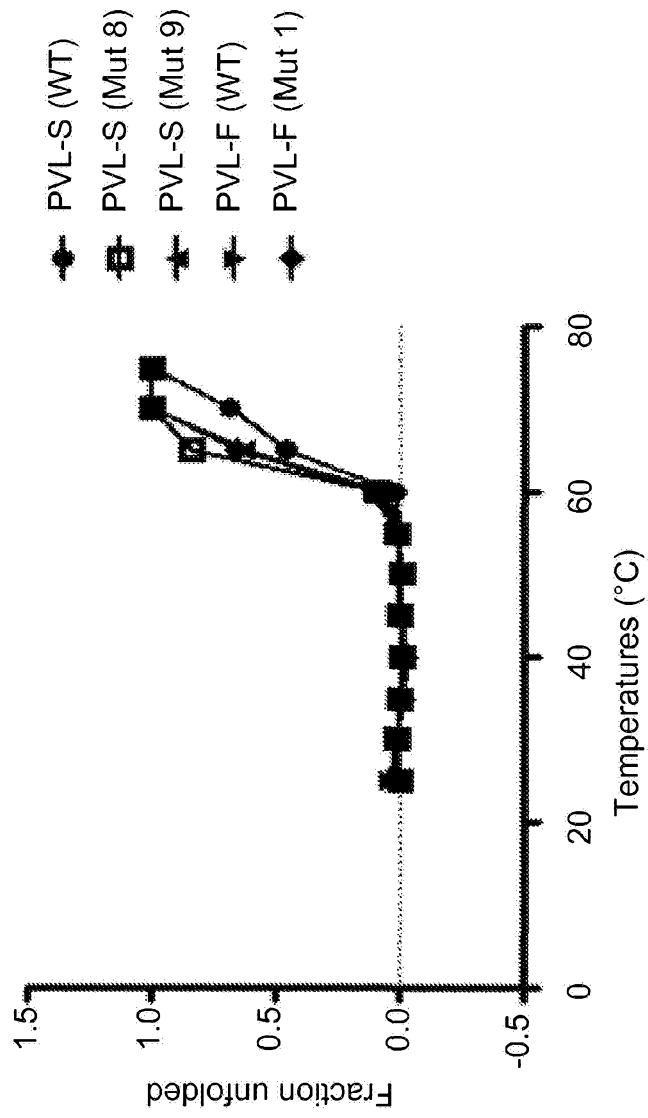


FIG. 9B

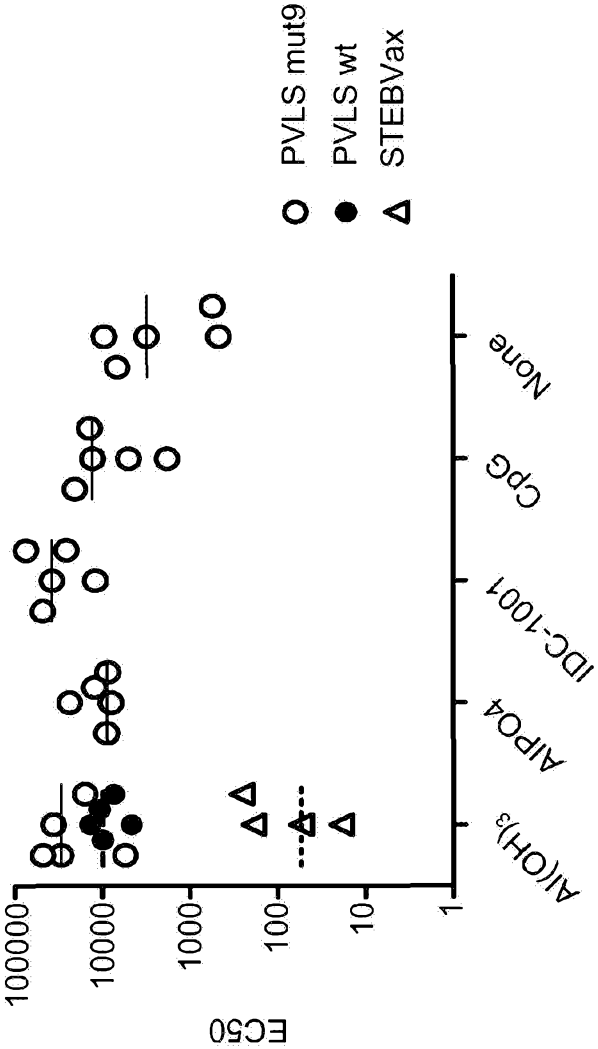


FIG. 10A

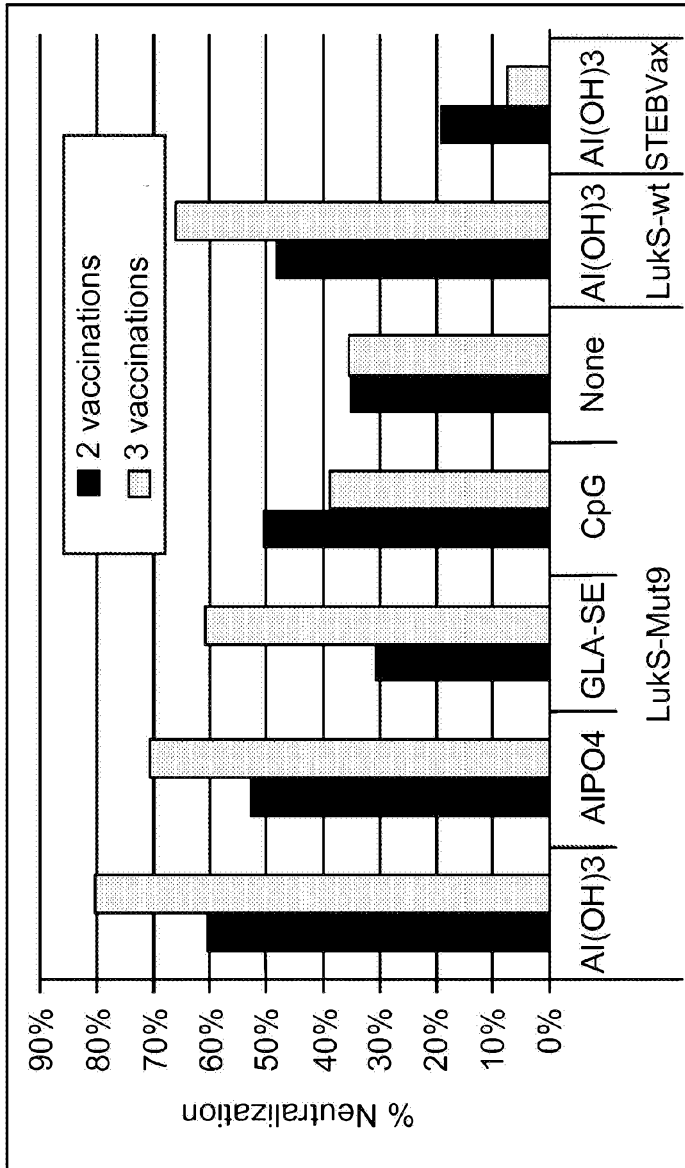
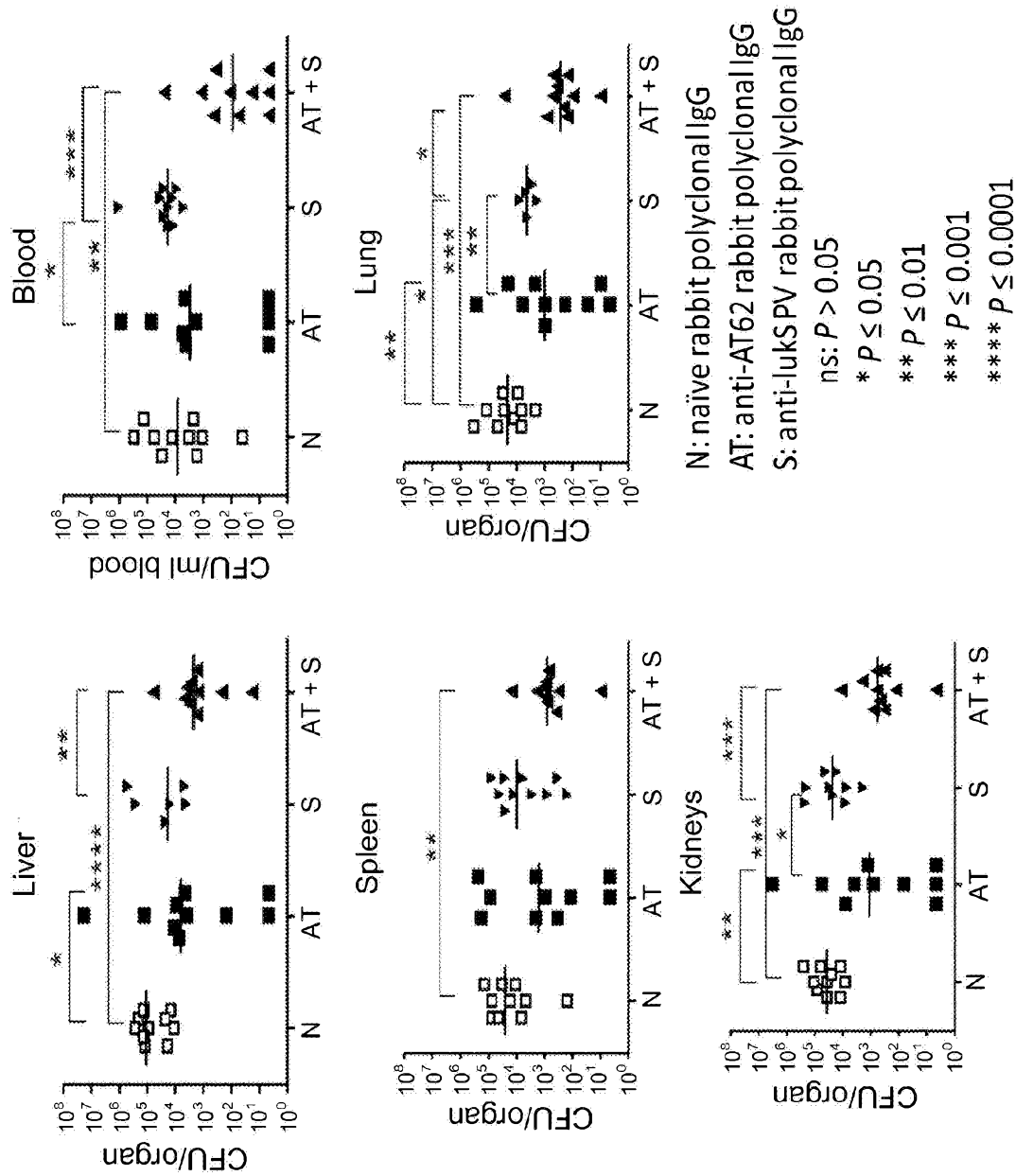


FIG. 10B



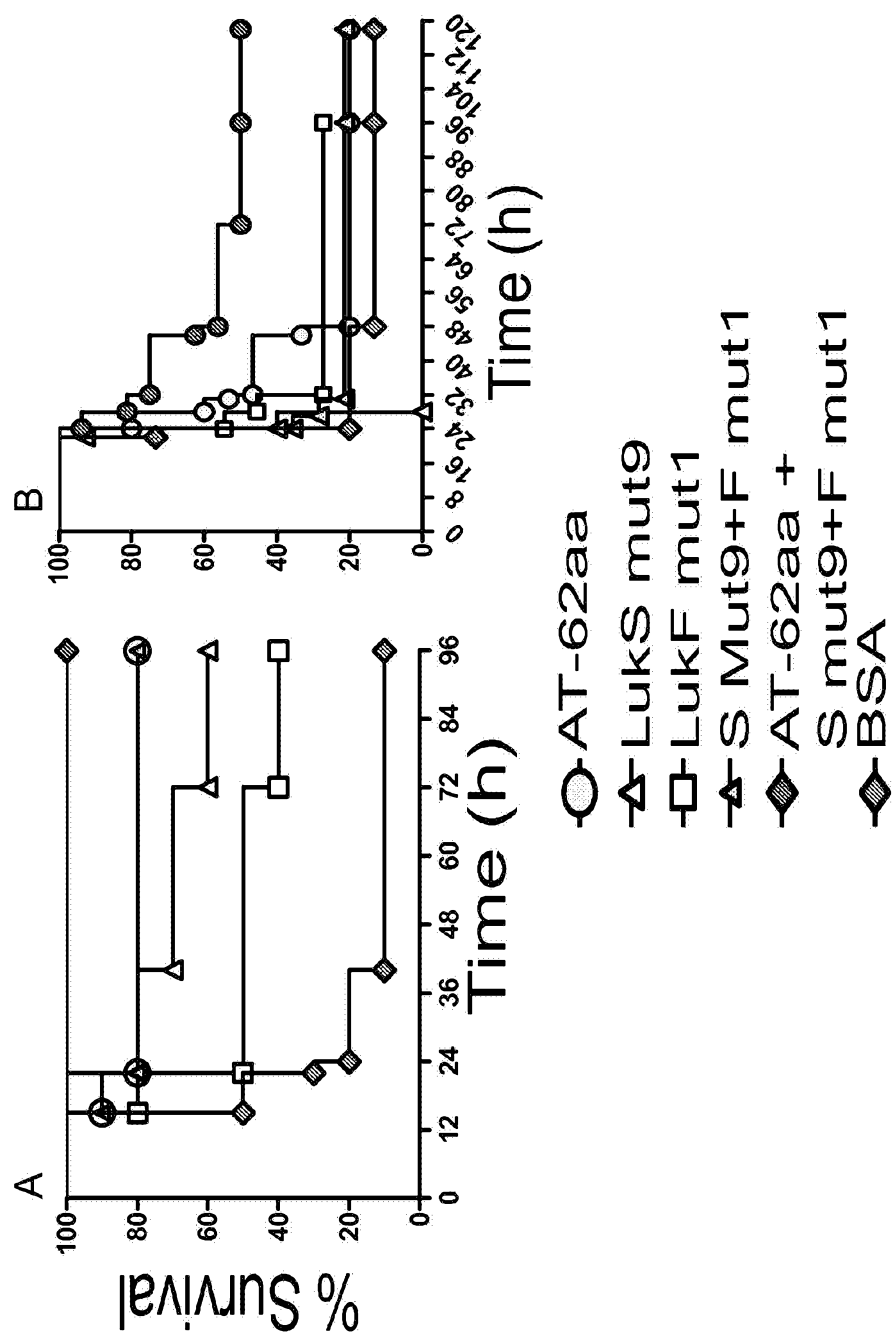


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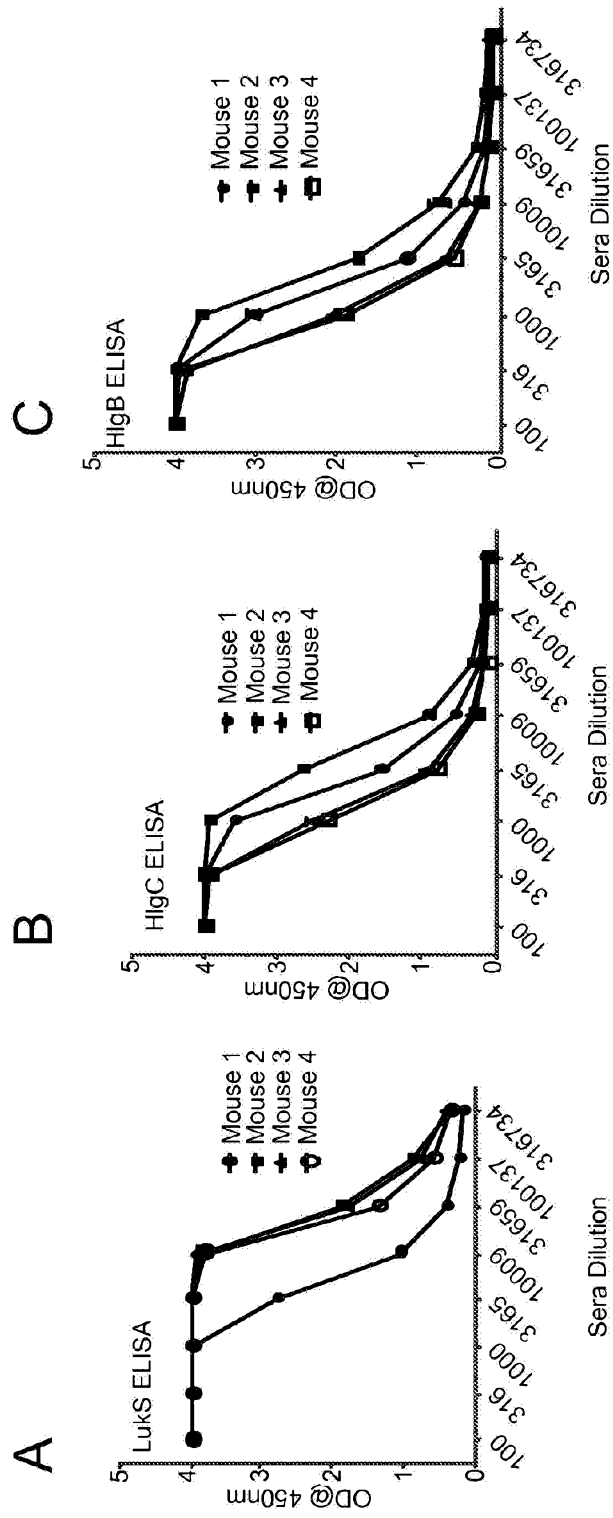


FIG. 13

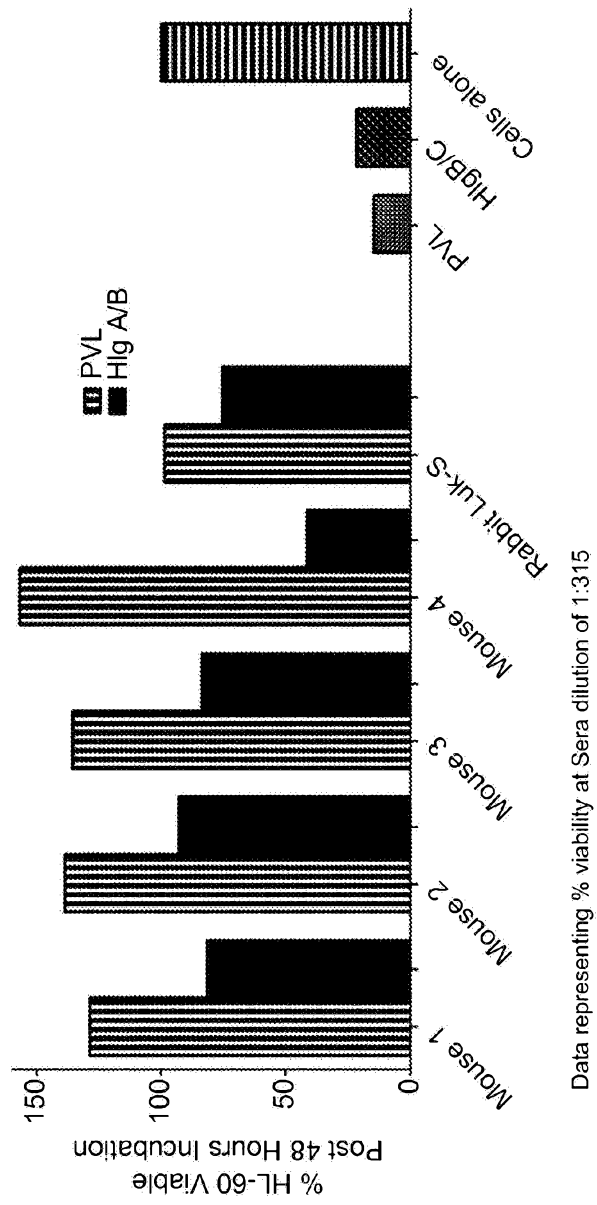


FIG. 13D

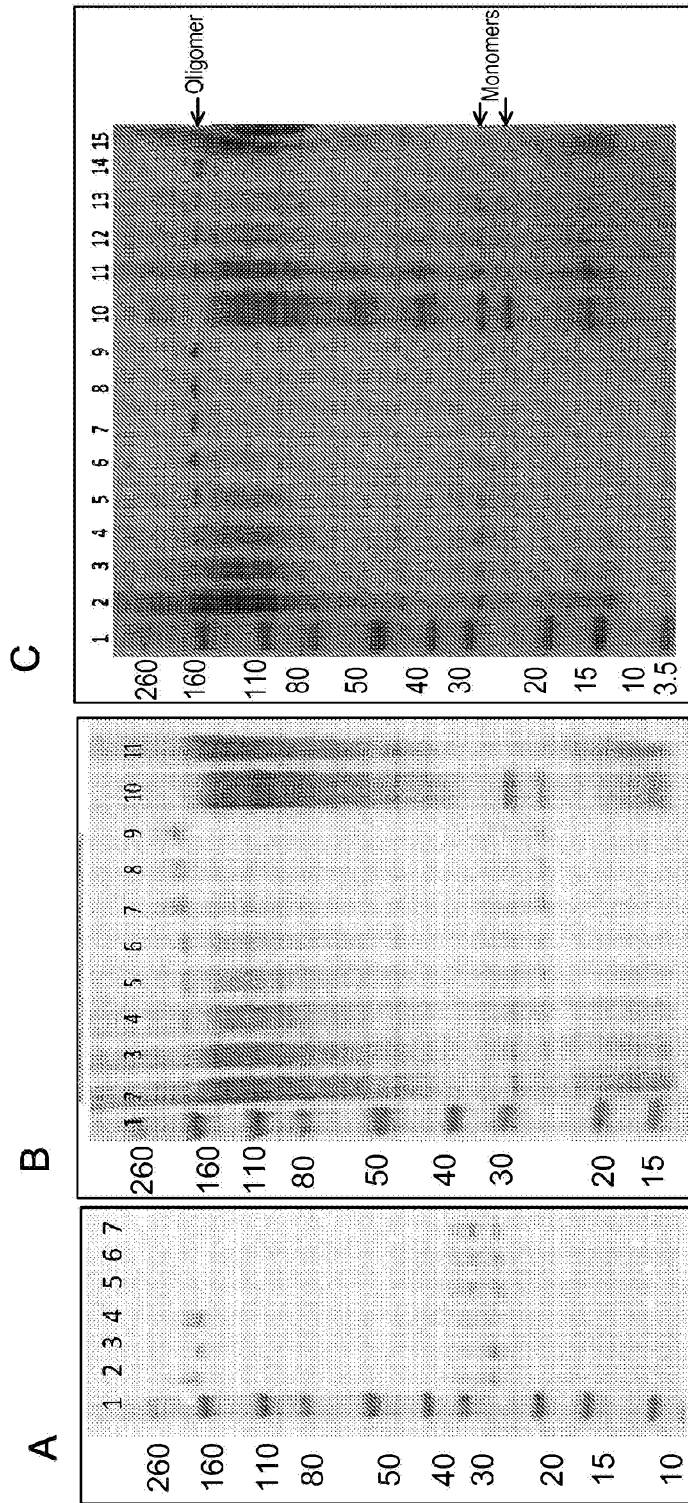


FIG. 14