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DESCRIPTION

Field of the invention

[0001] The invention relates to the field of medicine, specifically to the field of treatment of dermatitis or eczema, even more specifically to the field of treatment of atopic dermatitis. The invention relates to a novel composition and a novel kit of parts, both comprising an anti-inflammatory compound and a compound specifically targeting a bacterial cell, preferably a gram positive bacterial cell. The invention further relates to said composition for medical use, preferably for treating an individual suffering from eczema.

Background of the invention

[0002] Eczema is a common skin condition characterized by red, itchy skin and small blisters also known in the art as skin rash or rash or dermatitis. There is no cure for eczema, but there are many treatments, ranging from special diets to emollients and immunosuppressive ointments like e.g. corticosteroid ointment. While corticosteroids, such as hydrocortisone or clobetasol propionate (topical, oral or intradermal administration) usually bring about improvements, they also may have side effects. Prolonged use of topical corticosteroids is thought to increase the risk of side effects, the most common of which is the skin becoming thin and fragile (atrophy). Because of this, if used on the face or other delicate skin, a low-strength steroid should be used or applied less frequently. Additionally, high-strength steroids used over large areas, or under occlusion, may be absorbed into the body, causing hypothalamic-pituitary-adrenal axis suppression (HPA axis suppression).

[0003] Due to the impaired skin barrier in atopic dermatitis an increase in skin infections with bacteria such as *Staphylococcus aureus* or fungi might be the result. For more severe cases, dermatologists may also prescribe either topical or oral conventional antibiotics such as penicillin, streptomycin and chloramphenicol. The antibiotics prevent infection that can result from impaired skin barrier such as cracked skin. *S. aureus* colonization or infection is the most common cause of increased eczema severity. The effectiveness of antibiotic treatments varies from person to person. The well known disadvantages of conventional antibiotics are a-specificity, *i.e.* also non-pathogenic and/or beneficial bacteria are killed, and the risk of developing resistance, not only by the target bacterial cells but possibly also by other pathogenic bacteria. Furthermore, conventional, systemic antibiotic treatment can interact with other drugs, including contraceptive pills. Certain antibiotics cannot be combined with the use of alcohol. Accordingly, there is a need for improved treatment of eczema.

Description of the invention

[0004] The invention is defined by the subject matter of the claims herein.

[0005] In a first aspect, there is disclosed a novel composition comprising a first and a second compound, wherein said first compound is an anti-inflammatory compound and said second compound is a compound specifically targeting a bacterial cell, preferably a gram positive bacterial cell. Preferably, said gram positive bacterial cell is a *Staphylococcus*, more preferably a *Staphylococcus aureus*. Preferably, said composition is a medicament preferably for use in the treatment of eczema, most preferably for use in the treatment of atopic dermatitis, as further detailed herein. The state of the art for treating eczema is using immunosuppressive agents like corticosteroids and if indicated antibiotics topical or systemic. Disclosed is a novel composition comprising both an anti-inflammatory compound and a compound specifically targeting a bacterial cell, preferably a gram positive bacterial cell, preferably a *Staphylococcus aureus*, which combats most, if not all, of the disadvantages of using either an effective dosage regime of a corticosteroid and/or a conventional antibiotic alone or in combination and provides a unexpected synergy. In comparison to the use of an immunosuppressive agent alone like a corticosteroid alone, a disclosed composition decreases the risk and/or is more effective by combating eczema-related and/or corticosteroid induced infections induced by a bacterial cell, such as a gram positive bacterial cell, preferably *Staphylococcus aureus*. Furthermore, in comparison to the use of a corticosteroid alone, a disclosed composition may be as effective as using a corticosteroid alone while making use of a lower dosage and/or a shorter administration regimen resulting in a shorter exposure time of the corticosteroid thereby reducing possible side-effects like the risk of skin atrophy, hypothalamic-pituitary-adrenal axis suppression (HPA axis suppression) and/or (increased) skin infection.

[0006] In comparison to the use of a corticosteroid in combination with conventional antibiotics and/or conventional antibiotics alone, the disclosed composition selectively specifically targets a bacterial cell, preferably a gram positive bacterial cell, preferably a *Staphylococcus*, more preferably a *Staphylococcus aureus*, without affecting surrounding commensal and/or beneficial microflora. In addition, the risk of developing resistance against antibiotics is diminished or at least reduced since lower amounts of antibiotics or even no antibiotics at all are used.

[0007] An agent that specifically targets a gram positive bacterial cell preferably is an agent that shows at least 2, 5, 10, 50 or 100 times higher lytic activity towards a gram positive bacterial cell as compared to a gram negative bacterial cell. Preferably, an agent that specifically targets a gram positive bacterial cell is an agent that does not affect a gram negative bacterial cell in a concentration that is effective in lysing a gram positive bacterial cell. An agent that specifically targets a *Staphylococcus* bacterial cell preferably is an agent that shows at least 2, 5, 10, 50 or 100 times higher lytic activity towards a *Staphylococcus* bacterial cell as compared to a *non-Staphylococcus* bacterial cell. Preferably, an agent that specifically targets a *Staphylococcus* bacterial cell is an agent that does not affect a *non-Staphylococcus* bacterial cell in a concentration that is effective in lysing a *Staphylococcus* bacterial cell. An agent that specifically targets a *Staphylococcus aureus* bacterial cell preferably is an agent that shows at least 2, 5, 10, 50 or 100 times higher lytic activity towards a *Staphylococcus aureus*

bacterial cell as compared to a *non-Staphylococcus aureus* bacterial cell. Preferably, an agent that specifically targets a *Staphylococcus aureus* bacterial cell is an agent that does not affect a *non-Staphylococcus aureus* bacterial cell in a concentration that is effective in lysing a *Staphylococcus aureus* bacterial cell. Lytic activity is preferably assessed as exemplified herein.

[0008] Further disclosed is a composition comprising a first and a second compound, wherein said first compound is an anti-inflammatory compound and said second compound is a compound specifically targeting a bacterial cell, preferably a gram positive bacterial cell, and wherein said second compound comprises at least one cell wall binding domain specifically binding the peptidoglycan cell wall of said bacterial cell, preferably gram positive bacterial cell. A disclosed cell wall-binding domain is defined as an element, preferably a polypeptide within said second compound that directs said second compound to the bacterial wall of a bacterial cell.

[0009] A disclosed cell wall-binding domain may be any cell wall-binding domain known by the person skilled in the art. Preferably, a disclosed cell wall-binding domain is an element, preferably a polypeptide within said second compound, that directs said second compound to the peptidoglycan cell wall of a gram-positive bacterial cell, preferably the peptidoglycan cell wall of a *Staphylococcus* bacterial cell, more preferably the peptidoglycan cell wall of a *Staphylococcus aureus* bacterial cell.

[0010] Further disclosed is a composition comprising a first and a second compound, wherein said first compound is an anti-inflammatory compound and said second compound is a compound specifically targeting a bacterial cell, preferably a gram positive bacterial cell, and wherein said second compound comprises at least one cell wall binding domain specifically binding the peptidoglycan cell wall of *Staphylococcus*, more preferably, a *Staphylococcus aureus*.

[0011] Binding of a domain to the peptidoglycan cell wall of *Staphylococcus* genera may be assessed using assays well known to the person skilled in the art. In a preferred embodiment, an immunohistochemical technique and/or a gene fusion technique resulting in labelled constructs are used for assessing specific binding of compounds such as peptides, polypeptides, proteins or bacteriophages to the peptidoglycan cell wall of *Staphylococcus* genera. Quantification methods of signals used in the above mentioned immunohistochemical or fusion techniques are well known in the art.

[0012] In one embodiment, *Staphylococcus* peptidoglycan cell wall-binding is quantified using a fluorescent fusion construct comprising a cell wall-domain of interest. Such a cell wall-binding assay is described in detail by Loessner et al (Molecular Microbiology 2002, 44(2): 335-349). In this assay a solution comprising said fluorescent fusion construct or a negative control, preferably Green Fluorescent Protein (GFP), is subjected to *Staphylococcus* cells, preferably *S. aureus* cells, more preferably *S. aureus* BB255 for an indicated time period where after the cells are sedimented by centrifugation together with the bound fluorescent fusion constructs.

The fluorescent signal of the *Staphylococcus* cells exposed to a fluorescent fusion construct subtracted by the fluorescence signal of the *Staphylococcus* cells exposed to a negative control, preferably GFP, is a measure for cell binding as meant in this disclosure. Preferably, a disclosed domain is said to bind the peptidoglycan cell wall of *Staphylococcus* genera when using this assay an increase in fluorescent signal of the sedimented cells above the negative control as defined herein is detected. Further disclosed is a cell wall-binding domain which exhibits binding as defined herein of at least 50, 60, 70, 80, 90 or 100, 150 or 200% of peptidoglycan cell wall-binding of *S. aureus* bacteriophage Φ 2638a endolysin (Ply2638 endolysin defined by SEQ ID NO: 2) preferably encoded by SEQ ID NO: 1. Preferably, a fusion construct as represented by SEQ ID NO: 95 and encoded by SEQ ID NO: 96 serves as a positive control in this assay. An overview of all sequences included and their SEQ ID NO is given in table 2.

[0013] Further disclosed is a composition comprising a first and a second compound, wherein said first compound is an anti-inflammatory compound and said second compound is a compound specifically targeting a bacterial cell, preferably a gram positive bacterial cell, and wherein said second compound comprises at least one cell wall binding domain that originates from or is a homologue of a *Staphylococcus* phage endolysin, preferably said *Staphylococcus* phage endolysin is selected from, but not limited to, *S. aureus* bacteriophage Φ 2638a endolysin, *S. aureus* bacteriophage Φ 11 endolysin, *S. aureus* bacteriophage Φ Twort endolysin, *S. haemolyticus* JCSC1435, *S. aureus* Phage K endolysin, *S. warneri* phage WMY endolysin, *S. aureus* phage NM3 endolysin and *S. aureus* 80alpha endolysin.

[0014] Also preferred is a cell wall binding domain originating from or a homologue of *S. simulans* lysostaphin (represented by SEQ ID NO: 76, preferably encoded by SEQ ID NO: 75). A known homologue of *S. simulans* lysostaphin having cell wall binding properties is *S. capitis* ALE-1 enzyme.

[0015] Preferably, said cell wall binding domain has at least 80% identity to any of SEQ ID NO: 4, 6 or 8 and/or wherein said one or more enzymatic active domains has at least 80% identity to any of SEQ ID NO: 10, 12, 14, 16, 18, 98 or 100. Further disclosed is a cell wall-binding domain having at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with the cell wall binding domain of *S. simulans* lysostaphin defined herein by SEQ ID NO: 4 and preferably encoded by SEQ ID NO: 3. Also preferred is a cell wall-binding domain isolated from a native *Staphylococcus* bacteriophage endolysin. Further disclosed is a cell wall-binding domain that has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with the cell wall-binding domain of *S. aureus* bacteriophage Φ 2638a endolysin defined herein by SEQ ID NO: 6 and preferably encoded by SEQ ID NO: 5. Further disclosed is a cell wall-binding domain isolated from a native *Staphylococcus aureus* phage phiNM3 endolysin. Preferably, a cell wall-binding domain disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with the cell wall-binding domain of *S. aureus* phage phiNM3 endolysin defined herein by SEQ ID NO: 8 and preferably encoded by SEQ ID NO: 7.

[0016] Further disclosed is a composition comprising a first and a second compound, wherein said first compound is an anti-inflammatory compound and said second compound is a compound specifically targeting a bacterial cell, preferably a gram positive bacterial cell, wherein said second compound comprises one or more enzymatic active domains exhibiting target bond specificity. 'An enzymatic active domain' is defined herein is a domain having lytic activity, preferably exhibiting peptidoglycan hydrolase activity. Lytic activity can be assessed by methods well known by the person skilled in the art. In an embodiment, lytic activity is assessed spectrophotometrically by measuring the drop in turbidity of substrate cell suspensions. Turbidity is assessed by measuring optical density at a wavelength of 595 nm, typically a culture as turbid when it exhibits an optical density of at least 0.3 OD at a wavelength of 595 nm. Preferably, lytic activity is assessed spectrophotometrically measuring the drop in turbidity of a *S. aureus* suspension, wherein turbidity is quantified by measuring OD₅₉₅ spectrophotometrically (Libra S22, Biochrom). More preferably, 200 nM polypeptide comprising an enzymatic active domain as identified herein is incubated together with an *S. aureus* suspension having an initial OD₅₉₅ of 1 ± 0.05 , as assessed spectrophotometrically (Libra S22, Biochrom), in PBS buffer pH 7.4, 120 mM sodium chloride for 30 min at 37°C. The drop in turbidity is calculated by subtracting the OD₅₉₅ after 30 min of incubation from the OD₅₉₅ before 30 min of incubation. A polypeptide comprising an enzymatic active domain of as identified herein will be said to have lytic activity if, when using this assay, a drop in turbidity of at least 10, 20, 30, 40, 50 or 60% is detected. Preferably, a drop in turbidity of at least 70% is detected. Preferably, a polypeptide comprising an enzymatic active domain exhibits a lytic activity of at least 30, 40, 50, 60, 70, 80, 90, 100, 150 or 200% or more of a lytic activity of *S. aureus* bacteriophage Φ 2638a endolysin (Ply2638 endolysin identified by SEQ ID NO: 2) preferably encoded by SEQ ID NO: 1.

[0017] Further disclosed is a composition comprising a first and a second compound, wherein said first compound is an anti-inflammatory compound and said second compound is a compound specifically targeting a bacterial cell, preferably a gram positive bacterial cell, wherein said second compound comprises one or more enzymatic active domains exhibiting target bond specificity, and wherein said target bond is an essential bond in a peptidoglycan layer of said bacterial cell, preferably gram positive bacterial cell. An essential bond in a peptidoglycan layer of a bacterial cell, preferably a gram-positive bacterial cell is defined herein as a linkage within said peptidoglycan that is essential for said peptidoglycan to provide said bacterial cell shape and a rigid structure resistance to osmotic shock. Preferably, said essential bond in a peptidoglycan layer of a gram-positive bacterial cell is a bond between a D-alanine of the stem peptide and a glycine of the cross-bridge peptide (defined herein also as a bond between an N-terminal alanine and a glycine), a bond in a pentaglycin cross-bridge (defined herein also as a pentyglycin bridge glycyl-glycyl bond, a bond between an N-acetylmuramoyl and an L-alanine or a bond between an N-acetylmuramine and a N-acetylglucosamine or between a N-acetylglucosamine and an N-acetylmuramine. Other preferred essential bonds in a peptidoglycan layer of a gram-positive bacterial cell are a bond in a gamma-glutamyl stem peptide, a bond between an L-alanyl-iso-D-glutamic acid in a stem peptide and a bond between an iso-D-glutamic acid-L-Lysine in a stem peptide.

[0018] Most native *Staphylococcus* bacteriophage endolysins exhibiting peptidoglycan hydrolase activity consist of a C-terminal cell wall-binding domain (CBD), a central N-acetylmuramoyl-L-Alanine amidase domain, and an N-terminal alanyl-glycyl endopeptidase domain with cysteine, histidine-dependent amidohydrolases/peptidase (CHAP) homology, or in case of Ply2638, of an N-terminal glycyl-glycine endopeptidase domain with Peptidase_M23 homology, the latter three domains exhibiting peptidoglycan hydrolase activity each with distinct target bond specificity and generally named herein as enzymatically active domains. Preferably, said one or more enzymatic active domains is selected from or is a permutation of a domain of the group consisting of a cysteine, histidine dependent amidohydrolases/peptidase domain, an endopeptidase domain, an amidase domain and a glycosylhydrolase domain. Said glycosylhydrolase domain can be a muramidase domain or a glucosaminidase domain.

[0019] Preferably, said CHAP domain cleaves a bond between an N-terminal alanyl and a glycyl within a peptidoglycan layer. More preferably, said CHAP domain specifically cleaves a bond between an N-terminal alanyl and a glycyl within a peptidoglycan layer. Preferably, said endopeptidase domain cleaves pentaglycin bridge glycyl-glycyl bond within a peptidoglycan layer. More preferably, said endopeptidase domain specifically cleaves pentaglycin bridge glycyl-glycyl bond within a peptidoglycan layer. Preferably, said amidase domain cleaves a bond between a central N-acetylmuramoyl and an L-Alanine within a peptidoglycan layer. More preferably, said amidase domain specifically cleaves a bond between a central N-acetylmuramoyl and an L-Alanine within a peptidoglycan layer. Preferably, said muramidase domain cleaves a bond between an N-acetylmuramine and a N-acetylglucosamine within a peptidoglycan layer. More preferably, said muramidase domain specifically cleaves a bond between an N-acetylmuramine and a N-acetylglucosamine within a peptidoglycan layer. Preferably, said glucosaminidase domain cleaves a bond between an N-acetylglucosamine and an N-acetylmuramine within a peptidoglycan layer. More preferably, said glucosaminidase domain specifically cleaves a bond between an N-acetylglucosamine and an N-acetylmuramine within a peptidoglycan layer. Preferably said peptidoglycan layer is of a bacterial cell, preferably a gram positive bacterial cell, more preferably of a *Staphylococcus*, most preferably of a *Staphylococcus Aureus*. Preferably, the cleavage of a bond by an enzymatic active domain as defined herein is specific if such a bond is hydrolysed at least 2, 5, 10, 50 or a 100 times more efficient with said enzymatic active domain as compared to the hydrolyses of any other bond as defined herein above with said enzymatic active domain.

[0020] Preferably, a CHAP domain originates from *Staphylococcus* phage K, *Staphylococcus phage* Twort and/or *S. aureus* bacteriophage phi 11. Preferably, a CHAP domain is a domain that has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 10, 12 or 98 and/or is preferably encoded by SEQ ID NO: 9 or 11. Preferably, an endopeptidase domain originates from *S. aureus* bacteriophage Φ2638a and/or *S. simulans*. Preferably, an endopeptidase domain has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 14 or 16 and/or is preferably encoded by SEQ ID NO: 13 or 15. Preferably, an amidase domain originates from *S. aureus* bacteriophage Φ2638a or *S. aureus* bacteriophage phi 11. Preferably an amidase domain has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92,

93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 18 or 100 and/or is preferably encoded by SEQ ID NO: 17 or 99.

[0021] Further disclosed is a composition comprising a first and a second compound, wherein said first compound is an anti-inflammatory compound and said second compound is a compound specifically targeting a bacterial cell, preferably a gram positive bacterial cell, wherein said second compound is a naturally occurring or mutant bacteriophage, a naturally occurring endolysin or a mutant polypeptide.

[0022] A naturally occurring bacteriophage may be any bacteriophage specifically targeting and infecting a bacterial cell, preferably bacterial cell, preferably a *Staphylococcus*, most preferably a *Staphylococcus aureus*. Preferably, a naturally occurring bacteriophage is selected from, but not limited to, a group consisting of *S. aureus* bacteriophage Φ 2638a, *S. aureus* bacteriophage Φ 11, *S. aureus* bacteriophage Φ Twort, *S. haemolyticus* JCSC1435, *S. aureus* Phage K, *S. warneri* phage WMY, *S. aureus* phage NM3 and *S. aureus* 80alpha. Said naturally occurring endolysin may be synthesized and/or purified. A bacteriophage may be a mutant, chimeric and/or recombinant bacteriophage. The person skilled in the art may construct a bacteriophage by placing mutations in the genome and/or deleting and/or inserting coding sequences or parts thereof into the genome using methods known in the art.

A naturally occurring endolysin may be any wild type or native endolysin exhibiting peptidoglycan hydrolase activity. Preferred is a *Staphylococcus* phage endolysin, preferably said *Staphylococcus* phage endolysin is selected from, but not limited to, the group consisting of *S. aureus* bacteriophage Φ 2638a endolysin, *S. aureus* bacteriophage Φ 11 endolysin, *S. aureus* bacteriophage Φ Twort endolysin, *S. haemolyticus* JCSC1435, *S. aureus* Phage K endolysin, *S. warneri* phage WMY endolysin, *S. aureus* phage NM3 endolysin and *S. aureus* 80alpha endolysin. Also preferred is *S. simulans* lysostaphin and/or a homologue of *S. simulans* lysostaphin such as *S. capitis* ALE-1 enzyme. Most native *Staphylococcus* bacteriophage endolysins exhibiting peptidoglycan hydrolase activity consist of a C-terminal cell wall-binding domain (CBD), a central N-acetylmuramoyl-L-Alanine amidase domain, and an N-terminal Alanyl-glycyl endopeptidase domain with CHAP homology, or in case of Ply2638, of an N-terminal endopeptidase domain with Peptidase_M23 homology, the latter three domains exhibiting peptidoglycan hydrolase activity each with distinct target bond specificity and generally named herein as enzymatically active domains.

[0023] A mutant polypeptide as disclosed may be a chemically synthesized polypeptide or a recombinant or retrofitted polypeptide produced *in vitro*. A retrofitted construct is defined herein as a polynucleotide comprising heterologous nucleotide sequences. As used herein the term heterologous sequence or heterologous polynucleotide is one that is not naturally found operably linked as neighboring sequence of said first nucleotide sequence. As used herein, the term heterologous may mean recombinant. Recombinant refers to a genetic entity distinct from that generally found in nature. As applied to a nucleotide sequence or nucleic acid molecule, this means that said nucleotide sequence or nucleic acid molecule is the product of various combinations of cloning, restriction and/or ligation steps, and other procedures that result in the production of a construct that is distinct from a sequence or molecule found in nature.

Preferably, a mutant polypeptide disclosed comprises at least an enzymatic active domain and a cell binding domain as defined herein.

[0024] An endolysin or mutant polypeptide disclosed may be in a purified form or may be comprised within a crude composition, preferably of biological origin, such as a bacterial lysate, yeast lysate, fungal lysate, sonicate or fixate. Alternatively, said endolysin or mutant polypeptide may be a chemically synthesized endolysin or polypeptide or a recombinant polypeptide produced *in vitro*.

[0025] An endolysin or mutant polypeptide disclosed preferably comprises or consists of at least one enzymatic active domain and at least one cell binding domain and optionally a tag for ease of purification. Preferably, said tag is selected from, but is not limited to, the group consisting of a FLAG-tag, poly(His)-tag, HA-tag and Myc-tag. More preferably said tag is a 6xHis-tag. Even more preferably, said tag is an N-terminal 6xHis-tag (indicated herein as HXa) identical to SEQ ID NO: 74 and preferably encoded by SEQ ID NO: 73).

[0026] Preferably, a cell wall-binding domain disclosed is located on the C-terminal side of the enzymatic active domain within said naturally occurring endolysin or a mutant polypeptide. Preferably, said mutant naturally occurring or mutant polypeptide comprises at least two or more enzymatic active domains with distinct target bond specificities as distinct target bond specificities confer synergistic effects. Further disclosed is a composition comprises at least two distinct compounds targeting a bacterial cell, preferably a gram positive bacterial cell, preferably a *Staphylococcus*, more preferably a *Staphylococcus aureus*. Preferably said at least two distinct compounds are naturally occurring endolysin, which are optionally synthesized. Preferably said at least two distinct compounds are recombinant polypeptides each comprising a distinct enzymatic active domain and/or a different multiplicity of at least two distinct enzymatic active domains as defined herein below.

[0027] Further disclosed is a composition comprising a first and a second compound, wherein said first compound is an anti-inflammatory compound and said second compound is a compound specifically targeting a bacterial cell, preferably a gram positive bacterial cell, wherein said second compound is a recombinant polypeptide comprising a multiplicity of said one or more enzymatic active domains exhibiting target bond specificity. "Multiplicity" is to be understood as a number of copies and may be any integer varying from 1 to 20, preferably from 1 to 10, more preferably from 1 to 3, most preferably said multiplicity is 2, *i.e.* a duplicate. Polypeptides comprising a multiplicity of enzymatic active domains show superior lytic activity as compared to polypeptides comprising a single enzymatic active domain.

[0028] Preferably, said second compound is a polypeptide comprising and/or consisting of an enzymatic active domain, a cell wall binding and optionally a tag for ease of purification as defined herein, preferably said enzymatic active domain being a cysteine, histidine-dependent amidohydrolases/peptidase domain, an endopeptidase domain or an amidase domain, and preferably polypeptide comprises a multiplicity of said enzymatic active domain, preferably said multiplicity being 2, *i.e.* a duplicate. More preferably said polypeptide comprises and/or consists

of a duplicated amidase domain and a cell wall binding domain and optionally a tag for ease of purification as defined herein, preferably said amidase is from *S. aureus* bacteriophage Φ 2638a endolysin and said cell wall binding domain is of *S. simulans* lysostaphin. Most preferably said polypeptide comprises and/or consists of a duplicated endopeptidase domain and a cell wall binding domain and optionally a tag for ease of purification as defined herein, preferably said endopeptidase domain is a Peptidase_M23 domain of *S. simulans* lysostaphin and said cell wall binding domain is of *S. simulans* lysostaphin.

[0029] Preferably, said second compound is a polypeptide has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 98 or 100 and/or is encoded by a polynucleotide having at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity to any of SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 97 or 99. Preferably, said polypeptide has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 28, 34, 46, 52, 58 or 70, more preferably, said polypeptide has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 28, 46, 52, or 70, even more preferably, said polypeptide has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 46 or 70, most preferably said polypeptide has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 70.

[0030] Further disclosed is a composition comprising a first and a second compound, wherein said first compound is an anti-inflammatory compound and said second compound is a compound specifically targeting a bacterial cell, preferably a gram positive bacterial cell, wherein said first compound is selected from the group consisting of a corticosteroid, a calcineurin inhibitor, an immunotherapeutic compound, a recombinant human IFN-gamma, a microbial probiotic, a cytokine modulator, an inflammatory cell recruitment blocker, and a T cell activation inhibitor. Preferred calcineurin inhibitors are FK506, tacrolimus and pimecrolimus. A preferred immunotherapeutic compound is omalizumab, a humanized IgG1 monoclonal antibody against IgE that recognizes and masks an epitope in the CH3 region of IgE responsible for binding to the high-affinity Fc ϵ R on mast cells and basophils. Preferred cytokine modulators are a soluble IL-4 receptor, an anti-IL-5 monoclonal antibody and a TNF inhibitor. Preferred inflammatory cell recruitment blockers are a chemokine receptor antagonist and a CLA inhibitor. Preferred T cell activation inhibitors are alefacept and efalizumab. Corticosteroids that may be used include, but are not limited to, betamethasone dipropionate, fluocinolone acetonide, betamethasone valerate, triamcinolone acetonide, clobetasol propionate, desoximetasone, diflorasone diacetate, amcinonide, flurandrenolide, hydrocortisone valerate, hydrocortisone butyrate, desonide, hydrocortisone and methylprednisolone acetate. A further preferred anti-inflammatory compound is dapsone which has both antimicrobial and anti-inflammatory properties.

[0031] In all embodiments, the second compound specifically targeting a bacterial cell, preferably a gram positive bacterial cell may be comprised of a combination of a source of a first enzymatic active domain and a source of a second enzymatic active domain, wherein said first and second enzymatic active domains exhibit distinct target bond specificities and are comprised on a distinct first and second polypeptide, *i.e.* said first enzymatic active domain is comprised on a first polypeptide and said second enzymatic domain is comprised on a second polypeptide, wherein said first and second polypeptide each have a distinct amino acid sequence. In addition, the disclosed second compound according may be comprised of a combination of a source of a first enzymatic active domain, a source of a second enzymatic active domain and a source of a third enzymatic active domain, wherein said first, second and third enzymatic active domain exhibit distinct target bond specificities and are comprised on a distinct first, second and third polypeptide, *i.e.* said first enzymatic active domain is comprised on a first polypeptide, said second enzymatic domain is comprised on a second polypeptide, and said third enzymatic domain is comprised on a third polypeptide, wherein said first, second and third polypeptide each have a distinct amino acid sequence. Furthermore, the second compound disclosed may be comprised of a combination of a source of a first enzymatic active domain, a source of a second enzymatic active domain, a source of a third enzymatic active domain, and a source of a further enzymatic active domain, wherein said first, second, third and further enzymatic active domain exhibit distinct target bond specificities and are comprised on a distinct first, second, third and further polypeptide, *i.e.* said first enzymatic active domain is comprised on a first polypeptide, said second enzymatic domain is comprised on a second polypeptide, said third enzymatic domain is comprised on a third polypeptide, and said further enzymatic active domain is comprised on a further polypeptide, wherein said first, second, third and further polypeptide each have a distinct amino acid sequence. A further enzymatic active domain is meant herein as a fourth, fifth, sixth, seventh, eighth, ninth, tenth or more enzymatic active domain, preferably a fourth enzymatic active domain. A further polypeptide is meant herein as a fourth, fifth, sixth, seventh, eighth, ninth, tenth or more polypeptide, preferably a fourth polypeptide.

[0032] The inventors surprisingly found for the second compound disclosed, that simultaneous application of two or more enzymatically active domains with distinct target bond specificities confers synergistic effects. Surprisingly, this works not only when enzymatically active domains with different specificities are located on the same molecule as in native *Staphylococcus* endolysins, but works also when the enzymatically active domains with different specificities are separated on distinct polypeptides.

[0033] The benefit of having distinct enzymatic active domains located on separate individual polypeptides is that the resulting polypeptides are smaller which can be more easily produced. Furthermore, these smaller polypeptides have better diffusion properties in specific environments and can be more resistant to degradation and feature higher thermostability. Another advantage is that independent distinct enzymatic active domains located on separate distinct polypeptide molecules can be mixed and pooled in variable compositions, at a ratio that is best suited to hydrolyse the specific bacterial target cells. The second compound disclosed comprised of a combination as described herein can be supplemented and/or complemented

by the use of virtually any functional enzymatic active domain with virtually any target bond specificity from many different origins including phage lysins, bacteriocins, autolysins, or any other cell wall lytic enzymes.

[0034] Within the context of the second compound disclosed 'a combination' means that a source of a first enzymatic active domain and a source of a second enzymatic active domain are contemplated and encompassed. In addition, within the context of the second compound disclosed 'a combination' means that a source of a first enzymatic active domain, a source of a second enzymatic active domain and optionally a source of a third and/or further enzymatic active domain are contemplated and encompassed. Each source may be together or present together or combined together or physically in contact with the other source forming one single composition. Each source may alternatively be comprised within a distinct composition. However the disclosure provides the insight that both sources of a first and a second enzymatic active domain are preferably needed or are used in order to get an effect of the present invention as defined herein. If each source is not present in a same single composition, each source and/or each distinct composition comprising a source of a combination encompassing the second compound disclosed may be used sequentially or simultaneously.

[0035] 'A source of a first enzymatic active domain', 'a source of a second enzymatic active domain', 'a source of a third enzymatic active domain' and 'a source of a further enzymatic active domain' preferably comprises a protein-based source, *i.e.* a polypeptide, a protein, digest of a protein and/or fragment of a protein or digest, or a source not being protein based, *i.e.* a nucleic acid encoding a protein or derived peptide or protein fragment. Below we define preferred sources of a first enzymatic active domain, a source of a second enzymatic active domain, a source of a third enzymatic active domain and a source of a further enzymatic active domain that are encompassed by the disclosure. When the second compound disclosed relates to a combination of a source of a first enzymatic active domain, a source of a second enzymatic active domain and optionally a source of a third and/or further enzymatic active domain, each of the sources of a first enzymatic active domain defined herein may be combined with each of the sources of a second and optionally third and/or further enzymatic active domain defined herein. It is also disclosed to use a combination of a source of a first enzymatic active domain being protein-based with a source of a second and optionally a third and/or further enzymatic active domain being not protein-based, and vice versa.

[0036] 'Comprised on distinct polypeptides' is meant herein as any of said first, second and optionally third and/or further enzymatic active domain is comprised on a polypeptide which is distinct from the polypeptide that any of the other of said first, second and optionally third and/or further enzymatic active domain is comprised on.

[0037] In all embodiments, a polypeptide can be a natural polypeptide or an isolated polypeptide, preferably an isolated polypeptide. A nucleic acid may be a natural nucleic acid or an isolated nucleic acid, preferably an isolated nucleic acid. A nucleic acid construct can be a natural or an isolated construct, preferably an isolated nucleic acid construct.

[0038] Preferably, a first, a second and optionally a third and/or further enzymatic active domain together encompassing the second compound disclosed is a domain selected from the group consisting of a cysteine, histidine-dependent amidohydrolases/peptidase (CHAP) domain, an endopeptidase domain, and an amidase domain; all preferably as described previously herein.

[0039] Preferably, a first, second, third and/or further polypeptide together encompassing the second compound disclosed comprises a different multiplicity of a first, second, third and/or further enzymatic active domain as disclosed. A "multiplicity" is herein defined as a number of copies. A "different multiplicity" is defined herein as a multiplicity or number of copies of a specific enzymatic active domain disclosed, *i.e.* a first, second, third or further enzymatic active domain as defined herein, comprised within a specific polypeptide disclosed, *i.e.* a first, second, third or further polypeptide as defined herein, to be different from a multiplicity or number of copies of that same enzymatic active domain within another polypeptide of the combination encompassing the second compound disclosed. For example, a combination encompassing the second compound comprises a first polypeptide comprising a specific number of copies of a first enzymatic active domain, and a second polypeptide comprising a different number of copies of said first enzymatic active domain. Furthermore, said first polypeptide of said exemplified combination encompassing the second compound may further comprise a specific number of copies of second enzymatic active domain, which is different from the number of copies of said second enzymatic active domain as comprised on said second polypeptide of said combination. Furthermore, any further polypeptide of said exemplified combination encompassing the second compound may comprise a number of copies of further enzymatic active domain, which is different from the number of copies of said further enzymatic active domain as comprised on said first and second polypeptide of said combination. Although a combination of distinct polypeptides each comprising a single distinct enzymatic active domain showed synergistic lytic activity as compared to the lytic activity of each separate polypeptide, it was surprisingly found by the present inventors that polypeptides comprising a multiplicity of enzymatic active domains show superior lytic activity as compared to polypeptides comprising a single enzymatic active domain.

[0040] Moreover, a combination of distinct enzymatic domains on distinct polypeptides wherein at least one of said distinct polypeptides comprises a multiplicity of enzymatic active domains was found superior over a combination wherein all said distinct polypeptides comprise a single distinct enzymatic active domain. Moreover, a combination encompassing the second compound, wherein a first, second, third and/or further polypeptide comprise a multiplicity of a first, second, third and/or further enzymatic active domain, respectively, was found superior over a combination encompassing the second compound, wherein said first, second, third and/or further polypeptide comprise a single copy of said first, second, third and/or further enzymatic active domain, respectively, and preferably wherein said multiplicity, as defined herein, is 2, *i.e.* a duplicate. In a preferred embodiment, the synergistic effect of a combination encompassing the second compound disclosed, wherein a first, second, third and/or further polypeptide comprise a multiplicity of a first, second, third and/or further enzymatic active

domain, respectively, was found superior over a combination encompassing the second compound, wherein said first, second, third and further polypeptide comprise a single copy of said first, second, third and further enzymatic active domain, respectively, and preferably wherein said multiplicity, as defined herein below, is 2, *i.e.* a duplicate.

[0041] Preferably, a first and/or second polypeptide of a combination encompassing the second compound, comprises a different multiplicity of a first and/or second enzymatic active domain disclosed. Multiplicity of said first and second domain is defined as previously herein as a number of copies, preferably indicated by k , l , n and p , of said first and second domain indicated as follows:

k

indicates the number of copies of said first enzymatic active domain on said first polypeptide;

l

indicates the number of copies of said second enzymatic active domain on said first polypeptide;

n

indicates the number of copies of said first enzymatic active domain on said second polypeptide;

p

indicates the number of copies of said second enzymatic active domain on said second polypeptide;

and wherein k and p are independent integers from 1-10, 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, or preferably 1-2, and l and n are independent integers from 0-10, 0-9, 0-8, 0-7, 0-6, 0-5, 0-4, 0-3, or preferably 0-2, and wherein k is a different integer than n and/or l is a different integer than p , most preferably k and p are 2 and l and n are 0.

[0042] Preferably, a first, second and third polypeptide encompassing the second compound disclosed comprise a different multiplicity of a first, second and third enzymatic active domain disclosed.

[0043] Multiplicity of said first, second and third domain is defined as previously herein as a number of copies, preferably indicated by k , l , m , n , p , q , r , s and t , of said first, second and third domain indicated as follows:

k

indicates the number of copies of said first enzymatic active domain on said first polypeptide;

l

indicates the number of copies of said second enzymatic active domain on said first polypeptide;

m

indicates the number of copies of said third enzymatic active domain on said first

polypeptide;

n

indicates the number of copies of said first enzymatic active domain on said second polypeptide;

p

indicates the number of copies of said second enzymatic active domain on said second polypeptide;

q

indicates the number of copies of said third enzymatic active domain on said second polypeptide;

r

indicates the number of copies of said first enzymatic active domain on said third polypeptide;

s

indicates the number of copies of said second enzymatic active domain on said third polypeptide;

t

indicates the number of copies of said third enzymatic active domain on said third polypeptide;

and wherein *k*, *p* and *t* are independent integers from 1-10, 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, or preferably 1-2, and *l*, *m*, *n*, *q*, *r*, and *s* are independent integers from 0-10, 0-9, 0-8, 0-7, 0-6, 0-5, 0-4, 0-3, or preferably 0-2, and wherein *k* is a different integer than *n* and/or *r*, and/or *l* is a different integer than *p* and/or *s*, and/or *t* is a different integer than *m* or *q*, most preferably *k*, *p* and *t* are 2 and *l*, *m*, *n*, *q*, *r*, and *s* are 0 .

[0044] Preferably, a first, second, third and further polypeptide encompassing the second compound disclosed comprise a different multiplicity of a first, second, third and further enzymatic active domain disclosed. Multiplicity of said further enzymatic active domain in view of said first, second and third enzymatic active domain is to be construed herein in an analogous manner as defined herein above for a first, second and third enzymatic active domain.

[0045] Preferably a first, second, third or further polypeptide encompassing the second compound disclosed has a length of at least 140, 150, 160, 170, 180, 190, 200, 210, 220, 230, 240, 250, 260, 270, 280, 290, 300, 310, 320 or 330 amino acids and/or a length of at most 850, 800, 750, 700, 650, 600, 550, 500, 490, 480, 470, 460, 450, 440, 430, 420, 410, 400, 390, 380 or 370 amino acids. More preferably, a first, second or third polypeptide encompassing the second compound disclosed has a length of 140-850, 140-800, 140-750, 140-700, 140-650, 140-600, 140-550 140-500, 140-490, 140-480, 140-470, 140-460, 140-450, 140-440, 140-430, 140-420, 140-410, 140-400, 140-390, 140-380, 140-370, 150-850, 160-850, 170-850, 180-850, 190-850, 200-850, 210-850, 220-850, 230-850, 240-850, 250-850, 260-850, 270-850, 280-850, 290-850, 300-850, 310-850, 320-850 or 330-850 amino acids.

[0046] Preferably a first and second polypeptide encompassing the second compound disclosed each have a length of at least 140, 150, 160, 170, 180, 190, 200, 210, 220, 230, 240, 250, 260, 270, 280, 290, 300, 310, 320 or 330 amino acids and/or a length of at most 800, 850, 700, 650, 600, 550, 500, 490, 480, 470, 460, 450, 440, 430, 420, 410, 400, 390, 380 or 370 amino acids. More preferably, a first and second polypeptide disclosed each have a length of 140-850, 140-800, 140-750, 140-700, 140-650, 140-600, 140-550 140-500, 140-490, 140-480, 140-470, 140-460, 140-450, 140-440, 140-430, 140-420, 140-410, 140-400, 140-390, 140-380, 140-370, 150-850, 160-850, 170-850, 180-850, 190-850, 200-850, 210-850, 220-850, 230-850, 240-850, 250-850, 260-850, 270-850, 280-850, 290-850, 300-850, 310-850, 320-850 or 330-850 amino acids.

[0047] Preferably a first, second and third polypeptide encompassing the second compound disclosed each have a length of at least 140, 150, 160, 170, 180, 190, 200, 210, 220, 230, 240, 250, 260, 270, 280, 290, 300, 310, 320 or 330 amino acids and/or a length of at most 800, 850, 700, 650, 600, 550, 500, 490, 480, 470, 460, 450, 440, 430, 420, 410, 400, 390, 380 or 370 amino acids. More preferably, a first, second and third polypeptides encompassing the second compound disclosed each have a length of 140-850, 140-800, 140-750, 140-700, 140-650, 140-600, 140-550 140-500, 140-490, 140-480, 140-470, 140-460, 140-450, 140-440, 140-430, 140-420, 140-410, 140-400, 140-390, 140-380, 140-370, 150-850, 160-850, 170-850, 180-850, 190-850, 200-850, 210-850, 220-850, 230-850, 240-850, 250-850, 260-850, 270-850, 280-850, 290-850, 300-850, 310-850, 320-850 or 330-850 amino acids.

[0048] Preferably a first, second, third and further polypeptide encompassing the second compound disclosed each have a length of at least 140, 150, 160, 170, 180, 190, 200, 210, 220, 230, 240, 250, 260, 270, 280, 290, 300, 310, 320 or 330 amino acids and/or a length of at most 800, 850, 700, 650, 600, 550, 500, 490, 480, 470, 460, 450, 440, 430, 420, 410, 400, 390, 380 or 370 amino acids. More preferably, a first, second, third and further polypeptides encompassing the second compound disclosed each have a length of 140-850, 140-800, 140-750, 140-700, 140-650, 140-600, 140-550 140-500, 140-490, 140-480, 140-470, 140-460, 140-450, 140-440, 140-430, 140-420, 140-410, 140-400, 140-390, 140-380, 140-370, 150-850, 160-850, 170-850, 180-850, 190-850, 200-850, 210-850, 220-850, 230-850, 240-850, 250-850, 260-850, 270-850, 280-850, 290-850, 300-850, 310-850, 320-850 or 330-850 amino acids.

[0049] An embodiment provides a combination of a source of a first and a second enzymatic active domain encompassing the second compound disclosed, wherein said first and second enzymatic active domains are comprised on distinct, first and second polypeptides disclosed, wherein said first polypeptide is free of said second enzymatic active domain and said second polypeptide is free of said first enzymatic active domain. Moreover, provided is a combination disclosed, wherein l and n are 0.

[0050] Another embodiment provides a combination of a source of a first, second and third enzymatic active domain encompassing the second compound disclosed, wherein said first, second and third enzymatic active domains are comprised on distinct, first, second and third

polypeptides, wherein said first polypeptide is free of said second and third enzymatic active domain, said second polypeptide is free of said first and third enzymatic active domain, and said third polypeptide is free of said first and second enzymatic active domain. Moreover, provided is a combination disclosed, wherein *l*, *m*, *n*, *q*, *r* and *s* are 0. Further disclosed is a combination encompassing the second compound according to the present invention, wherein *l*, *m*, *n*, *q*, *r* and *s* are 0 and *k*, *p* and *t* are 2.

[0051] Another embodiment provides a combination of a source of a first, second, third and further enzymatic active domain encompassing the second compound disclosed, wherein said first, second, third and further enzymatic active domains are comprised on a distinct, first, second, third and further polypeptide, respectively, wherein preferably said first polypeptide is free of said second, third and further enzymatic active domain; preferably said second polypeptide is free of said first, third and further enzymatic active domain; preferably said third polypeptide is free of said first, second and further enzymatic active domain; and, preferably said further polypeptide is free of said first, second and third enzymatic active domain.

[0052] Preferably said first, second, third and further enzymatic active domain are comprised within said first, second, third and further polypeptide, respectively, in duplicate, *i.e.* wherein the multiplicity as identified herein is 2. Also encompassed is a combination encompassing the second compound disclosed, wherein a first, second and/or third polypeptide disclosed are not free of a first, second and/or third enzymatic active domain disclosed, but said first, second and/or third polypeptide differ in multiplicity of said first, second and/or third enzymatic active domain. Moreover, encompassed is a combination encompassing the second compound disclosed, wherein at least one of *k*, *l*, *m*, *n*, *p*, *q*, *r*, *s* or *t* is 2 and wherein any of the other *k*, *l*, *m*, *n*, *p*, *q*, *r*, *s* and/or *t* is 1 or 0.

[0053] Preferred is a combination encompassing the second compound disclosed, wherein a first, second, third and/or further polypeptide is a polypeptide that has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with a polypeptide selected from the group consisting of SEQ ID NO: 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 98 or 100.

[0054] Within the context of the disclosure, several preferred, non-limiting, combinations encompassing the second compound disclosed are envisaged, which are listed here below.

[0055] Preferred is a combination of a source of first enzymatic active domain and a second enzymatic active domain, wherein said first and second enzymatic active domains are comprised on distinct first and second polypeptides, and wherein said first enzymatic active domain is a cysteine, histidine-dependent amidohydrolases/peptidase domain and said second

enzymatic active domain is an endopeptidase domain or wherein said first enzymatic active domain is a cysteine, histidine-dependent amidohydrolases/peptidase domain and said second enzymatic active domain is amidase domain or wherein said first enzymatic active domain is an endopeptidase domain and said second enzymatic active domain is amidase domain, wherein said distinct first and second each further comprises a cell wall-binding domain, and wherein each of said distinct first and second polypeptides comprises a multiplicity of said first or second enzymatic active domain, preferably said multiplicity being 2, *i.e.* a duplicate.

[0056] Also preferred is a combination of a source of first and second enzymatic active domain, wherein said first and second enzymatic active domains are comprised on distinct first and second polypeptides, and wherein said first enzymatic domain is histidine-dependent amidohydrolases/peptidase domain and said second enzymatic active domain is an endopeptidase domain or said first enzymatic active domain is a cysteine, histidine-dependent amidohydrolases/peptidase domain and said second enzymatic active domain is amidase domain or said first enzymatic active domain is an endopeptidase domain and said second enzymatic active domain is amidase domain, and wherein said first and second polypeptide each further comprise a cell wall binding domain.

[0057] Also preferred is a combination of a source of first enzymatic active domain and a second enzymatic active domain, wherein said first and second enzymatic active domains are comprised on distinct first and second polypeptides, and wherein said first enzymatic active domain is a cysteine, histidine-dependent amidohydrolases/peptidase domain and said second enzymatic active domain is an endopeptidase domain, and wherein said combination further comprises a source of a third enzymatic active domain comprised on a distinct third polypeptide, wherein said third enzymatic active domain is an amidase domain and said distinct first, second and third polypeptide each further comprises a cell wall-binding domain, and wherein each of said distinct first, second and third polypeptides comprises a multiplicity of said first, second or third enzymatic active domain, preferably said multiplicity being 2, *i.e.* a duplicate.

[0058] Also preferred is a combination of a source of first, second and third enzymatic active domain, wherein said first, second and third enzymatic active domains are comprised on distinct first, second and third polypeptides, and wherein said first enzymatic domain is histidine-dependent amidohydrolases/peptidase domain, said second enzymatic active domain is an endopeptidase domain and said third enzymatic active domain is an amidase domain, and wherein said first, second and third polypeptide each further comprise a cell wall binding domain.

[0059] Also preferred is a combination wherein, a first enzymatic active domain disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 10 and a second enzymatic active domain disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 16.

[0060] Also preferred is a combination wherein, a first enzymatic active domain disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 10 and a second enzymatic active domain disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 18.

[0061] Also preferred is a combination wherein, a first enzymatic active disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 16 and a second enzymatic active domain disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 18.

[0062] Also preferred is a combination wherein, a first polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 34 and a second polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 46.

[0063] Also preferred is a combination wherein, a first polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 34 and a second polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 28.

[0064] Also preferred is a combination wherein, a first polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 46 and a second polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 28.

[0065] Also preferred is a combination wherein, a first polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 58 and a second polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 70.

[0066] Also preferred is a combination wherein, a first polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 58 and a second polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 52.

[0067] More preferred is a combination wherein, a first polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 70 and a second polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 52.

[0068] Also preferred is a combination wherein, a first polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with

SEQ ID NO: 58 and a second polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 46.

[0069] Also preferred is a combination wherein, a first polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 58 and a second polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 28.

[0070] Also preferred is a combination wherein, a first polypeptide according to the present invention has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 70 and a second polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 34.

[0071] More preferred is a combination wherein, a first polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 70 and a second polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 28.

[0072] Also preferred is a combination, wherein a first polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 52 and a second polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 34.

[0073] Also preferred is a combination wherein, a first polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 52 and a second polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 46.

[0074] Also preferred is a combination wherein, a first enzymatic active domain disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 10, a second enzymatic active domain disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 16 and a third enzymatic active domain disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 18.

[0075] Also preferred is a combination wherein, a first polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 34, a second polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 46 and a third polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 28.

[0076] Also preferred is a combination wherein, a first polypeptide disclosed has at least 80,

81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 32, a second polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 44 and a third polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 26.

[0077] Also preferred is a combination wherein, a first polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 34, a second polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 46 and a third polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 26.

[0078] Also preferred is a combination wherein, a first polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 36, a second polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 48 and a third polypeptide according to the present invention has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 30.

[0079] Also preferred is a combination wherein, a first polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 32, a second polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 46 and a third polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 26.

[0080] Also preferred is a combination wherein, a first polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 34, a second polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 44 and a third polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 26.

[0081] Also preferred is a combination wherein, a first polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 32, a second polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 44 and a third polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 28.

[0082] Also preferred is a combination wherein, a first polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 32, a second polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88,

[0095] Also preferred is a combination wherein, a first polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 58, a second polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 46 and a third polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 52.

[0096] Also preferred is a combination wherein, a first polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 34, a second polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 46 and a third polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 52.

[0097] Also preferred is a combination wherein, a first polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 58, a second polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 46 and a third polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 28.

[0098] Also preferred is a combination wherein, a first polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 34, a second polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 70 and a third polypeptide disclosed has at least 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 or 100% identity with SEQ ID NO: 28.

[0099] It is to be understood that a combination as described herein encompassing the second compound disclosed includes mixtures of a source of a first, a source of a second and optionally a source of a third and/or further enzymatic active domain according to in varying ratios. Preferably, such combination comprises a source a first and a source a second enzymatic active domain disclosed, wherein said first and second enzymatic active domain are present in equimolar amounts. Also preferred is a combination comprising a source a first, a source a second and a source a third enzymatic active domain disclosed, wherein said first, second and third enzymatic active domain are present in equimolar amounts. Also preferred is a combination comprising a source of a first, a source of a second, a source of a third and a source of a further enzymatic active domain disclosed, wherein said first, second, third and further enzymatic active domain are present in equimolar amounts.

[0100] In a **second aspect**, there is disclosed a kit of parts comprising:

1. a) a first vial containing a first composition comprising a first compound as defined in the first aspect; and,

2. b) a second vial containing a second composition comprising a second compound as defined in the first aspect; and optionally,
3. c) instructions for use, preferably comprising a dosage regime.

Preferably, said kit of parts, more specifically said first and second composition of said kit of parts, is for use as a medicament, preferably for use in the treatment of eczema, more preferably for use in the treatment of atopic dermatitis, as further detailed herein. A dosage regime is to be understood herein as an instruction for administration to an individual in the need thereof, preferably an instruction indicating an administration route, administration frequency and administration dosage, and optionally an instruction for admixing said first and second compound just before administration, as required for treatment, preferably required for treatment of eczema, more preferably for treatment of atopic dermatitis. Preferred administration routes, frequencies and dosages are further detailed herein. In an embodiment, said first composition according to a second aspect and/or said second composition according to a second aspect is administered separately, preferably as part of an overall treatment regimen. In an alternative embodiment, said first composition according to a second aspect and said second composition according to a second aspect are stored separately, and admixed just before administration. Preferably, "just before" is to be understood herein as less than 120, 60, 30, 15, 5, 4, 3, 2 or 1 minutes before administration, preferably less than 5 minutes before administration.

[0101] Said first and said second vial may be any vial, bottle, tube, ampoule, container, flask or the like, suitable for storing said first and second composition as defined herein, respectively. Preferably said first and/or second vial has a volume of between 0.1 and 500 mL, preferably between 1 and 100 mL, more preferably of about 5, 10, 50 or 100mL.

[0102] In a **third aspect**, there is disclosed a method of treatment comprising the administration of a composition according to the first aspect and/or the sequential or simultaneous administration of a first and second compound of a kit of parts according to the second aspect.

[0103] Preferably, said method of treatment is a method for preventing, delaying and/or curing an infectious disease, such as, but not limited to, a skin infection, mastitis, pneumonia, meningitis, endocarditis, Toxic Shock Syndrome (TSS), sepsis, septicemia, bacteremia, or osteomyelitis. Preferably, said skin infection is selected from the group of acne, rosacea, pimples, impetigo, boils, furuncles, cellulitis folliculitis, psoriasis, carbuncles, scaled skin syndrome and abscesses. Preferably, said method of treatment is a method for preventing, delaying and/or curing eczema such as atopic dermatitis, allergic contact eczema, contact eczema, dyshidrotic eczema, neurodermatitis, nummular eczema, seborrheic eczema, stasis dermatitis, preferably atopic dermatitis. Preferably, said method of treatment is topical treatment of a skin infection and/or eczema as identified herein, more preferably atopic dermatitis.

[0104] Encompassed is a composition according to the first aspect and/or a kit of parts

according to second aspect, for use as a medicament. Preferably, said composition according to the first aspect and/or said kit of parts according to second aspect is for preventing, delaying and/or curing an infectious disease, such as, but not limited to, a skin infection, mastitis, pneumonia, meningitis, endocarditis, Toxic Shock Syndrome (TSS), sepsis, septicemia, bacteremia, or osteomyelitis. Preferably, said skin infection is selected from the group of acne, rosacea, pimples, impetigo, boils, furuncles, cellulitis, folliculitis, psoriasis, carbuncles, scaled skin syndrome and abscesses. Preferably, said composition according to the first aspect and/or said kit of parts according to the second aspect is for use preventing, delaying and/or curing of eczema such as atopic dermatitis, allergic contact eczema, contact eczema, dyshidrotic eczema, neurodermatitis, nummular eczema, seborrheic eczema, stasis dermatitis, preferably atopic dermatitis.

[0105] Also encompassed is the use of a composition according to the first aspect and/or a kit of parts according to second aspect for the manufacture of a medicament. Preferably, said medicament is for preventing, delaying and/or curing an infectious disease, such as, but not limited to, a skin infection, mastitis, pneumonia, meningitis, endocarditis, Toxic Shock Syndrome (TSS), sepsis, septicemia, bacteremia, or osteomyelitis. Preferably, said skin infection is selected from the group of acne, rosacea, pimples, impetigo, boils, furuncles, cellulitis, folliculitis, psoriasis, carbuncles, scaled skin syndrome and abscesses. Preferably, said medicament is a medicament for preventing, delaying and/or curing eczema such as atopic dermatitis, allergic contact eczema, contact eczema, dyshidrotic eczema, neurodermatitis, nummular eczema, seborrheic eczema, stasis dermatitis, preferably atopic dermatitis.

[0106] Preferably, said composition according to the first aspect, a first composition of a kit of parts according to the second aspect and/or a second composition of a kit of parts according to the second aspect and/or medicament as defined herein is a topical formulation understood herein as a formulation, including a microencapsulated formulation, being suitable for topical administration and may be in the form of a cream, ointment, solution, powder, spray, aerosol, capsule, solid or gel, and/or may be bonded to a solid surface, e.g. by immobilization with affinity ligands or through ionic/hydrophobic interactions and covalent immobilization.

[0107] A composition according to the first aspect and/or a first and/or second composition of a kit of parts according to the second aspect may also form part of a body wash, soap, application stick or cosmetic.

[0108] A composition according to the first aspect and/or a second composition of a kit of parts according to the second aspect and/or a mixture resulting from admixing said first and second composition of a kit of parts according to the second aspect just before administration as earlier indicated herein, is preferably said to be active, functional or therapeutically active when it decreases the amount of bacterial cells, preferably gram positive bacterial cells, more preferably the amount of *Staphylococcus* bacterial cells, most preferably the amount of *Staphylococcus aureus* bacterial cells, present in a patient or in a cell of said patient or in a cell line or in a cell free *in vitro* system and preferably means that 99%, 90%, 80%, 70%, 60%,

50%, 40%, 30%, 20%, 10%, 5% or less of the initial amount of said bacterial cells is still detectable. More preferably, no bacterial cell, preferably no gram positive bacterial cell, more preferably no *Staphylococcus* bacterial cell, most preferably no *Staphylococcus aureus* bacterial cell, is detectable. In this paragraph, the expression "amount of bacterial cells" preferably means viable bacterial cells. Staphylococci of all genera may be detected using standard techniques known by the artisan such as immunohistochemical techniques using *Staphylococcus* specific antibodies, tube coagulase tests that detect staphylocoagulase or "free coagulase", detection of surface proteins such as clumping factor (slide coagulase test) and/or protein A (commercial latex tests). Viable Staphylococci may be detected using standard techniques known by the artisan such as microbiological bacterial culture techniques and/or real-time quantitative reverse transcription polymerase chain reaction to assay for bacterial mRNA. A decrease in amount of bacterial cells is preferably assessed in a tissue or in a cell of an individual or a patient by comparison to the amount present in said individual or patient before treatment with said composition or polypeptide disclosed. Alternatively, the comparison can be made with a tissue or cell of said individual or patient which has not yet been treated with said composition or polypeptide in case the treatment is local.

[0109] Preferably a composition according to the first aspect and/or a second composition of a kit of parts of the second aspect, and/or a resulting mixture resulting from admixing the first and second composition of the kit of part of the second aspect of the invention just before administration as identified herein before comprises an amount of a second compound as defined herein which is therapeutically active as earlier identified herein. Preferably, said composition is for topic administration to an individual in the need thereof, preferably to a patient suffering from eczema, and comprises said second compound in an effective amount, preferably a concentration of 0.001 - 10% by weight of the total composition. Depending on the specific activity of the second compound, the effective amount may be as low about a few micrograms/ml such as about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 microgram/ml to about several milligrams/ml such as about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 milligram/ml

[0110] Preferably a composition according to the first aspect and/or a first composition of a kit of parts of the second aspect, and/or a resulting mixture resulting from admixing the first and second composition of the kit of part of the second aspect just before administration as identified herein before is a composition for topic application for the treatment of eczema comprising an anti-inflammatory compound, selected from, but not limited to, a corticosteroid a calcineurin inhibitor, an immunotherapeutic compound, a recombinant human IFN-gamma, a microbial probiotic, a cytokine modulator, an inflammatory cell recruitment blocker, a T cell activation inhibitor, or a combination of these. Preferably, said composition is for topic administration to an individual in the need thereof, preferably to a patient suffering from eczema, and comprises said anti-inflammatory compound compound in an effective amount, preferably in the range of 0.01 to 10% by weight of the total composition, preferably in the range of 0.05 to 5%, more preferably in a range of 0.05 to 2.5%, even more preferably in a range of 0.1 to 1%.

[0111] Preferably a composition according to the first aspect and/or a first composition of a kit

of parts of the second aspect, and/or a resulting mixture resulting from admixing the first and second composition of the kit of part of the second aspect just before administration as identified herein before is a composition for topic application for the treatment of eczema comprising a corticosteroid in the range of 0.05 to 5%, by weight of the total composition preferably in a range of 0.05 to 2.5% more preferably in a range of 0.1 to 1%, even more preferably comprising about 0.05% clobetasol propionate, about 0.05% halobetasol propionate, about 0.1% fluocinonide, about 0.05% diflorasone diacetate, about 0.1% mometasone furoate, about 0.1% halcinonide, about 0.25% desoximetasone, about 0.05% fluocinonide, about 0.05% desoximetasone, about 0.1% clocortolone pivalate, about 0.1% mometasone furoate, about 0.1% triamcinolone acetonide, about 0.1% betamethasone valerate, about 0.025% fluocinolone acetonide, about 0.05% fluticasone propionate, about 0.1% prednicarbate, about 0.1% hydrocortisone probutate, about 0.1% triamcinolone acetonide, about 0.05% alclometasone dipropionate, about 0.05% desonide, about 0.025% triamcinolone acetonide, about 0.1% hydrocortisone butyrate, about 0.01% fluocinolone acetonide, about 1% hydrocortisone acetate, about 2% hydrocortisone, about 2.5% hydrocortisone and/or 0.5-1% hydrocortisone. About is defined herein as a value minus or plus 10% of the indicated value.

[0112] A composition according to the first aspect, a first composition of a kit of parts according to the second aspect and/or a second composition of a kit of parts according to the second aspect and/or medicament as defined herein may be in the liquid, solid or semi-liquid or semi-solid form, preferably further comprising a pharmaceutical acceptable carrier, excipient and/or stabilizer. Examples of pharmaceutically acceptable carriers, excipients and stabilizers include, but are not limited to, buffers such as phosphate, citrate, and other organic acids; antioxidants including ascorbic acid; low molecular weight polypeptides; proteins, such as serum albumin and gelatin; hydrophilic polymers such as polyvinylpyrrolidone; amino acids such as glycine, glutamine, asparagine, arginine or lysine; monosaccharides, disaccharides, and other carbohydrates including glucose mannose, or dextrans; chelating agents such as EDTA; sugar alcohols such as mannitol or sorbitol; salt-forming counterions such as sodium; and/or nonionic surfactants such as polysorbate (TWEEN™), polyethylene glycol (PEG), and poloxamers (PLURONICS™); and polymer thickeners such as hydrophilic and hydroalcoholic gelling agents frequently used in the cosmetic and pharmaceutical industries, preferably a gelling agent comprises between about 0.2% and about 4% by weight composition. A composition according to the first aspect, a first composition of a kit of parts according to the second aspect and/or a second composition of a kit of parts according to the second aspect and/or medicament as defined herein can also include a lubricant, a wetting agent, a sweetener, a flavoring agent, an emulsifier, a suspending agent, a sun screen such as, but not limited to, titanium dioxide or methyl cinnamate, and/or a preservative, in addition to the above ingredients, preferably a preservative is present as about 0.05% to 0.5% by weight of the total composition. A composition according to the first aspect, a first composition of a kit of parts according to the second aspect and/or a second composition of a kit of parts according to the second aspect and/or medicament as defined herein can also include a carrier which are known in the art (such as a carbohydrate and a sugar-alcohol) to aid in the exposure of the skin to a medicament.

[0113] Preferably, a composition according to the first aspect, a first composition of a kit of parts according to the second aspect and/or a second composition of a kit of parts according to the second aspect and/or a medicament as defined herein further comprises and additional active ingredient. An additional active ingredient may be any of, but is not limited to, an anti-inflammatory agent; a standard or conventional antibiotic agent such as, but not limited to penicillin, synthetic penicillins, bacitracin, methicillin, cephalosporin, polymyxin, cefaclor, Cefadroxil, cefamandole nafate, cefazolin, cefixime, cefmetazole, cefonid, cefoperazone, ceforanide, cefotanme, cefotaxime, cefotetan, cefoxitin, cefpodoxime proxetil, ceftazidime, ceftizoxime, ceftriaxone, cefriaxone moxalactam, cefuroxime, cephalixin, cephalosporin C, cephalosporin C sodium salt, cephalothin, cephalothin sodium salt, cephapirin, cephradine, cefuroximeaxetil, dihydratecephalothin, moxalactam, loracarbef mafate and/or chelating agents; an antifungal, such as, but not limited to, oxiconazole nitrate, ciclopirox olamine, ketoconazole, miconazole nitrate and butoconazole nitrate; an anti-androgen, such as, but not limited to, flutamide and/or finasterid; a local anesthetic agent, such as, but not limited to tetracaine, tetracaine hydrochloride, lidocaine, lidocaine hydrochloride, dyclonine, dyclonine hydrochloride, dimethisoquin hydrochloride, dibucaine, dibucaine hydrochloride, butambenpicrate and/or pramoxine hydrochloride; and dapsone which has both antimicrobial and anti-inflammatory properties. Preferred weight percentages of antimicrobial agents are 0.1% to 10% weight of the total composition. Preferred weight percentages for local anesthetics are 0.025% to 5% by weight of the total composition.

[0114] A composition according to the first aspect, a first composition according to a second aspect and/or a second composition according to a second aspect and/or medicament as defined herein can be used to treat animals, including humans, suffering from any of the an infectious diseases and/or eczema as identified herein above, preferably from atopic dermatitis.

[0115] A preferred route of administration of said composition and/or said medicament is any suitable route of administration that can be used to administer said composition according to the first aspect, said first composition according to a second aspect and/or said second composition according to a second aspect and/or medicament as defined herein including but not limited to: oral, aerosol or other device for delivery to the lungs, nasal spray, intravenous, intramuscular, intraperitoneal, intrathecal, vaginal, rectal, topical, lumbar puncture, intrathecal, and direct application to the brain and/or meninges. Preferably, said composition according to the first aspect, said first composition according to a second aspect and/or said second composition according to a second aspect and/or medicament as defined herein are administered topical, preferably at the side of infection and/or lesion and/or, in the case of eczema, preferably at the side of skin rash.

[0116] A preferred administration frequency of said composition and/or said medicament is once or twice a day, preferably to the area of the skin affected by the disease or the side of lesion known in the art as the side of rash. Preferably said treatment is continued as long as required for the rash to be cleared. Preferably said treatment is continued for 2 to 3 days, for 7

to 10 days and/or for 2 to 3 weeks. Preferably a total amount of composition for topic application is administered as identified herein resulting in a total application of about 1 gram of corticosteroid to the person in the need thereof.

[0117] A preferred dosage of administration of said composition and/or said medicament is a dosage containing an effective total amount of said first and second compound resulting in the prevention, delay and/or cure of an infectious disease and/or eczema as earlier identified herein, preferably eczema, more preferably atopic dermatitis.

Definitions

[0118] "Sequence identity" or "identity" in the context of amino acid- or nucleic acid-sequence is herein defined as a relationship between two or more amino acid (peptide, polypeptide, or protein) sequences or two or more nucleic acid (nucleotide, polynucleotide) sequences, as determined by comparing the sequences. In the art, "identity" also means the degree of sequence relatedness between amino acid or nucleotide sequences, as the case may be, as determined by the match between strings of such sequences. Herein, sequence identity with a particular sequence preferably means sequence identity over the entire length of said particular polypeptide or polynucleotide sequence. The sequence information as provided herein should not be so narrowly construed as to require inclusion of erroneously identified bases. The skilled person is capable of identifying such erroneously identified bases and knows how to correct for such errors.

"Similarity" between two amino acid sequences is determined by comparing the amino acid sequence and its conserved amino acid substitutes of one peptide or polypeptide to the sequence of a second peptide or polypeptide. In a preferred embodiment, identity or similarity is calculated over the whole SEQ ID NO as identified herein. "Identity" and "similarity" can be readily calculated by known methods, including but not limited to those described in Computational Molecular Biology, Lesk, A. M., ed., Oxford University Press, New York, 1988; Biocomputing: Informatics and Genome Projects, Smith, D. W., ed., Academic Press, New York, 1993; Computer Analysis of Sequence Data, Part I, Griffin, A. M., and Griffin, H. G., eds., Humana Press, New Jersey, 1994; Sequence Analysis in Molecular Biology, von Heine, G., Academic Press, 1987; and Sequence Analysis Primer, Gribskov, M. and Devereux, J., eds., M Stockton Press, New York, 1991; and Carillo, H., and Lipman, D., SIAM J. Applied Math., 48:1073 (1988).

[0119] Preferred methods to determine identity are designed to give the largest match between the sequences tested. Methods to determine identity and similarity are codified in publicly available computer programs. Preferred computer program methods to determine identity and similarity between two sequences include e.g. the GCG program package (Devereux, J., et al., Nucleic Acids Research 12 (1): 387 (1984)), BestFit, BLASTP, BLASTN, and FASTA (Altschul, S. F. et al., J. Mol. Biol. 215:403-410 (1990)). The BLAST X program is publicly available from NCBI and other sources (BLAST Manual, Altschul, S., et al., NCBI NLM NIH Bethesda, MD 20894; Altschul, S., et al., J. Mol. Biol. 215:403-410 (1990)). The well-known

Smith Waterman algorithm may also be used to determine identity.

[0120] Preferred parameters for polypeptide sequence comparison include the following: Algorithm: Needleman and Wunsch, J. Mol. Biol. 48:443-453 (1970); Comparison matrix: BLOSSUM62 from Hentikoff and Hentikoff, Proc. Natl. Acad. Sci. USA. 89:10915-10919 (1992); Gap Penalty: 12; and Gap Length Penalty: 4. A program useful with these parameters is publicly available as the "Ogap" program from Genetics Computer Group, located in Madison, WI. The aforementioned parameters are the default parameters for amino acid comparisons (along with no penalty for end gaps).

[0121] Preferred parameters for nucleic acid comparison include the following: Algorithm: Needleman and Wunsch, J. Mol. Biol. 48:443-453 (1970); Comparison matrix: matches=+10, mismatch=0; Gap Penalty: 50; Gap Length Penalty: 3. Available as the Gap program from Genetics Computer Group, located in Madison, Wis. Given above are the default parameters for nucleic acid comparisons.

[0122] Optionally, in determining the degree of amino acid similarity, the skilled person may also take into account so-called "conservative" amino acid substitutions, as will be clear to the skilled person. Conservative amino acid substitutions refer to the interchangeability of residues having similar side chains. For example, a group of amino acids having aliphatic side chains is glycine, alanine, valine, leucine, and isoleucine; a group of amino acids having aliphatic-hydroxyl side chains is serine and threonine; a group of amino acids having amide-containing side chains is asparagine and glutamine; a group of amino acids having aromatic side chains is phenylalanine, tyrosine, and tryptophan; a group of amino acids having basic side chains is lysine, arginine, and histidine; and a group of amino acids having sulphur-containing side chains is cysteine and methionine. Preferred conservative amino acids substitution groups are: valine-leucine-isoleucine, phenylalanine-tyrosine, lysine-arginine, alanine-valine, and asparagine-glutamine. Substitutional variants of the amino acid sequence disclosed herein are those in which at least one residue in the disclosed sequences has been removed and a different residue inserted in its place. Preferably, the amino acid change is conservative. Preferred conservative substitutions for each of the naturally occurring amino acids are as follows: Ala to ser; Arg to lys; Asn to gln or his; Asp to glu; Cys to ser or ala; Gln to asn; Glu to asp; Gly to pro; His to asn or gln; Ile to leu or val; Leu to ile or val; Lys to arg; gln or glu; Met to leu or ile; Phe to met, leu or tyr; Ser to thr; Thr to ser; Trp to tyr; Tyr to trp or phe; and, Val to ile or leu.

[0123] A polynucleotide is represented by a nucleotide sequence. A polypeptide is represented by an amino acid sequence. A nucleic acid construct is defined as a polynucleotide which is isolated from a naturally occurring gene or which has been modified to contain segments of polynucleotides which are combined or juxtaposed in a manner which would not otherwise exist in nature. Optionally, a polynucleotide present in a nucleic acid construct is operably linked to one or more control sequences, which direct the production or expression of said peptide or polypeptide in a cell or in a subject.

[0124] As used herein the term "heterologous sequence" or "heterologous nucleic acid" is one that is not naturally found operably linked as neighboring sequence of said first nucleotide sequence. As used herein, the term "heterologous" may mean "recombinant". "Recombinant" refers to a genetic entity distinct from that generally found in nature. As applied to a nucleotide sequence or nucleic acid molecule, this means that said nucleotide sequence or nucleic acid molecule is the product of various combinations of cloning, restriction and/or ligation steps, and other procedures that result in the production of a construct that is distinct from a sequence or molecule found in nature.

[0125] "Operably linked" is defined herein as a configuration in which a control sequence is appropriately placed at a position relative to the nucleotide sequence coding for the polypeptide disclosed herein such that the control sequence directs the production/expression of the peptide or polypeptide disclosed herein in a cell and/or in a subject.

[0126] "Operably linked" may also be used for defining a configuration in which a sequence is appropriately placed at a position relative to another sequence coding for a functional domain such that a chimeric polypeptide is encoded in a cell and/or in a subject.

Expression will be understood to include any step involved in the production of the peptide or polypeptide including, but not limited to, transcription, post-transcriptional modification, translation, post-translational modification and secretion.

Optionally, a promoter represented by a nucleotide sequence present in a nucleic acid construct is operably linked to another nucleotide sequence encoding a peptide or polypeptide as identified herein.

[0127] The term "transformation" refers to a permanent or transient genetic change induced in a cell following the incorporation of new DNA (*i.e.* DNA exogenous to the cell). When the cell is a bacterial cell, as is intended herein, the term usually refers to an extrachromosomal, self-replicating vector which harbors a selectable antibiotic resistance.

[0128] An expression vector may be any vector which can be conveniently subjected to recombinant DNA procedures and can bring about the expression of a nucleotide sequence encoding a disclosed polypeptide in a cell and/or in a subject. As used herein, the term "promoter" refers to a nucleic acid fragment that functions to control the transcription of one or more genes or nucleic acids, located upstream with respect to the direction of transcription of the transcription initiation site of the gene. It is related to the binding site identified by the presence of a binding site for DNA-dependent RNA polymerase, transcription initiation sites, and any other DNA sequences, including, but not limited to, transcription factor binding sites, repressor and activator protein binding sites, and any other sequences of nucleotides known to one skilled in the art to act directly or indirectly to regulate the amount of transcription from the promoter. Herein, a promoter preferably ends at nucleotide -1 of the transcription start site (TSS).

[0129] "Polypeptide" as used herein refers to any peptide, oligopeptide, polypeptide, gene product, expression product, or protein. A polypeptide is comprised of consecutive amino

acids. The term "polypeptide" encompasses naturally occurring or synthetic molecules.

[0130] The term "control sequences" is defined herein to include all components, which are necessary or advantageous for the expression of a polypeptide. Each control sequence may be native or foreign to the nucleic acid sequence encoding the polypeptide. Such control sequences include, but are not limited to, a leader, optimal translation initiation sequences (as described in Kozak, 1991, J. Biol. Chem. 266:19867-19870), a polyadenylation sequence, a pro-peptide sequence, a pre-pro-peptide sequence, a promoter, a signal sequence, and a transcription terminator. At a minimum, the control sequences include a promoter, and transcriptional and translational stop signals.

[0131] The control sequences may be provided with linkers for the purpose of introducing specific restriction sites facilitating ligation of the control sequences with the coding region of the nucleic acid sequence encoding a polypeptide.

[0132] The control sequence may be an appropriate promoter sequence, a nucleic acid sequence, which is recognized by a host cell for expression of the nucleic acid sequence. The promoter sequence contains transcriptional control sequences, which mediate the expression of the polypeptide. The promoter may be any nucleic acid sequence, which shows transcriptional activity in the cell including mutant, truncated, and hybrid promoters, and may be obtained from genes encoding extracellular or intracellular polypeptides either homologous or heterologous to the cell.

[0133] The control sequence may also be a suitable transcription terminator sequence, a sequence recognized by a host cell to terminate transcription. The terminator sequence is operably linked to the 3' terminus of the nucleic acid sequence encoding the polypeptide. Any terminator, which is functional in the cell, may be used herein.

[0134] The control sequence may also be a suitable leader sequence, a non-translated region of a mRNA which is important for translation by the host cell. The leader sequence is operably linked to the 5' terminus of the nucleic acid sequence encoding the polypeptide. Any leader sequence, which is functional in the cell, may be used herein.

[0135] The control sequence may also be a polyadenylation sequence, a sequence which is operably linked to the 3' terminus of the nucleic acid sequence and which, when transcribed, is recognized by the host cell as a signal to add polyadenosine residues to transcribed mRNA. Any polyadenylation sequence, which is functional in the cell, may be used herein.

[0136] In this document and in its claims, the verb "to comprise" and its conjugations is used in its non-limiting sense to mean that items following the word are included, but items not specifically mentioned are not excluded. In addition the verb "to consist" may be replaced by "to consist essentially of" meaning that a product or a composition or a nucleic acid molecule or a peptide or polypeptide of a nucleic acid construct or vector or cell as defined herein may comprise additional component(s) than the ones specifically identified; said additional

component(s) not altering the unique characteristic. In addition, reference to an element by the indefinite article "a" or "an" does not exclude the possibility that more than one of the elements is present, unless the context clearly requires that there be one and only one of the elements. The indefinite article "a" or "an" thus usually means "at least one".

[0137] The following examples are offered for illustrative purposes only, and are not intended to limit the scope of the invention in any way.

Examples

Use of corticosteroids and a compound specifically targeting *S. aureus* (Staphefekt™)

[0138] In several forms of dermatitis, courses of topical corticosteroid therapy are used to suppress symptoms of local inflammation. However, corticosteroids do not treat the underlying cause of the inflammation, and symptoms are known to return eventually. It was hypothesized that a second compound would be effective in combination with corticosteroid treatment. As a second compound specifically targeting *S. aureus* was used. The compound Staphefekt™ (Gladskin™) was obtained from Microcos Human Health B.V., The Netherlands. Since Staphefekt™ eradicates *S. aureus* as an etiological factor of local inflammation, it was speculated that during Staphefekt™ treatment less corticosteroids would be needed to alleviate symptoms.

[0139] To study the use of corticosteroid during Staphefekt™ treatment, corticosteroid use and symptom relief was monitored in eight patients, of whom the treatment of several kinds of dermatitis with Staphefekt™ was guided and observed by a physician (table 1). In the six cases where *S. aureus* was found, symptoms diminished during treatment with Staphefekt™, and patients reported less need of corticosteroids anamnestically. In one patient with severe constitutional eczema, the burden of *S. aureus* carriage was high and symptoms diminished only moderately with Staphefekt™, necessitating the unchanged use of corticosteroids and eventually even immune suppression with Neoral. In one case where no *S. aureus* was found, Staphefekt™ had no effect on symptoms and corticosteroid use remained unchanged.

[0140] The use of corticosteroids was not completely abandoned in the successfully treated patients, especially with the recurrence of symptoms after ceasing Staphefekt™ use. This suggests that a quick relief of symptoms at the stage of local inflammation is best achieved by combining symptomatic corticosteroid therapy with eradication of etiological *S. aureus* carriage by Staphefekt™.

[0141] The reduced need for corticosteroids as observed in customer feedback, questionnaires and the present physician guided Staphefekt™ study clearly indicates that a lower dose or shorter course of corticosteroids would be effective in combination therapy with a

second compound, *in casu* Staphefekt™.

Table 1. Physician guided Staphefekt™ cases.

gender (age)	treatment indication	site	<i>S. aureus</i> carriage	relief of symptoms	corticosteroid use during treatment
male (22)	eczema	neck/face	+++	moderate	unchanged corticosteroid use, Neoral because of relapse
male (32)	eczema	face	-	yes	less need
female (16)	eczema	arm, knee	+	yes	no need
female (19)	peri-oral dermatitis	peri-oral	+	yes	less need until relapse
female (16)	eczema	arm	-	no	unchanged
male (28)	contact dermatitis	hands	+++	yes	less need
male (57)	contact dermatitis	hands	+	yes	no need
female (30)	eczema	arm	+	yes	less need

Table 2: SEQ ID NO overview table

SEQ ID NO	Name construct	organism
1	Ply2638 endolysin CDS	Bacteriophage 2638A
2	Ply2638 endolysin PRT	Bacteriophage 2638A
3	CWT-LST CDS	<i>S. simulans</i>
4	CWT-LST PRT	<i>S. simulans</i>
5	CBD2638 CDS	Bacteriophage 2638A
6	CBD2638 PRT	Bacteriophage 2638A
7	CWT-NM3 CDS	<i>S. aureus</i> phage phiNM3
8	CWT-NM3 PRT	<i>S. aureus</i> phage phiNM3
9	CHAPK CDS	<i>S.</i> phage K
10	CHAPK PRT	<i>S.</i> phage K
11	CHAP- ϕ Twort CDS	<i>S.</i> phage Twort
12	CHAP- ϕ Twort PRT	<i>S.</i> phage Twort
13	M23-2638 CDS	Bacteriophage 2638A
14	M23-2638 PRT	Bacteriophage 2638A

SEQ ID NO	Name construct	organism
15	M23-LST CDS	<i>S. simulans</i>
16	M23-LST PRT	<i>S. simulans</i>
17	Ami2638 CDS	Bacteriophage 2638A
18	Ami2638 PRT	Bacteriophage 2638A
19	CHAPK_CHAPK_CWT-LST CDS	artificial construct
20	CHAPK_CHAPK_CWT-LST PRT	artificial construct
21	M23-LST_M23-LST_CWT-LST CDS	artificial construct
22	M23-LST_M23-LST_CWT-LST PRT	artificial construct
23	Ami2638_ami2638_CWT-LST CDS	artificial construct
24	Ami2638_ami2638_CWT-LST PRT	artificial construct
25	HXaAmi2638_CBD2638 CDS	artificial construct
26	HXaAmi2638_CBD2638 PRT	artificial construct
27	HXaAmi2638_CWT-LST CDS	artificial construct
28	HXaAmi2638_CWT-LST PRT	artificial construct
29	HXaAmi2638_CWT-NM3 CDS	artificial construct
30	HXaAmi2638_CWT-NM3 PRT	artificial construct
31	HXaCHAPK_CBD2638 CDS	artificial construct
32	HXaCHAPK_CBD2638 PRT	artificial construct
33	HXaCHAPK_CWT-LST CDS	artificial construct
34	HXaCHAPK_CWT-LST PRT	artificial construct
35	HXaCHAPK_CWT-NM3 CDS	artificial construct
36	HXaCHAPK_CWT-NM3 PRT	artificial construct
37	HXaCHAPT _w _CBD2638 CDS	artificial construct
38	HXaCHAPT _w _CBD2638 PRT	artificial construct
39	HXaCHAPT _w _CWT-LST CDS	artificial construct
40	HXaCHAPT _w _CWT-LST PRT	artificial construct
41	HXaCHAPT _w _CWT-NM3 CDS	artificial construct
42	HXaCHAPT _w _CWT-NM3 PRT	artificial construct
43	HXaM23-LST_CBD2638 CDS	artificial construct
44	HXaM23-LST_CBD2638 PRT	artificial construct
45	HXaM23-LST_CWT-LST CDS	artificial construct
46	HXaM23-LST_CWT-LST PRT	artificial construct
47	HXaM23-LST_CWT-NM3 CDS	artificial construct
48	HXaM23-LST_CWT-NM3 PRT	artificial construct
49	HXaAmi2638_Ami2638_CBD2638 CDS	artificial construct

SEQ ID NO	Name construct	organism
50	HXaAmi2638_Ami2638_CBD2638 PRT	artificial construct
51	HXaAmi2638_Ami2638_CWT-LST CDS	artificial construct
52	HXaAmi2638_Ami2638_CWT-LST PRT	artificial construct
53	HXaAmi2638_Ami2638_CWT-NM3 CDS	artificial construct
54	HXaAmi2638_Ami2638_CWT-NM3 PRT	artificial construct
55	HXaCHAPK_CHAPK_CBD2638 CDS	artificial construct
56	HXaCHAPK_CHAPK_CBD2638 PRT	artificial construct
57	HXaCHAPK_CHAPK_CWT-LST CDS	artificial construct
58	HXaCHAPK_CHAPK_CWT-LST PRT	artificial construct
59	HXaCHAPK_CHAPK_CWT-NM3 CDS	artificial construct
60	HXaCHAPK_CHAPK_CWT-NM3 PRT	artificial construct
61	HXaCHAPTw_CHAPTw_CBD2638 CDS	artificial construct
62	HXaCHAPTw_CHAPTw_CBD2638 PRT	artificial construct
63	HXaCHAPTw_CHAPTw_CWT-LST CDS	artificial construct
64	HXaCHAPTw_CHAPTw_CWT-LST PRT	artificial construct
65	HXaCHAPTw_CHAPTw_CWT-NM3 CDS	artificial construct
66	HXaCHAPTw_CHAPTw_CWT-NM3 PRT	artificial construct
67	HXaM23-LST_M23-LST_CBD2638 CDS	artificial construct
68	HXaM23-LST_M23-LST_CBD2638 PRT	artificial construct
69	HXaM23-LST_M23-LST_CWT-LST CDS	artificial construct
70	HXaM23-LST_M23-LST_CWT-LST PRT	artificial construct
71	HXaM23-LST_M23-LST_CWT-NM3 CDS	artificial construct
72	HXaM23-LST_M23-LST_CWT-NM3 PRT	artificial construct
73	His-tag with linker CDS	artificial construct
74	His-tag with linker PRT	artificial construct
75	LST CDS	<i>S. simulans</i>
76	LST PRT	<i>S. simulans</i>
77	HXaCHAP1 1_M23-2638_Ami2638_CBD2638 CDS	artificial construct
78	HXaCHAP1 1_M23-2638_Ami2638_CBD2638 PRT	artificial construct
79	HXaAmil 1_M23-2638_Ami2638_CBD2638 CDS	artificial construct
80	HXaAmi1 1_M23-2638_Ami2638_CBD2638 PRT	artificial construct
81	HXaCHAPTw_Ami2638_M23-LST_CBD2638	artificial construct

SEQ ID NO	Name construct	organism
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82	HXaCHAPTw_Ami2638_M23-LST_CBD2638 PRT	artificial construct
83	HXaM23-LST_Ami2638_CBD2638 CDS	artificial construct
84	HXaM23-LST_Ami2638_CBD2638 PRT	artificial construct
85	HXaM23-2638_Ami2638_CBD2638_CBD2638 CDS	artificial construct
86	HXaM23-2638_Ami2638_CBD2638_CBD2638 PRT	artificial construct
87	HXaM23-2638_CBD2638 CDS	artificial construct
88	HXaM23-2638_CBD2638 PRT	artificial construct
89	HXaPly2638-Ply2638 CDS	artificial construct
90	HXaPly2638-Ply2638 PRT	artificial construct
91	HXaCHAPTw_Ami2638_M23-LST_CWT-LST CDS	artificial construct
92	HXaCHAPTw_Ami2638_M23-LST_CWT-LST PRT	artificial construct
93	HXaLST_LST CDS	artificial construct
94	HXaLST_LST PRT	artificial construct
95	HXaGFP_CBD2638 CDS	artificial construct
96	HXaGFP_CBD2638 PRT	artificial construct
97	CHAPΦ11 CDS	S. aureus phage phi 11
98	CHAPΦ11 PRT	S. aureus phage phi 11
99	AmiΦ11 CDS	S. aureus phage phi 11
100	AmiΦ11 PRT	S. aureus phage phi 11

SEQUENCE LISTING

[0142]

<110> Microcos Human Health B.V.

<120> Combination treatment for atopic dermatitis

<130> P6045048PCT

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<170> PatentIn version 3.3

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Gln Gly Asp Ile Ile Gly Leu Gln Gly Asn Ser Asn Tyr Tyr Asp Asn
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Pro Met Ser Val His Leu His Leu Gln Leu Arg Pro Lys Asp Ala Lys
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Tyr Gly Ser Met Thr Pro Ser Gln Tyr Leu Pro Trp Leu Tyr Ala Arg
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Cys Gly Asn Gln Trp Ala Asn Ala Asn Leu Ile Gly Phe Glu Val Cys
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20 25 30

Ser Met Pro Gln Ser Gly Val Leu Lys Ala Gly Gln Thr Ile His Tyr
35 40 45

Asp Glu Val Met Lys Gln Asp Gly His Val Trp Val Gly Tyr Thr Gly
50 55 60

Asn Ser Gly Gln Arg Ile Tyr Leu Pro Val Arg Thr Trp Asn Lys Ser
65 70 75 80

Thr Asn Thr Leu Gly Val Leu Trp Gly Thr Ile Lys
85 90

<210> 5
<211> 285
<212> DNA
<213> Staphylococcus bacteriophage 2638A

<400> 5
tggaaacaga ataaagatgg catttggtat aaagctgaac atgcttcggt cacagtgaca 60
gcaccagagg gaattatcac aagatacaaa ggtccttgga ctggtcaccc acaagctggt 120
gtattacaaa aagggtcaaac gattaaatat gatgaggttc aaaaatttga cgggtcatgtt 180
tgggtatcgt gggaaacggt tgagggcgaa actgtataca tgccggtacg cacatgggac 240
gctaaaactg gtaaagttgg taagttgtgg ggcgaaatta aataa 285

<210> 6
<211> 94
<212> PRT
<213> Staphylococcus bacteriophage 2638A

<400> 6
Trp Lys Gln Asn Lys Asp Gly Ile Trp Tyr Lys Ala Glu His Ala Ser
1 5 10 15

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

Trp Thr Gly His Pro Gln Ala Gly Val Leu Gln Lys Gly Gln Thr Ile
35 40 45

Trp Thr Asn Gln Val Gln Thr Phe Asn Gln Val Thr Val Gln Thr

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

Glu Thr Phe Glu Gly Glu Thr Val Tyr Met Pro Val Arg Thr Trp Asp
65 70 75 80

Ala Lys Thr Gly Lys Val Gly Lys Leu Trp Gly Glu Ile Lys
85 90

<210> 7
<211> 282
<212> DNA
<213> Staphylococcus bacteriophage phiNM3

<400> 7
ggtaaactctg caagtaaaat aacagttgga agtaaagcgc cttataacct taaatgggtca 60
aaaggtgctt attttaatgc gaaaatcgac ggcttaggtg ctacttcagc cactagatac 120
ggtgataatc gtactaacta tagattcgat gttggacagg ctgtatacgc gcctggaaca 180
ttaatatatg tgtttgaaat tatagatggt tgggtgtcgca tttattggaa caatcataat 240
gagtggatat ggcattgagag attgattgtg aaagaagtgt tt 282

<210> 8
<211> 94
<212> PRT
<213> Staphylococcus bacteriophage phiNM3

<400> 8
Gly Lys Ser Ala Ser Lys Ile Thr Val Gly Ser Lys Ala Pro Tyr Asn
1 5 10 15

Leu Lys Trp Ser Lys Gly Ala Tyr Phe Asn Ala Lys Ile Asp Gly Leu
20 25 30

Gly Ala Thr Ser Ala Thr Arg Tyr Gly Asp Asn Arg Thr Asn Tyr Arg
35 40 45

Phe Asp Val Gly Gln Ala Val Tyr Ala Pro Gly Thr Leu Ile Tyr Val
50 55 60

Phe Glu Ile Ile Asp Gly Trp Cys Arg Ile Tyr Trp Asn Asn His Asn
65 70 75 80

Glu Trp Ile Trp His Glu Arg Leu Ile Val Lys Glu Val Phe
85 90

<210> 9
<211> 585
<212> DNA
<213> Staphylococcus bacteriophage K

<400> 9
atggctaaga ctcaagcaga aataaataaa cgtttagatg cttatgcaaa aggaacagta 60

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gatagccctt acagagttaa aaaagctaca agttatgacc catcatttgg tgtaatggaa 120
gcaggagcca ttgatgcaga tggttactat cacgctcagt gtcaagacct tattacagac 180
tatgttttat ggttaacaga taataaagtt agaacttggg gtaatgctaa agaccaaatt 240
aaacagagtt atggtactgg atttaaaata catgaaaata aaccttctac tgtacctaaa 300
aaaggttgga ttgcggtatt tacatccggt agttatgaac agtgggggtca cataggtatt 360
gtatatgatg gaggtaatat ttctacattt actatttttag agcaaaactg gaatggttat 420
gctaataaaa aacctacaaa acgtgtagat aattattacg gattaactca cttcattgaa 480
atacctgtaa aagcaggaac tactgttaaa aaagaaacag ctaagaaaag cgcaagtaaa 540
acgcctgcac ctaaaaagaa agcaacacta aaagtttcta agaatt 585

```

<210> 10

<211> 195

<212> PRT

<213> Staphylococcus bacteriophage K

<400> 10

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Met Ala Lys Thr Gln Ala Glu Ile Asn Lys Arg Leu Asp Ala Tyr Ala
1          5          10          15

Lys Gly Thr Val Asp Ser Pro Tyr Arg Val Lys Lys Ala Thr Ser Tyr
20          25          30

Asp Pro Ser Phe Gly Val Met Glu Ala Gly Ala Ile Asp Ala Asp Gly
35          40          45

Tyr Tyr His Ala Gln Cys Gln Asp Leu Ile Thr Asp Tyr Val Leu Trp
50          55          60

Leu Thr Asp Asn Lys Val Arg Thr Trp Gly Asn Ala Lys Asp Gln Ile
65          70          75          80

Lys Gln Ser Tyr Gly Thr Gly Phe Lys Ile His Glu Asn Lys Pro Ser
85          90          95

Thr Val Pro Lys Lys Gly Trp Ile Ala Val Phe Thr Ser Gly Ser Tyr
100         105         110

Glu Gln Trp Gly His Ile Gly Ile Val Tyr Asp Gly Gly Asn Thr Ser
115         120         125

Thr Phe Thr Ile Leu Glu Gln Asn Trp Asn Gly Tyr Ala Asn Lys Lys
130         135         140

Pro Thr Lys Arg Val Asp Asn Tyr Tyr Gly Leu Thr His Phe Ile Glu
145         150         155         160

Ile Pro Val Lys Ala Gly Thr Thr Val Lys Lys Glu Thr Ala Lys Lys
165         170         175

Ser Ala Ser Lys Thr Pro Ala Pro Lys Lys Lys Ala Thr Leu Lys Val
180         185         190

```

Ser Lys Asn
195

<210> 11

<211> 420

<212> DNA

<213> Staphylococcus bacteriophage Twort

<400> 11

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atgaaaaccc tgaaacaagc agagtcctac attaagagta aagtaaatac aggaactgat      60
tttgatgggtt tatatgggta tcagtgtatg gacttagcag tagattatat ttaccatgta      120
acagatggta aaataagaat gtggggtaat gctaaggatg cgataaataa ctcttttggt      180
ggtaactgcta cggatatataa aaactaccct gcttttagac ctaagtacgg tgatgtagtc      240
gtatggacta ctggtaattt tgcaacttat ggtcatatcg caatagttac taaccctgac      300
ccttatggag accttcaata tgttacagtt cttgaacaaa actggaacgg taacgggatt      360
tataaaaccg agttagctac aatcagaaca caggattaca caggaattac acattttatt      420

```

<210> 12

<211> 140

<212> PRT

<213> Staphylococcus bacteriophage Twort

<400> 12

```

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

Thr Gly Thr Asp Phe Asp Gly Leu Tyr Gly Tyr Gln Cys Met Asp Leu
20          25          30

Ala Val Asp Tyr Ile Tyr His Val Thr Asp Gly Lys Ile Arg Met Trp
35          40          45

Gly Asn Ala Lys Asp Ala Ile Asn Asn Ser Phe Gly Gly Thr Ala Thr
50          55          60

Val Tyr Lys Asn Tyr Pro Ala Phe Arg Pro Lys Tyr Gly Asp Val Val
65          70          75          80

Val Trp Thr Thr Gly Asn Phe Ala Thr Tyr Gly His Ile Ala Ile Val
85          90          95

Thr Asn Pro Asp Pro Tyr Gly Asp Leu Gln Tyr Val Thr Val Leu Glu
100         105         110

Gln Asn Trp Asn Gly Asn Gly Ile Tyr Lys Thr Glu Leu Ala Thr Ile
115         120         125

Arg Thr His Asp Tyr Thr Gly Ile Thr His Phe Ile
130         135         140

```

<210> 13

<211> 438

<212> DNA

<213> Staphylococcus bacteriophage 2638A

<400> 13

```

atgctaactg ctattgacta tcttacgaaa aaagggttgga aaatatcatc tgaccctcgc      60
acttacgatg gttaccctaa aaactacggc tacagaaatt accatgaaaa cggcattaat      120
tatgatgagt tttgtggtgg ttatcataga gcttttgatg tttacagtaa cgaaactaac      180
gacgtgcctg ctgttactag cggaacagtt attgaagcaa acgattacgg taattttggt      240
ggtacattcg ttattagaga cgctaacgat aacgattgga tatatgggca tctacaacgt      300
ggctcaatgc gatttgttgt aggcgacaaa gtcaatcaag gtgacattat tggttttacaa      360
ggtaatagca actattacga caatcctatg agtgtacatt tacatttaca attacgccct      420
aaagacgcaa agaaagat                                     438

```

<210> 14

<211> 146

<212> PRT

<213> Staphylococcus bacteriophage 2638A

<400> 14

```

Met Leu Thr Ala Ile Asp Tyr Leu Thr Lys Lys Gly Trp Lys Ile Ser
1              5              10              15

Ser Asp Pro Arg Thr Tyr Asp Gly Tyr Pro Lys Asn Tyr Gly Tyr Arg
                20              25              30

Asn Tyr His Glu Asn Gly Ile Asn Tyr Asp Glu Phe Cys Gly Gly Tyr
          35              40              45

His Arg Ala Phe Asp Val Tyr Ser Asn Glu Thr Asn Asp Val Pro Ala
          50              55              60

Val Thr Ser Gly Thr Val Ile Glu Ala Asn Asp Tyr Gly Asn Phe Gly
65              70              75              80

Gly Thr Phe Val Ile Arg Asp Ala Asn Asp Asn Asp Trp Ile Tyr Gly
          85              90              95

His Leu Gln Arg Gly Ser Met Arg Phe Val Val Gly Asp Lys Val Asn
          100             105             110

Gln Gly Asp Ile Ile Gly Leu Gln Gly Asn Ser Asn Tyr Tyr Asp Asn
          115             120             125

Pro Met Ser Val His Leu His Leu Gln Leu Arg Pro Lys Asp Ala Lys
          130             135             140

Lys Asp

```

145

<210> 15

<211> 420

<212> DNA

<213> Staphylococcus simulans

<400> 15

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gctgcaacac atgaacattc agcacaatgg ttgaataatt acaaaaaagg atatggttac      60
ggtccttatac cattaggtat aaatggcggg atgcactacg gagttgattt ttttatgaat      120
attggaacac cagtaaaagc tatttcaagc ggaaaaatag ttgaagctgg ttggagtaat      180
tacggaggag gtaatcaaat aggtcttatt gaaaatgatg gagtgcatag acaatggtat      240
atgcatctaa gtaaataataa tgttaaagta ggagattatg tcaaagctgg tcaaataatac      300
ggttggtctg gaagcactgg ttattctaca gcaccacatt tacacttcca aagaatggtt      360
aattcatttt caaattcaac tgcccaagat ccaatgcctt tcttaaagag cgcaggatat      420

```

<210> 16

<211> 140

<212> PRT

<213> Staphylococcus simulans

<400> 16

```

Ala Ala Thr His Glu His Ser Ala Gln Trp Leu Asn Asn Tyr Lys Lys
1              5              10              15

Gly Tyr Gly Tyr Gly Pro Tyr Pro Leu Gly Ile Asn Gly Gly Met His
20              25              30

Tyr Gly Val Asp Phe Phe Met Asn Ile Gly Thr Pro Val Lys Ala Ile
35              40              45

Ser Ser Gly Lys Ile Val Glu Ala Gly Trp Ser Asn Tyr Gly Gly Gly
50              55              60

Asn Gln Ile Gly Leu Ile Glu Asn Asp Gly Val His Arg Gln Trp Tyr
65              70              75              80

Met His Leu Ser Lys Tyr Asn Val Lys Val Gly Asp Tyr Val Lys Ala
85              90              95

Gly Gln Ile Ile Gly Trp Ser Gly Ser Thr Gly Tyr Ser Thr Ala Pro
100              105              110

His Leu His Phe Gln Arg Met Val Asn Ser Phe Ser Asn Ser Thr Ala
115              120              125

Gln Asp Pro Met Pro Phe Leu Lys Ser Ala Gly Tyr
130              135              140

```

<210> 17

<211> 510

<212> DNA

<213> Staphylococcus bacteriophage 2638A

<400> 17

```

ggtaacaaga ttacagcacc aaaacctagt attcaaggtg tggtcatcca caatgattat      60
ggtagtatga cacctagtca atacttacca tggttatatg cacgtgagaa taacgggtaca    120
cacgttaacg gttgggctag tgtttatgca aatagaaacg aagtgccttg gtatcatccg    180
acagactacg tagagtggca ttgtggtaat caatgggcaa atgctaactt aatcggattt    240
gaagtgtgtg agtcgtatcc tggtagaatc tcggacaaat tattcttaga aaatgaagaa    300
gcgacattga aagtagctgc ggatgtgatg aagtcgtacg gattaccagt taatcgcaac    360
actgtacgtc tgcataacga attcttcgga acttcttgtc cacatcgttc gtgggacttg    420
catgttggca aaggtgagcc ttacacaact actaatatta ataaaatgaa agactacttc    480
atcaaacgca tcaaacatta ttatgacggg      510

```

<210> 18

<211> 169

<212> PRT

<213> Staphylococcus bacteriophage 2638A

<400> 18

```

Asn Lys Ile Thr Ala Pro Lys Pro Ser Ile Gln Gly Val Val Ile His
1           5           10           15

Asn Asp Tyr Gly Ser Met Thr Pro Ser Gln Tyr Leu Pro Trp Leu Tyr
20           25           30

Ala Arg Glu Asn Asn Gly Thr His Val Asn Gly Trp Ala Ser Val Tyr
35           40           45

Ala Asn Arg Asn Glu Val Leu Trp Tyr His Pro Thr Asp Tyr Val Glu
50           55           60

Trp His Cys Gly Asn Gln Trp Ala Asn Ala Asn Leu Ile Gly Phe Glu
65           70           75           80

Val Cys Glu Ser Tyr Pro Gly Arg Ile Ser Asp Lys Leu Phe Leu Glu
85           90           95

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

Gly Leu Pro Val Asn Arg Asn Thr Val Arg Leu His Asn Glu Phe Phe
115          120          125

Gly Thr Ser Cys Pro His Arg Ser Trp Asp Leu His Val Gly Lys Gly
130          135          140

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

```

Lys Arg Ile Lys His Tyr Tyr Asp Gly
165

<210> 19

<211> 1407

<212> DNA

<213> artificial

<220>

<223> artificial construct

<400> 19

atggctaaga ctcaagcaga aataaataaa cgtttagatg cttatgcaaa aggaacagta	60
gatagccctt acagagttaa aaaagctaca agttatgacc catcatttgg tgtaatggaa	120
gcaggagcca ttgatgcaga tggttactat cacgctcagt gtcaagacct tattacagac	180
tatgtttttat ggttaacaga taataaagtt agaacttggg gtaatgctaa agaccaaatt	240
aaacagagtt atggtactgg atttaaaata catgaaaata aaccttctac tgtacctaaa	300
aaaggttgga ttgcggtatt tacatccggt agttatgaac agtggggtca cataggtatt	360
gtatatgatg gaggtaatac ttctacattt actatttttag agcaaaaactg gaatggttat	420
gctaataaaa aacctacaaa acgtgtagat aattattacg gattaactca cttcattgaa	480
atacctgtaa aagcaggaac tactgttaaa aaagaaacag ctaagaaaag cgcaagtaaa	540
acgcctgcac ctaaaaagaa agcaacacta aaagtttcta agaatgagct catggctaag	600
actcaagcag aaataaataa acgttttagat gcttatgcaa aaggaacagt agatagccct	660
tacagagtta aaaaagctac aagttatgac ccatcatttg gtgtaatgga agcaggagcc	720
attgatgcag atggttacta tcacgctcag tgtcaagacc ttattacaga ctatgtttta	780
tggttaacag ataataaagt tagaacttgg ggtaatgcta aagaccaaatt taaacagagt	840
tatggtactg gattttaaatt acatgaaaat aaaccttcta ctgtacctaa aaaaggttgg	900
attgcggtat ttacatccgg tagttatgaa cagtgggggtc acataggtat tgtatatgat	960
ggaggtaata cttctacatt tactatttta gagcaaaaact ggaatgggta tgctaataaa	1020
aaacctacaa aacgtgtaga taattattac ggattaactc acttcattga aatacctgta	1080
aaagcaggaa aagcaggtgg tacagtaact ccaacgccga atacagggttg gaaaacaaac	1140
aatatggca cactatataa atcagagtca gctagcttca cacctaatac agatataata	1200
acaagaacga ctggtccatt tagaagcatg ccgcagtcag gagtcttaaa agcaggtcaa	1260
acaattcatt atgatgaagt gatgaaacaa gacggtcatg tttgggtagg ttatacaggt	1320
aacagtggcc aacgtattta cttgcctgta agaacatgga ataaatctac taatacttta	1380
ggtgttcttt ggggaactat aaagtaa	1407

<210> 20

<211> 468

<212> PRT

<213> artificial

<220>

<223> artificial construct

<400> 20

Met	Ala	Lys	Thr	Gln	Ala	Glu	Ile	Asn	Lys	Arg	Leu	Asp	Ala	Tyr	Ala
1				5					10					15	

Lys	Gly	Thr	Val	Asp	Ser	Pro	Tyr	Arg	Val	Lys	Lys	Ala	Thr	Ser	Tyr
			20					25					30		

Asp	Pro	Ser	Phe	Gly	Val	Met	Glu	Ala	Gly	Ala	Ile	Asp	Ala	Asp	Gly
		35					40					45			

Tyr	Tyr	His	Ala	Gln	Cys	Gln	Asp	Leu	Ile	Thr	Asp	Tyr	Val	Leu	Trp
	50					55					60				

Leu	Thr	Asp	Asn	Lys	Val	Arg	Thr	Trp	Gly	Asn	Ala	Lys	Asp	Gln	Ile
65					70					75					80

Lys	Gln	Ser	Tyr	Gly	Thr	Gly	Phe	Lys	Ile	His	Glu	Asn	Lys	Pro	Ser
				85					90					95	

Thr	Val	Pro	Lys	Lys	Gly	Trp	Ile	Ala	Val	Phe	Thr	Ser	Gly	Ser	Tyr
			100					105					110		

Glu	Gln	Trp	Gly	His	Ile	Gly	Ile	Val	Tyr	Asp	Gly	Gly	Asn	Thr	Ser
		115					120					125			

Thr	Phe	Thr	Ile	Leu	Glu	Gln	Asn	Trp	Asn	Gly	Tyr	Ala	Asn	Lys	Lys
	130					135					140				

Pro	Thr	Lys	Arg	Val	Asp	Asn	Tyr	Tyr	Gly	Leu	Thr	His	Phe	Ile	Glu
145					150					155					160

Ile	Pro	Val	Lys	Ala	Gly	Thr	Thr	Val	Lys	Lys	Glu	Thr	Ala	Lys	Lys
			165						170					175	

Ser	Ala	Ser	Lys	Thr	Pro	Ala	Pro	Lys	Lys	Lys	Ala	Thr	Leu	Lys	Val
			180					185					190		

Ser	Lys	Asn	Glu	Leu	Met	Ala	Lys	Thr	Gln	Ala	Glu	Ile	Asn	Lys	Arg
		195					200					205			

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

Lys	Ala	Thr	Ser	Tyr	Asp	Pro	Ser	Phe	Gly	Val	Met	Glu	Ala	Gly	Ala
225					230					235					240

Ile	Asp	Ala	Asp	Gly	Tyr	Tyr	His	Ala	Gln	Cys	Gln	Asp	Leu	Ile	Thr
				245					250					255	

Asp	Tyr	Val	Leu	Trp	Leu	Thr	Asp	Asn	Lys	Val	Arg	Thr	Trp	Gly	Asn
		260						265					270		

Ala Lys Asp Gln Ile Lys Gln Ser Tyr Gly Thr Gly Phe Lys Ile His
275 280 285

Glu Asn Lys Pro Ser Thr Val Pro Lys Lys Gly Trp Ile Ala Val Phe
290 295 300

Thr Ser Gly Ser Tyr Glu Gln Trp Gly His Ile Gly Ile Val Tyr Asp
305 310 315 320

Gly Gly Asn Thr Ser Thr Phe Thr Ile Leu Glu Gln Asn Trp Asn Gly
325 330 335

Tyr Ala Asn Lys Lys Pro Thr Lys Arg Val Asp Asn Tyr Tyr Gly Leu
340 345 350

Thr His Phe Ile Glu Ile Pro Val Lys Ala Gly Lys Ala Gly Gly Thr
355 360 365

Val Thr Pro Thr Pro Asn Thr Gly Trp Lys Thr Asn Lys Tyr Gly Thr
370 375 380

Leu Tyr Lys Ser Glu Ser Ala Ser Phe Thr Pro Asn Thr Asp Ile Ile
385 390 395 400

Thr Arg Thr Thr Gly Pro Phe Arg Ser Met Pro Gln Ser Gly Val Leu
405 410 415

Lys Ala Gly Gln Thr Ile His Tyr Asp Glu Val Met Lys Gln Asp Gly
420 425 430

His Val Trp Val Gly Tyr Thr Gly Asn Ser Gly Gln Arg Ile Tyr Leu
435 440 445

Pro Val Arg Thr Trp Asn Lys Ser Thr Asn Thr Leu Gly Val Leu Trp
450 455 460

Gly Thr Ile Lys
465

<210> 21

<211> 1209

<212> DNA

<213> artificial

<220>

<223> artificial construct

<400> 21

gctgcaacac atgaacattc agcacaatgg ttgaataatt acaaaaaagg atatgggttac	60
ggtccttata cattaggtat aaatggcggt atgcactacg gagttgattt ttttatgaat	120
attggaacac cagtaaaagc tattttcaagc ggaaaaatag ttgaagctgg ttggagtaat	180
tacggaggag gtaatcaaat aggtcttatt gaaaatgatg gagtgcatag acaatgggtat	240
atgcatctaa ctaaatataa tctttaagta agagattatg tcaagctgg tgaataatac	300

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atgcattctaa gcaaatataa cyttaaagta yyagattatc tcaagctgg tcaataaatt 300
ggttggtctg gaagcactgg ttattctaca gcaccacatt tacacttcca aagaatggtt 360
aattcattttt caaattcaac tgcccaagat ccaatgcctt tcttaaagag cgcaggatat 420
ggaaaagcag gtggtacagt aactccaacg ccgaatacag gtgagctcgc tgcaacacat 480
gaacattcag cacaatgggt gaataattac aaaaaaggat atgggttacgg tccttatcca 540
ttaggtataa atggcggtat gcactacgga gttgattttt ttatgaatat tggaacacca 600
gtaaaagcta tttcaagcgg aaaaatagtt gaagctgggt ggagtaatta cggaggaggt 660
aatcaaatag gtcttattga aatgatgga gtgcatagac aatggtatat gcatctaagt 720
aaatataatg ttaaagtagg agattatgtc aaagctgggt aaataatcgg ttggtctgga 780
agcactgggt attctacagc accacattta cacttccaaa gaatgggtta ttcattttca 840
aattcaactg cccaagatcc aatgcctttc ttaaagagcg caggatatgg aaaagcaggt 900
ggtacagtaa ctccaacgcc gaatacaggt tggaaaacaa acaaatatgg cacactatat 960
aatcagagt cagctagctt cacaccta atacagatataa taacaagaac gactggtcca 1020
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gtgatgaaac aagacggtca tgtttgggta ggttatacag gtaacagtgg ccaacgtatt 1140
tacttgcttg taagaacatg gaataaatct actaatactt taggtgttct ttggggaact 1200
ataaagtaa 1209

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<210> 22

<211> 402

<212> PRT

<213> artificial

<220>

<223> artificial construct

<400> 22

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Ala Ala Thr His Glu His Ser Ala Gln Trp Leu Asn Asn Tyr Lys Lys
1          5          10          15

```

```

Gly Tyr Gly Tyr Gly Pro Tyr Pro Leu Gly Ile Asn Gly Gly Met His
20          25          30

```

```

Tyr Gly Val Asp Phe Phe Met Asn Ile Gly Thr Pro Val Lys Ala Ile
35          40          45

```

```

Ser Ser Gly Lys Ile Val Glu Ala Gly Trp Ser Asn Tyr Gly Gly Gly
50          55          60

```

```

Asn Gln Ile Gly Leu Ile Glu Asn Asp Gly Val His Arg Gln Trp Tyr
65          70          75          80

```

```

Met His Leu Ser Lys Tyr Asn Val Lys Val Gly Asp Tyr Val Lys Ala
85          90          95

```

```

Gly Gln Ile Ile Gly Trp Ser Gly Ser Thr Gly Tyr Ser Thr Ala Pro
100          105          110

```

His Leu His Phe Gln Arg Met Val Asn Ser Phe Ser Asn Ser Thr Ala
 115 120 125

Gln Asp Pro Met Pro Phe Leu Lys Ser Ala Gly Tyr Gly Lys Ala Gly
 130 135 140

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

Glu His Ser Ala Gln Trp Leu Asn Asn Tyr Lys Lys Gly Tyr Gly Tyr
 165 170 175

Gly Pro Tyr Pro Leu Gly Ile Asn Gly Gly Met His Tyr Gly Val Asp
 180 185 190

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

Ile Val Glu Ala Gly Trp Ser Asn Tyr Gly Gly Gly Asn Gln Ile Gly
 210 215 220

Leu Ile Glu Asn Asp Gly Val His Arg Gln Trp Tyr Met His Leu Ser
 225 230 235 240

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

Gly Trp Ser Gly Ser Thr Gly Tyr Ser Thr Ala Pro His Leu His Phe
 260 265 270

Gln Arg Met Val Asn Ser Phe Ser Asn Ser Thr Ala Gln Asp Pro Met
 275 280 285

Pro Phe Leu Lys Ser Ala Gly Tyr Gly Lys Ala Gly Gly Thr Val Thr
 290 295 300

Pro Thr Pro Asn Thr Gly Trp Lys Thr Asn Lys Tyr Gly Thr Leu Tyr
 305 310 315 320

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

Thr Thr Gly Pro Phe Arg Ser Met Pro Gln Ser Gly Val Leu Lys Ala
 340 345 350

Gly Gln Thr Ile His Tyr Asp Glu Val Met Lys Gln Asp Gly His Val
 355 360 365

Trp Val Gly Tyr Thr Gly Asn Ser Gly Gln Arg Ile Tyr Leu Pro Val
 370 375 380

Arg Thr Trp Asn Lys Ser Thr Asn Thr Leu Gly Val Leu Trp Gly Thr
 385 390 395 400

Ile Lys

<210> 23

<211> 1686

<212> DNA

<213> artificial

<220>

<223> artificial construct

<400> 23

gcaaagaaag atgaaaaatc acaagtatgt agtgggtttgg ctatggaaaa atatgacatt	60
acaaatttaa atgctaaaca agataaatca aagaatggga gcgtgaaaga gttgaaacat	120
atctattcaa accatattaa aggtaacaag attacagcac caaaacctag tattcaaggt	180
gtggatcatcc acaatgatta tggtagtatg acacctagtc aatacttacc atggttatat	240
gcacgtgaga ataacgggtac acacgttaac ggttgggcta gtgtttatgc aaatagaaac	300
gaagtgcctt ggtatcatcc gacagactac gtagagtggc attgtggtaa tcaatgggca	360
aatgctaact taatcggatt tgaagtgtgt gagtcgtatc ctggtagaat ctcggacaaa	420
ttattcttag aaaatgaaga agcgcatttg aaagtagctg cggatgtgat gaagtcgtac	480
ggattaccag ttaatcgcaa cactgtacgt ctgcataacg aattcttcgg aacttcttgt	540
ccacatcgtt cgtgggactt gcatgttggc aaaggtgagc cttacacaac tactaatatt	600
aataaaatga aagactactt catcaaacgc atcaaacatt attatgacgg tgagctcgca	660
aagaaagatg aaaaatcaca agtatgtagt ggtttggcta tggaaaaata tgacattaca	720
aatttaaagt ctaaacaaga taaatcaaag aatgggagcg tgaaagagtt gaaacatatc	780
tattcaaacc atattaaagg taacaagatt acagcaccaa aacctagtat tcaaggtgtg	840
gtcatccaca atgattatgg tagtatgaca cctagtcaat acttaccatg gttatatgca	900
cgtgagaata acggtacaca cgttaacggg tgggctagtg tttatgcaaa tagaaacgaa	960
gtgctttggg atcatccgac agactacgta gagtggcatt gtggtaatca atgggcaa	1020
gctaacttaa tcggatttga agtgtgtgag tcgtatcctg gtagaatctc ggacaaatta	1080
ttcttagaaa atgaagaagc gacattgaaa gtagctgcgg atgtgatgaa gtcgtacgga	1140
ttaccagtta atcgcaacac tgtacgtctg cataacgaat tcttcggaac ttcttgtcca	1200
catcgttcgt gggacttgca tgttggcaaa ggtgagcctt acacaactac taatattaat	1260
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gtaagcaaag cagcaactat caaacaatct gacgttaagc aagaagttaa aaagcaagaa	1380
gcaaaacaaa ttgtgaaagc aacagattgg aaaacaaaca aatatggcac actatataaa	1440
tcagagtcag ctagcttcac acctaataca gatataataa caagaacgac tgggtccattt	1500
agaagcatgc cgcagtcagg agtcttaaaa gcaggcaaa caattcatta tgatgaagtg	1560
atgaaacaag acggtcatgt ttgggtaggt tatacaggta acagtggcca acgtatttac	1620
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<210> 24

<211> 561

<212> PRT

<213> artificial

<220>

<223> artificial construct

<400> 24

Ala	Lys	Lys	Asp	Glu	Lys	Ser	Gln	Val	Cys	Ser	Gly	Leu	Ala	Met	Glu
1				5					10					15	

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

Gly	Ser	Val	Lys	Glu	Leu	Lys	His	Ile	Tyr	Ser	Asn	His	Ile	Lys	Gly
		35					40					45			

Asn	Lys	Ile	Thr	Ala	Pro	Lys	Pro	Ser	Ile	Gln	Gly	Val	Val	Ile	His
	50					55					60				

Asn	Asp	Tyr	Gly	Ser	Met	Thr	Pro	Ser	Gln	Tyr	Leu	Pro	Trp	Leu	Tyr
65					70				75						80

Ala	Arg	Glu	Asn	Asn	Gly	Thr	His	Val	Asn	Gly	Trp	Ala	Ser	Val	Tyr
			85						90					95	

Ala	Asn	Arg	Asn	Glu	Val	Leu	Trp	Tyr	His	Pro	Thr	Asp	Tyr	Val	Glu
			100					105					110		

Trp	His	Cys	Gly	Asn	Gln	Trp	Ala	Asn	Ala	Asn	Leu	Ile	Gly	Phe	Glu
		115					120					125			

Val	Cys	Glu	Ser	Tyr	Pro	Gly	Arg	Ile	Ser	Asp	Lys	Leu	Phe	Leu	Glu
	130					135					140				

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

Gly	Leu	Pro	Val	Asn	Arg	Asn	Thr	Val	Arg	Leu	His	Asn	Glu	Phe	Phe
				165					170					175	

Gly	Thr	Ser	Cys	Pro	His	Arg	Ser	Trp	Asp	Leu	His	Val	Gly	Lys	Gly
			180					185					190		

Glu	Pro	Tyr	Thr	Thr	Thr	Asn	Ile	Asn	Lys	Met	Lys	Asp	Tyr	Phe	Ile
		195				200						205			

Lys	Arg	Ile	Lys	His	Tyr	Tyr	Asp	Gly	Glu	Leu	Ala	Lys	Lys	Asp	Glu
	210					215					220				

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

Asn Leu Asn Ala Lys Gln Asp Lys Ser Lys Asn Gly Ser Val Lys Glu
 245 250 255
 Leu Lys His Ile Tyr Ser Asn His Ile Lys Gly Asn Lys Ile Thr Ala
 260 265 270
 Pro Lys Pro Ser Ile Gln Gly Val Val Ile His Asn Asp Tyr Gly Ser
 275 280 285
 Met Thr Pro Ser Gln Tyr Leu Pro Trp Leu Tyr Ala Arg Glu Asn Asn
 290 295 300
 Gly Thr His Val Asn Gly Trp Ala Ser Val Tyr Ala Asn Arg Asn Glu
 305 310 315 320
 Val Leu Trp Tyr His Pro Thr Asp Tyr Val Glu Trp His Cys Gly Asn
 325 330 335
 Gln Trp Ala Asn Ala Asn Leu Ile Gly Phe Glu Val Cys Glu Ser Tyr
 340 345 350
 Pro Gly Arg Ile Ser Asp Lys Leu Phe Leu Glu Asn Glu Glu Ala Thr
 355 360 365
 Leu Lys Val Ala Ala Asp Val Met Lys Ser Tyr Gly Leu Pro Val Asn
 370 375 380
 Arg Asn Thr Val Arg Leu His Asn Glu Phe Phe Gly Thr Ser Cys Pro
 385 390 395 400
 His Arg Ser Trp Asp Leu His Val Gly Lys Gly Glu Pro Tyr Thr Thr
 405 410 415
 Thr Asn Ile Asn Lys Met Lys Asp Tyr Phe Ile Lys Arg Ile Lys His
 420 425 430
 Tyr Tyr Asp Gly Gly Lys Leu Glu Val Ser Lys Ala Ala Thr Ile Lys
 435 440 445
 Gln Ser Asp Val Lys Gln Glu Val Lys Lys Gln Glu Ala Lys Gln Ile
 450 455 460
 Val Lys Ala Thr Asp Trp Lys Thr Asn Lys Tyr Gly Thr Leu Tyr Lys
 465 470 475 480
 Ser Glu Ser Ala Ser Phe Thr Pro Asn Thr Asp Ile Ile Thr Arg Thr
 485 490 495
 Thr Gly Pro Phe Arg Ser Met Pro Gln Ser Gly Val Leu Lys Ala Gly
 500 505 510
 Gln Thr Ile His Tyr Asp Glu Val Met Lys Gln Asp Gly His Val Trp
 515 520 525
 Val Gly Tyr Thr Gly Asn Ser Gly Gln Arg Ile Tyr Leu Pro Val Arg

530						535						540					
Thr	Trp	Asn	Lys	Ser	Thr	Asn	Thr	Leu	Gly	Val	Leu	Trp	Gly	Thr	Ile		
545					550					555					560		

Lys

<210> 25
<211> 1131
<212> DNA
<213> artificial

<220>
<223> artificial construct

<400> 25

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aggccttata	atggaactgg	atccgcatgc	gagctcgcaa	agaaagatga	aaaatcacaa	120
gtatgtagtg	gtttggctat	ggaaaaatat	gacattacaa	atttaaattgc	taaacaagat	180
aatcaaaga	atgggagcgt	gaaagagttg	aaacatatct	attcaaacca	tattaaaggt	240
aacaagatta	cagcaccaaa	acctagtatt	caagggtgtg	tcatccacaa	tgattatggt	300
agtatgacac	ctagtcaata	cttaccatgg	ttatatgcac	gtgagaataa	cggtagacac	360
gttaacggtt	gggctagtgt	ttatgcaaat	agaaacgaag	tgctttggta	tcatccgaca	420
gactacgtag	agtggcattg	tggtaatcaa	tgggcaaatg	ctaacttaat	cggatttgaa	480
gtgtgtgagt	cgtatcctgg	tagaatctcg	gacaaattat	tcttagaaaa	tgaagaagcg	540
acattgaaag	tagctgcgga	tgtgatgaag	tcgtacggat	taccagttaa	tcgcaacact	600
gtacgtctgc	ataacgaatt	cttcggaact	tcttgtccac	atcgttcgtg	ggacttgcac	660
gttggcaaag	gtgagcctta	cacaactact	aatattaata	aaatgaaaga	ctacttcac	720
aaacgcatca	aacattatta	tgacggtgga	aagctagaag	taagcaaagc	agcaactatc	780
aaacaatctg	acgttaagca	agaagttaa	aagcaagaag	caaaacaaat	tgtgaaagca	840
acagattgga	aacagaataa	agatggcatt	tggtataaag	ctgaacatgc	ttcgttcaca	900
gtgacagcac	cagagggaat	tatcacaaga	tacaaaggtc	cttggaactgg	tcaccacaaa	960
gctggtgtat	tacaaaaagg	tcaaacgatt	aatatgatg	aggttcaaaa	atttgacggt	1020
catgtttggg	tatcgtggga	aacgtttgag	ggcgaaactg	tatacatgcc	ggtacgcaca	1080
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<210> 26
<211> 376
<212> PRT
<213> artificial

<220>
<223> artificial construct

<400> 26

Met Arg Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser
1 5 10 15

Gly Ile Glu Gly Arg Pro Tyr Asn Gly Thr Gly Ser Ala Cys Glu Leu
20 25 30

Ala Lys Lys Asp Glu Lys Ser Gln Val Cys Ser Gly Leu Ala Met Glu
35 40 45

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

Gly Ser Val Lys Glu Leu Lys His Ile Tyr Ser Asn His Ile Lys Gly
65 70 75 80

Asn Lys Ile Thr Ala Pro Lys Pro Ser Ile Gln Gly Val Val Ile His
85 90 95

Asn Asp Tyr Gly Ser Met Thr Pro Ser Gln Tyr Leu Pro Trp Leu Tyr
100 105 110

Ala Arg Glu Asn Asn Gly Thr His Val Asn Gly Trp Ala Ser Val Tyr
115 120 125

Ala Asn Arg Asn Glu Val Leu Trp Tyr His Pro Thr Asp Tyr Val Glu
130 135 140

Trp His Cys Gly Asn Gln Trp Ala Asn Ala Asn Leu Ile Gly Phe Glu
145 150 155 160

Val Cys Glu Ser Tyr Pro Gly Arg Ile Ser Asp Lys Leu Phe Leu Glu
165 170 175

Asn Glu Glu Ala Thr Leu Lys Val Ala Ala Asp Val Met Lys Ser Tyr
180 185 190

Gly Leu Pro Val Asn Arg Asn Thr Val Arg Leu His Asn Glu Phe Phe
195 200 205

Gly Thr Ser Cys Pro His Arg Ser Trp Asp Leu His Val Gly Lys Gly
210 215 220

Glu Pro Tyr Thr Thr Thr Asn Ile Asn Lys Met Lys Asp Tyr Phe Ile
225 230 235 240

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

Ala Ala Thr Ile Lys Gln Ser Asp Val Lys Gln Glu Val Lys Lys Gln
260 265 270

Glu Ala Lys Gln Ile Val Lys Ala Thr Asp Trp Lys Gln Asn Lys Asp
275 280 285

Gly Ile Trp Tyr Lys Ala Glu His Ala Ser Phe Thr Val Thr Ala Pro
 290 295 300

Glu Gly Ile Ile Thr Arg Tyr Lys Gly Pro Trp Thr Gly His Pro Gln
 305 310 315 320

Ala Gly Val Leu Gln Lys Gly Gln Thr Ile Lys Tyr Asp Glu Val Gln
 325 330 335

Lys Phe Asp Gly His Val Trp Val Ser Trp Glu Thr Phe Glu Gly Glu
 340 345 350

Thr Val Tyr Met Pro Val Arg Thr Trp Asp Ala Lys Thr Gly Lys Val
 355 360 365

Gly Lys Leu Trp Gly Glu Ile Lys
 370 375

<210> 27

<211> 1125

<212> DNA

<213> artificial

<220>

<223> artificial construct

<400> 27

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aggccttata atggaactgg atccgcatgc gagctcgcaa agaaagatga aaaatcacaa	120
gtatgtagtg gtttggctat ggaaaaatat gacattacaa atttaaattgc taaacaagat	180
aatcaaaga atgggagcgt gaaagagttg aaacatatct attcaaacca tattaaaggt	240
aacaagatta cagcaccaaa acctagtatt caagggtgtg tcatccacaa tgattatggt	300
agtatgacac ctagtcaata cttaccatgg ttatatgcac gtgagaataa cggtagacac	360
gttaacggtt gggctagtgt ttatgcaaat agaaacgaag tgctttggta tcatccgaca	420
gactacgtag agtggcattg tggtaatcaa tgggcaaatt ctaacttaac cggatttgaa	480
gtgtgtgagt cgtatcctgg tagaatctcg gacaaattat tcttagaaaa tgaagaagcg	540
acattgaaag tagctgcgga tgtgatgaag tcgtacggat taccagttaa tcgcaacact	600
gtacgtctgc ataacgaatt cttcggaaact tcttgtccac atcgttcgtg ggacttgcac	660
gttggcaaag gtgagcctta cacaactact aatattaata aaatgaaaga ctacttcac	720
aaacgcacaa aacattatta tgacgggtgga aagctagaag taagcaaagc agcaactatc	780
aaacaatctg acgttaagca agaagttaaa aagcaagaag caaaacaaat tgtgaaagca	840
acagattgga aaacaaacaa atatggcaca ctatataaat cagagtcagc tagcttcaca	900
cctaatacag atataataac aagaacgact ggtccattta gaagcatgcc gcagtcagga	960
gtcttaaaag cagggtcaaac aattcattat gatgaagtga tgaaacaaga cggatcatgtt	1020
tgggtagggt atacaggtaa cagtggccaa cgtatttact tgccgtgtaag aacatggaat	1080

aaatctacta atacttttagg tgttcttttg ggaactataa agtaa

1125

<210> 28

<211> 374

<212> PRT

<213> artificial

<220>

<223> artificial construct

<400> 28

Met Arg Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser
1 5 10 15

Gly Ile Glu Gly Arg Pro Tyr Asn Gly Thr Gly Ser Ala Cys Glu Leu
20 25 30

Ala Lys Lys Asp Glu Lys Ser Gln Val Cys Ser Gly Leu Ala Met Glu
35 40 45

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

Gly Ser Val Lys Glu Leu Lys His Ile Tyr Ser Asn His Ile Lys Gly
65 70 75 80

Asn Lys Ile Thr Ala Pro Lys Pro Ser Ile Gln Gly Val Val Ile His
85 90 95

Asn Asp Tyr Gly Ser Met Thr Pro Ser Gln Tyr Leu Pro Trp Leu Tyr
100 105 110

Ala Arg Glu Asn Asn Gly Thr His Val Asn Gly Trp Ala Ser Val Tyr
115 120 125

Ala Asn Arg Asn Glu Val Leu Trp Tyr His Pro Thr Asp Tyr Val Glu
130 135 140

Trp His Cys Gly Asn Gln Trp Ala Asn Ala Asn Leu Ile Gly Phe Glu
145 150 155 160

Val Cys Glu Ser Tyr Pro Gly Arg Ile Ser Asp Lys Leu Phe Leu Glu
165 170 175

Asn Glu Glu Ala Thr Leu Lys Val Ala Ala Asp Val Met Lys Ser Tyr
180 185 190

Gly Leu Pro Val Asn Arg Asn Thr Val Arg Leu His Asn Glu Phe Phe
195 200 205

Gly Thr Ser Cys Pro His Arg Ser Trp Asp Leu His Val Gly Lys Gly
210 215 220

Glu Pro Tyr Thr Thr Thr Asn Ile Asn Lys Met Lys Asp Tyr Phe Ile
225 230 235 240

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

Ala Ala Thr Ile Lys Gln Ser Asp Val Lys Gln Glu Val Lys Lys Gln
260 265 270

Glu Ala Lys Gln Ile Val Lys Ala Thr Asp Trp Lys Thr Asn Lys Tyr
275 280 285

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

Ile Ile Thr Arg Thr Thr Gly Pro Phe Arg Ser Met Pro Gln Ser Gly
305 310 315 320

Val Leu Lys Ala Gly Gln Thr Ile His Tyr Asp Glu Val Met Lys Gln
325 330 335

Asp Gly His Val Trp Val Gly Tyr Thr Gly Asn Ser Gly Gln Arg Ile
340 345 350

Tyr Leu Pro Val Arg Thr Trp Asn Lys Ser Thr Asn Thr Leu Gly Val
355 360 365

Leu Trp Gly Thr Ile Lys
370

<210> 29

<211> 1131

<212> DNA

<213> artificial

<220>

<223> artificial construct

<400> 29

atgagaggat cgcacaccca tcaccatcac ggatctggct ctggatctgg tatcgaggga	60
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gtatgtagtg gtttggctat ggaaaaatat gacattacaa atttaaagtc taaacaagat	180
aatcaaaga atgggagcgt gaaagagttg aaacatatct attcaaacca tattaaaggt	240
aacaagatta cagcaccaaa acctagtatt caagggtgtg tcatccacaa tgattatggt	300
agtatgacac ctagtcaata cttaccatgg ttatatgcac gtgagaataa cggtagacac	360
gttaacggtt gggctagtgt ttatgcaaat agaaacgaag tgctttggtg tcatccgaca	420
gactacgtag agtggcattg tggtaatcaa tgggcaaagt ctaacttaat cggatttgaa	480
gtgtgtgagt cgtatcctgg tagaatctcg gacaaattat tcttagaaaa tgaagaagcg	540
acattgaaag tagctgcgga tgtgatgaag tcgtacggat taccagttaa tcgcaacact	600
gtacgtctgc ataacgaatt ctccggaact tcttgtccac atcgttcgtg ggacttgcac	660
gttggaagag gtgagcctta cacaactact aatattaata aaatgaaaga ctacttcac	720
aaacgcacat aacattatta tgacgggtgga aagctagaag taagcaaagc agcaactatc	780

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aaacaatctg acgttaagca agaagttaaa aagcaagaag caaaacaaat tgtgaaagca      840
acagatggta aatctgcaag taaaataaca gttggaagta aagcgcctta taaccttaaa      900
tggtcaaaag gtgcttattt taatgcgaaa atcgacggct taggtgctac ttcagccact      960
agatacgggtg ataatcgtac taactataga ttcgatgttg gacaggctgt atacgcgcct     1020
ggaacattaa tatatgtggt tgaaattata gatggttggt gtcgcattta ttggaacaat     1080
cataatgagt ggatatggca tgagagattg attgtgaaag aagtgtttta a               1131

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<210> 30

<211> 376

<212> PRT

<213> artificial

<220>

<223> artificial construct

<400> 30

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Met Arg Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser
1          5          10          15

```

```

Gly Ile Glu Gly Arg Pro Tyr Asn Gly Thr Gly Ser Ala Cys Glu Leu
20          25          30

```

```

Ala Lys Lys Asp Glu Lys Ser Gln Val Cys Ser Gly Leu Ala Met Glu
35          40          45

```

```

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

```

```

Gly Ser Val Lys Glu Leu Lys His Ile Tyr Ser Asn His Ile Lys Gly
65          70          75          80

```

```

Asn Lys Ile Thr Ala Pro Lys Pro Ser Ile Gln Gly Val Val Ile His
85          90          95

```

```

Asn Asp Tyr Gly Ser Met Thr Pro Ser Gln Tyr Leu Pro Trp Leu Tyr
100          105          110

```

```

Ala Arg Glu Asn Asn Gly Thr His Val Asn Gly Trp Ala Ser Val Tyr
115          120          125

```

```

Ala Asn Arg Asn Glu Val Leu Trp Tyr His Pro Thr Asp Tyr Val Glu
130          135          140

```

```

Trp His Cys Gly Asn Gln Trp Ala Asn Ala Asn Leu Ile Gly Phe Glu
145          150          155          160

```

```

Val Cys Glu Ser Tyr Pro Gly Arg Ile Ser Asp Lys Leu Phe Leu Glu
165          170          175

```

```

Asn Glu Glu Ala Thr Leu Lys Val Ala Ala Asp Val Met Lys Ser Tyr
180          185          190

```

Gly Leu Pro Val Asn Arg Asn Thr Val Arg Leu His Asn Glu Phe Phe
 195 200 205

Gly Thr Ser Cys Pro His Arg Ser Trp Asp Leu His Val Gly Lys Gly
 210 215 220

Glu Pro Tyr Thr Thr Thr Asn Ile Asn Lys Met Lys Asp Tyr Phe Ile
 225 230 235 240

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

Ala Ala Thr Ile Lys Gln Ser Asp Val Lys Gln Glu Val Lys Lys Gln
 260 265 270

Glu Ala Lys Gln Ile Val Lys Ala Thr Asp Gly Lys Ser Ala Ser Lys
 275 280 285

Ile Thr Val Gly Ser Lys Ala Pro Tyr Asn Leu Lys Trp Ser Lys Gly
 290 295 300

Ala Tyr Phe Asn Ala Lys Ile Asp Gly Leu Gly Ala Thr Ser Ala Thr
 305 310 315 320

Arg Tyr Gly Asp Asn Arg Thr Asn Tyr Arg Phe Asp Val Gly Gln Ala
 325 330 335

Val Tyr Ala Pro Gly Thr Leu Ile Tyr Val Phe Glu Ile Ile Asp Gly
 340 345 350

Trp Cys Arg Ile Tyr Trp Asn Asn His Asn Glu Trp Ile Trp His Glu
 355 360 365

Arg Leu Ile Val Lys Glu Val Phe
 370 375

<210> 31

<211> 975

<212> DNA

<213> artificial

<220>

<223> artificial construct

<400> 31

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aataaacgtt tagatgctta tgcaaaagga acagtagata gcccttacag agttaaaaaa	180
gctacaagtt atgacccatc atttggtgta atggaagcag gagccattga tgcagatggt	240
tactatcacg ctgagtgtca agaccttatt acagactatg ttttatgggtt aacagataat	300
aaagttagaa cttggggtaa tgctaaagac caaattaaac agagttatgg tactggattt	360

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aaaatacatg aaaataaacc ttctactgta cctaaaaaag gttggattgc ggtatttaca 420
tccggtagtt atgaacagtg gggtcacata ggtattgtat atgatggagg taatacttct 480
acatttacta ttttagagca aaactggaat ggttatgcta ataaaaaacc tacaaaacgt 540
gtagataatt attacggatt aactcacttc attgaaatac ctgtaaaagc aggaaagcta 600
gaagtaagca aagcagcaac tatcaaaca tctgacgtta agcaagaagt taaaaagcaa 660
gaagcaaaac aaattgtgaa agcaacagat tggaaacaga ataaagatgg catttggtat 720
aaagctgaac atgcttcggt cacagtgaca gcaccagagg gaattatcac aagatacaaa 780
ggtccttggg ctggtcaccc acaagctggg gtattacaaa aagggtcaaac gattaaatat 840
gatgagggtc aaaaatttga cggtcacgtt tgggtatcgt gggaaacgtt tgagggcgaa 900
actgtataca tgccgggtacg cacatgggac gctaaaactg gtaaagttgg taagttgtgg 960
ggcgaaatta aataa 975

```

<210> 32

<211> 324

<212> PRT

<213> artificial

<220>

<223> artificial construct

<400> 32

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Met Arg Gly Ser His His His His His Gly Ser Gly Ser Gly Ser
1           5           10           15

```

```

Gly Ile Glu Gly Arg Pro Tyr Asn Gly Thr Gly Ser Ala Cys Glu Leu
20           25           30

```

```

Met Ala Lys Thr Gln Ala Glu Ile Asn Lys Arg Leu Asp Ala Tyr Ala
35           40           45

```

```

Lys Gly Thr Val Asp Ser Pro Tyr Arg Val Lys Lys Ala Thr Ser Tyr
50           55           60

```

```

Asp Pro Ser Phe Gly Val Met Glu Ala Gly Ala Ile Asp Ala Asp Gly
65           70           75           80

```

```

Tyr Tyr His Ala Gln Cys Gln Asp Leu Ile Thr Asp Tyr Val Leu Trp
85           90           95

```

```

Leu Thr Asp Asn Lys Val Arg Thr Trp Gly Asn Ala Lys Asp Gln Ile
100          105          110

```

```

Lys Gln Ser Tyr Gly Thr Gly Phe Lys Ile His Glu Asn Lys Pro Ser
115          120          125

```

```

Thr Val Pro Lys Lys Gly Trp Ile Ala Val Phe Thr Ser Gly Ser Tyr
130          135          140

```

```

Glu Gln Trp Gly His Ile Gly Ile Val Tyr Asp Gly Gly Asn Thr Ser
145          150          155

```

145		150		155		160
Thr Phe Thr Ile Leu Glu Gln Asn Trp Asn Gly Tyr Ala Asn Lys Lys						
		165		170		175
Pro Thr Lys Arg Val Asp Asn Tyr Tyr Gly Leu Thr His Phe Ile Glu						
		180		185		190
Ile Pro Val Lys Ala Gly Lys Leu Glu Val Ser Lys Ala Ala Thr Ile						
		195		200		205
Lys Gln Ser Asp Val Lys Gln Glu Val Lys Lys Gln Glu Ala Lys Gln						
		210		215		220
Ile Val Lys Ala Thr Asp Trp Lys Gln Asn Lys Asp Gly Ile Trp Tyr						
		225		230		235
Lys Ala Glu His Ala Ser Phe Thr Val Thr Ala Pro Glu Gly Ile Ile						
		245		250		255
Thr Arg Tyr Lys Gly Pro Trp Thr Gly His Pro Gln Ala Gly Val Leu						
		260		265		270
Gln Lys Gly Gln Thr Ile Lys Tyr Asp Glu Val Gln Lys Phe Asp Gly						
		275		280		285
His Val Trp Val Ser Trp Glu Thr Phe Glu Gly Glu Thr Val Tyr Met						
		290		295		300
Pro Val Arg Thr Trp Asp Ala Lys Thr Gly Lys Val Gly Lys Leu Trp						
		305		310		315
						320

Gly Glu Ile Lys

<210> 33

<211> 912

<212> DNA

<213> artificial

<220>

<223> artificial construct

<400> 33

atgagaggat cgcacaccca tcaccatcac ggatctggct ctggatctgg tatcgaggga	60
aggccttata atggaactgg atccgcatgc gagctcatgg ctaagactca agcagaaata	120
aataaacggt tagatgctta tgcaaaagga acagtagata gcccttacag agttaaaaaa	180
gctacaagtt atgacccatc atttggtgta atggaagcag gagccattga tgcagatggt	240
tactatcacg ctcagtgtca agaccttatt acagactatg ttttatgggtt aacagataat	300
aaagttagaa cttggggtaa tgctaaagac caaattaaac agagttatgg tactggattt	360
aaaatacatg aaaataaacc ttctactgta cctaaaaaag gttggattgc ggtatttaca	420

```

tccggtagtt atgaacagtg gggtcacata ggtattgtat atgatggagg taatacttct 480
acatttacta ttttagagca aaactggaat ggttatgcta ataaaaaacc tacaaaacgt 540
gtagataatt attacggatt aactcacttc attgaaatac ctgtaaaagc aggaaaagca 600
ggtggtacag taactccaac gccgaatata ggttggaata caaacaata tggcacacta 660
tataaatcag agtcagctag cttcacacct aatacagata taataacaag aacgactggc 720
ccatttagaa gcatgccgca gtcaggagtc ttaaagcag gtcaaacaat tcattatgat 780
gaagtgatga aacaagacgg tcatgtttgg gtaggttata caggtaacag tggccaacgt 840
atttacttgc ctgtaagaac atggaataaa tctactaata ctttaggtgt tctttgggga 900
actataaagt aa 912

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<210> 34

<211> 303

<212> PRT

<213> artificial

<220>

<223> artificial construct

<400> 34

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Met Arg Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser
1           5           10           15

```

```

Gly Ile Glu Gly Arg Pro Tyr Asn Gly Thr Gly Ser Ala Cys Glu Leu
20           25           30

```

```

Met Ala Lys Thr Gln Ala Glu Ile Asn Lys Arg Leu Asp Ala Tyr Ala
35           40           45

```

```

Lys Gly Thr Val Asp Ser Pro Tyr Arg Val Lys Lys Ala Thr Ser Tyr
50           55           60

```

```

Asp Pro Ser Phe Gly Val Met Glu Ala Gly Ala Ile Asp Ala Asp Gly
65           70           75           80

```

```

Tyr Tyr His Ala Gln Cys Gln Asp Leu Ile Thr Asp Tyr Val Leu Trp
85           90           95

```

```

Leu Thr Asp Asn Lys Val Arg Thr Trp Gly Asn Ala Lys Asp Gln Ile
100          105          110

```

```

Lys Gln Ser Tyr Gly Thr Gly Phe Lys Ile His Glu Asn Lys Pro Ser
115          120          125

```

```

Thr Val Pro Lys Lys Gly Trp Ile Ala Val Phe Thr Ser Gly Ser Tyr
130          135          140

```

```

Glu Gln Trp Gly His Ile Gly Ile Val Tyr Asp Gly Gly Asn Thr Ser
145          150          155          160

```

Thr Phe Thr Ile Leu Glu Gln Asn Trp Asn Gly Tyr Ala Asn Lys Lys
165 170 175

Pro Thr Lys Arg Val Asp Asn Tyr Tyr Gly Leu Thr His Phe Ile Glu
180 185 190

Ile Pro Val Lys Ala Gly Lys Ala Gly Gly Thr Val Thr Pro Thr Pro
195 200 205

Asn Thr Gly Trp Lys Thr Asn Lys Tyr Gly Thr Leu Tyr Lys Ser Glu
210 215 220

Ser Ala Ser Phe Thr Pro Asn Thr Asp Ile Ile Thr Arg Thr Thr Gly
225 230 235 240

Pro Phe Arg Ser Met Pro Gln Ser Gly Val Leu Lys Ala Gly Gln Thr
245 250 255

Ile His Tyr Asp Glu Val Met Lys Gln Asp Gly His Val Trp Val Gly
260 265 270

Tyr Thr Gly Asn Ser Gly Gln Arg Ile Tyr Leu Pro Val Arg Thr Trp
275 280 285

Asn Lys Ser Thr Asn Thr Leu Gly Val Leu Trp Gly Thr Ile Lys
290 295 300

<210> 35

<211> 966

<212> DNA

<213> artificial

<220>

<223> artificial construct

<400> 35

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atgagaggat cgcacaccca tcaccatcac ggatctggct ctggatctgg tatcgaggga      60
aggccttata atggaactgg atccgcatgc gagctcatgg ctaagactca agcagaaata      120
aataaacggt tagatgctta tgcaaaagga acagtagata gcccttacag agttaaaaaa      180
gctacaagtt atgacccatc atttggtgta atggaagcag gagccattga tgcagatggt      240
tactatcacg ctcatgttca agaccttatt acagactatg ttttatgggt aacagataat      300
aaagttagaa cttggggtaa tgctaaagac caaattaaac agagttatgg tactggattt      360
aaaatacatg aaaataaacc ttctactgta cctaaaaaag gttggattgc ggtattttaca      420
tccggtagtt atgaacagtg gggtcacata ggtattgtat atgatggagg taatacttct      480
acattttacta ttttagagca aaactggaat ggttatgcta ataaaaaacc tacaaaacgt      540
gtagataatt attacggatt aactcacttc attgaaatac ctgtaaaagc aggaactact      600
gttaaaaaag aaacagctaa gaaaagcgca agtaaaacgc ctgcaccta aaagaaagca      660
acactaaaag tttctaagaa tggtaaactc gcaagtaaaa taacagttgg aagtaaagcg      720
tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt      780

```

```

ccttataacc ttaaatgggc aaaaggtgct tattttaatg cgaaaatcga cggcttaggt      780
gctacttcag ccactagata cggtgataat cgtactaact atagattcga tgttggacag      840
gctgtatacg cgcctggaac attaatatat gtgtttgaaa ttatagatgg ttggtgtcgc      900
atttattgga acaatcataa tgagtggata tggcatgaga gattgattgt gaaagaagtg      960
ttttaa                                          966

```

<210> 36

<211> 321

<212> PRT

<213> artificial

<220>

<223> artificial construct

<400> 36

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Met Arg Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser
1          5          10          15

Gly Ile Glu Gly Arg Pro Tyr Asn Gly Thr Gly Ser Ala Cys Glu Leu
20          25          30

Met Ala Lys Thr Gln Ala Glu Ile Asn Lys Arg Leu Asp Ala Tyr Ala
35          40          45

Lys Gly Thr Val Asp Ser Pro Tyr Arg Val Lys Lys Ala Thr Ser Tyr
50          55          60

Asp Pro Ser Phe Gly Val Met Glu Ala Gly Ala Ile Asp Ala Asp Gly
65          70          75          80

Tyr Tyr His Ala Gln Cys Gln Asp Leu Ile Thr Asp Tyr Val Leu Trp
85          90          95

Leu Thr Asp Asn Lys Val Arg Thr Trp Gly Asn Ala Lys Asp Gln Ile
100         105         110

Lys Gln Ser Tyr Gly Thr Gly Phe Lys Ile His Glu Asn Lys Pro Ser
115         120         125

Thr Val Pro Lys Lys Gly Trp Ile Ala Val Phe Thr Ser Gly Ser Tyr
130         135         140

Glu Gln Trp Gly His Ile Gly Ile Val Tyr Asp Gly Gly Asn Thr Ser
145         150         155         160

Thr Phe Thr Ile Leu Glu Gln Asn Trp Asn Gly Tyr Ala Asn Lys Lys
165         170         175

Pro Thr Lys Arg Val Asp Asn Tyr Tyr Gly Leu Thr His Phe Ile Glu
180         185         190

Ile Pro Val Lys Ala Gly Thr Thr Val Lys Lys Glu Thr Ala Lys Lys

```

195	200	205
Ser Ala Ser Lys Thr Pro	Ala Pro Lys Lys Lys	Ala Thr Leu Lys Val
210	215	220
Ser Lys Asn Gly Lys	Ser Ala Ser Lys Ile Thr	Val Gly Ser Lys Ala
225	230	235
Pro Tyr Asn Leu Lys	Trp Ser Lys Gly Ala Tyr Phe	Asn Ala Lys Ile
245	250	255
Asp Gly Leu Gly Ala Thr	Ser Ala Thr Arg Tyr Gly	Asp Asn Arg Thr
260	265	270
Asn Tyr Arg Phe Asp Val	Gly Gln Ala Val Tyr Ala	Pro Gly Thr Leu
275	280	285
Ile Tyr Val Phe Glu Ile	Ile Asp Gly Trp Cys Arg	Ile Tyr Trp Asn
290	295	300
Asn His Asn Glu Trp Ile	Trp His Glu Arg Leu Ile	Val Lys Glu Val
305	310	315
		320

Phe

<210> 37

<211> 927

<212> DNA

<213> artificial

<220>

<223> artificial construct

<400> 37

atgagaggat cgcacaccca tcaccatcac ggatctggct ctggatctgg tatcgaggga	60
aggccttata atggaactgg atccgcatgc gagctcatga aaaccctgaa acaagcagag	120
tcctacatta agagtaaagt aaatacagga actgattttg atggtttata tgggtatcag	180
tgtatggact tagcagtaga ttatatattac catgtaacag atggtaaaat aagaatgtgg	240
ggtaatgcta aggatgcgat aaataactct tttgggtggta ctgctacggg atataaaaac	300
taccctgctt ttagacctaa gtacgggtgat gtagtcgtat ggactactgg taattttgca	360
acttatgggc atatcgcaat agttactaac cctgaccctt atggagacct tcaatatggt	420
acagttcctg aacaaaactg gaacggtaac gggattttata aaaccgagtt agctacaatc	480
agaacacacg attacacagg aattacacat ttatttagac ctaactttgc tactgaatca	540
agtgtaaaaa agaaagatac aaagaaaaaa ccaaaaccat caaatagaga tggaataaat	600
aaagataaaa ttgtatatga tagaactaat attaattaca attggaaaca gaataaagat	660
ggcatttggt ataaagctga acatgcttcg ttcacagtga cagcaccaga gggaattatc	720
acaagataca aaggtccttg gactggtcac ccacaagctg gtgtattaca aaaaggtcaa	780
caatttcaat ctactcaact tcaaacattt caactcataa tttgactata ctggaacaaa	840

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acgattaaat atgatgaggt tcaaaaattt gacgggtcatg tttgggtatc gtgggaaacg      840
tttgagggcg aaactgtata catgccggta cgcacatggg acgctaaaac tggtaaagtt      900
ggtaagttgt ggggcgaaat taaataa      927

```

<210> 38

<211> 308

<212> PRT

<213> artificial

<220>

<223> artificial construct

<400> 38

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Met Arg Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser
1          5          10          15

Gly Ile Glu Gly Arg Pro Tyr Asn Gly Thr Gly Ser Ala Cys Glu Leu
20          25          30

Met Lys Thr Leu Lys Gln Ala Glu Ser Tyr Ile Lys Ser Lys Val Asn
35          40          45

Thr Gly Thr Asp Phe Asp Gly Leu Tyr Gly Tyr Gln Cys Met Asp Leu
50          55          60

Ala Val Asp Tyr Ile Tyr His Val Thr Asp Gly Lys Ile Arg Met Trp
65          70          75          80

Gly Asn Ala Lys Asp Ala Ile Asn Asn Ser Phe Gly Gly Thr Ala Thr
85          90          95

Val Tyr Lys Asn Tyr Pro Ala Phe Arg Pro Lys Tyr Gly Asp Val Val
100         105         110

Val Trp Thr Thr Gly Asn Phe Ala Thr Tyr Gly His Ile Ala Ile Val
115         120         125

Thr Asn Pro Asp Pro Tyr Gly Asp Leu Gln Tyr Val Thr Val Leu Glu
130         135         140

Gln Asn Trp Asn Gly Asn Gly Ile Tyr Lys Thr Glu Leu Ala Thr Ile
145         150         155         160

Arg Thr His Asp Tyr Thr Gly Ile Thr His Phe Ile Arg Pro Asn Phe
165         170         175

Ala Thr Glu Ser Ser Val Lys Lys Lys Asp Thr Lys Lys Lys Pro Lys
180         185         190

Pro Ser Asn Arg Asp Gly Ile Asn Lys Asp Lys Ile Val Tyr Asp Arg
195         200         205

Thr Asn Ile Asn Tyr Asn Trp Lys Gln Asn Lys Asp Gly Ile Trp Tyr
210         215         220

```

Lys Ala Glu His Ala Ser Phe Thr Val Thr Ala Pro Glu Gly Ile Ile
225 230 235 240

Thr Arg Tyr Lys Gly Pro Trp Thr Gly His Pro Gln Ala Gly Val Leu
245 250 255

Gln Lys Gly Gln Thr Ile Lys Tyr Asp Glu Val Gln Lys Phe Asp Gly
260 265 270

His Val Trp Val Ser Trp Glu Thr Phe Glu Gly Glu Thr Val Tyr Met
275 280 285

Pro Val Arg Thr Trp Asp Ala Lys Thr Gly Lys Val Gly Lys Leu Trp
290 295 300

Gly Glu Ile Lys
305

<210> 39

<211> 921

<212> DNA

<213> artificial

<220>

<223> artificial construct

<400> 39

atgagaggat cgcacaccca tcaccatcac ggatctggct ctggatctgg tatcgaggga	60
aggccttata atggaactgg atccgcatgc gagctcatga aaaccctgaa acaagcagag	120
tcctacatta agagtaaagt aaatacagga actgattttg atggtttata tgggtatcag	180
tgtatggact tagcagtaga ttatatattac catgtaacag atggtaaaat aagaatgtgg	240
ggtaatgcta aggatgcgat aaataactct tttgggtggta ctgctacggg atataaaaac	300
taccctgctt ttagacctaa gtacgggtgat gtagtcgtat ggactactgg taattttgca	360
acttatggtc atatcgcaat agttactaac cctgaccctt atggagacct tcaatatggt	420
acagttcttg aacaaaactg gaacggtaac gggattttata aaaccgagtt agctacaatc	480
agaacacacg attacacagg aattacacat tttattagac ctaactttgc tactgaatca	540
agtgtaaaaa agaaagatac aaagaaaaaa ccaaaccat caaatagaga tggaataaat	600
aaagataaaa ttgtatatga tagaactaat attaattaca attggaaaac aaacaaatat	660
ggcacactat ataaatcaga gtcagctagc ttcacaccta atacagatat aataacaaga	720
acgactggtc catttagaag catgccgcag tcaggagtct taaaagcagg tcaaacaatt	780
cattatgatg aagtgatgaa acaagacggg catgtttggg taggttatatc aggtaacagt	840
ggccaacgta tttacttgcc tgtaagaaca tggaataaat ctactaatac tttaggtggt	900
ctttggggaa ctataaagta a	921

<210> 40

<211> 306

<212> PRT

<213> artificial

<220>

<223> artificial construct

<400> 40

Met Arg Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser

1 5 10 15

Gly Ile Glu Gly Arg Pro Tyr Asn Gly Thr Gly Ser Ala Cys Glu Leu
20 25 30Met Lys Thr Leu Lys Gln Ala Glu Ser Tyr Ile Lys Ser Lys Val Asn
35 40 45Thr Gly Thr Asp Phe Asp Gly Leu Tyr Gly Tyr Gln Cys Met Asp Leu
50 55 60Ala Val Asp Tyr Ile Tyr His Val Thr Asp Gly Lys Ile Arg Met Trp
65 70 75 80Gly Asn Ala Lys Asp Ala Ile Asn Asn Ser Phe Gly Gly Thr Ala Thr
85 90 95Val Tyr Lys Asn Tyr Pro Ala Phe Arg Pro Lys Tyr Gly Asp Val Val
100 105 110Val Trp Thr Thr Gly Asn Phe Ala Thr Tyr Gly His Ile Ala Ile Val
115 120 125Thr Asn Pro Asp Pro Tyr Gly Asp Leu Gln Tyr Val Thr Val Leu Glu
130 135 140Gln Asn Trp Asn Gly Asn Gly Ile Tyr Lys Thr Glu Leu Ala Thr Ile
145 150 155 160Arg Thr His Asp Tyr Thr Gly Ile Thr His Phe Ile Arg Pro Asn Phe
165 170 175Ala Thr Glu Ser Ser Val Lys Lys Lys Asp Thr Lys Lys Lys Pro Lys
180 185 190Pro Ser Asn Arg Asp Gly Ile Asn Lys Asp Lys Ile Val Tyr Asp Arg
195 200 205Thr Asn Ile Asn Tyr Asn Trp Lys Thr Asn Lys Tyr Gly Thr Leu Tyr
210 215 220Lys Ser Glu Ser Ala Ser Phe Thr Pro Asn Thr Asp Ile Ile Thr Arg
225 230 235 240Thr Thr Gly Pro Phe Arg Ser Met Pro Gln Ser Gly Val Leu Lys Ala
245 250 255

Glv Gln Thr Ile His Trp Asp Glu Val Met Lys Gln Asp Glv His Val

260 265 270
Trp Val Gly Tyr Thr Gly Asn Ser Gly Gln Arg Ile Tyr Leu Pro Val
275 280 285
Arg Thr Trp Asn Lys Ser Thr Asn Thr Leu Gly Val Leu Trp Gly Thr
290 295 300

Ile Lys
305

<210> 41
<211> 927
<212> DNA
<213> artificial

<220>
<223> artificial construct

<400> 41
atgagaggat cgcacaccca tcaccatcac ggatctggct ctggatctgg tatcgaggga 60
aggccttata atggaactgg atccgcatgc gagctcatga aaaccctgaa acaagcagag 120
tcctacatta agagtaaagt aaatacagga actgattttg atggtttata tgggtatcag 180
tgtatggact tagcagtaga ttatatattac catgtaacag atggtaaaat aagaatgtgg 240
ggtaatgcta aggatgcat aaataactct tttgggtgga ctgctacggg atataaaaac 300
taccctgctt ttagacctaa gtacgggtgat gtagtcgtat ggactactgg taattttgca 360
acttatgggc atatcgcaat agttactaac cctgaccctt atggagacct tcaatatgtt 420
acagttcttg aacaaaactg gaacggtaac gggattttata aaaccgagtt agctacaatc 480
agaacacacg attacacagg aattacacat tttattagac ctaactttgc tactgaatca 540
agtgtaaaaa agaaagatac aaagaaaaaa ccaaaccat caaatagaga tggaataaat 600
aaagataaaa ttgtatatga tagaactaat attaattaca atggtaaata tgcaagtaaa 660
ataacagttg gaagtaaagc gccttataac cttaaattgt caaaagggtgc ttattttaat 720
gcgaaaatcg acggcttagg tgctacttca gccactagat acggtgataa tcgtactaac 780
tatagattcg atgttggaac ggctgtatac gcgcctggaa cattaatata tgtgtttgaa 840
attatagatg gttgggtgtc cattttattgg aacaatcata atgagtggat atggcatgag 900
agattgattg tgaaagaagt gtttttaa 927

<210> 42
<211> 308
<212> PRT
<213> artificial

<220>
<223> artificial construct

<400> 42

Met Arg Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser
 1 5 10 15

Gly Ile Glu Gly Arg Pro Tyr Asn Gly Thr Gly Ser Ala Cys Glu Leu
 20 25 30

Met Lys Thr Leu Lys Gln Ala Glu Ser Tyr Ile Lys Ser Lys Val Asn
 35 40 45

Thr Gly Thr Asp Phe Asp Gly Leu Tyr Gly Tyr Gln Cys Met Asp Leu
 50 55 60

Ala Val Asp Tyr Ile Tyr His Val Thr Asp Gly Lys Ile Arg Met Trp
 65 70 75 80

Gly Asn Ala Lys Asp Ala Ile Asn Asn Ser Phe Gly Gly Thr Ala Thr
 85 90 95

Val Tyr Lys Asn Tyr Pro Ala Phe Arg Pro Lys Tyr Gly Asp Val Val
 100 105 110

Val Trp Thr Thr Gly Asn Phe Ala Thr Tyr Gly His Ile Ala Ile Val
 115 120 125

Thr Asn Pro Asp Pro Tyr Gly Asp Leu Gln Tyr Val Thr Val Leu Glu
 130 135 140

Gln Asn Trp Asn Gly Asn Gly Ile Tyr Lys Thr Glu Leu Ala Thr Ile
 145 150 155 160

Arg Thr His Asp Tyr Thr Gly Ile Thr His Phe Ile Arg Pro Asn Phe
 165 170 175

Ala Thr Glu Ser Ser Val Lys Lys Lys Asp Thr Lys Lys Lys Pro Lys
 180 185 190

Pro Ser Asn Arg Asp Gly Ile Asn Lys Asp Lys Ile Val Tyr Asp Arg
 195 200 205

Thr Asn Ile Asn Tyr Asn Gly Lys Ser Ala Ser Lys Ile Thr Val Gly
 210 215 220

Ser Lys Ala Pro Tyr Asn Leu Lys Trp Ser Lys Gly Ala Tyr Phe Asn
 225 230 235 240

Ala Lys Ile Asp Gly Leu Gly Ala Thr Ser Ala Thr Arg Tyr Gly Asp
 245 250 255

Asn Arg Thr Asn Tyr Arg Phe Asp Val Gly Gln Ala Val Tyr Ala Pro
 260 265 270

Gly Thr Leu Ile Tyr Val Phe Glu Ile Ile Asp Gly Trp Cys Arg Ile
 275 280 285

Thr Thr Asp Asp His Asp Gly Thr Ile Thr His Gly Asp Leu Ile Val

LYS LEP ASN ASN HIS ASN GLU LEP LIE LEP HIS GLU ARG LEU LIE VAL
290 295 300

Lys Glu Val Phe
305

<210> 43
<211> 843
<212> DNA
<213> artificial

<220>
<223> artificial construct

<400> 43
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aggccttata atggaactgg atccgcatgc gagctcgctg caacacatga acattcagca 120
caatgggttga ataattacaa aaaaggatat ggttacggtc cttatccatt aggtataaat 180
ggcgggtatgc actacggagt tgattttttt atgaatattg gaacaccagt aaaagctatt 240
tcaagcggaa aaatagttga agctgggttg agtaattacg gaggaggtaa tcaaataagg 300
cttattgaaa atgatggagt gcatagacaa tggatatatgc atctaagtaa atataatgtt 360
aaagtaggag attatgtcaa agctgggtcaa ataatcggtt ggtctggaag cactgggttat 420
tctacagcac cacatttaca cttccaaaga atgggttaatt cattttcaaa ttcaactgcc 480
caagatccaa tgcctttctt aaagagcgcg ggatatggaa aagcaggtgg tacagtaact 540
ccaacgccga atacagggtg gaaacagaat aaagatggca tttggtataa agctgaacat 600
gcttcgttca cagtgcacgc accagaggga attatcacaa gatacaaagg tccttggact 660
ggtcacccac aagctgggtg attacaaaaa ggtcaaacga ttaaatatga tgaggttcaa 720
aaatttgacg gtcattgttg ggtatcgtgg gaaacgtttg agggcgaaac tgtatacatg 780
ccggtacgca catgggacgc taaaactggg aaagttggta agttgtgggg cgaaattaaa 840
taa 843

<210> 44
<211> 280
<212> PRT
<213> artificial

<220>
<223> artificial construct

<400> 44
Met Arg Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser
1 5 10 15

Gly Ile Glu Gly Arg Pro Tyr Asn Gly Thr Gly Ser Ala Cys Glu Leu
20 25 30

Ala Ala Thr His Glu His Ser Ala Gln Trp Leu Asn Asn Tyr Lys Lys
35 40 45 50 55 60

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

<210> 45

<211> 837

<212> DNA

<213> artificial

$\langle 220 \rangle$

<223> artificial construct

<400> 45

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aggccttata atggaactgg atccgcatgc gagctcgctg caacacatga acattcagca      120
caatgggttga ataattacaa aaaaggatat ggttacggtc cttatccatt aggtataaat      180
ggcggtatgc actacggagt tgattttttt atgaatattg gaacaccagt aaaagctatt      240
tcaagcggaa aaatagttga agctggttgg agtaattacg gaggaggtaa tcaaataagg      300
cttattgaaa atgatggagt gcatagacaa tggatatatgc atctaagtaa atataatgtt      360
aaagtaggag attatgtcaa agctgggtcaa ataatcggtt ggtctggaag cactgggttat      420
tctacagcac cacatttaca cttccaaaga atggttaatt cattttcaaa ttcaactgcc      480
caagatccaa tgcctttctt aaagagcgca ggatatggaa aagcagggtg tacagtaact      540
ccaacgccga atacagggtg gaaaacaaac aaatatggca cactatataa atcagagtca      600
gctagcttca cacctaatac agatataata acaagaacga ctgggtccatt tagaagcatg      660
ccgcagtcag gagtcttaaa agcagggtcaa acaattcatt atgatgaagt gatgaaacaa      720
gacggtcatg tttgggtagg ttatacaggt aacagtggcc aacgtattta cttgcctgta      780
agaacatgga ataaatctac taatacttta ggtgttcttt ggggaactat aaagtaa      837

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<210> 46

<211> 278

<212> PRT

<213> artificial

<220>

<223> artificial construct

<400> 46

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Met Arg Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser
1          5          10          15

Gly Ile Glu Gly Arg Pro Tyr Asn Gly Thr Gly Ser Ala Cys Glu Leu
20          25          30

Ala Ala Thr His Glu His Ser Ala Gln Trp Leu Asn Asn Tyr Lys Lys
35          40          45

Gly Tyr Gly Tyr Gly Pro Tyr Pro Leu Gly Ile Asn Gly Gly Met His
50          55          60

Tyr Gly Val Asp Phe Phe Met Asn Ile Gly Thr Pro Val Lys Ala Ile
65          70          75          80

Ser Ser Gly Lys Ile Val Glu Ala Gly Trp Ser Asn Tyr Gly Gly Gly
85          90          95

Asn Gln Ile Gly Leu Ile Glu Asn Asp Gly Val His Arg Gln Trp Tyr
100         105         110

Met His Leu Ser Lys Tyr Asn Val Lys Val Gly Asp Tyr Val Lys Ala
115         120         125

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Gly Gln Ile Ile Gly Trp Ser Gly Ser Thr Gly Tyr Ser Thr Ala Pro
130 135 140

His Leu His Phe Gln Arg Met Val Asn Ser Phe Ser Asn Ser Thr Ala
145 150 155 160

Gln Asp Pro Met Pro Phe Leu Lys Ser Ala Gly Tyr Gly Lys Ala Gly
165 170 175

Gly Thr Val Thr Pro Thr Pro Asn Thr Gly Trp Lys Thr Asn Lys Tyr
180 185 190

Gly Thr Leu Tyr Lys Ser Glu Ser Ala Ser Phe Thr Pro Asn Thr Asp
195 200 205

Ile Ile Thr Arg Thr Thr Gly Pro Phe Arg Ser Met Pro Gln Ser Gly
210 215 220

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

Asp Gly His Val Trp Val Gly Tyr Thr Gly Asn Ser Gly Gln Arg Ile
245 250 255

Tyr Leu Pro Val Arg Thr Trp Asn Lys Ser Thr Asn Thr Leu Gly Val
260 265 270

Leu Trp Gly Thr Ile Lys
275

<210> 47

<211> 843

<212> DNA

<213> artificial

<220>

<223> artificial construct

<400> 47

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caatgggttga ataattacaa aaaaggatat ggttacgggtc cttatccatt aggtataaat	180
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tctacagcac cacatttaca cttccaaaga atggttaatt cattttcaaa ttcaactgcc	480
caagatccaa tgcctttctt aaagagcgca ggatatggaa aagcaggtgg tacagtaact	540
ccaacgccga atacaggtgg taaatctgca agtaaaataa cagttggaag taaagcgcct	600

tataacctta aatgggtcaaa aggtgcttat tttaatgcga aaatcgacgg cttaggtgct 660
 acttcagcca ctagatacgg tgataatcgt actaactata gattcgatgt tggacaggct 720
 gtatacgcgc ctggaacatt aatatatgtg tttgaaatta tagatgggtg gtgtcgcatt 780
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 taa 843

<210> 48

<211> 280

<212> PRT

<213> artificial

<220>

<223> artificial construct

<400> 48

Met Arg Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser

1 5 10 15

Gly Ile Glu Gly Arg Pro Tyr Asn Gly Thr Gly Ser Ala Cys Glu Leu
 20 25 30

Ala Ala Thr His Glu His Ser Ala Gln Trp Leu Asn Asn Tyr Lys Lys
 35 40 45

Gly Tyr Gly Tyr Gly Pro Tyr Pro Leu Gly Ile Asn Gly Gly Met His
 50 55 60

Tyr Gly Val Asp Phe Phe Met Asn Ile Gly Thr Pro Val Lys Ala Ile
 65 70 75 80

Ser Ser Gly Lys Ile Val Glu Ala Gly Trp Ser Asn Tyr Gly Gly Gly
 85 90 95

Asn Gln Ile Gly Leu Ile Glu Asn Asp Gly Val His Arg Gln Trp Tyr
 100 105 110

Met His Leu Ser Lys Tyr Asn Val Lys Val Gly Asp Tyr Val Lys Ala
 115 120 125

Gly Gln Ile Ile Gly Trp Ser Gly Ser Thr Gly Tyr Ser Thr Ala Pro
 130 135 140

His Leu His Phe Gln Arg Met Val Asn Ser Phe Ser Asn Ser Thr Ala
 145 150 155 160

Gln Asp Pro Met Pro Phe Leu Lys Ser Ala Gly Tyr Gly Lys Ala Gly
 165 170 175

Gly Thr Val Thr Pro Thr Pro Asn Thr Gly Gly Lys Ser Ala Ser Lys
 180 185 190

Ile Thr Val Gly Ser Lys Ala Pro Tyr Asn Leu Lys Trp Ser Lys Gly
195 200 205

Ala Tyr Phe Asn Ala Lys Ile Asp Gly Leu Gly Ala Thr Ser Ala Thr
210 215 220

Arg Tyr Gly Asp Asn Arg Thr Asn Tyr Arg Phe Asp Val Gly Gln Ala
225 230 235 240

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

Trp Cys Arg Ile Tyr Trp Asn Asn His Asn Glu Trp Ile Trp His Glu
260 265 270

Arg Leu Ile Val Lys Glu Val Phe
275 280

<210> 49

<211> 1755

<212> DNA

<213> artificial

<220>

<223> artificial construct

<400> 49

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attacaaatt taaatgctaa acaagataaa tcaaagaatg ggagcgtgaa agagttgaaa	180
catatctatt caaacatat taaaggtaac aagattacag caccaaaacc tagtattcaa	240
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aacgaagtgc tttggtatca tccgacagac tacgtagagt ggcattgtgg taatcaatgg	420
gcaaatgcta acttaatcgg atttgaagtg tgtgagtcgt atcctggtag aatctcggac	480
aaattattct tagaaaatga agaagcgaca ttgaaagtag ctgcggatgt gatgaagtcg	540
tacggattac cagttaatcg caacactgta cgtctgcata acgaattctt cggaacttct	600
tgtccacatc gttcgtggga cttgcatggt ggcaaagggt agccttacac aactactaat	660
attaataaaa tgaaagacta cttcatcaaa cgcacaaac attattatga cggtgagctc	720
gcaaagaaag atgaaaaatc acaagtatgt agtggtttgg ctatggaaaa atatgacatt	780
acaaatttaa atgctaaaca agataaatca aagaatggga gcgtgaaaga gttgaaacat	840
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gaagtgcctt ggtatcatcc gacagactac gtagagtggc attgtggtaa tcaatgggca	1080
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gatgaggttc aaaaatttga cggtcatggt tgggtatcgt gggaaacggt tgagggcgaa 1680
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ggcgaaatta aataa 1755

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<210> 50

<211> 584

<212> PRT

<213> artificial

<220>

<223> artificial construct

<400> 50

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Met Arg Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser
1          5          10          15

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```

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

```

```

Gly Leu Ala Met Glu Lys Tyr Asp Ile Thr Asn Leu Asn Ala Lys Gln
35          40          45

```

```

Asp Lys Ser Lys Asn Gly Ser Val Lys Glu Leu Lys His Ile Tyr Ser
50          55          60

```

```

Asn His Ile Lys Gly Asn Lys Ile Thr Ala Pro Lys Pro Ser Ile Gln
65          70          75          80

```

```

Gly Val Val Ile His Asn Asp Tyr Gly Ser Met Thr Pro Ser Gln Tyr
85          90          95

```

```

Leu Pro Trp Leu Tyr Ala Arg Glu Asn Asn Gly Thr His Val Asn Gly
100         105         110

```

```

Trp Ala Ser Val Tyr Ala Asn Arg Asn Glu Val Leu Trp Tyr His Pro
115         120         125

```

```

Thr Asp Tyr Val Glu Trp His Cys Gly Asn Gln Trp Ala Asn Ala Asn
130         135         140

```

```

Trp Thr Glu Asn Glu Val Cys Gly Asp Thr Ser Gly Ser Thr Glu Ser
145         150         155         160         165

```

Leu Ile Gly Phe Glu Val Cys Glu Ser Tyr Pro Gly Arg Ile Ser Asp
145 150 155 160

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

Val Met Lys Ser Tyr Gly Leu Pro Val Asn Arg Asn Thr Val Arg Leu
180 185 190

His Asn Glu Phe Phe Gly Thr Ser Cys Pro His Arg Ser Trp Asp Leu
195 200 205

His Val Gly Lys Gly Glu Pro Tyr Thr Thr Thr Asn Ile Asn Lys Met
210 215 220

Lys Asp Tyr Phe Ile Lys Arg Ile Lys His Tyr Tyr Asp Gly Glu Leu
225 230 235 240

Ala Lys Lys Asp Glu Lys Ser Gln Val Cys Ser Gly Leu Ala Met Glu
245 250 255

Lys Tyr Asp Ile Thr Asn Leu Asn Ala Lys Gln Asp Lys Ser Lys Asn
260 265 270

Gly Ser Val Lys Glu Leu Lys His Ile Tyr Ser Asn His Ile Lys Gly
275 280 285

Asn Lys Ile Thr Ala Pro Lys Pro Ser Ile Gln Gly Val Val Ile His
290 295 300

Asn Asp Tyr Gly Ser Met Thr Pro Ser Gln Tyr Leu Pro Trp Leu Tyr
305 310 315 320

Ala Arg Glu Asn Asn Gly Thr His Val Asn Gly Trp Ala Ser Val Tyr
325 330 335

Ala Asn Arg Asn Glu Val Leu Trp Tyr His Pro Thr Asp Tyr Val Glu
340 345 350

Trp His Cys Gly Asn Gln Trp Ala Asn Ala Asn Leu Ile Gly Phe Glu
355 360 365

Val Cys Glu Ser Tyr Pro Gly Arg Ile Ser Asp Lys Leu Phe Leu Glu
370 375 380

Asn Glu Glu Ala Thr Leu Lys Val Ala Ala Asp Val Met Lys Ser Tyr
385 390 395 400

Gly Leu Pro Val Asn Arg Asn Thr Val Arg Leu His Asn Glu Phe Phe
405 410 415

Gly Thr Ser Cys Pro His Arg Ser Trp Asp Leu His Val Gly Lys Gly
420 425 430

Glu Pro Tyr Thr Thr Thr Asn Ile Asn Lys Met Lys Asp Tyr Phe Ile
435 440 445

Lys Arg Ile Lys His Tyr Tyr Asp Gly Gly Lys Leu Glu Val Ser Lys
450 455 460

Ala Ala Thr Ile Lys Gln Ser Asp Val Lys Gln Glu Val Lys Lys Gln
465 470 475 480

Glu Ala Lys Gln Ile Val Lys Ala Thr Asp Trp Lys Gln Asn Lys Asp
485 490 495

Gly Ile Trp Tyr Lys Ala Glu His Ala Ser Phe Thr Val Thr Ala Pro
500 505 510

Glu Gly Ile Ile Thr Arg Tyr Lys Gly Pro Trp Thr Gly His Pro Gln
515 520 525

Ala Gly Val Leu Gln Lys Gly Gln Thr Ile Lys Tyr Asp Glu Val Gln
530 535 540

Lys Phe Asp Gly His Val Trp Val Ser Trp Glu Thr Phe Glu Gly Glu
545 550 555 560

Thr Val Tyr Met Pro Val Arg Thr Trp Asp Ala Lys Thr Gly Lys Val
565 570 575

Gly Lys Leu Trp Gly Glu Ile Lys
580

<210> 51

<211> 1749

<212> DNA

<213> artificial

<220>

<223> artificial construct

<400> 51

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attacaaatt taaatgctaa acaagataaa tcaaagaatg ggagcgtgaa agagttgaaa	180
catatctatt caaacatat taaaggtaac aagattacag caccaaaacc tagtattcaa	240
ggtgtggtca tccacaatga ttatggtagt atgacaccta gtcaatactt accatgggta	300
tatgcacgtg agaataacgg tacacacgtt aacggttggg ctagtggtta tgcaaataga	360
aacgaagtgc tttggtatca tccgacagac tacgtagagt ggcattgtgg taatcaatgg	420
gcaaatgcta acttaatcgg atttgaagtg tgtgagtcgt atcctggtag aatctcggac	480
aaattattct tagaaaatga agaagcgaca ttgaaagtag ctgcggatgt gatgaagtgc	540
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<210> 52

<211> 582

<212> PRT

<213> artificial

<220>

<223> artificial construct

<400> 52

Met	Arg	Gly	Ser	His	His	His	His	His	His	Gly	Ser	Gly	Ser	Gly	Ser
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Gly	Ile	Glu	Gly	Arg	Ala	Lys	Lys	Asp	Glu	Lys	Ser	Gln	Val	Cys	Ser
			20					25					30		
Gly	Leu	Ala	Met	Glu	Lys	Tyr	Asp	Ile	Thr	Asn	Leu	Asn	Ala	Lys	Gln
		35					40					45			
Asp	Lys	Ser	Lys	Asn	Gly	Ser	Val	Lys	Glu	Leu	Lys	His	Ile	Tyr	Ser
	50				55					60					
Asn	His	Ile	Lys	Gly	Asn	Lys	Ile	Thr	Ala	Pro	Lys	Pro	Ser	Ile	Gln
65					70				75						80
Gly	Val	Val	Ile	His	Asn	Asp	Tyr	Gly	Ser	Met	Thr	Pro	Ser	Gln	Tyr
			85					90						95	

Leu Pro Trp Leu Tyr Ala Arg Glu Asn Asn Gly Thr His Val Asn Gly
 100 105 110

Trp Ala Ser Val Tyr Ala Asn Arg Asn Glu Val Leu Trp Tyr His Pro
 115 120 125

Thr Asp Tyr Val Glu Trp His Cys Gly Asn Gln Trp Ala Asn Ala Asn
 130 135 140

Leu Ile Gly Phe Glu Val Cys Glu Ser Tyr Pro Gly Arg Ile Ser Asp
 145 150 155 160

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

Val Met Lys Ser Tyr Gly Leu Pro Val Asn Arg Asn Thr Val Arg Leu
 180 185 190

His Asn Glu Phe Phe Gly Thr Ser Cys Pro His Arg Ser Trp Asp Leu
 195 200 205

His Val Gly Lys Gly Glu Pro Tyr Thr Thr Thr Asn Ile Asn Lys Met
 210 215 220

Lys Asp Tyr Phe Ile Lys Arg Ile Lys His Tyr Tyr Asp Gly Glu Leu
 225 230 235 240

Ala Lys Lys Asp Glu Lys Ser Gln Val Cys Ser Gly Leu Ala Met Glu
 245 250 255

Lys Tyr Asp Ile Thr Asn Leu Asn Ala Lys Gln Asp Lys Ser Lys Asn
 260 265 270

Gly Ser Val Lys Glu Leu Lys His Ile Tyr Ser Asn His Ile Lys Gly
 275 280 285

Asn Lys Ile Thr Ala Pro Lys Pro Ser Ile Gln Gly Val Val Ile His
 290 295 300

Asn Asp Tyr Gly Ser Met Thr Pro Ser Gln Tyr Leu Pro Trp Leu Tyr
 305 310 315 320

Ala Arg Glu Asn Asn Gly Thr His Val Asn Gly Trp Ala Ser Val Tyr
 325 330 335

Ala Asn Arg Asn Glu Val Leu Trp Tyr His Pro Thr Asp Tyr Val Glu
 340 345 350

Trp His Cys Gly Asn Gln Trp Ala Asn Ala Asn Leu Ile Gly Phe Glu
 355 360 365

Val Cys Glu Ser Tyr Pro Gly Arg Ile Ser Asp Lys Leu Phe Leu Glu
 370 375 380

Asn Glu Glu Ala Thr Leu Lys Val Ala Ala Asp Val Met Lys Ser Tyr
 385 390 395 400

Gly Leu Pro Val Asn Arg Asn Thr Val Arg Leu His Asn Glu Phe Phe
405 410 415

Gly Thr Ser Cys Pro His Arg Ser Trp Asp Leu His Val Gly Lys Gly
420 425 430

Glu Pro Tyr Thr Thr Thr Asn Ile Asn Lys Met Lys Asp Tyr Phe Ile
435 440 445

Lys Arg Ile Lys His Tyr Tyr Asp Gly Gly Lys Leu Glu Val Ser Lys
450 455 460

Ala Ala Thr Ile Lys Gln Ser Asp Val Lys Gln Glu Val Lys Lys Gln
465 470 475 480

Glu Ala Lys Gln Ile Val Lys Ala Thr Asp Trp Lys Thr Asn Lys Tyr
485 490 495

Gly Thr Leu Tyr Lys Ser Glu Ser Ala Ser Phe Thr Pro Asn Thr Asp
500 505 510

Ile Ile Thr Arg Thr Thr Gly Pro Phe Arg Ser Met Pro Gln Ser Gly
515 520 525

Val Leu Lys Ala Gly Gln Thr Ile His Tyr Asp Glu Val Met Lys Gln
530 535 540

Asp Gly His Val Trp Val Gly Tyr Thr Gly Asn Ser Gly Gln Arg Ile
545 550 555 560

Tyr Leu Pro Val Arg Thr Trp Asn Lys Ser Thr Asn Thr Leu Gly Val
565 570 575

Leu Trp Gly Thr Ile Lys
580

<210> 53
<211> 1755
<212> DNA
<213> artificial

<220>
<223> artificial construct

<400> 53
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 aaagaagtgt tttaa 1755

<210> 54

<211> 584

<212> PRT

<213> artificial

<220>

<223> artificial construct

<400> 54

Met Arg Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser
 1 5 10 15

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

Glv Leu Ala Met Glu Lys Trp Asp Ile Thr Asn Leu Asn Ala Lys Gln

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      35              40              45
Asp Lys Ser Lys Asn Gly Ser Val Lys Glu Leu Lys His Ile Tyr Ser
 50              55              60

Asn His Ile Lys Gly Asn Lys Ile Thr Ala Pro Lys Pro Ser Ile Gln
65              70              75              80

Gly Val Val Ile His Asn Asp Tyr Gly Ser Met Thr Pro Ser Gln Tyr
      85              90              95

Leu Pro Trp Leu Tyr Ala Arg Glu Asn Asn Gly Thr His Val Asn Gly
      100              105              110

Trp Ala Ser Val Tyr Ala Asn Arg Asn Glu Val Leu Trp Tyr His Pro
      115              120              125

Thr Asp Tyr Val Glu Trp His Cys Gly Asn Gln Trp Ala Asn Ala Asn
      130              135              140

Leu Ile Gly Phe Glu Val Cys Glu Ser Tyr Pro Gly Arg Ile Ser Asp
      145              150              155              160

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

Val Met Lys Ser Tyr Gly Leu Pro Val Asn Arg Asn Thr Val Arg Leu
      180              185              190

His Asn Glu Phe Phe Gly Thr Ser Cys Pro His Arg Ser Trp Asp Leu
      195              200              205

His Val Gly Lys Gly Glu Pro Tyr Thr Thr Thr Asn Ile Asn Lys Met
      210              215              220

Lys Asp Tyr Phe Ile Lys Arg Ile Lys His Tyr Tyr Asp Gly Glu Leu
      225              230              235              240

Ala Lys Lys Asp Glu Lys Ser Gln Val Cys Ser Gly Leu Ala Met Glu
      245              250              255

Lys Tyr Asp Ile Thr Asn Leu Asn Ala Lys Gln Asp Lys Ser Lys Asn
      260              265              270

Gly Ser Val Lys Glu Leu Lys His Ile Tyr Ser Asn His Ile Lys Gly
      275              280              285

Asn Lys Ile Thr Ala Pro Lys Pro Ser Ile Gln Gly Val Val Ile His
      290              295              300

Asn Asp Tyr Gly Ser Met Thr Pro Ser Gln Tyr Leu Pro Trp Leu Tyr
      305              310              315              320

Ala Arg Glu Asn Asn Gly Thr His Val Asn Gly Trp Ala Ser Val Tyr
      325              330              335

Ala Asn Arg Asn Glu Val Leu Trp Trp His Pro Thr Asp Trp Val Glu

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          340          345          350
Trp His Cys Gly Asn Gln Trp Ala Asn Ala Asn Leu Ile Gly Phe Glu
      355          360          365

Val Cys Glu Ser Tyr Pro Gly Arg Ile Ser Asp Lys Leu Phe Leu Glu
      370          375          380

Asn Glu Glu Ala Thr Leu Lys Val Ala Ala Asp Val Met Lys Ser Tyr
385          390          395          400

Gly Leu Pro Val Asn Arg Asn Thr Val Arg Leu His Asn Glu Phe Phe
          405          410          415

Gly Thr Ser Cys Pro His Arg Ser Trp Asp Leu His Val Gly Lys Gly
          420          425          430

Glu Pro Tyr Thr Thr Thr Asn Ile Asn Lys Met Lys Asp Tyr Phe Ile
      435          440          445

Lys Arg Ile Lys His Tyr Tyr Asp Gly Gly Lys Leu Glu Val Ser Lys
      450          455          460

Ala Ala Thr Ile Lys Gln Ser Asp Val Lys Gln Glu Val Lys Lys Gln
465          470          475          480

Glu Ala Lys Gln Ile Val Lys Ala Thr Asp Gly Lys Ser Ala Ser Lys
          485          490          495

Ile Thr Val Gly Ser Lys Ala Pro Tyr Asn Leu Lys Trp Ser Lys Gly
      500          505          510

Ala Tyr Phe Asn Ala Lys Ile Asp Gly Leu Gly Ala Thr Ser Ala Thr
      515          520          525

Arg Tyr Gly Asp Asn Arg Thr Asn Tyr Arg Phe Asp Val Gly Gln Ala
      530          535          540

Val Tyr Ala Pro Gly Thr Leu Ile Tyr Val Phe Glu Ile Ile Asp Gly
545          550          555          560

Trp Cys Arg Ile Tyr Trp Asn Asn His Asn Glu Trp Ile Trp His Glu
          565          570          575

Arg Leu Ile Val Lys Glu Val Phe
      580

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<210> 55

<211> 1533

<212> DNA

<213> artificial

<220>

<223> artificial construct

<400> 55

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gtagatagcc cttacagagt taaaaaagct acaagttatg acccatcatt tgggtgtaatg      180
gaagcaggag ccattgatgc agatgggttac tatcacgctc agtgtcaaga ccttattaca      240
gactatgttt tatggttaac agataataaa gttagaactt ggggtaatgc taaagaccaa      300
attaaacaga gttatgggtac tggattttaa atacatgaaa ataaaccttc tactgtacct      360
aaaaaagggt ggattgcggg atttacatcc ggtagttatg aacagtgggg tcacataggt      420
attgtatatg atggaggtaa tacttctaca ttactatatt tagagcaaaa ctggaatggg      480
tatgctaata aaaaacctac aaaacgtgta gataattatt acggattaac tcacttcatt      540
gaaataacctg taaaagcagg aactactgtt aaaaaagaaa cagctaagaa aagcgcaagt      600
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aagactcaag cagaaataaa taaacgttta gatgcttatg caaaaggaac agtagatagc      720
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gccattgatg cagatgggta ctatcacgct cagtgtcaag acctatttac agactatggt      840
ttatgggttaa cagataataa agttagaact tggggtaatg ctaaagacca aattaaacag      900
agttatggta ctggatttaa aatacatgaa aataaacctt ctactgtacc taaaaaagg      960
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gatggaggta atacttctac atttactatt ttagagcaaa actggaatgg ttatgctaatt     1080
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gtaaaagcag gaaagctaga agtaagcaaa gcagcaacta tcaaacaatc tgacgttaag     1200
caagaagtta aaaagcaaga agcaaaacaa attgtgaaag caacagattg gaaacagaat     1260
aaagatggca tttggtataa agctgaacat gcttcgttca cagtgcagc accagaggga     1320
attatcacia gatacaaagg tccttggact ggtcacccac aagctgggtg attacaaaaa     1380
ggtcaaacga ttaaatatga tgaggttcaa aaatttgacg gtcatgtttg ggtatcgtgg     1440
gaaacgtttg agggcgaaac tgtatacatg ccggtacgca catgggacgc taaaactggg     1500
aaagttggta agttgtgggg cgaaattaaa taa                                     1533

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<210> 56

<211> 510

<212> PRT

<213> artificial

<220>

<223> artificial construct

<400> 56

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Met Arg Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser
1          5          10          15

Gly Ile Glu Gly Arg Met Ala Lys Thr Gln Ala Glu Ile Asn Lys Arg
20          25          30

```

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

Lys Ala Thr Ser Tyr Asp Pro Ser Phe Gly Val Met Glu Ala Gly Ala
50 55 60

Ile Asp Ala Asp Gly Tyr Tyr His Ala Gln Cys Gln Asp Leu Ile Thr
65 70 75 80

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

Ala Lys Asp Gln Ile Lys Gln Ser Tyr Gly Thr Gly Phe Lys Ile His
100 105 110

Glu Asn Lys Pro Ser Thr Val Pro Lys Lys Gly Trp Ile Ala Val Phe
115 120 125

Thr Ser Gly Ser Tyr Glu Gln Trp Gly His Ile Gly Ile Val Tyr Asp
130 135 140

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

Tyr Ala Asn Lys Lys Pro Thr Lys Arg Val Asp Asn Tyr Tyr Gly Leu
165 170 175

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

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

Ala Thr Leu Lys Val Ser Lys Asn Glu Leu Met Ala Lys Thr Gln Ala
210 215 220

Glu Ile Asn Lys Arg Leu Asp Ala Tyr Ala Lys Gly Thr Val Asp Ser
225 230 235 240

Pro Tyr Arg Val Lys Lys Ala Thr Ser Tyr Asp Pro Ser Phe Gly Val
245 250 255

Met Glu Ala Gly Ala Ile Asp Ala Asp Gly Tyr Tyr His Ala Gln Cys
260 265 270

Gln Asp Leu Ile Thr Asp Tyr Val Leu Trp Leu Thr Asp Asn Lys Val
275 280 285

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

Gly Phe Lys Ile His Glu Asn Lys Pro Ser Thr Val Pro Lys Lys Gly
305 310 315 320

Trp Ile Ala Val Phe Thr Ser Glv Ser Trv Glu Gln Trp Glv His Ile

```

-----
          325          330          335
Gly Ile Val Tyr Asp Gly Gly Asn Thr Ser Thr Phe Thr Ile Leu Glu
          340          345          350
Gln Asn Trp Asn Gly Tyr Ala Asn Lys Lys Pro Thr Lys Arg Val Asp
          355          360          365
Asn Tyr Tyr Gly Leu Thr His Phe Ile Glu Ile Pro Val Lys Ala Gly
          370          375          380
Lys Leu Glu Val Ser Lys Ala Ala Thr Ile Lys Gln Ser Asp Val Lys
          385          390          395          400
Gln Glu Val Lys Lys Gln Glu Ala Lys Gln Ile Val Lys Ala Thr Asp
          405          410          415
Trp Lys Gln Asn Lys Asp Gly Ile Trp Tyr Lys Ala Glu His Ala Ser
          420          425          430
Phe Thr Val Thr Ala Pro Glu Gly Ile Ile Thr Arg Tyr Lys Gly Pro
          435          440          445
Trp Thr Gly His Pro Gln Ala Gly Val Leu Gln Lys Gly Gln Thr Ile
          450          455          460
Lys Tyr Asp Glu Val Gln Lys Phe Asp Gly His Val Trp Val Ser Trp
          465          470          475          480
Glu Thr Phe Glu Gly Glu Thr Val Tyr Met Pro Val Arg Thr Trp Asp
          485          490          495
Ala Lys Thr Gly Lys Val Gly Lys Leu Trp Gly Glu Ile Lys
          500          505          510

```

<210> 57

<211> 1470

<212> DNA

<213> artificial

<220>

<223> artificial construct

<400> 57

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gtagatagcc cttacagagt taaaaaagct acaagttatg acccatcatt tgggtgtaatg      180
gaagcaggag ccattgatgc agatgggttac tatcacgctc agtgtcaaga ccttattaca      240
gactatgttt tatggttaac agataataaa gtagaactt ggggtaatgc taaagaccaa      300
attaaacaga gttatggtac tggattttaa atacatgaaa ataaaccttc tactgtacct      360
aaaaaagggt ggattgcggt atttacatcc ggtagttatg aacagtgggg tcacataggt      420
attgtatatg atggaggtaa tacttctaca ttactatatt tagagcaaaa ctggaatggt      480

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tatgctaata aaaaacctac aaaacgtgta gataattatt acggattaac tcacttcatt 540
 gaaatacctg taaaagcagg aactactggt aaaaaagaaa cagctaagaa aagcgcaagt 600
 aaaacgcctg cacctaataaa gaaagcaaca ctaaaagttt ctaagaatga gctcatggct 660
 aagactcaag cagaaataaa taaacgttta gatgcttatg caaaaggaac agtagatagc 720
 ccttacagag ttaaaaaagc tacaagttat gacccatcat ttggtgtaat ggaagcagga 780
 gccattgatg cagatgggta ctatcacgct cagtgtcaag accttattac agactatggt 840
 ttatgggttaa cagataataa agttagaact tggggtaatg ctaaagacca aattaaacag 900
 agttatggta ctggatttaa aatacatgaa aataaacctt ctactgtacc taaaaaaggt 960
 tggattgctg tatttacatc cggtagtatt gaacagtggg gtcacatagg tattgtatat 1020
 gatggaggta atacttctac atttactatt ttagagcaaa actggaatgg ttatgctaata 1080
 aaaaaaccta caaacgtgt agataattat tacggattaa ctcacttcatt tgaaatacct 1140
 gtaaaagcag gaaaagcagg tgggtacagta actccaacgc cgaatacagg ttggaaaaca 1200
 aacaaatatg gcacactata taaatcagag tcagctagct tcacacctaa tacagatata 1260
 ataacaagaa cgactgggtcc atttagaagc atgccgcagt caggagtctt aaaagcaggt 1320
 caaacaattc attatgatga agtgatgaaa caagacggtc atgtttgggt aggttatata 1380
 ggtaacagtg gccaacgtat ttacttgcct gtaagaacat ggaataaatc tactaatact 1440
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<210> 58

<211> 489

<212> PRT

<213> artificial

<220>

<223> artificial construct

<400> 58

Met Arg Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser
1 5 10 15

Gly Ile Glu Gly Arg Met Ala Lys Thr Gln Ala Glu Ile Asn Lys Arg
20 25 30

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

Lys Ala Thr Ser Tyr Asp Pro Ser Phe Gly Val Met Glu Ala Gly Ala
50 55 60

Ile Asp Ala Asp Gly Tyr Tyr His Ala Gln Cys Gln Asp Leu Ile Thr
65 70 75 80

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

Ala Lys Asp Gln Ile Lys Gln Ser Tyr Gly Thr Gly Phe Lys Ile His
 100 105 110
 Glu Asn Lys Pro Ser Thr Val Pro Lys Lys Gly Trp Ile Ala Val Phe
 115 120 125
 Thr Ser Gly Ser Tyr Glu Gln Trp Gly His Ile Gly Ile Val Tyr Asp
 130 135 140
 Gly Gly Asn Thr Ser Thr Phe Thr Ile Leu Glu Gln Asn Trp Asn Gly
 145 150 155 160
 Tyr Ala Asn Lys Lys Pro Thr Lys Arg Val Asp Asn Tyr Tyr Gly Leu
 165 170 175
 Thr His Phe Ile Glu Ile Pro Val Lys Ala Gly Thr Thr Val Lys Lys
 180 185 190
 Glu Thr Ala Lys Lys Ser Ala Ser Lys Thr Pro Ala Pro Lys Lys Lys
 195 200 205
 Ala Thr Leu Lys Val Ser Lys Asn Glu Leu Met Ala Lys Thr Gln Ala
 210 215 220
 Glu Ile Asn Lys Arg Leu Asp Ala Tyr Ala Lys Gly Thr Val Asp Ser
 225 230 235 240
 Pro Tyr Arg Val Lys Lys Ala Thr Ser Tyr Asp Pro Ser Phe Gly Val
 245 250 255
 Met Glu Ala Gly Ala Ile Asp Ala Asp Gly Tyr Tyr His Ala Gln Cys
 260 265 270
 Gln Asp Leu Ile Thr Asp Tyr Val Leu Trp Leu Thr Asp Asn Lys Val
 275 280 285
 Arg Thr Trp Gly Asn Ala Lys Asp Gln Ile Lys Gln Ser Tyr Gly Thr
 290 295 300
 Gly Phe Lys Ile His Glu Asn Lys Pro Ser Thr Val Pro Lys Lys Gly
 305 310 315 320
 Trp Ile Ala Val Phe Thr Ser Gly Ser Tyr Glu Gln Trp Gly His Ile
 325 330 335
 Gly Ile Val Tyr Asp Gly Gly Asn Thr Ser Thr Phe Thr Ile Leu Glu
 340 345 350
 Gln Asn Trp Asn Gly Tyr Ala Asn Lys Lys Pro Thr Lys Arg Val Asp
 355 360 365
 Asn Tyr Tyr Gly Leu Thr His Phe Ile Glu Ile Pro Val Lys Ala Gly
 370 375 380
 Lys Ala Gly Gly Thr Val Thr Pro Thr Pro Asn Thr Gly Trp Lys Thr
 385 390 395 400

Asn Lys Tyr Gly Thr Leu Tyr Lys Ser Glu Ser Ala Ser Phe Thr Pro
 405 410 415

Asn Thr Asp Ile Ile Thr Arg Thr Thr Gly Pro Phe Arg Ser Met Pro
 420 425 430

Gln Ser Gly Val Leu Lys Ala Gly Gln Thr Ile His Tyr Asp Glu Val
 435 440 445

Met Lys Gln Asp Gly His Val Trp Val Gly Tyr Thr Gly Asn Ser Gly
 450 455 460

Gln Arg Ile Tyr Leu Pro Val Arg Thr Trp Asn Lys Ser Thr Asn Thr
 465 470 475 480

Leu Gly Val Leu Trp Gly Thr Ile Lys
 485

<210> 59

<211> 1524

<212> DNA

<213> artificial

<220>

<223> artificial construct

<400> 59

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gtagatagcc cttacagagt taaaaaagct acaagttatg acccatcatt tgggtgtaatg	180
gaagcaggag ccattgatgc agatgggttac tatcacgctc agtgtcaaga ccttattaca	240
gactatgttt tatggttaac agataataaa gtagaactt ggggtaatgc taaagaccaa	300
attaaacaga gttatggtac tggatttaaa atacatgaaa ataaaccttc tactgtacct	360
aaaaaagggt ggattgcggt atttacatcc ggtagttatg aacagtgggg tcacataggt	420
attgtatatg atggaggtaa tacttctaca ttactatatt tagagcaaaa ctggaatggt	480
tatgctaata aaaaacctac aaaacgtgta gataattatt acggattaac tcacttcatt	540
gaaataacctg taaaagcagg aactactgtt aaaaagaaa cagctaagaa aagcgcaagt	600
aaaacgcctg cacctaataaa gaaagcaaca ctaaaagttt ctaagaatga gctcatggct	660
aagactcaag cagaaataaa taaacgttta gatgcttatg caaaaggaa acgtagatagc	720
ccttacagag ttaaaaaagc tacaagttat gacccatcat ttggtgtaat ggaagcagga	780
gccattgatg cagatgggta ctatcacgct cagtgtcaag accttattac agactatggt	840
ttatgggttaa cagataataa agttagaact tggggtaatg ctaaagacca aattaaacag	900
agttatggta ctggatttaa aatacatgaa aataaacctt ctactgtacc taaaaaagggt	960
tggattgcgg tatttacatc cggtagttat gaacagtggg gtcacatagg tattgtatat	1020

gatggaggta atacttctac atttactatt ttagagcaaa actggaatgg ttatgctaata 1080
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gtaaaagcag gaactactgt taaaaaagaa acagctaaga aaagcgcaag taaaacgcct 1200
gcacctaaaa agaaagcaac actaaaagtt tctaagaatg gttaatctgc aagtaaaata 1260
acagttggaa gtaaagcgcc ttataacctt aaatgggtcaa aaggtgctta ttttaatgcg 1320
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agattcgatg ttggacaggc tgtatacgcg cctggaacat taatatatgt gtttgaaatt 1440
atagatgggtt ggtgtcgcat ttattggaac aatcataatg agtggatatg gcatgagaga 1500
ttgattgtga aagaagtgtt ttaa 1524

<210> 60

<211> 507

<212> PRT

<213> artificial

<220>

<223> artificial construct

<400> 60

Met Arg Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser
1 5 10 15

Gly Ile Glu Gly Arg Met Ala Lys Thr Gln Ala Glu Ile Asn Lys Arg
20 25 30

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

Lys Ala Thr Ser Tyr Asp Pro Ser Phe Gly Val Met Glu Ala Gly Ala
50 55 60

Ile Asp Ala Asp Gly Tyr Tyr His Ala Gln Cys Gln Asp Leu Ile Thr
65 70 75 80

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

Ala Lys Asp Gln Ile Lys Gln Ser Tyr Gly Thr Gly Phe Lys Ile His
100 105 110

Glu Asn Lys Pro Ser Thr Val Pro Lys Lys Gly Trp Ile Ala Val Phe
115 120 125

Thr Ser Gly Ser Tyr Glu Gln Trp Gly His Ile Gly Ile Val Tyr Asp
130 135 140

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

Tyr Ala Asn Lys Lys Pro Thr Lys Arg Val Asp Asn Tyr Tyr Gly Leu
165 170 175

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      180      185      190
Thr His Phe Ile Glu Ile Pro Val Lys Ala Gly Thr Thr Val Lys Lys
      195      200      205
Glu Thr Ala Lys Lys Ser Ala Ser Lys Thr Pro Ala Pro Lys Lys Lys

Ala Thr Leu Lys Val Ser Lys Asn Glu Leu Met Ala Lys Thr Gln Ala
      210      215      220

Glu Ile Asn Lys Arg Leu Asp Ala Tyr Ala Lys Gly Thr Val Asp Ser
      225      230      235      240

Pro Tyr Arg Val Lys Lys Ala Thr Ser Tyr Asp Pro Ser Phe Gly Val
      245      250      255

Met Glu Ala Gly Ala Ile Asp Ala Asp Gly Tyr Tyr His Ala Gln Cys
      260      265      270

Gln Asp Leu Ile Thr Asp Tyr Val Leu Trp Leu Thr Asp Asn Lys Val
      275      280      285

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

Gly Phe Lys Ile His Glu Asn Lys Pro Ser Thr Val Pro Lys Lys Gly
      305      310      315      320

Trp Ile Ala Val Phe Thr Ser Gly Ser Tyr Glu Gln Trp Gly His Ile
      325      330      335

Gly Ile Val Tyr Asp Gly Gly Asn Thr Ser Thr Phe Thr Ile Leu Glu
      340      345      350

Gln Asn Trp Asn Gly Tyr Ala Asn Lys Lys Pro Thr Lys Arg Val Asp
      355      360      365

Asn Tyr Tyr Gly Leu Thr His Phe Ile Glu Ile Pro Val Lys Ala Gly
      370      375      380

Thr Thr Val Lys Lys Glu Thr Ala Lys Lys Ser Ala Ser Lys Thr Pro
      385      390      395      400

Ala Pro Lys Lys Lys Ala Thr Leu Lys Val Ser Lys Asn Gly Lys Ser
      405      410      415

Ala Ser Lys Ile Thr Val Gly Ser Lys Ala Pro Tyr Asn Leu Lys Trp
      420      425      430

Ser Lys Gly Ala Tyr Phe Asn Ala Lys Ile Asp Gly Leu Gly Ala Thr
      435      440      445

Ser Ala Thr Arg Tyr Gly Asp Asn Arg Thr Asn Tyr Arg Phe Asp Val
      450      455      460

Gly Gln Ala Val Tyr Ala Pro Gly Thr Leu Ile Tyr Val Phe Glu Ile
      465      470      475      480

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Ile Asp Gly Trp Cys Arg Ile Tyr Trp Asn Asn His Asn Glu Trp Ile
485 490 495

Trp His Glu Arg Leu Ile Val Lys Glu Val Phe
500 505

<210> 61

<211> 1446

<212> DNA

<213> artificial

<220>

<223> artificial construct

<400> 61

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gattttgatg gtttatatgg gtatcagtgt atggacttag cagtagatta tattttaccat      180
gtaacagatg gtaaaataag aatgtgggggt aatgctaagg atgcgataaa taactctttt      240
ggtgggtactg ctacgggtata taaaaactac cctgcttttta gacctaaagta cgggtgatgta      300
gtcgtatgga ctactggtaa ttttgcaact tatggtcata tcgcaatagt tactaaccct      360
gacctttatg gagaccttca atatgttaca gttcttgaac aaaactggaa cggtaacggg      420
atttataaaa ccgagtttagc tacaatcaga acacacgatt acacaggaat tacacatttt      480
attagacctt actttgctac tgaatcaagt gtaaaaaaga aagatacaaa gaaaaaacca      540
aaaccatcaa atagagatgg aataaataaa gataaaattg tatatgatag aactaatatt      600
aattacaatg agctcatgaa aaccttgaaa caagcagagt cctacattaa gagtaaagta      660
aatacaggaa ctgattttga tggtttatat gggatcaggt gtatggactt agcagtagat      720
tatattttacc atgtaacaga tggtaaaata agaatgtggg gtaatgctaa ggatgcgata      780
aataactctt ttggtggtac tgctacggta tataaaaaact accctgcttt tagacctaa      840

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gttactaacc ctgacctta tggagacctt caatatgtta cagttcttga acaaaactgg      960
aacggtaacg ggatttataa aaccgagtta gctacaatca gaacacacga ttacacagga     1020
attacacatt ttattagacc taactttgct actgaatcaa gtgtaaaaaa gaaagatata     1080
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caaaaatttg acggtcatgt ttgggtatcg tgggaaacgt ttgagggcga aactgtatac     1380
atgccgggtac gcacatggga cgctaaaact ggtaaagttg gtaagttgtg gggcgaaatt     1440
aaataa                                           1446

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<210> 62

<211> 481

<212> PRT

<213> artificial

<220>

<223> artificial construct

<400> 62

Met Arg Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser
1 5 10 15

Gly Ile Glu Gly Arg Met Lys Thr Leu Lys Gln Ala Glu Ser Tyr Ile
20 25 30

Lys Ser Lys Val Asn Thr Gly Thr Asp Phe Asp Gly Leu Tyr Gly Tyr
35 40 45

Gln Cys Met Asp Leu Ala Val Asp Tyr Ile Tyr His Val Thr Asp Gly
50 55 60

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

Gly Gly Thr Ala Thr Val Tyr Lys Asn Tyr Pro Ala Phe Arg Pro Lys
85 90 95

Tyr Gly Asp Val Val Val Trp Thr Thr Gly Asn Phe Ala Thr Tyr Gly
100 105 110

His Ile Ala Ile Val Thr Asn Pro Asp Pro Tyr Gly Asp Leu Gln Tyr
115 120 125

Val Thr Val Leu Glu Gln Asn Trp Asn Gly Asn Gly Ile Tyr Lys Thr
130 135 140

Glu Leu Ala Thr Ile Arg Thr His Asp Tyr Thr Gly Ile Thr His Phe
145 150 155 160

Ile Arg Pro Asn Phe Ala Thr Glu Ser Ser Val Lys Lys Lys Asp Thr
165 170 175

Lys Lys Lys Pro Lys Pro Ser Asn Arg Asp Gly Ile Asn Lys Asp Lys
180 185 190

Ile Val Tyr Asp Arg Thr Asn Ile Asn Tyr Asn Glu Leu Met Lys Thr
195 200 205

Leu Lys Gln Ala Glu Ser Tyr Ile Lys Ser Lys Val Asn Thr Gly Thr
210 215 220

Asp Phe Asp Gly Leu Tyr Gly Tyr Gln Cys Met Asp Leu Ala Val Asp
225 230 235 240

Tyr Ile Tyr His Val Thr Asn Gly Lys Ile Arg Met Trp Gly Asn Ala

```

Tyr Ile Tyr His Val Thr Asp Gly Lys His Arg Asn Trp Gly Asn Ala
245                               250                               255

Lys Asp Ala Ile Asn Asn Ser Phe Gly Gly Thr Ala Thr Val Tyr Lys
260                               265                               270

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

Thr Gly Asn Phe Ala Thr Tyr Gly His Ile Ala Ile Val Thr Asn Pro
290                               295                               300

Asp Pro Tyr Gly Asp Leu Gln Tyr Val Thr Val Leu Glu Gln Asn Trp
305                               310                               315                               320

Asn Gly Asn Gly Ile Tyr Lys Thr Glu Leu Ala Thr Ile Arg Thr His
325                               330                               335

Asp Tyr Thr Gly Ile Thr His Phe Ile Arg Pro Asn Phe Ala Thr Glu
340                               345                               350

Ser Ser Val Lys Lys Lys Asp Thr Lys Lys Lys Pro Lys Pro Ser Asn
355                               360                               365

Arg Asp Gly Ile Asn Lys Asp Lys Ile Val Tyr Asp Arg Thr Asn Ile
370                               375                               380

Asn Tyr Asn Trp Lys Gln Asn Lys Asp Gly Ile Trp Tyr Lys Ala Glu
385                               390                               395                               400

His Ala Ser Phe Thr Val Thr Ala Pro Glu Gly Ile Ile Thr Arg Tyr
405                               410                               415

Lys Gly Pro Trp Thr Gly His Pro Gln Ala Gly Val Leu Gln Lys Gly
420                               425                               430

Gln Thr Ile Lys Tyr Asp Glu Val Gln Lys Phe Asp Gly His Val Trp
435                               440                               445

Val Ser Trp Glu Thr Phe Glu Gly Glu Thr Val Tyr Met Pro Val Arg
450                               455                               460

Thr Trp Asp Ala Lys Thr Gly Lys Val Gly Lys Leu Trp Gly Glu Ile
465                               470                               475                               480

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Lys

<210> 63

<211> 1440

<212> DNA

<213> artificial

<220>

<223> artificial construct

<400> 63

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gattttgatg gtttatatgg gtatcagtgt atggacttag cagtagatta tattttaccat      180
gtaacagatg gtaaaataag aatgtggggg aatgctaagg atgcgataaa taactctttt      240
ggtggtactg ctacggtata taaaaactac cctgctttta gacctaaagta cggatgatgta      300
gtcgtatgga ctactggtaa ttttgcaact tatggtcata tcgcaatagt tactaaccct      360
gacccttatg gagaccttca atatgttaca gttcttgaac aaaactggaa cggtaacggg      420
atttataaaa ccgagtttagc tacaatcaga acacacgatt acacaggaat tacacatttt      480
attagaccta actttgctac tgaatcaagt gtaaaaaaga aagatacaaa gaaaaaacca      540
aaaccatcaa atagagatgg aataaataaa gataaaattg tatatgatag aactaatatt      600
aattacaatg agctcatgaa aaccctgaaa caagcagagt cctacattaa gagtaaagta      660
aatacaggaa ctgattttga tggtttatat gggatcagt gtatggactt agcagtagat      720

tatattttacc atgtaacaga tggtaaaata agaatgtggg gtaatgctaa ggatgcgata      780
aataactctt ttggtggtac tgctacggta tataaaaact accctgcttt tagacctaa      840
tacggtgatg tagtcgtatg gactactggt aattttgcaa cttatggtca tatcgcaata      900
gttactaacc ctgaccctta tggagacctt caatatgtta cagttcttga acaaaactgg      960
aacggtaacg ggatttataa aaccgagtta gctacaatca gaacacacga ttacacagga     1020
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aagaaaaaac caaaaccatc aaatagagat ggaataaata aagataaaat tgtatatgat     1140
agaactaata ttaattacaa ttggaaaaca acaaatatg gcacactata taaatcagag     1200
tcagctagct tcacacctaa tacagatata ataacaagaa cgactgggtcc atttagaagc     1260
atgccgcagt caggagtctt aaaagcaggt caaacaattc attatgatga agtgatgaaa     1320
caagacggtc atgtttgggt aggttataca ggtaacagtg gccaacgtat ttacttgcct     1380
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<210> 64

<211> 479

<212> PRT

<213> artificial

<220>

<223> artificial construct

<400> 64

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Met Arg Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser
1           5           10           15

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Gly Ile Glu Gly Arg Met Lys Thr Leu Lys Gln Ala Glu Ser Tyr Ile
20           25           30

```

Lys Ser Lys Val Asn Thr Gly Thr Asp Phe Asp Gly Leu Tyr Gly Tyr
 35 40 45

Gln Cys Met Asp Leu Ala Val Asp Tyr Ile Tyr His Val Thr Asp Gly
 50 55 60

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

Gly Gly Thr Ala Thr Val Tyr Lys Asn Tyr Pro Ala Phe Arg Pro Lys
 85 90 95

Tyr Gly Asp Val Val Val Trp Thr Thr Gly Asn Phe Ala Thr Tyr Gly
 100 105 110

His Ile Ala Ile Val Thr Asn Pro Asp Pro Tyr Gly Asp Leu Gln Tyr
 115 120 125

Val Thr Val Leu Glu Gln Asn Trp Asn Gly Asn Gly Ile Tyr Lys Thr
 130 135 140

Glu Leu Ala Thr Ile Arg Thr His Asp Tyr Thr Gly Ile Thr His Phe
 145 150 155 160

Ile Arg Pro Asn Phe Ala Thr Glu Ser Ser Val Lys Lys Lys Asp Thr
 165 170 175

Lys Lys Lys Pro Lys Pro Ser Asn Arg Asp Gly Ile Asn Lys Asp Lys
 180 185 190

Ile Val Tyr Asp Arg Thr Asn Ile Asn Tyr Asn Glu Leu Met Lys Thr
 195 200 205

Leu Lys Gln Ala Glu Ser Tyr Ile Lys Ser Lys Val Asn Thr Gly Thr
 210 215 220

Asp Phe Asp Gly Leu Tyr Gly Tyr Gln Cys Met Asp Leu Ala Val Asp
 225 230 235 240

Tyr Ile Tyr His Val Thr Asp Gly Lys Ile Arg Met Trp Gly Asn Ala
 245 250 255

Lys Asp Ala Ile Asn Asn Ser Phe Gly Gly Thr Ala Thr Val Tyr Lys
 260 265 270

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

Thr Gly Asn Phe Ala Thr Tyr Gly His Ile Ala Ile Val Thr Asn Pro
 290 295 300

Asp Pro Tyr Gly Asp Leu Gln Tyr Val Thr Val Leu Glu Gln Asn Trp
 305 310 315 320

Asn Gly Asn Gly Ile Tyr Lys Thr Glu Leu Ala Thr Ile Arg Thr His
 325 330 335

Asp Tyr Thr Gly Ile Thr His Phe Ile Arg Pro Asn Phe Ala Thr Glu
340 345 350

Ser Ser Val Lys Lys Lys Asp Thr Lys Lys Lys Pro Lys Pro Ser Asn
355 360 365

Arg Asp Gly Ile Asn Lys Asp Lys Ile Val Tyr Asp Arg Thr Asn Ile
370 375 380

Asn Tyr Asn Trp Lys Thr Asn Lys Tyr Gly Thr Leu Tyr Lys Ser Glu
385 390 395 400

Ser Ala Ser Phe Thr Pro Asn Thr Asp Ile Ile Thr Arg Thr Thr Gly
405 410 415

Pro Phe Arg Ser Met Pro Gln Ser Gly Val Leu Lys Ala Gly Gln Thr
420 425 430

Ile His Tyr Asp Glu Val Met Lys Gln Asp Gly His Val Trp Val Gly
435 440 445

Tyr Thr Gly Asn Ser Gly Gln Arg Ile Tyr Leu Pro Val Arg Thr Trp
450 455 460

Asn Lys Ser Thr Asn Thr Leu Gly Val Leu Trp Gly Thr Ile Lys
465 470 475

<210> 65

<211> 1446

<212> DNA

<213> artificial

<220>

<223> artificial construct

<400> 65

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aggatgaaaa ccctgaaaca agcagagtcc tacattaaga gtaaagtaaa tacaggaact	120
gattttgatg gtttatatgg gtatcagtgt atggacttag cagtagatta tattttaccat	180
gtaacagatg gtaaaataag aatgtgggggt aatgctaagg atgcgataaa taactctttt	240
ggtggtactg ctacggtata taaaaactac cctgctttta gacctaaagta cggatgatgta	300
gtcgtatgga ctactggtaa ttttgcaact tatggtcata tcgcaatagt tactaacctt	360
gaccttatg gagaccttca atatgttaca gttcttgaac aaaactggaa cggtaacggg	420
atttataaaa ccgagtttagc tacaatcaga acacacgatt acacaggaat tacacatttt	480
attagacctt actttgctac tgaatcaagt gtaaaaaaga aagatacaaa gaaaaaacca	540
aaaccatcaa atagagatgg aataaataaa gataaaattg tatatgatag aactaatatt	600
aattacaatg agctcatgaa aacctgaaa caagcagagt cctacattaa gagtaaagta	660
aatacaggaa ctgattttga tggtttatat gggtatcagt gtatggactt agcagtagat	720

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tatatttacc atgtaacaga tggtaaaata agaatgtggg gtaatgctaa ggatgcgata 780
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tacggtgatg tagtcgtatg gactactggt aattttgcaa cttatgggtca tatcgcaata 900
gttactaacc ctgaccctta tggagacctt caatatgtta cagttcttga acaaaactgg 960
aacggtaacg ggatttataa aaccgagtta gctacaatca gaacacacga ttacacagga 1020
attacacatt ttattagacc taactttgct actgaatcaa gtgtaaaaaa gaaagataca 1080
aagaaaaaac caaaaccatc aaatagagat ggaataaata aagataaaat tgtatatgat 1140
agaactaata ttaattacaa tggtaaactct gcaagtaaaa taacagttgg aagtaaagcg 1200
ccttataacc ttaaattggtc aaaagggtgct tattttaatg cgaaaatcga cggcttaggt 1260
gctacttcag ccactagata cggtgataat cgtactaact atagattcga tgttggacag 1320
gctgtatacg cgcctggaac attaatatat gtgtttgaaa ttatagatgg ttggtgtcgc 1380
atattattgga acaatcataa tgagtggata tggcatgaga gattgattgt gaaagaagtg 1440
ttttaa 1446

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<210> 66

<211> 481

<212> PRT

<213> artificial

<220>

<223> artificial construct

<400> 66

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Met Arg Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser
1          5          10          15

Gly Ile Glu Gly Arg Met Lys Thr Leu Lys Gln Ala Glu Ser Tyr Ile
20          25          30

Lys Ser Lys Val Asn Thr Gly Thr Asp Phe Asp Gly Leu Tyr Gly Tyr
35          40          45

Gln Cys Met Asp Leu Ala Val Asp Tyr Ile Tyr His Val Thr Asp Gly
50          55          60

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

Gly Gly Thr Ala Thr Val Tyr Lys Asn Tyr Pro Ala Phe Arg Pro Lys
85          90          95

Tyr Gly Asp Val Val Val Trp Thr Thr Gly Asn Phe Ala Thr Tyr Gly
100         105         110

His Ile Ala Ile Val Thr Asn Pro Asp Pro Tyr Gly Asp Leu Gln Tyr
115         120         125

Val Thr Val Leu Glu Gln Asn Trp Asn Gly Asn Gly Ile Tyr Lys Thr
130         135         140

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Glu Leu Ala Thr Ile Arg Thr His Asp Tyr Thr Gly Ile Thr His Phe
 145 150 155 160

Ile Arg Pro Asn Phe Ala Thr Glu Ser Ser Val Lys Lys Lys Asp Thr
 165 170 175

Lys Lys Lys Pro Lys Pro Ser Asn Arg Asp Gly Ile Asn Lys Asp Lys
 180 185 190

Ile Val Tyr Asp Arg Thr Asn Ile Asn Tyr Asn Glu Leu Met Lys Thr
 195 200 205

Leu Lys Gln Ala Glu Ser Tyr Ile Lys Ser Lys Val Asn Thr Gly Thr
 210 215 220

Asp Phe Asp Gly Leu Tyr Gly Tyr Gln Cys Met Asp Leu Ala Val Asp
 225 230 235 240

Tyr Ile Tyr His Val Thr Asp Gly Lys Ile Arg Met Trp Gly Asn Ala
 245 250 255

Lys Asp Ala Ile Asn Asn Ser Phe Gly Gly Thr Ala Thr Val Tyr Lys
 260 265 270

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

Thr Gly Asn Phe Ala Thr Tyr Gly His Ile Ala Ile Val Thr Asn Pro
 290 295 300

Asp Pro Tyr Gly Asp Leu Gln Tyr Val Thr Val Leu Glu Gln Asn Trp
 305 310 315 320

Asn Gly Asn Gly Ile Tyr Lys Thr Glu Leu Ala Thr Ile Arg Thr His
 325 330 335

Asp Tyr Thr Gly Ile Thr His Phe Ile Arg Pro Asn Phe Ala Thr Glu
 340 345 350

Ser Ser Val Lys Lys Lys Asp Thr Lys Lys Lys Pro Lys Pro Ser Asn
 355 360 365

Arg Asp Gly Ile Asn Lys Asp Lys Ile Val Tyr Asp Arg Thr Asn Ile
 370 375 380

Asn Tyr Asn Gly Lys Ser Ala Ser Lys Ile Thr Val Gly Ser Lys Ala
 385 390 395 400

Pro Tyr Asn Leu Lys Trp Ser Lys Gly Ala Tyr Phe Asn Ala Lys Ile
 405 410 415

Asp Gly Leu Gly Ala Thr Ser Ala Thr Arg Tyr Gly Asp Asn Arg Thr
 420 425 430

Asn Tyr Arg Phe Asp Val Gly Gln Ala Val Tyr Ala Pro Gly Thr Leu
435 440 445

Ile Tyr Val Phe Glu Ile Ile Asp Gly Trp Cys Arg Ile Tyr Trp Asn
450 455 460

Asn His Asn Glu Trp Ile Trp His Glu Arg Leu Ile Val Lys Glu Val
465 470 475 480

Phe

<210> 67

<211> 1278

<212> DNA

<213> artificial

<220>

<223> artificial construct

<400> 67

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tacggtcctt atccattagg tataaatggc ggtatgcact acggagttga tttttttatg	180
aatattggaa caccagtaaa agctatttca agcggaaaaa tagttgaagc tggttggagt	240
aattacggag gaggtaatca aataggtcct attgaaaatg atggagtgc tagacaatgg	300
tatatgcac taagtaaata taatgttaaa gtaggagatt atgtcaaagc tgggtcaaata	360
atcggttggt ctggaagcac tggttattct acagcaccac atttacactt ccaaagaatg	420
gttaattcat tttcaaattc aactgcccaa gatccaatgc ctttcttaaa gagcgcagga	480
tatggaaaag caggtggtac agtaactcca acgccgaata caggtgagct cgctgcaaca	540
catgaacatt cagcacaatg gttgaataat tacaaaaaag gatatgggta cggtccttat	600
ccattaggtg taaatggcgg tatgcactac ggagttgatt tttttatgaa tattggaaca	660
ccagtaaaaag ctatttcaag cggaaaaata gttgaagctg gttggagtaa ttacggagga	720
ggtaatcaaa taggtcttat tgaaaatgat ggagtgcata gacaatggta tatgcaccta	780
agtaaataata atgttaaagt aggagattat gtcaaagctg gtcaaataat cggttggtct	840
ggaagcactg gttattctac agcaccacat ttacacttcc aaagaatggg taattcattt	900
tcaaattcaa ctgcccaaga tccaatgcct ttcttaaaga gcgcaggata tggaaaagca	960
ggtggtacag taactccaac gccgaatata ggttggaac agaataaaga tggcatttgg	1020
tataaagctg aacatgcttc gttcacagt acagcaccag agggaattat cacaagatac	1080
aaaggctcct ggactggtca cccacaagct ggtgtattac aaaaagggtca aacgattaaa	1140
tatgatgagg ttcaaaaatt tgacggtcat gtttgggtat cgtgggaaac gtttgagggc	1200
gaaactgtat acatgccggg acgcacatgg gacgctaaaa ctggtaaagt tggtaagttg	1260
tggggcgaaa ttaaataa	1278

<210> 68

<211> 425

<212> PRT

<213> artificial

<220>

<223> artificial construct

<400> 68

Met Arg Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser
1 5 10 15

Gly Ile Glu Gly Arg Ala Ala Thr His Glu His Ser Ala Gln Trp Leu
20 25 30

Asn Asn Tyr Lys Lys Gly Tyr Gly Tyr Gly Pro Tyr Pro Leu Gly Ile
35 40 45

Asn Gly Gly Met His Tyr Gly Val Asp Phe Phe Met Asn Ile Gly Thr
50 55 60

Pro Val Lys Ala Ile Ser Ser Gly Lys Ile Val Glu Ala Gly Trp Ser
65 70 75 80

Asn Tyr Gly Gly Gly Asn Gln Ile Gly Leu Ile Glu Asn Asp Gly Val
85 90 95

His Arg Gln Trp Tyr Met His Leu Ser Lys Tyr Asn Val Lys Val Gly
100 105 110

Asp Tyr Val Lys Ala Gly Gln Ile Ile Gly Trp Ser Gly Ser Thr Gly
115 120 125

Tyr Ser Thr Ala Pro His Leu His Phe Gln Arg Met Val Asn Ser Phe
130 135 140

Ser Asn Ser Thr Ala Gln Asp Pro Met Pro Phe Leu Lys Ser Ala Gly
145 150 155 160

Tyr Gly Lys Ala Gly Gly Thr Val Thr Pro Thr Pro Asn Thr Gly Glu
165 170 175

Leu Ala Ala Thr His Glu His Ser Ala Gln Trp Leu Asn Asn Tyr Lys
180 185 190

Lys Gly Tyr Gly Tyr Gly Pro Tyr Pro Leu Gly Ile Asn Gly Gly Met
195 200 205

His Tyr Gly Val Asp Phe Phe Met Asn Ile Gly Thr Pro Val Lys Ala
210 215 220

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

Gly Asn Gln Ile Gly Leu Ile Glu Asn Asp Gly Val His Arg Gln Trp

245										250					255				
Tyr	Met	His	Leu	Ser	Lys	Tyr	Asn	Val	Lys	Val	Gly	Asp	Tyr	Val	Lys				
			260					265					270						
Ala	Gly	Gln	Ile	Ile	Gly	Trp	Ser	Gly	Ser	Thr	Gly	Tyr	Ser	Thr	Ala				
		275					280					285							
Pro	His	Leu	His	Phe	Gln	Arg	Met	Val	Asn	Ser	Phe	Ser	Asn	Ser	Thr				
	290					295					300								
Ala	Gln	Asp	Pro	Met	Pro	Phe	Leu	Lys	Ser	Ala	Gly	Tyr	Gly	Lys	Ala				
305					310					315					320				
Gly	Gly	Thr	Val	Thr	Pro	Thr	Pro	Asn	Thr	Gly	Trp	Lys	Gln	Asn	Lys				
				325					330					335					
Asp	Gly	Ile	Trp	Tyr	Lys	Ala	Glu	His	Ala	Ser	Phe	Thr	Val	Thr	Ala				
		340						345					350						
Pro	Glu	Gly	Ile	Ile	Thr	Arg	Tyr	Lys	Gly	Pro	Trp	Thr	Gly	His	Pro				
		355					360					365							
Gln	Ala	Gly	Val	Leu	Gln	Lys	Gly	Gln	Thr	Ile	Lys	Tyr	Asp	Glu	Val				
	370					375					380								
Gln	Lys	Phe	Asp	Gly	His	Val	Trp	Val	Ser	Trp	Glu	Thr	Phe	Glu	Gly				
385					390					395					400				
Glu	Thr	Val	Tyr	Met	Pro	Val	Arg	Thr	Trp	Asp	Ala	Lys	Thr	Gly	Lys				
				405					410					415					
Val	Gly	Lys	Leu	Trp	Gly	Glu	Ile	Lys											
			420					425											

<210> 69

<211> 1272

<212> DNA

<213> artificial

<220>

<223> artificial construct

<400> 69

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tacggtcctt	atccattagg	tataaatggc	ggtatgcact	acggagttga	tttttttatg	180
aattattggaa	caccagtaaa	agctatttca	agcggaaaaa	tagttgaagc	tggttggagt	240
aattacggag	gaggtaatca	aataggtctt	attgaaaatg	atggagtgca	tagacaatgg	300
tatatgcac	taagtaaata	taatgttaaa	gtaggagatt	atgtcaaagc	tggtcaaata	360
atcggttggt	ctggaagcac	tggttattct	acagcaccac	atttacactt	ccaaagaatg	420
gttaattcat	tttcaaattc	aactgcccaa	gatccaatgc	ctttcttaaa	gagcgcagga	480

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tatggaaaag caggtggtac agtaactcca acgccgaata caggtgagct cgctgcaaca 540
catgaacatt cagcacaatg gttgaataat tacaaaaaag gatatggtta cggtccttat 600
ccattaggtta taaatggcgg tatgcactac ggagttgatt tttttatgaa tattggaaca 660
ccagtaaaaag ctatttcaag cggaaaaata gttgaagctg gttggagtaa ttacggagga 720
ggtaatcaaa taggtcttat tgaaaatgat ggagtgcata gacaatggta tatgcatcta 780
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tcaaattcaa ctgcccaga tccaatgcct ttcttaaaga gcgcaggata tggaaaagca 960
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tataaatcag agtcagctag cttcacacct aatacagata taataacaag aacgactggt 1080

ccatttagaa gcatgccgca gtcaggagtc ttaaagcag gtcaaacaat tcattatgat 1140
gaagtgatga aacaagacgg tcatgtttgg gtaggttata caggtaacag tggccaacgt 1200
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actataaagt aa 1272

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<210> 70

<211> 423

<212> PRT

<213> artificial

<220>

<223> artificial construct

<400> 70

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Met Arg Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser
1          5          10          15

Gly Ile Glu Gly Arg Ala Ala Thr His Glu His Ser Ala Gln Trp Leu
20          25          30

Asn Asn Tyr Lys Lys Gly Tyr Gly Tyr Gly Pro Tyr Pro Leu Gly Ile
35          40          45

Asn Gly Gly Met His Tyr Gly Val Asp Phe Phe Met Asn Ile Gly Thr
50          55          60

Pro Val Lys Ala Ile Ser Ser Gly Lys Ile Val Glu Ala Gly Trp Ser
65          70          75          80

Asn Tyr Gly Gly Gly Asn Gln Ile Gly Leu Ile Glu Asn Asp Gly Val
85          90          95

His Arg Gln Trp Tyr Met His Leu Ser Lys Tyr Asn Val Lys Val Gly
100          105          110

Asp Tyr Val Lys Ala Gly Gln Ile Ile Gly Trp Ser Gly Ser Thr Gly
115          120          125

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Tyr Ser Thr Ala Pro His Leu His Phe Gln Arg Met Val Asn Ser Phe
130 135 140

Ser Asn Ser Thr Ala Gln Asp Pro Met Pro Phe Leu Lys Ser Ala Gly
145 150 155 160

Tyr Gly Lys Ala Gly Gly Thr Val Thr Pro Thr Pro Asn Thr Gly Glu
165 170 175

Leu Ala Ala Thr His Glu His Ser Ala Gln Trp Leu Asn Asn Tyr Lys
180 185 190

Lys Gly Tyr Gly Tyr Gly Pro Tyr Pro Leu Gly Ile Asn Gly Gly Met
195 200 205

His Tyr Gly Val Asp Phe Phe Met Asn Ile Gly Thr Pro Val Lys Ala
210 215 220

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

Gly Asn Gln Ile Gly Leu Ile Glu Asn Asp Gly Val His Arg Gln Trp
245 250 255

Tyr Met His Leu Ser Lys Tyr Asn Val Lys Val Gly Asp Tyr Val Lys
260 265 270

Ala Gly Gln Ile Ile Gly Trp Ser Gly Ser Thr Gly Tyr Ser Thr Ala
275 280 285

Pro His Leu His Phe Gln Arg Met Val Asn Ser Phe Ser Asn Ser Thr
290 295 300

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

Gly Gly Thr Val Thr Pro Thr Pro Asn Thr Gly Trp Lys Thr Asn Lys
325 330 335

Tyr Gly Thr Leu Tyr Lys Ser Glu Ser Ala Ser Phe Thr Pro Asn Thr
340 345 350

Asp Ile Ile Thr Arg Thr Thr Gly Pro Phe Arg Ser Met Pro Gln Ser
355 360 365

Gly Val Leu Lys Ala Gly Gln Thr Ile His Tyr Asp Glu Val Met Lys
370 375 380

Gln Asp Gly His Val Trp Val Gly Tyr Thr Gly Asn Ser Gly Gln Arg
385 390 395 400

Ile Tyr Leu Pro Val Arg Thr Trp Asn Lys Ser Thr Asn Thr Leu Gly
405 410 415

Val Leu Trp Gly Thr Ile Lys
420

<210> 71

<211> 1278

<212> DNA

<213> artificial

<220>

<223> artificial construct

<400> 71

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tacggtcctt atccattagg tataaatggc ggtatgcact acggagttga tttttttatg	180
aattattggaa caccagtaaa agctattttca agcggaaaaa tagttgaagc tgggttgaggt	240
aattacggag gaggtaatca aataggtctt attgaaaatg atggagtgc tagacaatgg	300
tatatgcac taagtaaata taatgttaaa gtaggagatt atgtcaaagc tgggtcaaata	360
atcggttgggt ctggaagcac tggttattct acagcaccac atttacctt ccaaagaatg	420
gttaattcat tttcaaattc aactgcccaa gatccaatgc ctttcttaaa gagcgcagga	480
tatggaaaag caggtggtac agtaactcca acgccgaata caggtgagct cgctgcaaca	540
catgaacatt cagcacaatg gttgaataat tacaaaaaag gatatgggtta cggtccttat	600
ccattaggta taaatggcgg tatgcactac ggagttgatt tttttatgaa tattggaaca	660
ccagtaaaaag ctatttcaag cggaaaaata gttgaagctg gttggagtaa ttacggagga	720
ggtaatcaaa taggtcttat tgaaaatgat ggagtgcata gacaatggta tatgcaccta	780
agtaaatata atgttaaagt aggagattat gtcaaagctg gtcaaataat cggttggtct	840
ggaagcactg gttattctac agcaccacat ttacacttcc aaagaatgggt taattcattt	900
tcaaattcaa ctgccaaga tccaatgcct ttcttaaaga gcgcaggata tggaaaagca	960
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ggaagtaaag cgccttataa ccttaaattgg tcaaaagggtg cttattttta tgcgaaaatc	1080
gacggcttag gtgctacttc agccactaga tacggtgata atcgtactaa ctatagattc	1140
gatgttggac aggctgtata cgcgcctgga acattaatat atgtgtttga aattatagat	1200
ggttggtgtc gcatttattg gaacaatcat aatgagtgga tatggcatga gagattgatt	1260
gtgaaagaag tgttttta	1278

<210> 72

<211> 425

<212> PRT

<213> artificial

<220>

<223> artificial construct

<400> 72

Met Arg Glv Ser His His His His His His Glv Ser Glv Ser Glv Ser

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-----
1           5           10          15
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Gly Ile Glu Gly Arg Ala Ala Thr His Glu His Ser Ala Gln Trp Leu
      20              25              30

Asn Asn Tyr Lys Lys Gly Tyr Gly Tyr Gly Pro Tyr Pro Leu Gly Ile
      35              40              45

Asn Gly Gly Met His Tyr Gly Val Asp Phe Phe Met Asn Ile Gly Thr
      50              55              60

Pro Val Lys Ala Ile Ser Ser Gly Lys Ile Val Glu Ala Gly Trp Ser
      65              70              75              80

Asn Tyr Gly Gly Gly Asn Gln Ile Gly Leu Ile Glu Asn Asp Gly Val
      85              90              95

His Arg Gln Trp Tyr Met His Leu Ser Lys Tyr Asn Val Lys Val Gly
      100              105              110

Asp Tyr Val Lys Ala Gly Gln Ile Ile Gly Trp Ser Gly Ser Thr Gly
      115              120              125

Tyr Ser Thr Ala Pro His Leu His Phe Gln Arg Met Val Asn Ser Phe
      130              135              140

Ser Asn Ser Thr Ala Gln Asp Pro Met Pro Phe Leu Lys Ser Ala Gly
      145              150              155              160

Tyr Gly Lys Ala Gly Gly Thr Val Thr Pro Thr Pro Asn Thr Gly Glu
      165              170              175

Leu Ala Ala Thr His Glu His Ser Ala Gln Trp Leu Asn Asn Tyr Lys
      180              185              190

Lys Gly Tyr Gly Tyr Gly Pro Tyr Pro Leu Gly Ile Asn Gly Gly Met
      195              200              205

His Tyr Gly Val Asp Phe Phe Met Asn Ile Gly Thr Pro Val Lys Ala
      210              215              220

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

Gly Asn Gln Ile Gly Leu Ile Glu Asn Asp Gly Val His Arg Gln Trp
      245              250              255

Tyr Met His Leu Ser Lys Tyr Asn Val Lys Val Gly Asp Tyr Val Lys
      260              265              270

Ala Gly Gln Ile Ile Gly Trp Ser Gly Ser Thr Gly Tyr Ser Thr Ala
      275              280              285

Pro His Leu His Phe Gln Arg Met Val Asn Ser Phe Ser Asn Ser Thr
      290              295              300

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

Gly Gly Thr Val Thr Pro Thr Pro Asn Thr Gly Gly Lys Ser Ala Ser
325 330 335

Lys Ile Thr Val Gly Ser Lys Ala Pro Tyr Asn Leu Lys Trp Ser Lys
340 345 350

Gly Ala Tyr Phe Asn Ala Lys Ile Asp Gly Leu Gly Ala Thr Ser Ala
355 360 365

Thr Arg Tyr Gly Asp Asn Arg Thr Asn Tyr Arg Phe Asp Val Gly Gln
370 375 380

Ala Val Tyr Ala Pro Gly Thr Leu Ile Tyr Val Phe Glu Ile Ile Asp
385 390 395 400

Gly Trp Cys Arg Ile Tyr Trp Asn Asn His Asn Glu Trp Ile Trp His
405 410 415

Glu Arg Leu Ile Val Lys Glu Val Phe
420 425

<210> 73
<211> 63
<212> DNA
<213> artificial

<220>
<223> artificial his-tag

<400> 73
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agg 63

<210> 74
<211> 21
<212> PRT
<213> artificial

<220>
<223> artificial Hist-tag

<400> 74
Met Arg Gly Ser His His His His His His Gly Ser Gly Ser Gly Ser
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Gly Ile Glu Gly Arg
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<210> 75

<211> 741

<212> DNA

<213> Staphylococcus simulans

<400> 75

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attggaacac cagtaaaagc tatttcaagc ggaaaaatag ttgaagctgg ttggagtaat      180
tacggaggag gtaatcaa at aggtcttatt gaaaatgatg gagtgcatag acaatggtat      240
atgcatctaa gtaaatataa tgttaaagta ggagattatg tcaaagctgg tcaaataatc      300
ggttggtctg gaagcactgg ttattctaca gcaccacatt tacacttcca aagaatggtt      360
aattcatttt caaattcaac tgcccaagat ccaatgcctt tcttaaagag cgcaggatat      420
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cattatgatg aagtgatgaa acaagacggg catgtttggg taggttatac aggtaacagt      660
ggccaacgta tttacttgcc tgtaagaaca tggaataaat ctactaatac tttaggtggt      720
ctttggggaa ctataaagtg a                                     741

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<210> 76

<211> 246

<212> PRT

<213> Staphylococcus simulans

<400> 76

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Ala Ala Thr His Glu His Ser Ala Gln Trp Leu Asn Asn Tyr Lys Lys
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Gly Tyr Gly Tyr Gly Pro Tyr Pro Leu Gly Ile Asn Gly Gly Met His
20              25              30

Tyr Gly Val Asp Phe Phe Met Asn Ile Gly Thr Pro Val Lys Ala Ile
35              40              45

Ser Ser Gly Lys Ile Val Glu Ala Gly Trp Ser Asn Tyr Gly Gly Gly
50              55              60

Asn Gln Ile Gly Leu Ile Glu Asn Asp Gly Val His Arg Gln Trp Tyr
65              70              75              80

Met His Leu Ser Lys Tyr Asn Val Lys Val Gly Asp Tyr Val Lys Ala
85              90              95

Gly Gln Ile Ile Gly Trp Ser Gly Ser Thr Gly Tyr Ser Thr Ala Pro
100             105             110

His Leu His Phe Gln Arg Met Val Asn Ser Phe Ser Asn Ser Thr Ala
115             120             125

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Gln Asp Pro Met Pro Phe Leu Lys Ser Ala Gly Tyr Gly Lys Ala Gly
130 135 140

Gly Thr Val Thr Pro Thr Pro Asn Thr Gly Trp Lys Thr Asn Lys Tyr
145 150 155 160

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

Ile Ile Thr Arg Thr Thr Gly Pro Phe Arg Ser Met Pro Gln Ser Gly
180 185 190

Val Leu Lys Ala Gly Gln Thr Ile His Tyr Asp Glu Val Met Lys Gln
195 200 205

Asp Gly His Val Trp Val Gly Tyr Thr Gly Asn Ser Gly Gln Arg Ile
210 215 220

Tyr Leu Pro Val Arg Thr Trp Asn Lys Ser Thr Asn Thr Leu Gly Val
225 230 235 240

Leu Trp Gly Thr Ile Lys
245

<210> 77

<211> 2019

<212> DNA

<213> artificial

<220>

<223> artificial construct

<400> 77

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<210> 78

<211> 672

<212> PRT

<213> artificial

<220>

<223> artificial construct

<400> 78

Met Arg Gly Ser His His His His His His Gly Ser Met Gln Ala Lys
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Leu Thr Lys Asn Glu Phe Ile Glu Trp Leu Lys Thr Ser Glu Gly Lys
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Gln Phe Asn Val Asp Leu Trp Tyr Gly Phe Gln Cys Phe Asp Tyr Ala
 35 40 45

Asn Ala Gly Trp Lys Val Leu Phe Gly Leu Leu Leu Lys Gly Leu Gly
 50 55 60

Ala Lys Asp Ile Pro Phe Ala Asn Asn Phe Asp Gly Leu Ala Thr Val
 65 70 75 80

Tyr Gln Asn Thr Pro Asp Phe Leu Ala Gln Pro Gly Asp Met Val Val
85 90 95

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

Glu Ala Thr Leu Asp Tyr Ile Ile Val Tyr Glu Gln Asn Trp Leu Gly
115 120 125

Gly Gly Trp Thr Asp Gly Ile Glu Gln Pro Gly Trp Gly Trp Glu Lys
130 135 140

Val Thr Arg Arg Gln His Ala Tyr Asp Phe Pro Met Trp Phe Ile Arg
145 150 155 160

Pro Asn Phe Lys Ser Glu Thr Ala Pro Arg Ser Val Gln Ser Pro Thr
165 170 175

Gln Ala Pro Lys Lys Glu Thr Ala Gly Ser Met Leu Thr Ala Ile Asp
180 185 190

Tyr Leu Thr Lys Lys Gly Trp Lys Ile Ser Ser Asp Pro Arg Thr Tyr
195 200 205

Asp Gly Tyr Pro Lys Asn Tyr Gly Tyr Arg Asn Tyr His Glu Asn Gly
210 215 220

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

Tyr Ser Asn Glu Thr Asn Asp Val Pro Ala Val Thr Ser Gly Thr Val
245 250 255

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

Asp Ala Asn Asp Asn Asp Trp Ile Tyr Gly His Leu Gln Arg Gly Ser
275 280 285

Met Arg Phe Val Val Gly Asp Lys Val Asn Gln Gly Asp Ile Ile Gly
290 295 300

Leu Gln Gly Asn Ser Asn Tyr Tyr Asp Asn Pro Met Ser Val His Leu
305 310 315 320

His Leu Gln Leu Arg Pro Lys Asp Ala Lys Lys Asp Glu Lys Ser Gln
325 330 335

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

Ala Lys Gln Asp Lys Ser Lys Asn Gly Ser Val Lys Glu Leu Lys His
355 360 365

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

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Ser Ile Gln Gly Val Val Ile His Asn Asp Tyr Gly Ser Met Thr Pro
385                      390                      395                      400

Ser Gln Tyr Leu Pro Trp Leu Tyr Ala Arg Glu Asn Asn Gly Thr His
                      405                      410                      415

Val Asn Gly Trp Ala Ser Val Tyr Ala Asn Arg Asn Glu Val Leu Trp
                      420                      425                      430

Tyr His Pro Thr Asp Tyr Val Glu Trp His Cys Gly Asn Gln Trp Ala
                      435                      440                      445

Asn Ala Asn Leu Ile Gly Phe Glu Val Cys Glu Ser Tyr Pro Gly Arg
                      450                      455                      460

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

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

Val Arg Leu His Asn Glu Phe Phe Gly Thr Ser Cys Pro His Arg Ser
                    500                      505                      510

Trp Asp Leu His Val Gly Lys Gly Glu Pro Tyr Thr Thr Thr Asn Ile
                    515                      520                      525

Asn Lys Met Lys Asp Tyr Phe Ile Lys Arg Ile Lys His Tyr Tyr Asp
                    530                      535                      540

Gly Gly Lys Leu Glu Val Ser Lys Ala Ala Thr Ile Lys Gln Ser Asp
545                      550                      555                      560

Val Lys Gln Glu Val Lys Lys Gln Glu Ala Lys Gln Ile Val Lys Ala
                    565                      570                      575

Thr Asp Trp Lys Gln Asn Lys Asp Gly Ile Trp Tyr Lys Ala Glu His
                    580                      585                      590

Ala Ser Phe Thr Val Thr Ala Pro Glu Gly Ile Ile Thr Arg Tyr Lys
                    595                      600                      605

Gly Pro Trp Thr Gly His Pro Gln Ala Gly Val Leu Gln Lys Gly Gln
610                      615                      620

Thr Ile Lys Tyr Asp Glu Val Gln Lys Phe Asp Gly His Val Trp Val
625                      630                      635                      640

Ser Trp Glu Thr Phe Glu Gly Glu Thr Val Tyr Met Pro Val Arg Thr
                    645                      650                      655

Trp Asp Ala Lys Thr Gly Lys Val Gly Lys Leu Trp Gly Glu Ile Lys
660                      665                      670

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<210> 79

<211> 2145

<212> DNA

<213> artificial

<220>

<223> artificial construct

<400> 79

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aaaggtatag ttatacacia cgacgcaggg agcaaagggg cgactgctga agcatatcgt	180
aacggattag taaatgcacc tttatcaaga ttagaagcgg gcattgcgca tagttacgta	240
tcaggcaaca cagtttggca agccttagat gaatcacaaag taggttggca tacogctaata	300
caaataaggta ataaatatta ttacgggtatt gaagtatgtc aatcaatggg cgcagataac	360
gcgacattct taaaaaatga acaggcaact ttccaagaat gcgctagatt gttgaaaaaa	420
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tgccctcata gaagttcggg tttacacact ggttttgacc cagtaactcg cggctctattg	540
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gatggtaaaa taccggttgc cactgtctct aatgagtcaa gcgcttcaag taatacagtt	660
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caaggtgaca ttattggttt acaaggtaat agcaactatt acgacaatcc tatgagtgt	1080
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<210> 80

<211> 714

<212> PRT

<213> artificial

<220>

<223> artificial construct

<400> 80

Met Arg Gly Ser His His His His His His Gly Ser Lys Pro Gln Pro
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Lys Ala Val Glu Leu Lys Ile Ile Lys Asp Val Val Lys Gly Tyr Asp
 20 25 30

Leu Pro Lys Arg Gly Ser Asn Pro Lys Gly Ile Val Ile His Asn Asp
 35 40 45

Ala Gly Ser Lys Gly Ala Thr Ala Glu Ala Tyr Arg Asn Gly Leu Val
 50 55 60

Asn Ala Pro Leu Ser Arg Leu Glu Ala Gly Ile Ala His Ser Tyr Val
 65 70 75 80

Ser Gly Asn Thr Val Trp Gln Ala Leu Asp Glu Ser Gln Val Gly Trp
 85 90 95

His Thr Ala Asn Gln Ile Gly Asn Lys Tyr Tyr Tyr Gly Ile Glu Val
 100 105 110

Cys Gln Ser Met Gly Ala Asp Asn Ala Thr Phe Leu Lys Asn Glu Gln
 115 120 125

Ala Thr Phe Gln Glu Cys Ala Arg Leu Leu Lys Lys Trp Gly Leu Pro
 130 135 140

Ala Asn Arg Asn Thr Ile Arg Leu His Asn Glu Phe Thr Ser Thr Ser
 145 150 155 160

Cys Pro His Arg Ser Ser Val Leu His Thr Gly Phe Asp Pro Val Thr
 165 170 175

Arg Gly Leu Leu Pro Glu Asp Lys Arg Leu Gln Leu Lys Asp Tyr Phe
 180 185 190

Ile	Lys	Gln	Ile	Arg	Ala	Tyr	Met	Asp	Gly	Lys	Ile	Pro	Val	Ala	Thr		
		195					200					205					
Val	Ser	Asn	Glu	Ser	Ser	Ala	Ser	Ser	Asn	Thr	Val	Lys	Pro	Val	Ala		
	210					215					220						
Ser	Ala	Gly	Ser	Met	Leu	Thr	Ala	Ile	Asp	Tyr	Leu	Thr	Lys	Lys	Gly		
225					230					235					240		
Trp	Lys	Ile	Ser	Ser	Asp	Pro	Arg	Thr	Tyr	Asp	Gly	Tyr	Pro	Lys	Asn		
				245					250					255			
Tyr	Gly	Tyr	Arg	Asn	Tyr	His	Glu	Asn	Gly	Ile	Asn	Tyr	Asp	Glu	Phe		
			260					265					270				
Cys	Gly	Gly	Tyr	His	Arg	Ala	Phe	Asp	Val	Tyr	Ser	Asn	Glu	Thr	Asn		
		275					280					285					
Asp	Val	Pro	Ala	Val	Thr	Ser	Gly	Thr	Val	Ile	Glu	Ala	Asn	Asp	Tyr		
	290					295					300						
Gly	Asn	Phe	Gly	Gly	Thr	Phe	Val	Ile	Arg	Asp	Ala	Asn	Asp	Asn	Asp		
305					310					315					320		
Trp	Ile	Tyr	Gly	His	Leu	Gln	Arg	Gly	Ser	Met	Arg	Phe	Val	Val	Gly		
				325					330					335			
Asp	Lys	Val	Asn	Gln	Gly	Asp	Ile	Ile	Gly	Leu	Gln	Gly	Asn	Ser	Asn		
			340					345					350				
Tyr	Tyr	Asp	Asn	Pro	Met	Ser	Val	His	Leu	His	Leu	Gln	Leu	Arg	Pro		
		355					360					365					
Lys	Asp	Ala	Lys	Lys	Asp	Glu	Lys	Ser	Gln	Val	Cys	Ser	Gly	Leu	Ala		
	370					375					380						
Met	Glu	Lys	Tyr	Asp	Ile	Thr	Asn	Leu	Asn	Ala	Lys	Gln	Asp	Lys	Ser		
385					390					395					400		
Lys	Asn	Gly	Ser	Val	Lys	Glu	Leu	Lys	His	Ile	Tyr	Ser	Asn	His	Ile		
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Lys	Gly	Asn	Lys	Ile	Thr	Ala	Pro	Lys	Pro	Ser	Ile	Gln	Gly	Val	Val		
			420					425					430				
Ile	His	Asn	Asp	Tyr	Gly	Ser	Met	Thr	Pro	Ser	Gln	Tyr	Leu	Pro	Trp		
		435					440					445					
Leu	Tyr	Ala	Arg	Glu	Asn	Asn	Gly	Thr	His	Val	Asn	Gly	Trp	Ala	Ser		
	450					455					460						
Val	Tyr	Ala	Asn	Arg	Asn	Glu	Val	Leu	Trp	Tyr	His	Pro	Thr	Asp	Tyr		
465					470					475					480		
Val	Glu	Trp	His	Cys	Gly	Asn	Gln	Trp	Ala	Asn	Ala	Asn	Leu	Ile	Gly		
				485					490					495			

Phe Glu Val Cys Glu Ser Tyr Pro Gly Arg Ile Ser Asp Lys Leu Phe
500 505 510

Leu Glu Asn Glu Glu Ala Thr Leu Lys Val Ala Ala Asp Val Met Lys
515 520 525

Ser Tyr Gly Leu Pro Val Asn Arg Asn Thr Val Arg Leu His Asn Glu
530 535 540

Phe Phe Gly Thr Ser Cys Pro His Arg Ser Trp Asp Leu His Val Gly
545 550 555 560

Lys Gly Glu Pro Tyr Thr Thr Thr Asn Ile Asn Lys Met Lys Asp Tyr
565 570 575

Phe Ile Lys Arg Ile Lys His Tyr Tyr Asp Gly Gly Lys Leu Glu Val
580 585 590

Ser Lys Ala Ala Thr Ile Lys Gln Ser Asp Val Lys Gln Glu Val Lys
595 600 605

Lys Gln Glu Ala Lys Gln Ile Val Lys Ala Thr Asp Trp Lys Gln Asn
610 615 620

Lys Asp Gly Ile Trp Tyr Lys Ala Glu His Ala Ser Phe Thr Val Thr
625 630 635 640

Ala Pro Glu Gly Ile Ile Thr Arg Tyr Lys Gly Pro Trp Thr Gly His
645 650 655

Pro Gln Ala Gly Val Leu Gln Lys Gly Gln Thr Ile Lys Tyr Asp Glu
660 665 670

Val Gln Lys Phe Asp Gly His Val Trp Val Ser Trp Glu Thr Phe Glu
675 680 685

Gly Glu Thr Val Tyr Met Pro Val Arg Thr Trp Asp Ala Lys Thr Gly
690 695 700

Lys Val Gly Lys Leu Trp Gly Glu Ile Lys
705 710

<210> 81

<211> 1959

<212> DNA

<213> artificial

<220>

<223> artificial construct

<400> 81

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tgtatggact tagcagtaga ttatatattac catgtaacag atggtaaaat aagaatgtgg 180

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tcacaagtat gtagtggttt ggctatggaa aaatatgaca ttacaaattt aaatgctaaa 540
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<210> 82

<211> 652

<212> PRT

<213> artificial

<220>

<223> artificial construct

<400> 82

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Phe Asp Gly Leu Tyr Gly Tyr Gln Cys Met Asp Leu Ala Val Asp Tyr
 35 40 45

Ile Tyr His Val Thr Asp Gly Lys Ile Arg Met Trp Gly Asn Ala Lys
 50 55 60

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

Tyr Pro Ala Phe Arg Pro Lys Tyr Gly Asp Val Val Val Trp Thr Thr
 85 90 95

Gly Asn Phe Ala Thr Tyr Gly His Ile Ala Ile Val Thr Asn Pro Asp
 100 105 110

Pro Tyr Gly Asp Leu Gln Tyr Val Thr Val Leu Glu Gln Asn Trp Asn
 115 120 125

Gly Asn Gly Ile Tyr Lys Thr Glu Leu Ala Thr Ile Arg Thr His Asp
 130 135 140

Tyr Thr Gly Ile Thr His Phe Ile Lys Asp Ala Lys Lys Asp Glu Lys
 145 150 155 160

Ser Gln Val Cys Ser Gly Leu Ala Met Glu Lys Tyr Asp Ile Thr Asn
 165 170 175

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

Lys His Ile Tyr Ser Asn His Ile Lys Gly Asn Lys Ile Thr Ala Pro
 195 200 205

Lys Pro Ser Ile Gln Gly Val Val Ile His Asn Asp Tyr Gly Ser Met
 210 215 220

Thr Pro Ser Gln Tyr Leu Pro Trp Leu Tyr Ala Arg Glu Asn Asn Gly
 225 230 235 240

Thr His Val Asn Gly Trp Ala Ser Val Tyr Ala Asn Arg Asn Glu Val
 245 250 255

Leu Trp Tyr His Pro Thr Asp Tyr Val Glu Trp His Cys Gly Asn Gln
 260 265 270

Trp Ala Asn Ala Asn Leu Ile Gly Phe Glu Val Cys Glu Ser Tyr Pro
 275 280 285

Gly Arg Ile Ser Asp Lys Leu Phe Leu Glu Asn Glu Glu Ala Thr Leu
 290 295 300

```

250          255          300
Lys Val Ala Ala Asp Val Met Lys Ser Tyr Gly Leu Pro Val Asn Arg
305          310          315          320

Asn Thr Val Arg Leu His Asn Glu Phe Phe Gly Thr Ser Cys Pro His
325          330          335

Arg Ser Trp Asp Leu His Val Gly Lys Gly Glu Pro Tyr Thr Thr Thr
340          345          350

Asn Ile Asn Lys Met Lys Asp Tyr Phe Ile Lys Arg Ile Lys His Tyr
355          360          365

Tyr Asp Gly Gly Lys Leu Glu Val Ser Lys Ala Ala Thr Ile Lys Gln
370          375          380

Ser Asp Val Lys Gln Glu Val Lys Lys Gln Glu Ala Lys Gln Ile Val
385          390          395          400

Lys Ala Thr Asp Ala Ala Thr His Glu His Ser Ala Gln Trp Leu Asn
405          410          415

Asn Tyr Lys Lys Gly Tyr Gly Tyr Gly Pro Tyr Pro Leu Gly Ile Asn
420          425          430

Gly Gly Met His Tyr Gly Val Asp Phe Phe Met Asn Ile Gly Thr Pro
435          440          445

Val Lys Ala Ile Ser Ser Gly Lys Ile Val Glu Ala Gly Trp Ser Asn
450          455          460

Tyr Gly Gly Gly Asn Gln Ile Gly Leu Ile Glu Asn Asp Gly Val His
465          470          475          480

Arg Gln Trp Tyr Met His Leu Ser Lys Tyr Asn Val Lys Val Gly Asp
485          490          495

Tyr Val Lys Ala Gly Gln Ile Ile Gly Trp Ser Gly Ser Thr Gly Tyr
500          505          510

Ser Thr Ala Pro His Leu His Phe Gln Arg Met Val Asn Ser Phe Ser
515          520          525

Asn Ser Thr Ala Gln Asp Pro Met Pro Phe Leu Lys Ser Ala Gly Tyr
530          535          540

Gly Lys Ala Gly Gly Thr Val Thr Pro Thr Pro Asn Thr Gly Trp Lys
545          550          555          560

Gln Asn Lys Asp Gly Ile Trp Tyr Lys Ala Glu His Ala Ser Phe Thr
565          570          575

Val Thr Ala Pro Glu Gly Ile Ile Thr Arg Tyr Lys Gly Pro Trp Thr
580          585          590

```

Gly His Pro Gln Ala Gly Val Leu Gln Lys Gly Gln Thr Ile Lys Tyr
595 600 605

Asp Glu Val Gln Lys Phe Asp Gly His Val Trp Val Ser Trp Glu Thr
610 615 620

Phe Glu Gly Glu Thr Val Tyr Met Pro Val Arg Thr Trp Asp Ala Lys
625 630 635 640

Thr Gly Lys Val Gly Lys Leu Trp Gly Glu Ile Lys
645 650

<210> 83

<211> 1554

<212> DNA

<213> artificial

<220>

<223> artificial construct

<400> 83

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ggcgggtatgc actacggagt tgattttttt atgaatattg gaacaccagt aaaagctatt	180
tcaagcggaa aaatagttga agctgggttg agtaattacg gaggaggtaa tcaaataagg	240
cttattgaaa atgatggagt gcatagacaa tggatatatgc atctaagtaa atataatggt	300
aaagtaggag attatgtcaa agctgggtcaa ataatcggtt ggtctggaag cactgggttat	360
tctacagcac cacatttaca cttccaaaga atgggttaatt cattttcaaa ttcaactgcc	420
caagatccaa tgcctttctt aaagagcgca ggatatggaa aagcaggtgg tacagtaact	480
ccaacgccga atacaggtga gctcttacgc cctaaagacg caaagaaaga tgaaaaatca	540
caagtatgta gtgggtttggc tatggaaaaa tatgacatta caaatttaaa tgctaaacaa	600
gataaatcaa agaatgggag cgtgaaagag ttgaaacata tctattcaaa ccatattaaa	660
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ggtagtatga cacctagtca atacttacca tgggttatatg cacgtgagaa taacgggtaca	780
cacgttaacg gttgggctag tgtttatgca aatagaaacg aagtgccttg gtatcatccg	840
acagactacg tagagtggca ttgtggtaat caatgggcaa atgctaactt aatcggattt	900
gaagtgtgtg agtcgtatcc tggtagaatc tcggacaaat tattcttaga aaatgaagaa	960
gcgacattga aagtagctgc ggatgtgatg aagtcgtacg gattaccagt taatcgcaac	1020
actgtacgtc tgcataacga attcttcgga acttcttgtc cacatcggtc gtgggacttg	1080
catgttggca aaggtgagcc ttacacaact actaatatta ataaaatgaa agactacttc	1140
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gcaacagatt ggaaacagaa taaagatggc atttggtata aagctgaaca tgcttcgttc	1320

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 ggtcatgttt gggatatcgtg ggaaacgttt gagggcgaaa ctgtatacat gccggtacgc 1500
 acatgggacg ctaaaactgg taaagttggt aagttgtggg gcgaaattaa ataa 1554

<210> 84

<211> 517

<212> PRT

<213> artificial

<220>

<223> artificial construct

<400> 84

Met Arg Gly Ser His His His His His His Gly Ser Ala Ala Thr His
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Glu His Ser Ala Gln Trp Leu Asn Asn Tyr Lys Lys Gly Tyr Gly Tyr
 20 25 30

Gly Pro Tyr Pro Leu Gly Ile Asn Gly Gly Met His Tyr Gly Val Asp
 35 40 45

Phe Phe Met Asn Ile Gly Thr Pro Val Lys Ala Ile Ser Ser Gly Lys
 50 55 60

Ile Val Glu Ala Gly Trp Ser Asn Tyr Gly Gly Gly Asn Gln Ile Gly
 65 70 75 80

Leu Ile Glu Asn Asp Gly Val His Arg Gln Trp Tyr Met His Leu Ser
 85 90 95

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

Gly Trp Ser Gly Ser Thr Gly Tyr Ser Thr Ala Pro His Leu His Phe
 115 120 125

Gln Arg Met Val Asn Ser Phe Ser Asn Ser Thr Ala Gln Asp Pro Met
 130 135 140

Pro Phe Leu Lys Ser Ala Gly Tyr Gly Lys Ala Gly Gly Thr Val Thr
 145 150 155 160

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

Asp Glu Lys Ser Gln Val Cys Ser Gly Leu Ala Met Glu Lys Tyr Asp
 180 185 190

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

Lys Glu Leu Lys His Ile Tyr Ser Asn His Ile Lys Gly Asn Lys Ile
 210 215 220
 Thr Ala Pro Lys Pro Ser Ile Gln Gly Val Val Ile His Asn Asp Tyr
 225 230 235 240
 Gly Ser Met Thr Pro Ser Gln Tyr Leu Pro Trp Leu Tyr Ala Arg Glu
 245 250 255
 Asn Asn Gly Thr His Val Asn Gly Trp Ala Ser Val Tyr Ala Asn Arg
 260 265 270
 Asn Glu Val Leu Trp Tyr His Pro Thr Asp Tyr Val Glu Trp His Cys
 275 280 285
 Gly Asn Gln Trp Ala Asn Ala Asn Leu Ile Gly Phe Glu Val Cys Glu
 290 295 300
 Ser Tyr Pro Gly Arg Ile Ser Asp Lys Leu Phe Leu Glu Asn Glu Glu
 305 310 315 320
 Ala Thr Leu Lys Val Ala Ala Asp Val Met Lys Ser Tyr Gly Leu Pro
 325 330 335
 Val Asn Arg Asn Thr Val Arg Leu His Asn Glu Phe Phe Gly Thr Ser
 340 345 350
 Cys Pro His Arg Ser Trp Asp Leu His Val Gly Lys Gly Glu Pro Tyr
 355 360 365
 Thr Thr Thr Asn Ile Asn Lys Met Lys Asp Tyr Phe Ile Lys Arg Ile
 370 375 380
 Lys His Tyr Tyr Asp Gly Gly Lys Leu Glu Val Ser Lys Ala Ala Thr
 385 390 395 400
 Ile Lys Gln Ser Asp Val Lys Gln Glu Val Lys Lys Gln Glu Ala Lys
 405 410 415
 Gln Ile Val Lys Ala Thr Asp Trp Lys Gln Asn Lys Asp Gly Ile Trp
 420 425 430
 Tyr Lys Ala Glu His Ala Ser Phe Thr Val Thr Ala Pro Glu Gly Ile
 435 440 445
 Ile Thr Arg Tyr Lys Gly Pro Trp Thr Gly His Pro Gln Ala Gly Val
 450 455 460
 Leu Gln Lys Gly Gln Thr Ile Lys Tyr Asp Glu Val Gln Lys Phe Asp
 465 470 475 480
 Gly His Val Trp Val Ser Trp Glu Thr Phe Glu Gly Glu Thr Val Tyr
 485 490 495

Met Pro Val Arg Thr Trp Asp Ala Lys Thr Gly Lys Val Gly Lys Leu
500 505 510

Trp Gly Glu Ile Lys
515

<210> 85

<211> 1887

<212> DNA

<213> artificial

<220>

<223> artificial construct

<400> 85

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tacgggtaca gaaattacca tgaaaacggc attaattatg atgagttttg tgggtgggtat	180
catagagctt ttgatgttta cagtaacgaa actaacgacg tgcctgctgt tactagcggg	240
acagttattg aagcaaacga ttacggtaat tttgggtggta cattcggttat tagagacgct	300
aacgataacg attggatata tgggcatcta caacgtggct caatgcgatt tgttgtaggc	360
gacaaagtca atcaaggtga cattattggg ttacaaggta atagcaacta ttacgacaat	420
cctatgagtg tacattttaca tttaacaatta cgccctaaag acgcaaagaa agatgaaaaa	480
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caagataaat caaagaatgg gagcgtgaaa gagttgaaac atatctattc aaaccatatt	600
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tatggtagta tgacacctag tcaatactta ccatgggttat atgcacgtga gaataacggt	720
acacacgtta acggttgggc tagtggtttat gcaaatagaa acgaagtgc ttggtatcat	780
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gaagcgacat tgaaagtagc tgcggatgtg atgaagtcgt acggattacc agttaatcgc	960
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acaagataca aaggtccttg gactggtcac ccacaagctg gtgtattaca aaaaggtcaa 1740
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tttgagggcg aaactgtata catgccggta cgcacatggg acgctaaaac tggtaaagtt 1860
ggtaagttgt ggggcgaaat taaataa 1887

```

<210> 86

<211> 628

<212> PRT

<213> artificial

<220>

<223> artificial construct

<400> 86

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Met Arg Gly Ser His His His His His His Gly Ser Met Leu Thr Ala
1           5           10           15

```

```

Ile Asp Tyr Leu Thr Lys Lys Gly Trp Lys Ile Ser Ser Asp Pro Arg
20           25           30

```

```

Thr Tyr Asp Gly Tyr Pro Lys Asn Tyr Gly Tyr Arg Asn Tyr His Glu
35           40           45

```

```

Asn Gly Ile Asn Tyr Asp Glu Phe Cys Gly Gly Tyr His Arg Ala Phe
50           55           60

```

```

Asp Val Tyr Ser Asn Glu Thr Asn Asp Val Pro Ala Val Thr Ser Gly
65           70           75           80

```

```

Thr Val Ile Glu Ala Asn Asp Tyr Gly Asn Phe Gly Gly Thr Phe Val
85           90           95

```

```

Ile Arg Asp Ala Asn Asp Asn Asp Trp Ile Tyr Gly His Leu Gln Arg
100          105          110

```

```

Gly Ser Met Arg Phe Val Val Gly Asp Lys Val Asn Gln Gly Asp Ile
115          120          125

```

```

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

```

```

His Leu His Leu Gln Leu Arg Pro Lys Asp Ala Lys Lys Asp Glu Lys
145          150          155          160

```

```

Ser Gln Val Cys Ser Gly Leu Ala Met Glu Lys Tyr Asp Ile Thr Asn
165          170          175

```

```

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

```

```

Lys His Ile Tyr Ser Asn His Ile Lys Gly Asn Lys Ile Thr Ala Pro

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```

-      195      -      200      -      -      -      205

Lys Pro Ser Ile Gln Gly Val Val Ile His Asn Asp Tyr Gly Ser Met
210      215      220

Thr Pro Ser Gln Tyr Leu Pro Trp Leu Tyr Ala Arg Glu Asn Asn Gly
225      230      235      240

Thr His Val Asn Gly Trp Ala Ser Val Tyr Ala Asn Arg Asn Glu Val
245      250      255

Leu Trp Tyr His Pro Thr Asp Tyr Val Glu Trp His Cys Gly Asn Gln
260      265      270

Trp Ala Asn Ala Asn Leu Ile Gly Phe Glu Val Cys Glu Ser Tyr Pro
275      280      285

Gly Arg Ile Ser Asp Lys Leu Phe Leu Glu Asn Glu Glu Ala Thr Leu
290      295      300

Lys Val Ala Ala Asp Val Met Lys Ser Tyr Gly Leu Pro Val Asn Arg
305      310      315      320

Asn Thr Val Arg Leu His Asn Glu Phe Phe Gly Thr Ser Cys Pro His
325      330      335

Arg Ser Trp Asp Leu His Val Gly Lys Gly Glu Pro Tyr Thr Thr Thr
340      345      350

Asn Ile Asn Lys Met Lys Asp Tyr Phe Ile Lys Arg Ile Lys His Tyr
355      360      365

Tyr Asp Gly Gly Lys Leu Glu Val Ser Lys Ala Ala Thr Ile Lys Gln
370      375      380

Ser Asp Val Lys Gln Glu Val Lys Lys Gln Glu Ala Lys Gln Ile Val
385      390      395      400

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

Glu His Ala Ser Phe Thr Val Thr Ala Pro Glu Gly Ile Ile Thr Arg
420      425      430

Tyr Lys Gly Pro Trp Thr Gly His Pro Gln Ala Gly Val Leu Gln Lys
435      440      445

Gly Gln Thr Ile Lys Tyr Asp Glu Val Gln Lys Phe Asp Gly His Val
450      455      460

Trp Val Ser Trp Glu Thr Phe Glu Gly Glu Thr Val Tyr Met Pro Val
465      470      475      480

Arg Thr Trp Asp Ala Lys Thr Gly Lys Val Gly Lys Leu Trp Gly Glu
485      490      495

Tle Lys Glu Leu Gly Gly Lys Leu Glu Val Ser Lys Ala Ala Thr Tle

```

Lys Gln Ser Asp Val Lys Gln Glu Val Lys Lys Gln Glu Ala Lys Gln
500 505 510

Lys Gln Ser Asp Val Lys Gln Glu Val Lys Lys Gln Glu Ala Lys Gln
515 520 525

Ile Val Lys Ala Thr Asp Trp Lys Gln Asn Lys Asp Gly Ile Trp Tyr
530 535 540

Lys Ala Glu His Ala Ser Phe Thr Val Thr Ala Pro Glu Gly Ile Ile

545 550 555 560

Thr Arg Tyr Lys Gly Pro Trp Thr Gly His Pro Gln Ala Gly Val Leu
565 570 575

Gln Lys Gly Gln Thr Ile Lys Tyr Asp Glu Val Gln Lys Phe Asp Gly
580 585 590

His Val Trp Val Ser Trp Glu Thr Phe Glu Gly Glu Thr Val Tyr Met
595 600 605

Pro Val Arg Thr Trp Asp Ala Lys Thr Gly Lys Val Gly Lys Leu Trp
610 615 620

Gly Glu Ile Lys
625

<210> 87
<211> 1035
<212> DNA
<213> artificial

<220>
<223> artificial construct

<400> 87
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tacgggctaca gaaattacca tgaaaacggc attaattatg atgagttttg tgggtgggtat 180
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aacgataacg attggatata tgggcatcta caacgtggct caatgcgatt tggtgtaggc 360
gacaaagtca atcaaggtga cattattggg ttacaaggta atagcaacta ttacgacaat 420
cctatgagtg tacattttaca ttacaatta cgccctaaag acgcaaagaa agatgaaaaa 480
tcacaagtat gtagtggttt ggctatggaa aaatatgaca ttacaaattt aaatgctaaa 540
caagataaat caaagaatgg gagcgtgaaa gagttgaaac atatctattc aaaccatatt 600
aaaggtaaca agattacagc accaaaacct agtattcaag gtgagctcgg tggaaagcta 660
gaagtaagca aagcagcaac tatcaaacaa tctgacgtta agcaagaagt taaaaagcaa 720

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gatgaggttc aaaaatttga cggtcatggt tgggtatcgt gggaaacggt tgagggcgaa 960

actgtataca tgccggtacg cacatgggac gctaaaactg gtaaagttgg taagttgtgg 1020
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```

<210> 88

<211> 344

<212> PRT

<213> artificial

<220>

<223> artificial construct

<400> 88

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Met Arg Gly Ser His His His His His His Gly Ser Met Leu Thr Ala
1          5          10          15

```

```

Ile Asp Tyr Leu Thr Lys Lys Gly Trp Lys Ile Ser Ser Asp Pro Arg
20          25          30

```

```

Thr Tyr Asp Gly Tyr Pro Lys Asn Tyr Gly Tyr Arg Asn Tyr His Glu
35          40          45

```

```

Asn Gly Ile Asn Tyr Asp Glu Phe Cys Gly Gly Tyr His Arg Ala Phe
50          55          60

```

```

Asp Val Tyr Ser Asn Glu Thr Asn Asp Val Pro Ala Val Thr Ser Gly
65          70          75          80

```

```

Thr Val Ile Glu Ala Asn Asp Tyr Gly Asn Phe Gly Gly Thr Phe Val
85          90          95

```

```

Ile Arg Asp Ala Asn Asp Asn Asp Trp Ile Tyr Gly His Leu Gln Arg
100         105         110

```

```

Gly Ser Met Arg Phe Val Val Gly Asp Lys Val Asn Gln Gly Asp Ile
115         120         125

```

```

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

```

```

His Leu His Leu Gln Leu Arg Pro Lys Asp Ala Lys Lys Asp Glu Lys
145         150         155         160

```

```

Ser Gln Val Cys Ser Gly Leu Ala Met Glu Lys Tyr Asp Ile Thr Asn
165         170         175

```

```

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

```

Lys His Ile Tyr Ser Asn His Ile Lys Gly Asn Lys Ile Thr Ala Pro
 195 200 205

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

Ala Ala Thr Ile Lys Gln Ser Asp Val Lys Gln Glu Val Lys Lys Gln
 225 230 235 240

Glu Ala Lys Gln Ile Val Lys Ala Thr Asp Trp Lys Gln Asn Lys Asp
 245 250 255

Gly Ile Trp Tyr Lys Ala Glu His Ala Ser Phe Thr Val Thr Ala Pro
 260 265 270

Glu Gly Ile Ile Thr Arg Tyr Lys Gly Pro Trp Thr Gly His Pro Gln
 275 280 285

Ala Gly Val Leu Gln Lys Gly Gln Thr Ile Lys Tyr Asp Glu Val Gln
 290 295 300

Lys Phe Asp Gly His Val Trp Val Ser Trp Glu Thr Phe Glu Gly Glu
 305 310 315 320

Thr Val Tyr Met Pro Val Arg Thr Trp Asp Ala Lys Thr Gly Lys Val
 325 330 335

Gly Lys Leu Trp Gly Glu Ile Lys
 340

<210> 89

<211> 2961

<212> DNA

<213> artificial

<220>

<223> artificial construct

<400> 89

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tacgggtaca gaaattacca tgaaaacggc attaattatg atgagttttg tgggtggttat	180
catagagctt ttgatgttta cagtaacgaa actaacgacg tgccctgctgt tactagcgga	240
acagttattg aagcaaacga ttacggtaat tttgggtgga cattcgttat tagagacgct	300
aacgataacg attggatata tgggcatcta caacgtggct caatgcgatt tgttgtaggc	360
gacaaagtca atcaaggtga cattattggt ttacaaggta atagcaacta ttacgacaat	420
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caagataaat caaagaatgg gagcgtgaaa gagttgaaac atatctattc aaaccatatt	600

aaaggttaaca agattacagc accaaaacct agtattcaag gtgtggtcat ccacaatgat	660
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aaacatatct attcaaacca tattaaaggt aacaagatta cagcaccaaa acctagtatt	2100
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tcgtacggat taccagttaa tcgcaacact gtacgtctgc ataacgaatt cttcggaact	2460
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<210> 90

<211> 986

<212> PRT

<213> artificial

<220>

<223> artificial construct

<400> 90

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Thr Tyr Asp Gly Tyr Pro Lys Asn Tyr Gly Tyr Arg Asn Tyr His Glu
 35 40 45

Asn Gly Ile Asn Tyr Asp Glu Phe Cys Gly Gly Tyr His Arg Ala Phe
 50 55 60

Asp Val Tyr Ser Asn Glu Thr Asn Asp Val Pro Ala Val Thr Ser Gly
 65 70 75 80

Thr Val Ile Glu Ala Asn Asp Tyr Gly Asn Phe Gly Gly Thr Phe Val
 85 90 95

Ile Arg Asp Ala Asn Asp Asn Asp Trp Ile Tyr Gly His Leu Gln Arg
 100 105 110

Gly Ser Met Arg Phe Val Val Gly Asp Lys Val Asn Gln Gly Asp Ile
 115 120 125

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

His Leu His Leu Gln Leu Arg Pro Lys Asp Ala Lys Lys Asp Glu Lys
 145 150 155 160

Ser Gln Val Cys Ser Gly Leu Ala Met Glu Lys Tyr Asp Ile Thr Asn
 165 170 175

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

Lys His Ile Tyr Ser Asn His Ile Lys Gly Asn Lys Ile Thr Ala Pro
 195 200 205

Lys Pro Ser Ile Gln Gly Val Val Ile His Asn Asp Tyr Gly Ser Met
 210 215 220

Thr Pro Ser Gln Tyr Leu Pro Trp Leu Tyr Ala Arg Glu Asn Asn Gly
 225 230 235 240
 Thr His Val Asn Gly Trp Ala Ser Val Tyr Ala Asn Arg Asn Glu Val
 245 250 255
 Leu Trp Tyr His Pro Thr Asp Tyr Val Glu Trp His Cys Gly Asn Gln
 260 265 270
 Trp Ala Asn Ala Asn Leu Ile Gly Phe Glu Val Cys Glu Ser Tyr Pro
 275 280 285
 Gly Arg Ile Ser Asp Lys Leu Phe Leu Glu Asn Glu Glu Ala Thr Leu
 290 295 300
 Lys Val Ala Ala Asp Val Met Lys Ser Tyr Gly Leu Pro Val Asn Arg
 305 310 315 320
 Asn Thr Val Arg Leu His Asn Glu Phe Phe Gly Thr Ser Cys Pro His
 325 330 335
 Arg Ser Trp Asp Leu His Val Gly Lys Gly Glu Pro Tyr Thr Thr Thr
 340 345 350
 Asn Ile Asn Lys Met Lys Asp Tyr Phe Ile Lys Arg Ile Lys His Tyr
 355 360 365
 Tyr Asp Gly Gly Lys Leu Glu Val Ser Lys Ala Ala Thr Ile Lys Gln
 370 375 380
 Ser Asp Val Lys Gln Glu Val Lys Lys Gln Glu Ala Lys Gln Ile Val
 385 390 395 400
 Lys Ala Thr Asp Trp Lys Gln Asn Lys Asp Gly Ile Trp Tyr Lys Ala
 405 410 415
 Glu His Ala Ser Phe Thr Val Thr Ala Pro Glu Gly Ile Ile Thr Arg
 420 425 430
 Tyr Lys Gly Pro Trp Thr Gly His Pro Gln Ala Gly Val Leu Gln Lys
 435 440 445
 Gly Gln Thr Ile Lys Tyr Asp Glu Val Gln Lys Phe Asp Gly His Val
 450 455 460
 Trp Val Ser Trp Glu Thr Phe Glu Gly Glu Thr Val Tyr Met Pro Val
 465 470 475 480
 Arg Thr Trp Asp Ala Lys Thr Gly Lys Val Gly Lys Leu Trp Gly Glu
 485 490 495
 Ile Lys Glu Leu Met Leu Thr Ala Ile Asp Tyr Leu Thr Lys Lys Gly
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 Trp Lys Ile Ser Ser Asp Pro Arg Thr Tyr Asp Gly Tyr Pro Lys Asn
 515 520 525

Tyr Gly Tyr Arg Asn Tyr His Glu Asn Gly Ile Asn Tyr Asp Glu Phe
 530 535 540
 Cys Gly Gly Tyr His Arg Ala Phe Asp Val Tyr Ser Asn Glu Thr Asn
 545 550 555 560
 Asp Val Pro Ala Val Thr Ser Gly Thr Val Ile Glu Ala Asn Asp Tyr
 565 570 575
 Gly Asn Phe Gly Gly Thr Phe Val Ile Arg Asp Ala Asn Asp Asn Asp
 580 585 590
 Trp Ile Tyr Gly His Leu Gln Arg Gly Ser Met Arg Phe Val Val Gly
 595 600 605
 Asp Lys Val Asn Gln Gly Asp Ile Ile Gly Leu Gln Gly Asn Ser Asn
 610 615 620
 Tyr Tyr Asp Asn Pro Met Ser Val His Leu His Leu Gln Leu Arg Pro
 625 630 635 640
 Lys Asp Ala Lys Lys Asp Glu Lys Ser Gln Val Cys Ser Gly Leu Ala
 645 650 655
 Met Glu Lys Tyr Asp Ile Thr Asn Leu Asn Ala Lys Gln Asp Lys Ser
 660 665 670
 Lys Asn Gly Ser Val Lys Glu Leu Lys His Ile Tyr Ser Asn His Ile
 675 680 685
 Lys Gly Asn Lys Ile Thr Ala Pro Lys Pro Ser Ile Gln Gly Val Val
 690 695 700
 Ile His Asn Asp Tyr Gly Ser Met Thr Pro Ser Gln Tyr Leu Pro Trp
 705 710 715 720
 Leu Tyr Ala Arg Glu Asn Asn Gly Thr His Val Asn Gly Trp Ala Ser
 725 730 735
 Val Tyr Ala Asn Arg Asn Glu Val Leu Trp Tyr His Pro Thr Asp Tyr
 740 745 750
 Val Glu Trp His Cys Gly Asn Gln Trp Ala Asn Ala Asn Leu Ile Gly
 755 760 765
 Phe Glu Val Cys Glu Ser Tyr Pro Gly Arg Ile Ser Asp Lys Leu Phe
 770 775 780
 Leu Glu Asn Glu Glu Ala Thr Leu Lys Val Ala Ala Asp Val Met Lys
 785 790 795 800
 Ser Tyr Gly Leu Pro Val Asn Arg Asn Thr Val Arg Leu His Asn Glu
 805 810 815
 Phe Phe Gly Thr Ser Cys Pro His Arg Ser Trp Asp Leu His Val Gly
 820 825 830

Lys Gly Glu Pro Tyr Thr Thr Thr Asn Ile Asn Lys Met Lys Asp Tyr
835 840 845

Phe Ile Lys Arg Ile Lys His Tyr Tyr Asp Gly Gly Lys Leu Glu Val
850 855 860

Ser Lys Ala Ala Thr Ile Lys Gln Ser Asp Val Lys Gln Glu Val Lys

865 870 875 880

Lys Gln Glu Ala Lys Gln Ile Val Lys Ala Thr Asp Trp Lys Gln Asn
885 890 895

Lys Asp Gly Ile Trp Tyr Lys Ala Glu His Ala Ser Phe Thr Val Thr
900 905 910

Ala Pro Glu Gly Ile Ile Thr Arg Tyr Lys Gly Pro Trp Thr Gly His
915 920 925

Pro Gln Ala Gly Val Leu Gln Lys Gly Gln Thr Ile Lys Tyr Asp Glu
930 935 940

Val Gln Lys Phe Asp Gly His Val Trp Val Ser Trp Glu Thr Phe Glu
945 950 955 960

Gly Glu Thr Val Tyr Met Pro Val Arg Thr Trp Asp Ala Lys Thr Gly
965 970 975

Lys Val Gly Lys Leu Trp Gly Glu Ile Lys
980 985

<210> 91

<211> 1953

<212> DNA

<213> artificial

<220>

<223> artificial construct

<400> 91

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ggtaatgcta aggatgcgat aaataactct tttgggtggta ctgctacggt atataaaaac	240
taccctgctt ttagacctaa gtacgggtgat gtagtcgtat ggactactgg taattttgca	300
acttatggtc atatcgcaat agttactaac cctgaccctt atggagacct tcaatatggt	360
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agaacacacg attacacagg aattacacat tttatttaaag acgcaaagaa agatgaaaaa	480
tcacaagtat gtagtggttt ggctatggaa aaatatgaca ttacaaattt aaatgctaaa	540

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caagataaat caaagaatgg gagcgtgaaa gagttgaaac atatctattc aaaccatatt      600
aaaggtaaca agattacagc accaaaacct agtattcaag gtgtgggtcat ccacaatgat      660
tatggtagta tgacacctag tcaataactta ccatgggttat atgcacgtga gaataacggg      720

acacacgtta acggttgggc tagtgtttat gcaaatagaa acgaagtgct ttggtatcat      780
ccgacagact acgtagagtg gcattgtggg aatcaatggg caaatgctaa cttaatcgga      840
tttgaagtgt gtgagtcgta tcctggtaga atctcggaca aattattctt agaaaatgaa      900
gaagcgacat tgaaagtagc tgcggatgtg atgaagtcgt acggattacc agttaatcgc      960
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ggtcaaacaa ttcattatga tgaagtgatg aaacaagacg gtcatgtttg ggtaggttat     1860
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<210> 92

<211> 650

<212> PRT

<213> artificial

<220>

<223> artificial construct

<400> 92

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

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Phe Asp Gly Leu Tyr Gly Tyr Gln Cys Met Asp Leu Ala Val Asp Tyr

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Ile	Tyr	His	Val	Thr	Asp	Gly	Lys	Ile	Arg	Met	Trp	Gly	Asn	Ala	Lys				
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Pro	Tyr	Gly	Asp	Leu	Gln	Tyr	Val	Thr	Val	Leu	Glu	Gln	Asn	Trp	Asn				
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Tyr	Thr	Gly	Ile	Thr	His	Phe	Ile	Lys	Asp	Ala	Lys	Lys	Asp	Glu	Lys				
145					150					155					160				
Ser	Gln	Val	Cys	Ser	Gly	Leu	Ala	Met	Glu	Lys	Tyr	Asp	Ile	Thr	Asn				
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Leu	Asn	Ala	Lys	Gln	Asp	Lys	Ser	Lys	Asn	Gly	Ser	Val	Lys	Glu	Leu				
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Lys	His	Ile	Tyr	Ser	Asn	His	Ile	Lys	Gly	Asn	Lys	Ile	Thr	Ala	Pro				
		195					200					205							
Lys	Pro	Ser	Ile	Gln	Gly	Val	Val	Ile	His	Asn	Asp	Tyr	Gly	Ser	Met				
	210					215					220								
Thr	Pro	Ser	Gln	Tyr	Leu	Pro	Trp	Leu	Tyr	Ala	Arg	Glu	Asn	Asn	Gly				
225					230					235					240				
Thr	His	Val	Asn	Gly	Trp	Ala	Ser	Val	Tyr	Ala	Asn	Arg	Asn	Glu	Val				
				245					250					255					
Leu	Trp	Tyr	His	Pro	Thr	Asp	Tyr	Val	Glu	Trp	His	Cys	Gly	Asn	Gln				
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Trp	Ala	Asn	Ala	Asn	Leu	Ile	Gly	Phe	Glu	Val	Cys	Glu	Ser	Tyr	Pro				
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Gly	Arg	Ile	Ser	Asp	Lys	Leu	Phe	Leu	Glu	Asn	Glu	Glu	Ala	Thr	Leu				
	290					295					300								
Lys	Val	Ala	Ala	Asp	Val	Met	Lys	Ser	Tyr	Gly	Leu	Pro	Val	Asn	Arg				
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Asn	Thr	Val	Arg	Leu	His	Asn	Glu	Phe	Phe	Gly	Thr	Ser	Cys	Pro	His				
				325					330					335					

Arg Ser Trp Asp Leu His Val Gly Lys Gly Glu Pro Tyr Thr Thr Thr
 340 345 350
 Asn Ile Asn Lys Met Lys Asp Tyr Phe Ile Lys Arg Ile Lys His Tyr
 355 360 365
 Tyr Asp Gly Gly Lys Leu Glu Val Ser Lys Ala Ala Thr Ile Lys Gln
 370 375 380
 Ser Asp Val Lys Gln Glu Val Lys Lys Gln Glu Ala Lys Gln Ile Val
 385 390 395 400
 Lys Ala Thr Asp Ala Ala Thr His Glu His Ser Ala Gln Trp Leu Asn
 405 410 415
 Asn Tyr Lys Lys Gly Tyr Gly Tyr Gly Pro Tyr Pro Leu Gly Ile Asn
 420 425 430
 Gly Gly Met His Tyr Gly Val Asp Phe Phe Met Asn Ile Gly Thr Pro
 435 440 445
 Val Lys Ala Ile Ser Ser Gly Lys Ile Val Glu Ala Gly Trp Ser Asn
 450 455 460
 Tyr Gly Gly Gly Asn Gln Ile Gly Leu Ile Glu Asn Asp Gly Val His
 465 470 475 480
 Arg Gln Trp Tyr Met His Leu Ser Lys Tyr Asn Val Lys Val Gly Asp
 485 490 495
 Tyr Val Lys Ala Gly Gln Ile Ile Gly Trp Ser Gly Ser Thr Gly Tyr
 500 505 510
 Ser Thr Ala Pro His Leu His Phe Gln Arg Met Val Asn Ser Phe Ser
 515 520 525
 Asn Ser Thr Ala Gln Asp Pro Met Pro Phe Leu Lys Ser Ala Gly Tyr
 530 535 540
 Gly Lys Ala Gly Gly Thr Val Thr Pro Thr Pro Asn Thr Gly Trp Lys
 545 550 555 560
 Thr Asn Lys Tyr Gly Thr Leu Tyr Lys Ser Glu Ser Ala Ser Phe Thr
 565 570 575
 Pro Asn Thr Asp Ile Ile Thr Arg Thr Thr Gly Pro Phe Arg Ser Met
 580 585 590
 Pro Gln Ser Gly Val Leu Lys Ala Gly Gln Thr Ile His Tyr Asp Glu
 595 600 605
 Val Met Lys Gln Asp Gly His Val Trp Val Gly Tyr Thr Gly Asn Ser
 610 615 620
 Gly Gln Arg Ile Tyr Leu Pro Val Arg Thr Trp Asn Lys Ser Thr Asn
 625 630 635 640

Thr Leu Gly Val Leu Trp Gly Thr Ile Lys
645 650

<210> 93

<211> 1521

<212> DNA

<213> artificial

<220>

<223> artificial construct

<400> 93

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cttattgaaa atgatggagt gcatagacaa tggatatatgc atctaagtaa atataatgtt	300
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ccaacgccga atacagggtg gaaaacaaac aaatatggca cactatataa atcagagtca	540
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agaacatgga ataaatctac taatacttta ggtgttcttt ggggaactat aaaggagctc	780
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<210> 94

<211> 506

<212> PRT

<213> artificial

<220>

<223> artificial construct

<400> 94

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			20				25						30		

Gly	Pro	Tyr	Pro	Leu	Gly	Ile	Asn	Gly	Gly	Met	His	Tyr	Gly	Val	Asp
		35					40					45			

Phe	Phe	Met	Asn	Ile	Gly	Thr	Pro	Val	Lys	Ala	Ile	Ser	Ser	Gly	Lys
	50					55					60				

Ile	Val	Glu	Ala	Gly	Trp	Ser	Asn	Tyr	Gly	Gly	Gly	Asn	Gln	Ile	Gly
65					70					75					80

Leu	Ile	Glu	Asn	Asp	Gly	Val	His	Arg	Gln	Trp	Tyr	Met	His	Leu	Ser
			85						90					95	

Lys	Tyr	Asn	Val	Lys	Val	Gly	Asp	Tyr	Val	Lys	Ala	Gly	Gln	Ile	Ile
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100

105

110

Gly	Trp	Ser	Gly	Ser	Thr	Gly	Tyr	Ser	Thr	Ala	Pro	His	Leu	His	Phe
		115					120					125			

Gln	Arg	Met	Val	Asn	Ser	Phe	Ser	Asn	Ser	Thr	Ala	Gln	Asp	Pro	Met
	130					135					140				

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

Thr	Thr	Gly	Pro	Phe	Arg	Ser	Met	Pro	Gln	Ser	Gly	Val	Leu	Lys	Ala
		195					200					205			

Gly	Gln	Thr	Ile	His	Tyr	Asp	Glu	Val	Met	Lys	Gln	Asp	Gly	His	Val
	210					215					220				

Trp	Val	Gly	Tyr	Thr	Gly	Asn	Ser	Gly	Gln	Arg	Ile	Tyr	Leu	Pro	Val
225					230					235					240

Arg Thr Trp Asn Lys Ser Thr Asn Thr Leu Gly Val Leu Trp Gly Thr
245 250 255

Ile Lys Glu Leu Ala Ala Thr His Glu His Ser Ala Gln Trp Leu Asn
260 265 270

Asn Tyr Lys Lys Gly Tyr Gly Tyr Gly Pro Tyr Pro Leu Gly Ile Asn
275 280 285

Gly Gly Met His Tyr Gly Val Asp Phe Phe Met Asn Ile Gly Thr Pro
290 295 300

Val Lys Ala Ile Ser Ser Gly Lys Ile Val Glu Ala Gly Trp Ser Asn
305 310 315 320

Tyr Gly Gly Gly Asn Gln Ile Gly Leu Ile Glu Asn Asp Gly Val His
325 330 335

Arg Gln Trp Tyr Met His Leu Ser Lys Tyr Asn Val Lys Val Gly Asp
340 345 350

Tyr Val Lys Ala Gly Gln Ile Ile Gly Trp Ser Gly Ser Thr Gly Tyr
355 360 365

Ser Thr Ala Pro His Leu His Phe Gln Arg Met Val Asn Ser Phe Ser
370 375 380

Asn Ser Thr Ala Gln Asp Pro Met Pro Phe Leu Lys Ser Ala Gly Tyr
385 390 395 400

Gly Lys Ala Gly Gly Thr Val Thr Pro Thr Pro Asn Thr Gly Trp Lys
405 410 415

Thr Asn Lys Tyr Gly Thr Leu Tyr Lys Ser Glu Ser Ala Ser Phe Thr
420 425 430

Pro Asn Thr Asp Ile Ile Thr Arg Thr Thr Gly Pro Phe Arg Ser Met
435 440 445

Pro Gln Ser Gly Val Leu Lys Ala Gly Gln Thr Ile His Tyr Asp Glu
450 455 460

Val Met Lys Gln Asp Gly His Val Trp Val Gly Tyr Thr Gly Asn Ser
465 470 475 480

Gly Gln Arg Ile Tyr Leu Pro Val Arg Thr Trp Asn Lys Ser Thr Asn
485 490 495

Thr Leu Gly Val Leu Trp Gly Thr Ile Lys
500 505

<210> 95

<211> 1143

<212> DNA

<213> artificial

<220>

<223> artificial construct

<400> 95

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<210> 96

<211> 380

<212> PRT

<213> artificial

<220>

<223> artificial construct

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Asp Val Asn Gly His Lys Phe Ser Val Ser Gly Glu Gly Glu Gly Asp
35          40          45

Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile Cys Thr Thr Gly Lys
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Gln	Cys	Phe	Ala	Arg 85	Tyr	Pro	Asp	His	Met 90	Lys	Arg	His	Asp	Phe	Phe 95		
Lys	Ser	Ala	Met 100	Pro	Glu	Gly	Tyr	Val 105	Gln	Glu	Arg	Thr	Ile	Phe	Phe 110		
Lys	Asp	Asp 115	Gly	Asn	Tyr	Lys	Thr 120	Arg	Ala	Glu	Val	Lys 125	Phe	Glu	Gly		
Asp	Thr 130	Leu	Val	Asn	Arg	Ile 135	Glu	Leu	Lys	Gly	Ile 140	Asp	Phe	Lys	Glu		
Asp 145	Gly	Asn	Ile	Leu	Gly 150	His	Lys	Leu	Glu	Tyr 155	Asn	Tyr	Asn	Ser	His 160		
Asn	Val	Tyr	Ile	Met 165	Ala	Asp	Lys	Gln	Lys 170	Asn	Gly	Ile	Lys	Val 175	Asn		
Phe	Lys	Ile	Arg 180	His	Asn	Ile	Glu	Asp 185	Gly	Ser	Val	Gln	Leu 190	Ala	Asp		
His	Tyr	Gln 195	Gln	Asn	Thr	Pro	Ile 200	Gly	Asp	Gly	Pro	Val 205	Leu	Leu	Pro		
Asp	Asn 210	His	Tyr	Leu	Ser	Thr 215	Gln	Ser	Ala	Leu	Ser 220	Lys	Asp	Pro	Asn		
Glu 225	Lys	Arg	Asp	His	Met 230	Val	Leu	Leu	Glu	Phe 235	Val	Thr	Ala	Ala	Gly 240		
Ile	Thr	His	Gly	Met 245	Asp	Glu	Leu	Tyr	Lys 250	Glu	Leu	Gly	Gly	Lys 255	Leu		
Glu	Val	Ser	Lys 260	Ala	Ala	Thr	Ile	Lys 265	Gln	Ser	Asp	Val	Lys 270	Gln	Glu		
Val	Lys	Lys 275	Gln	Glu	Ala	Lys	Gln 280	Ile	Val	Lys	Ala	Thr 285	Asp	Trp	Lys		
Gln	Asn 290	Lys	Asp	Gly	Ile	Trp 295	Tyr	Lys	Ala	Glu	His 300	Ala	Ser	Phe	Thr		
Val 305	Thr	Ala	Pro	Glu	Gly 310	Ile	Ile	Thr	Arg	Tyr 315	Lys	Gly	Pro	Trp	Thr 320		
Gly	His	Pro	Gln	Ala 325	Gly	Val	Leu	Gln	Lys 330	Gly	Gln	Thr	Ile	Lys 335	Tyr		
Asp	Glu	Val	Gln 340	Lys	Phe	Asp	Gly	His 345	Val	Trp	Val	Ser	Trp 350	Glu	Thr		

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355

360

365

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<212> DNA

<213> Staphylococcus bacteriophage phi 11

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aacttcgacg gattagctac tgtataccaa aatacaccgg acttcttagc acaacctggc      240
gacatgggtg tattcggtag caactacggg gctggatatg gtcacgttgc atgggtaatt      300
gaagcaactt tagattacat cattgtatat gagcagaatt ggctaggcgg tggctggact      360
gacggaatcg aacaaccggg ctgggggttg gaaaaagtta caagacgaca acatgcttat      420
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<213> Staphylococcus bacteriophage phi 11

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

Val Asp Leu Trp Tyr Gly Phe Gln Cys Phe Asp Tyr Ala Asn Ala Gly
          35           40           45

Trp Lys Val Leu Phe Gly Leu Leu Leu Lys Gly Leu Gly Ala Lys Asp
50           55           60

Ile Pro Phe Ala Asn Asn Phe Asp Gly Leu Ala Thr Val Tyr Gln Asn
65           70           75           80

Thr Pro Asp Phe Leu Ala Gln Pro Gly Asp Met Val Val Phe Gly Ser
          85           90           95

Asn Tyr Gly Ala Gly Tyr Gly His Val Ala Trp Val Ile Glu Ala Thr
100          105          110

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Leu Asp Tyr Ile Ile Val Tyr Glu Gln Asn Trp Leu Gly Gly Gly Trp
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Thr Asp Gly Ile Glu Gln Pro Gly Trp Gly Trp Glu Lys Val Thr Arg
 130 135 140

Arg Gln His Ala Tyr Asp Phe Pro Met Trp Phe Ile Arg Pro
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<211> 642

<212> DNA

<213> Staphylococcus bacteriophage phi 11

<400> 99

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ggggcgactg ctgaagcata tcgtaacgga ttagtaaattg cacctttatc aagattagaa      180
gcgggcattg cgcatagtta cgtatcaggc aacacagttt ggcaagcctt agatgaatca      240
caagtaggtt ggcataccgc taatcaaata ggtaataaat attattacgg tattgaagta      300
tgtcaatcaa tgggcgcaga taacgcgaca ttcttaaaaa atgaacaggc aactttccaa      360
gaatgcgcta gattgttgaa aaaatgggga ttaccagcaa acagaaatac aatcagattg      420
cacaatgaat ttacttcaac atcatgccct catagaagtt cggttttaca cactggtttt      480
gacccagtaa ctgcggtct attgccagaa gacaagcggg tgcaacttaa agactacttt      540
atcaagcaga ttagggcgta catggatggg aaaataccgg ttgccactgt ctctaagtag      600
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<210> 100

<211> 163

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<213> Staphylococcus bacteriophage phi 11

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Asn Pro Lys Gly Ile Val Ile His Asn Asp Ala Gly Ser Lys Gly Ala
1          5          10          15

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

Leu Glu Ala Gly Ile Ala His Ser Tyr Val Ser Gly Asn Thr Val Trp
35          40          45

Gln Ala Leu Asp Glu Ser Gln Val Gly Trp His Thr Ala Asn Gln Ile
50          55          60

Gly Asn Lys Tyr Tyr Tyr Gly Ile Glu Val Cys Gln Ser Met Gly Ala
65          70          75          80

Asp Asn Ala Thr Phe Leu Lys Asn Glu Gln Ala Thr Phe Gln Glu Cys
85          90          95

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Ala Arg Leu Leu Lys Lys Trp Gly Leu Pro Ala Asn Arg Asn Thr Ile
 100 105 110

Arg Leu His Asn Glu Phe Thr Ser Thr Ser Cys Pro His Arg Ser Ser
 115 120 125

Val Leu His Thr Gly Phe Asp Pro Val Thr Arg Gly Leu Leu Pro Glu
 130 135 140

Asp Lys Arg Leu Gln Leu Lys Asp Tyr Phe Ile Lys Gln Ile Arg Ala
 145 150 155 160

Tyr Met Asp

REFERENCES CITED IN THE DESCRIPTION

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P a t e n t k r a v

- 5 **1.** Sammensætning omfattende en første og en anden forbindelse, hvor den første forbindelse er et corticosteroid og den anden forbindelse omfatter mindst et cellevægbindingsdomæne, der specifikt binder peptidoglycan-cellevæggen af en bakteriel celle, fortrinsvis en grampositiv bakteriel celle, og hvor den anden forbindelse er et polypeptid, som har mindst 80 % identitet med SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 76, 78, 80, 10 82, 84, 86, 88, 90, 92, 94, 98 eller 100; og/eller cellevægbindingsdomænet har mindst 80 % identitet med en hvilken som helst af SEQ ID NO: 4, 6 eller 8; og/eller hvor det ene eller de flere enzymatiske aktive domæner har mindst 80 % identitet med en hvilken som helst af SEQ ID NO: 10, 12, 14, 16, 18, 98 eller 100.
- 15 **2.** Kit med dele omfattende:
- a) et første hætteglas indeholdende en første sammensætning omfattende en første forbindelse som defineret i krav 1; og,
- b) et andet hætteglas indeholdende en anden sammensætning omfattende en anden forbindelse som defineret i krav 1; og eventuelt,
- 20 c) brugsanvisninger, fortrinsvis omfattende et doseringsregime.
- 3.** Sammensætning ifølge krav 1 til anvendelse ved en fremgangsmåde til behandling, omfattende
- 25 den sekventielle eller simultane indgivelse af den første og anden forbindelse.
- 4.** Sammensætning til anvendelse ifølge krav 3, til anvendelse til forebyggelse, forsinkelse og/eller helbredelse af dermatitis eller eksem.
- 30 **5.** Sammensætning og/eller et kit med dele ifølge et af de foregående krav, hvor den anden forbindelse omfatter et eller flere enzymatiske aktive domæner, der udviser en targetbindingsspecifitet.
- 35 **6.** Sammensætning og/eller kit med dele ifølge krav 5, hvor targetbindingen er en essential binding i et peptidoglycan-lag af den bakterielle celle, fortrinsvis

grampositive bakterielle celle.

- 5 **7.** Sammensætning og/eller kit med dele ifølge krav 5 og/eller 6, hvor det ene eller de flere enzymatiske aktive domæner er udvalgt fra eller er en kombination af et domæne fra gruppen bestående af et cystein, histidinafhængigt amidohydrolases/peptidase-domæne, et endopeptidasedomæne, et amidasedomæne og et glycosylhydrolasedomæne.
- 10 **8.** Sammensætning og/eller kit med dele ifølge et af de foregående krav, hvor den bakterielle celle, fortrinsvis den grampositive bakterielle celle er en *Staphylococcus*.
- 15 **9.** Sammensætning og/eller kit med dele ifølge krav 8, hvor cellevægbindingsdomænet stammer fra eller er en homolog af et *Staphylococcus*-fagendolysin og/eller et *S. simulans* lysostaphin og/eller et *S. capitis* ALE-1-bakteriocin.
- 20 **10.** Sammensætning og/eller kit med dele ifølge et af de foregående krav, hvor den anden forbindelse er en naturligt forekommende eller muteret bakteriofag, et naturligt forekommende endolysin eller et muteret polypeptid.
- 11.** Sammensætning og/eller kit med dele ifølge et af kravene 8-10, hvor den anden forbindelse er et rekombinant polypeptid omfattende en flerhed af det ene eller de flere enzymatiske aktive domæner, der udviser targetbindingsspecificitet.