Toxin Peptide Therapeutic Agents

This application claims the benefit of U.S. Nonprovisional Application, serial number not yet available, filed April 17, 2006, which claims the benefit of U. S. Provisional Application No. 60/672,342, filed April 22, 2005, both of which are hereby incorporated by reference.

This application incorporates by reference all subject matter contained on the compact disc, which is identified by the name of the file, A-1006.ST25.txt created on April 17, 2006, the size of which file is 744 KB.

Throughout this application various publications are referenced within parentheses or brackets. The disclosures of these publications in their entireties are hereby incorporated by reference in this application in order to more fully describe the state of the art to which this invention pertains.

Background of the Invention

1. Field of the Invention

The present invention is related to the biochemical arts, in particular to therapeutic peptides and conjugates.

2. Discussion of the Related Art

Ion channels are a diverse group of molecules that permit the exchange of small inorganic ions across membranes. All cells require ion channels for function, but this is especially so for excitable cells such as those present in the nervous system and the heart. The electrical signals orchestrated by ion channels control the thinking brain, the beating heart and the contracting muscle. Ion channels play a role in regulating cell volume, and they control a wide variety of signaling processes.

The ion channel family includes Na^+, K^+, and Ca^{2+} cation and Cl^- anion channels. Collectively, ion channels are distinguished as either ligand-gated or voltage-gated. Ligand-gated channels include both extracellular and intracellular ligand-gated channels. The extracellular ligand-gated channels include the nicotinic acetylcholine receptor (nAChR), the serotonin (5-hdroxytryptamine, 5-HT) receptors, the glycine and γ-butyric acid receptors (GABA) and the glutamate-activated channels including kanate, α-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (AMPA) and N-methyl-D-aspartate receptors (NMDA) receptors. (Harte and Ouzounis (2002),

FEBS Lett. 514: 129-34). Intracellular ligand gated channels include those activated by cyclic nucleotides (e.g. cAMP, cGMP), Ca^{2+} and G-proteins. (Harte and Ouzounis (2002), FEBS Lett. 514: 129-34). The voltage-gated ion channels are categorized by their selectivity for inorganic ion species, including sodium, potassium, calcium and chloride ion channels. (Harte and Ouzounis (2002), FEBS Lett. 514: 129-34).

A unified nomenclature for classification of voltage-gated channels was recently presented. (Catterall et al. (2000), Pharmacol. Rev. 55: 573-4; Gutman et al. (2000), Pharmacol. Rev. 55, 583-6; Catterall et al. (2000) Pharmacol. Rev. 55: 579-81; Catterall et al. (2000), Pharmacol. Rev. 55: 575-8; Hofmann et al. (2000), Pharmacol. Rev. 55: 587-9; Clapham et al. (2000), Pharmacol Rev. 55: 591-6; Chandy (1991), Nature 352: 26; Goldin et al. (2000), Neuron 28: 365-8; Ertel et al. (2000), Neuron 25: 533-5).

The K^+ channels constitute the largest and best characterized family of ion channels described to date. Potassium channels are subdivided into three general groups: the 6 transmembrane (6TM) K^+ channels, the 2TM-2TM/leak K^+ channels and the 2TM/Kir inward rectifying channels. (Tang et al. (2004), Ann. Rev. Physiol. 66, 131-159). These three groups are further subdivided into families based on sequence similarity. The voltage-gated K^+ channels, including (Kv1-6, Kv8-9), EAG, KQT, and Slo (BKCa), are family members of the 6TM group. The 2TM-2TM group comprises TWIK, TREK, TASK, TRAAK, and THIK, whereas the 2TM/Kir group consists of Kir1-7. Two additional classes of ion channels include the inward rectifier potassium (IRK) and ATP-gated purinergic (P2X) channels. (Harte and Ouzounis (2002), FEBS Lett. 514: 129-34).

Toxin peptides produced by a variety of organisms have evolved to target ion channels. Snakes, scorpions, spiders, bees, snails and sea anemone are a few examples of organisms that produce venom that can serve as a rich source of small bioactive toxin peptides or "toxins" that potently and selectively target ion channels and receptors. In most cases, these toxin peptides have evolved as potent antagonists or inhibitors of ion channels, by binding to the channel pore and physically blocking the ion conduction pathway. In some other cases, as with some of the tarantula toxin peptides, the peptide is found to antagonize channel function by binding to a region outside the pore (e.g., the voltage sensor domain).

The toxin peptides are usually between about 20 and about 80 amino acids in length, contain 2-5 disulfide linkages and form a very compact structure (see, e.g., Figure 10). Toxin peptides (e.g., from the venom of scorpions, sea anemones and cone snails) have been isolated and characterized for their impact on ion channels. Such peptides appear to have evolved from a

relatively small number of structural frameworks that are particularly well suited to addressing the critical issues of potency and stability. The majority of scorpion and Conus toxin peptides, for example, contain 10-40 amino acids and up to five disulfide bonds, forming extremely compact and constrained structure (microproteins) often resistant to proteolysis. The conotoxin and scorpion toxin peptides can be divided into a number of superfamilies based on their disulfide connections and peptide folds. The solution structure of many of these has been determined by NMR spectroscopy, illustrating their compact structure and verifying conservation of their family fold. (E.g., Tudor et al., Ionisation behaviour and solution properties of the potassium-channel blocker ShK toxin, Eur. J. Biochem. 251(1-2):133-41(1998); Pennington et al., Role of disulfide bonds in the structure and potassium channel blocking activity of ShK toxin, Biochem. 38(44): 14549-58 (1999); Jaravine et al., Three-dimensional structure of toxin OSK1 from Orthochirus scrobiculosus scorpion venom, Biochem. 36(6):1223-32 (1997); del Rio-Portillo et al.; NMR solution structure of Cn12, a novel peptide from the Mexican scorpion Centruroides noxius with a typical beta-toxin sequence but with alpha-like physiological activity, Eur. J. Biochem. 271(12): 2504-16 (2004); Prochnicka-Chalufour et al., Solution structure of discrepin, a new K+-channel blocking peptide from the alpha-KTx15 subfamily, Biochem. 45(6):1795-1804 (2006)).

Conserved disulfide structures can also reflect the individual pharmacological activity of the toxin family. (Nicke et al. (2004), Eur. J. Biochem. 271: 2305-19, Table 1; Adams (1999), Drug Develop. Res.46: 219-34). For example, α-conotoxins have well-defined four cysteine/two disulfide loop structures (Loughnan, 2004) and inhibit nicotinic acetylcholine receptors. In contrast, ω-conotoxins have six cysteine/three disulfide loop consensus structures (Nielsen, 2000) and block calcium channels. Structural subsets of toxins have evolved to inhibit either voltage-gated or calcium-activated potassium channels. Figure 9 shows that a limited number of conserved disulfide architectures shared by a variety of venomous animals from bee to snail and scorpion to snake target ion channels. Figure 7A-B shows alignment of alpha-scorpion toxin family and illustrates that a conserved structural framework is used to derive toxins targeting a vast array of potassium channels.

Due to their potent and selective blockade of specific ion channels, toxin peptides have been used for many years as tools to investigate the pharmacology of ion channels. Other than excitable cells and tissues such as those present in heart, muscle and brain, ion channels are also important to non-excitable cells such as immune cells. Accordingly, the potential therapeutic utility of toxin peptides has been considered for treating various immune disorders, in particular by inhibition of potassium channels such as Kv1.3 and IKCa1 since these channels indirectly control

calcium signaling pathway in lymphocytes. [e.g., Kem et al., ShK toxin compositions and methods of use, US Patent No. 6,077,680; Lebrun et al., Neuropeptides originating in scorpion, US Patent No. 6,689,749; Beeton et al., Targeting effector memory T cells with a selective peptide inhibitor of Kv1.3 channnels for therapy of autoimmune diseases, Molec. Pharmacol. 67(4):1369-81 (2005); Mouhat et al., K^+ channel types targeted by synthetic OSK1, a toxin from Orthochirus scrobiculosus scorpion venom, Biochem. J. 385:95-104 (2005); Mouhat et al., Pharmacological profiling of Orthochirus scrobiculosus toxin 1 analogs with a trimmed N-terminal domain, Molec. Pharmacol. 69:354- 62 (2006); Mouhat et al., OsK1 derivatives, WO 2006/002850 A2; B.S. Jensen et al. The Ca^{2+}-activated K+ Channel of Intermediate Conductance: A Molecular Target for Novel Treatments?, Current Drug Targets 2:401-422 (2001); Rauer et al., Structure-guided Transformation of Charybdotoxin Yields an Analog That Selectively Targets Ca^{2+}-activated over Voltage-gated K^+ Channels, J. Biol. Chem. 275: 1201-1208 (2000); Castle et al., Maurotoxin: A Potent Inhibitor of Intermediate Conductance Ca^{2+}-Activated Potassium Channels, Molecular Pharmacol. 63: 409-418 (2003); Chandy et al., K^+ channels as targets for specific Immunomodulation, Trends in Pharmacol. Sciences 25: 280-289 (2004); Lewis & Garcia, Therapeutic Potential of Venom Peptides, Nat. Rev. Drug Discov. 2: 790-802 (2003)].

Small molecules inhibitors of Kv1.3 and IKCa1 potassium channels and the major calcium entry channel in T cells, CRAC, have also been developed to treat immune disorders [A. Schmitz et al. (2005) Molecul. Pharmacol. 68, 1254; K.G. Chandy et al. (2004) TIPS 25, 280; H. Wulff et al. (2001) J. Biol. Chem. 276, 32040; C. Zitt et al. (2004) J. Biol. Chem. 279, 12427], but obtaining small molecules with selectivity toward some of these targets has been difficult.

Calcium mobilization in lymphocytes is known to be a critical pathway in activation of inflammatory responses [M.W. Winslow et al. (2003) Current Opinion Immunol. 15, 299]. Compared to other cells, T cells show a unique sensitivity to increased levels of intracellular calcium and ion channels both directly and indirectly control this process. Inositol triphosphate (IP3) is the natural second messenger which activates the calcium signaling pathway. IP3 is produced following ligand-induced activation of the T cell receptor (TCR) and upon binding to its intracellular receptor (a channel) causes unloading of intracellular calcium stores. The endoplasmic reticulum provides one key calcium store. Thapsigargin, an inhibitor of the sarcoplasmic-endoplasmic reticulum calcium ATPase (SERCA), also causes unloading of intracellular stores and activation of the calcium signaling pathway in lymphocytes. Therefore, thapsigargin can be used as a specific stimulus of the calcium signaling pathway in T cells. The unloading of intracellular calcium stores in T cells is known to cause activation of a calcium

channel on the cell surface which allows for influx of calcium from outside the cell. This store operated calcium channel (SOCC) on T cells is referred to as "CRAC" (calcium release activated channel) and sustained influx of calcium through this channel is known to be critical for full T cell activation [S. Feske et al. (2005) J. Exp. Med. 202, 651 and N. Venkatesh et al. (2004) PNAS 101, 8969]. For many years it has been appreciated that in order to maintain continued calcium influx into T cells, the cell membrane must remain in a hyperpolarized condition through efflux of potassium ions. In T cells, potassium efflux is accomplished by the voltage-gated potassium channel Kv1.3 and the calcium-activated potassium channel IKCa1 [K.G. Chandy et al. (2004) TIPS 25, 280]. These potassium channels therefore indirectly control the calcium signaling pathway, by allowing for the necessary potassium efflux that allows for a sustained influx of calcium through CRAC.

Sustained increases in intracellular calcium activate a variety of pathways in T cells, including those leading to activation of NFAT, NF-kB and AP-1 [Quintana-A (2005) Pflugers Arch. – Eur. J. Physiol. 450, 1]. These events lead to various T cell responses including alteration of cell size and membrane organization, activation of cell surface effector molecules, cytokine production and proliferation. Several calcium sensing molecules transmit the calcium signal and orchestrate the cellular response. Calmodulin is one molecule that binds calcium, but many others have been identified (M.J. Berridge et al. (2003) Nat. Rev. Mol. Cell. Biol. 4,517). The calcium-calmodulin dependent phosphatase calcineurin is activated upon sustained increases in intracellular calcium and dephosphorylates cytosolic NFAT. Dephosphorylated NFAT quickly translocates to the nucleus and is widely accepted as a critical transcription factor for T cell activation (F. Macian (2005) Nat. Rev. Immunol. 5, 472 and N. Venkatesh et al. (2004) PNAS 101, 8969). Inhibitors of calcineurin, such as cyclosporin A (Neoral, SandImmune) and FK506 (Tacrolimus) are a main stay for treatment of severe immune disorders such as those resulting in rejection following solid organ transplant (I.M. Gonzalez-Pinto et al. (2005) Transplant. Proc. 37, 1713 and D.R.J. Kuypers (2005) Transplant International 18, 140). Neoral has been approved for the treatment of transplant rejection, severe rheumatoid arthritis (D.E. Yocum et al. (2000) Rheumatol. 39, 156) and severe psoriasis (J. Koo (1998) British J. Dermatol. 139, 88). Preclinical and clinical data has also been provided suggesting calcineurin inhibitors may have utility in treatment of inflammatory bowel disease (IBD; Baumgart DC (2006) Am. J. Gastroenterol. Mar 30; Epub ahead of print), multiple sclerosis (Ann. Neurol. (1990) 27, 591) and asthma (S. Rohatagi et al. (2000) J. Clin. Pharmacol. 40, 1211). Lupus represents another disorder that may benefit from agents blocking activation of helper T cells. Despite the importance of calcineurin in regulating NFAT in T cells, calcineurin is

also expressed in other tissues (e.g. kidney) and cyclosporine A & FK506 have a narrow safety margin due to mechanism based toxicity. Renal toxicity and hypertension are common side effects that have limited the promise of cyclosporine & FK506. Due to concerns regarding toxicity, calcineurin inhibitors are used mostly to treat only severe immune disease (Bissonnette-R et al. (2006) J. Am. Acad. Dermatol. 54, 472). Kv1.3 inhibitors offer a safer alternative to calcineurin inhibitors for the treatment of immune disorders. This is because Kv1.3 also operates to control the calcium signaling pathway in T cells, but does so through a distinct mechanism to that of calcineurin inhibitors, and evidence on Kv1.3 expression and function show that Kv1.3 has a more restricted role in T cell biology relative to calcineurin, which functions also in a variety of non-lymphoid cells and tissues.

Calcium mobilization in immune cells also activates production of the cytokines interleukin 2 (IL-2) and interferon gamma (IFNg) which are critical mediators of inflammation. IL-2 induces a variety of biological responses ranging from expansion and differentiation of $CD4^+$ and $CD8^+$ T cells, to enhancement of proliferation and antibody secretion by B cells, to activation of NK cells [S.L. Gaffen & K.D. Liu (2004) Cytokine 28, 109]. Secretion of IL-2 occurs quickly following T cell activation and T cells represent the predominant source of this cytokine. Shortly following activation, the high affinity IL-2 receptor (IL2-R) is upregulated on T cells endowing them with an ability to proliferate in response to IL-2. T cells, NK cells, B cells and professional antigen presenting cells (APCs) can all secrete IFNg upon activation. T cells represent the principle source of IFNg production in mediating adaptive immune responses, whereas natural killer (NK) cells & APCs are likely an important source during host defense against infection [K. Schroder et al. (2004) J. Leukoc. Biol. 75, 163]. IFNg, originally called macrophage-activating factor, upregulates antigen processing and presentation by monocytes, macrophages and dendritic cells. IFNg mediates a diverse array of biological activities in many cell types [U. Boehm et al. (1997) Annu. Rev. Immunol. 15, 749] including growth & differentiation, enhancement of NK cell activity and regulation of B cell immunoglobulin production and class switching.

CD40L is another cytokine expressed on activated T cells following calcium mobilization and upon binding to its receptor on B cells provides critical help allowing for B cell germinal center formation, B cell differentiation and antibody isotype switching. CD40L-mediated activation of CD40 on B cells can induce profound differentiation and clonal expansion of immunoglobulin (Ig) producing B cells [S. Quezada et al. (2004) Annu. Rev. Immunol. 22, 307]. The CD40 receptor can also be found on dendritic cells and CD40L signaling can mediate dendritic cell activation and differentiation as well. The antigen presenting capacity of B cells and dendritic cells is promoted

by CD40L binding, further illustrating the broad role of this cytokine in adaptive immunity. Given the essential role of CD40 signaling to B cell biology, neutralizing antibodies to CD40L have been examined in preclinical and clinical studies for utility in treatment of systemic lupus erythematosis (SLE), - a disorder characterized by deposition of antibody complexes in tissues, inflammation and organ damage [J. Yazdany and J Davis (2004) Lupus 13, 377].

Production of toxin peptides is a complex process in venomous organisms, and is an even more complex process synthetically. Due to their conserved disulfide structures and need for efficient oxidative refolding, toxin peptides present challenges to synthesis. Although toxin peptides have been used for years as highly selective pharmacological inhibitors of ion channels, the high cost of synthesis and refolding of the toxin peptides and their short half-life in vivo have impeded the pursuit of these peptides as a therapeutic modality. Far more effort has been expended to identify small molecule inhibitors as therapeutic antagonists of ion channels, than has been given the toxin peptides themselves. One exception is the recent approval of the small ω-conotoxin MVIIA peptide (Ziconotide™) for treatment of intractable pain. The synthetic and refolding production process for Ziconotide™, however, is costly and only results in a small peptide product with a very short half-life in vivo (about 4 hours).

A cost-effective process for producing therapeutics, such as but not limited to, inhibitors of ion channels, is a desideratum provided by the present invention, which involves toxin peptides fused, or otherwise covalently conjugated to a vehicle.

Summary of the Invention

The present disclosure relates to a composition of matter of the formula:

$$(X^1)_a\text{-}(F^1)_d\text{-}(X^2)_b\text{-}(F^2)_e\text{-}(X^3)_c$$

(I)

and multimers thereof, wherein:

F^1 and F^2 are half-life extending moieties, and d and e are each independently 0 or 1, provided that at least one of d and e is 1;

X^1, X^2, and X^3 are each independently $-(L)_f\text{-}P\text{-}(L)_g-$, and f and g are each independently 0 or 1;

P is a toxin peptide of no more than about 80 amino acid residues in length, comprising at least two intrapeptide disulfide bonds;

L is an optional linker (present when f=1 and/or g =1); and

a, b, and c are each independently 0 or 1, provided that at least one of a, b and c is 1.

In a first aspect, there is provided a composition of matter of the formula

$$(X^1)_a\text{-}(F^1)_d\text{-}(X^2)_b\text{-}(F^2)_e\text{-}(X^3)_c$$

or multimers thereof, wherein:

F^1 and F^2 are half-life extending moieties, and d and e are each independently 0 or 1, provided that at least one of d and e is 1;

X^1, X^2, and X^3 are each independently $-(L)_f\text{-}P\text{-}(L)_g-$, and f and g are each independently 0 or 1;

P is a ShK toxin peptide or a ShK peptide analog of no more than about 80 amino acid residues in length, comprising at least two intrapeptide disulfide bonds;

L is a linker; and

a, b, and c are each independently 0 or 1, provided that at least one of a, b and c is 1; or

a physiologically acceptable salt thereof.

The present disclosure thus concerns molecules having variations on Formula 1, such as the formulae:

(II) $P\text{-}(L)_g\text{-}F^1$ (i.e., b, c, and e equal to 0);

(III) $F^1\text{-}(L)_f\text{-}P$ (i.e., a, c, and e equal to 0);

(IV) $P\text{-}(L)_g\text{-}F^1\text{-}(L)_f\text{-}P$ or $(X^1)_a\text{–}F^1\text{–}(X^2)_b$ (i.e., c and e equal to 0);

(V) $F^1\text{-}(L)_f\text{-}P\text{-}(L)_g\text{-}F^2$ (i.e., a and c equal to 0);

(VI) $F^1\text{-}(L)_f\text{-}P\text{-}(L)_g\text{-}F^2\text{-}(L)_f\text{-}P$ (i.e., a equal to 0);

(VII) $F^1\text{-}F^2\text{-}(L)_f\text{-}P$ (i.e., a and b equal to 0);

(VIII) $P\text{-}(L)_g\text{-}F^1\text{-}F^2$ (i.e., b and c equal to 0);

(IX) $P\text{-}(L)_g\text{-}F^1\text{-}F^2\text{-}(L)_f\text{-}P$ (i.e., b equal to 0);

and any multimers of any of these, when stated conventionally with the N-terminus of the peptide(s) on the left. All of such molecules of Formulae II-IX are within the meaning of Structural Formula I. Within the meaning of Formula I, the toxin peptide (P), if more than one is present , can be independently the same or different from any other toxin peptide(s) also present in the inventive composition, and the linker moiety ($(L)_f$ and/or $(L)_g$), if present, can be independently the same or different from any other linker, or linkers, that may be present in the inventive composition. Conjugation of the toxin peptide(s) to the half-life extending moiety, or moieties, can be via the N-terminal and/or C-terminal of the toxin peptide, or can be intercalary as to its primary amino acid sequence, F^1 being linked closer to the toxin peptide's N-terminus than is linked F^2. Examples of

useful half-life extending moieties (F^1 or F^2) include immunoglobulin Fc domain, human serum albumin (HSA), or poly(ethylene glycol) (PEG). These and other half-life extending moieties described herein are useful, either individually or in combination.

In a second aspect, there is provided a DNA encoding a composition of matter as defined above.

In a third aspect, there is provided an expression vector comprising the DNA as defined above.

In a fourth aspect, there is provided a host cell comprising the expression vector as defined above.

In a fifth aspect, there is provided a composition of matter, comprising a ShK peptide analog that comprises an amino acid sequence selected from the group consisting of SEQ ID NOS: 88, 89, 92, 148 through 200, 548 through 561, 884 through 949, and 1295 through 1300 as set forth in Table 2, or a physiologically acceptable salt thereof.

The present disclosure also relates to a composition of matter, which includes, conjugated or unconjugated, a toxin peptide analog of ShK, OSK1, ChTx, or Maurotoxin modified from the native sequences at one or more amino acid residues, having greater Kv1.3 or IKCa1antagonist activity, and/or target selectivity, compared to a ShK, OSK1, or Maurotoxin (MTX) peptides having a native sequence. The toxin peptide analogs may comprise an amino acid sequence selected from any of the following:

SEQ ID NOS: 88, 89, 92, 148 through 200, 548 through 561, 884 through 949, or 1295 through 1300 as set forth in Table 2; or

SEQ ID NOS: 980 through 1274, 1303, or 1308 as set forth in Table 7; or

SEQ ID NOS: 330 through 337, 341, 1301, 1302, 1304 through 1307, 1309, 1311, 1312, and 1315 through 1336 as set forth in Table 13; or

SEQ ID NOS: 36, 59, 344-346, or 1369 through 1390 as set forth in Table 14.

The present disclosure also relates to other toxin peptide analogs that comprise an amino acid sequence selected from any of the following:

SEQ ID NOS: 201 through 225 as set forth in Table 3; or

SEQ ID NOS: 242 through 248 or 250 through 260 as set forth in Table 4; or

SEQ ID NOS: 261 through 275 as set forth in Table 5; or

SEQ ID NOS: 276 through 293 as set forth in Table 6; or

SEQ ID NOS: 299 through 315 as set forth in Table 8; or

SEQ ID NOS: 316 through 318 as set forth in Table 9; or

SEQ ID NO: 319 as set forth in Table 10; or

SEQ ID NO: 327 or 328 as set forth in Table 11; or

SEQ ID NOS: 330 through 337, 341, 1301, 1302, 1304 through 1307, 1309, 1311, 1312, or 1315 through 1336 as set forth in Table 13;

SEQ ID NOS: 1369 through 1390 as set forth in Table 14; or

SEQ ID NOS: 348 through 353 as set forth in Table 16; or

SEQ ID NOS: 357 through 362, 364 through 368, 370, 372 through 385, or 387 through 398 as set forth in Table 19; or

SEQ ID NOS: 399 through 408 as set forth in Table 20; or

SEQ ID NOS: 410 through 421 as set forth in Table 22; or

SEQ ID NOS: 422, 424, 426, or 428 as set forth in Table 23; or
SEQ ID NOS: 430 through 437 as set forth in Table 24; or
SEQ ID NOS: 438 through 445 as set forth in Table 25; or
SEQ ID NOS: 447, 449, 451, 453, 455, or 457 as set forth in Table 26; or
SEQ ID NOS: 470 through 482 or 484 through 493 as set forth in Table 28; or
SEQ ID NOS: 495 through 506 as set forth in Table 29; or
SEQ ID NOS: 507 through 518 as set forth in Table 30.

In a sixth aspect, there is provided a pharmaceutical composition comprising the disclosed composition of matter and a pharmaceutically acceptable carrier.

The compositions of this disclosure can be prepared by conventional synthetic methods, recombinant DNA techniques, or any other methods of preparing peptides and fusion proteins well known in the art. Compositions of this disclosure that have non-peptide portions can be synthesized by conventional organic chemistry reactions, in addition to conventional peptide chemistry reactions when applicable.

The primary use contemplated is as therapeutic and/or prophylactic agents. The inventive compositions incorporating the toxin peptide can have activity and/or ion channel target selectivity comparable to—or even greater than—the unconjugated peptide.

In a seventh aspect, there is provided the use of composition of matter for the preparation of a medicament for preventing or mitigating a relapse of a symptom of multiple sclerosis in a patient, wherein the composition of matter is selected from:

a composition as defined above; and

a composition of matter comprising a ShK peptide analog that comprises an amino acid sequence selected from the group consisting of SEQ ID NOS: 88, 89, 92, 148 through 200, 548 through 561, 884 through 949, and 1295 through 1300 as set forth in Table 2, or a physiologically acceptable salt thereof.

In an eighth aspect, there is provided the use of composition of matter for the preparation of a medicament for treating an autoimmune disorder in a patient selected from the group consisting of multiple sclerosis, type 1 diabetes, psoriasis, inflammatory bowel disease, contact-mediated dermatitis, rheumatoid arthritis, psoriatic arthritis, asthma, allergy, restinosis, systemic sclerosis, fibrosis, scleroderma, glomerulonephritis, Sjogren syndrome, inflammatory

bone resorption, transplant rejection, graft-versus-host disease, and lupus, a therapeutically effective amount of a composition of matter whereby at least one symptom of the disorder is alleviated in the patient, wherein the composition of matter is selected from:

a composition as defined above; and

a composition of matter comprising a ShK peptide analog that comprises an amino acid sequence selected from the group consisting of SEQ ID NOS: 88, 89, 92, 148 through 200, 548 through 561, 884 through 949, and 1295 through 1300 as set forth in Table 2, or a physiologically acceptable salt thereof.

The present disclosure also includes a method of treating an autoimmune disorder, which involves administering to a patient who has been diagnosed with an autoimmune disorder, such as multiple sclerosis, type 1 diabetes, psoriasis, inflammatory bowel disease, contact-mediated dermatitis, rheumatoid arthritis, psoriatic arthritis, asthma, allergy, restinosis, systemic sclerosis, fibrosis, scleroderma, glomerulonephritis, Sjogren syndrome, inflammatory bone resorption, transplant rejection, graft-versus-host disease, or lupus, a therapeutically effective amount of the inventive composition of matter (preferably comprising a Kv1.3 antagonist peptide or IKCa1 antagonist peptide), whereby at least one symptom of the disorder is alleviated in the patient.

The present disclosure is further directed to a method of preventing or mitigating a relapse of a symptom of multiple sclerosis, which method involves administering to a patient, who has previously experienced at least one symptom of multiple sclerosis, a prophylactically effective amount of the inventive composition of matter (preferably comprising a Kv1.3 antagonist peptide or IKCa1 antagonist peptide), such that the at least one symptom of multiple sclerosis is prevented from recurring or is mitigated.

Although mostly contemplated as therapeutic agents, compositions of this disclosure can also be useful in screening for therapeutic or diagnostic agents. For example, one can use an Fc-peptide in an assay employing anti-Fc coated plates. The half-life extending moiety, such as Fc, can make insoluble peptides soluble and thus useful in a number of assays.

Numerous additional aspects and advantages of the present disclosure will become apparent upon consideration of the figures and detailed description of the disclosure.

Brief Description of the Figures

Figure 1 shows schematic structures of some exemplary Fc dimers that can be derived from an IgG1 antibody. "Fc" in the figure represents any of the Fc variants within the meaning of "Fc domain" herein. "X1" and "X2" represent peptides or linker-peptide combinations as defined hereinafter. The specific dimers are as follows:

Figure 1A and Figure 1D: Single disulfide-bonded dimers;

Figure 1B and Figure 1E: Doubly disulfide-bonded dimers;

Figure 1C and Figure 1F: Noncovalent dimers.

Figure 2 shows schematic structures of some embodiments of the composition of the invention that shows a single unit of the pharmacologically active toxin peptide. Figure 2A shows a single chain molecule and can also represent the DNA construct for the molecule. Figure 2B shows a dimer in which the linker-peptide portion is present on only one chain of the dimer. Figure 2C shows a dimer having the peptide portion on both chains. The dimer of Figure 2C will form spontaneously in certain host cells upon expression of a DNA construct encoding the single chain shown in Figure 2A. In other host cells, the cells could be placed in conditions favoring formation of dimers or the dimers can be formed in vitro.

Figure 3A-B shows exemplary nucleic acid and amino acid sequences (SEQ ID NOS: 1 and 2, respectively) of human IgG1 Fc that is optimized for mammalian expression and can be used in this invention.

Figure 4A-B shows exemplary nucleic acid and amino acid sequences (SEQ ID NOS: 3 and 4, respectively) of human IgG1 Fc that is optimized for bacterial expression and can be used in this invention.

Figure 5A shows the amino acid sequence of the mature ShK peptide (SEQ ID NO: 5), which can be encoded for by a nucleic acid sequence containing codons optimized for expression in mammalian cell, bacteria or yeast.

Figure 5B shows the three disulfide bonds (--S—S--) formed by the six cysteines within the ShK peptide (SEQ ID NO: 10).

Figure 6 shows an alignment of the voltage-gated potassium channel inhibitor Stichodactyla helianthus (ShK) with other closely related members of the sea anemone toxin family. The sequence of the 35 amino acid mature ShK toxin (Accession #P29187) isolated from the venom of Stichodactyla helianthus is shown aligned to other closely related members of the sea anemone family. The consensus sequence and predicted disulfide linkages are shown, with highly conserved residues being shaded. The HmK peptide toxin sequence shown (Swiss-Protein

Accession #097436) is of the immature precursor from the Magnificent sea anemone (Radianthus magnifica; Heteractis magnifica) and the putative signal peptide is underlined. The mature HmK peptide toxin would be predicted to be 35 amino acids in length and span residues 40 through 74. AeK is the mature peptide toxin, isolated from the venom of the sea anemone Actinia equine (Accession #P81897). The sequence of the mature peptide toxin AsKS (Accession #Q9TWG1) and BgK (Accession #P29186) isolated from the venom of the sea anemone Anemonia sulcata and Bunodosoma granulifera, respectively, are also shown. Figure 6A shows the amino acid alignment (SEQ ID NO: 10) of ShK to other members of the sea anemone family of toxins, HmK (SEQ ID NO: 6 (Mature Peptide), (SEQ ID NO: 542, Signal and Mature Peptide portions)), AeK (SEQ ID NO: 7), AsKs (SEQ ID NO: 8), and BgK (SEQ ID NO: 9). The predicted disulfide linkages are shown and conserved residues are highlighted. (HmK, SEQ ID NO: 543; ShK, SEQ ID NO: 10; AeK, SEQ ID NO: 544; AsKS, SEQ ID NO: 545). Figure 6B shows a disulfide linkage map for this family having 3 disulfide linkages (C1-C6, C2-C4, C3-C5).

Figure 7A-B shows an amino acid alignment of the alpha-scorpion toxin family of potassium channel inhibitors. (BmKK1, SEQ ID NO: 11; BmKK4, SEQ ID NO: 12; PBTx1, SEQ ID NO: 14; Tc32, SEQ ID NO: 13; BmKK6, SEQ ID NO: 15; P01, SEQ ID NO: 16; Pi2, SEQ ID NO: 17; Pi3, SEQ ID NO: 18; Pi4, SEQ ID NO: 19; MTX, SEQ ID NO: 20; Pi1, SEQ ID NO: 21; HsTx1, SEQ ID NO: 61; AgTx2, SEQ ID NO: 23; KTX1, SEQ ID NO: 24; OSK1, SEQ ID NO: 25; BmKTX, SEQ ID NO: 22; HgTX1, SEQ ID NO: 27; MgTx, SEQ ID NO: 28; C11Tx1, SEQ ID NO: 29; NTX, SEQ ID NO: 30; Tc30, SEQ ID NO: 31; TsTX-Ka, SEQ ID NO: 32; PBTx3, SEQ ID NO: 33; Lqh 15-1, SEQ ID NO: 34; MartenTx, SEQ ID NO: 37; ChTx, SEQ ID NO:36; ChTx-Lq2, SEQ ID NO: 42; IbTx, SEQ ID NO: 38; SloTx, SEQ ID NO: 39; BmTx1; SEQ ID NO: 43; BuTx, SEQ ID NO: 41; AmmTx3, SEQ ID NO: 44; AaTX1, SEQ ID NO: 45; BmTX3, SEQ ID NO: 46; Tc1, SEQ ID NO: 48; OSK2, SEQ ID NO: 49; TsK, SEQ ID NO: 54; CoTx1, SEQ ID NO:55; CoTx2, SEQ ID NO: 871; BmPo5, SEQ ID NO: 60; ScyTx, SEQ ID NO: 51; P05, SEQ ID NO: 52; Tamapin, SEQ ID NO: 53; and TmTx, SEQ ID NO: 691. Highly conserved residues are shaded and a consensus sequence is listed. Subfamilies of the α-KTx are listed and are from Rodriguez de la Vega, R.C. et al. (2003) TIPS 24: 222-227. A list of some ion channels reported to antagonized is listed (IK = IKCa, BK=BKCa, SK=SKCa, Kv=voltage-gated K+ channels). Although most family members in this alignment represent the mature peptide product, several represent immature or modified forms of the peptide and these include: BmKK1, BmKK4, BmKK6, BmKTX, MartenTx, ChTx, ChTx-Lq2, BmTx1, AaTx1, BmTX3, TsK, CoTx1, BmP05.

Figure 8 shows an alignment of toxin peptides converted to peptibodies in this invention (Apamin, SEQ ID NO: 68; HaTx1, SEQ ID NO: 494; ProTx1, SEQ ID NO: 56; PaTx2, SEQ ID NO: 57; ShK[2-35], SEQ ID NO: 92; ShK[1-35], SEQ ID NO: 5; HmK, SEQ ID NO: 6; ChTx (K32E), SEQ ID NO: 59; ChTx, SEQ ID NO: 36; IbTx, SEQ ID NO: 38; OSK1 (E16K, K20D), SEQ ID NO: 296; OSK1, SEQ ID NO: 25; AgTx2, SEQ ID NO: 23; KTX1, SEQ ID NO: 24; MgTx, SEQ ID NO: 28; NTX, SEQ ID NO: 30; MTX, SEQ ID NO: 20; Pi2, SEQ ID NO: 17; HsTx1, SEQ ID NO: 61; Anuroctoxin [AnTx], SEQ ID NO: 62; BeKm1, SEQ ID NO: 63; ScyTx, SEQ ID NO: 51; ωGVIA, SEQ ID NO: 64; ωMVIIa, SEQ ID NO: 65; Ptu1, SEQ ID NO: 66; and CTX, SEQ ID NO: 67). The original sources of the toxins is indicated, as well as, the number of cysteines in each. Key ion channels targeted are listed. The alignment shows clustering of toxin peptides based on their source and ion channel target impact.

Figure 9 shows disulfide arrangements within the toxin family. The number of disulfides and the disulfide bonding order for each subfamily is indicated. A partial list of toxins that fall within each disulfide linkage category is presented.

Figure 10 illustrates that solution structures of toxins reveal a compact structure. Solution structures of native toxins from sea anemone (ShK), scorpion (MgTx, MTX, HsTx1), marine cone snail (wGVIA) and tarantula (HaTx1) indicate the 28 to 39 amino acid peptides all form a compact structure. The toxins shown have 3 or 4 disulfide linkages and fall within 4 of the 6 subfamilies shown in Figure 9. The solution structures of native toxins from sea anemone (ShK), scorpion (MgTx, MTX, HsTx1), marine cone snail (wGVIA) and tarantula (HaTx1) were derived from Protein Data Bank (PDB) accession numbers 1ROO (mmdbId:5247), 1MTX (mmdbId:4064), 1TXM (mmdbId:6201), 1QUZ (mmdbId:36904), 1OMZ (mmdbId:1816) and 1D1H (mmdbId:14344) using the MMDB Entrez 3D-structure database [J. Chen et al. (2003) Nucleic Acids Res. 31, 474] and viewer.

Figure 11A-C shows the nucleic acid (SEQ ID NO: 69 and SEQ ID NO: 1358) and encoded amino acid (SEQ ID NO:70, SEQ ID NO:1359 and SEQ ID NO: 1360) sequences of residues 5131-6660 of pAMG21ampR-Fc-pep. The sequences of the Fc domain (SEQ ID NOS: 71 and 72) exclude the five C-terminal glycine residues. This vector enables production of peptibodies in which the peptide-linker portion is at the C-terminus of the Fc domain.

Figure 11D shows a circle diagram of a peptibody bacterial expression vector pAMG21ampR-Fc-pep having a chloramphenicol acetyltransferase gene (cat; "CmR" site) that is replaced with the peptide-linker sequence.

Figure 12A-C shows the nucleic acid (SEQ ID NO: 73 and SEQ ID NO: 1361) and encoded amino acid (SEQ ID NO:74, SEQ ID NO: 1362 and SEQ ID NO: 1363) sequences of residues 5131-6319 of pAMG21ampR-Pep-Fc. The sequences of the Fc domain (SEQ ID NOS: 75 and 76) exclude the five N-terminal glycine residues. This vector enables production of peptibodies in which the peptide-linker portion is at the N-terminus of the Fc domain.

Figure 12D shows a circle diagram of a peptibody bacterial expression vector having a zeocin resistance (ble; "ZeoR") site that is replaced with the peptide-linker sequence.

Figure 12E-G shows the nucleic acid (SEQ ID NO:1339) and encoded amino acid sequences of pAMG21ampR-Pep-Fc (SEQ ID NO:1340, SEQ ID NO:1341, and SEQ ID NO:1342). The sequences of the Fc domain (SEQ ID NOS: 75 and 76) exclude the five N-terminal glycine residues. This vector enables production of peptibodies in which the peptide-linker portion is at the N-terminus of the Fc domain.

Figure 13A is a circle diagram of mammalian expression vector pCDNA3.1(+) CMVi.

Figure 13B is a circle diagram of mammalian expression vector pCDNA3.1(+)CMVi-Fc-2xG4S-Activin RIIb that contains a Fc region from human IgG1, a 10 amino acid linker and the activin RIIb gene.

Figure 13C is a circle diagram of the CHO expression vector pDSRa22 containing the Fc-L10-ShK[2-35] coding sequence.

Figure 14A-B shows the nucleotide and encoded amino acid sequences (SEQ. ID. NOS: 77 and 78, respectively) of the molecule identified as "Fc-L10-ShK[1-35]" in Example 1 hereinafter. The L10 linker amino acid sequence (SEQ ID NO: 79) is underlined.

Figure 15A-B shows the nucleotide and encoded amino acid sequences (SEQ. ID. NOS: 80 and 81, respectively) of the molecule identified as "Fc-L10-ShK[2-35]" in Example 2 hereinafter. The same L10 linker amino acid sequence (SEQ ID NO: 79) as used in Fc-L10-ShK[1-35] (Figure 14A-B) is underlined.

Figure 16A-B shows the nucleotide and encoded amino acid sequences (SEQ. ID. NOS: 82 and 83, respectively) of the molecule identified as "Fc-L25-ShK[2-35]" in Example 2 hereinafter. The L25 linker amino acid sequence (SEQ ID NO: 84) is underlined.

Figure 17 shows a scheme for N-terminal PEGylation of ShK peptide (SEQ ID NO: 5 and SEQ ID NO:10) by reductive amination, which is also described in Example 32 hereinafter.

Figure 18 shows a scheme for N-terminal PEGylation of ShK peptide (SEQ ID NO: 5 and SEQ ID NO:10) via amide formation, which is also described in Example 34 hereinafter.

Figure 19 shows a scheme for N-terminal PEGylation of ShK peptide (SEQ ID NO: 5 and SEQ ID NO:10) by chemoselective oxime formation, which is also described in Example 33 hereinafter.

Figure 20A shows a reversed-phase HPLC analysis at 214 nm and Figure 20B shows electrospray mass analysis of folded ShK[2-35], also described as folded-"Des-Arg1-ShK" (Peptide 2).

Figure 21 shows reversed phase HPLC analysis at 214 nm of N-terminally PEGylated ShK[2-35], also referred to as N-Terminally PEGylated-"Des-Arg1-ShK".

Figure 22A shows a reversed-phase HPLC analysis at 214 nm of folded ShK[1-35], also referred to as "ShK".

Figure 22B shows electrospray mass analysis of folded ShK[1-35], also referred to as "ShK".

Figure 23 illustrates a scheme for N-terminal PEGylation of ShK[2-35] (SEQ ID NO: 92 and SEQ ID NO: 58, also referred to as "Des-Arg1-ShK" or "ShK d1") by reductive amination, which is also described in Example 31 hereinafter.

Figure 24A shows a western blot of conditioned medium from HEK 293 cells transiently transfected with Fc-L10-ShK[1-35]. Lane 1: molecular weight markers; Lane 2: 15 μl Fc-L10-ShK; Lane 3: 10 μl Fc-L10-ShK; Lane 4: 5 μl Fc-L10-ShK; Lane 5; molecular weight markers; Lane 6: blank; Lane 7: 15 μl No DNA control; Lane 8: 10 μl No DNA control; Lane 9: 5 μl No DNA control; Lane 10; molecular weight markers.

Figure 24B shows a western blot of with 15 μl ofconditioned medium from clones of Chinese Hamster Ovary (CHO) cells stably transfected with Fc-L-ShK[1-35]. Lanes 1 – 15 were loaded as follows: blank, BB6, molecular weight markers, BB5, BB4, BB3, BB2, BB1, blank, BD6, BD5, molecular weight markers, BD4, BD3, BD2.

Figure 25A shows a western blot of a non-reducing SDS-PAGE gel containing conditioned medium from 293T cells transiently transfected with Fc-L-SmIIIA.

Figure 25B shows a western blot of a reducing SDS-PAGE gel containing conditioned medium from 293T cells transiently transfected with Fc-L-SmIIIA.

Figure 26A shows a Spectral scan of 10 μl purified Fc-L10-ShK[1-35] product from stably transfected CHO cells diluted in 700 μl PBS (blanking buffer) using a Hewlett Packard 8453 spectrophotometer and a 1-cm path length quartz cuvette.

Figure 26B shows Coomassie brilliant blue stained tris-glycine 4-20% SDS-PAGE of the final Fc-L10-ShK[1-35] product. Lanes 1 – 12 were loaded as follows: Novex Mark12 wide range

protein standards, 0.5 μg product non-reduced, blank, 2.0 μg product non-reduced, blank, 10 μg product non-reduced, Novex Mark12 wide range protein standards, 0.5 μg product reduced, blank, 2.0 μg product reduced, blank, and 10 μg product reduced.

Figure 26C shows size exclusion chromatography on 20 μg of the final Fc-L10-ShK[1-35] product injected on to a Phenomenex BioSep SEC 3000 column (7.8 x 300 mm) in 50 mM NaH_2PO_4, 250 mM NaCl, and pH 6.9 at 1 ml/min observing the absorbance at 280 nm.

Figure 26D shows a MALDI mass spectral analysis of the final sample of Fc-L10-ShK[1-35] analyzed using a Voyager DE-RP time-of-flight mass spectrometer equipped with a nitrogen laser (337 nm, 3 ns pulse). The positive ion/linear mode was used, with an accelerating voltage of 25 kV. Each spectrum was produced by accumulating data from ~ 200 laser shots. External mass calibration was accomplished using purified proteins of known molecular masses.

Figure 27A shows a Coomassie brilliant blue stained tris-glycine 4-20% SDS-PAGE of the final purified Fc-L10-ShK[2-35] product from stably transfected CHO cells. Lane 1 – 12 were loaded as follows: Novex Mark12 wide range protein standards, 0.5 μg product non-reduced, blank, 2.0 μg product non-reduced, blank, 10 μg product non-reduced, Novex Mark12 wide range protein standards, 0.5 μg product reduced, blank, 2.0 μg product reduced, blank, and 10 μg product reduced.

Figure 27B shows size exclusion chromatography on 50 μg of the purified Fc-L10-ShK[2-35] injected on to a Phenomenex BioSep SEC 3000 column (7.8 x 300 mm) in 50 mM NaH_2PO_4, 250 mM NaCl, and pH 6.9 at 1 ml/min observing the absorbance at 280 nm.

Figure 27C shows a Coomassie brilliant blue stained tris-glycine 4-20% SDS-PAGE of Fc-L5-ShK[2-35] purified from stably transfected CHO cells. Lane 1 – 12 are loaded as follows: Novex Mark12 wide range protein standards, 0.5 μg product non-reduced, blank, 2.0 μg product non-reduced, blank, 10 μg product non-reduced, Novex Mark12 wide range protein standards, 0.5 μg product reduced, blank, 2.0 μg product reduced, blank, and 10 μg product reduced.

Figure 27D shows a Coomassie brilliant blue stained tris-glycine 4-20% SDS-PAGE of Fc-L25-ShK[2-35] purified from stably transfected CHO cells. Lane 1 – 12 are loaded as follows: Novex Mark12 wide range protein standards, 0.5 μg product non-reduced, blank, 2.0 μg product non-reduced, blank, 10 μg product non-reduced, Novex Mark12 wide range protein standards, 0.5 μg product reduced, blank, 2.0 μg product reduced, blank, and 10 μg product reduced.

Figure 27E shows a spectral scan of 10 µl of the Fc-L10-ShK[2-35] product diluted in 700 µl PBS (blanking buffer) using a Hewlett Packard 8453 spectrophotometer and a 1 cm path length quartz cuvette.

Figure 27F shows a MALDI mass spectral analysis of the final sample of Fc-L10-ShK[2-35] analyzed using a Voyager DE-RP time-of-flight mass spectrometer equipped with a nitrogen laser (337 nm, 3 ns pulse). The positive ion/linear mode was used, with an accelerating voltage of 25 kV. Each spectrum was produced by accumulating data from about 200 laser shots. External mass calibration was accomplished using purified proteins of known molecular masses.

Figure 27G shows a spectral scan of 10 µl of the Fc-L5-ShK[2-35] product diluted in 700 µl PBS (blanking buffer) using a Hewlett Packard 8453 spectrophotometer and a 1 cm path length quartz cuvette.

Figure 27H shows the size exclusion chromatography on 50 mg of the final Fc-L5-ShK[2-35] product injected on to a Phenomenex BioSep SEC 3000 column (7.8 x 300 mm) in 50 mM NaH2PO4, 250 mM NaCl, pH 6.9 at 1 ml/min observing the absorbance at 280 nm.

Figure 27I shows a MALDI mass spectral analysis of the final sample of Fc-L5-ShK[2-35] analyzed using a Voyager DE-RP time-of-flight mass spectrometer equipped with a nitrogen laser (337 nm, 3 ns pulse). The positive ion/linear mode was used, with an accelerating voltage of 25 kV. Each spectrum was produced by accumulating data from ~ 200 laser shots. External mass calibration was accomplished using purified proteins of known molecular masses.

Figure 27J shows a Spectral scan of 20 µl of the product diluted in 700 µl PBS (blanking buffer) using a Hewlett Packard 8453 spectrophotometer and a 1 cm path length quartz cuvette.

Figure 27K shows the size exclusion chromatography on 50 µg of the final Fc-L25-ShK[2-35] product injected on to a Phenomenex BioSep SEC 3000 column (7.8 x 300 mm) in 50 mM NaH_2PO_4, 250 mM NaCl, pH 6.9 at 1 ml/min observing the absorbance at 280 nm.

Figure 27L shows a MALDI mass spectral analysis of the final sample of Fc-L25-ShK[2-35] analyzed using a Voyager DE-RP time-of-flight mass spectrometer equipped with a nitrogen laser (337 nm, 3 ns pulse). The positive ion/linear mode was used, with an accelerating voltage of 25 kV. Each spectrum was produced by accumulating data from about 200 laser shots. External mass calibration was accomplished using purified proteins of known molecular masses.

Figure 28A shows a Coomassie brilliant blue stained tris-glycine 4-20% SDS-PAGE of Fc-L10-KTX1 purified and refolded from bacterial cells. Lane 1 – 12 are loaded as follows: Novex Mark12 wide range protein standards, 0.5 µg product non-reduced, blank, 2.0 µg product non-

reduced, blank, 10 μg product non-reduced, Novex Mark12 wide range protein standards, 0.5 μg product reduced, blank, 2.0 μg product reduced, blank, and 10 μg product reduced.

Figure 28B shows size exclusion chromatography on 45 μg of purified Fc-L10-KTX1 injected on to a Phenomenex BioSep SEC 3000 column (7.8 x 300 mm) in 50 mM NaH_2PO_4, 250 mM NaCl, pH 6.9 at 1 ml/min observing the absorbance at 280 nm.

Figure 28C shows a Spectral scan of 20 μl of the Fc-L10-KTX1 product diluted in 700 μl PBS (blanking buffer) using a Hewlett Packard 8453 spectrophotometer and a 1 cm path length quartz cuvette.

Figure 28D shows a MALDI mass spectral analysis of the final sample of Fc-L10-KTX1 analyzed using a Voyager DE-RP time-of-flight mass spectrometer equipped with a nitrogen laser (337 nm, 3 ns pulse). The positive ion/linear mode was used, with an accelerating voltage of 25 kV. Each spectrum was produced by accumulating data from ~ 200 laser shots. External mass calibration was accomplished using purified proteins of known molecular masses.

Figure 29A shows a Coomassie brilliant blue stained tris-glycine 4-20% SDS-PAGE of Fc-L-AgTx2 purified and refolded from bacterial cells. Lane 1 – 12 are loaded as follows: Novex Mark12 wide range protein standards, 0.5 μg product non-reduced, blank, 2.0 μg product non-reduced, blank, 10 μg product non-reduced, Novex Mark12 wide range protein standards, 0.5 μg product reduced, blank, 2.0 μg product reduced, blank, and 10 μg product reduced.

Figure 29B shows a Coomassie brilliant blue stained tris-glycine 4-20% SDS-PAGE of Fc-L10-HaTx1 purified and refolded from bacterial cells. Lane 1 – 12 are loaded as follows: Novex Mark12 wide range protein standards, 0.5 μg product non-reduced, blank, 2.0 μg product non-reduced, blank, 10 μg product non-reduced, Novex Mark12 wide range protein standards, 0.5 μg product reduced, blank, 2.0 μg product reduced, blank, and 10 μg product reduced, spectral scan of the purified material.

Figure 29C shows a Spectral scan of 20 μl of the Fc-L10-AgTx2 product diluted in 700 μl PBS (blanking buffer) using a Hewlett Packard 8453 spectrophotometer and a 1 cm path length quartz cuvette.

Figure 29D shows the Size exclusion chromatography on 20 μg of the final Fc-L10-AgTx2 product injected on to a Phenomenex BioSep SEC 3000 column (7.8 x 300 mm) in 50 mM NaH_2PO_4, 250 mM NaCl, pH 6.9 at 1 ml/min observing the absorbance at 280 nm.

Figure 29E shows a MALDI mass spectral analysis of the final sample of Fc-L10-AgTx2 analyzed using a Voyager DE-RP time-of-flight mass spectrometer equipped with a nitrogen laser (337 nm, 3 ns pulse). The positive ion/linear mode was used, with an accelerating voltage of 25

kV. Each spectrum was produced by accumulating data from about 200 laser shots. External mass calibration was accomplished using purified proteins of known molecular masses.

Figure 29F shows a Spectral scan of 20 µl of the Fc-L10-HaTx1 product diluted in 700 µl PBS (blanking buffer) using a Hewlett Packard 8453 spectrophotometer and a 1 cm path length quartz cuvette.

Figure 29G shows the size exclusion chromatography on 20 µg of the final Fc-L10-HaTx1 product injected on to a Phenomenex BioSep SEC 3000 column (7.8 x 300 mm) in 50 mM NaH_2PO_4, 250 mM NaCl, pH 6.9 at 1 ml/min observing the absorbance at 280 nm.

Figure 29H shows a MALDI mass spectral analysis of the final sample of Fc-L10-HaTx1 analyzed using a Voyager DE-RP time-of-flight mass spectrometer equipped with a nitrogen laser (337 nm, 3 ns pulse). The positive ion/linear mode was used, with an accelerating voltage of 25 kV. Each spectrum was produced by accumulating data from ~ 200 laser shots. External mass calibration was accomplished using purified proteins of known molecular masses.

Figure 30A shows Fc-L10-ShK[1-35] purified from CHO cells produces a concentration dependent block of the outward potassium current recorded from HEK293 cell stably expressing the human Kv1.3 channel.

Figure 30B shows the time course of potassium current block by Fc-L10-ShK[1-35] at various concentrations. The IC50 was estimated to be 15 ± 2 pM (n = 4 cells).

Figure 30C shows synthetic ShK[1-35] (also referred to as "ShK" alone) produces a concentration dependent block of the outward potassium current recorded from HEK293 cell stably expressing human Kv1.3 channel.

Figure 30D shows the time course of ShK[1-35] block at various concentrations. The IC50 for ShK was estimated to be 12 ± 1 pM (n =4 cells).

Figure 31A shows synthetic peptide analog ShK[2-35] producing a concentration dependent block of the outward potassium current as recorded from HEK293 cells stably expressing human Kv1.3 channel with an IC50 of 49 ± 5 pM (n = 3 cells).

Figure 31B shows the CHO-derived Fc-L10-ShK[2-35] peptibody producing a concentration dependent block of the outward potassium current as recorded from HEK293 cell stably expressing human Kv1.3 channel with an IC50 of 115 ± 18 pM (n = 3 cells).

Figure 31C shows the Fc-L5-ShK[2-35] peptibody produces a concentration dependent block of the outward potassium current recorded from HEK293 cell stably expressing human Kv1.3 channel with an IC50 of 100 pM (n = 3 cells).

Figure 32A shows Fc-L-KTX1 peptibody purified from bacterial cells producing a concentration dependent block of the outward potassium current as recorded from HEK293 cell stably expressing human Kv1.3 channel.

Figure 32B shows the time course of potassium current block by Fc-L10-KTX1 at various concentrations.

Figure 33 shows by immunohistochemistry that CHO-derived Fc-L10-ShK[1-35] peptibody stains HEK 293 cells stably transfected with human Kv1.3 (Figure 33A), whereas untransfected HEK 293 cells are not stained with the peptibody (Figure 33B).

Figure 34 shows results of an enzyme-immunoassay using fixed HEK 293 cells stably transfected with human Kv1.3. Figure 34A shows the CHO-derived Fc-L10-ShK[1-35] (referred to here simply as "Fc-L10-ShK") peptibody shows a dose-dependent increase in response, whereas the CHO-Fc control ("Fc control") does not. Figure 34B shows the Fc-L10-ShK[1-35] peptibody (referred to here as "Fc-ShK") does not elicit a response from untransfected HEK 293 cells using similar conditions and also shows other negative controls.

Figure 35 shows the CHO-derived Fc-L10-ShK[1-35] peptibody shows a dose-dependent inhibition of IL-2 (Figure 35A) and IFNγ (Figure 35B) production from PMA and αCD3 antibody stimulated human PBMCs. The peptibody shows a novel pharmacology exhibiting a complete inhibition of the response, whereas the synthetic ShK[1-35] peptide alone shows only a partial inhibition.

Figure 36 shows the mammalian-derived Fc-L10-ShK[1-35] peptibody inhibits T cell proliferation (^{3}H-thymidine incorporation) in human PBMCs from two normal donors stimulated with antibodies to CD3 and CD28. Figure 36A shows the response of donor 1 and Figure 36B the response of donor 2. Pre-incubation with the anti-CD32 (FcgRII) blocking antibody did not alter the sensitivity toward the peptibody.

Figure 37 shows the purified CHO-derived Fc-L10-ShK[1-35] peptibody causes a dose-dependent inhibition of IL-2 (Figure 37A) and IFNγ (Figure 37B) production from αCD3 and αCD28 antibody stimulated human PBMCs.

Figure 38A shows the PEGylated ShK[2-35] synthetic peptide produces a concentration dependent block of the outward potassium current recorded from HEK293 cell stably expressing human Kv1.3 channel and the time course of potassium current block at various concentrations is shown in Figure 38B.

Figure 39A shows a spectral scan of 50 µl of the Fc-L10-ShK(1-35) product diluted in 700 µl PBS (blanking buffer) using a Hewlett Packard 8453 spectrophotometer and a 1 cm path length quartz cuvette.

Figure 39B shows a Coomassie brilliant blue stained tris-glycine 4-20% SDS-PAGE of the final Fc-L10-ShK(1-35) product. Lane 1 – 12 are loaded as follows: Novex Mark12 wide range protein standards, 0.5 µg product non-reduced, blank, 2.0 µg product non-reduced, blank, 10 µg product non-reduced, Novex Mark12 wide range protein standards, 0.5 µg product reduced, blank, 2.0 µg product reduced, blank, and 10 µg product reduced.

Figure 39C shows the Size exclusion chromatography on 50 µg of the final Fc-L10-ShK(1-35) product injected on to a Phenomenex BioSep SEC 3000 column (7.8 x 300 mm) in 50 mM NaH_2PO_4, 250 mM NaCl, pH 6.9 at 1 ml/min observing the absorbance at 280 nm.

Figure 40A shows a Spectral scan of 20 µl of the Fc-L10-ShK(2-35) product diluted in 700 µl PBS (blanking buffer) using a Hewlett Packard 8453 spectrophotometer and a 1 cm path length quartz cuvette.

Figure 40B shows a Coomassie brilliant blue stained tris-glycine 4-20% SDS-PAGE of the final Fc-L10-ShK(2-35) product. Lanes 1 – 12 are loaded as follows: Novex Mark12 wide range protein standards, 0.5 µg product non-reduced, blank, 2.0 µg product non-reduced, blank, 10 µg product non-reduced, Novex Mark12 wide range protein standards, 0.5 µg product reduced, blank, 2.0 µg product reduced, blank, and 10 µg product reduced.

Figure 40C shows the size exclusion chromatography on 50 µg of the final Fc-L10-ShK(2-35) product injected on to a Phenomenex BioSep SEC 3000 column (7.8 x 300 mm) in 50 mM NaH_2PO_4, 250 mM NaCl, pH 6.9 at 1 ml/min observing the absorbance at 280 nm.

Figure 40D shows a MALDI mass spectral analysis of the final sample of Fc-L10-ShK(2-35) analyzed using a Voyager DE-RP time-of-flight mass spectrometer equipped with a nitrogen laser (337 nm, 3 ns pulse). The positive ion/linear mode was used, with an accelerating voltage of 25 kV. Each spectrum was produced by accumulating data from ~ 200 laser shots. External mass calibration was accomplished using purified proteins of known molecular masses.

Figure 41A shows spectral scan of 50 µl of the Fc-L10-OSK1 product diluted in 700 µl Formulation Buffer using a Hewlett Packard 8453 spectrophotometer and a 1 cm path length quartz cuvette.

Figure 41B shows Coomassie brilliant blue stained tris-glycine 4-20% SDS-PAGE of the final Fc-L10-OSK1 product. Lanes 1 – 12 are loaded as follows: Novex Mark12 wide range protein standards, 0.5 µg product non-reduced, blank, 2.0 µg product non-reduced, blank, 10 µg product

non-reduced, Novex Mark12 wide range protein standards, 0.5 μg product reduced, blank, 2.0 μg product reduced, blank, and 10 μg product reduced.

Figure 41C shows size exclusion chromatography on 123 μg of the final Fc-L10-OSK1 product injected on to a Phenomenex BioSep SEC 3000 column (7.8 x 300 mm) in 50 mM NaH_2PO_4, 250 mM NaCl, pH 6.9 at 1 ml/min observing the absorbance at 280 nm.

Figure 41D shows liquid chromatography - mass spectral analysis of approximately 4 μg of the final Fc-L10-OSK1 sample using a Vydac C_4 column with part of the effluent directed into a LCQ ion trap mass spectrometer. The mass spectrum was deconvoluted using the Bioworks software provided by the mass spectrometer manufacturer.

Figure 42A-B shows nucleotide and amino acid sequences (SEQ ID NO: 1040 and SEQ ID NO: 1041, respectively) of Fc-L10-OSK1.

Figure 43A-B shows nucleotide and amino acid sequences (SEQ ID NO: 1042 and SEQ ID NO: 1043, respectively) of Fc-L10-OSK1[K7S].

Figure 44A-B shows nucleotide and amino acid sequences (SEQ ID NO: 1044 and SEQ ID NO: 1045, respectively) of Fc-L10-OSK1[E16K,K20D].

Figure 45A-B shows nucleotide and amino acid sequences (SEQ ID NO: 1046 and SEQ ID NO: 1047, respectively) of Fc-L10-OSK1[K7S,E16K,K20D].

Figure 46 shows a Western blot (from tris-glycine 4-20% SDS-PAGE) with anti-human Fc antibodies. Lanes 1 – 6 were loaded as follows: 15μl of Fc-L10-OSK1[K7S,E16K,K20D];15μl of Fc-L10-OSK1[E16K,K20D];15μl of Fc-L10-OSK1[K7S];15μl of Fc-L10-OSK1;15μl of "No DNA" control; molecular weight markers

Figure 47 shows a Western blot (from tris-glycine 4-20% SDS-PAGE) with anti-human Fc antibodies. Lanes 1-5 were loaded as follows: 2μl of Fc-L10-OSK1; 5μl of Fc-L10-OSK1;10μl of Fc-L10-OSK1; 20ng Human IgG standard; molecular weight markers.

Figure 48 shows a Western blot (from tris-glycine 4-20% SDS-PAGE) with anti-human Fc antibodies. Lanes 1-13 were loaded as follows: 20 ng Human IgG standard; D1; C3; C2; B6; B5; B2; B1; A6; A5; A4; A3; A2 (5 μl of clone-conditioned medium loaded in lanes 2-13).

Figure 49A shows a spectral scan of 50 μl of the Fc-L10-OsK1 product diluted in 700 μl PBS (blanking buffer) using a Hewlett Packard 8453 spectrophotometer and a 1 cm path length quartz cuvette.

Figure 49B shows Coomassie brilliant blue stained tris-glycine 4-20% SDS-PAGE of the final Fc-L10-OsK1 product. Lane 1 – 12 are loaded as follows: Novex Mark12 wide range protein standards, 0.5 μg product non-reduced, blank, 2.0 μg product non-reduced, blank, 10 μg product

non-reduced, Novex Mark12 wide range protein standards, 0.5 μg product reduced, blank, 2.0 μg product reduced, blank, and 10 μg product reduced.

Figure 49C shows Size exclusion chromatography on 149 μg of the final Fc-L10-OsK1 product injected on to a Phenomenex BioSep SEC 3000 column (7.8 x 300 mm) in 50 mM NaH_2PO_4, 250 mM NaCl, pH 6.9 at 1 ml/min observing the absorbance at 280 nm.

Figure 49D shows MALDI mass spectral analysis of the final sample of Fc-L10-OsK1 analyzed using a Voyager DE-RP time-of-flight mass spectrometer equipped with a nitrogen laser (337 nm, 3 ns pulse). The positive ion/linear mode was used, with an accelerating voltage of 25 kV. Each spectrum was produced by accumulating data from ~ 200 laser shots. External mass calibration was accomplished using purified proteins of known molecular masses.

Figure 50A shows a spectral scan of 50 μl of the Fc-L10-OsK1(K7S) product diluted in 700 μl PBS (blanking buffer) using a Hewlett Packard 8453 spectrophotometer and a 1 cm path length quartz cuvette.

Figure 50B shows Coomassie brilliant blue stained tris-glycine 4-20% SDS-PAGE of the final Fc-L10-OsK1(K7S) product. Lane 1 – 12 are loaded as follows: Novex Mark12 wide range protein standards, 0.5 μg product non-reduced, blank, 2.0 μg product non-reduced, blank, 10 μg product non-reduced, Novex Mark12 wide range protein standards, 0.5 μg product reduced, blank, 2.0 μg product reduced, blank, and 10 μg product reduced.

Figure 50C shows size exclusion chromatography on 50 μg of the final Fc-L10-OsK1(K7S) product injected on to a Phenomenex BioSep SEC 3000 column (7.8 x 300 mm) in 50 mM NaH_2PO_4, 250 mM NaCl, pH 6.9 at 1 ml/min observing the absorbance at 280 nm.

Figure 50D shows MALDI mass spectral analysis of a sample of the final product Fc-L10-OsK1(K7S) analyzed using a Voyager DE-RP time-of-flight mass spectrometer equipped with a nitrogen laser (337 nm, 3 ns pulse). The positive ion/linear mode was used, with an accelerating voltage of 25 kV. Each spectrum was produced by accumulating data from ~ 200 laser shots. External mass calibration was accomplished using purified proteins of known molecular masses.

Figure 51A shows a spectral scan of 50 μl of the Fc-L10-OsK1(E16K, K20D) product diluted in 700 μl PBS (blanking buffer) using a Hewlett Packard 8453 spectrophotometer and a 1 cm path length quartz cuvette.

Figure 51B shows Coomassie brilliant blue stained tris-glycine 4-20% SDS-PAGE of the final Fc-L10-OsK1(E16K, K20D) product. Lane 1 – 12 are loaded as follows: Novex Mark12 wide range protein standards, 0.5 μg product non-reduced, blank, 2.0 μg product non-reduced, blank,

10 μg product non-reduced, Novex Mark12 wide range protein standards, 0.5 μg product reduced, blank, 2.0 μg product reduced, blank, and 10 μg product reduced.

Figure 51C shows size exclusion chromatography on 50 μg of the final Fc-L10-OsK1(E16K, K20D) product injected on to a Phenomenex BioSep SEC 3000 column (7.8 x 300 mm) in 50 mM NaH_2PO_4, 250 mM NaCl, pH 6.9 at 1 ml/min observing the absorbance at 280 nm.

Figure 51D shows MALDI mass spectral analysis of a sample of the final product Fc-L10-OsK1(E16K, K20D) analyzed using a Voyager DE-RP time-of-flight mass spectrometer equipped with a nitrogen laser (337 nm, 3 ns pulse). The positive ion/linear mode was used, with an accelerating voltage of 25 kV. Each spectrum was produced by accumulating data from ~ 200 laser shots. External mass calibration was accomplished using purified proteins of known molecular masses.

Figure 52A shows a spectral scan of 50 μl of the Fc-L10-OsK1(K7S, E16K, K20D) product diluted in 700 μl PBS (blanking buffer) using a Hewlett Packard 8453 spectrophotometer and a 1 cm path length quartz cuvette.

Figure 52B shows Coomassie brilliant blue stained tris-glycine 4-20% SDS-PAGE of the final Fc-L10-OsK1(K7S, E16K, K20D) product. Lanes 1 – 12 are loaded as follows: Novex Mark12 wide range protein standards, 0.5 μg product non-reduced, blank, 2.0 μg product non-reduced, blank, 10 μg product non-reduced, Novex Mark12 wide range protein standards, 0.5 μg product reduced, blank, 2.0 μg product reduced, blank, and 10 μg product reduced.

Figure 52C shows size exclusion chromatography on 50 μg of the final Fc-L10-OsK1(K7S, E16K, K20D) product injected on to a Phenomenex BioSep SEC 3000 column (7.8 x 300 mm) in 50 mM NaH_2PO_4, 250 mM NaCl, pH 6.9 at 1 ml/min observing the absorbance at 280 nm.

Figure 52D shows MALDI mass spectral analysis of a sample of the final product Fc-L10-OsK1(K7S, E16K, K20D) analyzed using a Voyager DE-RP time-of-flight mass spectrometer equipped with a nitrogen laser (337 nm, 3 ns pulse). The positive ion/linear mode was used, with an accelerating voltage of 25 kV. Each spectrum was produced by accumulating data from ~ 200 laser shots. External mass calibration was accomplished using purified proteins of known molecular masses.

Figure 53 shows inhibition of the outward potassium current recorded from HEK293 cell stably expressing human Kv1.3 channel by synthetic Osk1, a 38-residue toxin peptide of the Asian scorpion *Orthochirus scrobiculosus* venom. Figure 53A shows a concentration dependent block of the outward potassium current recorded from HEK293 cell stably expressing human Kv1.3 channel

by the synthetic Osk1 toxin peptide. Figure 53B shows the time course of the synthetic Osk1 toxin peptide block at various concentrations. The IC50 for the synthetic Osk1 toxin peptide was estimated to be 39 ± 12 pM (n =4 cells).

Figure 54 shows that modification of the synthetic OSK1 toxin peptide by fusion to the Fc-fragment of an antibody (OSK1-peptibody) retained the inhibitory activity against the human Kv1.3 channel. Figure 54A shows a concentration dependent block of the outward potassium current recorded from HEK293 cells stably expressing human Kv1.3 channel by OSK1 linked to a human IgG1 Fc-fragment with a linker chain length of 10 amino acid residues (Fc-L10-OSK1). The fusion construct was stably expressed in Chinese Hamster Ovarian (CHO) cells. Figure 54B shows the time course of the Fc-L10-OSK1 block at various concentrations. The IC50 for Fc-L10-OSK1 was estimated to be 198 ± 35 pM (n = 6 cells), approximately 5-fold less potent than the synthetic OSK1 toxin peptide.

Figure 55 shows that a single amino-acid residue substitution of the OSK1-peptibody retained the inhibitory activity against the human Kv1.3 channel. Figure 55A shows a concentration dependent block of the outward potassium current recorded from HEK293 cell stably expressing human Kv1.3 channel by OSK1-peptibody with a single amino acid substitution (lysine to serine at the 7th position from N-terminal, [K7S]) and linked to a human IgG1 Fc-fragment with a linker chain length of 10 amino acid residues (Fc-L10-OSK1[K7S]). The fusion construct was stably expressed in Chinese Hamster Ovarian (CHO) cells. Figure 55B shows the time course of potassium current block by Fc-L10-OSK1[K7S] at various concentrations. The IC50 was estimated to be 372 ± 71 pM (n = 4 cells), approximately 10-fold less potent than the synthetic OSK1 toxin peptide.

Figure 56 shows that a two amino-acid residue substitution of the OSK1-peptibody retained the inhibitory activity against the human Kv1.3 channel. Figure 56A shows a concentration dependent block of the outward potassium current recorded from HEK293 cell stably expressing human Kv1.3 channel by OSK1-peptibody with two amino acid substitutions (glutamic acid to lysine and lysine to aspartic acid at the 16th and 20th position from N-terminal respectively, [E16KK20D]) and linked to a human IgG1 Fc-fragment with a linker chain length of 10 amino acid residues (Fc-L10-OSK1[E16KK20D]). The fusion construct was stably expressed in Chinese Hamster Ovarian (CHO) cells. Figure 56B shows the time course of potassium current block by Fc-L10-OSK1[E16KK20D] at various concentrations. The IC50 was estimated to be 248 ± 63 pM (n = 3 cells), approximately 6-fold less potent than the synthetic OSK1 toxin peptide.

Figure 57 shows that a triple amino-acid residue substitution of the OSK1-peptibody retained the inhibitory activity against the human Kv1.3 channel, but the potency of inhibition was significantly reduced when compared to the synthetic OSK1 toxin peptide. Figure 57A shows a concentration dependent block of the outward potassium current recorded from HEK293 cell stably expressing human Kv1.3 channel by OSK1-peptibody with triple amino acid substitutions (lysine to serine, glutamic acid to lysine and lysine to aspartic acid at the 7th, 16th and 20th position from N-terminal respectively, [K7SE16KK20D]) and linked to a human IgG1 Fc-fragment with a linker chain length of 10 amino acid residues (Fc-L10-OSK1[K7SE16KK20D]). The fusion construct was stably expressed in Chinese Hamster Ovarian (CHO) cells. Figure 57B shows the time course of potassium current block by Fc-L10-OSK1[K7SE16KK20D] at various concentrations. The IC50 was estimated to be 812 ± 84 pM (n = 3 cells), approximately 21-fold less potent than the synthetic OSK1 toxin peptide.

Figure 58 shows Standard curves for ShK (Figure 58A) and 20K PEG-ShK[1-35] (Figure 58B) containing linear regression equations for each Standard at a given percentage of serum.

Figure 59 shows the pharmacokinetic profile in rats of 20K PEG ShK[1-35] molecule after IV injection.

Figure 60 shows Kv1.3 inhibitory activity in serum samples (5%) of rats receiving a single equal molar IV injection of Kv1.3 inhibitors ShK versus 20K PEG-ShK[1-35].

Figure 61 illustrates an Adoptive Transfer EAE model experimental design (n = 5 rats per treatment group). Dosing values in microgram per kilogram (mg/kg) are based on peptide content.

Figure 62 shows that treatment with PEG-ShK ameliorated disease in rats in the adoptive transfer EAE model. Clinical scoring: 0 = No signs, 0.5 = distal limp tail, 1.0 = limp tail, 2.0 = mild paraparesis, ataxia, 3.0 = moderate paraparesis, 3.5 = one hind leg paralysis, 4.0 = complete hind leg paralysis, 5.0 = complete hind leg paralysis and incontinence, 5.5 = tetraplegia, 6.0 = moribund state or death. Rats reaching a score of 5.5 to 6 died or were euthanized. Mean ± sem values are shown. (n = 5 rats per treatment group.)

Figure 63 shows that treatment with PEG-ShK prevented loss of body weight in the adoptive transfer EAE model. Rats were weighed on days –1, 4, 6, and 8 (for surviving rats). Mean ± sem values are shown.

Figure 64 shows that thapsigargin-induced IL-2 production in human whole blood was suppressed by the Kv1.3 channel inhibitors ShK[1-35] and Fc-L10-ShK[2-35]. The calcineurin inhibitor cyclosporine A also blocked the response. The BKCa channel inhibitor iberiotoxin (IbTx)

showed no significant activity. The response of whole blood from two separate donors is shown in Figure 64A and Figure 64B.

Figure 65 shows that thapsigargin-induced IFN-g production in human whole blood was suppressed by the Kv1.3 channel inhibitors ShK[1-35] and Fc-L10-ShK[2-35]. The calcineurin inhibitor cyclosporine A also blocked the response. The BKCa channel inhibitor iberiotoxin (IbTx) showed no significant activity. The response of whole blood from two separate donors is shown in Figure 65A and Figure 65B.

Figure 66 shows that thapsigargin-induced upregulation of CD40L on T cells in human whole blood was suppressed by the Kv1.3 channel inhibitors ShK[1-35] and Fc-L10-ShK[1-35] (Fc-ShK). The calcineurin inhibitor cyclosporine A (CsA) also blocked the response. Figure 66A shows results of an experiment looking at the response of total CD4+ T cells. Figure 66B shows results of an experiment that looked at total CD4+ T cells, as well as CD4+CD45+ and CD4+CD45- T cells. In Figure 66B, the BKCa channel inhibitor iberiotoxin (IbTx) and the Kv1.1 channel inhibitor dendrotoxin-K (DTX-K) showed no significant activity.

Figure 67 shows that thapsigargin-induced upregulation of the IL-2R on T cells in human whole blood was suppressed by the Kv1.3 channel inhibitors ShK[1-35] and Fc-L10-ShK[1-35] (Fc-ShK). The calcineurin inhibitor cyclosporine A (CsA) also blocked the response. Figure 67A shows results of an experiment looking at the response of total CD4+ T cells. Figure 67B shows results of an experiment that looked at total CD4+ T cells, as well as CD4+CD45+ and CD4+CD45- T cells. In Figure 67B, the BKCa channel inhibitor iberiotoxin (IbTx) and the Kv1.1 channel inhibitor dendrotoxin-K (DTX-K) showed no significant activity.

Figure 68 shows cation exchange chromatograms of PEG-peptide purification on SP Sepharose HP columns for PEG-Shk purification (Figure 68A) and PEG-OSK-1 purification (Figure 68B).

Figure 69 shows RP-HPLC chromatograms on final PEG-peptide pools to demonstrate purity of PEG-Shk purity >99% (Figure 69A) and PEG-Osk1 purity >97% (Figure 69B).

Figure 70 shows the amino acid sequence (SEQ ID NO: 976) of an exemplary FcLoop-L2-OsK1-L2 having three linked domains: Fc N-terminal domain (amino acid residues 1-139); OsK1(underlined amino acid residues 142-179); and Fc C-terminal domain (amino acid residues 182-270).

Figure 71 shows the amino acid sequence (SEQ ID NO: 977) of an exemplary FcLoop-L2-ShK-L2 having three linked domains: Fc N-terminal domain (amino acid residues 1-139); ShK

(underlined amino acid residues 142-176); and Fc C-terminal domain (amino acid residues 179-267).

Figure 72 shows the amino acid sequence (SEQ ID NO: 978) of an exemplary FcLoop-L2-ShK-L4 having three linked domains: Fc N-terminal domain (amino acid residues 1-139); ShK (underlined amino acid residues 142-176); and Fc C-terminal domain (amino acid residues 181-269).

Figure 73 shows the amino acid sequence (SEQ ID NO: 979) of an exemplary FcLoop-L4-OsK1-L2 having three linked domains: Fc N-terminal domain (amino acid residues 1-139); OsK1(underlined amino acid residues 144-181); and Fc C-terminal domain (amino acid residues 184-272).

Figure 74 shows that the 20K PEGylated ShK[1-35] provided potent blockade of human Kv1.3 as determined by whole cell patch clamp electrophysiology on HEK293/Kv1.3 cells. The data represents blockade of peak current.

Figure 75 shows schematic structures of some other exemplary embodiments of the composition of matter of the invention. "X^2" and "X^3" represent toxin peptides or linker-toxin peptide combinations (i.e., $-(L)_f-P-(L)_g-$) as defined herein. As described herein but not shown in Figure 75, an additional X^1 domain and one or more additional PEG moieties are also encompassed in other embodiments. The specific embodiments shown here are as follows:

Figure 75C, Figure 75D, Figure 75G and Figure 75H: show a single chain molecule and can also represent the DNA construct for the molecule.

Figure 75A, Figure 75B, Figure 75E and Figure 75F: show doubly disulfide-bonded Fc dimers (in position F^2); Figure 75A and Figure 75B show a dimer having the toxin peptide portion on both chains in position X^3; Figure 75E and Figure 75F show a dimer having the toxin peptide portion on both chains In position X^2.

Figure 76A shows a spectral scan of 50 µl of the ShK[2-35]-Fc product diluted in 700 µl PBS (blanking buffer) using a Hewlett Packard 8453 spectrophotometer and a 1 cm path length quartz cuvette.

Figure 76B shows Coomassie brilliant blue stained tris-glycine 4-20% SDS-PAGE of the final ShK[2-35]-Fc product. Lanes 1 – 12 were loaded as follows: Novex Mark12 wide range protein standards, 0.5 µg product non-reduced, blank, 2.0 µg product non-reduced, blank, 10 µg product non-reduced, Novex Mark12 wide range protein standards, 0.5 µg product reduced, blank, 2.0 µg product reduced, blank, and 10 µg product reduced.

Figure 76C shows size exclusion chromatography on 70 μg of the final ShK[2-35]-Fc product injected on to a Phenomenex BioSep SEC 3000 column (7.8 x 300 mm) in 50 mM NaH_2PO_4, 250 mM NaCl, pH 6.9 at 1 ml/min observing the absorbance at 280 nm.

Figure 76D shows LC-MS analysis of the final ShK[2-35]-Fc sample using an Agilent 1100 HPCL running reverse phase chromatography, with the column effluent directly coupled to an electrospray source of a Thermo Finnigan LCQ ion trap mass spectrometer. Relevant spectra were summed and deconvoluted to mass data with the Bioworks software package.

Figure 77A shows a spectral scan of 20 μl of the met-ShK[1-35]-Fc product diluted in 700 μl PBS (blanking buffer) using a Hewlett Packard 8453 spectrophotometer and a 1 cm path length quartz cuvette.

Figure 77B shows Coomassie brilliant blue stained tris-glycine 4-20% SDS-PAGE of the final met-ShK[1-35]-Fc product. Lanes 1 – 12 were loaded as follows: Novex Mark12 wide range protein standards, 0.5 μg product non-reduced, blank, 2.0 μg product non-reduced, blank, 10 μg product non-reduced, Novex Mark12 wide range protein standards, 0.5 μg product reduced, blank, 2.0 μg product reduced, blank, and 10 μg product reduced.

Figure 77C shows size exclusion chromatography on 93 μg of the final met-ShK[1-35]-Fc product injected on to a Phenomenex BioSep SEC 3000 column (7.8 x 300 mm) in 50 mM NaH_2PO_4, 250 mM NaCl, pH 6.9 at 1 ml/min observing the absorbance at 280 nm.

Figure 77D shows MALDI mass spectral analysis of the final met-ShK[1-35]-Fc sample analyzed using a Voyager DE-RP time-of-flight mass spectrometer equipped with a nitrogen laser (337 nm, 3 ns pulse). The positive ion/linear mode was used, with an accelerating voltage of 25 kV. Each spectrum was produced by accumulating data from ~ 200 laser shots. External mass calibration was accomplished using purified proteins of known molecular masses.

Detailed Description of Embodiments of the Invention

Definition of Terms

The terms used throughout this specification are defined as follows, unless otherwise limited in specific instances. As used in the specification and the appended claims, the singular forms "a", "an", and "the" include plural referents unless the context clearly dictates otherwise.

The term "half-life extending moiety" (i.e., F^1 or F^2 in Formula I) refers to a pharmaceutically acceptable moiety, domain, or "vehicle" covalently linked or conjugated to the toxin peptide, that prevents or mitigates in vivo proteolytic degradation or other activity-diminishing chemical modification of the toxin peptide, increases half-life or other pharmacokinetic properties such as but not limited to increasing the rate of absorption, reduces toxicity, improves solubility, increases biological activity and/or target selectivity of the toxin peptide with respect to a target ion channel of interest, increases manufacturability, and/or reduces immunogenicity of the toxin peptide, compared to an unconjugated form of the toxin peptide.

By "PEGylated peptide" is meant a peptide or protein having a polyethylene glycol (PEG) moiety covalently bound to an amino acid residue of the peptide itself or to a peptidyl or non-peptidyl linker (including but not limited to aromatic linkers) that is covalently bound to a residue of the peptide.

By "polyethylene glycol" or "PEG" is meant a polyalkylene glycol compound or a derivative thereof, with or without coupling agents or derivatization with coupling or activating moieties (e.g., with aldehyde, hydroxysuccinimidyl, hydrazide, thiol, triflate, tresylate, azirdine, oxirane, orthopyridyl disulphide, vinylsulfone, iodoacetamide or a maleimide moiety). In accordance with the present invention, useful PEG includes substantially linear, straight chain PEG, branched PEG, or dendritic PEG. (See, e.g., Merrill, US Patent No. 5,171,264; Harris et al., Multiarmed, monofunctional, polymer for coupling to molecules and surfaces, US Patent No. 5,932,462; Shen, N-maleimidyl polymer derivatives, US Patent No. 6,602,498).

The term "peptibody" refers to molecules of Formula I in which F^1 and/or F^2 is an immunoglobulin Fc domain or a portion thereof, such as a CH2 domain of an Fc, or in which the toxin peptide is inserted into a human IgG1 Fc domain loop, such that F^1 and F^2 are each a portion of an Fc domain with a toxin peptide inserted between them (See, e.g., Figures 70-73 and Example 49 herein). Peptibodies of the present invention can also be PEGylated as described further herein, at either an Fc domain or portion thereof, or at the toxin peptide(s) portion of the inventive composition, or both.

The term "native Fc" refers to molecule or sequence comprising the sequence of a non-antigen-binding fragment resulting from digestion of whole antibody, whether in monomeric or multimeric form. The original immunoglobulin source of the native Fc is preferably of human origin and can be any of the immunoglobulins, although IgG1 or IgG2 are preferred. Native Fc's are made up of monomeric polypeptides that can be linked into dimeric or multimeric forms by covalent (i.e., disulfide bonds) and non-covalent association. The number of intermolecular disulfide bonds between monomeric subunits of native Fc molecules ranges from 1 to 4 depending on class (e.g., IgG, IgA, IgE) or subclass (e.g., IgG1, IgG2, IgG3, IgA1, IgGA2). One example of a native Fc is a disulfide-bonded dimer resulting from papain digestion of an IgG (see Ellison et al. (1982), Nucleic Acids Res. 10: 4071-9). The term "native Fc" as used herein is generic to the monomeric, dimeric, and multimeric forms.

The term "Fc variant" refers to a molecule or sequence that is modified from a native Fc but still comprises a binding site for the salvage receptor, FcRn. Several published patent documents describe exemplary Fc variants, as well as interaction with the salvage receptor. See International applications WO 97/34 631 (published 25 September 1997; WO 96/32 478, corresponding to US Pat. No. 6,096,891, issued August 1, 2000, hereby incorporated by reference in its entirety; and WO 04/110 472. Thus, the term "Fc variant" includes a molecule or sequence that is humanized from a non-human native Fc. Furthermore, a native Fc comprises sites that can be removed because they provide structural features or biological activity that are not required for the fusion molecules of the present invention. Thus, the term "Fc variant" includes a molecule or sequence that lacks one or more native Fc sites or residues that affect or are involved in (1) disulfide bond formation, (2) incompatibility with a selected host cell (3) N-terminal heterogeneity upon expression in a selected host cell, (4) glycosylation, (5) interaction with complement, (6) binding to an Fc receptor other than a salvage receptor, or (7) antibody-dependent cellular cytotoxicity (ADCC). Fc variants are described in further detail hereinafter.

The term "Fc domain" encompasses native Fc and Fc variant molecules and sequences as defined above. As with Fc variants and native Fc's, the term "Fc domain" includes molecules in monomeric or multimeric form, whether digested from whole antibody or produced by other means.

The term "multimer" as applied to Fc domains or molecules comprising Fc domains refers to molecules having two or more polypeptide chains associated covalently, noncovalently, or by both covalent and non-covalent interactions. IgG molecules typically form dimers; IgM, pentamers; IgD, dimers; and IgA, monomers, dimers, trimers, or tetramers. One skilled in the art can form

multimers by exploiting the sequence and resulting activity of the native Ig source of the Fc or by derivatizing (as defined below) such a native Fc.

The term "dimer" as applied to Fc domains or molecules comprising Fc domains refers to molecules having two polypeptide chains associated covalently or non-covalently. Thus, exemplary dimers within the scope of this invention are as shown in Figure 2.

The terms "derivatizing" and "derivative" or "derivatized" comprise processes and resulting compounds respectively in which (1) the compound has a cyclic portion; for example, cross-linking between cysteinyl residues within the compound; (2) the compound is cross-linked or has a cross-linking site; for example, the compound has a cysteinyl residue and thus forms cross-linked dimers in culture or in vivo; (3) one or more peptidyl linkage is replaced by a non-peptidyl linkage; (4) the N-terminus is replaced by -NRR^1, NRC(O)R^1, -NRC(O)OR^1, -NRS(O)$_2$R^1, -NHC(O)NHR, a succinimide group, or substituted or unsubstituted benzyloxycarbonyl-NH-, wherein R and R^1 and the ring substituents are as defined hereinafter; (5) the C-terminus is replaced by -C(O)R^2 or -NR^{3}R^4 wherein R^2, R^3 and R^4 are as defined hereinafter; and (6) compounds in which individual amino acid moieties are modified through treatment with agents capable of reacting with selected side chains or terminal residues. Derivatives are further described hereinafter.

The term "peptide" refers to molecules of 2 to about 80 amino acid residues, with molecules of about 10 to about 60 amino acid residues preferred and those of about 30 to about 50 amino acid residuess most preferred. Exemplary peptides can be randomly generated by any known method, carried in a peptide library (e.g., a phage display library), or derived by digestion of proteins. In any peptide portion of the inventive compositions, for example a toxin peptide or a peptide linker moiety described herein, additional amino acids can be included on either or both of the N- or C- termini of the given sequence. Of course, these additional amino acid residues should not significantly interfere with the functional activity of the composition. "Toxin peptides" include peptides having the same amino acid sequence of a naturally occurring pharmacologically active peptide that can be isolated from a venom, and also include modified peptide analogs of such naturally occurring molecules. Examples of toxin peptides useful in practicing the present invention are listed in Tables 1-32. The toxin peptide ("P", or equivalently shown as "P^1" in Figure 2) comprises at least two intrapeptide disulfide bonds, as shown, for example, in Figure 9. Accordingly, this invention concerns molecules comprising:

a) C^1-C^3 and C^2-C^4 disulfide bonding in which C^1, C^2, C^3, and C^4 represent the order in which cysteine residues appear in the primary sequence of the toxin peptide stated conventionally with the N-terminus of the peptide on the left, with the first and third

cysteines in the amino acid sequence forming a disulfide bond, and the second and fourth cysteines forming a disulfide bond. Examples of toxin peptides with such a C^1-C^3, C^2-C^4 disulfide bonding pattern include, but are not limited to, apamin peptides, α-conopeptides, PnIA peptides, PnIB peptides, and MII peptides, and analogs of any of the foregoing.

b) C^1-C^6, C^2-C^4 and C^3-C^5 disulfide bonding in which, as described above, C^1, C^2, C^3, C^4, C^5 and C^6 represent the order of cysteine residues appearing in the primary sequence of the toxin peptide stated conventionally with the N-terminus of the peptide(s) on the left, with the first and sixth cysteines in the amino acid sequence forming a disulfide bond, the second and fourth cysteines forming a disulfide bond, and the third and fifth cysteines forming a disulfide bond. Examples of toxin peptides with such a C^1-C^6, C^2-C^4, C^3-C^5 disulfide bonding pattern include, but are not limited to, ShK, BgK, HmK, AeKS, AsK, and DTX1, and analogs of any of the foregoing.

c) C^1-C^4, C^2-C^5 and C^3-C^6 disulfide bonding in which, as described above, C^1, C^2, C^3, C^4, C^5 and C^6 represent the order of cysteine residues appearing in the primary sequence of the toxin peptide stated conventionally with the N-terminus of the peptide(s) on the left, with the first and fourth cysteines in the amino acid sequence forming a disulfide bond, the second and fifth cysteines forming a disulfide bond, and the third and sixth cysteines forming a disulfide bond. Examples of toxin peptides with such a C^1-C^4, C^2-C^5, C^3-C^6 disulfide bonding pattern include, but are not limited to, ChTx, MgTx, OSK1, KTX1, AgTx2, Pi2, Pi3, NTX, HgTx1, BeKM1, BmKTX, P01, BmKK6, Tc32, Tc1, BmTx1, BmTX3, IbTx, P05, ScyTx, TsK, HaTx1, ProTX1, PaTX2, Ptu1, ωGVIA, ωMVIIA, and SmIIIa, and analogs of any of the foregoing.

d) C^1-C^5, C^2-C^6, C^3-C^7, and C^4-C^8 disulfide bonding in which C^1, C^2, C^3, C^4, C^5, C^6, C^7 and C^8 represent the order of cysteine residues appearing in the primary sequence of the toxin peptide stated conventionally with the N-terminus of the peptide(s) on the left, with the first and fifth cysteines in the amino acid sequence forming a disulfide bond, the second and sixth cysteines forming a disulfide bond, the third and seventh cysteines forming a disulfide bond, and the fourth and eighth cysteines forming a disulfide bond. Examples of toxin peptides with such a C^1-C^5, C^2-C^6, C^3-C^7, C^4-C^8 disulfide bonding pattern include, but are not limited to, Anuroctoxin (AnTx), Pi1, HsTx1, MTX (P12A, P20A), and Pi4 peptides, and analogs of any of the foregoing.

e) C^1-C^4, C^2-C^6, C^3-C^7, and C^5-C^8 disulfide bonding in which C^1, C^2, C^3, C^4, C^5, C^6, C^7 and C^8 represent the order of cysteine residues appearing in the primary sequence of the toxin peptide stated conventionally with the N-terminus of the peptide(s) on the left, with the first and fourth cysteines in the amino acid sequence forming a disulfide bond, the second and sixth cysteines forming a disulfide bond, the third and seventh cysteines forming a disulfide bond, and the fifth and eighth cysteines forming a disulfide bond. Examples of toxin peptides with such a C^1-C^4, C^2-C^6, C^3-C^7, C^5-C^8 disulfide bonding pattern include, but are not limited to, Chlorotoxin, Bm-12b, and, and analogs of either.

f) C^1-C^5, C^2-C^6, C^3-C^4, and C^7-C^8 disulfide bonding in which C^1, C^2, C^3, C^4, C^5, C^6, C^7 and C^8 represent the order of cysteine residues appearing in the primary sequence of the toxin peptide stated conventionally with the N-terminus of the peptide(s) on the left, with the first and fifth cysteines in the amino acid sequence forming a disulfide bond, the second and sixth cysteines forming a disulfide bond, the third and fourth cysteines forming a disulfide bond, and the seventh and eighth cysteines forming a disulfide bond. Examples of toxin peptides with such a C^1-C^5, C^2-C^6, C^3-C^4, C^7-C^8 disulfide bonding pattern include, but are not limited to, Maurotoxin peptides and analogs thereof.

The term "randomized" as used to refer to peptide sequences refers to fully random sequences (e.g., selected by phage display methods) and sequences in which one or more residues of a naturally occurring molecule is replaced by an amino acid residue not appearing in that position in the naturally occurring molecule. Exemplary methods for identifying peptide sequences include phage display, E. coli display, ribosome display, yeast-based screening, RNA-peptide screening, chemical screening, rational design, protein structural analysis, and the like.

The term "pharmacologically active" means that a substance so described is determined to have activity that affects a medical parameter (e.g., blood pressure, blood cell count, cholesterol level) or disease state (e.g., cancer, autoimmune disorders). Thus, pharmacologically active peptides comprise agonistic or mimetic and antagonistic peptides as defined below.

The terms "-mimetic peptide" and "-agonist peptide" refer to a peptide having biological activity comparable to a naturally occurring toxin peptide molecule, e.g., naturally occurring ShK toxin peptide. These terms further include peptides that indirectly mimic the activity of a naturally occurring toxin peptide molecule, such as by potentiating the effects of the naturally occurring molecule.

The term "-antagonist peptide" or "inhibitor peptide" refers to a peptide that blocks or in some way interferes with the biological activity of a receptor of interest, or has biological activity comparable to a known antagonist or inhibitor of a receptor of interest (such as, but not limited to, an ion channel).

The term "acidic residue" refers to amino acid residues in D- or L-form having sidechains comprising acidic groups. Exemplary acidic residues include D and E.

The term "amide residue" refers to amino acids in D- or L-form having sidechains comprising amide derivatives of acidic groups. Exemplary residues include N and Q.

The term "aromatic residue" refers to amino acid residues in D- or L-form having sidechains comprising aromatic groups. Exemplary aromatic residues include F, Y, and W.

The term "basic residue" refers to amino acid residues in D- or L-form having sidechains comprising basic groups. Exemplary basic residues include H, K, R, N-methyl-arginine, ω-aminoarginine, ω-methyl-arginine, 1-methyl-histidine, 3-methyl-histidine, and homoarginine (hR) residues.

The term "hydrophilic residue" refers to amino acid residues in D- or L-form having sidechains comprising polar groups. Exemplary hydrophilic residues include C, S, T, N, Q, D, E, K, and citrulline (Cit) residues.

The term "nonfunctional residue" refers to amino acid residues in D- or L-form having sidechains that lack acidic, basic, or aromatic groups. Exemplary nonfunctional amino acid residues include M, G, A, V, I, L and norleucine (Nle).

The term "neutral polar residue" refers to amino acid residues in D- or L-form having sidechains that lack basic, acidic, or polar groups. Exemplary neutral polar amino acid residues include A, V, L, I, P, W, M, and F.

The term "polar hydrophobic residue" refers to amino acid residues in D- or L-form having sidechains comprising polar groups. Exemplary polar hydrophobic amino acid residues include T, G, S, Y, C, Q, and N.

The term "hydrophobic residue" refers to amino acid residues in D- or L-form having sidechains that lack basic or acidic groups. Exemplary hydrophobic amino acid residues include A, V, L, I, P, W, M, F, T, G, S, Y, C, Q, and N.

In some useful embodiments of the compositions of the invention, the amino acid sequence of the toxin peptide is modified in one or more ways relative to a native toxin peptide sequence of interest, such as, but not limited to, a native ShK or OSK1 sequence, their peptide analogs, or any other toxin peptides having amino acid sequences as set for in any of Tables 1-32.

The one or more useful modifications can include amino acid additions or insertions, amino acid deletions, peptide truncations, amino acid substitutions, and/or chemical derivatization of amino acid residues, accomplished by known chemical techniques. Such modifications can be, for example, for the purpose of enhanced potency, selectivity, and/or proteolytic stability, or the like. Those skilled in the art are aware of techniques for designing peptide analogs with such enhanced properties, such as alanine scanning, rational design based on alignment mediated mutagenesis using known toxin peptide sequences and/or molecular modeling. For example, ShK analogs can be designed to remove protease cleavage sites (e.g., trypsin cleavage sites at K or R residues and/or chymotrypsin cleavage sites at F, Y, or W residues) in a ShK peptide- or ShK analog-containing composition of the invention, based partially on alignment mediated mutagenesis using HmK (see, e.g., Figure 6) and molecular modeling. (See, e.g., Kalman et al., ShK-Dap22, a potent Kv1.3-specific immunosuppressive polypeptide, J. Biol. Chem. 273(49):32697-707 (1998); Kem et al., US Patent No. 6,077,680; Mouhat *et al.*, *OsK1 derivatives*, WO 2006/002850 A2)).

The term "protease" is synonymous with "peptidase". Proteases comprise two groups of enzymes: the endopeptidases which cleave peptide bonds at points within the protein, and the exopeptidases, which remove one or more amino acids from either N- or C-terminus respectively. The term "proteinase" is also used as a synonym for endopeptidase. The four mechanistic classes of proteinases are: serine proteinases, cysteine proteinases, aspartic proteinases, and metallo-proteinases. In addition to these four mechanistic classes, there is a section of the enzyme nomenclature which is allocated for proteases of unidentified catalytic mechanism. This indicates that the catalytic mechanism has not been identified.

Cleavage subsite nomenclature is commonly adopted from a scheme created by Schechter and Berger (Schechter I. & Berger A., On the size of the active site in proteases. I. Papain, Biochemical and Biophysical Research Communication, 27:157 (1967); Schechter I. & Berger A., On the active site of proteases. 3. Mapping the active site of papain; specific inhibitor peptides of papain, Biochemical and Biophysical Research Communication, 32:898 (1968)). According to this model, amino acid residues in a substrate undergoing cleavage are designated P1,P2, P3, P4 etc. in the N-terminal direction from the cleaved bond. Likewise, the residues in the C-terminal direction are designated P1', P2', P3', P4'. etc.

The skilled artisan is aware of a variety of tools for identifying protease binding or protease cleavage sites of interest. For example, the PeptideCutter software tool is available through the ExPASy (Expert Protein Analysis System) proteomics server of the Swiss Institute of Bioinformatics (SIB; www.expasy.org/tools/peptidecutter). PeptideCutter searches a protein

sequence from the SWISS-PROT and/or TrEMBL databases or a user-entered protein sequence for protease cleavage sites. Single proteases and chemicals, a selection or the whole list of proteases and chemicals can be used. Different forms of output of the results are available: tables of cleavage sites either grouped alphabetically according to enzyme names or sequentially according to the amino acid number. A third option for output is a map of cleavage sites. The sequence and the cleavage sites mapped onto it are grouped in blocks, the size of which can be chosen by the user. Other tools are also known for determining protease cleavage sites. (E.g., Turk, B. et al., Determination of protease cleavage site motifs using mixture-based oriented peptide libraries, Nature Biotechnology, 19:661-667 (2001); Barrett A. et al., Handbook of proteolytic enzymes, Academic Press (1998)).

The serine proteinases include the chymotrypsin family, which includes mammalian protease enzymes such as chymotrypsin, trypsin or elastase or kallikrein. The serine proteinases exhibit different substrate specificities, which are related to amino acid substitutions in the various enzyme subsites interacting with the substrate residues. Some enzymes have an extended interaction site with the substrate whereas others have a specificity restricted to the P1 substrate residue.

Trypsin preferentially cleaves at R or K in position P1. A statistical study carried out by Keil (1992) described the negative influences of residues surrounding the Arg- and Lys- bonds (i.e. the positions P2 and P1', respectively) during trypsin cleavage. (Keil, B., Specificity of proteolysis, Springer-Verlag Berlin-Heidelberg-NewYork, 335 (1992)). A proline residue in position P1' normally exerts a strong negative influence on trypsin cleavage. Similarly, the positioning of R and K in P1' results in an inhibition, as well as negatively charged residues in positions P2 and P1'.

Chymotrypsin preferentially cleaves at a W, Y or F in position P1 (high specificity) and to a lesser extent at L, M or H residue in position P1. (Keil, 1992). Exceptions to these rules are the following: When W is found in position P1, the cleavage is blocked when M or P are found in position P1' at the same time. Furthermore, a proline residue in position P1' nearly fully blocks the cleavage independent of the amino acids found in position P1. When an M residue is found in position P1, the cleavage is blocked by the presence of a Y residue in position P1'. Finally, when H is located in position P1, the presence of a D, M or W residue also blocks the cleavage.

Membrane metallo-endopeptidase (NEP; neutral endopeptidase, kidney-brush-border neutral proteinase, enkephalinase, EC 3.4.24.11) cleaves peptides at the amino side of hydrophobic amino acid residues. (Connelly, JC et al., Neutral Endopeptidase 24.11 in Human Neutrophils: Cleavage of Chemotactic Peptide, PNAS, 82(24):8737-8741 (1985)).

Thrombin preferentially cleaves at an R residue in position P1. (Keil, 1992). The natural substrate of thrombin is fibrinogen. Optimum cleavage sites are when an R residue is in position P1 and Gly is in position P2 and position P1'. Likewise, when hydrophobic amino acid residues are found in position P4 and position P3, a proline residue in position P2, an R residue in position P1, and non-acidic amino acid residues in position P1' and position P2'. A very important residue for its natural substrate fibrinogen is a D residue in P10.

Caspases are a family of cysteine proteases bearing an active site with a conserved amino acid sequence and which cleave peptides specifically following D residues. (Earnshaw WC et al., Mammalian caspases: Structure, activation, substrates, and functions during apoptosis, Annual Review of Biochemistry, 68:383-424 (1999)).

The Arg-C proteinase preferentially cleaves at an R residue in position P1. The cleavage behavior seems to be only moderately affected by residues in position P1'. (Keil, 1992). The Asp-N endopeptidase cleaves specifically bonds with a D residue in position P1'. (Keil, 1992).

The foregoing is merely exemplary and by no means an exhaustive treatment of knowledge available to the skilled artisan concerning protease binding and/or cleavage sites that the skilled artisan may be interested in eliminating in practicing the invention.

In other examples, a toxin peptide amino acid sequence modified from a naturally occurring toxin peptide amino acid sequence includes at least one amino acid residue inserted or substituted therein, relative to the amino acid sequence of the native toxin peptide sequence of interest, in which the inserted or substituted amino acid residue has a side chain comprising a nucleophilic or electrophilic reactive functional group by which the peptide is conjugated to a linker or half-life extending moiety. In accordance with the invention, useful examples of such a nucleophilic or electrophilic reactive functional group include, but are not limited to, a thiol, a primary amine, a seleno, a hydrazide, an aldehyde, a carboxylic acid, a ketone, an aminooxy, a masked (protected) aldehyde, or a masked (protected) keto functional group. Examples of amino acid residues having a side chain comprising a nucleophilic reactive functional group include, but are not limited to, a lysine residue, an α,β-diaminopropionic acid residue, an α,γ-diaminobutyric acid residue, an ornithine residue, a cysteine, a homocysteine, a glutamic acid residue, an aspartic acid residue, or a selenocysteine residue.

In further describing toxin peptides herein, a one-letter abbreviation system is frequently applied to designate the identities of the twenty "canonical" amino acid residues generally incorporated into naturally occurring peptides and proteins (Table 1A). Such one-letter abbreviations are entirely interchangeable in meaning with three-letter abbreviations, or non-

abbreviated amino acid names. Within the one-letter abbreviation system used herein, an uppercase letter indicates a L-amino acid, and a lower case letter indicates a D-amino acid, unless otherwise noted herein. For example, the abbreviation "R" designates L-arginine and the abbreviation "r" designates D-arginine.

Table 1A. One-letter abbreviations for the canonical amino acids. Three-letter abbreviations are in parentheses.

Alanine (Ala)	A
Glutamine (Gln)	Q
Leucine (Leu)	L
Serine (Ser)	S
Arginine (Arg)	R
Glutamic Acid (Glu)	E
Lysine (Lys)	K
Threonine (Thr)	T
Asparagine (Asn)	N
Glycine (Gly)	G
Methionine (Met)	M
Tryptophan (Trp)	W
Aspartic Acid (Asp)	D
Histidine (His)	H
Phenylalanine (Phe)	F
Tyrosine (Tyr)	Y
Cysteine (Cys)	C
Isoleucine (Ile)	I
Proline (Pro)	P
Valine (Val)	V

An amino acid substitution in an amino acid sequence is typically designated herein with a one-letter abbreviation for the amino acid residue in a particular position, followed by the numerical amino acid position relative to the native toxin peptide sequence of interest, which is then followed by the one-letter symbol for the amino acid residue substituted in. For example, "T30D" symbolizes a substitution of a threonine residue by an aspartate residue at amino acid position 30, relative to a hypothetical native toxin peptide sequence. By way of further example, "R18hR" or "R18Cit" indicates a substitution of an arginine residue by a homoarginine or a citrulline residue, respectively, at amino acid position 18, relative to the hypothetical native toxin peptide. An amino acid position within the amino acid sequence of any particular toxin peptide (or peptide analog) described herein may differ from its position relative to the native sequence, i.e., as determined in an alignment of the N-terminal or C-terminal end of the peptide's amino acid sequence with the N-terminal or C-terminal end, as appropriate, of the native toxin peptide sequence. For example, amino acid position 1 of the sequence SCIDTIPKSRCTAFQCKHSMKYRLSFCRKTCGTC (ShK(2-

35); SEQ ID NO:92), a N-terminal truncation of the native ShK sequence, thus aligned with the C-terminal of native ShK(1-35) (SEQ ID NO:5), corresponds to amino acid position 2 relative to the native sequence, and amino acid position 34 of SEQ ID NO:92 corresponds to amino acid position 35 relative to the native sequence (SEQ ID NO:5).

In certain embodiments of the present invention, amino acid substitutions encompass, non-canonical amino acid residues, which can include naturally rare (in peptides or proteins) amino acid residues or unnatural amino acid residues. Non-canonical amino acid residues can be incorporated into the peptide by chemical peptide synthesis rather than by synthesis in biological systems, such as recombinantly expressing cells, or alternatively the skilled artisan can employ known techniques of protein engineering that use recombinantly expressing cells. (See, e.g., Link et al., Non-canonical amino acids in protein engineering, Current Opinion in Biotechnology, 14(6):603-609 (2003)). The term "non-canonical amino acid residue" refers to amino acid residues in D- or L-form that are not among the 20 canonical amino acids generally incorporated into naturally occurring proteins, for example, β-amino acids, homoamino acids, cyclic amino acids and amino acids with derivatized side chains. Examples include (in the L-form or D-form): citrulline (Cit), homocitrulline (hCit), *N*-methylcitrulline (NMeCit), *N*-methylhomocitrulline (NMeHoCit), ornithine (Orn or O), *N*-Methylornithine (NMeOrn), sarcosine (Sar), homolysine (hK or Hlys), homoarginine (hR or hArg), homoglutamine (hQ), *N*-methylarginine (NMeR), *N*-methylleucine (NMeL), *N*-methylhomolysine (NMeHoK), *N*-methylglutamine (NMeQ), norleucine (Nle), norvaline (Nva), 1,2,3,4-tetrahydroisoquinoline (Tic), nitrophenylalanine (nitrophe), aminophenylalanine (aminophe), benzylphenyalanine (benzylphe), γ-carboxyglutamic acid (γ-carboxyglu), hydroxyproline (hydroxypro), *p*-carboxyl-phenylalanine (Cpa), α-aminoadipic acid (Aad), acetylarginine (acetylarg), α, β-diaminopropionoic acid (Dpr), α, γ-diaminobutyric acid (Dab), diaminopropionic acid (Dap), β-(1-Naphthyl)-alanine (1Na1), β-(2-Naphthyl)-alanine (2Na1), cyclohexylalanine (Cha), 4-methyl-phenylalanine (MePhe), β, β-diphenyl-alanine (BiPhA), aminobutyric acid (Abu), 4-phenyl-phenylalanine (4Bip), α-amino-isobutyric acid (Aib), and derivatized forms of any of these as described herein. Nomenclature and Symbolism for Amino Acids and Peptides by the UPAC-IUB Joint Commission on Biochemical Nomenclature (JCBN) have been published in the following documents: Biochem. J., 1984, 219, 345-373; Eur. J. Biochem., 1984, 138, 9-37; 1985, 152, 1; 1993, 213, 2; Internat. J. Pept. Prot. Res., 1984, 24, following p 84; J. Biol. Chem., 1985, 260,14-42; Pure Appl. Chem., 1984, 56, 595-624; Amino Acids and Peptides, 1985, 16, 387-410; Biochemical Nomenclature and Related Documents, 2nd edition, Portland Press, 1992, pages 39-69].

As stated herein, in accordance with the present invention, peptide portions of the inventive compositions, such as the toxin peptide or a peptide linker, can also be chemically derivatized at one or more amino acid residues. Peptides that contain derivatized amino acid residues can be synthesized by known organic chemistry techniques. "Chemical derivative" or "chemically derivatized" in the context of a peptide refers to a subject peptide having one or more residues chemically derivatized by reaction of a functional side group. Such derivatized molecules include, for example, those molecules in which free amino groups have been derivatized to form amine hydrochlorides, p-toluene sulfonyl groups, carbobenzoxy groups, t-butyloxycarbonyl groups, chloroacetyl groups or formyl groups. Free carboxyl groups may be derivatized to form salts, methyl and ethyl esters or other types of esters or hydrazides. Free hydroxyl groups may be derivatized to form O-acyl or O-alkyl derivatives. The imidazole nitrogen of histidine may be derivatized to form N-im-benzylhistidine. Also included as chemical derivatives are those peptides which contain one or more naturally occurring amino acid derivatives of the twenty canonical amino acids, whether in L- or D- form. For example, 4-hydroxyproline may be substituted for proline; 5-hydroxylysine maybe substituted for lysine; 3-methylhistidine may be substituted for histidine; homoserine may be substituted for serine; and ornithine may be substituted for lysine.

In some embodiments of the present invention, basic residues (e.g., lysine) of the toxin peptide of interest can be replaced with other residues (nonfunctional residues preferred). Such molecules will be less basic than the molecules from which they are derived and otherwise retain the activity of the molecules from which they are derived, which can result in advantages in stability and immunogenicity; the present invention should not, however, be limited by this theory.

Additionally, physiologically acceptable salts of the inventive compositions are also encompassed, including when the inventive compositons are referred to herein as "molecules" or "compounds.". By "physiologically acceptable salts" is meant any salts that are known or later discovered to be pharmaceutically acceptable. Some examples are: acetate; trifluoroacetate; hydrohalides, such as hydrochloride and hydrobromide; sulfate; citrate; maleate; tartrate; glycolate; gluconate; succinate; mesylate; besylate; and oxalate salts.

Structure of compounds:

In general. Recombinant proteins have been developed as therapeutic agents through, among other means, covalent attachment to half-life extending moieties. Such moieties include the "Fc" domain of an antibody, as is used in Enbrel® (etanercept) , as well as biologically suitable polymers (e.g., polyethylene glycol, or "PEG"), as is used in Neulasta® (pegfilgrastim). Feige *et al.*

described the use of such half-life extenders with peptides in U.S. Pat. No. 6,660,843, issued December 9, 2003 (hereby incorporated by reference in its entirety).

The present inventors have determined that molecules of this invention—peptides of about 80 amino acids or less with at least two intrapeptide disulfide bonds—possess therapeutic advantages when covalently attached to half-life extending moieties. Molecules of the present invention can further comprise an additional pharmacologically active, covalently bound peptide, which can be bound to the half-life extending moiety ($F^1$and/or F^2) or to the peptide portion (P). Embodiments of the inventive compositions containing more than one half-life extending moiety (F^1 and F^2) include those in which F^1 and F^2 are the same or different half-life extending moieties. Examples (with or without a linker between each domain) include structures as illustrated in Figure 75 as well as the following embodiments (and others described herein and in the working Examples):

20KPEG – toxin peptide – Fc domain, consistent with the formula $[(F^1)_1\text{-}(X^2)_1\text{-}(F^2)_1]$;

20KPEG – toxin peptide - Fc CH2 domain, consistent with the formula $[(F^1)_1\text{-}(X^2)_1\text{-}(F^2)_1]$;

20KPEG – toxin peptide – HSA, consistent with the formula $[(F^1)_1\text{-}(X^2)_1\text{-}(F^2)_1]$;

20KPEG - Fc domain– toxin peptide, consistent with the formula $[(F^1)_1\text{-}(F^2)_1\text{-}(X^3)_1]$;

20KPEG – Fc CH2 domain– toxin peptide, consistent with the formula $[(F^1)_1\text{-}(F^2)_1\text{-}(X^3)_1]$;

and

20KPEG - HSA – toxin peptide, consistent with the formula $[(F^1)_1\text{-}(F^2)_1\text{-}(X^3)_1]$.

Toxin peptides. Any number of toxin peptides (i.e., "P", or equivalently shown as "P^1" in Figure 2) can be used in conjunction with the present invention. Of particular interest are the toxin peptides ShK, HmK, MgTx, AgTx2, OsK1 (also referred to as "OSK1"), Agatoxins, and HsTx1, as well as modified analogs of these, and other peptides that mimic the activity of such toxin peptides. As stated herein above, if more than one toxin peptide "P" is present in the inventive composition, "P" can be independently the same or different from any other toxin peptide(s) also present in the inventive composition. For example, in a composition having the formula $P\text{-}(L)_g\text{-}F^1\text{-}(L)_f\text{-}P$, both of the toxin peptides, "P", can be the same peptide analog of ShK, different peptide analogs of ShK, or one can be a peptide analog of ShK and the other a peptide analog of OSK1.

In some embodiments of the invention, other peptides of interest are especially useful in molecules having additional features over the molecules of structural Formula I. In such molecules, the molecule of Formula I further comprises an additional pharmacologically active, covalently bound peptide, which is an agonistic peptide, an antagonistic peptide, or a targeting

peptide; this peptide can be conjugated to F^1 or F^2 or P. Such agonistic peptides have activity agonistic to the toxin peptide but are not required to exert such activity by the same mechanism as the toxin peptide. Peptide antagonists are also useful in embodiments of the invention, with a preference for those with activity that can be complementary to the activity of the toxin peptide. Targeting peptides are also of interest, such as peptides that direct the molecule to particular cell types, organs, and the like. These classes of peptides can be discovered by methods described in the references cited in this specification and other references. Phage display, in particular, is useful in generating toxin peptides for use in the present invention. Affinity selection from libraries of random peptides can be used to identify peptide ligands for any site of any gene product. Dedman et al. (1993), J. Biol. Chem. 268: 23025-30. Phage display is particularly well suited for identifying peptides that bind to such proteins of interest as cell surface receptors or any proteins having linear epitopes. Wilson et al. (1998), Can. J. Microbiol. 44: 313-29; Kay et al. (1998), Drug Disc. Today 3: 370-8. Such proteins are extensively reviewed in Herz et al. (1997), J. Receptor and Signal Transduction Res. 17(5): 671-776, which is hereby incorporated by reference in its entirety. Such proteins of interest are preferred for use in this invention.

Particularly preferred peptides appear in the following tables. These peptides can be prepared by methods disclosed in the art or as described hereinafter. Single letter amino acid abbreviations are used. Unless otherwise specified, each X is independently a nonfunctional residue.

Table 1—Kv1.3 inhibitor peptide sequences

Sequence/structure	Short-hand designation	SEQ ID NO:
LVKCRGTSDCGRPCQQQTGCPNSKCINRMCKCYGC	Pi1	21
TISCTNPKQCYPHCKKETGYPNAKCMNRKCKCFGR	Pi2	17
TISCTNEKQCYPHCKKETGYPNAKCMNRKCKCFGR	Pi3	18
IEAIRCGGSRDCYRPCQKRTGCPNAKCINKTCKCYGCS	Pi4	19
ASCRTPKDCADPCRKETGCPYGKCMNRKCKCNRC	HsTx1	61
GVPINVSCTGSPQCIKPCKDAGMRFGKCMNRKCHCTPK	AgTx2	23
GVPINVKCTGSPQCLKPCKDAGMRFGKCINGKCHCTPK	AgTx1	85
GVIINVKCKISRQCLEPCKKAGMRFGKCMNGKCHCTPK	OSK1	25
ZKECTGPQHCTNFCRKNKCTHGKCMNRKCKCFNCK	Anuroctoxin	62
TIINVKCTSPKQCSKPCKELYGSSAGAKCMNGKCKCYNN	NTX	30
TVIDVKCTSPKQCLPPCKAQFGIRAGAKCMNGKCKCYPH	HgTx1	27
QFTNVSCTTSKECWSVCQRLHNTSRGKCMNKKCRCYS	ChTx	36
VFINAKCRGSPECLPKCKEAIGKAAGKCMNGKCKCYP	Titystoxin-Ka	86
VCRDWFKETACRHAKSLGNCRTSQKYRANCAKTCELC	BgK	9
VGINVKCKHSGQCLKPCKDAGMRFGKCINGKCDCTPKG	BmKTX	26
QFTDVKCTGSKQCWPVCKQMFGKPNGKCMNGKCRCYS	BmTx1	40
VFINVKCRGSKECLPACKAAVGKAAGKCMNGKCKCYP	Tc30	87
TGPQTTCQAAMCEAGCKGLGKSMESCQGDTCKCKA	Tc32	13

Table 2—ShK peptide and ShK peptide analog sequences

Sequence/structure	Short-hand designation	SEQ ID NO:
RSCIDTIPKSRCTAFQCKHSMKYRLSFCRKTCGTC	ShK	5
RSCIDTIPKSRCTAFQSKHSMKYRLSFCRKTSGTC	ShK-S17/S32	88
RSSIDTIPKSRCTAFQCKHSMKYRLSFCRKTCGTS	ShK-S3/S35	89
SSCIDTIPKSRCTAFQCKHSMKYRLSFCRKTCGTC	ShK-S1	90
(N-acetylarg) SCIDTIPKSRCTAFQCKHSMKYRLSFCRKTCGTC	ShK-N-acetylarg1	91
SCIDTIPKSRCTAFQCKHSMKYRLSFCRKTCGTC	ShK-d1	92
CIDTIPKSRCTAFQCKHSMKYRLSFCRKTCGTC	ShK-d2	93
ASCIDTIPKSRCTAFQCKHSMKYRLSFCRKTCGTC	ShK-A1	94
RSCADTIPKSRCTAFQCKHSMKYRLSFCRKTCGTC	ShK-A4	95
RSCADTIPKSRCTAAQCKHSMKYRLSFCRKTCGTC	ShK-A4/A15	96
RSCADTIPKSRCTAAQCKHSMKYRASFCRKTCGTC	ShK-A4/A15/A25	97
RSCIDAIPKSRCTAFQCKHSMKYRLSFCRKTCGTC	ShK-A6	98
RSCIDTAPKSRCTAFQCKHSMKYRLSFCRKTCGTC	ShK-A7	99
RSCIDTIAKSRCTAFQCKHSMKYRLSFCRKTCGTC	ShK-A8	100
RSCIDTIPASRCTAFQCKHSMKYRLSFCRKTCGTC	ShK-A9	101
RSCIDTIPESRCTAFQCKHSMKYRLSFCRKTCGTC	ShK-E9	102
RSCIDTIPQSRCTAFQCKHSMKYRLSFCRKTCGTC	ShK-Q9	103
RSCIDTIPKARCTAFQCKHSMKYRLSFCRKTCGTC	ShK-A10	104
RSCIDTIPKSACTAFQCKHSMKYRLSFCRKTCGTC	ShK-A11	105
RSCIDTIPKSECTAFQCKHSMKYRLSFCRKTCGTC	ShK-E11	106
RSCIDTIPKSQCTAFQCKHSMKYRLSFCRKTCGTC	ShK-Q11	107
RSCIDTIPKSRCAAFQCKHSMKYRLSFCRKTCGTC	ShK-A13	108
RSCIDTIPKSRCTAAQCKHSMKYRLSFCRKTCGTC	ShK-A15	109
RSCIDTIPKSRCTAWQCKHSMKYRLSFCRKTCGTC	ShK-W15	110
RSCIDTIPKSRCTAX^{813}QCKHSMKYRLSFCRKTCGTC	ShK-X15	111
RSCIDTIPKSRCTAAQCKHSMKYRASFCRKTCGTC	ShK-A15/A25	112
RSCIDTIPKSRCTAFACKHSMKYRLSFCRKTCGTC	ShK-A16	113
RSCIDTIPKSRCTAFECKHSMKYRLSFCRKTCGTC	ShK-E16	114
RSCIDTIPKSRCTAFQCAHSMKYRLSFCRKTCGTC	ShK-A18	115
RSCIDTIPKSRCTAFQCEHSMKYRLSFCRKTCGTC	ShK-E18	116
RSCIDTIPKSRCTAFQCKASMKYRLSFCRKTCGTC	ShK-A19	117
RSCIDTIPKSRCTAFQCKKSMKYRLSFCRKTCGTC	ShK-K19	118
RSCIDTIPKSRCTAFQCKHAMKYRLSFCRKTCGTC	ShK-A20	119
RSCIDTIPKSRCTAFQCKHSAKYRLSFCRKTCGTC	ShK-A21	120
RSCIDTIPKSRCTAFQCKHSX^{821}KYRLSFCRKTCGTC	ShK-X21	121
RSCIDTIPKSRCTAFQCKHS(norleu)KYRLSFCRKTCGTC	ShK-Nle21	122
RSCIDTIPKSRCTAFQCKHSMAYRLSFCRKTCGTC	ShK-A22	123
RSCIDTIPKSRCTAFQCKHSMEYRLSFCRKTCGTC	ShK-E22	124
RSCIDTIPKSRCTAFQCKHSMRYRLSFCRKTCGTC	ShK-R22	125
RSCIDTIPKSRCTAFQCKHSMX^{822}YRLSFCRKTCGTC	ShK-X22	126
RSCIDTIPKSRCTAFQCKHSM(norleu)YRLSFCRKTCGTC	ShK- Nle22	127
RSCIDTIPKSRCTAFQCKHSM(orn)YRLSFCRKTCGTC	ShK- Orn22	128
RSCIDTIPKSRCTAFQCKHSM(homocit)YRLSFCRKTCGTC	ShK- Homocit22	129
RSCIDTIPKSRCTAFQCKHSM(diaminopropionic)YRLS FCRKTCGTC	ShK- Diamino-propionic22	130
RSCIDTIPKSRCTAFQCKHSMKARLSFCRKTCGTC	ShK-A23	131
RSCIDTIPKSRCTAFQCKHSMKSRLSFCRKTCGTC	ShK-S23	132

RSCIDTIPKSRCTAFQCKHSMKFRLSFCRKTCGTC	ShK-F23	133
RSCIDTIPKSRCTAFQCKHSMKX[823]RLSFCRKTCGTC	ShK-X23	134
RSCIDTIPKSRCTAFQCKHSMK(nitrophe)RLSFCRKTCGTC	ShK-Nitrophe23	135
RSCIDTIPKSRCTAFQCKHSMK(aminophe)RLSFCRKTCGTC	ShK-Aminophe23	136
RSCIDTIPKSRCTAFQCKHSMK(benzylphe)RLSFCRKTCGTC	ShK-Benzylphe23	137
RSCIDTIPKSRCTAFQCKHSMKYALSFCRKTCGTC	ShK-A24	138
RSCIDTIPKSRCTAFQCKHSMKYELSFCRKTCGTC	ShK-E24	139
RSCIDTIPKSRCTAFQCKHSMKYRASFCRKTCGTC	ShK-A25	140
RSCIDTIPKSRCTAFQCKHSMKYRLAFCRKTCGTC	ShK-A26	141
RSCIDTIPKSRCTAFQCKHSMKYRLSACRKTCGTC	ShK-A27	142
RSCIDTIPKSRCTAFQCKHSMKYRLSX[827]CRKTCGTC	ShK-X27	143
RSCIDTIPKSRCTAFQCKHSMKYRLSFCAKTCGTC	ShK-A29	144
RSCIDTIPKSRCTAFQCKHSMKYRLSFCRATCGTC	ShK-A30	145
RSCIDTIPKSRCTAFQCKHSMKYRLSFCRKACGTC	ShK-A31	146
RSCIDTIPKSRCTAFQCKHSMKYRLSFCRKTCGAC	ShK-A34	147
SCADTIPKSRCTAFQCKHSMKYRLSFCRKTCGTC	ShK-A4d1	148
SCADTIPKSRCTAAQCKHSMKYRLSFCRKTCGTC	ShK-A4/A15d1	149
SCADTIPKSRCTAAQCKHSMKYRASFCRKTCGTC	ShK-A4/A15/A25 d1	150
SCIDAIPKSRCTAFQCKHSMKYRLSFCRKTCGTC	ShK-A6 d1	151
SCIDTAPKSRCTAFQCKHSMKYRLSFCRKTCGTC	ShK-A7 d1	152
SCIDTIAKSRCTAFQCKHSMKYRLSFCRKTCGTC	ShK-A8 d1	153
SCIDTIPASRCTAFQCKHSMKYRLSFCRKTCGTC	ShK-A9 d1	154
SCIDTIPESRCTAFQCKHSMKYRLSFCRKTCGTC	ShK-E9 d1	155
SCIDTIPQSRCTAFQCKHSMKYRLSFCRKTCGTC	ShK-Q9 d1	156
SCIDTIPKARCTAFQCKHSMKYRLSFCRKTCGTC	ShK-A10 d1	157
SCIDTIPKSACTAFQCKHSMKYRLSFCRKTCGTC	ShK-A11 d1	158
SCIDTIPKSECTAFQCKHSMKYRLSFCRKTCGTC	ShK-E11 d1	159
SCIDTIPKSQCTAFQCKHSMKYRLSFCRKTCGTC	ShK-Q11 d1	160
SCIDTIPKSRCAAFQCKHSMKYRLSFCRKTCGTC	ShK-A13 d1	161
SCIDTIPKSRCTAAQCKHSMKYRLSFCRKTCGTC	ShK-A15 d1	162
SCIDTIPKSRCTAWQCKHSMKYRLSFCRKTCGTC	ShK-W15 d1	163
SCIDTIPKSRCTAX[815]QCKHSMKYRLSFCRKTCGTC	ShK-X15 d1	164
SCIDTIPKSRCTAAQCKHSMKYRASFCRKTCGTC	ShK-A15/A25 d1	165
SCIDTIPKSRCTAFACKHSMKYRLSFCRKTCGTC	ShK-A16 d1	166
SCIDTIPKSRCTAFECKHSMKYRLSFCRKTCGTC	ShK-E16 d1	167
SCIDTIPKSRCTAFQCAHSMKYRLSFCRKTCGTC	ShK-A18 d1	168
SCIDTIPKSRCTAFQCEHSMKYRLSFCRKTCGTC	ShK-E18 d1	169
SCIDTIPKSRCTAFQCKASMKYRLSFCRKTCGTC	ShK-A19 d1	170
SCIDTIPKSRCTAFQCKKSMKYRLSFCRKTCGTC	ShK-K19 d1	171
SCIDTIPKSRCTAFQCKHAMKYRLSFCRKTCGTC	ShK-A20 d1	172
SCIDTIPKSRCTAFQCKHSAKYRLSFCRKTCGTC	ShK-A21 d1	173
SCIDTIPKSRCTAFQCKHSX[821]KYRLSFCRKTCGTC	ShK-X21 d1	174
SCIDTIPKSRCTAFQCKHS(norleu)KYRLSFCRKTCGTC	ShK-Nle21 d1	175
SCIDTIPKSRCTAFQCKHSMAYRLSFCRKTCGTC	ShK-A22 d1	176
SCIDTIPKSRCTAFQCKHSMEYRLSFCRKTCGTC	ShK-E22 d1	177
SCIDTIPKSRCTAFQCKHSMRYRLSFCRKTCGTC	ShK-R22 d1	178
SCIDTIPKSRCTAFQCKHSMX[822]YRLSFCRKTCGTC	ShK-X22 d1	179
SCIDTIPKSRCTAFQCKHSM(norleu)YRLSFCRKTCGTC	ShK- Nle22 d1	180

SCIDTIPKSRCTAFQCKHSM(orn)YRLSFCRKTCGTC	ShK- Orn22 d1	181
SCIDTIPKSRCTAFQCKHSM(homocit)YRLSFCRKTCGTC	ShK- Homocit22 d1	182
SCIDTIPKSRCTAFQCKHSM(diaminopropionic)YRLSFCRKTCGTC	ShK- Diamino-propionic22 d1	183
SCIDTIPKSRCTAFQCKHSMKARLSFCRKTCGTC	ShK-A23 d1	184
SCIDTIPKSRCTAFQCKHSMKSRLSFCRKTCGTC	ShK-S23 d1	185
SCIDTIPKSRCTAFQCKHSMKFRLSFCRKTCGTC	ShK-F23 d1	186
SCIDTIPKSRCTAFQCKHSMKX^{823}RLSFCRKTCGTC	ShK-X23 d1	187
SCIDTIPKSRCTAFQCKHSMK(nitrophe)RLSFCRKTCGTC	ShK-Nitrophe23 d1	188
SCIDTIPKSRCTAFQCKHSMK(aminophe)RLSFCRKTCGTC	ShK-Aminophe23 d1	189
SCIDTIPKSRCTAFQCKHSMK(benzylphe)RLSFCRKTCGTC	ShK-Benzylphe23 d1	190
SCIDTIPKSRCTAFQCKHSMKYALSFCRKTCGTC	ShK-A24 d1	191
SCIDTIPKSRCTAFQCKHSMKYELSFCRKTCGTC	ShK-E24 d1	192
SCIDTIPKSRCTAFQCKHSMKYRASFCRKTCGTC	ShK-A25 d1	193
SCIDTIPKSRCTAFQCKHSMKYRLAFCRKTCGTC	ShK-A26 d1	194
SCIDTIPKSRCTAFQCKHSMKYRLSACRKTCGTC	ShK-A27 d1	195
SCIDTIPKSRCTAFQCKHSMKYRLSX^{827}CRKTCGTC	ShK-X27 d1	196
SCIDTIPKSRCTAFQCKHSMKYRLSFCAKTCGTC	ShK-A29 d1	197
SCIDTIPKSRCTAFQCKHSMKYRLSFCRATCGTC	ShK-A30 d1	198
SCIDTIPKSRCTAFQCKHSMKYRLSFCRKACGTC	ShK-A31 d1	199
SCIDTIPKSRCTAFQCKHSMKYRLSFCRKTCGAC	ShK-A34 d1	200
YSCIDTIPKSRCTAFQCKHSMKYRLSFCRKTCGTC	ShK-Y1	548
KSCIDTIPKSRCTAFQCKHSMKYRLSFCRKTCGTC	ShK-K1	549
HSCIDTIPKSRCTAFQCKHSMKYRLSFCRKTCGTC	ShK-H1	550
QSCIDTIPKSRCTAFQCKHSMKYRLSFCRKTCGTC	ShK-Q1	551
PPRSCIDTIPKSRCTAFQCKHSMKYRLSFCRKTCGTC	PP-ShK	552
MRSCIDTIPKSRCTAFQCKHSMKYRLSFCRKTCGTC	M-ShK	553
GRSCIDTIPKSRCTAFQCKHSMKYRLSFCRKTCGTC	G-ShK	554
YSCIDTIPKSRCTAFQCKHSMAYRLSFCRKTCGTC	ShK-Y1/A22	555
KSCIDTIPKSRCTAFQCKHSMAYRLSFCRKTCGTC	ShK-K1/A22	556
HSCIDTIPKSRCTAFQCKHSMAYRLSFCRKTCGTC	ShK-H1/A22	557
QSCIDTIPKSRCTAFQCKHSMAYRLSFCRKTCGTC	ShK-Q1/A22	558
PPRSCIDTIPKSRCTAFQCKHSMAYRLSFCRKTCGTC	PP-ShK-A22	559
MRSCIDTIPKSRCTAFQCKHSMAYRLSFCRKTCGTC	M-ShK-A22	560
GRSCIDTIPKSRCTAFQCKHSMAYRLSFCRKTCGTC	G-ShK-A22	561
RSCIDTIPASRCTAFQCKHSMAYRLSFCRKTCGTC	ShK-A9/A22	884
SCIDTIPASRCTAFQCKHSMAYRLSFCRKTCGTC	ShK-A9/A22 d1	885
RSCIDTIPVSRCTAFQCKHSMKYRLSFCRKTCGTC	ShK-V9	886
RSCIDTIPVSRCTAFQCKHSMAYRLSFCRKTCGTC	ShK-V9/A22	887
SCIDTIPVSRCTAFQCKHSMKYRLSFCRKTCGTC	ShK-V9 d1	888
SCIDTIPVSRCTAFQCKHSMAYRLSFCRKTCGTC	ShK-V9/A22 d1	889
RSCIDTIPESRCTAFQCKHSMAYRLSFCRKTCGTC	ShK-E9/A22	890
SCIDTIPESRCTAFQCKHSMAYRLSFCRKTCGTC	ShK-E9/A22 d1	891
RSCIDTIPKSACTAFQCKHSMAYRLSFCRKTCGTC	ShK-A11/A22	892
SCIDTIPKSACTAFQCKHSMAYRLSFCRKTCGTC	ShK-A11/22 d1	893
RSCIDTIPKSECTAFQCKHSMAYRLSFCRKTCGTC	ShK-E11/A22	894
SCIDTIPKSECTAFQCKHSMAYRLSFCRKTCGTC	ShK-E11/A22 d1	895
RSCIDTIPKSRCTDFQCKHSMKYRLSFCRKTCGTC	ShK-D14	896

RSCIDTIPKSRCTDFQCKHSMAYRLSFCRKTCGTC	ShK-D14/A22	897
SCIDTIPKSRCTDFQCKHSMKYRLSFCRKTCGTC	ShK-D14 d1	898
SCIDTIPKSRCTDFQCKHSMAYRLSFCRKTCGTC	ShK-D14/A22 d1	899
RSCIDTIPKSRCTAAQCKHSMAYRLSFCRKTCGTC	ShK-A15A/22	900
SCIDTIPKSRCTAAQCKHSMAYRLSFCRKTCGTC	ShK-A15/A22 d1	901
RSCIDTIPKSRCTAIQCKHSMKYRLSFCRKTCGTC	ShK-I15	902
RSCIDTIPKSRCTAIQCKHSMAYRLSFCRKTCGTC	ShK-I15/A22	903
SCIDTIPKSRCTAIQCKHSMKYRLSFCRKTCGTC	ShK-I15 d1	904
SCIDTIPKSRCTAIQCKHSMAYRLSFCRKTCGTC	ShK-I15/A22 d1	905
RSCIDTIPKSRCTAVQCKHSMKYRLSFCRKTCGTC	ShK-V15	906
RSCIDTIPKSRCTAVQCKHSMAYRLSFCRKTCGTC	ShK-V15/A22	907
SCIDTIPKSRCTAVQCKHSMKYRLSFCRKTCGTC	ShK-V15 d1	908
SCIDTIPKSRCTAVQCKHSMAYRLSFCRKTCGTC	ShK-V15/A22 d1	909
RSCIDTIPKSRCTAFRCKHSMKYRLSFCRKTCGTC	ShK-R16	910
RSCIDTIPKSRCTAFRCKHSMAYRLSFCRKTCGTC	ShK-R16/A22	911
SCIDTIPKSRCTAFRCKHSMKYRLSFCRKTCGTC	ShK-R16 d1	912
SCIDTIPKSRCTAFRCKHSMAYRLSFCRKTCGTC	ShK-R16/A22 d1	913
RSCIDTIPKSRCTAFKCKHSMKYRLSFCRKTCGTC	ShK-K16	914
RSCIDTIPKSRCTAFKCKHSMAYRLSFCRKTCGTC	ShK-K16/A22	915
SCIDTIPKSRCTAFKCKHSMKYRLSFCRKTCGTC	ShK-K16 d1	916
SCIDTIPKSRCTAFKCKHSMAYRLSFCRKTCGTC	ShK-K16/A22 d1	917
RSCIDTIPASECTAFQCKHSMKYRLSFCRKTCGTC	ShK-A9/E11	918
RSCIDTIPASECTAFQCKHSMAYRLSFCRKTCGTC	ShK-A9/E11/A22	919
SCIDTIPASECTAFQCKHSMKYRLSFCRKTCGTC	ShK-A9/E11 d1	920
SCIDTIPASECTAFQCKHSMAYRLSFCRKTCGTC	ShK-A9/E11/A22 d1	921
RSCIDTIPVSECTAFQCKHSMKYRLSFCRKTCGTC	ShK-V9/E11	922
RSCIDTIPVSECTAFQCKHSMAYRLSFCRKTCGTC	ShK-V9/E11/A22	923
SCIDTIPVSECTAFQCKHSMKYRLSFCRKTCGTC	ShK-V9/E11 d1	924
SCIDTIPVSECTAFQCKHSMAYRLSFCRKTCGTC	ShK-V9/E11/A22 d1	925
RSCIDTIPVSACTAFQCKHSMKYRLSFCRKTCGTC	ShK-V9/A11	926
RSCIDTIPVSACTAFQCKHSMAYRLSFCRKTCGTC	ShK-V9/A11/A22	927
SCIDTIPVSACTAFQCKHSMKYRLSFCRKTCGTC	ShK-V9/A11 d1	928
SCIDTIPVSACTAFQCKHSMAYRLSFCRKTCGTC	ShK-V9/A11/A22 d1	929
RSCIDTIPASACTAFQCKHSMKYRLSFCRKTCGTC	ShK-A9/A11	930
RSCIDTIPASACTAFQCKHSMAYRLSFCRKTCGTC	ShK-A9/A11/A22	931
SCIDTIPASACTAFQCKHSMKYRLSFCRKTCGTC	ShK-A9/A11 d1	932
SCIDTIPASACTAFQCKHSMAYRLSFCRKTCGTC	ShK-A9/A11/A22 d1	933
RSCIDTIPKSECTDIRCKHSMKYRLSFCRKTCGTC	ShK-E11/D14/I15/R16	934
RSCIDTIPKSECTDIRCKHSMAYRLSFCRKTCGTC	ShK-E11/D14/I15/R16/A22	935
SCIDTIPKSECTDIRCKHSMKYRLSFCRKTCGTC	ShK-E11/D14/I15/R16 d1	936
SCIDTIPKSECTDIRCKHSMAYRLSFCRKTCGTC	ShK-E11/D14/I15//R16 A22 d1	937

RSCIDTIPVSECTDIRCKHSMKYRLSFCRKTCGTC	ShK-V9/E11/D14/I15/R16	938
RSCIDTIPVSECTDIRCKHSMAYRLSFCRKTCGTC	ShK-V9/E11/D14/I15/R16/A22	939
SCIDTIPVSECTDIRCKHSMKYRLSFCRKTCGTC	ShK-V9/E11/D14/I15/R16 d1	940
SCIDTIPVSECTDIRCKHSMAYRLSFCRKTCGTC	ShK-V9/E11/D14/I15/R16/A22 d1	941
RSCIDTIPVSECTDIQCKHSMKYRLSFCRKTCGTC	ShK-V9/E11/D14/I15	942
RSCIDTIPVSECTDIQCKHSMAYRLSFCRKTCGTC	ShK-V9/E11/D14/I15/A22	943
SCIDTIPVSECTDIQCKHSMKYRLSFCRKTCGTC	ShK-V9/E11/D14/I15 d1	944
SCIDTIPVSECTDIQCKHSMAYRLSFCRKTCGTC	ShK-V9/E11/D14/I15/A22 d1	945
RTCKDLIPVSECTDIRCKHSMKYRLSFCRKTCGTC	ShK-T2/K4/L6/V9/E11/D14/I15/R16	946
RTCKDLIPVSECTDIRCKHSMAYRLSFCRKTCGTC	ShK-T2/K4/L6/V9/E11/D14/I15/R16/A22	947
TCKDLIPVSECTDIRCKHSMKYRLSFCRKTCGTC	ShK-T2/K4/L6/V9/E11/D14/I15/R16 d1	948
TCKDLIPVSECTDIRCKHSMAYRLSFCRKTCGTC	ShK-T2/K4/L6/V9/E11/D14/I15/R16/A22 d1	949
(L-Phosphotyrosine)-AEEARSCIDTIPKSRCTAFQCKHSMKYRLSFCRKTCGTC	ShK(L5)	950
QSCADTIPKSRCTAAQCKHSMKYRLSFCRKTCGTC	ShK Q1/A4/A15	1295
QSCADTIPKSRCTAAQCKHSMAYRLSFCRKTCGTC	ShK Q1/A4/A15/A22	1296
QSCADTIPKSRCTAAQCKHSM(Dap)YRLSFCRKTCGTC	ShK Q1/A4/A15/Dap22	1297
QSCADTIPKSRCTAAQCKHSMKYRASFCRKTCGTC	ShK Q1/A4/A15/A25	1298
QSCADTIPKSRCTAAQCKHSMAYRASFCRKTCGTC	ShK Q1/A4/A15/A22/A25	1299
QSCADTIPKSRCTAAQCKHSM(Dap)YRASFCRKTCGTC	ShK Q1/A4/A15/Dap22/A25	1300

Many peptides as described in Table 2 can be prepared as described in U.S. Pat. No. 6,077,680 issued June 20, 2000 to Kem et al., which is hereby incorporated by reference in its entirety. Other peptides of Table 2 can be prepared by techniques known in the art. For example, ShK(L5) (SEQ ID NO: 950) can be prepared as described in Beeton et al., Targeting effector memory T cells with a selective peptide inhibitor of Kv1.3 channels for therapy of autoimmune diseases, Molec. Pharmacol. 67(4): 1369- 81 (2005), which is hereby incorporated by reference in its entirety. In Table 2 and throughout the specification, X^{s15}, X^{s21}, X^{s22}, X^{s23} and X^{s27} each independently refer to nonfunctional amino acid residues.

Table 3—HmK, BgK, AeK and AsKS peptide and peptide analog sequences

Sequence/structure	Short-hand designation	SEQ ID NO:
RTCKDLIPVSECTDIRCRTSMKYRLNLCRKTCGSC	HmK	6
ATCKDLIPVSECTDIRCRTSMKYRLNLCRKTCGSC	HmK-A1	201
STCKDLIPVSECTDIRCRTSMKYRLNLCRKTCGSC	HmK-S1	202
TCKDLIPVSECTDIRCRTSMKYRLNLCRKTCGSC	HmK-d1	203
SCKDLIPVSECTDIRCRTSMKYRLNLCRKTCGSC	HmK-d1/S2	204
TCIDLIPVSECTDIRCRTSMKYRLNLCRKTCGSC	HmK-d1/I4	205
TCKDTIPVSECTDIRCRTSMKYRLNLCRKTCGSC	HmK-d1/T6	206
TCKDLIPKSECTDIRCRTSMKYRLNLCRKTCGSC	HmK-d1/K9	207
TCKDLIPVSRCTDIRCRTSMKYRLNLCRKTCGSC	HmK-d1/R11	208
TCKDLIPVSECTAIRCRTSMKYRLNLCRKTCGSC	HmK-d1/A14	209
TCKDLIPVSECTDFRCRTSMKYRLNLCRKTCGSC	HmK-d1/F15	210
TCKDLIPVSECTDIQCRTSMKYRLNLCRKTCGSC	HmK-d1/Q16	211
TCKDLIPVSECTDIRCKTSMKYRLNLCRKTCGSC	HmK-d1/K18	212
TCKDLIPVSECTDIRCRHSMKYRLNLCRKTCGSC	HmK-d1/H19	213
TCKDLIPVSECTDIRCRTSMKYRLSLCRKTCGSC	HmK-d1/S26	214
TCKDLIPVSECTDIRCRTSMKYRLNFCRKTCGSC	HmK-d1/F27	215
TCKDLIPVSECTDIRCRTSMKYRLNLCRKTCGTC	HmK-d1/T34	216
TCKDLIPVSRCTDIRCRTSMKYRLNFCRKTCGSC	HmK-d1/R11/F27	217
ATCKDLIPVSRCTDIRCRTSMKYRLNFCRKTCGSC	HmK-A1/R11/F27	218
TCIDTIPKSRCTAFQCKHSMKYRLSFCRKTCGSC	HmK-d1/Z1	219
TCIDTIPKSRCTAFQCRTSMKYRLNFCRKTCGSC	HmK-d1/Z2	220
TCADLIPASRCTAIACRTSMKYRLNFCRKTCGSC	HmK-d1/Z3	221
TCADLIPASRCTAIACKHSMKYRLNFCRKTCGSC	HmK-d1/Z4	222
TCADLIPASRCTAIACAHSMKYRLNFCRKTCGSC	HmK-d1/Z5	223
RTCKDLIPVSECTDIRCRTSMX^{h22}YRLNLCRKTCGSC	HmK-X22	224
ATCKDLX^{h6}PVSRCTDIRCRTSMKX^{h22}RLNX^{h25}CRKTCGSC	HmK-X6, 22, 26	225

VCRDWFKETACRHAKSLGNCRTSQKYRANCAKTCELC	BgK	9
ACRDWFKETACRHAKSLGNCRTSQKYRANCAKTCELC	BgK-A1	226
VCADWFKETACRHAKSLGNCRTSQKYRANCAKTCELC	BgK-A3	227
VCRDAFKETACRHAKSLGNCRTSQKYRANCAKTCELC	BgK-A5	228
VCRDWFKATACRHAKSLGNCRTSQKYRANCAKTCELC	BgK-A8	229
VCRDWFKEAACRHAKSLGNCRTSQKYRANCAKTCELC	BgK-A9	230
VCRDWFKETACAHAKSLGNCRTSQKYRANCAKTCELC	BgK-A12	231
VCRDWFKETACRHAASLGNCRTSQKYRANCAKTCELC	BgK-A15	232
VCRDWFKETACRHAKALGNCRTSQKYRANCAKTCELC	BgK-A16	233
VCRDWFKETACRHAKSAGNCRTSQKYRANCAKTCELC	BgK-A17	234
VCRDWFKETACRHAKSLGNCATSQKYRANCAKTCELC	BgK-A21	235
VCRDWFKETACRHAKSLGNCRASQKYRANCAKTCELC	BgK-A22	236
VCRDWFKETACRHAKSLGNCRTSQKYAANCAKTCELC	BgK-A27	237
VCRDWFKETACRHAKSLGNCRTSQKYRANCAATCELC	BgK-A32	238
VCRDWFKETACRHAKSLGNCRTSQKYRANCAKACELC	BgK-A33	239
VCRDWFKETACRHAKSLGNCRTSQKYRANCAKTCALC	BgK-A35	240
VCRDWFKETACRHAKSLGNCRTSQKYRANCAKTCEAC	BgK-A37	241
GCKDNFSANTCKHVKANNNCGSQKYATNCAKTCGKC	AeK	7
ACKDNFAAATCKHVKENKNCGSQKYATNCAKTCGKC	AsKS	8

In Table 3 and throughout the specification, X^{h6}, X^{h22}, X^{h26} are each independently nonfunctional residues.

Table 4—MgTx peptide and MgTx peptide analog sequences

Sequence/structure	Short-hand designation	SEQ ID NO:
TIINVKCTSPKQCLPPCKAQFGQSAGAKCMNGKCKCYPH	MgTx	28
TIINVACTSPKQCLPPCKAQFGQSAGAKCMNGKCKCYPH	MgTx-A6	242
TIINVSCTSPKQCLPPCKAQFGQSAGAKCMNGKCKCYPH	MgTx-S6	243
TIINVKCTSPAQCLPPCKAQFGQSAGAKCMNGKCKCYPH	MgTx-A11	244
TIINVKCTSPKQCLPPCAAQFGQSAGAKCMNGKCKCYPH	MgTx-A18	245
TIINVKCTSPKQCLPPCKAQFGQSAGAACMNGKCKCYPH	MgTx-A28	246
TIINVKCTSPKQCLPPCKAQFGQSAGAKCMNGACKCYPH	MgTx-A33	247
TIINVKCTSPKQCLPPCKAQFGQSAGAKCMNGKCACYPH	MgTx-A35	248
TIINVKCTSPKQCLPPCKAQFGQSAGAKCMNGKCKCYPN	MgTx-H39N	249
TIINVACTSPKQCLPPCKAQFGQSAGAKCMNGKCKCYPN	MgTx-A6/H39N	250
TIINVSCTSPKQCLPPCKAQFGQSAGAKCMNGKCKCYS	MgTx-S6/38/d39	251
TIITISCTSPKQCLPPCKAQFGQSAGAKCMNGKCKCYPH	MgTx-T4/I5/S6	252
TISCTSPKQCLPPCKAQFGQSAGAKCMNGKCKCYPH	MgTx-d3/T4/I5/S6	253
TISCTSPKQCLPPCKAQFGQSAGAKCMNGKCKCFGR	MgTx-Pi2	254
NVACTSPKQCLPPCKAQFGQSAGAKCMNGKCKCYPH	MgTx-d3/A6	255
QFTNVSCTSPKQCLPPCKAQFGQSAGAKCMNGKCKCYS	MgTx-ChTx	256
QFTDVDCTSPKQCLPPCKAQFGQSAGAKCMNGKCKCYQ	MgTx-IbTx	257
IINVSCTSPKQCLPPCKAQFGQSAGAKCMNGKCKCYPH	MgTx-Z1	258

IITISCTSPKQCLPPCKAQFGQSAGAKCMNGKCKCYPH	MgTx-Z2	259
GVIINVSCTSPKQCLPPCKAQFGQSAGAKCMNGKCKCYPH	MgTx-Z3	260

Many peptides as described in Table 4 can be prepared as described in WO 95/03065, published February 2, 1995, for which the applicant is Merck & Co., Inc. That application corresponds to U.S. Ser. No. 07/096,942, filed 22 July 1993, which is hereby incorporated by reference in its entirety.

Table 5—AgTx2 peptide and AgTx2 peptide analog sequences

Sequence/structure	Short-hand designation	SEQ ID NO:
GVPINVSCTGSPQCIKPCKDAGMRFGKCMNRKCHCTPK	AgTx2	23
GVPIAVSCTGSPQCIKPCKDAGMRFGKCMNRKCHCTPK	AgTx2-A5	261
GVPINVSCTGSPQCIAPCKDAGMRFGKCMNRKCHCTPK	AgTx2-A16	262
GVPINVSCTGSPQCIKPCADAGMRFGKCMNRKCHCTPK	AgTx2-A19	263
GVPINVSCTGSPQCIKPCKDAGMAFGKCMNRKCHCTPK	AgTx2-A24	264
GVPINVSCTGSPQCIKPCKDAGMRFGACMNRKCHCTPK	AgTx2-A27	265
GVPINVSCTGSPQCIKPCKDAGMRFGKCMNAKCHCTPK	AgTx2-A31	266
GVPINVSCTGSPQCIKPCKDAGMRFGKCMNRACHCTPK	AgTx2-A32	267
GVPINVSCTGSPQCIKPCKDAGMRFGKCMNRKCHCTPA	AgTx2-A38	268
GVPIAVSCTGSPQCIKPCKDAGMRFGKCMNRKCHCTPA	AgTx2-A5/A38	269
GVPINVSCTGSPQCIKPCKDAGMRFGKCMNGKCHCTPK	AgTx2-G31	270
GVPIIVSCKGSRQCIKPCKDAGMRFGKCMNGKCHCTPK	AgTx2-OSK_z1	271
GVPIIVSCKISRQCIKPCKDAGMRFGKCMNGKCHCTPK	AgTx2-OSK_z2	272
GVPIIVKCKGSRQCIKPCKDAGMRFGKCMNGKCHCTPK	AgTx2-OSK_z3	273
GVPIIVKCKISRQCIKPCKDAGMRFGKCMNGKCHCTPK	AgTx2-OSK_z4	274
GVPIIVKCKISRQCIKPCKDAGMRFGKCMNGKCHCTPK	AgTx2-OSK_z5	275

Table 6—*Heteromitrus spinnifer* (HsTx1) peptide and HsTx1 peptide analog sequences

Sequence/structure	Short-hand designation	SEQ ID NO:
ASCRTPKDCADPCRKETGCPYGKCMNRKCKCNRC	HsTx1	61
ASCXTPKDCADPCRKETGCPYGKCMNRKCKCNRC	HsTx1-X4	276
ASCATPKDCADPCRKETGCPYGKCMNRKCKCNRC	HsTx1-A4	277
ASCRTPXDCADPCRKETGCPYGKCMNRKCKCNRC	HsTx1-X7	278
ASCRTPADCADPCRKETGCPYGKCMNRKCKCNRC	HsTx1-A7	279
ASCRTPKDCADPCXKETGCPYGKCMNRKCKCNRC	HsTx1-X14	280
ASCRTPKDCADPCAKETGCPYGKCMNRKCKCNRC	HsTx1-A14	281
ASCRTPKDCADPCRXETGCPYGKCMNRKCKCNRC	HsTx1-X15	282
ASCRTPKDCADPCRAETGCPYGKCMNRKCKCNRC	HsTx1-A15	283
ASCRTPKDCADPCRKETGCPYGXCMNRKCKCNRC	HsTx1-X23	284
ASCRTPKDCADPCRKETGCPYGACMNRKCKCNRC	HsTx1-A23	285
ASCRTPKDCADPCRKETGCPYGKCMNXKCKCNRC	HsTx1-X27	286
ASCRTPKDCADPCRKETGCPYGKCMNAKCKCNRC	HsTx1-A27	287

ASCRTPKDCADPCRKETGCPYGKCMNRXCKCNRC	HsTx1-X28	288
ASCRTPKDCADPCRKETGCPYGKCMNRACKCNRC	HsTx1-A28	289
ASCRTPKDCADPCRKETGCPYGKCMNRKCXCNRC	HsTx1-X30	290
ASCRTPKDCADPCRKETGCPYGKCMNRKCACNRC	HsTx1-A30	291
ASCRTPKDCADPCRKETGCPYGKCMNRKCKCNXC	HsTx1-X33	292
ASCRTPKDCADPCRKETGCPYGKCMNRKCKCNAC	HsTx1-A33	293

Peptides as described in Table 5 can be prepared as described in U.S. Pat. No. 6,689,749, issued February 10, 2004 to Lebrun et al., which is hereby incorporated by reference in its entirety.

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Table 7— Orthochirus scrobiculosus (OSK1) peptide and OSK1 peptide analog sequences

Sequence/structure	Short-hand designation	SEQ ID NO:
GVIINVKCKISRQCLEPCKKAGMRFGKCMNGKCHCTPK	OSK1	25
GVIINVSCKISRQCLEPCKKAGMRFGKCMNGKCHCTPK	OSK1-S7	1303
GVIINVKCKISRQCLKPCKKAGMRFGKCMNGKCHCTPK	OSK1-K16	294
GVIINVKCKISRQCLEPCKDAGMRFGKCMNGKCHCTPK	OSK1-D20	295
GVIINVKCKISRQCLKPCKDAGMRFGKCMNGKCHCTPK	OSK1-K16,D20	296
GVIINVSCKISRQCLKPCKDAGMRFGKCMNGKCHCTPK	OSK1-S7,K16,D20	1308
GVIINVKCKISPQCLKPCKDAGMRFGKCMNGKCHCTPK	OSK1-P12,K16,D20	297
GVIINVKCKISRQCLKPCKDAGMRFGKCMNGKCHCYPK	OSK1-K16,D20,Y36	298
Ac-GVIINVKCKISPQCLKPCKDAGMRFGKCMNGKCHCTPK	Ac-OSK1-P12, K16, D20	562
GVIINVKCKISPQCLKPCKDAGMRFGKCMNGKCHCTPK-NH_2	OSK1-P12,K16, D20-NH_2	563
Ac-GVIINVKCKISPQCLKPCKDAGMRFGKCMNGKCHCTPK-NH_2	Ac-OSK1-P12, K16, D20-NH_2	564
GVIINVKCKISRQCLKPCKDAGMRFGKCMNGKCHCYPK-NH_2	OSK1-K16, D20, Y36-NH_2	565
Ac-GVIINVKCKISRQCLKPCKDAGMRFGKCMNGKCHCYPK	Ac-OSK1-K16, D20, Y36	566
Ac-GVIINVKCKISRQCLKPCKDAGMRFGKCMNGKCHCYPK-NH_2	Ac-OSK1-K16, D20, Y36-NH_2	567
GVIINVKCKISRQCLKPCKKAGMRFGKCMNGKCHCTPK-NH_2	OSK1-K16-NH_2	568
Ac-GVIINVKCKISRQCLKPCKKAGMRFGKCMNGKCHCTPK	Ac-OSK1-K16	569
Ac-GVIINVKCKISRQCLKPCKKAGMRFGKCMNGKCHCTPK-NH_2	Ac-OSK1-K16-NH_2	570
Ac-GVIINVKCKISRQCLEPCKDAGMRFGKCMNGKCHCTPK	Ac-OSK1-D20	571
GVIINVKCKISRQCLEPCKDAGMRFGKCMNGKCHCTPK-NH_2	OSK1-D20-NH_2	572
Ac-GVIINVKCKISRQCLEPCKDAGMRFGKCMNGKCHCTPK- NH_2	Ac-OSK1-D20-NH_2	573
GVIINVKCKISRQCLEPCKKAGMRFGKCMNGKCHCTPK-NH_2	OSK1-NH_2	574
Ac-GVIINVKCKISRQCLEPCKKAGMRFGKCMNGKCHCTPK	Ac-OSK1	575
Ac-GVIINVKCKISRQCLEPCKKAGMRFGKCMNGKCHCTPK-NH_2	Ac-OSK1-NH_2	576
GVIINVKCKISRQCLKPCKDAGMRFGKCMNGKCHCTPK-NH_2	OSK1-K16, D20-NH_2	577
Ac-GVIINVKCKISRQCLKPCKDAGMRFGKCMNGKCHCTPK	Ac-OSK1-K16, D20	578
Ac-GVIINVKCKISRQCLKPCKDAGMRFGKCMNGKCHCTPK-NH_2	Ac-OSK1-K16, D20-NH_2	579

VIINVKCKISRQCLEPCKKAGMRFGKCMNGKCHCTPK	Δ1-OSK1	580
Ac-VIINVKCKISRQCLEPCKKAGMRFGKCMNGKCHCTPK	Ac-Δ1-OSK1	581
VIINVKCKISRQCLEPCKKAGMRFGKCMNGKCHCTPK-NH_2	Δ1-OSK1- NH_2	582
Ac-VIINVKCKISRQCLEPCKKAGMRFGKCMNGKCHCTPK-NH_2	Ac-Δ1-OSK1-NH_2	583
GVIINVKCKISRQCLEPCKKAGMRFGKCMNGKCACTPK	OSK1-A34	584
Ac-GVIINVKCKISRQCLEPCKKAGMRFGKCMNGKCACTPK	Ac-OSK1-A34	585
GVIINVKCKISRQCLEPCKKAGMRFGKCMNGKCACTPK-NH_2	OSK1-A34-NH_2	586
Ac-GVIINVKCKISRQCLEPCKKAGMRFGKCMNGKCACTPK-NH_2	Ac-OSK1-A34-NH_2	587
VIINVKCKISRQCLKPCKDAGMRFGKCMNGKCHCTPK	Δ1-OSK1-K16, D20	588
Ac-VIINVKCKISRQCLKPCKDAGMRFGKCMNGKCHCTPK	Ac-Δ1-OSK1-K16, D20	589
VIINVKCKISRQCLKPCKDAGMRFGKCMNGKCHCTPK-NH_2	Δ1-OSK1-K16, D20-NH_2	590
Ac-VIINVKCKISRQCLKPCKDAGMRFGKCMNGKCHCTPK-NH_2	Ac-Δ1-OSK1-K16, D20-NH_2	591
NVKCKISRQCLKPCKDAGMRFGKCMNGKCHCTPK	(Δ1-4)-OSK1-K16, D20	592
Ac-NVKCKISRQCLKPCKDAGMRFGKCMNGKCHCTPK	Ac-(Δ1-4)-OSK1-K16, D20	593
NVKCKISRQCLKPCKDAGMRFGKCMNGKCHCTPK-NH_2	(Δ1-4)-OSK1-K16, D20-NH_2	594
Ac-NVKCKISRQCLKPCKDAGMRFGKCMNGKCHCTPK-NH_2	Ac-(Δ1-4)-OSK1-K16, D20-NH_2	595
KCKISRQCLKPCKDAGMRFGKCMNGKCHCTPK	(Δ1-6)-OSK1-K16, D20	596
Ac-KCKISRQCLKPCKDAGMRFGKCMNGKCHCTPK	Ac-(Δ1-6)-OSK1-K16, D20	597
KCKISRQCLKPCKDAGMRFGKCMNGKCHCTPK-NH_2	(Δ1-6)-OSK1-K16, D20-NH_2	598
Ac-KCKISRQCLKPCKDAGMRFGKCMNGKCHCTPK-NH_2	Ac-(Δ1-6)-OSK1-K16, D20-NH_2	599
CKISRQCLKPCKDAGMRFGKCMNGKCHCTPK	(Δ1-7)-OSK1-K16, D20	600
Ac-CKISRQCLKPCKDAGMRFGKCMNGKCHCTPK	Ac-(Δ1-7)-OSK1-K16, D20	601
CKISRQCLKPCKDAGMRFGKCMNGKCHCTPK-NH_2	(Δ1-7)-OSK1-K16, D20-NH_2	602
Ac-CKISRQCLKPCKDAGMRFGKCMNGKCHCTPK-NH_2	Ac-(Δ1-7)-OSK1-K16, D20-NH_2	603
GVIINVKCKISRQCLKPCKDAGMRNGKCMNGKCHCTPK	OSK1-K16, D20, N25	604
GVIINVKCKISRQCLKPCKDAGMRNGKCMNGKCHCTPK-NH_2	OSK1-K16, D20, N25-NH_2	605
Ac-GVIINVKCKISRQCLKPCKDAGMRNGKCMNGKCHCTPK	Ac-OSK1-K16, D20, N25	606
Ac-GVIINVKCKISRQCLKPCKDAGMRNGKCMNGKCHCTPK-NH_2	Ac-OSK1-K16, D20, N25-NH_2	607
GVIINVKCKISRQCLKPCKDAGMRFGKCMNRKCHCTPK	OSK1-K16, D20, R31	608
GVIINVKCKISRQCLKPCKDAGMRFGKCMNRKCHCTPK-NH_2	OSK1-K16, D20, R31-NH_2	609

Ac-GVIINVKCKISRQCLKPCKDAGMRFGKCMNRKCHCTPK	Ac-OSK1-K16, D20, R31	610
Ac-GVIINVKCKISRQCLKPCKDAGMRFGKCMNRKCHCTPK-NH_2	Ac-OSK1-K16, D20, R31-NH_2	611
GVIINVKCKISKQCLKPCRDAGMRFGKCMNGKCHCTPK	OSK1-K12, K16, R19, D20	612
Ac-GVIINVKCKISKQCLKPCRDAGMRFGKCMNGKCHCTPK	Ac-OSK1-K12, K16, R19, D20	613
GVIINVKCKISKQCLKPCRDAGMRFGKCMNGKCHCTPK-NH_2	OSK1-K12, K16, R19, D20-NH_2	614
Ac-GVIINVKCKISKQCLKPCRDAGMRFGKCMNGKCHCTPK-NH_2	Ac-OSK1-K12, K16, R19, D20-NH_2	615
TIINVKCKISRQCLKPCKDAGMRFGKCMNGKCHCTPK	Δ1-OSK1-T2, K16, D20	616
Ac-TIINVKCKISRQCLKPCKDAGMRFGKCMNGKCHCTPK	Ac-Δ1-OSK1-T2, K16, D20	617
TIINVKCKISRQCLKPCKDAGMRFGKCMNGKCHCTPK-NH_2	Δ1-OSK1-T2, K16, D20-NH_2	618
Ac-TIINVKCKISRQCLKPCKDAGMRFGKCMNGKCHCTPK-NH_2	Ac-Δ1-OSK1-T2, K16, D20-NH_2	619
GVKINVKCKISRQCLEPCKKAGMRFGKCMNGKCHCTPK	OSK1-K3	620
Ac-GVKINVKCKISRQCLEPCKKAGMRFGKCMNGKCHCTPK	Ac-OSK1-K3	621
GVKINVKCKISRQCLEPCKKAGMRFGKCMNGKCHCTPK-NH_2	OSK1-K3-NH_2	622
Ac-GVKINVKCKISRQCLEPCKKAGMRFGKCMNGKCHCTPK-NH_2	Ac-OSK1-K3-NH_2	623
GVKINVKCKISRQCLEPCKKAGMRFGKCMNGKCACTPK	OSK1-K3, A34	624
GVKINVKCKISRQCLKPCKDAGMRFGKCMNGKCHCTPK	OSK1-K3, K16, D20	625
GVKINVKCKISRQCLKPCKDAGMRFGKCMNGKCACTPK	OSK1-K3, K16, D20, A34	626
Ac-GVKINVKCKISRQCLEPCKKAGMRFGKCMNGKCACTPK	Ac-OSK1-K3, A34	627
GVKINVKCKISRQCLEPCKKAGMRFGKCMNGKCACTPK-NH_2	OSK1-K3, A34-NH_2	628
Ac-GVKINVKCKISRQCLEPCKKAGMRFGKCMNGKCACTPK-NH_2	Ac-OSK1-K3, A34-NH_2	629
Ac-GVKINVKCKISRQCLKPCKDAGMRFGKCMNGKCACTPK	Ac-OSK1-K3, K16, D20, A34	630
GVKINVKCKISRQCLKPCKDAGMRFGKCMNGKCACTPK-NH_2	OSK1-K3, K16, D20, A34-NH_2	631
Ac-GVKINVKCKISRQCLKPCKDAGMRFGKCMNGKCACTPK-NH_2	Ac-OSK1-K3, K16, D20, A34-NH_2	632
Ac-GVKINVKCKISRQCLKPCKDAGMRFGKCMNGKCHCTPK	Ac-OSK1-K3, K16, D20	633
GVKINVKCKISRQCLKPCKDAGMRFGKCMNGKCHCTPK-NH_2	OSK1-K3, K16, D20-NH_2	634
Ac-GVKINVKCKISRQCLKPCKDAGMRFGKCMNGKCHCTPK-NH_2	Ac-OSK1-K3, K16, D20-NH_2	635
GVIINVKCKISRQCLKPCKDAGMRFGKCMNGKCHCT	Δ36-38-OSK1-K16, D20	636
GVIINVKCKISRQCLOPCKDAGMRFGKCMNGKCHCTPK	OSK1-O16,D20	980
GVIINVKCKISRQCL[hLys]PCKDAGMRFGKCMNGKCHCTPK	OSK1-hLys 16,D20	981
GVIINVKCKISRQCL[hArg]PCKDAGMRFGKCMNGKCHCTPK	OSK1-hArg 16,D20	982

GVIINVKCKISRQCL[Cit]PCKDAGMRFGKCMNGKCHCTPK	OSK1-Cit 16,D20	983
GVIINVKCKISRQCL[hCit]PCKDAGMRFGKCMNGKCHCTPK	OSK1-hCit 16,D20	984
GVIINVKCKISRQCL[Dpr]PCKDAGMRFGKCMNGKCHCTPK	OSK1-Dpr 16,D20	985
GVIINVKCKISRQCL[Dab]PCKDAGMRFGKCMNGKCHCTPK	OSK1-Dab 16,D20	986
GVIINVKCKISRQCLOPCKDAGMRFGKCMNGKCHCYPK	OSK1-O16,D20,Y36	987
GVIINVKCKISRQCL[hLys]PCKDAGMRFGKCMNGKCHCYPK	OSK1-hLys 16,D20,Y36	988
GVIINVKCKISRQCL[hArg]PCKDAGMRFGKCMNGKCHCYPK	OSK1-hArg 16,D20,Y36	989
GVIINVKCKISRQCL[Cit]PCKDAGMRFGKCMNGKCHCYPK	OSK1-Cit 16,D20,Y36	990
GVIINVKCKISRQCL[hCit]PCKDAGMRFGKCMNGKCHCYPK	OSK1-hCit 16,D20,Y36	991
GVIINVKCKISRQCL[Dpr]PCKDAGMRFGKCMNGKCHCYPK	OSK1-Dpr 16,D20,Y36	992
GVIINVKCKISRQCL[Dab]PCKDAGMRFGKCMNGKCHCYPK	OSK1-Dab 16,D20,Y36	993
GVIINVKCKISRQCLKPCKDAGMRFGKCMNGKCACYPK	OSK1-K16,D20,A34,Y36	994
GVIINVKCKISRQCLKPCKDAGMRFGKCMNGKCGCYPK	OSK1-K16,D20,G34,Y36	995
GVIINVKCKISRQCLKPCKDAGMRFGKCMNGKCACFPK	OSK1-K16,D20,A34,F36	996
GVIINVKCKISRQCLKPCKDAGMRFGKCMNGKCACWPK	OSK1-K16,D20,A34,W36	997
GVIINVKCKISRQCLKPCKEAGMRFGKCMNGKCACYPK	OSK1-K16,E20,A34,Y36	998
GVIINVKCKISRQCLOPCKDAGMRFGKCMNGKCACTPK	OSK1-O16,D20,A34	999
GVIINVKCKISRQCL[hLys]PCKDAGMRFGKCMNGKCACTPK	OSK1-hLys 16,D20,A34	1000
GVIINVKCKISRQCL[hArg]PCKDAGMRFGKCMNGKCACTPK	OSK1-hArg 16,D20,A34	1001
GVIINVKCKISRQCL[Cit]PCKDAGMRFGKCMNGKCACTPK	OSK1-Cit 16,D20,A34	1002
GVIINVKCKISRQCL[hCit]PCKDAGMRFGKCMNGKCHCTPK	OSK1-hCit 16,D20,A34	1003
GVIINVKCKISRQCL[Dpr]PCKDAGMRFGKCMNGKCACTPK	OSK1-Dpr 16,D20,A34	1004
GVIINVKCKISRQCL[Dab]PCKDAGMRFGKCMNGKCACTPK	OSK1-Dab 16,D20,A34	1005
GVIINVKCKISRQCLOPCKDAGMRFGKCMNGKCHC	Δ36-38, OSK1-O16,D20,	1006
GVIINVKCKISRQCL[hLys]PCKDAGMRFGKCMNGKCHC	Δ36-38, OSK1-hLys 16,D20	1007
GVIINVKCKISRQCL[hArg]PCKDAGMRFGKCMNGKCHC	Δ36-38, OSK1-hArg 16,D20	1008
GVIINVKCKISRQCL[Cit]PCKDAGMRFGKCMNGKCHC	Δ36-38, OSK1-Cit 16,D20	1009
GVIINVKCKISRQCL[hCit]PCKDAGMRFGKCMNGKCHC	Δ36-38, OSK1-hCit 16,D20	1010

GVIINVKCKISRQCL[Dpr]PCKDAGMRFGKCMNGKCHC	Δ36-38, OSK1-Dpr 16,D20	1011
GVIINVKCKISRQCL[Dab]PCKDAGMRFGKCMNGKCHC	Δ36-38, OSK1-Dab16,D20	1012
GVIINVKCKISRQCLOPCKDAGMRFGKCMNGKCAC	Δ36-38, OSK1-O16,D20,A34	1013
GVIINVKCKISRQCL[hLys]PCKDAGMRFGKCMNGKCAC	Δ36-38, OSK1-hLys 16,D20,A34	1014
GVIINVKCKISRQCL[hArg]PCKDAGMRFGKCMNGKCAC	Δ36-38, OSK1-hArg 16,D20,A34	1015
GVIINVKCKISRQCL[Cit]PCKDAGMRFGKCMNGKCAC	Δ36-38, OSK1-Cit 16,D20,A34	1016
GVIINVKCKISRQCL[hCit]PCKDAGMRFGKCMNGKCHC	Δ36-38, OSK1-hCit 16,D20,A34	1017
GVIINVKCKISRQCL[Dpr]PCKDAGMRFGKCMNGKCAC	Δ36-38, OSK1-Dpr 16,D20,A34	1018
GVIINVKCKISRQCL[Dab]PCKDAGMRFGKCMNGKCAC	Δ36-38, OSK1-Dab 16,D20,A34	1019
GVIINVKCKISRQCLKPCKDAGMRFGKCMNGKCGCYGG	OSK1-K16,D20,G34,Y36,G37,G38	1020
GVIINVKCKISRQCLOPCKDAGMRFGKCMNGKCHCYGG	OSK1-O16,D20,Y36,G37,G38	1021
GVIINVKCKISRQCL[hLys]PCKDAGMRFGKCMNGKCHCYGG	OSK1-hLys 16,D20,Y36,G37,G38	1022
GVIINVKCKISRQCL[hArg]PCKDAGMRFGKCMNGKCHCYGG	OSK1-hArg 16,D20,Y36,G37,G38	1023
GVIINVKCKISRQCL[Cit]PCKDAGMRFGKCMNGKCHCYGG	OSK1-Cit 16,D20,Y36,G37,G38	1024
GVIINVKCKISRQCL[hCit]PCKDAGMRFGKCMNGKCHCYGG	OSK1-hCit 16,D20,Y36,G37,G38	1025
GVIINVKCKISRQCL[Dpr]PCKDAGMRFGKCMNGKCHCYGG	OSK1-Dpr 16,D20,Y36,G37,G38	1026
GVIINVKCKISRQCLKPCKDAGMRFGKCMNGKCACYGG	OSK1-K16,D20,A34,Y36,G37,G38	1027
GVIINVKCKISRQCLOPCKDAGMRFGKCMNGKCACYGG	OSK1-O16,D20,A34,Y36,G37,G38	1028
GVIINVKCKISRQCL[hLys]PCKDAGMRFGKCMNGKCACYGG	OSK1-hLys 16,D20,A34,Y36,G37,G38	1029
GVIINVKCKISRQCL[hArg]PCKDAGMRFGKCMNGKCACYGG	OSK1-hArg 16,D20,A34,Y36,G37,G38	1030

GVIINVKCKISRQCL[Cit]PCKDAGMRFGKCMNGKCACYGG	OSK1-Cit 16,D20,A34,Y36,G37,G38	1031
GVIINVKCKISRQCL[hCit]PCKDAGMRFGKCMNGKCHCYGG	OSK1-hCit 16,D20,A34,Y3,G37, G38	1032
GVIINVKCKISRQCL[Dpr]PCKDAGMRFGKCMNGKCACYGG	OSK1-Dpr 16,D20,A34,Y36,G37,G38	1033
GVIINVKCKISRQCL[Dab]PCKDAGMRFGKCMNGKCACYGG	OSK1-Dab 16,D20,A34,Y36,G37,G38	1034
GVIINVKCKISRQCLKPCKDAGMRFGKCMNGKCACYG	Δ38, OSK1-K16,D20,A34,Y36,G37	1035
GVIINVKCKISRQCLOPCKDAGMRFGKCMNGKCHCGGG	OSK1-O16,D20,G36-38	1036
GVIINVKCKISRQCL[hLys]PCKDAGMRFGKCMNGKCHCGGG	OSK1-hLys 16,D20,G36-38	1037
GVIINVKCKISRQCL[hArg]PCKDAGMRFGKCMNGKCHCGGG	OSK1-hArg 16,D20,G36-38	1038
GVIINVKCKISRQCL[Cit]PCKDAGMRFGKCMNGKCHCGGG	OSK1-Cit 16,D20,G36-38	1039
GVIINVKCKISRQCL[hCit]PCKDAGMRFGKCMNGKCHCGGG	OSK1-hCit 16,D20,G36-38	1040
GVIINVKCKISRQCL[Dpr]PCKDAGMRFGKCMNGKCHCGGG	OSK1-Dpr 16,D20,G36-38	1041
GVIINVKCKISRQCLKPCKDAGMRFGKCMNGKCACFGG	OSK1-K16,D20,A34,F36,G37,G38	1042
GVIINVKCKISRQCLOPCKDAGMRFGKCMNGKCACGGG	OSK1-O16,D20,A34,G36-38	1043
GVIINVKCKISRQCL[hLys]PCKDAGMRFGKCMNGKCACGGG	OSK1-hLys 16,D20,A34,G36-38	1044
GVIINVKCKISRQCL[hArg]PCKDAGMRFGKCMNGKCACGGG	OSK1-hArg 16,D20,A34,G36-38	1045
GVIINVKCKISRQCL[Cit]PCKDAGMRFGKCMNGKCACGGG	OSK1-Cit 16,D20,A34,G36-38	1046
GVIINVKCKISRQCL[hCit]PCKDAGMRFGKCMNGKCACGGG	OSK1-hCit 16,D20,A34,G36-38	1047
GVIINVKCKISRQCL[Dpr]PCKDAGMRFGKCMNGKCACGGG	OSK1-Dpr 16,D20,A34,G36-38	1048
GVIINVKCKISRQCL[Dab]PCKDAGMRFGKCMNGKCACGGG	OSK1-Dab 16,D20,A34,G36-38	1049
GVIINVKCKISRQCLKPCKDAGMRFGKCMNGKCACGG	Δ38, OSK1-K16,D20,A34,G36-37	1050
GVIINVKCKISRQCLKPCKDAGMRFGKCMNGKCACYG	Δ38, OSK1-K16,D20,A35,Y36,G37	1051

GVIINVKCKISRQCLOPCKDAGMRFGKCMNGKCACGG	Δ38, OSK1-O16,D20,A35,Y36,G37	1052
GVIINVKCKISRQCL[hLys]PCKEAGMRFGKCMNGKCHCTPK	OSK1-hLys 16,E20	1053
GVIINVKCKISRQCL[hArg]PCKEAGMRFGKCMNGKCHCTPK	OSK1-hArg 16,E20	1054
GVIINVKCKISRQCL[Cit]PCKEAGMRFGKCMNGKCHCTPK	OSK1-Cit 16,E20	1055
GVIINVKCKISRQCL[hCit]PCKEAGMRFGKCMNGKCHCTPK	OSK1-hCit 16,E20	1056
GVIINVKCKISRQCL[Dpr]PCKEAGMRFGKCMNGKCHCTPK	OSK1-Dpr 16,E20	1057
GVIINVKCKISRQCL[Dab]PCKEAGMRFGKCMNGKCHCTPK	OSK1-Dab 16,E20	1058
GVIINVKCKISRQCLOPCKEAGMRFGKCMNGKCHCYPK	OSK1-O16,E20,Y36	1059
GVIINVKCKISRQCL[hLys]PCKEAGMRFGKCMNGKCHCYPK	OSK1-hLys 16,E20,Y36	1060
GVIINVKCKISRQCL[hArg]PCKEAGMRFGKCMNGKCHCYPK	OSK1-hArg 16,E20,Y36	1061
GVIINVKCKISRQCL[Cit]PCKEAGMRFGKCMNGKCHCYPK	OSK1-Cit 16,E20,Y36	1062
GVIINVKCKISRQCL[hCit]PCKEAGMRFGKCMNGKCHCYPK	OSK1-hCit 16,E20,Y36	1063
GVIINVKCKISRQCL[Dpr]PCKEAGMRFGKCMNGKCHCYPK	OSK1-Dpr 16,E20,Y36	1064
GVIINVKCKISRQCL[Dab]PCKEAGMRFGKCMNGKCHCYPK	OSK1-Dab 16,E20,Y36	1065
GVIINVKCKISRQCLOPCKEAGMRFGKCMNGKCACTPK	OSK1-O16,E20,A34	1066
GVIINVKCKISRQCL[hLys]PCKEAGMRFGKCMNGKCACTPK	OSK1-hLys 16,E20,A34	1067
GVIINVKCKISRQCL[hArg]PCKEAGMRFGKCMNGKCACTPK	OSK1-hArg 16,E20,A34	1068
GVIINVKCKISRQCL[Cit]PCKEAGMRFGKCMNGKCACTPK	OSK1-Cit 16,E20,A34	1069
GVIINVKCKISRQCL[hCit]PCKEAGMRFGKCMNGKCHCTPK	OSK1-hCit 16,E20,A34	1070
GVIINVKCKISRQCL[Dpr]PCKEAGMRFGKCMNGKCACTPK	OSK1-Dpr 16,E20,A34	1071
GVIINVKCKISRQCL[Dab]PCKEAGMRFGKCMNGKCACTPK	OSK1-Dab 16,E20,A34	1072
GVIINVKCKISRQCLOPCKEAGMRFGKCMNGKCHC	Δ36-38, OSK1-O16,E20,	1073
GVIINVKCKISRQCL[hLys]PCKEAGMRFGKCMNGKCHC	Δ36-38, OSK1-hLys 16,E20	1074
GVIINVKCKISRQCL[hArg]PCKEAGMRFGKCMNGKCHC	Δ36-38, OSK1-hArg 16,E20	1075
GVIINVKCKISRQCL[Cit]PCKEAGMRFGKCMNGKCHC	Δ36-38, OSK1-Cit 16,E20	1076
GVIINVKCKISRQCL[hCit]PCKEAGMRFGKCMNGKCHC	Δ36-38, OSK1-hCit16,E20	1077
GVIINVKCKISRQCL[Dpr]PCKEAGMRFGKCMNGKCHC	Δ36-38, OSK1-Dpr 16,E20	1078

GVIINVKCKISRQCLOPCKEAGMRFGKCMNGKCAC	Δ36-38, OSK1-O16,E20,A34	1079
GVIINVKCKISRQCL[hLys]PCKEAGMRFGKCMNGKCAC	Δ36-38, OSK1-hLys 16,E20,A34	1080
GVIINVKCKISRQCL[hArg]PCKEAGMRFGKCMNGKCAC	Δ36-38, OSK1-hArg 16,E20,A34	1081
GVIINVKCKISRQCL[Cit]PCKEAGMRFGKCMNGKCAC	Δ36-38, OSK1-Cit 16,E20,A34	1082
GVIINVKCKISRQCL[hCit]PCKEAGMRFGKCMNGKCHC	Δ36-38, OSK1-hCit 16,E20,A34	1083
GVIINVKCKISRQCL[Dpr]PCKEAGMRFGKCMNGKCAC	Δ36-38, OSK1-Dpr 16,E20,A34	1084
GVIINVKCKISRQCL[Dab]PCKEAGMRFGKCMNGKCAC	Δ36-38, OSK1-Dab 16,E20,A34	1085
GVIINVKCKISRQCLKPCKEAGMRFGKCMNGKCHCYGG	OSK1-K16,E20,Y36,G37,G38	1086
GVIINVKCKISRQCLOPCKEAGMRFGKCMNGKCHCYGG	OSK1-O16,E20,Y36,G37,G38	1087
GVIINVKCKISRQCLKPCKEAGMRFGKCMNGKCHCYG	Δ38 OSK1-K16,E20,Y36,G37	1088
GVIINVKCKISRQCLKPCKEAGMRFGKCMNGKCACYG	Δ38 OSK1-K16,E20,A34, Y36,G37	1089
GVIINVKCKISRQCL[hLys]PCKEAGMRFGKCMNGKCHCYGG	OSK1-hLys 16,E20,Y36,G37,G38	1090
GVIINVKCKISRQCL[hArg]PCKEAGMRFGKCMNGKCHCYGG	OSK1-hArg 16,E20,Y36,G37,G38	1091
GVIINVKCKISRQCL[Cit]PCKEAGMRFGKCMNGKCHCYGG	OSK1-Cit 16,E20,Y36,G37,G38	1092
GVIINVKCKISRQCL[hCit]PCKEAGMRFGKCMNGKCHCYGG	Δ37-38, OSK1-hCit 16,E20,Y36,G37,G38	1093
GVIINVKCKISRQCL[Dpr]PCKEAGMRFGKCMNGKCHCYGG	OSK1-Dpr 16,E20,Y36,G37,G38	1094
GVIINVKCKISRQCL[Dab]PCKEAGMRFGKCMNGKCHCYGG	OSK1-Dab 16,E20,Y36,G37,G38	1095
GVIINVKCKISRQCLKPCKEAGMRFGKCMNGKCACYG	Δ38, OSK1-K16,E20,A34,Y36,G37	1096
GVIINVKCKISRQCLOPCKEAGMRFGKCMNGKCACYGG	OSK1-O16,E20,A34,Y36,G37,G38	1097

GVIINVKCKISRQCL[hLys]PCKEAGMRFGKCMNGKCACYGG	OSK1-hLys 16,E20,A34,Y36,G37,G38	1098
GVIINVKCKISRQCL[hArg]PCKEAGMRFGKCMNGKCACYGG	OSK1-hArg 16,E20,A34,Y36,G37,G38	1099
GVIINVKCKISRQCL[Cit]PCKEAGMRFGKCMNGKCACYGG	OSK1-Cit 16,E20,A34,Y36,G37,G38	1100
GVIINVKCKISRQCL[hCit]PCKEAGMRFGKCMNGKCHCYGG	OSK1-hCit 16,E20,A34,Y3,G37,G38	1101
GVIINVKCKISRQCL[Dpr]PCKEAGMRFGKCMNGKCACYGG	OSK1-Dpr 16,E20,A34,Y36,G37,G38	1102
GVIINVKCKISRQCL[Dab]PCKEAGMRFGKCMNGKCACYGG	OSK1-Dab 16,E20,A34,Y36,G37,G38	1103
GVIINVKCKISRQCLKPCKEAGMRFGKCMNGKCACFGG	OSK1-K16,D20,A34,F36,G37,G38	1104
GVIINVKCKISRQCLOPCKEAGMRFGKCMNGKCHCGGG	OSK1-O16,E20,G36-38	1105
GVIINVKCKISRQCL[hLys]PCKEAGMRFGKCMNGKCHCGGG	OSK1-hLys 16,E20,G36-38	1106
GVIINVKCKISRQCL[hArg]PCKEAGMRFGKCMNGKCHCGGG	OSK1-hArg 16,E20,G36-38	1107
GVIINVKCKISRQCL[Cit]PCKEAGMRFGKCMNGKCHCGGG	OSK1-Cit 16,E20,G36-38	1108
GVIINVKCKISRQCL[hCit]PCKEAGMRFGKCMNGKCHCGGG	OSK1-hCit 16,E20,G36-38	1109
GVIINVKCKISRQCL[Dpr]PCKEAGMRFGKCMNGKCHCGGG	OSK1-Dpr 16,E20,G36-38	1110
GVIINVKCKISRQCLOPCKEAGMRFGKCMNGKCACGGG	OSK1-O16,E20,A34,G36-38	1111
GVIINVKCKISRQCL[hLys]PCKEAGMRFGKCMNGKCACGGG	OSK1-hLys 16,E20,A34,G36-38	1112
GVIINVKCKISRQCL[hArg]PCKEAGMRFGKCMNGKCACGGG	OSK1-hArg 16,E20,A34,G36-38	1113
GVIINVKCKISRQCL[Cit]PCKEAGMRFGKCMNGKCACGGG	OSK1-Cit 16,E20,A34,G36-38	1114
GVIINVKCKISRQCL[hCit]PCKEAGMRFGKCMNGKCACTP	OSK1-hCit 16,E20,A34,G36-38	1115
GVIINVKCKISRQCL[Dpr]PCKEAGMRFGKCMNGKCACTP	OSK1-Dpr 16,E20,A34,G36-38	1116
GVIINVKCKISRQCL[Dab]PCKEAGMRFGKCMNGKCACTP	OSK1-Dab 16,E20,A34,G36-38	1117
GVIINVKCKISRQCLOPCKDAGMRFGKCMNGKCHCTPK-NH2	OSK1-O16,D20-amide	1118
GVIINVKCKISRQCL[hLys]PCKDAGMRFGKCMNGKCHCTPK-NH2	OSK1-hLys 16,D20-amide	1119

GVIINVKCKISRQCL[hArg]PCKDAGMRFGKCMNGKCHCTPK-NH2	OSK1-hArg 16,D20-amide	1120
GVIINVKCKISRQCL[Cit]PCKDAGMRFGKCMNGKCHCTPK-NH2	OSK1-Cit 16,D20-amide	1121
GVIINVKCKISRQCL[hCit]PCKDAGMRFGKCMNGKCHCTPK-NH2	OSK1-hCit 16,D20-amide	1122
GVIINVKCKISRQCL[Dpr]PCKDAGMRFGKCMNGKCHCTPK-NH2	OSK1-Dpr 16,D20-amide	1123
GVIINVKCKISRQCL[Dab]PCKDAGMRFGKCMNGKCHCTPK-NH2	OSK1-Dab 16,D20	1124
GVIINVKCKISRQCLOPCKDAGMRFGKCMNGKCHCYPK-NH2	OSK1-O16,D20,Y36-amide	1125
GVIINVKCKISRQCL[hLys]PCKDAGMRFGKCMNGKCHCYPK-NH2	OSK1-hLys 16,D20,Y36-amide	1126
GVIINVKCKISRQCL[hArg]PCKDAGMRFGKCMNGKCHCYPK-NH2	OSK1-hArg 16,D20,Y36-amide	1127
GVIINVKCKISRQCL[Cit]PCKDAGMRFGKCMNGKCHCYPK-NH2	OSK1-Cit 16,D20,Y36-amide	1128
GVIINVKCKISRQCL[hCit]PCKDAGMRFGKCMNGKCHCYPK-NH2	OSK1-hCit 16,D20,Y36-amide	1129
GVIINVKCKISRQCL[Dpr]PCKDAGMRFGKCMNGKCHCYPK-NH2	OSK1-Dpr 16,D20,Y36-amide	1130
GVIINVKCKISRQCL[Dab]PCKDAGMRFGKCMNGKCHCYPK-NH2	OSK1-Dab 16,D20,Y36-amide	1131
GVIINVKCKISRQCLOPCKDAGMRFGKCMNGKCACTPK-NH2	OSK1-O16,D20,A34-amide	1132
GVIINVKCKISRQCL[hLys]PCKDAGMRFGKCMNGKCACTPK-NH2	OSK1-hLys 16,D20,A34-amide	1133
GVIINVKCKISRQCL[hArg]PCKDAGMRFGKCMNGKCACTPK-NH2	OSK1-hArg 16,D20,A34-amide	1134
GVIINVKCKISRQCL[Cit]PCKDAGMRFGKCMNGKCACTPK-NH2	OSK1-Cit 16,D20,A34-amide	1135
GVIINVKCKISRQCL[hCit]PCKDAGMRFGKCMNGKCACTPK-NH2	OSK1-hCit 16,D20,A34-amide	1136
GVIINVKCKISRQCL[Dpr]PCKDAGMRFGKCMNGKCACTPK-NH2	OSK1-Dpr 16,D20,A34-amide	1137
GVIINVKCKISRQCL[Dab]PCKDAGMRFGKCMNGKCACTPK-NH2	OSK1-Dab 16,D20,A34-amide	1138

GVIINVKCKISRQCLOPCKDAGMRFGKCMNGKCHC-NH2	Δ36-38, OSK1-O16,D20, -amide	1139
GVIINVKCKISRQCL[hLys]PCKDAGMRFGKCMNGKCHC-NH2	Δ36-38, OSK1-hLys 16,D20-amide	1140
GVIINVKCKISRQCL[hArg]PCKDAGMRFGKCMNGKCHC-NH2	Δ36-38, OSK1-hArg 16,D20-amide	1141
GVIINVKCKISRQCL[Cit]PCKDAGMRFGKCMNGKCHC-NH2	Δ36-38, OSK1-Cit 16,D20-amide	1142
GVIINVKCKISRQCL[hCit]PCKDAGMRFGKCMNGKCHC-NH2	Δ36-38, OSK1-hCit16,D20-amide	1143
GVIINVKCKISRQCL[Dpr]PCKDAGMRFGKCMNGKCHC-NH2	Δ36-38, OSK1-Dpr 16,D20-amide	1144
GVIINVKCKISRQCLOPCKDAGMRFGKCMNGKCAC-NH2	Δ36-38, OSK1-O16,D20,A34-amide	1145
GVIINVKCKISRQCL[hLys]PCKDAGMRFGKCMNGKCAC-NH2	Δ36-38, OSK1-hLys 16,D20,A34-amide	1146
GVIINVKCKISRQCL[hArg]PCKDAGMRFGKCMNGKCAC-NH2	Δ36-38, OSK1-hArg 16,D20,A34-amide	1147
GVIINVKCKISRQCL[Cit]PCKDAGMRFGKCMNGKCAC-NH2	Δ36-38, OSK1-Cit 16,D20,A34-amide	1148
GVIINVKCKISRQCL[hCit]PCKDAGMRFGKCMNGKCHC-NH2	Δ36-38, OSK1-hCit16,D20,A34	1149
GVIINVKCKISRQCL[Dpr]PCKDAGMRFGKCMNGKCAC-NH2	Δ36-38, OSK1-Dpr 16,D20,A34-amide	1150
GVIINVKCKISRQCL[Dab]PCKDAGMRFGKCMNGKCAC-NH2	Δ36-38, OSK1-Dab 16,D20,A34-amide	1151
GVIINVKCKISRQCLKPCKDAGMRFGKCMNGKCHCYGG-NH2	OSK1-O16,D20,Y36,G37,G38-amide	1152
GVIINVKCKISRQCLOPCKDAGMRFGKCMNGKCHCYGG-NH2	OSK1-O16,D20,Y36,G37,G38	1153
GVIINVKCKISRQCL[hLys]PCKDAGMRFGKCMNGKCHCYGG-NH2	OSK1-hLys 16,D20,Y36,G37,G38-amide	1154
GVIINVKCKISRQCL[hArg]PCKDAGMRFGKCMNGKCHCYGG-NH2	OSK1-hArg 16,D20,Y36,G37,G38-amide	1155
GVIINVKCKISRQCL[Cit]PCKDAGMRFGKCMNGKCHCYGG-NH2	OSK1-Cit 16,D20,Y36,G37,G38-amide	1156

GVIINVKCKISRQCL[hCit]PCKDAGMRFGKCMNGKCHCYGG-NH2	OSK1-hCit16,D20,Y36,G37,G38-amide	1157
GVIINVKCKISRQCL[Dpr]PCKDAGMRFGKCMNGKCHCYGG-NH2	OSK1-Dpr16,D20,Y36,G37,G38-amide	1158
GVIINVKCKISRQCLKPCKDAGMRFGKCMNGKCHCFGG-NH2	OSK1-K16,D20,F36,G37,G38-amide	1159
GVIINVKCKISRQCLKPCKDAGMRFGKCMNGKCHCYG-NH2	Δ38-OSK1-K16,D20,Y36,G37-amide	1160
GVIINVKCKISRQCLKPCKDAGMRFGKCMNGKCACYG-NH2	Δ38-OSK1-K16,D20,A34,Y36,G37-amide	1161
GVIINVKCKISRQCLOPCKDAGMRFGKCMNGKCACYGG-NH2	OSK1-O16,D20,A34,Y36,G37,G38-amide	1162
GVIINVKCKISRQCL[hLys]PCKDAGMRFGKCMNGKCACYGG-NH2	OSK1-hLys16,D20,A34,Y36,G37,G38-amide	1163
GVIINVKCKISRQCL[hArg]PCKDAGMRFGKCMNGKCACYGG-NH2	OSK1-hArg16,D20,A34,Y36,G37,G38-amide	1164
GVIINVKCKISRQCL[Cit]PCKDAGMRFGKCMNGKCACYGG-NH2	OSK1-Cit16,D20,A34,Y36,G37,G38	1165
GVIINVKCKISRQCL[hCit]PCKDAGMRFGKCMNGKCACYGG-NH2	OSK1-hCit16,D20,A34,Y3,G37,G38-amide	1166
GVIINVKCKISRQCL[Dpr]PCKDAGMRFGKCMNGKCACYGG-NH2	OSK1-Dpr16,D20,A34,Y36,G37,G38-amide	1167
GVIINVKCKISRQCL[Dab]PCKDAGMRFGKCMNGKCACYGG-NH2	OSK1-Dab16,D20,A34,Y36,G37,G38-amide	1168
GVIINVKCKISRQCLKPCKDAGMRFGKCMNGKCACYGG-NH2	OSK1-K16,D20,A34,Y36,G37,G38-amide	1169
GVIINVKCKISRQCLOPCKDAGMRFGKCMNGKCHCGGG-NH2	OSK1-O16,D20,G36-38-amide	1170
GVIINVKCKISRQCL[hLys]PCKDAGMRFGKCMNGKCHCGGG-NH2	OSK1-hLys16,D20,G36-38-amide	1171
GVIINVKCKISRQCL[hArg]PCKDAGMRFGKCMNGKCHCGGG-NH2	OSK1-hArg16,D20,G36-38-amide	1172
GVIINVKCKISRQCL[Cit]PCKDAGMRFGKCMNGKCHCGGG-NH2	OSK1-Cit16,D20,G36-38-amide	1173

GVIINVKCKISRQCL[hCit]PCKDAGMRFGKCMNGKCHCGGG-NH2	OSK1-hCit16,D20,G36-38-amide	1174
GVIINVKCKISRQCL[Dpr]PCKDAGMRFGKCMNGKCHCGGG-NH2	OSK1-Dpr 16,D20,G36-38-amide	1175
GVIINVKCKISRQCLKPCKDAGMRFGKCMNGKCACGGG-NH2	OSK1-K16,D20,A34,G36-38-amide	1176
GVIINVKCKISRQCLOPCKDAGMRFGKCMNGKCACFGG-NH2	OSK1-O16,D20,A34,F36,G37-38-amide	1177
GVIINVKCKISRQCLOPCKDAGMRFGKCMNGKCACGGG-NH2	OSK1-O16,D20,A34,G36-38-amide	1178
GVIINVKCKISRQCL[hLys]PCKDAGMRFGKCMNGKCACGGG-NH2	OSK1-hLys 16,D20,A34,G36-38-amide	1179
GVIINVKCKISRQCL[hArg]PCKDAGMRFGKCMNGKCACGGG-NH2	OSK1-hArg 16,D20,A34,G36-38-amide	1180
GVIINVKCKISRQCL[Cit]PCKDAGMRFGKCMNGKCACGGG-NH2	OSK1-Cit 16,D20,A34,G36-38-amide	1181
GVIINVKCKISRQCL[hCit]PCKDAGMRFGKCMNGKCACGGG-NH2	OSK1-hCit16,D20,A34,G36-38-amide	1182
GVIINVKCKISRQCL[Dpr]PCKDAGMRFGKCMNGKCACGGG-NH2	OSK1-Dpr 16,D20,A34,G36-38-amide	1183
GVIINVKCKISRQCL[Dab]PCKDAGMRFGKCMNGKCACGGG-NH2	OSK1-Dab 16,D20,A34,G36-38-amide	1184
GVIINVKCKISRQCLOPCKEAGMRFGKCMNGKCHCTPK-NH2	OSK1-O16,E20-amide	1185
GVIINVKCKISRQCL[hLys]PCKEAGMRFGKCMNGKCHCTPK-NH2	OSK1-hLys 16,E20-amide	1186
GVIINVKCKISRQCL[hArg]PCKEAGMRFGKCMNGKCHCTPK-NH2	OSK1-hArg 16,E20-amide	1187
GVIINVKCKISRQCL[Cit]PCKEAGMRFGKCMNGKCHCTPK-NH2	OSK1-Cit 16,E20-amide	1188
GVIINVKCKISRQCL[hCit]PCKEAGMRFGKCMNGKCHCTPK-NH2	OSK1-hCit16,E20-amide	1189
GVIINVKCKISRQCL[Dpr]PCKEAGMRFGKCMNGKCHCTPK-NH2	OSK1-Dpr 16,E20-amide	1190
GVIINVKCKISRQCL[Dab]PCKEAGMRFGKCMNGKCHCTPK-NH2	OSK1-Dab 16,E20-amide	1191
GVIINVKCKISRQCLOPCKEAGMRFGKCMNGKCHCYPK-NH2	OSK1-O16,E20,Y36-amide	1192

GVIINVKCKISRQCL[hLys]PCKEAGMRFGKCMNGKCHCYPK-NH2	OSK1-hLys 16,E20,Y36-amide	1193
GVIINVKCKISRQCL[hArg]PCKEAGMRFGKCMNGKCHCYPK-NH2	OSK1-hArg 16,E20,Y36-amide	1194
GVIINVKCKISRQCL[Cit]PCKEAGMRFGKCMNGKCHCYPK-NH2	OSK1-Cit 16,E20,Y36-amide	1195
GVIINVKCKISRQCL[hCit]PCKEAGMRFGKCMNGKCHCYPK-NH2	OSK1-hCit16,E20,Y36-amide	1196
GVIINVKCKISRQCL[Dpr]PCKEAGMRFGKCMNGKCHCYPK-NH2	OSK1-Dpr 16,E20,Y36-amide	1197
GVIINVKCKISRQCL[Dab]PCKEAGMRFGKCMNGKCHCYPK-NH2	OSK1-Dab 16,E20,Y36-amide	1198
GVIINVKCKISRQCLOPCKEAGMRFGKCMNGKCACTPK-NH2	OSK1-O16,E20,A34-amide	1199
GVIINVKCKISRQCL[hLys]PCKEAGMRFGKCMNGKCACTPK-NH2	OSK1-hLys 16,E20,A34-amide	1200
GVIINVKCKISRQCL[hArg]PCKEAGMRFGKCMNGKCACTPK-NH2	OSK1-hArg 16,E20,A34-amide	1201
GVIINVKCKISRQCL[Cit]PCKEAGMRFGKCMNGKCACTPK-NH2	OSK1-Cit 16,E20,A34-amide	1202
GVIINVKCKISRQCL[hCit]PCKEAGMRFGKCMNGKCACTPK-NH2	OSK1-hCit16,E20,A34-amide	1203
GVIINVKCKISRQCL[Dpr]PCKEAGMRFGKCMNGKCACTPK-NH2	OSK1-Dpr 16,E20,A34-amide	1204
GVIINVKCKISRQCL[Dab]PCKEAGMRFGKCMNGKCACTPK-NH2	OSK1-Dab 16,E20,A34-amide	1205
GVIINVKCKISRQCLOPCKEAGMRFGKCMNGKCHC-NH2	Δ36-38, OSK1-O16,E20, -amide	1206
GVIINVKCKISRQCL[hLys]PCKEAGMRFGKCMNGKCHC-NH2	Δ36-38, OSK1-hLys 16,E20-amide	1207
GVIINVKCKISRQCL[hArg]PCKEAGMRFGKCMNGKCHC-NH2	Δ36-38, OSK1-hArg 16,E20-amide	1208
GVIINVKCKISRQCL[Cit]PCKEAGMRFGKCMNGKCHC-NH2	Δ36-38, OSK1-Cit 16,E20-amide	1209
GVIINVKCKISRQCL[hCit]PCKEAGMRFGKCMNGKCHC-NH2	Δ36-38, OSK1-hCit16,E20-amide	1210

GVIINVKCKISRQCL[Dpr]PCKEAGMRFGKCMNGKCHC-NH2	Δ36-38, OSK1-Dpr 16,E20-amide	1211
GVIINVKCKISRQCLOPCKEAGMRFGKCMNGKCAC-NH2	Δ36-38, OSK1-O16,E20,A34-amide	1212
GVIINVKCKISRQCL[hLys]PCKEAGMRFGKCMNGKCAC-NH2	Δ36-38, OSK1-hLys16,E20,A34-amide	1213
GVIINVKCKISRQCL[hArg]PCKEAGMRFGKCMNGKCAC-NH2	Δ36-38, OSK1-hArg16,E20,A34-amide	1214
GVIINVKCKISRQCL[Cit]PCKEAGMRFGKCMNGKCAC-NH2	Δ36-38, OSK1-Cit 16,E20,A34-amide	1215
GVIINVKCKISRQCL[hCit]PCKEAGMRFGKCMNGKCHC-NH2	Δ36-38, OSK1-hCit16,E20,A34-amide	1216
GVIINVKCKISRQCL[Dpr]PCKEAGMRFGKCMNGKCAC-NH2	Δ36-38, OSK1-Dpr 16,E20,A34-amide	1217
GVIINVKCKISRQCL[Dab]PCKEAGMRFGKCMNGKCAC-NH2	Δ36-38, OSK1-Dab 16,E20,A34-amide	1218
GVIINVKCKISRQCLKPCKEAGMRFGKCMNGKCHCWGG-NH2	OSK1-O16,E20,W36,G37, G38-amide	1219
GVIINVKCKISRQCLOPCKEAGMRFGKCMNGKCHCYGG-NH2	OSK1-O16,E20,Y36,G37,G38-amide	1220
GVIINVKCKISRQCL[hLys]PCKEAGMRFGKCMNGKCHCYGG-NH2	OSK1-hLys 16,E20,Y36,G37,G38-amide	1221
GVIINVKCKISRQCL[hArg]PCKEAGMRFGKCMNGKCHCYGG-NH2	OSK1-hArg 16,E20,Y36,G37,G38-amide	1222
GVIINVKCKISRQCL[Cit]PCKEAGMRFGKCMNGKCHCYGG-NH2	OSK1-Cit 16,E20,Y36,G37,G38-amide	1223
GVIINVKCKISRQCL[hCit]PCKEAGMRFGKCMNGKCHCYGG-NH2	OSK1-hCit 16,E20,Y36,G37,G38-amide	1224
GVIINVKCKISRQCL[Dpr]PCKEAGMRFGKCMNGKCHCYGG-NH2	OSK1-Dpr 16,E20,Y36,G37,G38-amide	1225
GVIINVKCKISRQCL[Dab]PCKEAGMRFGKCMNGKCHCYGG-NH2	OSK1-Dpr 16,E20,Y36,G37,G38-amide	1226
GVIINVKCKISRQCLKPCKEAGMRFGKCMNGKCACYGG-NH2	OSK1-K16,E20,A34,Y36,G37,G38-amide	1227
GVIINVKCKISRQCLOPCKEAGMRFGKCMNGKCACYGG-NH2	OSK1-O16,E20,A34,Y36,G37,G38-amide	1228

GVIINVKCKISRQCL[hLys]PCKEAGMRFGKCMNGKCACYGG-NH2	OSK1-hLys 16,E20,A34,Y36,G37,G38-amide	1229
GVIINVKCKISRQCL[hArg]PCKEAGMRFGKCMNGKCACYGG-NH2	OSK1-hArg 16,E20,A34,Y36,G37,G38-amide	1230
GVIINVKCKISRQCL[Cit]PCKEAGMRFGKCMNGKCACYGG-NH2	OSK1-Cit 16,E20,A34,Y36,G37,G38-amide	1231
GVIINVKCKISRQCL[hCit]PCKEAGMRFGKCMNGKCHCYGG-NH2	OSK1- hCit 16,E20,A34,Y3,G37,G38-amide	1232
GVIINVKCKISRQCL[Dpr]PCKEAGMRFGKCMNGKCACYGG-NH2	OSK1-Dpr 16,E20,A34,Y36,G37,G38-amide	1233
GVIINVKCKISRQCL[Dab]PCKEAGMRFGKCMNGKCACYGG-NH2	OSK1-Dab 16,E20,A34,Y36,G37,G38-amide	1234
GVIINVKCKISRQCLOPCKEAGMRFGKCMNGKCHCGGG-NH2	OSK1-O16,E20,G36-38-amide	1235
GVIINVKCKISRQCL[hLys]PCKEAGMRFGKCMNGKCHCGGG-NH2	OSK1-hLys 16,E20,G36-38-amide	1236
GVIINVKCKISRQCL[hArg]PCKEAGMRFGKCMNGKCHCGGG-NH2	OSK1-hArg 16,E20,G36-38-amide	1237
GVIINVKCKISRQCL[Cit]PCKEAGMRFGKCMNGKCHCGGG-NH2	OSK1-Cit 16,E20,G36-38-amide	1238
GVIINVKCKISRQCL[hCit]PCKEAGMRFGKCMNGKCHCGGG-NH2	OSK1-hCit 16,E20,G36-38-amide	1239
GVIINVKCKISRQCL[Dpr]PCKEAGMRFGKCMNGKCHCGGG-NH2	OSK1-Dpr 16,E20,G36-38-amide	1240
GVIINVKCKISRQCLOPCKEAGMRFGKCMNGKCACGGG-NH2	OSK1-O16,E20,A34,G36-38-amide	1241
GVIINVKCKISRQCL[hLys]PCKEAGMRFGKCMNGKCACGGG-NH2	OSK1-hLys 16,E20,A34,G36-38-amide	1242
GVIINVKCKISRQCL[hArg]PCKEAGMRFGKCMNGKCACGGG-NH2	OSK1-hArg 16,E20,A34,G36-38-amide	1243
GVIINVKCKISRQCL[Cit]PCKEAGMRFGKCMNGKCACGGG-NH2	OSK1-Cit 16,E20,A34,G36-38-amide	1244
GVIINVKCKISRQCL[hCit]PCKEAGMRFGKCMNGKCACTP-NH2	Δ38 OSK1-hCit 16,E20,A34-amide	1245

GVIINVKCKISRQCL[Dpr]PCKEAGMRFGKCMNGKCACGGG-NH2	OSK1-Dpr 16,E20,A34,G36-38-amide	1246
GVIINVKCKISRQCL[Dab]PCKEAGMRFGKCMNGKCACGGG-NH2	OSK1-Dab 16,E20,A34,G36-38-amide	1247
GVIINVKCKISRQCLKPCK[Cpa]AGMRFGKCMNGKCACYGG-NH2	OSK1-K 16,CPA20,A34,Y36, G37,G38-amide	1248
GVIINVKCKISRQCLKPCK[Cpa]AGMRFGKCMNGKCACGGG-NH2	OSK1-K 16,CPA20,A34,G36-38-amide	1249
GVIINVKCKISRQCLKPCK[Cpa]AGMRFGKCMNGKCACY-NH2	Δ37-38OSK1-K 16,CPA20,A34,Y36 -amide	1250
Ac-GVIINVKCKISRQCLKPCKDAGMRFGKCMNGKCACYGG-NH2	Acetyl-OSK1-K 16,D20,A34,Y36,G3 7,G38-amide	1251
GVIINVKCKISRQCLKPCK[Aad]AGMRFGKCMNGKCACYGG-NH2	OSK1-K 16, Aad20,A34,Y36,G37 ,G38-amide	1252
GVIINVKCKISRQCLKPCK[Aad]AGMRFGKCMNGKCHCYGG-NH2	OSK1-K 16, Aad20,Y36,G37,G38 -amide	1253
GVIINVKCKISRQCLKPCK[Aad]AGMRFGKCMNGKCACYGG	OSK1-K 16, Aad20,A34,Y36,G37 ,G38	1254
GVIINVKCKISRQCLHPCKDAGMRFGKCMNGKCACYGG-NH2	OSK1-H 16,D20,A34,Y36,G3 7,G38-amide	1255
GVIINVKCKISRQCLHPCKDAGMRFGKCMNGKCACYGG	OSK1-H 16,D20,A34,Y36,G3 7,G38	1256
GVIINVKCKISRQCLHPCKDAGMRFGKCMNGKCACY-NH2	Δ37-38-OSK1-H 16,D20,A34,Y36-amide	1257
GVIINVKCKISRQCLHPCKDAGMRFGKCMNGKCHCYGG-NH2	OSK1-H 16,D20,A34,Y36,G3 7,G38-amide	1258
GVIINVKCKISRQCLHPCKDAGMRFGKCMNGKCHCYGG	OSK1-H 16,D20,A34,Y36,G3 7,G38	1259
GVIINVKCKISRQCLHPCKDAGMRFGKCMNGKCHCYPK	OSK1-H 16,D20,A34,Y36,	1260
GVIINVKCKISRQCLHPCKDAGMRFGKCMNGKCAC	Δ36-38 OSK1-H 16,D20,A34,Y36,	1261
GVIINVKCKISRQCLKPCKDAGMRFGKCMNGKCAC[1Nal]GG-NH2	OSK1-K 16,D20,A34,1Nal36, G37,G38-amide	1262
GVIINVKCKISRQCLKPCKDAGMRFGKCMNGKCAC[1Nal]PK-NH2	OSK1-K 16,D20,A34,1Nal36 -amide	1263

GVIINVKCKISRQCLKPCKDAGMRFGKCMNGKCAC[2Nal]GG-NH2	OSK1-K 16,D20,A34,2Nal36, G37,G38-amide	1264
GVIINVKCKISRQCLKPCKDAGMRFGKCMNGKCAC[Cha]GG-NH2	OSK1-K 16,D20,A34,Cha36, G37,G38-amide	1265
GVIINVKCKISRQCLKPCKDAGMRFGKCMNGKCAC[MePhe]GG-NH2	OSK1-K 16,D20,A34, MePhe36,G37,G38 -amide	1266
GVIINVKCKISRQCLKPCKDAGMRFGKCMNGKCAC[BiPhA]GG-NH2	OSK1-K 16,D20,A34, BiPhA36,G37,G38 -amide	1267
GVIINVKCKISRQCLKPCKDAGMRFGKCMNGKC[Aib]CYGG-NH2	OSK1-K 16,D20, Aib34,Y36,G37,G3 8-amide	1268
GVIINVKCKISRQCLKPCKDAGMRFGKCMNGKC[Abu]CYGG-NH2	OSK1-K 16,D20, Abu34,Y36,G37,G3 8-amide	1269
GVIINVKCKISRQCLKPCKDAGMRFGKCMNGKCAC[1Nal]	Δ37-38 OSK1-H 16,D20,A34,1Nal36, -amide	1270
GVIINVKCKISRQCLHPCKDAGMRFGKCMNGKCAC[1Nal]GG-NH2	OSK1-H 16,D20,A34, 1Nal36,G37,G38- amide	1271
GVIINVKCKISRQCLKPCKDAGMRFGKCMNGKCAC[4Bip]-NH2	Δ37-38 OSK1-H 16,D20,A34, 4Bip 36,-amide	1272
GVIINVKCKISRQCLHPCKDAGMRFGKCMNGKCAC[4Bip]GG-NH2	OSK1-H 16,D20,A34, 4Bip 36,G37,G38- amide	1273
GVIINVKCKISRQCLKPCKDAGMRFGKCMNGKCHCGGG	OSK1-K16,E20,G36-38	1274

Any of the sequences set forth in Table 7, can also be derivatized at either its N-terminal or C-terminal with a fatty acid having from 4 to 10 carbon atoms and from 0 to 2 carbon-carbon double bonds, or a derivative thereof such as an ω-amino-fatty acid. (E.g., Mouhat *et al.*, WO 2006/002850 A2, which is incorporated by reference in its entirety). Examples of such fatty acids include valeric acid or (for the C-terminal) ω-amino-valeric acid

Table 8—Pi2 peptide and PiP2 s peptide analog equences

Sequence/structure	Short-hand designation	SEQ ID NO:
TISCTNPKQCYPHCKKETGYPNAKCMNRKCKCFGR	Pi2	17
TISCTNPXQCYPHCKKETGYPNAKCMNRKCKCFGR	Pi2-X8	299
TISCTNPAQCYPHCKKETGYPNAKCMNRKCKCFGR	Pi2-A8	300

TISCTNPKQCYPHCXKETGYPNAKCMNRKCKCFGR	Pi2-X15	301
TISCTNPKQCYPHCAKETGYPNAKCMNRKCKCFGR	Pi2-A15	302
TISCTNPKQCYPHCKXETGYPNAKCMNRKCKCFGR	Pi2-X16	303
TISCTNPKQCYPHCKAETGYPNAKCMNRKCKCFGR	Pi2-A16	304
TISCTNPKQCYPHCKKETGYPNAXCMNRKCKCFGR	Pi2-X24	305
TISCTNPKQCYPHCKKETGYPNAACMNRKCKCFGR	Pi2-A24	306
TISCTNPKQCYPHCKKETGYPNAKCMNXKCKCFGR	Pi2-X28	307
TISCTNPKQCYPHCKKETGYPNAKCMNAKCKCFGR	Pi2-A28	308
TISCTNPKQCYPHCKKETGYPNAKCMNRXCKCFGR	Pi2-X29	309
TISCTNPKQCYPHCKKETGYPNAKCMNRACKCFGR	Pi2-A29	310
TISCTNPKQCYPHCKKETGYPNAKCMNRKCXCFGR	Pi2-X31	311
TISCTNPKQCYPHCKKETGYPNAKCMNRKCACFGR	Pi2-A31	312
TISCTNPKQCYPHCKKETGYPNAKCMNRKCKCFGX	Pi2-X35	313
TISCTNPKQCYPHCKKETGYPNAKCMNRKCKCFGA	Pi2-A35	314
TISCTNPKQCYPHCKKETGYPNAKCMNRKCKCFG	Pi2-d35	315

Table 9—Anuroctoxin (AnTx) peptide and peptide analog sequences

Sequence/structure	Short-hand designation	SEQ ID NO:
ZKECTGPQHCTNFCRKNKCTHGKCMNRKCKCFNCK	Anuroctoxin (AnTx)	62
KECTGPQHCTNFCRKNKCTHGKCMNRKCKCFNCK	AnTx-d1	316
XECTGPQHCTNFCRKNKCTHGKCMNRKCKCFNCK	AnTx-d1,X2	317
AECTGPQHCTNFCRKNKCTHGKCMNRKCKCFNCK	AnTx-d1,A2	318

Table 10—Noxiustoxin (NTX) peptide and NTX peptide analog sequences

Sequence/structure	Short-hand designation	SEQ ID NO:
TIINVKCTSPKQCSKPCKELYGSSAGAKCMNGKCKCYNN	NTX	30
TIINVACTSPKQCSKPCKELYGSSAGAKCMNGKCKCYNN	NTX-A6	319
TIINVKCTSPKQCSKPCKELYGSSRGAKCMNGKCKCYNN	NTX-R25	320
TIINVKCTSSKQCSKPCKELYGSSAGAKCMNGKCKCYNN	NTX-S10	321
TIINVKCTSPKQCWKPCKELYGSSAGAKCMNGKCKCYNN	NTX-W14	322
TIINVKCTSPKQCSKPCKELYGSSGAKCMNGKCKCYNN	NTX-A25d	323
TIINVKCTSPKQCSKPCKELFGVDRGKCMNGKCKCYNN	NTX-IbTx1	324
TIINVKCTSPKQCWKPCKELFGVDRGKCMNGKCKCYN	NTX-IBTX2	325

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Table 11—Kaliotoxin1 (KTX1) peptide and KTX1 peptide analog sequences

Sequence/structure	Short-hand designation	SEQ ID NO:
GVEINVKCSGSPQCLKPCKDAGMRFGKCMNRKCHCTPK	KTX1	24
VRIPVSCKHSGQCLKPCKDAGMRFGKCMNGKCDCTPK	KTX2	326
GVEINVSCSGSPQCLKPCKDAGMRFGKCMNRKCHCTPK	KTX1-S7	327
GVEINVACSGSPQCLKPCKDAGMRFGKCMNRKCHCTPK	KTX1-A7	328

Table 12—IKCa1 inhibitor peptide sequences

Sequence/structure	Short-hand designation	SEQ ID NO:
VSCTGSKDCYAPCRKQTGCPNAKCINKSCKCYGC	MTX	20
QFTNVSCTTSKECWSVCQRLHNTSRGKCMNKKCRCYS	ChTx	36
QFTQESCTASNQCWSICKRLHNTNRGKCMNKKCRCYS	ChTx-Lq2	329

Table 13—Maurotoxin (MTx) peptide amd MTx peptide analog sequences

Sequence/structure	Short-hand designation	SEQ ID NO:
VSCTGSKDCYAPCRKQTGCPNAKCINKSCKCYGC	MTX	20
VSCAGSKDCYAPCRKQTGCPNAKCINKSCKCYGC	MTX-A4	330
VSCTGAKDCYAPCRKQTGCPNAKCINKSCKCYGC	MTX-A6	331
VSCTGSADCYAPCRKQTGCPNAKCINKSCKCYGC	MTX-A7	332
VSCTGSKDCAAPCRKQTGCPNAKCINKSCKCYGC	MTX-A10	333
VSCTGSKDCYAPCQKQTGCPNAKCINKSCKCYGC	MTX-Q14	334
VSCTGSKDCYAPCRQQTGCPNAKCINKSCKCYGC	MTX-Q15	335
VSCTGSKDCYAPCQQQTGCPNAKCINKSCKCYGC	MTX-Q14,15	336
VSCTGSKDCYAPCRKQTGCPNAKCINKSCKCYAC	MTX-A33	337
VSCTGSKDCYAPCRKQTGCPYGKCMNRKCKCNRC	MTX-HsTx1	338
VSCTGSKDCYAACRKQTGCANAKCINKSCKCYGC	MTX-A12,20	339
VSCTGSKDCYAPCRKQTGX^{M19}PNAKCINKSCKCYGX^{M34}	MTX-X19, 34	340
VSCTGSKDCYAPCRKQTGSPNAKCINKSCKCYGS	MTX-S19,34	341
VSCTGSADCYAPCRKQTGCPNAKCINKSCKCYGC	MTX-A7	342
VVIGQRCTGSKDCYAPCRKQTGCPNAKCINKSCKCYGC	TsK-MTX	343
VSCRGSKDCYAPCRKQTGCPNAKCINKSCKCYGC	MTX-R4	1301
VSCGGSKDCYAPCRKQTGCPNAKCINKSCKCYGC	MTX-G4	1302
VSCTTSKDCYAPCRKQTGCPNAKCINKSCKCYGC	MTX-T5	1304
VSCTASKDCYAPCRKQTGCPNAKCINKSCKCYGC	MTX-A5	1305
VSCTGTKDCYAPCRKQTGCPNAKCINKSCKCYGC	MTX-T6	1306
VSCTGPKDCYAPCRKQTGCPNAKCINKSCKCYGC	MTX-P6	1307
VSCTGSKDCGAPCRKQTGCPNAKCINKSCKCYGC	MTX-G10	1309
VSCTGSKDCYRPCRKQTGCPNAKCINKSCKCYGC	MTX-R11	1311
VSCTGSKDCYDPCRKQTGCPNAKCINKSCKCYGC	MTX-D11	1312
VSCTGSKDCYAPCRKRTGCPNAKCINKSCKCYGC	MTX-R16	1315
VSCTGSKDCYAPCRKETGCPNAKCINKSCKCYGC	MTX-E16	1316
VSCTGSKDCYAPCRKQTGCPYAKCINKSCKCYGC	MTX-Y21	1317
VSCTGSKDCYAPCRKQTGCPNSKCINKSCKCYGC	MTX-S22	1318
VSCTGSKDCYAPCRKQTGCPNGKCINKSCKCYGC	MTX-G22	1319
VSCTGSKDCYAPCRKQTGCPNAKCINRSCKCYGC	MTX-R27	1320
VSCTGSKDCYAPCRKQTGCPNAKCINKTCKCYGC	MTX-T28	1321
VSCTGSKDCYAPCRKQTGCPNAKCINKMCKCYGC	MTX-M28	1322
VSCTGSKDCYAPCRKQTGCPNAKCINKKCKCYGC	MTX-K28	1323
VSCTGSKDCYAPCRKQTGCPNAKCINKSCKCNGC	MTX-N32	1324
VSCTGSKDCYAPCRKQTGCPNAKCINKSCKCYRC	MTX-R33	1325
VSCTGSKDCYAPCRKQTGCPNAKCINKSCKCYGCS	MTX-S35	1326
SCTGSKDCYAPCRKQTGCPNAKCINKSCKCYGC	MTX-d1	1327
SCTGSKDCYAPCRKQTGCPNAKCINKSCKCYGCS	MTX-S35 d1	1328
VSCTGSKDCYAPCAKQTGCPNAKCINKSCKCYGC	MTX-A14	1329

VSCTGSKDCYAPCRAQTGCPNAKCINKSCKCYGC	MTX-A15	1330
VSCTGSKDCYAPCRKQTGCPNAACINKSCKCYGC	MTX-A23	1331
VSCTGSKDCYAPCRKQTGCPNAKCINASCKCYGC	MTX-A27	1332
VSCTGSKDCYAPCRKQTGCPNAKCINKSCACYGC	MTX-A30	1333
VSCTGSKDCYAPCRKQTGCPNAKCINKSCKCAGC	MTX-A32	1334
ASCTGSKDCYAPCRKQTGCPNAKCINKSCKCYGC	MTX-A1	1335
MSCTGSKDCYAPCRKQTGCPNAKCINKSCKCYGC	MTX-M1	1336

In Table 13 and throughout this specification, X^{m19} and X^{m34} are each independently nonfunctional residues.

Table 14—Charybdotoxin(ChTx) peptide and ChTx peptide analog sequences

Sequence/structure	Short-hand designation	SEQ ID NO:
QFTNVSCTTSKECWSVCQRLHNTSRGKCMNKKCRCYS	ChTx	36
QFTNVSCTTSKECWSVCQRLHNTSRGKCMNKECRCYS	ChTx-E32	59
QFTNVSCTTSKECWSVCQRLHNTSRGKCMNKDCRCYS	ChTx-D32	344
CTTSKECWSVCQRLHNTSRGKCMNKKCRCYS	ChTx-d1-d6	345
QFTNVSCTTSKECWSVCQRLFGVDRGKCMGKKCRCYQ	ChTx-IbTx	346
QFTNVSCTTSKECWSVCQRLHNTSRGKCMNGKCRCYS	ChTx-G31	1369
QFTNVSCTTSKECLSVCQRLHNTSRGKCMNKKCRCYS	ChTx-L14	1370
QFTNVSCTTSKECASVCQRLHNTSRGKCMNKKCRCYS	ChTx-A14	1371
QFTNVSCTTSKECWAVCQRLHNTSRGKCMNKKCRCYS	ChTx-A15	1372
QFTNVSCTTSKECWPVCQRLHNTSRGKCMNKKCRCYS	ChTx-P15	1373
QFTNVSCTTSKECWSACQRLHNTSRGKCMNKKCRCYS	ChTx-A16	1374
QFTNVSCTTSKECWSPCQRLHNTSRGKCMNKKCRCYS	ChTx-P16	1375
QFTNVSCTTSKECWSVCQRLHNTSAGKCMNKKCRCYS	ChTx-A25	1376
QFTNVACTTSKECWSVCQRLHNTSRGKCMNKKCRCYS	ChTx-A6	1377
QFTNVKCTTSKECWSVCQRLHNTSRGKCMNKKCRCYS	ChTx-K6	1378
QFTNVSCTTAKECWSVCQRLHNTSRGKCMNKKCRCYS	ChTx-A10	1379
QFTNVSCTTPKECWSVCQRLHNTSRGKCMNKKCRCYS	ChTx-P10	1380
QFTNVSCTTSKACWSVCQRLHNTSRGKCMNKKCRCYS	ChTx-A12	1381
QFTNVSCTTSKQCWSVCQRLHNTSRGKCMNKKCRCYS	ChTx-Q12	1382

AFTNVSCTTSKECWSVCQRLHNTSRGKCMNKKCRCYS	ChTx-A1	1383
TFTNVSCTTSKECWSVCQRLHNTSRGKCMNKKCRCYS	ChTx-T1	1384
QATNVSCTTSKECWSVCQRLHNTSRGKCMNKKCRCYS	ChTx-A2	1385
QITNVSCTTSKECWSVCQRLHNTSRGKCMNKKCRCYS	ChTx-I2	1386
QFANVSCTTSKECWSVCQRLHNTSRGKCMNKKCRCYS	ChTx-A3	1387
QFINVSCTTSKECWSVCQRLHNTSRGKCMNKKCRCYS	ChTx-I3	1388
TIINVKCTSPKQCLPPCKAQFGTSRGKCMNKKCRCYSP	ChTx-MgTx	1389
TIINVSCTSPKQCLPPCKAQFGTSRGKCMNKKCRCYSP	ChTx-MgTx-b	1390

Table 15—SKCa inhibitor peptide sequences

Sequence/structure	Short-hand designation	SEQ ID NO:
CNCKAPETALCARRCQQHG	Apamin	68
AFCNLRMCQLSCRSLGLLGKCIGDKCECVKH	ScyTx	51
AVCNLKRCQLSCRSLGLLGKCIGDKCECVKHG	BmP05	50
TVCNLRRCQLSCRSLGLLGKCIGVKCECVKH	P05	52
AFCNLRRCELSCRSLGLLGKCIGEECKCVPY	Tamapin	53
VSCEDCPEHCSTQKAQAKCDNDKCVCEPI	P01	16
VVIGQRCYRSPDCYSACKKLVGKATGKCTNGRCDC	TsK	47

Table 16—Apamin peptide and peptide analog inhibitor sequences

Sequence/structure	Short-hand designation	SEQ ID NO:
CNCKAPETALCARRCQQHG	Apamin (Ap)	68
CNCXAPETALCARRCQQHG	Ap-X4	348
CNCAAPETALCARRCQQHG	Ap-A4	349
CNCKAPETALCAXRCQQHG	Ap-X13	350
CNCKAPETALCAARCQQHG	Ap-A13	351
CNCKAPETALCARXCQQHG	Ap-X14	352
CNCKAPETALCARACQQHG	Ap-A14	353

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Table 17—Scyllatoxin (ScyTx), BmP05, P05, Tamapin, P01 peptide and peptide analog inhibitor sequences

Sequence/structure	Short-hand designation	SEQ ID NO:
AFCNLRMCQLSCRSLGLLGKCIGDKCECVKH	ScyTx	51
AFCNLRRCQLSCRSLGLLGKCIGDKCECVKH	ScyTx-R7	354
AFCNLRMCQLSCRSLGLLGKCMGKKCRCVKH	ScyTx-IbTx	355
AFSNLRMCQLSCRSLGLLGKSIGDKCECVKH	ScyTx-C/S	356
AFCNLRRCELSCRSLGLLGKCIGEECKCVPY	Tamapin	53

Table 18—BKCa inhibitor peptide sequences

Sequence/structure	Short-hand designation	SEQ ID NO:
QFTDVDCSVSKECWSVCKDLFGVDRGKCMGKKCRCYQ	IbTx	38
TFIDVDCTVSKECWAPCKAAFGVDRGKCMGKKCKCYV	Slotoxin (SloTx)	39
QFTDVKCTGSKQCWPVCKQMFGKPNGKCMNGKCRCYS	BmTx1	40
WCSTCLDLACGASRECYDPCFKAFGRAHGKCMNNKCRCYTN	BuTx	41
FGLIDVKCFASSECWTACKKVTGSGQGKCQNNQCRCY	MartenTx	35
ITINVKCTSPQQCLRPCKDRFGQHAGGKCINGKCKCYP	CllTx1	29

Table 19—IbTx, Slotoxin, BmTx1, & BuTX (Slotoxin family) peptide and peptide analog inhibitor sequences

Sequence/structure	Short-hand designation	SEQ ID NO:
QFTDVDCSVSKECWSVCKDLFGVDRGKCMGKKCRCYQ	IbTx	38
QFTDVDCSVSXECWSVCKDLFGVDRGKCMGKKCRCYQ	IbTx-X11	357
QFTDVDCSVSAECWSVCKDLFGVDRGKCMGKKCRCYQ	IbTx-A11	358
QFTDVDCSVSKECWSVCXDLFGVDRGKCMGKKCRCYQ	IbTx-X18	359
QFTDVDCSVSKECWSVCADLFGVDRGKCMGKKCRCYQ	IbTx-A18	360
QFTDVDCSVSKECWSVCKDLFGVDXGKCMGKKCRCYQ	IbTx-X25	361
QFTDVDCSVSKECWSVCKDLFGVDAGKCMGKKCRCYQ	IbTx-A25	362
QFTDVDCSVSKECWSVCKDLFGVDRGXCMGKKCRCYQ	IbTx-X27	363
QFTDVDCSVSKECWSVCKDLFGVDRGACMGKKCRCYQ	IbTx-A27	364
QFTDVDCSVSKECWSVCKDLFGVDRGKCMGXKCRCYQ	IbTx-X31	365
QFTDVDCSVSKECWSVCKDLFGVDRGKCMGAKCRCYQ	IbTx-A31	366
QFTDVDCSVSKECWSVCKDLFGVDRGKCMGKXCRCYQ	IbTx-X32	367
QFTDVDCSVSKECWSVCKDLFGVDRGKCMGKACRCYQ	IbTx-A32	368
QFTDVDCSVSKECWSVCKDLFGVDRGKCMGKKCXCYQ	IbTx-X34	369
QFTDVDCSVSKECWSVCKDLFGVDRGKCMGKKCACYQ	IbTx-A34	370
QFTDVKCTGSKQCWPVCKQMFGKPNGKCMNGKCRCYS	BmTx1	371
QFTDVXCTGSKQCWPVCKQMFGKPNGKCMNGKCRCYS	BmTx1-X6	372
QFTDVACTGSKQCWPVCKQMFGKPNGKCMNGKCRCYS	BmTx1-A6	373
QFTDVKCTGSXQCWPVCKQMFGKPNGKCMNGKCRCYS	BmTx1-X11	374
QFTDVKCTGSAQCWPVCKQMFGKPNGKCMNGKCRCYS	BmTx1-A11	375
QFTDVKCTGSKQCWPVCXQMFGKPNGKCMNGKCRCYS	BmTx1-X18	376
QFTDVKCTGSKQCWPVCAQMFGKPNGKCMNGKCRCYS	BmTx1-A18	377

QFTDVKCTGSKQCWPVCKQMFGXPNGKCMNGKCRCYS	BmTx1-X23	378
QFTDVKCTGSKQCWPVCKQMFGAPNGKCMNGKCRCYS	BmTx1-A23	379
QFTDVKCTGSKQCWPVCKQMFGKPNGXCMNGKCRCYS	BmTx1-X27	380
QFTDVKCTGSKQCWPVCKQMFGKPNGACMNGKCRCYS	BmTx1-A27	381
QFTDVKCTGSKQCWPVCKQMFGKPNGKCMNGXCRCYS	BmTx1-X32	382
QFTDVKCTGSKQCWPVCKQMFGKPNGKCMNGARCYS	BmTx1-A32	383
QFTDVKCTGSKQCWPVCKQMFGKPNGKCMNGKCXYS	BmTx1-X34	384
QFTDVKCTGSKQCWPVCKQMFGKPNGKCMNGKCAYS	BmTx1-A34	385
WCSTCLDLACGASRECYDPCFKAFGRAHGKCMNNKCRCYTN	BuTx	386
WCSTCLDLACGASXCYDPCFKAFGRAHGKCMNNKCRCYTN	BuTx-X14	387
WCSTCLDLACGASACYDPCFKAFGRAHGKCMNNKCRCYTN	BuTx-A14	388
WCSTCLDLACGASRECYDPCFXFGRAHGKCMNNKCRCYTN	BuTx-X22	389
WCSTCLDLACGASRECYDPCFAGRAHGKCMNNKCRCYTN	BuTx-A22	390
WCSTCLDLACGASRECYDPCFKAFGXHGKCMNNKCRCYTN	BuTx-X26	391
WCSTCLDLACGASRECYDPCFKAFGAHGKCMNNKCRCYTN	BuTx-A26	392
WCSTCLDLACGASRECYDPCFKAFGRAHGXMNNKCRCYTN	BuTx-X30	393
WCSTCLDLACGASRECYDPCFKAFGRAHGAMNNKCRCYTN	BuTx-A30	394
WCSTCLDLACGASRECYDPCFKAFGRAHGKCMNNXRCYTN	BuTx-X35	395
WCSTCLDLACGASRECYDPCFKAFGRAHGKCMNNARCYTN	BuTx-A35	396
WCSTCLDLACGASRECYDPCFKAFGRAHGKCMNNKCXYTN	BuTx-X37	397
WCSTCLDLACGASRECYDPCFKAFGRAHGKCMNNKCAYTN	BuTx-A37	398

Table 20—Martentoxin peptide and peptide analog inhibitor sequences

Sequence/structure	Short-hand designation	SEQ ID NO:
FGLIDVKCFASSECWTACKKVTGSGQGKCQNNQCRCY	MartenTx	35
FGLIDVXCFASSECWTACKKVTGSGQGKCQNNQCRCY	MartenTx-X7	399
FGLIDVACFASSECWTACKKVTGSGQGKCQNNQCRCY	MartenTx-A7	400
FGLIDVKCFASSECWTACXKVTGSGQGKCQNNQCRCY	MartenTx-X19	401
FGLIDVKCFASSECWTACAKVTGSGQGKCQNNQCRCY	MartenTx-A19	402
FGLIDVKCFASSECWTACKXVTGSGQGKCQNNQCRCY	MartenTx-X20	403
FGLIDVKCFASSECWTACKAVTGSGQGKCQNNQCRCY	MartenTx-A20	404
FGLIDVKCFASSECWTACKKVTGSGQGXCQNNQCRCY	MartenTx-X28	405
FGLIDVKCFASSECWTACKKVTGSGQGACQNNQCRCY	MartenTx-A28	406
FGLIDVKCFASSECWTACKKVTGSGQGKCQNNQCXCY	MartenTx-X35	407
FGLIDVKCFASSECWTACKKVTGSGQGKCQNNQCACY	MartenTx-A35	408

Table 21—N type Ca^{2+} channel inhibitor peptide sequences

Sequence/structure	Short-hand designation	SEQ ID NO:
CKGKGAKCSRLMYDCCTGSCRSGKC	MVIIA	65
CKSPGSSCSPTSYNCCRSCNPYTKRCY	GVIA	64
CKSKGAKCSKLMYDCCTGSCSGTVGRC	CVIA	409
CKLKGQSCRKTSYDCCSGSCGRSGKC	SVIB	347
AEKDCIAPGAPCFGTDKPCCNPRAWCSSYANKCL	Ptu1	66
CKGKGASCRKTMYDCCRGSCRSGRC	CVIB	1364
CKGKGQSCSKLMYDCCTGSCSRRGKC	CVIC	1365
CKSKGAKCSKLMYDCCSGSCSGTVGRC	CVID	1366
CLSXGSSCSXTSYNCCRSCNXYSRKCY	TVIA	1367

Table 22—ωMVIIA peptide and peptide analog inhibitor sequences

Sequence/structure	Short-hand designation	SEQ ID NO:
CKGKGAKCSRLMYDCCTGSCRSGKC	MVIIA	65
CXGKGAKCSRLMYDCCTGSCRSGKC	MVIIA-X2	410
CAGKGAKCSRLMYDCCTGSCRSGKC	MVIIA-A2	411
CKGXGAKCSRLMYDCCTGSCRSGKC	MVIIA-X4	412
CKGAGAKCSRLMYDCCTGSCRSGKC	MVIIA-A4	413
CKGKGAXCSRLMYDCCTGSCRSGKC	MVIIA-X7	414
CKGKGAACSRLMYDCCTGSCRSGKC	MVIIA-A7	415
CKGKGAKCSXLMYDCCTGSCRSGKC	MVIIA-X10	416
CKGKGAKCSALMYDCCTGSCRSGKC	MVIIA-A10	417
CKGKGAKCSRLMYDCCTGSCXSGKC	MVIIA-X21	418
CKGKGAKCSRLMYDCCTGSCASGKC	MVIIA-A21	419
CKGKGAKCSRLMYDCCTGSCRSGXC	MVIIA-X24	420
CKGKGAKCSRLMYDCCTGSCRSGAC	MVIIA-A24	421

Table 23—ωGVIA peptide and peptide analog inhibitor sequences

Sequence/structure	Short-hand designation	SEQ ID NO:
CKSPGSSCSPTSYNCCRSCNPYTKRCY	GVIA	64
CXSPGSSCSPTSYNCCRSCNPYTKRCY	GVIA-X2	422
CASPGSSCSPTSYNCCRSCNPYTKRCY	GVIA-A2	423
CKSPGSSCSPTSYNCCXSCNPYTKRCY	GVIA-X17	424
CKSPGSSCSPTSYNCCASCNPYTKRCY	GVIA-A17	425
CKSPGSSCSPTSYNCCRSCNPYTXRCY	GVIA-X24	426
CKSPGSSCSPTSYNCCRSCNPYTARCY	GVIA-A24	427
CKSPGSSCSPTSYNCCRSCNPYTKXCY	GVIA-X25	428
CKSPGSSCSPTSYNCCRSCNPYTKACY	GVIA-A25	429

Table 24—Ptu1 peptide and peptide analog inhibitor sequences

Sequence/structure	Short-hand designation	SEQ ID NO:
AEKDCIAPGAPCFGTDKPCCNPRAWCSSYANKCL	Ptu1	66
AEXDCIAPGAPCFGTDKPCCNPRAWCSSYANKCL	Ptu1-X3	430
AEADCIAPGAPCFGTDKPCCNPRAWCSSYANKCL	Ptu1-A3	431
AEKDCIAPGAPCFGTDXPCCNPRAWCSSYANKCL	Ptu1-X17	432
AEKDCIAPGAPCFGTDAPCCNPRAWCSSYANKCL	Ptu1-A17	433
AEKDCIAPGAPCFGTDKPCCNPXAWCSSYANKCL	Ptu1-X23	434
AEKDCIAPGAPCFGTDKPCCNPAAWCSSYANKCL	Ptu1-A23	435
AEKDCIAPGAPCFGTDKPCCNPRAWCSSYANXCL	Ptu1-X32	436
AEKDCIAPGAPCFGTDKPCCNPRAWCSSYANACL	Ptu1-A32	437

Table 25— Thrixopelma pruriens (ProTx1) and ProTx1 peptide analogs and other T type Ca^{2+} channel inhibitor peptide sequences

Sequence/structure	Short-hand designation	SEQ ID NO:
ECRYWLGGCSAGQTCCKHLVCSRRHGWCVWDGTFS	ProTx1	56
ECXYWLGGCSAGQTCCKHLVCSRRHGWCVWDGTFS	ProTx1-X3	438
ECAYWLGGCSAGQTCCKHLVCSRRHGWCVWDGTFS	ProTx1-A3	439
ECRYWLGGCSAGQTCCXHLVCSRRHGWCVWDGTFS	ProTx1-X17	440
ECRYWLGGCSAGQTCCAHLVCSRRHGWCVWDGTFS	ProTx1-A17	441
ECRYWLGGCSAGQTCCKHLVCSXRHGWCVWDGTFS	ProTx1-X23	442
ECRYWLGGCSAGQTCCKHLVCSARHGWCVWDGTFS	ProTx1-A23	443
ECRYWLGGCSAGQTCCKHLVCSRXHGWCVWDGTFS	ProTx1-X24	444
ECRYWLGGCSAGQTCCKHLVCSRAHGWCVWDGTFS	ProTx1-A24	445
KIDGYPVDYW NCKRICWYNN KYCNDLCKGL KADSGYCWGW TLSCYCQGLP DNARIKRSGR CRA	Kurtoxin	1276

Table 26— BeKM1 M current inhibitor peptide and BeKM1 peptide analog sequences

Sequence/structure	Short-hand designation	SEQ ID NO:
RPTDIKCSESYQCFPVCKSRFGKTNGRCVNGFCDCF	BeKM1	63
PTDIKCSESYQCFPVCKSRFGKTNGRCVNGFCDCF	BeKM1-d1	446
XPTDIKCSESYQCFPVCKSRFGKTNGRCVNGFCDCF	BeKM1-X1	447
APTDIKCSESYQCFPVCKSRFGKTNGRCVNGFCDCF	BeKM1-A1	448
RPTDIXCSESYQCFPVCKSRFGKTNGRCVNGFCDCF	BeKM1-X6	449
RPTDIACSESYQCFPVCKSRFGKTNGRCVNGFCDCF	BeKM1-A6	450
RPTDIKCSESYQCFPVCXSRFGKTNGRCVNGFCDCF	BeKM1-X18	451
RPTDIKCSESYQCFPVCASRFGKTNGRCVNGFCDCF	BeKM1-A18	452
RPTDIKCSESYQCFPVCKSXFGKTNGRCVNGFCDCF	BeKM1-X20	453
RPTDIKCSESYQCFPVCKSAFGKTNGRCVNGFCDCF	BeKM1-A20	454
RPTDIKCSESYQCFPVCKSRFGXTNGRCVNGFCDCF	BeKM1-X23	455
RPTDIKCSESYQCFPVCKSRFGATNGRCVNGFCDCF	BeKM1-A23	456
RPTDIKCSESYQCFPVCKSRFGKTNGXCVNGFCDCF	BeKM1-X27	457
RPTDIKCSESYQCFPVCKSRFGKTNGACVNGFCDCF	BeKM1-A27	458

Table 27—Na^+ channel inhibitor peptide sequences

Sequence/structure	Short-hand designation	SEQ ID NO:
QRCCNGRRGCSSRWCRDHSRCC	SmIIIa	459
RDCCTOOKKCKDRQCKOQRCCA	μ-GIIIA	460
RDCCTOORKCKDRRCKOMRCCA	μ-GIIIB	461
ZRLCCGFOKSCRSRQCKOHRCC	μ-PIIIA	462
ZRCCNGRRGCSSRWCRDHSRCC	μ-SmIIIA	463
ACRKKWEYCIVPIIGFIYCCPGLICGPFVCV	μO-MrVIA	464
ACSKKWEYCIVPIIGFIYCCPGLICGPFVCV	μO-MrVIB	465
EACYAOGTFCGIKOGLCCSEFCLPGVCFG	δ-PVIA	466
DGCSSGGTFCGIHOGLCCSEFCFLWCITFID	δ–SVIE	467
WCKQSGEMCNLLDQNCCDGYCIVLVCT	δ-TxVIA	468
VKPCRKEGQLCDPIFQNCCRGWNCVLFCV	δ-GmVIA	469

Table 28—Cl- channel inhibitor peptide sequences

Sequence/structure	Short-hand designation	SEQ ID NO:
MCMPCFTTDHQMARKCDDCCGGKGRGKCYGPQCLCR	CTX	67
MCMPCFTTDHQMAXKCDDCCGGKGRGKCYGPQCLCR	CTX-X14	470
MCMPCFTTDHQMAAKCDDCCGGKGRGKCYGPQCLCR	CTX-A14	471
MCMPCFTTDHQMARXCDDCCGGKGRGKCYGPQCLCR	CTX-X15	472
MCMPCFTTDHQMARACDDCCGGKGRGKCYGPQCLCR	CTX-A15	473
MCMPCFTTDHQMARKCDDCCGGXGRGKCYGPQCLCR	CTX-X23	474
MCMPCFTTDHQMARKCDDCCGGAGRGKCYGPQCLCR	CTX-A23	475
MCMPCFTTDHQMARKCDDCCGGKGXGKCYGPQCLCR	CTX-X25	476
MCMPCFTTDHQMARKCDDCCGGKGAGKCYGPQCLCR	CTX-A25	477
MCMPCFTTDHQMARKCDDCCGGKGRGXCYGPQCLCR	CTX-X27	478
MCMPCFTTDHQMARKCDDCCGGKGRGACYGPQCLCR	CTX-A27	479
MCMPCFTTDHQMARKCDDCCGGKGRGKCYGPQCLCX	CTX-X36	480
MCMPCFTTDHQMARKCDDCCGGKGRGKCYGPQCLCA	CTX-A36	481
MCMPCFTTDHQMARKCDDCCGGKGRGKCYGPQCLC	CTX-d36	482
QTDGCGPCFTTDANMARKCRECCGGNGKCFGPQCLCNRE	Bm-12b	483
QTDGCGPCFTTDANMAXKCRECCGGNGKCFGPQCLCNRE	Bm-12b-X17	484
QTDGCGPCFTTDANMAAKCRECCGGNGKCFGPQCLCNRE	Bm-12b-A17	485
QTDGCGPCFTTDANMARXCRECCGGNGKCFGPQCLCNRE	Bm-12b-X18	486
QTDGCGPCFTTDANMARACRECCGGNGKCFGPQCLCNRE	Bm-12b-A18	487
QTDGCGPCFTTDANMARKCXECCGGNGKCFGPQCLCNRE	Bm-12b-X20	488
QTDGCGPCFTTDANMARKCAECCGGNGKCFGPQCLCNRE	Bm-12b-A20	489
QTDGCGPCFTTDANMARKCRECCGGNGXCFGPQCLCNRE	Bm-12b-X28	490
QTDGCGPCFTTDANMARKCRECCGGNGACFGPQCLCNRE	Bm-12b-A28	491
QTDGCGPCFTTDANMARKCRECCGGNGKCFGPQCLCNXE	Bm-12b-X38	492
QTDGCGPCFTTDANMARKCRECCGGNGKCFGPQCLCNAE	Bm-12b-A38	493

Table 29—Kv2.1 inhibitor peptide sequences

Sequence/structure	Short-hand designation	SEQ ID NO:
ECRYLFGGCKTTSDCCKHLGCKFRDKYCAWDFTFS	HaTx1	494
ECXYLFGGCKTTSDCCKHLGCKFRDKYCAWDFTFS	HaTx1-X3	495
ECAYLFGGCKTTSDCCKHLGCKFRDKYCAWDFTFS	HaTx1-A3	496
ECRYLFGGCXTTSDCCKHLGCKFRDKYCAWDFTFS	HaTx1-X10	497
ECRYLFGGCATTSDCCKHLGCKFRDKYCAWDFTFS	HaTx1-A10	498
ECRYLFGGCKTTSDCCXHLGCKFRDKYCAWDFTFS	HaTx1-X17	499
ECRYLFGGCKTTSDCCAHLGCKFRDKYCAWDFTFS	HaTx1-A17	500
ECRYLFGGCKTTSDCCKHLGCXFRDKYCAWDFTFS	HaTx1-X22	501
ECRYLFGGCKTTSDCCKHLGCAFRDKYCAWDFTFS	HaTx1-A22	502
ECRYLFGGCKTTSDCCKHLGCKFXDKYCAWDFTFS	HaTx1-X24	503
ECRYLFGGCKTTSDCCKHLGCKFADKYCAWDFTFS	HaTx1-A24	504
ECRYLFGGCKTTSDCCKHLGCKFRDXYCAWDFTFS	HaTx1-X26	505
ECRYLFGGCKTTSDCCKHLGCKFRDAYCAWDFTFS	HaTx1-A26	506

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Table 30—Kv4.3 & Kv4.2 inhibitor peptide sequences

Sequence/structure	Short-hand designation	SEQ ID NO:
YCQKWMWTCDEERKCCEGLVCRLWCKRIINM	PaTx2	57
YCQXWMWTCDEERKCCEGLVCRLWCKRIINM	PaTx2-X4	507
YCQAWMWTCDEERKCCEGLVCRLWCKRIINM	PaTx2-A4	508
YCQKWMWTCDEEXKCCEGLVCRLWCKRIINM	PaTx2-X13	509
YCQKWMWTCDEEAKCCEGLVCRLWCKRIINM	PaTx2-A13	510
YCQKWMWTCDEERXCCEGLVCRLWCKRIINM	PaTx2-X14	511
YCQKWMWTCDEERACCEGLVCRLWCKRIINM	PaTx2-A14	512
YCQKWMWTCDEERKCCEGLVCXLWCKRIINM	PaTx2-X22	513
YCQKWMWTCDEERKCCEGLVCALWCKRIINM	PaTx2-A22	514
YCQKWMWTCDEERKCCEGLVCRLWCXRIINM	PaTx2-X26	515
YCQKWMWTCDEERKCCEGLVCRLWCARIINM	PaTx2-A26	516
YCQKWMWTCDEERKCCEGLVCRLWCKXIINM	PaTx2-X27	517
YCQKWMWTCDEERKCCEGLVCRLWCKAIINM	PaTx2-A27	518

Table 31—nACHR channel inhibitor peptide sequences

Sequence/structure	Short-hand designation	SEQ ID NO:
GCCSLPPCAANNPDYC	PnIA	519
GCCSLPPCALNNPDYC	PnIA-L10	520
GCCSLPPCAASNPDYC	PnIA-S11	521
GCCSLPPCALSNPDYC	PnIB	522
GCCSLPPCAASNPDYC	PnIB-A10	523
GCCSLPPCALNNPDYC	PnIB-N11	524
GCCSNPVCHLEHSNLC	MII	525
GRCCHPACGKNYSC	α-MI	526
RD(hydroxypro)CCYHPTCNMSNPQIC	α-EI	527
GCCSYPPCFATNPDC	α-AuIB	528
RDPCCSNPVCTVHNPQIC	α-PIA	529
GCCSDPRCAWRC	α-ImI	530
ACCSDRRCRWRC	α-ImII	531
ECCNPACGRHYSC	α-GI	532
GCCGSY(hydroxypro)NAACH(hydroxypro)CSCKDR (hydroxypro)SYCGQ	αA-PIVA	533
GCCPY(hydroxypro)NAACH(hydroxypro)CGCKVGR (hydroxypro)(hydroxypro)YCDR(hydroxypro)S GG	αA-EIVA	534
H(hydroxypro)(hydroxypro)CCLYGKCRRY(hydro xypro)GCSSASCCQR	ψ-PIIIE	535
GCCSDPRCNMNNPDYC	EpI	536
GCCSHPACAGNNQHIC	GIC	537
IRD(γ-carboxyglu) CCSNPACRVNN (hydroxypro)HVC	GID	538
GGCCSHPACAANNQDYC	AnIB	539
GCCSYPPCFATNSDYC	AuIA	540
GCCSYPPCFATNSGYC	AuIC	541

Table 32- Agelenopsis aperta (Agatoxin) toxin peptides and peptide analogs and other Ca^{2+} channel inhibiter peptides

Sequence/structure	Short-hand designation	SEQ ID NO:
KKKCIAKDYG RCKWGGTPCC RGRGCICSIM GTNCECKPRL IMEGLGLA	ω-Aga-IVA	959
EDNCIAEDYG KCTWGGTKCC RGRPCRCSMI GTNCECTPRL IMEGLSFA	ω-Aga-IVB	960
SCIDIGGDCD GEKDDCQCCR RNGYCSCYSL FGYLKSGCKC VVGTSAEFQG ICRRKARQCY NSDPDKCESH NKPKRR	ω-Aga-IIIA	961
SCIDIGGDCD GEKDDCQCCR RNGYCSCYSL FGYLKSGCKC VVGTSAEFQG ICRRKARTCY NSDPDKCESH NKPKRR	ω-Aga-IIIA-T58	962
SCIDFGGDCD GEKDDCQCCR SNGYCSCYSL FGYLKSGCKC EVGTSAEFRR ICRRKAKQCY NSDPDKCVSV YKPKRR	ω-Aga-IIIB	963
SCIDFGGDCD GEKDDCQCCR SNGYCSCYNL FGYLKSGCKC EVGTSAEFRR ICRRKAKQCYNSDPDKCVSV YKPKRR	ω-Aga-IIIB-N29	964
SCIDFGGDCD GEKDDCQCCR SNGYCSCYNL FGYLRSGCKC EVGTSAEFRR ICRRKAKQCY NSDPDKCVSV YKPKRR	ω-Aga-IIIB-N29/R35	965
NCIDFGGDCD GEKDDCQCCX RNGYCSCYNL FGYLKRGCKX EVG	ω-Aga-IIIC	966
SCIKIGEDCD GDKDDCQCCR TNGYCSXYXL FGYLKSG	ω-Aga-IIID	967
GCIEIGGDCD GYQEKSYCQC CRNNGFCS	ω-Aga-IIA	968
AKAL PPGSVCDGNE SDCKCYGKWH KCRCPWKWHF TGEGPCTCEK GMKHTCITKL HCPNKAEWGL DW	ω-Aga-IA (major chain)	969
ECVPENGHCR DWYDECCEGF YCSCRQPPKC ICRNNNX	μ-Aga	970
DCVGESQQCA DWAGPHCCDG YYCTCRYFPK CICVNNN	μ-Aga-6	971
ACVGENKQCA DWAGPHCCDG YYCTCRYFPK CICRNNN	μ-Aga-5	972
ACVGENQQCA DWAGPHCCDG YYCTCRYFPK CICRNNN	μ-Aga-4	973
ADCVGDGQRC ADWAGPYCCS GYYCSCRSMP YCRCRSDS	μ-Aga-3	1275
ECATKNKRCA DWAGPWCCDG LYCSCRSYPG CMCRPSS	μ-Aga-2	974
ECVPENGHCR DWYDECCEGF YCSCRQPPKC ICRNNN	μ-Aga-1	975
AELTSCFPVGHECDGDASNCNCCGDDVYCGCGWGRWNCKC KVADQSYAYGICKDKVNCPNRHLWPAKVCKKPCRREC	Tx-1	1277
GCANAYKSCNGPHTCCWGYNGYKKACICSGXNWK	Tx3-3	1278
SCINVGDFCDGKKDCCQCDRDNAFCSCSVIFGYKTNCRCE	Tx3-4	1279
SCINVGDFCDGKKDDCQCCRDNAFCSCSVIFGYKTNCRCE VGTTATSYGICMAKHKCGRQTTCTKPCLSKRCKKNH	ω-PtXIIA	1280
AECLMIGDTSCVPRLGRRCCYGAWCYCDQQLSCRRVGRKR ECGWVEVNCKCGWSWSQRIDDWRADYSCKCPEDQ	Dw13.3	1281
GGCLPHNRFCNALSGPRCCSGLKCKELSIWDSRCL	Agelenin	1282
DCVRFWGKCSQTSDCCPHLACKSKWPRNICVWDGSV	ω-GTx-SIA	1283
GCLEVDYFCG IPFANNGLCC SGNCVFVCTP Q	ω-conotoxin PnVIA	1284
DDDCEPPGNF CGMIKIGPPC CSGWCFFACA	ω-conotoxin PnVIB	1285
VCCGYKLCHP C	Lambda-conotoxin CMrVIA	1286

MRCLPVLIIL LLLTASAPGV VVLPKTEDDV PMSSVYGNGK SILRGILRNG VCCGYKLCHP C	Lambda-conotoxin CMrVIB	1287
KIDGYPVDYW NCKRICWYNN KYCNDLCKGL KADSGYCWGW TLSCYCQGLP DNARIKRSGR CRA	Kurtoxin	1276
CKGKGAPCRKTMYDCCSGSCGRRGKC	MVIIC	1368

In accordance with this invention are molecules in which at least one of the toxin peptide (P) portions of the molecule comprises a Kv1.3 antagonist peptide. Amino acid sequences selected from ShK, HmK, MgTx, AgTx1, AgTx2, Heterometrus spinnifer (HsTx1), OSK1, Anuroctoxin(AnTx), Noxiustoxin (NTX), KTX1, Hongotoxin, ChTx, Titystoxin, BgK, BmKTX, BmTx, AeK, AsKS Tc30, Tc32, Pi1, Pi2, and/or Pi3 toxin peptides and peptide analogs of any of these are preferred. Examples of useful Kv1.3 antagonist peptide sequences include those having any amino acid sequence set forth in Table 1, Table 2, Table 3, Table 4, Table 5, Table 6, Table 7, Table 8, Table 9, Table 10, and/or Table 11 herein above;

Other embodiments of the inventive composition include at least one toxin peptide (P) that is an IKCa1 antagonist peptide. Useful IKCa1 antagonist peptides include Maurotoxin (MTx), ChTx,peptides and peptide analogs of either of these, examples of which include those having any amino acid sequence set forth in Table 12, Table 13, and/or Table 14;

Other embodiments of the inventive composition include at least one toxin peptide (P) that is a SKCa inhibitor peptide. Useful SKCa inhibitor peptides include, Apamin, ScyTx, BmP05, P01, P05, Tamapin, TsK, and peptide analogs of any of these, examples of which include those having any amino acid sequence set forth in Table 15;

Other embodiments of the inventive composition include at least one toxin peptide (P) that is an apamin peptide, and peptide analogs of apamin, examples of which include those having any amino acid sequence set forth in Table 16;

Other embodiments of the inventive composition include at least one toxin peptide (P) that is a *Scyllotoxin* family peptide, and peptide analogs of any of these, examples of which include those having any amino acid sequence set forth in Table 17;

Other embodiments of the inventive composition include at least one toxin peptide (P) that is a BKCa inhibitor peptide, examples of which include those having any amino acid sequence set forth in Table 18;

Other embodiments of the inventive composition include at least one toxin peptide (P) that is a *Slotoxin* family peptide, and peptide analogs of any of these, examples of which include those having any amino acid sequence set forth in Table 19;

Other embodiments of the inventive composition include at least one toxin peptide (P) that is a Martentoxin peptide, and peptide analogs thereof, examples of which include those having any amino acid sequence set forth in Table 20;

Other embodiments of the inventive composition include at least one toxin peptide (P) that is a N-type Ca^{2+} channel inhibitor peptide, examples of which include those having any amino acid sequence set forth in Table 21;

Other embodiments of the inventive composition include at least one toxin peptide (P) that is a ωMVIIA peptide, and peptide analogs thereof, examples of which include those having any amino acid sequence set forth in Table 22;

Other embodiments of the inventive composition include at least one toxin peptide (P) that is a ωGVIA peptide, and peptide analogs thereof, examples of which include those having any amino acid sequence set forth in Table 23;

Other embodiments of the inventive composition include at least one toxin peptide (P) that is a Ptu1 peptide, and peptide analogs thereof, examples of which include those having any amino acid sequence set forth in Table 24;

Other embodiments of the inventive composition include at least one toxin peptide (P) that is a ProTx1 peptide, and peptide analogs thereof, examples of which include those having any amino acid sequence set forth in Table 25;

Other embodiments of the inventive composition include at least one toxin peptide (P) that is a BeKM1 peptide, and peptide analogs thereof, examples of which include those having any amino acid sequence set forth in Table 26;

Other embodiments of the inventive composition include at least one toxin peptide (P) that is a Na^+ channel inhibitor peptide, examples of which include those having any amino acid sequence set forth in Table 27;

Other embodiments of the inventive composition include at least one toxin peptide (P) that is a Cl^- channel inhibitor peptide, examples of which include those having any amino acid sequence set forth in Table 28;

Other embodiments of the inventive composition include at least one toxin peptide (P) that is a Kv2.1 inhibitor peptide, examples of which include those having any amino acid sequence set forth in Table 29;

Other embodiments of the inventive composition include at least one toxin peptide (P) that is a Kv4.2/Kv4.3 inhibitor peptide, examples of which include those having any amino acid sequence set forth in Table 30;

Other embodiments of the inventive composition include at least one toxin peptide (P) that is a nACHR inhibitor peptide, examples of which include those having any amino acid sequence set forth in Table 31; and

Other embodiments of the inventive composition include at least one toxin peptide (P) that is an Agatoxin peptide, a peptide analog thereof or other calcium channel inhibitor peptide, examples of which include those having any amino acid sequence set forth in Table 32.

Half-life extending moieties. This invention involves the presence of at least one half-life extending moiety (F^1 and/or F^2 in Formula I) attached to a peptide through the N-terminus, C-terminus or a sidechain of one of the intracalary amino acid residues. Multiple half-life extending moieties can also be used; e.g., Fc's at each terminus or an Fc at a terminus and a PEG group at the other terminus or at a sidechain. In other embodiments the Fc domain can be PEGylated (e.g., in accordance with the formulae F^1-F^2-$(L)_f$-P; P-$(L)_g$-F^1-F^2; or P-$(L)_g$-F^1-F^2-$(L)_f$-P).

The half-life extending moiety can be selected such that the inventive composition achieves a sufficient hydrodynamic size to prevent clearance by renal filtration *in vivo*. For example, a half-life extending moiety can be selected that is a polymeric macromolecule, which is substantially straight chain, branched-chain, or dendritic in form. Alternatively, a half-life extending moiety can be selected such that, *in vivo*, the inventive composition of matter will bind to a serum protein to form a complex, such that the complex thus formed avoids substantial renal clearance. The half-life extending moiety can be, for example, a lipid; a cholesterol group (such as a steroid); a carbohydrate or oligosaccharide; or any natural or synthetic protein, polypeptide or peptide that binds to a salvage receptor.

Exemplary half-life extending moieties that can be used, in accordance with the present invention, include an immunoglobulin Fc domain, or a portion thereof, or a biologically suitable polymer or copolymer, for example, a polyalkylene glycol compound, such as a polyethylene glycol or a polypropylene glycol. Other appropriate polyalkylene glycol compounds include, but are not limited to, charged or neutral polymers of the following types: dextran, polylysine, colominic acids or other carbohydrate based polymers, polymers of amino acids, and biotin derivatives.

Other examples of the half-life extending moiety, in accordance with the invention, include a copolymer of ethylene glycol, a copolymer of propylene glycol, a carboxymethylcellulose, a polyvinyl pyrrolidone, a poly-1,3-dioxolane, a poly-1,3,6-trioxane, an ethylene/maleic anhydride copolymer, a polyaminoacid (e.g., polylysine), a dextran n-vinyl pyrrolidone, a poly n-vinyl pyrrolidone, a propylene glycol homopolymer, a propylene oxide polymer, an ethylene oxide polymer, a polyoxyethylated polyol, a polyvinyl alcohol, a linear or branched glycosylated chain, a

polyacetal, a long chain fatty acid, a long chain hydrophobic aliphatic group, an immunoglobulin F_c domain or a portion thereof (see, e.g., Feige et al., *Modified peptides as therapeutic agents*, US Patent No. 6,660,843), a CH2 domain of Fc, an albumin (e.g., human serum albumin (HSA)); see, e.g., Rosen et al., *Albumin fusion proteins*, US Patent No. 6,926,898 and US 2005/0054051; Bridon et al., *Protection of endogenous therapeutic peptides from peptidase activity through conjugation to blood components*, US 6,887,470), a transthyretin (TTR; see, e.g., Walker et al., *Use of transthyretin peptide/protein fusions to increase the serum half-life of pharmacologically active peptides/proteins*, US 2003/0195154 A1; 2003/0191056 A1), or a thyroxine-binding globulin (TBG). Thus, exemplary embodiments of the inventive compositions also include HSA fusion constructs such as but not limited to: HSA fusions with ShK, OSK1, or modified analogs of those toxin peptides. Examples include HSA-L10-ShK(2-35); HSA-L10-OsK1(1-38); HSA-L10-ShK(2-35); and HSA-L10-OsK1(1-38).

Other embodiments of the half-life extending moiety, in accordance with the invention, include peptide ligands or small (organic) molecule ligands that have binding affinity for a long half-life serum protein under physiological conditions of temperature, pH, and ionic strength. Examples include an albumin-binding peptide or small molecule ligand, a transthyretin-binding peptide or small molecule ligand, a thyroxine-binding globulin-binding peptide or small molecule ligand, an antibody-binding peptide or small molecule ligand, or another peptide or small molecule that has an affinity for a long half-life serum protein. (See, e.g., Blaney et al., Method and compositions for increasing the serum half-life of pharmacologically active agents by binding to transthyretin-selective ligands, US Patent. No. 5,714,142; Sato et al., Serum albumin binding moieties, US 2003/0069395 A1; Jones et al., Pharmaceutical active conjugates, US Patent No. 6,342,225). A "long half-life serum protein" is one of the hundreds of different proteins dissolved in mammalian blood plasma, including so-called "carrier proteins" (such as albumin, transferrin and haptoglobin), fibrinogen and other blood coagulation factors, complement components, immunoglobulins, enzyme inhibitors, precursors of substances such as angiotensin and bradykinin and many other types of proteins. The invention encompasses the use of any single species of pharmaceutically acceptable half-life extending moiety, such as, but not limited to, those described herein, or the use of a combination of two or more different half-life extending moieties, such as PEG and immunoglobulin Fc domain or a CH2 domain of Fc, albumin (e.g., HSA), an albumin-binding protein, transthyretin or TBG.

In some embodiments of the invention an Fc domain or portion thereof, such as a CH2 domain of Fc, is used as a half-life extending moiety. The Fc domain can be fused to the N-

terminal (e.g., in accordance with the formula F^1–$(L)_f$–P) or C-terminal (e.g., in accordance with the formula P–$(L)_g$–F^1) of the toxin peptides or at both the N and C termini (e.g., in accordance with the formulae F^1–$(L)_f$–P–$(L)_g$–F^2 or P–$(L)_g$–F^1–$(L)_f$–P). A peptide linker sequence can be optionally included between the Fc domain and the toxin peptide, as described herein. Examples of the the formula F^1–$(L)_f$–P include: Fc-L10-ShK(K22A)[2-35]; Fc-L10-ShK(R1K/K22A)[1-35]; Fc-L10-ShK(R1H/K22A)[1-35]; Fc-L10-ShK(R1Q /K22A)[1-35]; Fc-L10-ShK(R1Y /K22A)[1-35]; Fc-L10-PP-ShK(K22A) [1-35]; and any other working examples described herein. Examples of the the formula P–$(L)_g$–F^1 include: ShK(1-35)-L10-Fc; OsK1(1-38)-L10-Fc; Met-ShK(1-35)-L10-Fc; ShK(2-35)-L10-Fc; Gly-ShK(1-35)-L10-Fc; Osk1(1-38)-L10-Fc; and any other working examples described herein.

Fc variants are suitable half-life extending moieties within the scope of this invention. A native Fc can be extensively modified to form an Fc variant in accordance with this invention, provided binding to the salvage receptor is maintained; see, for example WO 97/34631, WO 96/32478, and WO 04/110 472. In such Fc variants, one can remove one or more sites of a native Fc that provide structural features or functional activity not required by the fusion molecules of this invention. One can remove these sites by, for example, substituting or deleting residues, inserting residues into the site, or truncating portions containing the site. The inserted or substituted residues can also be altered amino acids, such as peptidomimetics or D-amino acids. Fc variants can be desirable for a number of reasons, several of which are described below. Exemplary Fc variants include molecules and sequences in which:

1. Sites involved in disulfide bond formation are removed. Such removal can avoid reaction with other cysteine-containing proteins present in the host cell used to produce the molecules of the invention. For this purpose, the cysteine-containing segment at the N-terminus can be truncated or cysteine residues can be deleted or substituted with other amino acids (e.g., alanyl, seryl). In particular, one can truncate the N-terminal 20-amino acid segment of SEQ ID NO: 2 or delete or substitute the cysteine residues at positions 7 and 10 of SEQ ID NO: 2. Even when cysteine residues are removed, the single chain Fc domains can still form a dimeric Fc domain that is held together non-covalently.
2. A native Fc is modified to make it more compatible with a selected host cell. For example, one can remove the PA sequence near the N-terminus of a typical native Fc, which can be recognized by a digestive enzyme in E. coli such as proline iminopeptidase. One can also add an N-terminal methionine residue, especially when the molecule is expressed recombinantly in

a bacterial cell such as E. coli. The Fc domain of SEQ ID NO: 2 (Figure 4A-B) is one such Fc variant.

3. A portion of the N-terminus of a native Fc is removed to prevent N-terminal heterogeneity when expressed in a selected host cell. For this purpose, one can delete any of the first 20 amino acid residues at the N-terminus, particularly those at positions 1, 2, 3, 4 and 5.
4. One or more glycosylation sites are removed. Residues that are typically glycosylated (e.g., asparagine) can confer cytolytic response. Such residues can be deleted or substituted with unglycosylated residues (e.g., alanine).
5. Sites involved in interaction with complement, such as the C1q binding site, are removed. For example, one can delete or substitute the EKK sequence of human IgG1. Complement recruitment may not be advantageous for the molecules of this invention and so can be avoided with such an Fc variant.
6. Sites are removed that affect binding to Fc receptors other than a salvage receptor. A native Fc can have sites for interaction with certain white blood cells that are not required for the fusion molecules of the present invention and so can be removed.
7. The ADCC site is removed. ADCC sites are known in the art; see, for example, Molec. Immunol. 29 (5): 633-9 (1992) with regard to ADCC sites in IgG1. These sites, as well, are not required for the fusion molecules of the present invention and so can be removed.
8. When the native Fc is derived from a non-human antibody, the native Fc can be humanized. Typically, to humanize a native Fc, one will substitute selected residues in the non-human native Fc with residues that are normally found in human native Fc. Techniques for antibody humanization are well known in the art.

Preferred Fc variants include the following. In SEQ ID NO: 2, the leucine at position 15 can be substituted with glutamate; the glutamate at position 99, with alanine; and the lysines at positions 101 and 103, with alanines. In addition, phenyalanine residues can replace one or more tyrosine residues.

An alternative half-life extending moiety would be a protein, polypeptide, peptide, antibody, antibody fragment, or small molecule (e.g., a peptidomimetic compound) capable of binding to a salvage receptor. For example, one could use as a half-life extending moiety a polypeptide as described in U.S. Pat. No. 5,739,277, issued April 14, 1998 to Presta et al. Peptides could also be selected by phage display for binding to the FcRn salvage receptor. Such salvage receptor-binding compounds are also included within the meaning of "half-life extending moiety" and are within the scope of this invention. Such half-life extending moieties should be

selected for increased half-life (e.g., by avoiding sequences recognized by proteases) and decreased immunogenicity (e.g., by favoring non-immunogenic sequences, as discovered in antibody humanization).

As noted above, polymer half-life extending moieties can also be used for F^1 and F^2. Various means for attaching chemical moieties useful as half-life extending moieties are currently available, see, e.g., Patent Cooperation Treaty ("PCT") International Publication No. WO 96/11953, entitled "N-Terminally Chemically Modified Protein Compositions and Methods," herein incorporated by reference in its entirety. This PCT publication discloses, among other things, the selective attachment of water-soluble polymers to the N-terminus of proteins.

In some embodiments of the inventive compositions, the polymer half-life extending moiety is polyethylene glycol (PEG), as F^1 and/or F^2, but it should be understood that the inventive composition of matter, beyond positions F^1 and/or F^2, can also include one or more PEGs conjugated at other sites in the molecule, such as at one or more sites on the toxin peptide. Accordingly, some embodiments of the inventive composition of matter further include one or more PEG moieties conjugated to a non-PEG half-life extending moiety, which is F^1 and/or F^2, or to the toxin peptide(s) (P), or to any combination of any of these. For example, an Fc domain or portion thereof (as F1 and/or F2) in the inventive composition can be made mono-PEGylated, di-PEGylated, or otherwise multi-PEGylated, by the process of reductive alkylation.

Covalent conjugation of proteins and peptides with poly(ethylene glycol) (PEG) has been widely recognized as an approach to significantly extend the *in vivo* circulating half-lives of therapeutic proteins. PEGylation achieves this effect predominately by retarding renal clearance, since the PEG moiety adds considerable hydrodynamic radius to the protein. (Zalipsky, S., et al., Use of functionalized poly(ethylene glycol)s for modification of polypeptides., in poly(ethylene glycol) chemistry: Biotechnical and biomedical applications., J.M. Harris, Ed., Plenum Press: New York., 347-370 (1992)). Additional benefits often conferred by PEGylation of proteins and peptides include increased solubility, resistance to proteolytic degradation, and reduced immunogenicity of the therapeutic polypeptide. The merits of protein PEGylation are evidenced by the commercialization of several PEGylated proteins including PEG-Adenosine deaminase (Adagen™/Enzon Corp.), PEG-L-asparaginase (Oncaspar™/Enzon Corp.), PEG-Interferon α-2b (PEG-Intron™/Schering/Enzon), PEG-Interferon α-2a (PEGASYS™/Roche) and PEG-G-CSF (Neulasta™/Amgen) as well as many others in clinical trials. It

Briefly, the PEG groups are generally attached to the peptide portion of the composition of the invention via acylation or reductive alkylation through a reactive group on the PEG moiety (e.g.,

an aldehyde, amino, thiol, or ester group) to a reactive group on the inventive compound (e.g., an aldehyde, amino, or ester group).

A useful strategy for the PEGylation of synthetic peptides consists of combining, through forming a conjugate linkage in solution, a peptide and a PEG moiety, each bearing a special functionality that is mutually reactive toward the other. The peptides can be easily prepared with conventional solid phase synthesis (see, for example, Figures 5 and 6 and the accompanying text herein). The peptides are "preactivated" with an appropriate functional group at a specific site. The precursors are purified and fully characterized prior to reacting with the PEG moiety. Ligation of the peptide with PEG usually takes place in aqueous phase and can be easily monitored by reverse phase analytical HPLC. The PEGylated peptides can be easily purified by preparative HPLC and characterized by analytical HPLC, amino acid analysis and laser desorption mass spectrometry.

PEG is a well-known, water soluble polymer that is commercially available or can be prepared by ring-opening polymerization of ethylene glycol according to methods well known in the art (Sandler and Karo, Polymer Synthesis, Academic Press, New York, Vol. 3, pages 138-161). In the present application, the term "PEG" is used broadly to encompass any polyethylene glycol molecule, in mono-, bi-, or poly- functional form, without regard to size or to modification at an end of the PEG, and can be represented by the formula:

$$X\text{-}O(CH_2CH_2O)_{n-1}CH_2CH_2OH, \qquad (X)$$

where n is 20 to 2300 and X is H or a terminal modification, e.g., a C_{1-4} alkyl.

In some useful embodiments, a PEG used in the invention terminates on one end with hydroxy or methoxy, i.e., X is H or CH_3 ("methoxy PEG"). It is noted that the other end of the PEG, which is shown in formula (II) terminating in OH, covalently attaches to an activating moiety via an ether oxygen bond, an amine linkage, or amide linkage. When used in a chemical structure, the term "PEG" includes the formula (II) above without the hydrogen of the hydroxyl group shown, leaving the oxygen available to react with a free carbon atom of a linker to form an ether bond. More specifically, in order to conjugate PEG to a peptide, the peptide must be reacted with PEG in an "activated" form. Activated PEG can be represented by the formula:

$$(PEG)\text{-}(A) \qquad (XI)$$

where PEG (defined *supra*) covalently attaches to a carbon atom of the activation moiety (A) to form an ether bond, an amine linkage, or amide linkage, and (A) contains a reactive group which can react with an amino, imino, or thiol group on an amino acid residue of a peptide or a linker moiety covalently attached to the peptide.

Techniques for the preparation of activated PEG and its conjugation to biologically active peptides are well known in the art. (E.g., see U.S. Pat. Nos. 5,643,575, 5,919,455, 5,932,462, and 5,990,237; Thompson et al., PEGylation of polypeptides, EP 0575545 B1; Petit, Site specific protein modification, US Patent Nos. 6,451,986, and 6,548,644; S. Herman et al., Poly(ethylene glycol) with reactive endgroups: I. Modification of proteins, J. Bioactive Compatible Polymers, 10:145-187 (1995); Y. Lu et al., Pegylated peptides III: Solid-phase synthesis with PEGylating reagents of varying molecular weight: synthesis of multiply PEGylated peptides, Reactive Polymers, 22:221-229 (1994); A.M. Felix et al., PEGylated Peptides IV: Enhanced biological activity of site-directed PEGylated GRF analogs, Int. J. Peptide Protein Res., 46:253-264 (1995); A.M. Felix, Site-specific poly(ethylene glycol)ylation of peptides, ACS Symposium Series 680(poly(ethylene glycol)): 218-238 (1997); Y. Ikeda et al., Polyethylene glycol derivatives, their modified peptides, methods for producing them and use of the modified peptides, EP 0473084 B1; G.E. Means et al., Selected techniques for the modification of protein side chains, in: Chemical modification of proteins, Holden Day, Inc., 219 (1971)).

Activated PEG, such as PEG-aldehydes or PEG-aldehyde hydrates, can be chemically synthesized by known means or obtained from commercial sources, e.g., Shearwater Polymers, (Huntsville, Al) or Enzon, Inc. (Piscataway, N.J.).

An example of a useful activated PEG for purposes of the present invention is a PEG-aldehyde compound (e.g., a methoxy PEG-aldehyde), such as PEG-propionaldehyde, which is commercially available from Shearwater Polymers (Huntsville, Al). PEG-propionaldehyde is represented by the formula PEG-CH_2CH_2CHO. (See, e.g., U.S. Pat. No. 5,252,714). Other examples of useful activated PEG are PEG acetaldehyde hydrate and PEG bis aldehyde hydrate, which latter yields a bifunctionally activated structure. (See., e.g., Bentley et al., Poly(ethylene glycol) aldehyde hydrates and related polymers and applications in modifying amines, US Patent No. 5,990,237).

Another useful activated PEG for generating the PEG-conjugated peptides of the present invention is a PEG-maleimide compound, such as, but not limited to, a methoxy PEG-maleimide, such as maleimido monomethoxy PEG, are particularly useful for generating the PEG-conjugated peptides of the invention. (E.g., Shen, *N*-maleimidyl polymer derivatives, US Patent No. 6,602,498;

C. Delgado et al., The uses and properties of PEG-linked proteins., Crit. Rev. Therap. Drug Carrier Systems, 9:249-304 (1992); S. Zalipsky et al., Use of functionalized poly(ethylene glycol)s for modification of polypeptides, in: Poly(ethylene glycol) chemistry: Biotechnical and biomedical applications (J.M. Harris, Editor, Plenum Press: New York, 347-370 (1992); S. Herman et al., Poly(ethylene glycol) with reactive endgroups: I. Modification of proteins, J. Bioactive Compatible Polymers, 10:145-187 (1995); P.J. Shadle et al., Conjugation of polymer to colony stimulating factor-1, U.S. Patent No. 4,847,325; G. Shaw et al., Cysteine added variants IL-3 and chemical modifications thereof, U.S. Patent No. 5,166,322 and EP 0469074 B1; G. Shaw et al., Cysteine added variants of EPO and chemical modifications thereof, EP 0668353 A1; G. Shaw et al., Cysteine added variants G-CSF and chemical modifications thereof, EP 0668354 A1; N.V. Katre et al., Interleukin-2 muteins and polymer conjugation thereof, U.S. Patent No. 5,206,344; R.J. Goodson and N.V. Katre, Site-directed pegylation of recombinant interleukin-2 at its glycosylation site, Biotechnology, 8:343-346 (1990)).

A poly(ethylene glycol) vinyl sulfone is another useful activated PEG for generating the PEG-conjugated peptides of the present invention by conjugation at thiolated amino acid residues, e.g., at C residues. (E.g., M. Morpurgo et al., Preparation and characterization of poly(ethylene glycol) vinyl sulfone, Bioconj. Chem., 7:363-368 (1996); see also Harris, Functionalization of polyethylene glycol for formation of active sulfone-terminated PEG derivatives for binding to proteins and biologically compatible materials, U.S. Patent Nos. 5,446,090; 5,739,208; 5,900,461; 6,610,281 and 6,894,025; and Harris, Water soluble active sulfones of poly(ethylene glycol), WO 95/13312 A1).

Another activated form of PEG that is useful in accordance with the present invention, is a PEG-N-hydroxysuccinimide ester compound, for example, methoxy PEG-N-hydroxysuccinimidyl (NHS) ester.

Heterobifunctionally activated forms of PEG are also useful. (See, e.g., Thompson et al., PEGylation reagents and biologically active compounds formed therewith, U.S. Patent No. 6,552,170).

Typically, a toxin peptide or, a fusion protein comprising the toxin peptide, is reacted by known chemical techniques with an activated PEG compound, such as but not limited to, a thiol-activated PEG compound, a diol-activated PEG compound, a PEG-hydrazide compound, a PEG-oxyamine compound, or a PEG-bromoacetyl compound. (See, e.g., S. Herman, Poly(ethylene glycol) with Reactive Endgroups: I. Modification of Proteins, J. Bioactive and Compatible Polymers, 10:145-187 (1995); S. Zalipsky, Chemistry of Polyethylene Glycol Conjugates with Biologically

Active Molecules, Advanced Drug Delivery Reviews, 16:157-182 (1995); R. Greenwald et al., Poly(ethylene glycol) conjugated drugs and prodrugs: a comprehensive review, Critical Reviews in Therapeutic Drug Carrier Systems, 17:101-161 (2000)).

Methods for N-terminal PEGylation are exemplified herein in Examples 31-34, 45 and 47-48, but these are in no way limiting of the PEGylation methods that can be employed by one skilled in the art.

Any molecular mass for a PEG can be used as practically desired, e.g., from about 1,000 or 2,000 Daltons (Da) to about 100,000 Da (n is 20 to 2300). Preferably, the combined or total molecular mass of PEG used in a PEG-conjugated peptide of the present invention is from about 3,000 Da or 5,000 Da, to about 50,000 Da or 60,000 Da (total n is from 70 to 1,400), more preferably from about 10,000 Da to about 40,000 Da (total n is about 230 to about 910). The most preferred combined mass for PEG is from about 20,000 Da to about 30,000 Da (total n is about 450 to about 680). The number of repeating units "n" in the PEG is approximated for the molecular mass described in Daltons. It is preferred that the combined molecular mass of PEG on an activated linker is suitable for pharmaceutical use. Thus, the combined molecular mass of the PEG molecule should not exceed about 100,000 Da.

Polysaccharide polymers are another type of water-soluble polymer that can be used for protein modification. Dextrans are polysaccharide polymers comprised of individual subunits of glucose predominantly linked by α1-6 linkages. The dextran itself is available in many molecular weight ranges, and is readily available in molecular weights from about 1 kD to about 70 kD. Dextran is a suitable water-soluble polymer for use in the present invention as a half-life extending moiety by itself or in combination with another half-life extending moiety (e.g., Fc). See, for example, WO 96/11953 and WO 96/05309. The use of dextran conjugated to therapeutic or diagnostic immunoglobulins has been reported; see, for example, European Patent Publication No. 0 315 456, which is hereby incorporated by reference in its entirety. Dextran of about 1 kD to about 20 kD is preferred when dextran is used as a half-life extending moiety in accordance with the present invention.

Linkers. Any "linker" group or moiety (i.e., "-$(L)_f$-" or "-$(L)_g$-" in Formulae I-IX) is optional. When present, its chemical structure is not critical, since it serves primarily as a spacer. As stated herein above, the linker moiety (-$(L)_f$- and/or -$(L)_g$-), if present, can be independently the same or different from any other linker, or linkers, that may be present in the inventive composition. For example, an "$(L)_f$" can represent the same moiety as, or a different moiety from, any other "$(L)_f$" or any "$(L)_g$" in accordance with the invention. The linker is preferably made up of amino acids linked

together by peptide bonds. Thus, in some embodiments, the linker is made up of from 1 to about 30 amino acids linked by peptide bonds, wherein the amino acids are selected from the 20 naturally occurring amino acids. Some of these amino acids can be glycosylated, as is well understood by those in the art. For example, a useful linker sequence constituting a sialylation site is $X_1X_2NX_4X_5G$ (SEQ ID NO: 637), wherein X_1, X_2,X_4 and X_5 are each independently any amino acid residue.

In some embodiments, the 1 to 20 amino acids are selected from glycine, alanine, proline, asparagine, glutamine, and lysine. Even more preferably, a linker is made up of a majority of amino acids that are sterically unhindered, such as glycine and alanine. Thus, preferred linkers include polyglycines (particularly $(Gly)_4$, $(Gly)_5$), poly(Gly-Ala), and polyalanines. Other preferred linkers are those identified herein as "L5" (GGGGS; SEQ ID NO: 638), "L10" (GGGGSGGGGS; SEQ ID NO:79), "L25" GGGGSGGGGSGGGGSGGGGSGGGGS; SEQ ID NO:84) and any linkers used in the working examples hereinafter. The linkers described herein, however, are exemplary; linkers within the scope of this invention can be much longer and can include other residues.

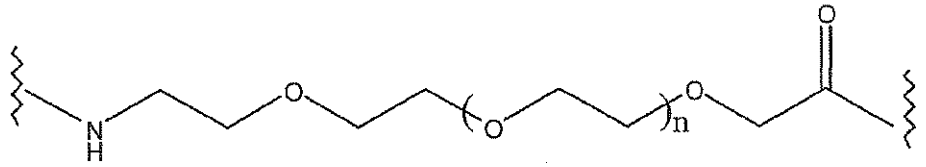
In some embodiments of the compositions of this invention, which comprise a peptide linker moiety (L), acidic residues, for example, glutamate or aspartate residues, are placed in the amino acid sequence of the linker moiety (L). Examples include the following peptide linker sequences:

GGEGGG (SEQ ID NO: 639);
GGEEEGGG (SEQ ID NO: 640);
GEEEG (SEQ ID NO: 641);
GEEE (SEQ ID NO: 642);
GGDGGG (SEQ ID NO: 643);
GGDDDGG (SEQ ID NO: 644);
GDDDG (SEQ ID NO: 645);
GDDD (SEQ ID NO: 646);
GGGGSDDSDEGSDGEDGGGGS (SEQ ID NO: 647);
WEWEW (SEQ ID NO: 648);
FEFEF (SEQ ID NO: 649);
EEEWWW (SEQ ID NO: 650);
EEEFFF (SEQ ID NO: 651);
WWEEEWW (SEQ ID NO: 652); or
FFEEEFF (SEQ ID NO: 653).

In other embodiments, the linker constitutes a phosphorylation site, e.g., $X_1X_2YX_3X_4G$ (SEQ ID NO: 654), wherein X_1, X_2,X_3 and X_4 are each independently any amino acid residue; $X_1X_2SX_3X_4G$ (SEQ ID NO: 655), wherein X_1, X_2,X_3 and X_4 are each independently any amino acid residue; or $X_1X_2TX_3X_4G$ (SEQ ID NO: 656), wherein X_1, X_2,X_3 and X_4 are each independently any amino acid residue.

Non-peptide linkers are also possible. For example, alkyl linkers such as -NH-$(CH_2)_s$-C(O)-, wherein s = 2-20 could be used. These alkyl linkers can further be substituted by any non-sterically hindering group such as lower alkyl (e.g., C_1-C_6) lower acyl, halogen (e.g., Cl, Br), CN, NH_2, phenyl, etc. An exemplary non-peptide linker is a PEG linker,

(XII)

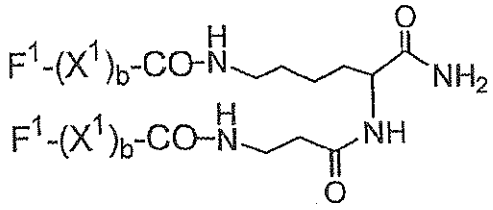


wherein n is such that the linker has a molecular weight of 100 to 5000 kD, preferably 100 to 500 kD. The peptide linkers can be altered to form derivatives in the same manner as described above.

Derivatives. The inventors also contemplate derivatizing the peptide and/or half-life extending moiety portion of the compounds. Such derivatives can improve the solubility, absorption, biological half-life, and the like of the compounds. The moieties can alternatively eliminate or attenuate any undesirable side-effect of the compounds and the like. Exemplary derivatives include compounds in which:

1. The compound or some portion thereof is cyclic. For example, the peptide portion can be modified to contain two or more Cys residues (e.g., in the linker), which could cyclize by disulfide bond formation.
2. The compound is cross-linked or is rendered capable of cross-linking between molecules. For example, the peptide portion can be modified to contain one Cys residue and thereby be able to form an intermolecular disulfide bond with a like molecule. The compound can also be cross-linked through its C-terminus, as in the molecule shown below.

(XIII)



3. Non-peptidyl linkages (bonds) replace one or more peptidyl [-C(O)NR-] linkages. Exemplary non-peptidyl linkages are -CH_2-carbamate [-CH_2-OC(O)NR-], phosphonate , -CH_2-sulfonamide [-CH_2-S(O)$_2$NR-], urea [-NHC(O)NH-], -CH_2-secondary amine, and alkylated peptide [-C(O)NR^6- wherein R^6 is lower alkyl].
4. The N-terminus is chemically derivatized. Typically, the N-terminus can be acylated or modified to a substituted amine. Exemplary N-terminal derivative groups include -NRR^1 (other than -NH_2), -$NRC(O)R^1$, -$NRC(O)OR^1$, -$NRS(O)_2R^1$, -$NHC(O)NHR^1$, succinimide, or benzyloxycarbonyl-NH- (CBZ-NH-), wherein R and R^1 are each independently hydrogen or lower alkyl and wherein the phenyl ring can be substituted with 1 to 3 substituents selected from the group consisting of C_1-C_4 alkyl, C_1-C_4 alkoxy, chloro, and bromo.
5. The free C-terminus is derivatized. Typically, the C-terminus is esterified or amidated. For example, one can use methods described in the art to add (NH-CH_2-CH_2-NH_2)$_2$ to compounds of this invention having any of SEQ ID NOS: 504 to 508 at the C-terminus. Likewise, one can use methods described in the art to add -NH_2 to compounds of this invention having any of SEQ ID NOS: 924 to 955, 963 to 972, 1005 to 1013, or 1018 to 1023 at the C-terminus. Exemplary C-terminal derivative groups include, for example, -$C(O)R^2$ wherein R^2 is lower alkoxy or -NR^3R^4 wherein R^3 and R^4 are independently hydrogen or C_1-C_8 alkyl (preferably C_1-C_4 alkyl).
6. A disulfide bond is replaced with another, preferably more stable, cross-linking moiety (e.g., an alkylene). See, e.g., Bhatnagar et al. (1996), J. Med. Chem. 39: 3814-9; Alberts et al. (1993) Thirteenth Am. Pep. Symp., 357-9.
7. One or more individual amino acid residues are modified. Various derivatizing agents are known to react specifically with selected sidechains or terminal residues, as described in detail below.

Lysinyl residues and amino terminal residues can be reacted with succinic or other carboxylic acid anhydrides, which reverse the charge of the lysinyl residues. Other suitable reagents for derivatizing alpha-amino-containing residues include imidoesters such as methyl picolinimidate; pyridoxal phosphate;

pyridoxal; chloroborohydride; trinitrobenzenesulfonic acid; O-methylisourea; 2,4 pentanedione; and transaminase-catalyzed reaction with glyoxylate.

Arginyl residues can be modified by reaction with any one or combination of several conventional reagents, including phenylglyoxal, 2,3-butanedione, 1,2-cyclohexanedione, and ninhydrin. Derivatization of arginyl residues requires that the reaction be performed in alkaline conditions because of the high pKa of the guanidine functional group. Furthermore, these reagents can react with the groups of lysine as well as the arginine epsilon-amino group.

Specific modification of tyrosyl residues has been studied extensively, with particular interest in introducing spectral labels into tyrosyl residues by reaction with aromatic diazonium compounds or tetranitromethane. Most commonly, N-acetylimidizole and tetranitromethane are used to form O-acetyl tyrosyl species and 3-nitro derivatives, respectively.

Carboxyl sidechain groups (aspartyl or glutamyl) can be selectively modified by reaction with carbodiimides (R'-N=C=N-R') such as 1-cyclohexyl-3-(2-morpholinyl-(4-ethyl) carbodiimide or 1-ethyl-3-(4-azonia-4,4-dimethylpentyl) carbodiimide. Furthermore, aspartyl and glutamyl residues can be converted to asparaginyl and glutaminyl residues by reaction with ammonium ions.

Glutaminyl and asparaginyl residues can be deamidated to the corresponding glutamyl and aspartyl residues. Alternatively, these residues are deamidated under mildly acidic conditions. Either form of these residues falls within the scope of this invention.

Cysteinyl residues can be replaced by amino acid residues or other moieties either to eliminate disulfide bonding or, conversely, to stabilize cross-linking. See, e.g., Bhatnagar et al. (1996), J. Med. Chem. 39: 3814-9.

Derivatization with bifunctional agents is useful for cross-linking the peptides or their functional derivatives to a water-insoluble support matrix or to other macromolecular half-life extending moieties. Commonly used cross-linking agents include, e.g., 1,1-bis(diazoacetyl)-2-phenylethane, glutaraldehyde, N-hydroxysuccinimide esters, for example, esters with 4-azidosalicylic acid, homobifunctional imidoesters, including disuccinimidyl esters such as 3,3'-dithiobis(succinimidylpropionate), and bifunctional maleimides such as bis-N-maleimido-1,8-octane. Derivatizing agents such as methyl-3-[(p-azidophenyl)dithio]propioimidate yield photoactivatable intermediates that are capable of forming crosslinks in the presence of light. Alternatively, reactive water-insoluble matrices such as cyanogen bromide-activated carbohydrates and the reactive substrates described in U.S. Pat. Nos. 3,969,287; 3,691,016; 4,195,128; 4,247,642; 4,229,537; and 4,330,440 are employed for protein immobilization.

Carbohydrate (oligosaccharide) groups can conveniently be attached to sites that are known to be glycosylation sites in proteins. Generally, O-linked oligosaccharides are attached to

serine (Ser) or threonine (Thr) residues while N-linked oligosaccharides are attached to asparagine (Asn) residues when they are part of the sequence Asn-X-Ser/Thr, where X can be any amino acid except proline. X is preferably one of the 19 naturally occurring amino acids other than proline. The structures of N-linked and O-linked oligosaccharides and the sugar residues found in each type are different. One type of sugar that is commonly found on both is N-acetylneuraminic acid (referred to as sialic acid). Sialic acid is usually the terminal residue of both N-linked and O-linked oligosaccharides and, by virtue of its negative charge, can confer acidic properties to the glycosylated compound. Such site(s) can be incorporated in the linker of the compounds of this invention and are preferably glycosylated by a cell during recombinant production of the polypeptide compounds (e.g., in mammalian cells such as CHO, BHK, COS). However, such sites can further be glycosylated by synthetic or semi-synthetic procedures known in the art.

Other possible modifications include hydroxylation of proline and lysine, phosphorylation of hydroxyl groups of seryl or threonyl residues, oxidation of the sulfur atom in Cys, methylation of the alpha-amino groups of lysine, arginine, and histidine side chains. Creighton, Proteins: Structure and Molecule Properties (W. H. Freeman and Co., San Francisco), pp. 79-86 (1983).

Compounds of the present invention can be changed at the DNA level, as well. The DNA sequence of any portion of the compound can be changed to codons more compatible with the chosen host cell. For E. coli, which is the preferred host cell, optimized codons are known in the art. Codons can be substituted to eliminate restriction sites or to include silent restriction sites, which can aid in processing of the DNA in the selected host cell. The half-life extending moiety, linker and peptide DNA sequences can be modified to include any of the foregoing sequence changes.

A process for preparing conjugation derivatives is also contemplated. Tumor cells, for example, exhibit epitopes not found on their normal counterparts. Such epitopes include, for example, different post-translational modifications resulting from their rapid proliferation. Thus, one aspect of this invention is a process comprising:

a) selecting at least one randomized peptide that specifically binds to a target epitope; and

b) preparing a pharmacologic agent comprising (i) at least one half-life extending moiety (Fc domain preferred), (ii) at least one amino acid sequence of the selected peptide or peptides, and (iii) an effector molecule.

The target epitope is preferably a tumor-specific epitope or an epitope specific to a pathogenic organism. The effector molecule can be any of the above-noted conjugation partners and is preferably a radioisotope.

Methods of Making

The present invention also relates to nucleic acids, expression vectors and host cells useful in producing the polypeptides of the present invention. Host cells can be eukaryotic cells, with mammalian cells preferred and CHO cells most preferred. Host cells can also be prokaryotic cells, with E. coli cells most preferred.

The compounds of this invention largely can be made in transformed host cells using recombinant DNA techniques. To do so, a recombinant DNA molecule coding for the peptide is prepared. Methods of preparing such DNA molecules are well known in the art. For instance, sequences coding for the peptides could be excised from DNA using suitable restriction enzymes. Alternatively, the DNA molecule could be synthesized using chemical synthesis techniques, such as the phosphoramidate method. Also, a combination of these techniques could be used

The invention also includes a vector capable of expressing the peptides in an appropriate host. The vector comprises the DNA molecule that codes for the peptides operatively linked to appropriate expression control sequences. Methods of effecting this operative linking, either before or after the DNA molecule is inserted into the vector, are well known. Expression control sequences include promoters, activators, enhancers, operators, ribosomal binding sites, start signals, stop signals, cap signals, polyadenylation signals, and other signals involved with the control of transcription or translation.

The resulting vector having the DNA molecule thereon is used to transform an appropriate host. This transformation can be performed using methods well known in the art.

Any of a large number of available and well-known host cells can be used in the practice of this invention. The selection of a particular host is dependent upon a number of factors recognized by the art. These include, for example, compatibility with the chosen expression vector, toxicity of the peptides encoded by the DNA molecule, rate of transformation, ease of recovery of the peptides, expression characteristics, bio-safety and costs. A balance of these factors must be struck with the understanding that not all hosts can be equally effective for the expression of a particular DNA sequence. Within these general guidelines, useful microbial hosts include bacteria (such as E. coli sp.), yeast (such as Saccharomyces sp.) and other fungi, insects, plants, mammalian (including human) cells in culture, or other hosts known in the art.

Next, the transformed host is cultured and purified. Host cells can be cultured under conventional fermentation conditions so that the desired compounds are expressed. Such fermentation conditions are well known in the art. Finally, the peptides are purified from culture by methods well known in the art.

The compounds can also be made by synthetic methods. Solid phase synthesis is the preferred technique of making individual peptides since it is the most cost-effective method of making small peptides. For example, well known solid phase synthesis techniques include the use of protecting groups, linkers, and solid phase supports, as well as specific protection and deprotection reaction conditions, linker cleavage conditions, use of scavengers, and other aspects of solid phase peptide synthesis. Suitable techniques are well known in the art. (E.g., Merrifield (1973), Chem. Polypeptides, pp. 335-61 (Katsoyannis and Panayotis eds.); Merrifield (1963), J. Am. Chem. Soc. 85: 2149; Davis et al. (1985), Biochem. Intl. 10: 394-414; Stewart and Young (1969), Solid Phase Peptide Synthesis; U.S. Pat. No. 3,941,763; Finn et al. (1976), The Proteins (3rd ed.) 2: 105-253; and Erickson et al. (1976), The Proteins (3rd ed.) 2: 257-527; "Protecting Groups in Organic Synthesis," 3rd Edition, T. W. Greene and P. G. M. Wuts, Eds., John Wiley & Sons, Inc., 1999; NovaBiochem Catalog, 2000; "Synthetic Peptides, A User's Guide," G. A. Grant, Ed., W.H. Freeman & Company, New York, N.Y., 1992; "Advanced Chemtech Handbook of Combinatorial & Solid Phase Organic Chemistry," W. D. Bennet, J. W. Christensen, L. K. Hamaker, M. L. Peterson, M. R. Rhodes, and H. H. Saneii, Eds., Advanced Chemtech, 1998; "Principles of Peptide Synthesis, 2nd ed.," M. Bodanszky, Ed., Springer-Verlag, 1993; "The Practice of Peptide Synthesis, 2nd ed.," M. Bodanszky and A. Bodanszky, Eds., Springer-Verlag, 1994; "Protecting Groups," P. J. Kocienski, Ed., Georg Thieme Verlag, Stuttgart, Germany, 1994; "Fmoc Solid Phase Peptide Synthesis, A Practical Approach," W. C. Chan and P. D. White, Eds., Oxford Press, 2000, G. B. Fields et al., Synthetic Peptides: A User's Guide, 1990, 77-183).

Whether the compositions of the present invention are prepared by synthetic or recombinant techniques, suitable protein purification techniques can also be involved, when applicable. In some embodiments of the compositions of the invention, the toxin peptide portion and/or the half-life extending portion, or any other portion, can be prepared to include a suitable isotopic label (e.g., ^{125}I, ^{14}C, ^{13}C, ^{35}S, ^{3}H, ^{2}H, ^{13}N, ^{15}N, ^{18}O, ^{17}O, *etc.*), for ease of quantification or detection.

Compounds that contain derivatized peptides or which contain non-peptide groups can be synthesized by well-known organic chemistry techniques.

Uses of the Compounds

In general. The compounds of this invention have pharmacologic activity resulting from their ability to bind to proteins of interest as agonists, mimetics or antagonists of the native ligands of such proteins of interest. Heritable diseases that have a known linkage to ion channels ("channelopathies") cover various fields of medicine, some of which include neurology, nephrology, myology and cardiology. A list of inherited disorders attributed to ion channels includes:

- cystic fibrosis (Cl^- channel; CFTR),
- Dent's disease (proteinuria and hypercalciuria; Cl^- channel; CLCN5),
- osteopetrosis (Cl^- channel; CLCN7),
- familial hyperinsulinemia (SUR1; KCNJ11; K channel),
- diabetes (KATP / SUR channel),
- Andersen syndrome (KCNJ2, Kir2.1 K channel),
- Bartter syndrome (KCNJ1; Kir1.1/ROMK; K channel),
- hereditary hearing loss (KCNQ4; K channel),
- hereditary hypertension (Liddle's syndrome; SCNN1; epithelial Na channel),
- dilated cardiomyopathy (SUR2, K channel),
- long-QT syndrome or cardiac arrhythmias (cardiac potassium and sodium channels),
- Thymothy syndrome (CACNA1C, Cav1.2),
- myasthenic syndromes (CHRNA,CHRNB,CNRNE; nAChR), and a variety of other myopathies,
- hyperkalemic periodic paralysis (Na and K channels),
- epilepsy (Na^+ and K^+ channels),
- hemiplegic migraine (CACNA1A, Cav2.1 Ca^{2+} channel and ATP1A2),
- central core disease (RYR1, RyR1; Ca^{2+} channel), and
- paramyotonia and myotonia (Na^+, Cl^- channels)

See L.J. Ptacek and Y-H Fu (2004), Arch. Neurol. 61: 166-8; B.A. Niemeyer et al. (2001), EMBO reports 21: 568-73; F. Lehmann-Horn and K. Jurkat-Rott (1999), Physiol. Rev. 79: 1317-72. Although the foregoing list concerned disorders of inherited origin, molecules targeting the channels cited in these disorders can also be useful in treating related disorders of other, or indeterminate, origin.

In addition to the aforementioned disorders, evidence has also been provided supporting ion channels as targets for treatment of:

- sickle cell anemia (IKCa1) – in sickle cell anemia, water loss from erythrocytes leads to hemoglobin polymerization and subsequent hemolysis and vascular obstruction. The water loss is consequent to potassium efflux through the so-called Gardos channel i.e., IKCa1. Therefore, block of IKCa1 is a potential therapeutic treatment for sickle cell anemia.
- glaucoma (BKCa), – In glaucoma the intraocular pressure is too high leading to optic nerve damage, abnormal eye function and possibly blindness. Block of BKCa potassium channels can reduce intraocular fluid secretion and increase smooth muscle contraction, possibly leading to lower intraocular pressure and neuroprotection in the eye.
- multiple sclerosis (Kv, KCa),
- psoriasis (Kv, KCa),
- arthritis (Kv, KCa),
- asthma (KCa, Kv),
- allergy(KCa, Kv),
- COPD (KCa, Kv, Ca),
- allergic rhinitis (KCa, Kv),
- pulmonary fibrosis,
- lupus (IKCa1, Kv),
- transplantation, GvHD (KCa, Kv),
- inflammatory bone resorption (KCa, Kv),
- periodontal disease (KCa, Kv),
- diabetes, type I (Kv), – type I diabetes is an autoimmune disease that is characterized by abnormal glucose, protein and lipid metabolism and is associated with insulin deficiency or resistance. In this disease, Kv1.3-expressing T-lymphocytes attack and destroy pancreatic islets leading to loss of beta-cells. Block of Kv1.3 decreases inflammatory cytokines. In addition block of Kv1.3 facilitates the translocation of GLUT4 to the plasma membrane, thereby increasing insulin sensitivity.
- obesity (Kv), – Kv1.3 appears to play a critical role in controlling energy homeostasis and in protecting against diet-induced obesity. Consequently, Kv1.3 blockers could increase metabolic rate, leading to greater energy utilization and decreased body weight.

- restenosis (KCa, Ca^{2+}), – proliferation and migration of vascular smooth muscle cells can lead to neointimal thickening and vascular restenosis. Excessive neointimal vascular smooth muscle cell proliferation is associated with elevated expression of IKCa1. Therefore, block of IKCa1 could represent a therapeutic strategy to prevent restenosis after angioplasty.
- ischaemia (KCa, Ca^{2+}), – in neuronal or cardiac ischemia, depolarization of cell membranes leads to opening of voltage-gated sodium and calcium channels. In turn this can lead to calcium overload, which is cytotoxic. Block of voltage-gated sodium and/or calcium channels can reduce calcium overload and provide cytoprotective effects. In addition, due to their critical role in controlling and stabilizing cell membrane potential, modulators of voltage- and calcium-activated potassium channels can also act to reduce calcium overload and protect cells.
- renal incontinence (KCa), renal incontinence is associated with overactive bladder smooth muscle cells. Calcium-activated potassium channels are expressed in bladder smooth muscle cells, where they control the membrane potential and indirectly control the force and frequency of cell contraction. Openers of calcium-activated potassium channels therefore provide a mechanism to dampen electrical and contractile activity in bladder, leading to reduced urge to urinate.
- osteoporosis (Kv),
- pain, including migraine (Na_v, TRP [transient receptor potential channels], P2X, Ca^{2+}), N-type voltage-gated calcium channels are key regulators of nociceptive neurotransmission in the spinal cord. Ziconotide, a peptide blocker of N-type calcium channels reduces nociceptive neurotransmission and is approved worldwide for the symptomatic alleviation of severe chronic pain in humans. Novel blockers of nociceptor-specific N-type calcium channels would be improved analgesics with reduced side-effect profiles.
- hypertension (Ca^{2+}), – L-type and T-type voltage-gated calcium channels are expressed in vascular smooth muscle cells where they control excitation-contraction coupling and cellular proliferation. In particular, T-type calcium channel activity has been linked to neointima formation during hypertension. Blockers of L-type and T-type calcium channels are useful for the clinical treatment of hypertension because they reduce calcium influx and inhibit smooth muscle cell contraction.
- wound healing, cell migration serves a key role in wound healing. Intracellular calcium gradients have been implicated as important regulators of cellular migration machinery in keratinocytes and fibroblasts. In addition, ion flux across cell membranes is associated with cell volume changes. By controlling cell volume, ion

channels contribute to the intracellular environment that is required for operation of the cellular migration machinery. In particular, IKCa1 appears to be required universally for cell migration. In addition, Kv1.3, Kv3.1, NMDA receptors and N-type calcium channels are associated with the migration of lymphocytes and neurons.

- stroke,
- Alzheimer's,
  Parkenson's Disease (nACHR, Nav)
  Bipolar Disorder (Nav, Cav)
- cancer, many potassium channel genes are amplified and protein subunits are upregulated in many cancerous condition. Consistent with a pathophysiological role for potassium channel upregulation, potassium channel blockers have been shown to suppress proliferation of uterine cancer cells and hepatocarcinoma cells, presumably through inhibition of calcium influx and effects on calcium-dependent gene expression.
- a variety of neurological, cardiovascular, metabolic and autoimmune diseases.

Both agonists and antagonists of ion channels can achieve therapeutic benefit. Therapeutic benefits can result, for example, from antagonizing Kv1.3, IKCa1, SKCa, BKCa, N-type or T-type Ca^{2+} channels and the like. Small molecule and peptide antagonists of these channels have been shown to possess utility in vitro and in vivo. Limitations in production efficiency and pharmacokinetics, however, have largely prevented clinical investigation of inhibitor peptides of ion channels.

Compositions of this invention incorporating peptide antagonists of the voltage-gated potassium channel Kv1.3 are useful as immunosuppressive agents with therapeutic value for autoimmune diseases. For example, such molecules are useful in treating multiple sclerosis, type 1 diabetes, psoriasis, inflammatory bowel disease, and rheumatoid arthritis. (See, e.g., H. Wulff et al. (2003) J. Clin. Invest. 111, 1703-1713 and H. Rus et al. (2005) PNAS 102, 11094-11099; Beeton et al., Targeting effector memory T cells with a selective inhibitor peptide of Kv1.3 channnels for therapy of autoimmune diseases, Molec. Pharmacol. 67(4):1369-81 (2005);1 Beeton et al. (2006), Kv1.3: therapeutic target for cell-mediated autoimmune disease, electronic preprint at //webfiles.uci.edu/xythoswfs/webui/ 2670029.1). Inhibitors of the voltage-gated potassium channel Kv1.3 have been examined in a variety of preclinical animal models of inflammation. Small molecule and peptide inhibitors of Kv1.3 have been shown to block delayed type hypersensitivity responses to ovalbumin [C. Beeton et al. (2005) Mol. Pharmacol. 67, 1369] and tetanus toxoid

[G.C. Koo et al. (1999) Clin. Immunol. 197, 99]. In addition to suppressing inflammation in the skin, inhibitors also reduced antibody production [G.C. Koo et al. (1997) J. Immunol. 158, 5120]. Kv1.3 antagonists have shown efficacy in a rat adoptive-transfer experimental autoimmune encephalomyelitis (AT-EAE) model of multiple sclerosis (MS). The Kv1.3 channel is overexpressed on myelin-specific T cells from MS patients, lending further support to the utility Kv1.3 inhibitors may provide in treating MS. Inflammatory bone resorption was also suppressed by Kv1.3 inhibitors in a preclinical adoptive-transfer model of periodontal disease [P. Valverde et al. (2004) J. Bone Mineral Res. 19, 155]. In this study, inhibitors additionally blocked antibody production to a bacterial outer membrane protein, - one component of the bacteria used to induce gingival inflammation. Recently in preclinical rat models, efficacy of Kv1.3 inhibitors was shown in treating pristane-induced arthritis and diabetes [C. Beeton et al. (2006) preprint available at //webfiles.uci.edu/xythoswfs/webui/_xy-2670029_1.]. The Kv1.3 channel is expressed on all subsets of T cells and B cells, but effector memory T cells and class-switched memory B cells are particularly dependent on Kv1.3 [H. Wulff et al. (2004) J. Immunol. 173, 776]. Gad5 / insulin-specific T cells from patients with new onset type 1 diabetes, myelin-specific T cells from MS patients and T cells from the synovium of rheumatoid arthritis patients all overexpress Kv1.3 [C. Beeton et al. (2006) preprint at //webfiles.uci.edu/xythoswfs/webui/_xy-2670029_1.]. Because mice deficient in Kv1.3 gained less weight when placed on a high fat diet [J. Xu et al. (2003) Human Mol. Genet. 12, 551] and showed altered glucose utilization [J. Xu et al. (2004) Proc. Natl. Acad. Sci. 101, 3112], Kv1.3 is also being investigated for the treatment of obesity and diabetes. Breast cancer specimens [M. Abdul et al. (2003)Anticancer Res. 23, 3347] and prostate cancer cell lines [S.P. Fraser et al. (2003) Pflugers Arch. 446, 559] have also been shown to express Kv1.3, and Kv1.3 blockade may be of utility for treatment of cancer. Disorders that can be treated in accordance with the inventive method of treating an autoimmune disorder, involving Kv1.3 inhibitor toxin peptide(s), include multiple sclerosis, type 1 diabetes, psoriasis, inflammatory bowel disease, contact-mediated dermatitis, rheumatoid arthritis, psoriatic arthritis, asthma, allergy, restinosis, systemic sclerosis, fibrosis, scleroderma, glomerulonephritis, Sjogren syndrome, inflammatory bone resorption, transplant rejection, graft-versus-host disease, and systemic lupus erythematosus (SLE) and other forms of lupus.

Some of the cells that express the calcium-activated potassium of intermediate conductance IKCa1 include T cells, B cells, mast cells and red blood cells (RBCs). T cells and RBCs from mice deficient in IKCa1 show defects in volume regulation [T. Begenisich et al. (2004) J. Biol. Chem. 279, 47681]. Preclinical and clinical studies have demonstrated IKCa1 inhibitors

utility in treating sickle cell anemia [J. W. Stocker et al. (2003) Blood 101, 2412; www.icagen.com]. Blockers of the IKCa1 channel have also been shown to block EAE, indicating they may possess utility in treatment of MS [E. P. Reich et al. (2005) Eur. J. Immunol. 35, 1027]. IgE-mediated histamine production from mast cells is also blocked by IKCa1 inhibitors [S. Mark Duffy et al. (2004) J. Allergy Clin. Immunol. 114, 66], therefore they may also be of benefit in treating asthma. The IKCa1 channel is overexpressed on activated T and B lymphocytes [H. Wulff et al. (2004) J. Immunol. 173, 776] and thus may show utility in treatment of a wide variety of immune disorders. Outside of the immune system, IKCa1 inhibitors have also shown efficacy in a rat model of vascular restinosis and thus might represent a new therapeutic strategy to prevent restenosis after angioplasty [R. Kohler et al. (2003) Circulation 108, 1119]. It is also thought that IKCa1 antagonists are of utility in treatment of tumor angiogenesis since inhibitors suppressed endothelial cell proliferation and angionenesis in vivo [I. Grgic et al. (2005) Arterioscler. Thromb. Vasc. Biol. 25, 704]. The IKCa1 channel is upregulated in pancreatic tumors and inhibitors blocked proliferation of pancreatic tumor cell lines [H. Jager et al. (2004) Mol Pharmacol. 65, 630]. IKCa1 antagonists may also represent an approach to attenuate acute brain damage caused by traumatic brain injury [F. Mauler (2004) Eur. J. Neurosci. 20, 1761]. Disorders that can be treated with IKCa1 inhibitors include multiple sclerosis, asthma, psoriasis, contact-mediated dermatitis, rheumatoid & psoriatic arthritis, inflammatory bowel disease, transplant rejection, graft-versus-host disease, Lupus, restinosis, pancreatic cancer, tumor angiogenesis and traumatic brain injury.

Accordingly, molecules of this invention incorporating peptide antagonists of the calcium-activated potassium channel of intermediate conductance, IKCa can be used to treat immune dysfunction, multiple sclerosis, type 1 diabetes, psoriasis, inflammatory bowel disease, contact-mediated dermatitis, rheumatoid arthritis, psoriatic arthritis, asthma, allergy, restinosis, systemic sclerosis, fibrosis, scleroderma, glomerulonephritis, Sjogren syndrome, inflammatory bone resorption, transplant rejection, graft-versus-host disease, and lupus.

Accordingly, the present invention includes a method of treating an autoimmune disorder, which involves administering to a patient who has been diagnosed with an autoimmune disorder, such as multiple sclerosis, type 1 diabetes, psoriasis, inflammatory bowel disease, contact-mediated dermatitis, rheumatoid arthritis, psoriatic arthritis, asthma, allergy, restinosis, systemic sclerosis, fibrosis, scleroderma, glomerulonephritis, Sjogren syndrome, inflammatory bone resorption, transplant rejection, graft-versus-host disease, or lupus, a therapeutically effective amount of the inventive composition of matter, whereby at least one symptom of the disorder is alleviated in the patient. "Alleviated" means to be lessened, lightened, diminished, softened,

mitigated (i.e., made more mild or gentle), quieted, assuaged, abated, relieved, nullified, or allayed, regardless of whether the symptom of interest is entirely erased, eradicated, eliminated, or prevented in a particular patient.

The present invention is further directed to a method of preventing or mitigating a relapse of a symptom of multiple sclerosis, which method involves administering to a patient, who has previously experienced at least one symptom of multiple sclerosis, a prophylactically effective amount of the inventive composition of matter, such that the at least one symptom of multiple sclerosis is prevented from recurring or is mitigated.

The inventive compositions of matter preferred for use in practicing the inventive method of treating an autoimmune disorder and the method of preventing or mitigating a relapse of a symptom of multiple sclerosis include as P (conjugated as in Formula I), a Kv1.3 or IKCa1 antagonist peptide, such as a ShK peptide, an OSK1 peptide, a ChTx peptide and/or a Maurotoxin (MTx) peptide, or peptide analogs of any of these.

For example, the conjugated ShK peptide peptide or ShK peptide analog can comprise an amino acid sequence selected from the following:
SEQ ID NOS: 5, 88 through 200, 548 through 561, 884 through 950, or 1295 through 1300 as set forth in Table 2.

The conjugated OSK1 peptide peptide or OSK1 peptide analog can comprise an amino acid sequence selected from the following:
SEQ ID NOS: 25, 294 through 298, 562 through 636, 980 through 1274, GVIINVSCKISRQCLEPCKKAGMRFGKCMNGKCHCTPK (OSK1-S7)(SEQ ID NO: 1303), or GVIINVSCKISRQCLKPCKDAGMRFGKCMNGKCHCTPK (OSK1-S7,K16,D20)(SEQ ID NO: 1308) as set forth in Table 7.

Also by way of example, a the conjugated MTX peptide, MTX peptide analog, ChTx peptide or ChTx peptide analog can comprise an amino acid sequence selected from:
SEQ ID NOS: 20, 330 through 343, 1301, 1302, 1304 through 1307, 1309, 1311, 1312, or 1315 through 1336 as set forth in Table 13; or SEQ ID NOS: 36, 59, 344 through 346, or 1369 through 1390 as set forth in Table 14.

Also useful in these methods conjugated, or unconjugated, are a Kv1.3 or IKCa1 inhibitor toxin peptide analog that comprises an amino acid sequence selected from:
SEQ ID NOS: 88, 89, 92, 148 through 200, 548 through 561, 884 through 949, or 1295 through 1300 as set forth in Table 2; or

SEQ ID NOS: 980 through 1274, GVIINVSCKISRQCLEPCKKAGMRFGKCMNGKCHCTPK (OSK1-S7)(SEQ ID NO: 1303), or GVIINVSCKISRQCLKPCKDAGMRFGKCMNGKCHCTPK (OSK1-S7,K16,D20)(SEQ ID NO: 1308) as set forth in Table 7; or

SEQ ID NOS: 330 through 337, 341, 1301, 1302, 1304 through 1307, 1309, 1311, 1312, and 1315 through 1336 as set forth in Table 13.

In accordance with these inventive methods, a patient who has been diagnosed with an autoimmune disorder, such as, but not limited to multiple sclerosis, type 1 diabetes, psoriasis, inflammatory bowel disease, contact-mediated dermatitis, rheumatoid arthritis, psoriatic arthritis, asthma, allergy, restinosis, systemic sclerosis, fibrosis, scleroderma, glomerulonephritis, Sjogren syndrome, inflammatory bone resorption, transplant rejection, graft-versus-host disease, or lupus, or a patient who has previously experienced at least one symptom of multiple sclerosis, are well-recognizable and/or diagnosed by the skilled practitioner, such as a physician, familiar with autoimmune disorders and their symptoms.

For example, symptoms of multiple sclerosis can include the following:

visual symptoms, such as, optic neuritis (blurred vision, eye pain, loss of color vision, blindness); diplopia (double vision); nystagmus (jerky eye movements); ocular dysmetria (constant under- or overshooting eye movements); internuclear ophthalmoplegia (lack of coordination between the two eyes, nystagmus, diplopia); movement and sound phosphenes (flashing lights when moving eyes or in response to a sudden noise); afferent pupillary defect (abnormal pupil responses);

motor symptoms, such as, paresis, monoparesis, paraparesis, hemiparesis, quadraparesis (muscle weakness - partial or mild paralysis); plegia, paraplegia, hemiplegia, tetraplegia, quadraplegia (paralysis - total or near total loss of muscle strength); spasticity (loss of muscle tone causing stiffness, pain and restricting free movement of affected limbs); dysarthria (slurred speech and related speech problems); muscle atrophy (wasting of muscles due to lack of use); spasms, cramps (involuntary contraction of muscles); hypotonia, clonus (problems with posture); myoclonus, myokymia (jerking and twitching muscles, tics); restless leg syndrome (involuntary leg movements, especially bothersome at night); footdrop (foot drags along floor during walking); dysfunctional reflexes (MSRs, Babinski's, Hoffman's, Chaddock's);

sensory symptoms, such as, paraesthesia (partial numbness, tingling, buzzing and vibration sensations); anaesthesia (complete numbness/loss of sensation); neuralgia, neuropathic and neurogenic pain (pain without apparent cause, burning, itching and electrical shock sensations); L'Hermitte's (electric shocks and buzzing sensations when moving head);

proprioceptive dysfunction (loss of awareness of location of body parts); trigeminal neuralgia (facial pain);

coordination and balance symptoms, such as, ataxia (loss of coordination); intention tremor (shaking when performing fine movements); dysmetria (constant under- or overshooting limb movements); vestibular ataxia (abnormal balance function in the inner ear); vertigo (nausea/vomitting/sensitivity to travel sickness from vestibular ataxia); speech ataxia (problems coordinating speech, stuttering); dystonia (slow limb position feedback); dysdiadochokinesia (loss of ability to produce rapidly alternating movements, for example to move to a rhythm);

bowel, bladder and sexual symptoms, such as, frequent micturation, bladder spasticity (urinary urgency and incontinence); flaccid bladder, detrusor-sphincter dyssynergia (urinary hesitancy and retention); erectile dysfunction (male and female impotence); anorgasmy (inability to achieve orgasm); retrograde ejaculation (ejaculating into the bladder); frigidity (inability to become sexually aroused); constipation (infrequent or irregular bowel movements); fecal urgency (bowel urgency); fecal incontinence (bowel incontinence);

cognitive symptoms, such as, depression; cognitive dysfunction (short-term and long-term memory problems, forgetfulness, slow word recall); dementia; mood swings, emotional lability, euphoria; bipolar syndrome; anxiety; aphasia, dysphasia (impairments to speech comprehension and production); and

other symptoms, such as, fatigue; Uhthoff's Symptom (increase in severity of symptoms with heat); gastroesophageal reflux (acid reflux); impaired sense of taste and smell; epileptic seizures; swallowing problems, respiratory problems; and sleeping disorders.

The symptoms of multiple sclerosis enumerated above, are merely illustrative and are not intended to be an exhaustive description of all possible symptoms experienced by a single patient or by several sufferers in composite, and to which the present invention is directed. Those skilled in the art are aware of various clinical symptoms and constellations of symptoms of autoimmune disorders suffered by individual patients, and to those symptoms are also directed the present inventive methods of treating an autoimmune disorder or of preventing or mitigating a relapse of a symptom of multiple sclerosis.

The therapeutically effective amount, prophylactically effective amount, and dosage regimen involved in the inventive methods of treating an autoimmune disorder or of preventing or mitigating a relapse of a symptom of multiple sclerosis, will be determined by the attending physician, considering various factors which modify the action of therapeutic agents, such as the age, condition, body weight, sex and diet of the patient, the severity of the condition being treated,

time of administration, and other clinical factors. Generally, the daily amount or regimen should be in the range of about 1 to about 10,000 micrograms (μg) of the vehicle-conjugated peptide per kilogram (kg) of body mass, preferably about 1 to about 5000 μg per kilogram of body mass, and most preferably about 1 to about 1000 μg per kilogram of body mass.

Molecules of this invention incorporating peptide antagonists of the voltage-gated potassium channel Kv2.1 can be used to treat type II diabetes.

Molecules of this invention incorporating peptide antagonists of the M current (e.g., BeKm-1) can be used to treat Alzheimer's disease and enhance cognition.

Molecules of this invention incorporating peptide antagonists of the voltage-gated potassium channel Kv4.3 can be used to treat Alzheimer's disease.

Molecules of this invention incorporating peptide antagonists of the calcium-activated potassium channel of small conductance, SKCa can be used to treat epilepsy, memory, learning, neuropsychiatric, neurological, neuromuscular, and immunological disorders, schizophrenia, bipolar disorder, sleep apnea, neurodegeneration, and smooth muscle disorders.

Molecules of this invention incorporating N-type calcium channel antagonist peptides are useful in alleviating pain. Peptides with such activity (e.g., Ziconotide™, ω-conotoxin-MVIIA) have been clinically validated.

Molecules of this invention incorporating T-type calcium channel antagonist peptides are useful in alleviating pain. Several lines of evidence have converged to indicate that inhibition of Cav3.2 in dorsal root ganglia may bring relief from chronic pain. T-type calcium channels are found at extremely high levels in the cell bodies of a subset of neurons in the DRG; these are likely mechanoreceptors adapted to detect slowly-moving stimuli (Shin et al., Nature Neuroscience 6:724-730, 2003), and T-type channel activity is likely responsible for burst spiking (Nelson et al., J Neurosci 25:8766-8775, 2005). Inhibition of T-type channels by either mibefradil or ethosuximide reverses mechanical allodynia in animals induced by nerve injury (Dogrul et al., Pain 105:159-168, 2003) or by chemotherapy (Flatters and Bennett, Pain 109:150-161, 2004). Antisense to Cav3.2, but not Cav3.1 or Cav3.3, increases pain thresholds in animals and also reduces expression of Cav3.2 protein in the DRG (Bourinet et al., EMBO J 24:315-324, 2005). Similarly, locally injected reducing agents produce pain and increase Cav3.2 currents, oxidizing agents reduce pain and inhibit Cav3.2 currents, and peripherally administered neurosteroids are analgesic and inhibit T-type currents from DRG (Todorovic et al., Pain 109:328-339, 2004; Pathirathna et al., Pain 114:429-443, 2005). Accordingly, it is thought that inhibition of Cav3.2 in the cell bodies of DRG neurons can inhibit the repetitive spiking of these neurons associated with chronic pain states.

Molecules of this invention incorporating L-type calcium channel antagonist peptides are useful in treating hypertension. Small molecules with such activity (e.g., DHP) have been clinically validated.

Molecules of this invention incorporating peptide antagonists of the Na_V1 (TTX_S-type) channel can be used to alleviate pain. Local anesthetics and tricyclic antidepressants with such activity have been clinically validated. Such molecules of this invention can in particular be useful as muscle relaxants.

Molecules of this invention incorporating peptide antagonists of the Na_V1(TTX_R-type) channel can be used to alleviate pain arising from nerve and or tissue injury.

Molecules of this invention incorporating peptide antagonists of glial & epithelial cell Ca^{2+}-activated chloride channel can be used to treat cancer and diabetes.

Molecules of this invention incorporating peptide antagonists of NMDA receptors can be used to treat pain, epilepsy, brain and spinal cord injury.

Molecules of this invention incorporating peptide antagonists of nicotinic receptors can be used as muscle relaxants. Such molecules can be used to treat pain, gastric motility disorders, urinary incontinence, nicotine addiction, and mood disorders.

Molecules of this invention incorporating peptide antagonists of 5HT3 receptor can be used to treat Nausea, pain, and anxiety.

Molecules of this invention incorporating peptide antagonists of the norepinephrine transporter can be used to treat pain, anti-depressant, learning, memory, and urinary incontinence.

Molecules of this invention incorporating peptide antagonists of the Neurotensin receptor can be used to treat pain.

In addition to therapeutic uses, the compounds of the present invention can be useful in diagnosing diseases characterized by dysfunction of their associated protein of interest. In one embodiment, a method of detecting in a biological sample a protein of interest (e.g., a receptor) that is capable of being activated comprising the steps of: (a) contacting the sample with a compound of this invention; and (b) detecting activation of the protein of interest by the compound. The biological samples include tissue specimens, intact cells, or extracts thereof. The compounds of this invention can be used as part of a diagnostic kit to detect the presence of their associated proteins of interest in a biological sample. Such kits employ the compounds of the invention having an attached label to allow for detection. The compounds are useful for identifying normal or abnormal proteins of interest.

The therapeutic methods, compositions and compounds of the present invention can also

be employed, alone or in combination with other molecules in the treatment of disease.

Pharmaceutical Compositions

In General. The present invention also provides pharmaceutical compositions comprising the inventive composition of matter and a pharmaceutically acceptable carrier. Such pharmaceutical compositions can be configured for administration to a patient by a wide variety of delivery routes, e.g., an intravascular delivery route such as by injection or infusion, subcutaneous, intramuscular, intraperitoneal, epidural, or intrathecal delivery routes, or for oral, enteral, pulmonary (e.g., inhalant), intranasal, transmucosal (e.g., sublingual administration), transdermal or other delivery routes and/or forms of administration known in the art. The inventive pharmaceutical compositions may be prepared in liquid form, or may be in dried powder form, such as lyophilized form. For oral or enteral use, the pharmaceutical compositions can be configured, for example, as tablets, troches, lozenges, aqueous or oily suspensions, dispersible powders or granules, emulsions, hard or soft capsules, syrups, elixirs or enteral formulas.

In the practice of this invention the "pharmaceutically acceptable carrier" is any physiologically tolerated substance known to those of ordinary skill in the art useful in formulating pharmaceutical compositions, including, any pharmaceutically acceptable diluents, excipients, dispersants, binders, fillers, glidants, anti-frictional agents, compression aids, tablet-disintegrating agents (disintegrants), suspending agents, lubricants, flavorants, odorants, sweeteners, permeation or penetration enhancers, preservatives, surfactants, solubilizers, emulsifiers, thickeners, adjuvants, dyes, coatings, encapsulating material(s), and/or other additives singly or in combination. Such pharmaceutical compositions can include diluents of various buffer content (*e.g.*, Tris-HCl, acetate, phosphate), pH and ionic strength; additives such as detergents and solubilizing agents (*e.g.*, Tween® 80, Polysorbate 80), anti-oxidants (*e.g.*, ascorbic acid, sodium metabisulfite), preservatives (*e.g.*, Thimersol®, benzyl alcohol) and bulking substances (*e.g.*, lactose, mannitol); incorporation of the material into particulate preparations of polymeric compounds such as polylactic acid, polyglycolic acid, etc. or into liposomes. Hyaluronic acid can also be used, and this can have the effect of promoting sustained duration in the circulation. Such compositions can influence the physical state, stability, rate of in vivo release, and rate of in vivo clearance of the present proteins and derivatives. See, e.g., Remington's Pharmaceutical Sciences, 18th Ed. (1990, Mack Publishing Co., Easton, PA 18042) pages 1435-1712, which are herein incorporated by reference in their entirety. The compositions can be prepared in liquid form, or can be in dried powder, such as lyophilized form. Implantable sustained release formulations are also useful, as are transdermal or transmucosal formulations. Additionally (or alternatively), the present invention provides compositions for use in any of the various slow or sustained release formulations or microparticle formulations known to

the skilled artisan, for example, sustained release microparticle formulations, which can be administered via pulmonary, intranasal, or subcutaneous delivery routes.

One can dilute the inventive compositions or increase the volume of the pharmaceutical compositions of the invention with an inert material. Such diluents can include carbohydrates, especially, mannitol, α-lactose, anhydrous lactose, cellulose, sucrose, modified dextrans and starch. Certain inorganic salts may also be used as fillers, including calcium triphosphate, magnesium carbonate and sodium chloride. Some commercially available diluents are Fast-Flo, Emdex, STA-Rx 1500, Emcompress and Avicell.

A variety of conventional thickeners are useful in creams, ointments, suppository and gel configurations of the pharmaceutical composition, such as, but not limited to, alginate, xanthan gum, or petrolatum, may also be employed in such configurations of the pharmaceutical composition of the present invention. A permeation or penetration enhancer, such as polyethylene glycol monolaurate, dimethyl sulfoxide, N-vinyl-2-pyrrolidone, N-(2-hydroxyethyl)-pyrrolidone, or 3-hydroxy-N-methyl-2-pyrrolidone can also be employed. Useful techniques for producing hydrogel matrices are known. (E.g., Feijen, Biodegradable hydrogel matrices for the controlled release of pharmacologically active agents, U.S. Patent No. 4,925,677; Shah et al., Biodegradable pH/thermosensitive hydrogels for sustained delivery of biologically active agents, WO 00/38651 A1). Such biodegradable gel matrices can be formed, for example, by crosslinking a proteinaceous component and a polysaccharide or mucopolysaccharide component, then loading with the inventive composition of matter to be delivered.

Liquid pharmaceutical compositions of the present invention that are sterile solutions or suspensions can be administered to a patient by injection, for example, intramuscularly, intrathecally, epidurally, intravascularly (e.g., intravenously or intraarterially), intraperitoneally or subcutaneously. (See, e.g., Goldenberg et al., Suspensions for the sustained release of proteins, U.S. Patent No. 6,245,740 and WO 00/38652 A1). Sterile solutions can also be administered by intravenous infusion. The inventive composition can be included in a sterile solid pharmaceutical composition, such as a lyophilized powder, which can be dissolved or suspended at a convenient time before administration to a patient using sterile water, saline, buffered saline or other appropriate sterile injectable medium.

Implantable sustained release formulations are also useful embodiments of the inventive pharmaceutical compositions. For example, the pharmaceutically acceptable carrier, being a biodegradable matrix implanted within the body or under the skin of a human or non-human vertebrate, can be a hydrogel similar to those described above. Alternatively, it may be formed from a poly-alpha-amino acid component. (Sidman, Biodegradable, implantable drug delivery device, and process for

preparing and using same, U.S. Patent No. 4,351,337). Other techniques for making implants for delivery of drugs are also known and useful in accordance with the present invention.

In powder forms, the pharmaceutically acceptable carrier is a finely divided solid, which is in admixture with finely divided active ingredient(s), including the inventive composition. For example, in some embodiments, a powder form is useful when the pharmaceutical composition is configured as an inhalant. (See, e.g., Zeng et al., Method of preparing dry powder inhalation compositions, WO 2004/017918; Trunk et al., Salts of the CGRP antagonist BIBN4096 and inhalable powdered medicaments containing them, U.S. Patent No. 6,900,317).

One can dilute or increase the volume of the compound of the invention with an inert material. These diluents could include carbohydrates, especially mannitol, α-lactose, anhydrous lactose, cellulose, sucrose, modified dextrans and starch. Certain inorganic salts can also be used as fillers including calcium triphosphate, magnesium carbonate and sodium chloride. Some commercially available diluents are Fast-Flo™, Emdex™, STA-Rx™ 1500, Emcompress™ and Avicell™.

Disintegrants can be included in the formulation of the pharmaceutical composition into a solid dosage form. Materials used as disintegrants include but are not limited to starch including the commercial disintegrant based on starch, Explotab™. Sodium starch glycolate, Amberlite™, sodium carboxymethylcellulose, ultramylopectin, sodium alginate, gelatin, orange peel, acid carboxymethyl cellulose, natural sponge and bentonite can all be used. Insoluble cationic exchange resin is another form of disintegrant. Powdered gums can be used as disintegrants and as binders and these can include powdered gums such as agar, Karaya or tragacanth. Alginic acid and its sodium salt are also useful as disintegrants.

Binders can be used to hold the therapeutic agent together to form a hard tablet and include materials from natural products such as acacia, tragacanth, starch and gelatin. Others include methyl cellulose (MC), ethyl cellulose (EC) and carboxymethyl cellulose (CMC). Polyvinyl pyrrolidone (PVP) and hydroxypropylmethyl cellulose (HPMC) could both be used in alcoholic solutions to granulate the therapeutic.

An antifrictional agent can be included in the formulation of the therapeutic to prevent sticking during the formulation process. Lubricants can be used as a layer between the therapeutic and the die wall, and these can include but are not limited to; stearic acid including its magnesium and calcium salts, polytetrafluoroethylene (PTFE), liquid paraffin, vegetable oils and waxes. Soluble lubricants can also be used such as sodium lauryl sulfate, magnesium lauryl sulfate, polyethylene glycol of various molecular weights, Carbowax 4000 and 6000.

Glidants that might improve the flow properties of the drug during formulation and to aid rearrangement during compression might be added. The glidants can include starch, talc, pyrogenic silica and hydrated silicoaluminate.

To aid dissolution of the compound of this invention into the aqueous environment a surfactant might be added as a wetting agent. Surfactants can include anionic detergents such as sodium lauryl sulfate, dioctyl sodium sulfosuccinate and dioctyl sodium sulfonate. Cationic detergents might be used and could include benzalkonium chloride or benzethonium chloride. The list of potential nonionic detergents that could be included in the formulation as surfactants are lauromacrogol 400, polyoxyl 40 stearate, polyoxyethylene hydrogenated castor oil 10, 50 and 60, glycerol monostearate, polysorbate 40, 60, 65 and 80, sucrose fatty acid ester, methyl cellulose and carboxymethyl cellulose. These surfactants could be present in the formulation of the protein or derivative either alone or as a mixture in different ratios.

Oral dosage forms. Also useful are oral dosage forms of the inventive compositionss. If necessary, the composition can be chemically modified so that oral delivery is efficacious. Generally, the chemical modification contemplated is the attachment of at least one moiety to the molecule itself, where said moiety permits (a) inhibition of proteolysis; and (b) uptake into the blood stream from the stomach or intestine. Also desired is the increase in overall stability of the compound and increase in circulation time in the body. Moieties useful as covalently attached half-life extending moieties in this invention can also be used for this purpose. Examples of such moieties include: PEG, copolymers of ethylene glycol and propylene glycol, carboxymethyl cellulose, dextran, polyvinyl alcohol, polyvinyl pyrrolidone and polyproline. See, for example, Abuchowski and Davis (1981), Soluble Polymer-Enzyme Adducts, Enzymes as Drugs (Hocenberg and Roberts, eds.), Wiley-Interscience, New York, NY, pp 367-83; Newmark, et al. (1982), J. Appl. Biochem. 4:185-9. Other polymers that could be used are poly-1,3-dioxolane and poly-1,3,6-tioxocane. Preferred for pharmaceutical usage, as indicated above, are PEG moieties.

For oral delivery dosage forms, it is also possible to use a salt of a modified aliphatic amino acid, such as sodium N-(8-[2-hydroxybenzoyl] amino) caprylate (SNAC), as a carrier to enhance absorption of the therapeutic compounds of this invention. The clinical efficacy of a heparin formulation using SNAC has been demonstrated in a Phase II trial conducted by Emisphere Technologies. See US Patent No. 5,792,451, "Oral drug delivery composition and methods."

In one embodiment, the pharmaceutically acceptable carrier can be a liquid and the pharmaceutical composition is prepared in the form of a solution, suspension, emulsion, syrup,

elixir or pressurized composition. The active ingredient(s) (e.g., the inventive composition of matter) can be dissolved, diluted or suspended in a pharmaceutically acceptable liquid carrier such as water, an organic solvent, a mixture of both, or pharmaceutically acceptable oils or fats. The liquid carrier can contain other suitable pharmaceutical additives such as detergents and/or solubilizers (e.g., Tween 80, Polysorbate 80), emulsifiers, buffers at appropriate pH (e.g., Tris-HCl, acetate, phosphate), adjuvants, anti-oxidants (e.g., ascorbic acid, sodium metabisulfite), preservatives (e.g., Thimersol, benzyl alcohol), sweeteners, flavoring agents, suspending agents, thickening agents, bulking substances (e.g., lactose, mannitol), colors, viscosity regulators, stabilizers, electrolytes, osmolutes or osmo-regulators. Additives can also be included in the formulation to enhance uptake of the inventive composition. Additives potentially having this property are for instance the fatty acids oleic acid, linoleic acid and linolenic acid.

Useful are oral solid dosage forms, which are described generally in Remington's Pharmaceutical Sciences (1990), supra, in Chapter 89, which is hereby incorporated by reference in its entirety. Solid dosage forms include tablets, capsules, pills, troches or lozenges, cachets or pellets. Also, liposomal or proteinoid encapsulation can be used to formulate the present compositions (as, for example, proteinoid microspheres reported in U.S. Patent No. 4,925,673). Liposomal encapsulation can be used and the liposomes can be derivatized with various polymers (e.g., U.S. Patent No. 5,013,556). A description of possible solid dosage forms for the therapeutic is given in Marshall, K., Modern Pharmaceutics (1979), edited by G. S. Banker and C. T. Rhodes, in Chapter 10, which is hereby incorporated by reference in its entirety. In general, the formulation will include the inventive compound, and inert ingredients that allow for protection against the stomach environment, and release of the biologically active material in the intestine.

The composition of this invention can be included in the formulation as fine multiparticulates in the form of granules or pellets of particle size about 1 mm. The formulation of the material for capsule administration could also be as a powder, lightly compressed plugs or even as tablets. The therapeutic could be prepared by compression.

Colorants and flavoring agents can all be included. For example, the protein (or derivative) can be formulated (such as by liposome or microsphere encapsulation) and then further contained within an edible product, such as a refrigerated beverage containing colorants and flavoring agents.

In tablet form, the active ingredient(s) are mixed with a pharmaceutically acceptable carrier having the necessary compression properties in suitable proportions and compacted in the shape and size desired.

The powders and tablets preferably contain up to 99% of the active ingredient(s). Suitable solid carriers include, for example, calcium phosphate, magnesium stearate, talc, sugars, lactose, dextrin, starch, gelatin, cellulose, polyvinylpyrrolidine, low melting waxes and ion exchange resins.

Controlled release formulation can be desirable. The composition of this invention could be incorporated into an inert matrix that permits release by either diffusion or leaching mechanisms e.g., gums. Slowly degenerating matrices can also be incorporated into the formulation, e.g., alginates, polysaccharides. Another form of a controlled release of the compositions of this invention is by a method based on the Oros™ therapeutic system (Alza Corp.), i.e., the drug is enclosed in a semipermeable membrane which allows water to enter and push drug out through a single small opening due to osmotic effects. Some enteric coatings also have a delayed release effect.

Other coatings can be used for the formulation. These include a variety of sugars that could be applied in a coating pan. The therapeutic agent could also be given in a film-coated tablet and the materials used in this instance are divided into 2 groups. The first are the nonenteric materials and include methylcellulose, ethyl cellulose, hydroxyethyl cellulose, methylhydroxy-ethyl cellulose, hydroxypropyl cellulose, hydroxypropyl-methyl cellulose, sodium carboxymethyl cellulose, providone and the polyethylene glycols. The second group consists of the enteric materials that are commonly esters of phthalic acid.

A mix of materials might be used to provide the optimum film coating. Film coating can be carried out in a pan coater or in a fluidized bed or by compression coating.

Pulmonary delivery forms. Pulmonary delivery of the inventive compositions is also useful. The protein (or derivative) is delivered to the lungs of a mammal while inhaling and traverses across the lung epithelial lining to the blood stream. (Other reports of this include Adjei et al., Pharma. Res. (1990) 7: 565-9; Adjei et al. (1990), Internatl. J. Pharmaceutics 63: 135-44 (leuprolide acetate); Braquet et al. (1989), J. Cardiovasc. Pharmacol. 13 (suppl.5): s.143-146 (endothelin-1); Hubbard et al. (1989), Annals Int. Med. 3: 206-12 (α1-antitrypsin); Smith et al. (1989), J. Clin. Invest. 84: 1145-6 (α1-proteinase); Oswein et al. (March 1990), "Aerosolization of Proteins," Proc. Symp. Resp. Drug Delivery II, Keystone, Colorado (recombinant human growth hormone); Debs et al. (1988), J. Immunol. 140: 3482-8 (interferon-γ and tumor necrosis factor α) and Platz et al., U.S. Patent No. 5,284,656 (granulocyte colony stimulating factor).

Useful in the practice of this invention are a wide range of mechanical devices designed for pulmonary delivery of therapeutic products, including but not limited to nebulizers, metered dose inhalers, and powder inhalers, all of which are familiar to those skilled in the art. Some specific

examples of commercially available devices suitable for the practice of this invention are the Ultravent nebulizer, manufactured by Mallinckrodt, Inc., St. Louis, Missouri; the Acorn II nebulizer, manufactured by Marquest Medical Products, Englewood, Colorado; the Ventolin metered dose inhaler, manufactured by Glaxo Inc., Research Triangle Park, North Carolina; and the Spinhaler powder inhaler, manufactured by Fisons Corp., Bedford, Massachusetts. (See, e.g., Helgesson et al., Inhalation device, U.S. Patent No. 6,892,728; McDerment et al., Dry powder inhaler, WO 02/11801 A1; Ohki et al., Inhalant medicator, U.S. Patent No. 6,273,086).

All such devices require the use of formulations suitable for the dispensing of the inventive compound. Typically, each formulation is specific to the type of device employed and can involve the use of an appropriate propellant material, in addition to diluents, adjuvants and/or carriers useful in therapy.

The inventive compound should most advantageously be prepared in particulate form with an average particle size of less than 10 μm (or microns), most preferably 0.5 to 5 μm, for most effective delivery to the distal lung.

Pharmaceutically acceptable carriers include carbohydrates such as trehalose, mannitol, xylitol, sucrose, lactose, and sorbitol. Other ingredients for use in formulations can include DPPC, DOPE, DSPC and DOPC. Natural or synthetic surfactants can be used. PEG can be used (even apart from its use in derivatizing the protein or analog). Dextrans, such as cyclodextran, can be used. Bile salts and other related enhancers can be used. Cellulose and cellulose derivatives can be used. Amino acids can be used, such as use in a buffer formulation.

Also, the use of liposomes, microcapsules or microspheres, inclusion complexes, or other types of carriers is contemplated.

Formulations suitable for use with a nebulizer, either jet or ultrasonic, will typically comprise the inventive compound dissolved in water at a concentration of about 0.1 to 25 mg of biologically active protein per mL of solution. The formulation can also include a buffer and a simple sugar (e.g., for protein stabilization and regulation of osmotic pressure). The nebulizer formulation can also contain a surfactant, to reduce or prevent surface induced aggregation of the protein caused by atomization of the solution in forming the aerosol.

Formulations for use with a metered-dose inhaler device will generally comprise a finely divided powder containing the inventive compound suspended in a propellant with the aid of a surfactant. The propellant can be any conventional material employed for this purpose, such as a chlorofluorocarbon, a hydrochlorofluorocarbon, a hydrofluorocarbon, or a hydrocarbon, including trichlorofluoromethane, dichlorodifluoromethane, dichlorotetrafluoroethanol, and 1,1,1,2-

tetrafluoroethane, or combinations thereof. Suitable surfactants include sorbitan trioleate and soya lecithin. Oleic acid can also be useful as a surfactant. (See, e.g., Bäckström et al., Aerosol drug formulations containing hydrofluoroalkanes and alkyl saccharides, U.S. Patent No. 6,932,962).

Formulations for dispensing from a powder inhaler device will comprise a finely divided dry powder containing the inventive compound and can also include a bulking agent, such as lactose, sorbitol, sucrose, mannitol, trehalose, or xylitol in amounts which facilitate dispersal of the powder from the device, e.g., 50 to 90% by weight of the formulation.

Nasal delivery forms.In accordance with the present invention, intranasal delivery of the inventive composition of matter and/or pharmaceutical compositions is also useful, which allows passage thereof to the blood stream directly after administration to the inside of the nose, without the necessity for deposition of the product in the lung. Formulations suitable for intransal administration include those with dextran or cyclodextran, and intranasal delivery devices are known. (See, e.g, Freezer, Inhaler, U.S. Patent No. 4,083,368).

Transdermal and transmucosal (e.g., buccal) delivery forms). In some embodiments, the inventive composition is configured as a part of a pharmaceutically acceptable transdermal or transmucosal patch or a troche. Transdermal patch drug delivery systems, for example, matrix type transdermal patches, are known and useful for practicing some embodiments of the present pharmaceutical compositions. (E.g., Chien et al., Transdermal estrogen/progestin dosage unit, system and process, U.S. Patent Nos. 4,906,169 and 5,023,084; Cleary et al., Diffusion matrix for transdermal drug administration and transdermal drug delivery devices including same, U.S. Patent No. 4,911,916; Teillaud et al., EVA-based transdermal matrix system for the administration of an estrogen and/or a progestogen, U.S. Patent No. 5.605,702; Venkateshwaran et al., Transdermal drug delivery matrix for coadministering estradiol and another steroid, U.S. Patent No. 5,783,208; Ebert et al., Methods for providing testosterone and optionally estrogen replacement therapy to women, U.S. Patent No. 5,460,820). A variety of pharmaceutically acceptable systems for transmucosal delivery of therapeutic agents are also known in the art and are compatible with the practice of the present invention. (E.g., Heiber et al., Transmucosal delivery of macromolecular drugs, U.S. Patent Nos. 5,346,701 and 5,516,523; Longenecker et al., Transmembrane formulations for drug administration, U.S. Patent No. 4,994,439).

Buccal delivery of the inventive compositions is also useful. Buccal delivery formulations are known in the art for use with peptides. For example, known tablet or patch systems configured for drug delivery through the oral mucosa (e.g., sublingual mucosa), include some embodiments that comprise an inner layer containing the drug, a permeation enhancer, such as a bile salt or

fusidate, and a hydrophilic polymer, such as hydroxypropyl cellulose, hydroxypropyl methylcellulose, hydroxyethyl cellulose, dextran, pectin, polyvinyl pyrrolidone, starch, gelatin, or any number of other polymers known to be useful for this purpose. This inner layer can have one surface adapted to contact and adhere to the moist mucosal tissue of the oral cavity and can have an opposing surface adhering to an overlying non-adhesive inert layer. Optionally, such a transmucosal delivery system can be in the form of a bilayer tablet, in which the inner layer also contains additional binding agents, flavoring agents, or fillers. Some useful systems employ a non-ionic detergent along with a permeation enhancer. Transmucosal delivery devices may be in free form, such as a cream, gel, or ointment, or may comprise a determinate form such as a tablet, patch or troche. For example, delivery of the inventive composition can be via a transmucosal delivery system comprising a laminated composite of, for example, an adhesive layer, a backing layer, a permeable membrane defining a reservoir containing the inventive composition, a peel seal disc underlying the membrane, one or more heat seals, and a removable release liner. (E.g., Ebert et al., Transdermal delivery system with adhesive overlay and peel seal disc, U.S. Patent No. 5,662,925; Chang et al., Device for administering an active agent to the skin or mucosa, U.S. Patent Nos. 4,849,224 and 4,983,395). These examples are merely illustrative of available transmucosal drug delivery technology and are not limiting of the present invention.

Dosages. The dosage regimen involved in a method for treating the above-described conditions will be determined by the attending physician, considering various factors which modify the action of drugs, e.g. the age, condition, body weight, sex and diet of the patient, the severity of any infection, time of administration and other clinical factors. Generally, the daily regimen should be in the range of 0.1-1000 micrograms of the inventive compound per kilogram of body weight, preferably 0.1-150 micrograms per kilogram.

Working examples

The compositions described above can be prepared as described below. These examples are not to be construed in any way as limiting the scope of the present invention.

Example 1

Fc-L10-ShK[1-35] mammalian expression

Fc-L10-ShK[1-35], also referred to as "Fc-2xL-ShK[1-35]", an inhibitor of Kv1.3. A DNA sequence coding for the Fc region of human IgG1 fused in-frame to a linker sequence and a monomer of the Kv1.3 inhibitor peptide ShK[1-35] was constructed as described below. Methods for expressing and purifying the peptibody from mammalian cells (HEK 293 and Chinese Hamster Ovary cells) are disclosed herein.

The expression vector pcDNA3.1(+)CMVi (Figure 13A) was constructed by replacing the CMV promoter between MluI and HindIII in pcDNA3.1(+) with the CMV promoter plus intron (Invitrogen). The expression vector pcDNA3.1(+)CMVi-hFc-ActivinRIIB (Figure 13B) was generated by cloning a HindIII-NotI digested PCR product containing a 5' Kozak sequence, a signal peptide and the human Fc-linker–ActivinRIIB fusion protein with the large fragment of HindIII-NotI digested pcDNA3.1(+)CMVi. The nucleotide and amino acid sequence of the human IgG1 Fc region in pcDNA3.1(+)CMVi-hFc-ActivinRIIB is shown in Figure 3A-B. This vector also has a GGGGSGGGGS ("L10"; SEQ ID NO:79) linker split by a BamHI site thus enabling with the oligo below formation of the 10 amino acid linker between Fc and the ShK[1-35] peptide (see Figure 14A-B) for the final Fc-L10-ShK[1-35] nucleotide and amino acid sequence (Figure 14A-B and SEQ ID NO: 77 and SEQ ID NO:78).

The Fc-L10-ShK[1-35] expression vector was constructing using PCR stategies to generate the full length ShK gene linked to a four glycine and one serine amino acid linker (lower case letters here indicate linker sequence of L-form amino acid residues) with two stop codons and flanked by BamHI and NotI restriction sites as shown below.

```
BamHI
GGATCCGGAGGAGGAGGAAGCCGCAGCTGCATCGACACCATCCCCAAGAGCCGCTGCACCGCCTTCCAG
     g  g  g  g  s  R  S  C  I  D  T  I  P  K  S  R  C  T  A  F  Q

TGCAAGCACAGCATGAAGTACCGCCTGAGCTTCTGCCGCAAGACCTGCGGCACCTGCTAATGAGCGGCCGC//SEQ ID NO:657
C  K  H  S  M  K  Y  R  L  S  F  C  R  K  T  C  G  T  C          NotI
//SEQ ID NO:658
```

Two oligos with the sequence as depicted below were used in a PCR reaction with Herculase™ polymerase (Stratagene) at 94°C-30sec, 50°C-30sec, and 72°C-1min for 30 cycles.

```
cat gga tcc gga gga gga gga agc cgc agc tgc atc gac acc atc ccc aag agc
cgc tgc acc gcc ttc cag tgc aag cac  //SEQ ID NO:659

cat gcg gcc gct cat tag cag gtg ccg cag gtc ttg cgg cag aag ctc agg cgg
tac ttc atg ctg tgc ttg cac tgg aag g  //SEQ ID NO:660
```

The resulting PCR products were resolved as the 150bp bands on a one percent agarose gel. The 150bp PCR product was digested with BamHI and NotI (Roche) restriction enzymes and agarose gel purified by Gel Purification Kit (Qiagen). At the same time, the pcDNA3.1(+)CMVi-hFc-ActivinRIIB vector (Figure 13B) was digested with BamHI and NotI restriction enzymes

and the large fragment was purified by Gel Purification Kit. The gel purified PCR fragment was ligated to the purified large fragment and transformed into XL-1blue bacteria (Stratagene). DNAs from transformed bacterial colonies were isolated and digested with BamHI and NotI restriction enzyme digestion and resolved on a one percent agarose gel. DNAs resulting in an expected pattern were submitted for sequencing. Although, analysis of several sequences of clones yielded a 100% percent match with the above sequence, only one clone was selected for large scaled plasmid purification. The DNA from Fc-2xL-ShK in pcDNA3.1(+)CMVi clone was resequenced to confirm the Fc and linker regions and the sequence was 100% identical to the predicted coding sequence, which is shown in Figure 14A-B.

HEK-293 cells used in transient transfection expression of Fc-2xL-ShK[1-35] in pcDNA3.1(+)CMVi protein were cultured in growth medium containing DMEM High Glucose (Gibco), 10% fetal bovine serum (FBS from Gibco) and 1X non-essential amino acid (NEAA from Gibco). 5.6ug of Fc-2xL-ShK[1-35] in pcDNA3.1(+)CMVi plasmid that had been phenol/chloroform extracted was transfected into HEK-293 cells using Fugene 6 (Roche). The cells recovered for 24 hours, and then placed in DMEM High Glucose and 1x NEAA medium for 48 hours. The conditioned medium was concentrated 50X by running 30ml through Centriprep YM-10 filter (Amicon) and further concentrated by a Centricon YM-10 (Amicon) filter. Various amounts of concentrated medium were mixed with an in-house 4x Loading Buffer (without B-mercaptoethanol) and electrophoresed on a Novex 4-20% tris-glycine gel using a Novex Xcell II apparatus at 101V/46mA for 2 hours in a 5x Tank buffer solution (0.123 Tris Base, 0.96M Glycine) along with 10ul of BenchMark Pre-Stained Protein ladder (Invitrogen). The gel was then soaked in Electroblot buffer (35mM Tris base, 20%methanol, 192mM glycine) for 30 minutes. A PVDF membrane from Novex (Cat. No. LC2002, 0.2um pores size) was soaked in methanol for 30 seconds to activate the PVDF, rinsed with deionized water, and soaked in Electroblot buffer. The pre-soaked gel was blotted to the PVDF membrane using the XCell II Blot module according to the manufacturer instructions (Novex) at 40mA for 2 hours. Then, the blot was first soaked in a 5% milk (Carnation) in Tris buffered saline solution pH7.5 (TBS) for 1 hour at room temperature and incubated with 1:500 dilution in TBS with 0.1%Tween-20 (TBST Sigma) and 1% milk buffer of the HRP-conjugated murine anti-human Fc antibody (Zymed Laboratores Cat. no. 05-3320) for two hours shaking at room temperature. The blot was then washed three times in TBST for 15 minutes per wash at room temperature. The primary antibody was detected using Amersham Pharmacia Biotech's ECL western blotting detection reagents according to manufacturer's instructions. Upon

ECL detection, the western blot analysis displayed the expected size of 66kDa under non-reducing gel conditions (Figure 24A).

AM1 CHOd- (Amgen Proprietary) cells used in the stable expression of Fc-L10-ShK[1-35] protein were cultured in AM1 CHOd- growth medium containing DMEM High Glucose, 10% fetal bovine serum, 1x hypoxantine/thymidine (HT from Gibco) and 1X NEAA. 6.5ug of pcDNA3.1(+)CMVi-Fc-ShK plasmid was also transfected into AM1 CHOd- cells using Fugene 6. The following day, the transfected cells were plated into twenty 15cm dishes and selected using DMEM high glucose, 10%FBS, 1xHT, 1xNEAA and Geneticin (800ug/ml G418 from Gibco) for thirteen days. Forty-eight surviving colonies were picked into two 24-well plates. The plates were allowed to grow up for a week and then replicated for freezing. One set of each plate was transferred to AM1 CHOd- growth medium without 10% FBS for 48 hours and the conditioned media were harvested. Western Blot analysis similar to the transient Western blot analysis with detection by the same anti-human Fc antibody was used to screen 15ul of conditioned medium for expressing stable CHO clones. Of the 48 stable clones, more than 50% gave ShK expression at the expected size of 66kDa. The BB6, BD5 and BD6 clones were selected with BD5 and BD6 as a backup to the primary clone BB6 (Figure 24B).

The BB6 clone was scaled up into ten roller bottles (Corning) using AM1 CHOd- growth medium and grown to confluency as judged under the microscope. Then, the medium was exchanged with a serum-free medium containing to 50% DMEM high glucose and 50% Ham's F12 (Gibco) with 1xHT and 1xNEAA and let incubate for one week. The conditioned medium was harvested at the one-week incubation time, filtered through 0.45 μm filter (Corning) and frozen. Fresh serum-free medium was added and incubated for an additional week. The conditioned serum-free medium was harvested like the first time and frozen.

Approximately 4 L of conditioned medium was thawed in a water bath at room temperature. The medium was concentrated to about 450 ml using a Satorius Sartocon Polysulfon 10 tangential flow ultra-filtration cassette (0.1 m^2) at room temperature. The retentate was then filtered through a 0.22 μm cellulose acetate filter with a pre-filter. The retentate was then loaded on to a 5 ml Amersham HiTrap Protein A column at 5 ml/min 7 °C, and the column was washed with several column volumes of Dulbecco's phosphate buffered saline without divalent cations (PBS) and sample was eluted with a step to 100 mM glycine pH 3.0. The protein A elution pool (approximately 9 ml) was diluted to 50 ml with water and loaded on to a 5 ml Amersham HiTrap SP-HP column in S-Buffer A (20 mM NaH_2PO_4, pH 7.0) at 5 ml/min and 7 °C. The column was then washed with several column volumes S-Buffer A, and then developed using a linear gradient

from 25% to 75% S-Buffer B (20 mM NaH_2PO_4, 1 M NaCl, pH 7.0) at 5 ml/min followed by a step to 100% S-Buffer B at 7 °C. Fractions were then analyzed using a Coomassie brilliant blue stained tris-glycine 4-20% SDS-PAGE, and the fractions containing the desired product were pooled based on these data. The pooled material was then concentrated to about 3.4 ml using a Pall Life Sciences Macrosep 10K Omega centrifugal ultra-filtration device and then filtered though a Costar 0.22 μm cellulose acetate syringe filter.

A spectral scan was then conducted on 10 μl of the filtered material diluted in 700 μl PBS using a Hewlett Packard 8453 spectrophotometer (Figure 26A). The concentration of the filtered material was determined to be 5.4 mg/ml using a calculated molecular mass of 32,420 g/mol and extinction coefficient of 47,900 M^{-1} cm^{-1}. The purity of the filtered material was then assessed using a Coomassie brilliant blue stained tris-glycine 4-20% SDS-PAGE (Figure 26B). The endotoxin level was then determined using a Charles River Laboratories Endosafe-PTS system (0.05 – 5 EU/ml sensitivity) using a 108-fold dilution of the sample in PBS yielding a result of <1 EU/mg protein. The macromolecular state of the product was then determined using size exclusion chromatography on 20 μg of the product injected on to a Phenomenex BioSep SEC 3000 column (7.8 x 300 mm) in 50 mM NaH_2PO_4, 250 mM NaCl, pH 6.9 at 1 ml/min observing the absorbance at 280 nm (Figure 26C). The product was then subject to mass spectral analysis by diluting 1 μl of the sample into 10 μl of sinapinic acid (10 mg per ml in 0.05% trifluroacetic acid, 50% acetonitrile) . The resultant solution (1 μl) was spotted onto a MALDI sample plate. The sample was allowed to dry before being analyzed using a Voyager DE-RP time-of-flight mass spectrometer equipped with a nitrogen laser (337 nm, 3 ns pulse). The positive ion/linear mode was used, with an accelerating voltage of 25 kV. Each spectrum was produced by accumulating data from ~ 200 laser shots. External mass calibration was accomplished using purified proteins of known molecular masses (Figure 26D) and confirmed (within experimental error) the integrity of the purified peptibody. The product was then stored at –80 °C.

Purified Fc-L10-ShK[1-35] potently blocked human Kv1.3 (Figure 30A and Figure 30B) as determined by electrophysiology (see Example 36). The purified Fc-L10-ShK[1-35] molecule also blocked T cell proliferation (Figure 36A and Figure 36B) and production of the cytokines IL-2 (Figure 35A and Figure 37A) and IFN-g (Figure 35B and Figure 37B).

Example 2

Fc-L-ShK[2-35] mammalian expression

A DNA sequence coding for the Fc region of human IgG1 fused in-frame to a monomer of the Kv1.3 inhibitor peptide ShK[2-35] was constructed using standard PCR technology. The ShK[2-35] and the 5, 10, or 25 amino acid linker portion of the molecule were generated in a PCR reaction using the original Fc-2xL-ShK[1-35] in pcDNA3.1(+)CMVi as a template (Example 1, Figure 14A-B). All ShK constructs should have the following amino acid sequence of

SCIDTIPKSRCTAFQCKHSMKYRLSFCRKTCGTC

(SEQ ID NO: 92)

with the first amino acid of the wild-type sequence deleted.

The sequences of the primers used to generate Fc-L5-ShK[2-35], also referred to as "Fc-1xL-ShK[2-35]", are shown below:

cat gga tcc agc tgc atc gac acc atc//SEQ ID NO:661;

cat gcg gcc gct cat tag c// SEQ ID NO:662;

The sequences of the primers used to generate Fc-L10-ShK[2-35], also referred to as "Fc-2xL-ShK[2-35]" are shown below:

cat gga tcc gga gga gga gga agc agc tgc a //SEQ ID NO:663;

cat gcg gcc gct cat tag cag gtg c //SEQ ID NO:664;

The sequences of the primers used to generate Fc-L25-ShK[2-35], also referred to as "Fc-5xL-ShK[2-35]", are shown below:

cat gga tcc ggg ggt ggg ggt tct ggg ggt ggg ggt tct gga gga gga gga agc gga gga gga gga agc agc tgc a//SEQ ID NO:665;

cat gcg gcc gct cat tag cag gtg c//SEQ ID NO:666;

The PCR products were digested with BamHI and NotI (Roche) restriction enzymes and agarose gel purified by Gel Purification Kit. At the same time, the pcDNA3.1(+)CMVi-hFc-ActivinRIIB vector was digested with BamHI and NotI restriction enzymes and the large fragment was purified by Gel Purification Kit. Each purified PCR product was ligated to the large fragment and transformed into XL-1blue bacteria. DNAs from transformed bacterial colonies were isolated and subjected to BamHI and NotI restriction enzyme digestions and resolved on a one percent agarose gel. DNAs resulting in an expected pattern were submitted for sequencing. Although, analysis of several sequences of clones yielded a 100% percent match with the above sequence, only one clone was selected for large scaled plasmid purification. The DNA from this clone was resequenced to confirm the Fc and linker regions and the sequence was 100% identical to the expected sequence.

Plasmids containing the Fc-1xL-Shk[2-35], Fc-2xL-Shk[2-35] and Fc-5xL-Shk[2-35] inserts in pcDNA3.1(+)CMVi vector were digested with Xba1 and Xho1 (Roche) restriction enzymes and gel purified. The inserts were individually ligated into Not1 and Sall (Roche) digested pDSRα-22 (Amgen Proprietary) expression vector. Integrity of the resulting constructs were confirmed by DNA sequencing. The final plasmid DNA expression vector constructs were pDSRα-22-Fc-1xL-Shk[2-35], pDSRα-22- Fc-2xL-Shk[2-35] (Figure 13C and Figure 15A-B) and pDSRα-22- Fc-5xL-Shk[2-35] (Figure 16A-B) and contained 5, 10 and 25 amino acid linkers, respectively.

Twenty-four hours prior to transfection, 1.2e7 AM-1/D CHOd- (Amgen Proprietary) cells were plated into a T-175 cm sterile tissue culture flask, to allow 70-80% confluency on the day of transfection. The cells had been maintained in the AM-1/D CHOd- culture medium containing DMEM High Glucose, 5% FBS, 1X Glutamine Pen/Strep (Gibco), 1X HT, 1X NEAA's and 1X sodium pyruvate (Gibco). The following day, eighteen micrograms of each of the linearized pDSRα22:Fc-1xL-ShK[2-35], pDSRα22:Fc-2xL-ShK[2-35] and pDSRα22:Fc-5xL-ShK[2-35] (RDS's # 20050037685, 20050053709, 20050073295) plasmids were mixed with 72 µg of linearized Selexis MAR plasmid and pPAGO1 (RDS 20042009896) and diluted into 6ml of OptiMEM in a 50ml conical tube and incubate for five minutes. LF2000 (210 µl) was added to 6ml of OptiMEM and incubated for five minutes. The diluted DNA and LF2000 were mixed together and incubated for 20 minutes at room temperature. In the meantime, the cells were washed one time with PBS and then 30ml OptiMEM without antibiotics were added to the cells. tThe OptiMEM was aspirated off, and the cells were incubated with 12ml of DNA/LF2000 mixture for 6 hours or overnight in the 37°C incubator with shaking. Twenty-four hours post transfection, the cells were split 1:5 into AM-1/D CHOd- culture medium and at differing dilutions for colony selection. Seventy-two hours post transfection, the cell medium was replaced with DHFR selection medium containing 10% Dialyzed FBS (Gibco) in DMEM High Glucose, plus 1X Glutamine Pen/Strep, 1X NEAA's and 1X Na Pyr to allow expression and secretion of protein into the cell medium. The selection medium was changed two times a week until the colonies are big enough to pick. The pDSRa22 expression vector contains a DHFR expression cassette, which allows transfected cells to grow in the absence of hypoxanthine and thymidine. The five T-175 pools of the resulting colonies were scaled up into roller bottles and cultured under serum free conditions. The conditioned media were harvested and replaced at one-week intervals. The resulting 3 liters of conditioned medium was filtered through a 0.45 um cellulose acetate filter (Corning, Acton, MA) and transferred to Protein Chemistry for purification. As a backup, twelve colonies were selected from the 10 cm plates after 10-14 days on DHFR selection medium and expression levels evaluated by western blot using

HRP conjugated anti human IgGFc as a probe. The three best clones expressing the highest level of each of the different linker length Fc-L-ShK[2-35] fusion proteins were expanded and frozen for future use.

Purification of Fc-L10-ShK(2-35). Approximately 1 L of conditioned medium was thawed in a water bath at room temperature. The medium was loaded on to a 5 ml Amersham HiTrap Protein A column at 5 ml/min 7 °C, and the column was washed with several column volumes of Dulbecco's phosphate buffered saline without divalent cations (PBS) and sample was eluted with a step to 100 mM glycine pH 3.0. The protein A elution pool (approximately 8.5 ml) combined with 71 µl 3 M sodium acetate and then diluted to 50 ml with water. The diluted material was then loaded on to a 5 ml Amersham HiTrap SP-HP column in S-Buffer A (20 mM NaH_2PO_4, pH 7.0) at 5 ml/min 7 °C. The column was then washed with several column volumes S-Buffer A, and then developed using a linear gradient from 0% to 75% S-Buffer B (20 mM NaH_2PO_4, 1 M NaCl, pH 7.0) at 5 ml/min followed by a step to 100% S-Buffer B at 7 °C. Fractions were then analyzed using a Coomassie brilliant blue stained tris-glycine 4-20% SDS-PAGE, and the fractions containing the desired product were pooled based on these data. The pooled material was then filtere through a 0.22 µm cellulose acetate filter and concentrated to about 3.9 ml using a Pall Life Sciences Macrosep 10K Omega centrifugal ultra-filtration device. The concentrated material was then filtered though a Pall Life Sciences Acrodisc with a 0.22 µm, 25 mm Mustang E membrane at 2 ml/min room temperature. A spectral scan was then conducted on 10 µl of the filtered material diluted in 700 µl PBS using a Hewlett Packard 8453 spectrophotometer (Figure 27E). The concentration of the filtered material was determined to be 2.76 mg/ml using a calculated molecular mass of 30,008 g/mol and extinction coefficient of 36,900 M^{-1} cm^{-1}. Since material was found in the permeate, repeated concentration step on the permeate using a new Macrosep cartridge. The new batch of concentrated material was then filtered though a Pall Life Sciences Acrodisc with a 0.22 µm, 25 mm Mustang E membrane at 2 ml/min room temperature. Both lots of concentrated material were combined into one pool.

A spectral scan was then conducted on 10 µl of the combined pool diluted in 700 µl PBS using a Hewlett Packard 8453 spectrophotometer. The concentration of the filtered material was determined to be 3.33 mg/ml using a calculated molecular mass of 30,008 g/mol and extinction coefficient of 36,900 M^{-1} cm^{-1}. The purity of the filtered material was then assessed using a Coomassie brilliant blue stained tris-glycine 4-20% SDS-PAGE (Figure 27A). The endotoxin level was then determined using a Charles River Laboratories Endosafe-PTS system (0.05 – 5 EU/ml sensitivity) using a 67-fold dilution of the sample in PBS yielding a result of <1 EU/mg protein. The

macromolecular state of the product was then determined using size exclusion chromatography on 50 μg of the product injected on to a Phenomenex BioSep SEC 3000 column (7.8 x 300 mm) in 50 mM NaH_2PO_4, 250 mM NaCl, pH 6.9 at 1 ml/min observing the absorbance at 280 nm (Figure 27B). The product was then subject to mass spectral analysis by diluting 1 μl of the sample into 10 μl of sinapinic acid (10 mg per ml in 0.05% trifluroacetic acid, 50% acetonitrile) . The resultant solution (1 μl) was spotted onto a MALDI sample plate. The sample was allowed to dry before being analyzed using a Voyager DE-RP time-of-flight mass spectrometer equipped with a nitrogen laser (337 nm, 3 ns pulse). The positive ion/linear mode was used, with an accelerating voltage of 25 kV. Each spectrum was produced by accumulating data from ~ 200 laser shots. External mass calibration was accomplished using purified proteins of known molecular masses (Figure 27F) and the experiment confirmed the itegrity of the peptibody, within experimental error. The product was then stored at –80 °C.

Figure 31B shows that purified Fc-L10-ShK[2-35] potently blocks human Kv1.3 current (electrophysiology was done as described in Example 36). The purified Fc-L10-ShK[2-35] molecule also blocked IL-2 (Figure 64A and Figure 64B) and IFN-g (Figure 65A and Figure 65B) production in human whole blood, as well as, upregulation of CD40L (Figure 66A and Figure 66B) and IL-2R (Figure 67A and Figure 67B) on T cells.

Purification of Fc-L5-ShK(2-35). Approximately 1 L of conditioned medium was loaded on to a 5 ml Amersham HiTrap Protein A column at 5 ml/min 7 °C, and the column was washed with several column volumes of Dulbecco's phosphate buffered saline without divalent cations (PBS) and sample was eluted with a step to 100 mM glycine pH 3.0. The protein A elution pool (approximately 9 ml) combined with 450 μl 1 M tris HCl pH 8.5 followed by 230 μl 2 M acetic acid and then diluted to 50 ml with water. The pH adjusted material was then filtered through a 0.22 μm cellulose acetate filter and loaded on to a 5 ml Amersham HiTrap SP-HP column in S-Buffer A (20 mM NaH_2PO_4, pH 7.0) at 5 ml/min 7 °C. The column was then washed with several column volumes S-Buffer A, and then developed using a linear gradient from 0% to 75% S-Buffer B (20 mM NaH_2PO_4, 1 M NaCl, pH 7.0) at 5 ml/min followed by a step to 100% S-Buffer B at 7 °C. Fractions were then analyzed using a Coomassie brilliant blue stained tris-glycine 4-20% SDS-PAGE, and the fractions containing the desired product were pooled based on these data. The pooled material was then concentrated to about 5.5 ml using a Pall Life Sciences Macrosep 10K Omega centrifugal ultra-filtration device. The concentrated material was then filtered though a Pall Life Sciences Acrodisc with a 0.22 μm, 25 mm Mustang E membrane at 2 ml/min room temperature.

A spectral scan was then conducted on 10 µl of the combined pool diluted in 700 µl PBS using a Hewlett Packard 8453 spectrophotometer (Figure 27G). The concentration of the filtered material was determined to be 4.59 mg/ml using a calculated molecular mass of 29,750 g/mol and extinction coefficient of 36,900 M^{-1} cm^{-1}. The purity of the filtered material was then assessed using a Coomassie brilliant blue stained tris-glycine 4-20% SDS-PAGE (Figure 27C). The endotoxin level was then determined using a Charles River Laboratories Endosafe-PTS system (0.05 – 5 EU/ml sensitivity) using a 92-fold dilution of the sample in Charles Rivers Endotoxin Specific Buffer BG120 yielding a result of <1 EU/mg protein. The macromolecular state of the product was then determined using size exclusion chromatography on 50 µg of the product injected on to a Phenomenex BioSep SEC 3000 column (7.8 x 300 mm) in 50 mM NaH_2PO_4, 250 mM NaCl, pH 6.9 at 1 ml/min observing the absorbance at 280 nm (Figure 27H). The product was then subject to mass spectral analysis by diluting 1 µl of the sample into 10 µl of sinapinic acid (10 mg per ml in 0.05% trifluroacetic acid, 50% acetonitrile) . The resultant solution (1 µl) was spotted onto a MALDI sample plate. The sample was allowed to dry before being analyzed using a Voyager DE-RP time-of-flight mass spectrometer equipped with a nitrogen laser (337 nm, 3 ns pulse). The positive ion/linear mode was used, with an accelerating voltage of 25 kV. Each spectrum was produced by accumulating data from ~ 200 laser shots. External mass calibration was accomplished using purified proteins of known molecular masses (Figure 27I) and confirmed the integrity of the peptibody, within experimental error. The product was then stored at –80°C.

Figure 31C shows that purified Fc-L5-ShK[2-35] is highly active and blocks human Kv1.3 as determined by whole cell patch clamp electrophysiology (see Example 36).

Purification of Fc-L25-ShK(2-35). Approximately 1 L of conditioned medium was loaded on to a 5 ml Amersham HiTrap Protein A column at 5 ml/min 7 °C, and the column was washed with several column volumes of Dulbecco's phosphate buffered saline without divalent cations (PBS) and sample was eluted with a step to 100 mM glycine pH 3.0. The protein A elution pool (approximately 9.5 ml) combined with 119 µl 3 M sodium acetate and then diluted to 50 ml with water. The pH adjusted material was then loaded on to a 5 ml Amersham HiTrap SP-HP column in S-Buffer A (20 mM NaH_2PO_4, pH 7.0) at 5 ml/min 7 °C. The column was then washed with several column volumes S-Buffer A, and then developed using a linear gradient from 0% to 75% S-Buffer B (20 mM NaH_2PO_4, 1 M NaCl, pH 7.0) at 5 ml/min followed by a step to 100% S-Buffer B at 7 °C. Fractions containing the main peak from the chromatogram were pooled and filtered through a 0.22 µm cellulose acetate filter.

A spectral scan was then conducted on 20 µl of the combined pool diluted in 700 µl PBS using a Hewlett Packard 8453 spectrophotometer Figure 27J. The concentration of the filtered material was determined to be 1.40 mg/ml using a calculated molecular mass of 31,011 g/mol and extinction coefficient of 36,900 M^{-1} cm^{-1}. The purity of the filtered material was then assessed using a Coomassie brilliant blue stained tris-glycine 4-20% SDS-PAGE (Figure 27D). The endotoxin level was then determined using a Charles River Laboratories Endosafe-PTS system (0.05 – 5 EU/ml sensitivity) using a 28-fold dilution of the sample in Charles Rivers Endotoxin Specific Buffer BG120 yielding a result of <1 EU/mg protein. The macromolecular state of the product was then determined using size exclusion chromatography on 50 µg of the product injected on to a Phenomenex BioSep SEC 3000 column (7.8 x 300 mm) in 50 mM NaH_2PO_4, 250 mM NaCl, pH 6.9 at 1 ml/min observing the absorbance at 280 nm (Figure 27K). The product was then subject to mass spectral analysis by diluting 1 µl of the sample into 10 µl of sinapinic acid (10 mg per ml in 0.05% trifluroacetic acid, 50% acetonitrile). The resultant solution (1 µl) was spotted onto a MALDI sample plate. The sample was allowed to dry before being analyzed using a Voyager DE-RP time-of-flight mass spectrometer equipped with a nitrogen laser (337 nm, 3 ns pulse). The positive ion/linear mode was used, with an accelerating voltage of 25 kV. Each spectrum was produced by accumulating data from ~ 200 laser shots. External mass calibration was accomplished using purified proteins of known molecular masses (Figure 27L) and this confirmed the itegrity of the peptibody, within experimental error. The product was then stored at –80°C.

Purified Fc-L25-ShK[2-35] inhibited human Kv1.3 with an IC_{50} of ~150 pM by whole cell patch clamp electrophysiology on HEK293/Kv1.3 cells (Example 36).

Example 3

Fc-L-ShK[1-35] bacterial expression

Description of bacterial peptibody expression vectors and procedures for cloning and expression of peptibodies. The cloning vector used for bacterial expression (Examples 3-30) is based on pAMG21 (originally described in U.S. Patent 2004/0044188). It has been modified in that the kanamycin resistance component has been replaced with ampicillin resistance by excising the DNA between the unique BstBI and NsiI sites of the vector and replacing with an appropriately digested PCR fragment bearing the beta-lactamase gene using PCR primers CCA ACA CAC TTC GAA AGA CGT TGA TCG GCA C (SEQ ID NO:667) and CAC CCA ACA ATG CAT CCT TAA AAA AAT TAC GCC C (SEQ ID NO:668) with pUC19 DNA as the template source of

the beta-lactamase gene conferring resistance to ampicillin. The new version is called pAMG21ampR.

Description of cloning vector pAMG21ampR-Fc-Pep used in examples 3 to 30, excluding 15 and 16. Figure 11A-C and Figure 11D (schematic diagram) show the ds-DNA that has been added to the basic vector pAMG21ampR to permit the cloning of peptide fusions to the C-terminus of the Fc gene. The DNA has been introduced between the unique NdeI and BamHI sites in the pAMG21ampR vector. This entire region of DNA is shown in Figure11A-C. The coding region for Fc extends from nt 5134 to 5817 and the protein sequence appears below the DNA sequence. This is followed in frame by a glyX5 linker (nt's 5818-5832). A BsmBI site (GAGACG) spans nt's 5834-5839. DNA cleavage occurs between nt's 5828 and 5829 on the upper DNA strand and between nt's 5832 and 5833 on the lower DNA strand. Digestion creates 4 bp cohesive termini as shown here. The BsmBI site is underlined.

```
                AGGTGG                  TGGTTGAGACG SEQ ID NO:683
                TCCACCACCA                   ACTCTGC
                SEQ ID NO:684
```

A second BsmBI site occurs at nt's 6643 through 6648; viz., CGTCTC. DNA cleavage occurs between nt's 6650 and 6651 on the upper strand and between 6654 and 6655 on the lower strand.

```
                CGTCTCT                 TAAGGATCCG SEQ ID NO:685
                GCAGAGAATTC                  CTAGGC
                SEQ ID NO:686
```

Between the two BsmBI sites is a dispensable chloramphenicol resistance cassette constitutively expressing chloramphenicol acetyltransferase (cat gene). The cat protein sequence:

```
  1  MEKKITGYTT VDISQWHRKE HFEAFQSVAQ CTYNQTVQLD ITAFLKTVKK
 51  NKHKFYPAFI HILARLMNAH PEFRMAMKDG ELVIWDSVHP CYTVFHEQTE
101  TFSSLWSEYH DDFRQFLHIY SQDVACYGEN LAYFPKGFIE NMFFVSANPW
151  VSFTSFDLNV ANMDNFFAPV FTMGKYYTQG DKVLMPLAIQ VHHAVCDGFH
201  VGRMLNELQQ YCDEWQGGA //SEQ ID NO:1337
```

is shown in Fig. 11A-C and extends from nt's 5954 to 6610. The peptide encoding duplexes in each example (except Examples 15 and 16) bear cohesive ends complementary to those presented by the vector.

Description of the cloning vector pAMG21ampR-Pep-Fc used in examples 15 and 16. Figure 12A-C, and the schematic diagram in Figure 12D, shows the ds-DNA sequence that has

been added to the basic vector pAMG21ampR to permit the cloning of peptide fusions to the N-terminus of the Fc gene. The DNA has been introduced between the unique NdeI and BamHI sites in the pAMG21ampR vector. The coding region for Fc extends from nt 5640 to 6309 and the protein sequence appears below the DNA sequence. This is preceded in frame by a glyX5 linker (nt's 5614-5628). A BsmBI site spans nt's 5138 to 5143; viz., GAGACG. The cutting occurs between nt's 5132 and 5133 on the upper DNA strand and between 5136 and 5137 on the lower DNA strand.

Digestion creates 4 bp cohesive termini as shown. The BsmBI site is underlined.

```
AATAACA                    TATGCGAGACG SEQ ID NO:687
TTATTGTATAC                    GCTCTGC
SEQ ID NO:688
```

A second BsmBI site occurs at nt's 5607 through 5612; viz., CGTCTC. Cutting occurs between nt's 5613 and 5614 on the upper strand and between 5617 and 5618 on the lower strand.

```
CGTCTCA                    GGTGGTGGT
GCAGAGTCCAC                    CACCA
SEQ ID NO:689
```

Between the BsmBI sites is a dispensable zeocin resistance cassette constitutively expressing the Shigella ble protein. The ble protein sequence:

```
  1  MAKLTSAVPV LTARDVAGAV EFWTDRLGFS RDFVEDDFAG VVRDDVTLFI
 51  SAVQDQVVPD NTLAWVWVRG LDELYAEWSE VVSTNFRDAS GPAMTEIGEQ
101  PWGREFALRD PAGNCVHFVA EEQD //SEQ ID NO:1338
```

is shown extending from nt's 5217 to 5588 in Figure 12A-C. The peptide encoding duplexes in Examples 15 and 16 bear cohesive ends complementary to those presented by the vector.

Description of the cloning vector pAMG21ampR-Pep-Fc used in Examples 52 and 53.

Figure 12E-G shows the ds-DNA sequence that has been added to the basic vector pAMG21ampR to permit the cloning of peptide fusions to the N-terminus of the Fc gene in which the first two codons of the peptide are to be met-gly. The DNA has been introduced between the unique NdeI and BamHI sites in the pAMG21ampR vector. The coding region for Fc extends from nt 5632 to 6312 and the protein sequence appears below the DNA sequence. This is preceded in frame by a glyX5 linker (nt's 5617-5631). A BsmBI site spans nt's 5141 to 5146; viz., GAGACG. The cutting occurs between nt's 5135 and 5136 on the upper DNA strand and between 5139 and 5140 on the lower DNA strand.

Digestion creates 4 bp cohesive termini as shown. The BsmBI site is underlined.

AATAACATAT GGGTCGAGACG SEQ ID NO:1344
SEQ ID NO:1343
TTATTGTATACCCA GCTCTGC
SEQ ID NO:1345

A second BsmBI site occurs at nt's 5607 through 5612; viz., CGTCTC. Cutting occurs between nt's 5613 and 5614 on the upper strand and between 5617 and 5618 on the lower strand.

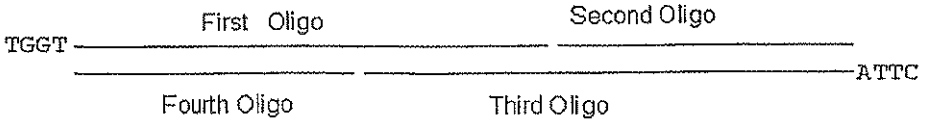
CGTCTCA GGTGGTGGT
GCAGAGTCCAC CACCA
SEQ ID NO:1346

Between the BsmBI sites is a dispensable zeocin resistance cassette constitutively expressing the Shigella ble protein. The ble protein sequence, as described above, is shown extending from nt's 5220 to 5591. The peptide encoding duplexes in Examples 52 and 53 herein below bear cohesive ends complementary to those presented by the vector.

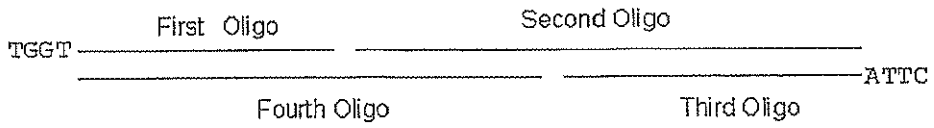
For Examples 3 to 30 for which all are for bacterial expression, cloned peptide sequences are all derived from the annealing of oligonucleotides to create a DNA duplex that is directly ligated into the appropriate vector. Two oligos suffice for Example 20, four are required for all other examples. When the duplex is to be inserted at the N-terminus of Fc (see, Examples 15, 16, 52, and 53 herein) the design is as follows with the ordinal numbers matching the listing of oligos in each example:



When the duplex is to be inserted at the C-terminus of Fc (Examples 3, 4, 5, 10, 11, 12, 13, and 30) the design is as follows:



All remaining examples have the duplex inserted at the C-terminus of Fc and utilize the following design.



No kinasing step is required for the phosphorylation of any of the oligos. A successful insertion of a duplex results in the replacement of the dispensable antibiotic resistance cassette (Zeocin resistance for pAMG21ampR-Pep-Fc and chloramphenicol resistance for pAMG21ampR-Fc-Pep). The resulting change in phenotype is useful for discriminating recombinant from nonrecombinant clones.

The following description gives the uniform method for carrying out the cloning of all 30 bacterially expressed recombinant proteins exemplified herein. Only the set of oligonucleotides and the vector are varied. These spefications are given below in each example.

An oligonucleotide duplex containing the coding region for a given peptide was formed by annealing the oligonucleotides listed in each example. Ten picomoles of each oligo was mixed in a final volume of 10 µl containing 1X ligation buffer along with 0.3 µg of appropriate vector that had been previously digested with restriction endonuclease BsmBI. The mix was heated to 80°C and allowed to cool at 0.1 degree/sec to room temperature. To this was added 10 µl of 1X ligase buffer plus 400 units of T4 DNA ligase. The sample was incubated at 14C for 20 min. Ligase was inactivated by heating at 65°C for 10 minutes. Next, 10 units of restriction endonucleases BsmBI were added follwed by incubation at 55C for one hour to cleave any reformed parental vector molecules. Fifty ul of chemically competent *E. coli* cells were added and held at 2C for 20 minutes followed by heat shock at 42C for 5 second. The entire volume was spread onto Luria Agar plates supplemented with carbenicillin at 200 ug/ml and incubated overnight at 37C. Colonies were tested for the loss of resistance to the replaceable antibiotic resistance marker. A standard PCR test can be used to confirm the expected size of the duplex insert. Plasmid preparations were obtained and the recombinant insert was verified by DNA sequencing. Half liter cultures of a sequence confirmed construct were grown in Terrific Broth, expression of the peptibody was induced by addition of N-(3-oxo-hexanoyl)-homoserine lactone at 50 ng/ml and after 4-6 hours of shaking at 37C the cells were centrifuged and the cell paste stored at –20C.

The following gives for each example the cloning vector and the set of oligonucleotides used for constructing each fusion protein. Also shown is a DNA/protein map.

Bacterial expression of Fc-L-ShK[1-35] inhibitor of Kv1.3. The methods to clone and express the peptibody in bacteria are described above. The vector used was pAMG21ampR-Fc-

Pep and the oligos listed below were used to generate a duplex (see below) for cloning and expression in bacteria of Fc-L-ShK[1-35].

Oligos used to form the duplex:

TGGTTCCGGTGGTGGTGGTTCCCGTTCCTGCATCGACACCAT //SEQ ID NO:669;

CCCGAAATCCCGTTGCACCGCTTTCCAGTGCAAACACTCCATGAAATACCGTCTGTCCTTCTGCCGTAAAACC TGCGGTACCTGC //SEQ ID NO:670;

CTTAGCAGGTACCGCAGGTTTTACGGCAGAAGGACAGACGGT //SEQ ID NO:671;

ATTTCATGGAGTGTTTGCACTGGAAAGCGGTGCAACGGGATTTCGGGATGGTGTCGATGCAGGAACGGGAACC ACCACCACCGGA //SEQ ID NO:672;

The oligo duplex is shown below:

```
   TGGTTCCGGTGGTGGTGGTTCCCGTTCCTGCATCGACACCATCCCGAAATCCCGTTGCAC
 1 ---------+---------+---------+---------+---------+---------+ 60
     AGGCCACCACCACCAAGGGCAAGGACGTAGCTGTGGTAGGGCTTTAGGGCAACGTG

    G  S  G  G  G  G  S  R  S  C  I  D  T  I  P  K  S  R  C  T  -

   CGCTTTCCAGTGCAAACACTCCATGAAATACCGTCTGTCCTTCTGCCGTAAAACCTGCGG
61 ---------+---------+---------+---------+---------+---------+ 120
   GCGAAAGGTCACGTTTGTGAGGTACTTTATGGCAGACAGGAAGACGGCATTTTGGACGCC

    A  F  Q  C  K  H  S  M  K  Y  R  L  S  F  C  R  K  T  C  G  -

   TACCTGC //SEQ ID NO:673
121 -------
   ATGGACGATTC //SEQ ID NO:675

    T  C   - //SEQ ID NO:674
```

Bacterial expression of the peptibody was as described in Example 3 and paste was stored frozen. Purification of bacterially expressed Fc-L10-ShK(1-35) is further described in Example 38 herein below.

Example 4

Fc-L-ShK[2-35] bacterial expression

Bacterial expression of Fc-L-ShK[2-35] . The methods to clone and express the peptibody in bacteria are described in Example 3. The vector used was pAMG21ampR-Fc-Pep and the oligos listed below were used to generate a duplex (see below) for cloning and expression in bacteria of Fc-L-ShK[2-35].

Oligos used to form duplex are shown below:

TGGTTCCGGTGGTGGTGGTTCCTGCATCGACACCATCCCGAAATCCCGTTGCACCGCTTTCCAGTGCAAACACTCCATGAAA T //SEQ ID NO:676;

ACCGTCTGTCCTTCTGCCGTAAAACCTGCGGTACCTGC //SEQ ID NO:677;

CTTAGCAGGTACCGCAGGTTTTACGGCAGAAGGACAGACGGTATTTCATGGAGTGTTTGCACTGGAAAGCGGTGCAACGGGA //SEQ ID NO:678;

TTTCGGGATGGTGTCGATGCAGGAACCACCACCACCGGA //SEQ ID NO:679;

The oligo duplex formed is shown below:

```
    TGGTTCCGGTGGTGGTGGTTCCTGCATCGACACCATCCCGAAATCCCGTTGCACCGCTTT
 1  ---------+---------+---------+---------+---------+---------+ 60
      AGGCCACCACCACCAAGGACGTAGCTGTGGTAGGGCTTTAGGGCAACGTGGCGAAA

     G  S  G  G  G  G  S  C  I  D  T  I  P  K  S  R  C  T  A  F  -

    CCAGTGCAAACACTCCATGAAATACCGTCTGTCCTTCTGCCGTAAAACCTGCGGTACCTG
61  ---------+---------+---------+---------+---------+---------+ 120
    GGTCACGTTTGTGAGGTACTTTATGGCAGACAGGAAGACGGCATTTTGGACGCCATGGAC

     Q  C  K  H  S  M  K  Y  R  L  S  F  C  R  K  T  C  G  T  C  - //SEQ ID NO:681

    C //SEQ ID NO:680
121 -
    GATTC //SEQ ID NO:682
```

Bacterial expression of the peptibody was as described in Example 3 and paste was stored frozen. Purification of bacterially expressed Fc-L10-ShK(2-35) is further described in Example 39 herein below.

Example 5

Fc-L-HmK bacterial expression

Bacterial expression of Fc-L-HmK. The methods to clone and express the peptibody in bacteria are described in Example 3. The vector used was pAMG21ampR-Fc-Pep and the oligos listed below were used to generate a duplex (see below) for cloning and expression in bacteria of Fc-L-HmK.

Oligos used to form duplex are shown below:

TGGTTCCGGTGGTGGTGGTTCCCGTACCTGCAAAGACCTGAT //SEQ ID NO:690;

CCCGGTTTCCGAATGCACCGACATCCGTTGCCGTACCTCCATGAAATACCGTCTGAACCTGTGCCGTAAAACCTGCGGTTCC TGC SEQ ID NO:692;

CTTAGCAGGAACCGCAGGTTTTACGGCACAGGTTCAGACGGT //SEQ ID NO:693;

4142-94
ATTTCATGGAGGTACGGCAACGGATGTCGGTGCATTCGGAAACCGGGATCAGGTCTTTGCAGGTACGGGAACCAC CACCACCGGA //SEQ ID NO:694

The oligo duplex formed is shown below:

```
    TGGTTCCGGTGGTGGTGGTTCCCGTACCTGCAAAGACCTGATCCCGGTTTCCGAATGCAC
 1  ---------+---------+---------+---------+---------+---------+ 60
      AGGCCACCACCACCAAGGGCATGGACGTTTCTGGACTAGGGCCAAAGGCTTACGTG

     G  S  G  G  G  G  S  R  T  C  K  D  L  I  P  V  S  E  C  T  -

    CGACATCCGTTGCCGTACCTCCATGAAATACCGTCTGAACCTGTGCCGTAAAACCTGCGG
61  ---------+---------+---------+---------+---------+---------+ 120
    GCTGTAGGCAACGGCATGGAGGTACTTTATGGCAGACTTGGACACGGCATTTTGGACGCC
```

```
      D  I  R  C  R  T  S  M  K  Y  R  L  N  L  C  R  K  T  C  G  - //SEQ ID NO:696

    TTCCTGC //SEQ ID NO:695
121 -------
    AAGGACGATTC //SEQ ID NO:697

     S  C  -
```

Bacterial expression of the peptibody was as described in Example 3 and paste was stored frozen.

Example 6

Fc-L-KTX1 bacterial expression

Bacterial expression of Fc-L-KTX1. The methods to clone and express the peptibody in bacteria are described in Example 3. The vector used was pAMG21ampR-Fc-Pep and the oligos listed below were used to generate a duplex (see below) for cloning and expression in bacteria of Fc-L-KTX1.

Oligos used to form duplex are shown below:

TGGTTCCGGTGGTGGTGGTTCCGGTGTTGAAATCAACGTTAAATGCT //SEQ ID NO:698;

CCGGTTCCCCGCAGTGCCTGAAACCGTGCAAAGACGCTGGTATGCGTTTCGGTAAATGCATGAACCGTAAATGCCACTGCAC
CCCGAAA //SEQ ID NO:699;

CTTATTTCGGGGTGCAGTGGCATTTACGGTTCATGCATTTACCGAAA //SEQ ID NO:700;

CGCATACCAGCGTCTTTGCACGGTTTCAGGCACTGCGGGGAACCGGAGCATTTAACGTTGATTTCAACACCGGAACCACCAC
CACCGGA //SEQ ID NO:701;

The oligo duplex formed is shown below:

```
    TGGTTCCGGTGGTGGTGGTTCCGGTGTTGAAATCAACGTTAAATGCTCCGGTTCCCCGCA
  1 ---------+---------+---------+---------+---------+---------+ 60
      AGGCCACCACCACCAAGGCCACAACTTTAGTTGCAATTTACGAGGCCAAGGGGCGT

     G  S  G  G  G  G  S  G  V  E  I  N  V  K  C  S  G  S  P  Q  -

    GTGCCTGAAACCGTGCAAAGACGCTGGTATGCGTTTCGGTAAATGCATGAACCGTAAATG
 61 ---------+---------+---------+---------+---------+---------+ 120
    CACGGACTTTGGCACGTTTCTGCGACCATACGCAAAGCCATTTACGTACTTGGCATTTAC

     C  L  K  P  C  K  D  A  G  M  R  F  G  K  C  M  N  R  K  C  -

    CCACTGCACCCCGAAA //SEQ ID NO:702
121 ---------+------
    GGTGACGTGGGGCTTTATTC  //SEQ ID NO:704

     H  C  T  P  K  - //SEQ ID NO:703
```

Bacterial expression of the peptibody was as described in Example 3 and paste was stored frozen.

Purification and refolding of Fc-L-KTX1 expressed in bacteria. Frozen, *E. coli* paste (28 g) was combined with 210 ml of room temperature 50 mM tris HCl, 5 mM EDTA, pH 8.0 and was brought to about 0.1 mg/ml hen egg white lysozyme. The suspended paste was passed through a chilled microfluidizer twice at 12,000 PSI. The cell lysate was then centrifuged at 22,000 g for 20 min at 4 °C. The pellet was then resuspended in 200 ml 1% deoxycholic acid using a tissue

grinder and then centrifuged at 22,000 g for 20 min at 4 °C. The pellet was then resuspended in 200 ml water using a tissue grinder and then centrifuged at 22,000 g for 20 min at 4 °C. The pellet (4.8 g) was then dissolved in 48 ml 8 M guanidine HCl, 50 mM tris HCl, pH 8.0. The dissolved pellet was then reduced by adding 30 µl 1 M dithiothreitol to 3 ml of the solution and incubating at 37 °C for 30 minutes. The reduced pellet solution was then centrifuged at 14,000 g for 5 min at room temperature, and then 2.5 ml of the supernatant was transferred to 250 ml of the refolding buffer (2 M urea, 50 mM tris, 160 mM arginine HCl, 5 mM EDTA, 1 mM cystamine HCl, 4 mM cysteine, pH 8.5) at 4 °C with vigorous stirring. The stirring rate was then slowed and the incubation was continued for 2 days at 4 °C. The refolding solution was then filtered through a 0.22 µm cellulose acetate filter and stored at 4 °C for 3 days.

The stored refold was then diluted with 1 L of water and the pH was adjusted to 7.5 using 1 M H_3PO_4. The pH adjusted material was then loaded on to a 10 ml Amersham SP-HP HiTrap column at 10 ml/min in S-Buffer A (20 mM NaH_2PO_4, pH 7.3) at 7 °C. The column was then washed with several column volumes of S-Buffer A, followed by elution with a linear gradient from 0% to 60% S-Buffer B (20 mM NaH_2PO_4, 1 M NaCl, pH 7.3) followed by a step to 100% S-Buffer B at 5 ml/min 7 °C. Fractions were then analyzed using a Coomassie brilliant blue stained tris-glycine 4-20% SDS-PAGE, and the fractions containing the desired product were pooled based on these data (45 ml). The pool was then loaded on to a 1 ml Amersham rProtein A HiTrap column in PBS at 2 ml/min 7 °C. Then column was then washed with several column volumes of PBS and eluted with 100 mM glycine pH 3.0. To the elution peak (2.5 ml), 62.5 µl 2 M tris base was added, and then the pH adjusted material was filtered though a Pall Life Sciences Acrodisc with a 0.22 µm, 25 mm Mustang E membrane at 2 ml/min room temperature.

A spectral scan was then conducted on 20 µl of the combined pool diluted in 700 µl PBS using a Hewlett Packard 8453 spectrophotometer (Figure 28C). The concentration of the filtered material was determined to be 2.49 mg/ml using a calculated molecular mass of 30,504 g/mol and extinction coefficient of 35,410 M^{-1} cm^{-1}. The purity of the filtered material was then assessed using a Coomassie brilliant blue stained tris-glycine 4-20% SDS-PAGE (Figure 28A). The endotoxin level was then determined using a Charles River Laboratories Endosafe-PTS system (0.05 – 5 EU/ml sensitivity) using a 50-fold dilution of the sample in Charles Rivers Endotoxin Specific Buffer BG120 yielding a result of <1 EU/mg protein. The macromolecular state of the product was then determined using size exclusion chromatography on 45 µg of the product injected on to a Phenomenex BioSep SEC 3000 column (7.8 x 300 mm) in 50 mM NaH_2PO_4, 250 mM NaCl, pH 6.9 at 1 ml/min observing the absorbance at 280 nm (Figure 28B). The product was

then subject to mass spectral analysis by diluting 1 µl of the sample into 10 µl of sinapinic acid (10 mg per ml in 0.05% trifluroacetic acid, 50% acetonitrile) . The resultant solution (1 µl) was spotted onto a MALDI sample plate. The sample was allowed to dry before being analyzed using a Voyager DE-RP time-of-flight mass spectrometer equipped with a nitrogen laser (337 nm, 3 ns pulse). The positive ion/linear mode was used, with an accelerating voltage of 25 kV. Each spectrum was produced by accumulating data from ~ 200 laser shots. External mass calibration was accomplished using purified proteins of known molecular masses (Figure 28D) and these studies confirmed the integrity of the purified peptibody, within experimental error. The product was then stored at –80°C.

Purified Fc-L-KTX1 blocked the human Kv1.3 current in a dose-dependent fashion (Figure 32A and Figure 32B) by electrophysiology (method was as described in Example 36).

Example 7

Fc-L-HsTx1 bacterial expression

Bacterial expression of Fc-L-HsT1 . The methods to clone and express the peptibody in bacteria are described in Example 3. The vector used was pAMG21ampR-Fc-Pep and the oligos listed below were used to generate a duplex (see below) for cloning and expression in bacteria of Fc-L-HsTx1.

Oligos used to form duplex are shown below:

TGGTTCCGGTGGTGGTGGTTCCGCTTCCTGCCGTACCCCGAAAGAC //SEQ ID NO:705;

TGCGCTGACCCGTGCCGTAAAGAAACCGGTTGCCCGTACGGTAAATGCATGAACCGTAAATGCAAATGCAACC
GTTGC //SEQ ID NO:706;

CTTAGCAACGGTTGCATTTGCATTTACGGTTCATGCATTTACCGTACG //SEQ ID NO:707;

GGCAACCGGTTTCTTTACGGCACGGGTCAGCGCAGTCTTTCGGGGTACGGCAGGAAGCGGAACCACCACCACC
GGA //SEQ ID NO:708;

The duplex formed by the oligos above is shown below:

```
   TGGTTCCGGTGGTGGTGGTTCCGCTTCCTGCCGTACCCCGAAAGACTGCGCTGACCCGTG
 1 ---------+---------+---------+---------+---------+---------+ 60
     AGGCCACCACCACCAAGGCGAAGGACGGCATGGGGCTTTCTGACGCGACTGGGCAC
   G S G G G G S A S C R T P K D C A D P C -

   CCGTAAAGAAACCGGTTGCCCGTACGGTAAATGCATGAACCGTAAATGCAAATGCAACCG
61 ---------+---------+---------+---------+---------+---------+ 120
   GGCATTTCTTTGGCCAACGGGCATGCCATTTACGTACTTGGCATTTACGTTTACGTTGGC
   R K E T G C P Y G K C M N R K C K C N R -


   TTGC SEQ ID NO:709
121 ---- 124
   AACGATTC SEQ ID NO:711

    C   - SEQ ID NO:710
```

Bacterial expression of the peptibody was as described in Example 3 and paste was stored frozen.

Example 8

Fc-L-MgTx bacterial expression

Bacterial expression of Fc-L-MgTx. The methods to clone and express the peptibody in bacteria are described in Example 3. The vector used was pAMG21ampR-Fc-Pep and the oligos listed below were used to generate a duplex (see below) for cloning and expression in bacteria of Fc-L-MgTx.

Oligos used to form duplex are shown below:

```
TGGTTCCGGTGGTGGTGGTTCCACCATCATCAACGTTAAATGCACCTC //SEQ ID NO:712;

CCCGAAACAGTGCCTGCCGCCGTGCAAAGCTCAGTTCGGTCAGTCCGCTGGTGCTAAATGCATGAACGGTAAA
TGCAAATGCTACCCGCAC //SEQ ID NO:713;

CTTAGTGCGGGTAGCATTTGCATTTACCGTTCATGCATTTAGCACCAG //SEQ ID NO:714;

CGGACTGACCGAACTGAGCTTTGCACGGCGGCAGGCACTGTTTCGGGGAGGTGCATTTAACGTTGATGATGGT
GGAACCACCACCACCGGA //SEQ ID NO:715;
```

The oligos above were used to form the duplex shown below:

```
    TGGTTCCGGTGGTGGTGGTTCCACCATCATCAACGTTAAATGCACCTCCCCGAAACAGTG
  1 ---------+---------+---------+---------+---------+---------+ 60
      AGGCCACCACCACCAAGGTGGTAGTAGTTGCAATTTACGTGGAGGGGCTTTGTCAC

     G  S  G  G  G  G  S  T  I  I  N  V  K  C  T  S  P  K  Q  C  -

    CCTGCCGCCGTGCAAAGCTCAGTTCGGTCAGTCCGCTGGTGCTAAATGCATGAACGGTAA
 61 ---------+---------+---------+---------+---------+---------+ 120
    GGACGGCGGCACGTTTCGAGTCAAGCCAGTCAGGCGACCACGATTTACGTACTTGCCATT

     L  P  P  C  K  A  Q  F  G  Q  S  A  G  A  K  C  M  N  G  K  -

    ATGCAAATGCTACCCGCAC SEQ ID NO:716
121 ---------+---------
    TACGTTTACGATGGGCGTGATTC SEQ ID NO:718

     C  K  C  Y  P  H   - SEQ ID NO:717
```

Bacterial expression of the peptibody was as described in Example 3 and paste was stored frozen.

Example 9

Fc-L-AgTx2 bacterial expression

Bacterial expression of Fc-L-AgTx2. The methods to clone and express the peptibody in bacteria are described in Example 3. The vector used was pAMG21ampR-Fc-Pep and the oligos listed below were used to generate a duplex (see below) for cloning and expression in bacteria of Fc-L-AgTx2.

Oligos used to form duplex are shown below:

TGGTTCCGGTGGTGGTGGTTCCGGTGTTCCGATCAACGTTTCCTGCACCGGT //SEQ ID NO:719;

TCCCCGCAGTGCATCAAACCGTGCAAAGACGCTGGTATGCGTTTCGGTAAATGCATGAACCGTAAATGCCACT GCACCCCGAAA //SEQ ID NO:720;

CTTATTTCGGGGTGCAGTGGCATTTACGGTTCATGCATTTACCGAAACGCATA //SEQ ID NO:721;

CCAGCGTCTTTGCACGGTTTGATGCACTGCGGGGAACCGGTGCAGGAAACGTTGATCGGAACACCGGAACCAC CACCACCGGA //SEQ ID NO:722;

The oligos listed above were used to form the duplex shown below:

```
    TGGTTCCGGTGGTGGTGGTTCCGGTGTTCCGATCAACGTTTCCTGCACCGGTTCCCCGCA
  1 ---------+---------+---------+---------+---------+---------+ 60
      AGGCCACCACCACCAAGGCCACAAGGCTAGTTGCAAAGGACGTGGCCAAGGGGCGT

     G  S  G  G  G  G  S  G  V  P  I  N  V  S  C  T  G  S  P  Q  -

    GTGCATCAAACCGTGCAAAGACGCTGGTATGCGTTTCGGTAAATGCATGAACCGTAAATG
 61 ---------+---------+---------+---------+---------+---------+ 120
    CACGTAGTTTGGCACGTTTCTGCGACCATACGCAAAGCCATTTACGTACTTGGCATTTAC

     C  I  K  P  C  K  D  A  G  M  R  F  G  K  C  M  N  R  K  C  -

    CCACTGCACCCCGAAA_SEQ ID NO:723
121 ---------+------
    GGTGACGTGGGGCTTTATTC SEQ ID NO:725

     H  C  T  P  K   - SEQ ID NO:724
```

Bacterial expression of the peptibody was as described in Example 3 and paste was stored frozen.

Refolding and purification of Fc-L-AgTx2 expressed in bacteria. Frozen, E. coli paste (15 g) was combined with 120 ml of room temperature 50 mM tris HCl, 5 mM EDTA, pH 8.0 and was brought to about 0.1 mg/ml hen egg white lysozyme. The suspended paste was passed through a chilled microfluidizer twice at 12,000 PSI. The cell lysate was then centrifuged at 22,000 g for 20 min at 4 °C. The pellet was then resuspended in 200 ml 1% deoxycholic acid using a tissue grinder and then centrifuged at 22,000 g for 20 min at 4 °C. The pellet was then resuspended in 200 ml water using a tissue grinder and then centrifuged at 22,000 g for 20 min at 4 °C. The pellet (4.6 g) was then dissolved in 46 ml 8 M guanidine HCl, 50 mM tris HCl, pH 8.0. The dissolved pellet was then reduced by adding 30 µl 1 M dithiothreitol to 3 ml of the solution and incubating at 37 °C for 30 minutes. The reduced pellet solution was then centrifuged at 14,000 g for 5 min at room temperature, and then 2.5 ml of the supernatant was transferred to 250 ml of the refolding buffer (2 M urea, 50 mM tris, 160 mM arginine HCl, 5 mM EDTA, 1 mM cystamine HCl, 4 mM cysteine, pH 9.5) at 4 °C with vigorous stirring. The stirring rate was then slowed and the incubation was continued for 2 days at 4 °C. The refolding solution was then filtered through a 0.22 µm cellulose acetate filter and stored at -70 °C.

The stored refold was defrosted and then diluted with 1 L of water and the pH was adjusted to 7.5 using 1 M H_3PO_4. The pH adjusted material was then filtered through a 0.22 µm

cellulose acetate filter and loaded on to a 10 ml Amersham SP-HP HiTrap column at 10 ml/min in S-Buffer A (20 mM NaH_2PO_4, pH 7.3) at 7 °C. The column was then washed with several column volumes of S-Buffer A, followed by elution with a linear gradient from 0% to 60% S-Buffer B (20 mM NaH_2PO_4, 1 M NaCl, pH 7.3) followed by a step to 100% S-Buffer B at 5 ml/min 7 °C. Fractions were then analyzed using a Coomassie brilliant blue stained tris-glycine 4-20% SDS-PAGE, and the fractions containing the desired product were pooled based on these data (15 ml). The pool was then loaded on to a 1 ml Amersham rProtein A HiTrap column in PBS at 2 ml/min 7 °C. Then column was then washed with several column volumes of 20 mM NaH_2PO_4 pH 6.5, 1 M NaCl and eluted with 100 mM glycine pH 3.0. To the elution peak (1.5 ml), 70 µl 1 M tris HCl pH 8.5 was added, and then the pH -adjusted material was filtered though a 0.22 µm cellulose acetate filter.

A spectral scan was then conducted on 20 µl of the combined pool diluted in 700 µl PBS using a Hewlett Packard 8453 spectrophotometer (Figure 29C). The concentration of the filtered material was determined to be 1.65 mg/ml using a calculated molecular mass of 30,446 g/mol and extinction coefficient of 35,410 M^{-1} cm^{-1}. The purity of the filtered material was then assessed using a Coomassie brilliant blue stained tris-glycine 4-20% SDS-PAGE (Figure 29A). The endotoxin level was then determined using a Charles River Laboratories Endosafe-PTS system (0.05 – 5 EU/ml sensitivity) using a 33-fold dilution of the sample in Charles Rivers Endotoxin Specific Buffer BG120 yielding a result of <4 EU/mg protein. The macromolecular state of the product was then determined using size exclusion chromatography on 20 µg of the product injected on to a Phenomenex BioSep SEC 3000 column (7.8 x 300 mm) in 50 mM NaH_2PO_4, 250 mM NaCl, pH 6.9 at 1 ml/min observing the absorbance at 280 nm (Figure 29D). The product was then subject to mass spectral analysis by diluting 1 µl of the sample into 10 µl of sinapinic acid (10 mg per ml in 0.05% trifluroacetic acid, 50% acetonitrile) . The resultant solution (1 µl) was spotted onto a MALDI sample plate. The sample was allowed to dry before being analyzed using a Voyager DE-RP time-of-flight mass spectrometer equipped with a nitrogen laser (337 nm, 3 ns pulse). The positive ion/linear mode was used, with an accelerating voltage of 25 kV. Each spectrum was produced by accumulating data from ~ 200 laser shots. External mass calibration was accomplished using purified proteins of known molecular masses (Figure 29E) and these studies confirmed the integrity of the purified peptibody, within experimental error . The product was then stored at –80 °C.

Example 10

Fc-L-OSK1 bacterial expression

Bacterial expression of Fc-L-OSK1. The methods used to clone and express the peptibody in bacteria were as described in Example 3. The vector used was pAMG21ampR-Fc-Pep and the oligos listed below were used to generate a duplex (see below) for cloning and expression in bacteria of Fc-L-OSK1.

Oligos used to form duplex are shown below:

```
TGGTTCCGGTGGTGGTGGTTCCGGTGTTATCATCAACGTTAAATGCAAAATCTCCCGTCAGTGCCTGGAACCG
TGCAAAAAAG //SEQ ID NO:726;

CTGGTATGCGTTTCGGTAAATGCATGAACGGTAAATGCCACTGCACCCCGAAA //SEQ ID NO:727;

CTTATTTCGGGGTGCAGTGGCATTTACCGTTCATGCATTTACCGAAACGCATACCAGCTTTTTTGCACGGTTC
CAGGCACTGA //SEQ ID NO:728;

CGGGAGATTTTGCATTTAACGTTGATGATAACACCGGAACCACCACCACCGGA //SEQ ID NO:729;
```

The oligos shown above were used to form the duplex below:

```
   TGGTTCCGGTGGTGGTGGTTCCGGTGTTATCATCAACGTTAAATGCAAAATCTCCCGTCA
 1 ----------+---------+---------+---------+---------+---------+ 60
     AGGCCACCACCACCAAGGCCACAATAGTAGTTGCAATTTACGTTTTAGAGGGCAGT

   G  S  G  G  G  G  S  G  V  I  I  N  V  K  C  K  I  S  R  Q  -

   GTGCCTGGAACCGTGCAAAAAAGCTGGTATGCGTTTCGGTAAATGCATGAACGGTAAATG
61 ----------+---------+---------+---------+---------+---------+ 120
   CACGGACCTTGGCACGTTTTTTCGACCATACGCAAAGCCATTTACGTACTTGCCATTTAC

   C  L  E  P  C  K  K  A  G  M  R  F  G  K  C  M  N  G  K  C  -

   CCACTGCACCCCGAAA SEQ ID NO:730
121 ----------+------
   GGTGACGTGGGGCTTTATTC SEQ ID NO:732

   H  C  T  P  K   - SEQ ID NO:731
```

Bacterial expression of the peptibody was as described in Example 3 and paste was stored frozen for later use. Purification of Fc-L10-OSK1 from *E. coli* paste is described in Example 40 herein below.

Example 11

Fc-L-OSK1(E16K,K20D) bacterial expression

Bacterial expression of Fc-L-OSK1(E16K, K20D). The methods to clone and express the peptibody in bacteria are described in Example 3. The vector used was pAMG21ampR-Fc-Pep and the oligos listed below were used to generate a duplex (see below) for cloning and expression in bacteria of Fc-L-OSK1(E16K,K20D).

Oligos used to form duplex are shown below:

TGGTTCCGGTGGTGGTGGTTCCGGTGTTATCATCAACGTTAAATGCAAAATCTCCCGTCAGTGCCTGAAACCG
TGCAAAGACG //SEQ ID NO:733;

CTGGTATGCGTTTCGGTAAATGCATGAACGGTAAATGCCACTGCACCCCGAAA //SEQ ID NO:734;

CTTATTTCGGGGTGCAGTGGCATTTACCGTTCATGCATTTACCGAAACGCATACCAGCGTCTTTGCACGGTTT
CAGGCACTGA //SEQ ID NO:735;

CGGGAGATTTTGCATTTAACGTTGATGATAACACCGGAACCACCACCACCGGA //SEQ ID NO:736;

The oligos shown above were used to form the duplex below:

```
    TGGTTCCGGTGGTGGTGGTTCCGGTGTTATCATCAACGTTAAATGCAAAATCTCCCGTCA
  1 ----------+---------+---------+---------+---------+---------+ 60
      AGGCCACCACCACCAAGGCCACAATAGTAGTTGCAATTTACGTTTTAGAGGGCAGT

      G  S  G  G  G  G  S  G  V  I  I  N  V  K  C  K  I  S  R  Q  -

    GTGCCTGAAACCGTGCAAAGACGCTGGTATGCGTTTCGGTAAATGCATGAACGGTAAATG
 61 ----------+---------+---------+---------+---------+---------+ 120
    CACGGACTTTGGCACGTTTCTGCGACCATACGCAAAGCCATTTACGTACTTGCCATTTAC

      C  L  K  P  C  K  D  A  G  M  R  F  G  K  C  M  N  G  K  C  -

    CCACTGCACCCCGAAA SEQ ID NO:737
121 ----------+-------
    GGTGACGTGGGGCTTTATTC SEQ ID NO:739

      H  C  T  P  K   - SEQ ID NO:738
```

Bacterial expression of the peptibody was as described in Example 3 and paste was stored frozen for later use.

Example 12

Fc-L-Anuroctoxin bacterial expression

Bacterial expression of Fc-L-Anuroctoxin. The methods to clone and express the peptibody in bacteria are described in Example 3. The vector used was pAMG21ampR-Fc-Pep and the oligos listed below were used to generate a duplex (see below) for cloning and expression in bacteria of Fc-L-Anuroctoxin.

Oligos used to form duplex are shown below:

TGGTTCCGGTGGTGGTGGTTCCAAAGAATGCACCGGTCCGCAGCACTGCACCAACTTCTGCCGTAAAAACAAA
TGCACCCACG //SEQ ID NO:740;

GTAAATGCATGAACCGTAAATGCAAATGCTTCAACTGCAAA //SEQ ID NO:741;

CTTATTTGCAGTTGAAGCATTTGCATTTACGGTTCATGCATTTACCGTGGGTGCATTTGTTTTTACGGCAGAA
GTTGGTGCAG //SEQ ID NO:742;

TGCTGCGGACCGGTGCATTCTTTGGAACCACCACCACCGGA //SEQ ID NO:743;

The oligos shown above were used to form the duplex below:

```
    TGGTTCCGGTGGTGGTGGTTCCAAAGAATGCACCGGTCCGCAGCACTGCACCAACTTCTG
  1 ---------+---------+---------+---------+---------+---------+ 60
      AGGCCACCACCACCAAGGTTTCTTACGTGGCCAGGCGTCGTGACGTGGTTGAAGAC

      G  S  G  G  G  G  S  K  E  C  T  G  P  Q  H  C  T  N  F  C  -
```

```
    CCGTAAAAACAAATGCACCCACGGTAAATGCATGAACCGTAAATGCAAATGCTTCAACTG
 61 ---------+---------+---------+---------+---------+---------+ 120
    GGCATTTTTGTTTACGTGGGTGCCATTTACGTACTTGGCATTTACGTTTACGAAGTTGAC

     R  K  N  K  C  T  H  G  K  C  M  N  R  K  C  K  C  F  N  C  -

    CAAA SEQ ID NO:744
121 ----
    GTTTATTC SEQ ID NO:746

     K   - SEQ ID NO:745
```

Bacterial expression of the peptibody was as described in Example 3 and paste was stored frozen.

Example 13

Fc-L-Noxiustoxin bacterial expression

Bacterial expression of Fc-L-Noxiustoxin or Fc-L-NTX. The methods to clone and express the peptibody in bacteria are described in Example 3. The vector used was pAMG21ampR-Fc-Pep and the oligos listed below were used to generate a duplex (see below) for cloning and expression in bacteria of Fc-L-NTX.

Oligos used to form duplex are shown below:

TGGTTCCGGTGGTGGTGGTTCCACCATCATCAACGTTAAATGCACCTCCCCGAAACAGTGCTCCAAACCGTGC AAAGAACTGT //SEQ ID NO:747;

ACGGTTCCTCCGCTGGTGCTAAATGCATGAACGGTAAATGCAAATGCTACAACAAC //SEQ ID NO:748;

CTTAGTTGTTGTAGCATTTGCATTTACCGTTCATGCATTTAGCACCAGCGGAGGAACCGTACAGTTCTTTGCA CGGTTTGGAG //SEQ ID NO:749;

CACTGTTTCGGGGAGGTGCATTTAACGTTGATGATGGTGGAACCACCACCACCGGA //SEQ ID NO:750;

The oligos shown above were used to form the duplex below:

```
    TGGTTCCGGTGGTGGTGGTTCCACCATCATCAACGTTAAATGCACCTCCCCGAAACAGTG
  1 ---------+---------+---------+---------+---------+---------+ 60
        AGGCCACCACCACCAAGGTGGTAGTAGTTGCAATTTACGTGGAGGGGCTTTGTCAC

     G  S  G  G  G  G  S  T  I  I  N  V  K  C  T  S  P  K  Q  C  -

    CTCCAAACCGTGCAAAGAACTGTACGGTTCCTCCGCTGGTGCTAAATGCATGAACGGTAA
 61 ---------+---------+---------+---------+---------+---------+ 120
    GAGGTTTGGCACGTTTCTTGACATGCCAAGGAGGCGACCACGATTTACGTACTTGCCATT

     S  K  P  C  K  E  L  Y  G  S  S  A  G  A  K  C  M  N  G  K  -

    ATGCAAATGCTACAACAAC SEQ ID NO:751
121 ---------+---------
    TACGTTTACGATGTTGTTGATTC SEQ ID NO:753

     C  K  C  Y  N  N   - SEQ ID NO:752
```

Bacterial expression of the peptibody was as described in Example 3 and paste was stored frozen.

Example 14

Fc-L-Pi2 bacterial expression

Bacterial expression of Fc-L-Pi2. The methods to clone and express the peptibody in bacteria are described in Example 3. The vector used was pAMG21ampR-Fc-Pep and the oligos listed below were used to generate a duplex (see below) for cloning and expression in bacteria of Fc-L-Pi2.

Oligos used to form duplex are shown below:

TGGTTCCGGTGGTGGTGGTTCCACCATCTCCTGCACCAACCCG //SEQ ID NO:754;

AAACAGTGCTACCCGCACTGCAAAAAAGAAACCGGTTACCCGAACGCTAAATGCATGAACCGTAAATGCAAAT GCTTCGGTCGT //SEQ ID NO:755;

CTTAACGACCGAAGCATTTGCATTTACGGTTCATGCATTTAGCG //SEQ ID NO:756;

TTCGGGTAACCGGTTTCTTTTTTGCAGTGCGGGTAGCACTGTTTCGGGTTGGTGCAGGAGATGGTGGAACCAC CACCACCGGA //SEQ ID NO:757;

The oligos above were used to form the duplex below:

```
   TGGTTCCGGTGGTGGTGGTTCCACCATCTCCTGCACCAACCCGAAACAGTGCTACCCGCA
 1 ---------+---------+---------+---------+---------+---------+ 60
     AGGCCACCACCACCAAGGTGGTAGAGGACGTGGTTGGGCTTTGTCACGATGGGCGT

     G  S  G  G  G  G  S  T  I  S  C  T  N  P  K  Q  C  Y  P  H  -

   CTGCAAAAAAGAAACCGGTTACCCGAACGCTAAATGCATGAACCGTAAATGCAAATGCTT
61 ---------+---------+---------+---------+---------+---------+ 120
   GACGTTTTTTCTTTGGCCAATGGGCTTGCGATTTACGTACTTGGCATTTACGTTTACGAA

     C  K  K  E  T  G  Y  P  N  A  K  C  M  N  R  K  C  K  C  F  -

   CGGTCGT SEQ ID NO:758
121 -------
   GCCAGCAATTC SEQ ID NO:760

     G  R   - SEQ ID NO:759
```

Bacterial expression of the peptibody was as described in Example 3 and paste was stored frozen.

Example 15

ShK[1-35]-L-Fc bacterial expression

Bacterial expression of ShK[1-35]-L-Fc. The methods to clone and express the peptibody in bacteria are described in Example 3. The vector used was pAMG21ampR-Pep-Fc and the oligos listed below were used to generate a duplex (see below) for cloning and expression in bacteria of ShK[1-35]-L-Fc.

Oligos used to form duplex are shown below:

TATGCGTTCTTGTATTGATACTATTCCAAAATCTCGTTGTACTGCTTTTCAATGTAAACATTCTATGAAATAT CGTCTTTCTT //SEQ ID NO:761;

TTTGTCGTAAAACTTGTGGTACTTGTTCTGGTGGTGGTGGTTCT //SEQ ID NO:762;

CACCAGAACCACCACCACCAGAACAAGTACCACAAGTTTTACGACAAAAAGAAAGACGATATTTCATAGAATG
TTTACATTGA //SEQ ID NO:763;

AAAGCAGTACAACGAGATTTTGGAATAGTATCAATACAAGAACG //SEQ ID NO:764;

The oligos shown above were used to form the duplex shown below:

```
    TATGCGTTCTTGTATTGATACTATTCCAAAATCTCGTTGTACTGCTTTTCAATGTAAACA
  1 ---------+---------+---------+---------+---------+---------+ 60
      GCAAGAACATAACTATGATAAGGTTTTAGAGCAACATGACGAAAAGTTACATTTGT

     M  R  S  C  I  D  T  I  P  K  S  R  C  T  A  F  Q  C  K  H  -

    TTCTATGAAATATCGTCTTTCTTTTTGTCGTAAAACTTGTGGTACTTGTTCTGGTGGTGG
 61 ---------+---------+---------+---------+---------+---------+ 120
    AAGATACTTTATAGCAGAAAGAAAAACAGCATTTTGAACACCATGAACAAGACCACCACC

     S  M  K  Y  R  L  S  F  C  R  K  T  C  G  T  C  S  G  G  G  -

    TGGTTCT SEQ ID NO:765
121 ------- 127
    ACCAAGACCAC SEQ ID NO:767

     G  S   - SEQ ID NO:766
```

Bacterial expression of the peptibody was as described in Example 3 and paste was stored frozen. Purification of met-ShK[1-35]-Fc was as described in Example 51 herein below.

Example 16

ShK[2-35]-L-Fc bacterial expression

Bacterial expression of ShK[2-35]-L-Fc. The methods to clone and express the peptibody in bacteria are described in Example 3. The vector used was pAMG21ampR-Pep-Fc and the oligos listed below were used to generate a duplex (see below) for cloning and expression in bacteria of ShK[2-35]-L-Fc.

Oligos used to form duplex are shown below:

TATGTCTTGTATTGATACTATTCCAAAATCTCGTTGTACTGCTTTTCAATGTAAACATTCTATGAAATATCGT
CTTTCTT //SEQ ID NO:768;

TTTGTCGTAAAACTTGTGGTACTTGTTCTGGTGGTGGTGGTTCT //SEQ ID NO:769;

CACCAGAACCACCACCACCAGAACAAGTACCACAAGTTTTACGACAAAAAGAAAGACGATATTTCATAGAATG
TTTACATTGA //SEQ ID NO:770;

AAAGCAGTACAACGAGATTTTGGAATAGTATCAATACAAGA SEQ ID NO:771;

The oligos above were used to form the duplex shown below:

```
    TATGTCTTGTATTGATACTATTCCAAAATCTCGTTGTACTGCTTTTCAATGTAAACATTC
  1 ---------+---------+---------+---------+---------+---------+ 60
      AGAACATAACTATGATAAGGTTTTAGAGCAACATGACGAAAAGTTACATTTGTAAG

     M  S  C  I  D  T  I  P  K  S  R  C  T  A  F  Q  C  K  H  S  -

    TATGAAATATCGTCTTTCTTTTTGTCGTAAAACTTGTGGTACTTGTTCTGGTGGTGGTGG
 61 ---------+---------+---------+---------+---------+---------+ 120
    ATACTTTATAGCAGAAAGAAAAACAGCATTTTGAACACCATGAACAAGACCACCACCACC

     M  K  Y  R  L  S  F  C  R  K  T  C  G  T  C  S  G  G  G  G  -
```

```
    TTCT SEQ ID NO:772
121 ----
    AAGACCAC SEQ ID NO:774
      S   - SEQ ID NO:773
```

Bacterial expression of the peptibody was as described in Example 3 and paste was stored frozen. Purification of the ShK[2-35]-Fc was as described in Example 50 herein below.

Example 17

Fc-L-ChTx bacterial expression

Bacterial expression of Fc-L-ChTx. The methods to clone and express the peptibody in bacteria are described in Example 3. The vector used was pAMG21ampR-Fc-Pep and the oligos listed below were used to generate a duplex (see below) for cloning and expression in bacteria of Fc-L-ChTx.

Oligos used to form duplex are shown below:

```
TGGTTCCGGTGGTGGTGGTTCCCAGTTCACCAACGTT //SEQ ID NO:775;

TCCTGCACCACCTCCAAAGAATGCTGGTCCGTTTGCCAGCGTCTGCACAACACCTCCCGTGGTAAATGCATGA
ACAAAAAATGCCGTTGCTACTCC //SEQ ID NO:776;

CTTAGGAGTAGCAACGGCATTTTTTGTTCATGCATTTA //SEQ ID NO:777;

CCACGGGAGGTGTTGTGCAGACGCTGGCAAACGGACCAGCATTCTTTGGAGGTGGTGCAGGAAACGTTGGTGA
ACTGGGAACCACCACCACCGGA //SEQ ID NO:778;
```

The oligos shown above were used to form the duplex below:

```
    TGGTTCCGGTGGTGGTGGTTCCCAGTTCACCAACGTTTCCTGCACCACCTCCAAAGAATG
  1 ---------+---------+---------+---------+---------+---------+ 60
      AGGCCACCACCACCAAGGGTCAAGTGGTTGCAAAGGACGTGGTGGAGGTTTCTTAC

       G   S   G   G   G   G   S   Q   F   T   N   V   S   C   T   T   S   K   E   C   -

    CTGGTCCGTTTGCCAGCGTCTGCACAACACCTCCCGTGGTAAATGCATGAACAAAAAATG
 61 ---------+---------+---------+---------+---------+---------+ 120
    GACCAGGCAAACGGTCGCAGACGTGTTGTGGAGGGCACCATTTACGTACTTGTTTTTTAC

       W   S   V   C   Q   R   L   H   N   T   S   R   G   K   C   M   N   K   K   C   -

    CCGTTGCTACTCC SEQ ID NO:779
121 ----------+---
    GGCAACGATGAGGATTC SEQ ID NO:781
      R   C   Y   S   - SEQ ID NO:780
```

Bacterial expression of the peptibody was as described in Example 3 and paste was stored frozen.

Example 18

Fc-L-MTX bacterial expression

Bacterial expression of Fc-L-MTX. The methods to clone and express the peptibody in bacteria are described in Example 3. The vector used was pAMG21ampR-Fc-Pep and the oligos

listed below were used to generate a duplex (see below) for cloning and expression in bacteria of Fc-L-MTX.

Oligos used to form duplex are shown below:

TGGTTCCGGTGGTGGTGGTTCCGTTTCCTGCACCGGT //SEQ ID NO:782;

TCCAAAGACTGCTACGCTCCGTGCCGTAAACAGACCGGTTGCCCGAACGCTAAATGCATCAACAAATCCTGCA
AATGCTACGGTTGC //SEQ ID NO:783;

CTTAGCAACCGTAGCATTTGCAGGATTTGTTGATGCAT //SEQ ID NO:784;

TTAGCGTTCGGGCAACCGGTCTGTTTACGGCACGGAGCGTAGCAGTCTTTGGAACCGGTGCAGGAAACGGAAC
CACCACCACCGGA //SEQ ID NO:785;

The oligos above were used to form the duplex shown below:

```
    TGGTTCCGGTGGTGGTGGTTCCGTTTCCTGCACCGGTTCCAAAGACTGCTACGCTCCGTG
 1  ----------+---------+---------+---------+---------+---------+ 60
      AGGCCACCACCACCAAGGCAAAGGACGTGGCCAAGGTTTCTGACGATGCGAGGCAC

     G  S  G  G  G  G  S  V  S  C  T  G  S  K  D  C  Y  A  P  C  -

    CCGTAAACAGACCGGTTGCCCGAACGCTAAATGCATCAACAAATCCTGCAAATGCTACGG
 61 ----------+---------+---------+---------+---------+---------+ 120
    GGCATTTGTCTGGCCAACGGGCTTGCGATTTACGTAGTTGTTTAGGACGTTTACGATGCC

     R  K  Q  T  G  C  P  N  A  K  C  I  N  K  S  C  K  C  Y  G  -

    TTGC SEQ ID NO:786
121 ----
    AACGATTC SEQ ID NO:788

     C   - SEQ ID NO:787
```

Bacterial expression of the peptibody was as described in Example 3 and paste was stored frozen.

Example 19

Fc-L-ChTx(K32E) bacterial expression

Bacterial expression of Fc-L-ChTx(K32E). The methods to clone and express the peptibody in bacteria are described in Example 3. The vector used was pAMG21ampR-Fc-Pep and the oligos listed below were used to generate a duplex (see below) for cloning and expression in bacteria of Fc-L-ChTx(K32E).

Oligos used to form duplex are shown below:

TGGTTCCGGTGGTGGTGGTTCCCAGTTCACCAACGTTTCCTG //SEQ ID NO:789;

CACCACCTCCAAAGAATGCTGGTCCGTTTGCCAGCGTCTGCACAACACCTCCCGTGGTAAATGCATGAACAAA
GAATGCCGTTGCTACTCC //SEQ ID NO:790;

CTTAGGAGTAGCAACGGCATTCTTTGTTCATGCATTTACCACG //SEQ ID NO:791;

GGAGGTGTTGTGCAGACGCTGGCAAACGGACCAGCATTCTTTGGAGGTGGTGCAGGAAACGTTGGTGAACTGG
GAACCACCACCACCGGA //SEQ ID NO:792;

The oligos shown above were used to form the duplex below:

```
   TGGTTCCGGTGGTGGTGGTTCCCAGTTCACCAACGTTTCCTGCACCACCTCCAAAGAATG
 1 ---------+---------+---------+---------+---------+---------+ 60
     AGGCCACCACCACCAAGGGTCAAGTGGTTGCAAAGGACGTGGTGGAGGTTTCTTAC

     G  S  G  G  G  G  S  Q  F  T  N  V  S  C  T  T  S  K  E  C  -

   CTGGTCCGTTTGCCAGCGTCTGCACAACACCTCCCGTGGTAAATGCATGAACAAAGAATG
61 ---------+---------+---------+---------+---------+---------+ 120
   GACCAGGCAAACGGTCGCAGACGTGTTGTGGAGGGCACCATTTACGTACTTGTTTCTTAC

     W  S  V  C  Q  R  L  H  N  T  S  R  G  K  C  M  N  K  E  C  -

   CCGTTGCTACTCC SEQ ID NO:793
121 ----------+---
   GGCAACGATGAGGATTC SEQ ID NO:795

     R  C  Y  S   - SEQ ID NO:794
```

Bacterial expression of the peptibody was as described in Example 3 and paste was stored frozen.

Example 20

Fc-L-Apamin bacterial expression

Bacterial expression of Fc-L-Apamin. The methods to clone and express the peptibody in bacteria are described in Example 3. The vector used was pAMG21ampR-Fc-Pep and the oligos listed below were used to generate a duplex (see below) for cloning and expression in bacteria of Fc-L-Apamin.

Oligos used to form duplex are shown below:

```
TGGTTCCGGTGGTGGTGGTTCCTGCAACTGCAAAGCTCCGGAAACCGCTCTGTGCGCTCGTCGTTGCCAGCAG
CACGGT //SEQ ID NO:796;

CTTAACCGTGCTGCTGGCAACGACGAGCGCACAGAGCGGTTTCCGGAGCTTTGCAGTTGCAGGAACCACCACC
ACCGGA //SEQ ID NO:797;
```

The oligos above were used to form the duplex shown below:

```
   TGGTTCCGGTGGTGGTGGTTCCTGCAACTGCAAAGCTCCGGAAACCGCTCTGTGCGCTCG
 1 ---------+---------+---------+---------+---------+---------+ 60
     AGGCCACCACCACCAAGGACGTTGACGTTTCGAGGCCTTTGGCGAGACACGCGAGC

     G  S  G  G  G  G  S  C  N  C  K  A  P  E  T  A  L  C  A  R  -

   TCGTTGCCAGCAGCACGGT SEQ ID NO:798
61 ---------+---------
   AGCAACGGTCGTCGTGCCAATTC SEQ ID NO:800

     R  C  Q  Q  H  G   - SEQ ID NO:799
```

Bacterial expression of the peptibody was as described in Example 3 and paste was stored frozen.

Example 21

Fc-L-Scyllatoxin bacterial expression

Bacterial expression of Fc-L-Scyllatoxin or Fc-L-ScyTx. The methods to clone and express the peptibody in bacteria are described in Example 3. The vector used was

pAMG21ampR-Fc-Pep and the oligos listed below were used to generate a duplex (see below) for cloning and expression in bacteria of Fc-L-ScyTx.

Oligos used to form duplex are shown below:

TGGTTCCGGTGGTGGTGGTTCCGCTTTCTGCAACCTGCG //SEQ ID NO:801;

TATGTGCCAGCTGTCCTGCCGTTCCCTGGGTCTGCTGGGTAAATGCATCGGTGACAAATGCGAATGCGTTAAA CAC //SEQ ID NO:802;

CTTAGTGTTTAACGCATTCGCATTTGTCACCGATGCATTT //SEQ ID NO:803;

ACCCAGCAGACCCAGGGAACGGCAGGACAGCTGGCACATACGCAGGTTGCAGAAAGCGGAACCACCACCACCG GA //SEQ ID NO:804;

The oligos above were used to form the duplex below:

```
   TGGTTCCGGTGGTGGTGGTTCCGCTTTCTGCAACCTGCGTATGTGCCAGCTGTCCTGCCG
 1 ---------+---------+---------+---------+---------+---------+ 60
      AGGCCACCACCACCAAGGCGAAAGACGTTGGACGCATACACGGTCGACAGGACGGC
```

G S G G G G S A F C N L R M C Q L S C R -

```
   TTCCCTGGGTCTGCTGGGTAAATGCATCGGTGACAAATGCGAATGCGTTAAACAC SEQ ID NO:805
61 ---------+---------+---------+---------+---------+------
   AAGGGACCCAGACGACCCATTTACGTAGCCACTGTTTACGCTTACGCAATTTGTGATTC SEQ ID NO:807
```

S L G L L G K C I G D K C E C V K H - SEQ ID NO:806

Bacterial expression of the peptibody was as described in Example 3 and paste was stored frozen.

Example 22

Fc-L-IbTx bacterial expression

Bacterial expression of Fc-L-IbTx. The methods to clone and express the peptibody in bacteria are described in Example 3. The vector used was pAMG21ampR-Fc-Pep and the oligos listed below were used to generate a duplex (see below) for cloning and expression in bacteria of Fc-L-IbTx.

Oligos used to form duplex are shown below:

TGGTTCCGGTGGTGGTGGTTCCCAGTTCACCGACGTTGACTGCTCCGT //SEQ ID NO:808;

TTCCAAAGAATGCTGGTCCGTTTGCAAAGACCTGTTCGGTGTTGACCGTGGTAAATGCATGGGTAAAAAATGC CGTTGCTACCAG //SEQ ID NO:809;

CTTACTGGTAGCAACGGCATTTTTTACCCATGCATTTACCACGGTCAA //SEQ ID NO:810;

CACCGAACAGGTCTTTGCAAACGGACCAGCATTCTTTGGAAACGGAGCAGTCAACGTCGGTGAACTGGGAACC ACCACCACCGGA //SEQ ID NO:811;

The oligos above were used to form the duplex below:

```
   TGGTTCCGGTGGTGGTGGTTCCCAGTTCACCGACGTTGACTGCTCCGTTTCCAAAGAATG
 1 ---------+---------+---------+---------+---------+---------+ 60
      AGGCCACCACCACCAAGGGTCAAGTGGCTGCAACTGACGAGGCAAAGGTTTCTTAC
```

```
      G  S  G  G  G  G  S  Q  F  T  D  V  D  C  S  V  S  K  E  C  -

    CTGGTCCGTTTGCAAAGACCTGTTCGGTGTTGACCGTGGTAAATGCATGGGTAAAAAATG
 61 ---------+---------+---------+---------+---------+---------+ 120
    GACCAGGCAAACGTTTCTGGACAAGCCACAACTGGCACCATTTACGTACCCATTTTTTAC

      W  S  V  C  K  D  L  F  G  V  D  R  G  K  C  M  G  K  K  C  -

    CCGTTGCTACCAG SEQ ID NO:812
121 ----------+---
    GGCAACGATGGTCATTC SEQ ID NO:814

      R  C  Y  Q   - SEQ ID NO:813
```

Bacterial expression of the peptibody was as described in Example 3 and paste was stored frozen.

Example 23

Fc-L-HaTx1 bacterial expression

Bacterial expression of Fc-L-HaTx1. The methods to clone and express the peptibody in bacteria are described in Example 3. The vector used was pAMG21ampR-Fc-Pep and the oligos listed below were used to generate a duplex (see below) for cloning and expression in bacteria of Fc-L-HaTx1.

Oligos used to form duplex are shown below:

TGGTTCCGGTGGTGGTGGTTCCGAATGCCGTTACCTGTTCGGTGGTTG //SEQ ID NO:815;

CAAAACCACCTCCGACTGCTGCAAACACCTGGGTTGCAAATTCCGTGACAAATACTGCGCTTGGGACTTCACC
TTCTCC //SEQ ID NO:816;

CTTAGGAGAAGGTGAAGTCCCAAGCGCAGTATTTGTCACGGAATTTGC //SEQ ID NO:817;

AACCCAGGTGTTTGCAGCAGTCGGAGGTGGTTTTGCAACCACCGAACAGGTAACGGCATTCGGAACCACCACC
ACCGGA //SEQ ID NO:818;

The oligos above were used to form the duplex below:

```
    TGGTTCCGGTGGTGGTGGTTCCGAATGCCGTTACCTGTTCGGTGGTTGCAAAACCACCTC
  1 ---------+---------+---------+---------+---------+---------+ 60
      AGGCCACCACCACCAAGGCTTACGGCAATGGACAAGCCACCAACGTTTTGGTGGAG

      G  S  G  G  G  G  S  E  C  R  Y  L  F  G  G  C  K  T  T  S  -

    CGACTGCTGCAAACACCTGGGTTGCAAATTCCGTGACAAATACTGCGCTTGGGACTTCAC
 61 ---------+---------+---------+---------+---------+---------+ 120
    GCTGACGACGTTTGTGGACCCAACGTTTAAGGCACTGTTTATGACGCGAACCCTGAAGTG

      D  C  C  K  H  L  G  C  K  F  R  D  K  Y  C  A  W  D  F  T  -

    CTTCTCC SEQ ID NO:819
121 -------
    GAAGAGGATTC SEQ ID NO:821

      F  S   - SEQ ID NO:820
```

Bacterial expression of the peptibody was as described in Example 3 and paste was stored frozen.

Refolding and purification of Fc-L-HaTx1 expressed in bacteria. Frozen, *E. coli* paste (13 g) was combined with 100 ml of room temperature 50 mM tris HCl, 5 mM EDTA, pH 8.0 and was brought to about 0.1 mg/ml hen egg white lysozyme. The suspended paste was passed through a chilled microfluidizer twice at 12,000 PSI. The cell lysate was then centrifuged at 22,000 g for 20 min at 4 °C. The pellet was then resuspended in 200 ml 1% deoxycholic acid using a tissue grinder and then centrifuged at 22,000 g for 20 min at 4 °C. The pellet was then resuspended in 200 ml water using a tissue grinder and then centrifuged at 22,000 g for 20 min at 4 °C. The pellet (2.6 g) was then dissolved in 26 ml 8 M guanidine HCl, 50 mM tris HCl, pH 8.0. The dissolved pellet was then reduced by adding 30 µl 1 M dithiothreitol to 3 ml of the solution and incubating at 37 °C for 30 minutes. The reduced pellet solution was then centrifuged at 14,000 g for 5 min at room temperature, and then 2.5 ml of the supernatant was transferred to 250 ml of the refolding buffer (2 M urea, 50 mM tris, 160 mM arginine HCl, 5 mM EDTA, 1 mM cystamine HCl, 4 mM cysteine, pH 8.5) at 4 °C with vigorous stirring. The stirring rate was then slowed and the incubation was continued for 2 days at 4 °C. The refolding solution was then filtered through a 0.22 µm cellulose acetate filter and stored at -70 °C.

The stored refold was defrosted and then diluted with 1 L of water and the pH was adjusted to 7.5 using 1 M H_3PO_4. The pH adjusted material was then filtered through a 0.22 µm cellulose acetate filter and loaded on to a 10 ml Amersham SP-HP HiTrap column at 10 ml/min in S-Buffer A (20 mM NaH_2PO_4, pH 7.3) at 7 °C. The column was then washed with several column volumes of S-Buffer A, followed by elution with a linear gradient from 0% to 60% S-Buffer B (20 mM NaH_2PO_4, 1 M NaCl, pH 7.3) followed by a step to 100% S-Buffer B at 5 ml/min 7 °C. Fractions were then analyzed using a Coomassie brilliant blue stained tris-glycine 4-20% SDS-PAGE, and the fractions containing the desired product were pooled based on these data (15 ml). The pool was then loaded on to a 1 ml Amersham rProtein A HiTrap column in PBS at 2 ml/min 7 °C. Then column was then washed with several column volumes of 20 mM NaH_2PO_4 pH 6.5, 1 M NaCl and eluted with 100 mM glycine pH 3.0. To the elution peak (1.4 ml), 70 µl 1 M tris HCl pH 8.5 was added, and then the pH adjusted material was filtered though a 0.22 µm cellulose acetate filter.

A spectral scan was then conducted on 20 µl of the combined pool diluted in 700 µl PBS using a Hewlett Packard 8453 spectrophotometer (Figure 29F). The concentration of the filtered material was determined to be 1.44 mg/ml using a calculated molecular mass of 30,469 g/mol and extinction coefficient of 43,890 M^{-1} cm^{-1}. The purity of the filtered material was then assessed using a Coomassie brilliant blue stained tris-glycine 4-20% SDS-PAGE (Figure 29B). The

endotoxin level was then determined using a Charles River Laboratories Endosafe-PTS system (0.05 – 5 EU/ml sensitivity) using a 33-fold dilution of the sample in Charles Rivers Endotoxin Specific Buffer BG120 yielding a result of <4 EU/mg protein. The macromolecular state of the product was then determined using size exclusion chromatography on 20 μg of the product injected on to a Phenomenex BioSep SEC 3000 column (7.8 x 300 mm) in 50 mM NaH_2PO_4, 250 mM NaCl, pH 6.9 at 1 ml/min observing the absorbance at 280 nm (Figure 29G). The product was then subject to mass spectral analysis by diluting 1 μl of the sample into 10 μl of sinapinic acid (10 mg per ml in 0.05% trifluroacetic acid, 50% acetonitrile) . The resultant solution (1 μl) was spotted onto a MALDI sample plate. The sample was allowed to dry before being analyzed using a Voyager DE-RP time-of-flight mass spectrometer equipped with a nitrogen laser (337 nm, 3 ns pulse). The positive ion/linear mode was used, with an accelerating voltage of 25 kV. Each spectrum was produced by accumulating data from ~ 200 laser shots. External mass calibration was accomplished using purified proteins of known molecular masses (Figure 29H) and these studies confirmed the integrity of the purified peptibody, within experimental error. The product was then stored at –80 °C.

Example 24
Fc-L-PaTx2 bacterial expression

Bacterial expression of Fc-L-PaTx2. The methods to clone and express the peptibody in bacteria are described in Example 3. The vector used was pAMG21ampR-Fc-Pep and the oligos listed below were used to generate a duplex (see below) for cloning and expression in bacteria of Fc-L-PaTx2.

Oligos used to form duplex are shown below:

TGGTTCCGGTGGTGGTGGTTCCTACTGCCAGAAATGGA //SEQ ID NO:822;

TGTGGACCTGCGACGAAGAACGTAAATGCTGCGAAGGTCTGGTTTGCCGTCTGTGGTGCAAACGTATCATCAA CATG //SEQ ID NO:823;

CTTACATGTTGATGATACGTTTGCACCACAGACGGCAAA //SEQ ID NO:824;

CCAGACCTTCGCAGCATTTACGTTCTTCGTCGCAGGTCCACATCCATTTCTGGCAGTAGGAACCACCACCACC GGA //SEQ ID NO:825;

The oligos above were used to form the duplex below:

```
   TGGTTCCGGTGGTGGTGGTTCCTACTGCCAGAAATGGATGTGGACCTGCGACGAAGAACG
 1 ---------+---------+---------+---------+---------+---------+ 60
     AGGCCACCACCACCAAGGATGACGGTCTTTACCTACACCTGGACGCTGCTTCTTGC

    G  S  G  G  G  G  S  Y  C  Q  K  W  M  W  T  C  D  E  E  R  -

   TAAATGCTGCGAAGGTCTGGTTTGCCGTCTGTGGTGCAAACGTATCATCAACATG SEQ ID NO:826
61 ---------+---------+---------+---------+---------+---------+-----
   ATTTACGACGCTTCCAGACCAAACGGCAGACACCACGTTTGCATAGTAGTTGTACATTC SEQ ID NO:828

    K  C  C  E  G  L  V  C  R  L  W  C  K  R  I  I  N  M  - SEQ ID NO:827
```

Bacterial expression of the peptibody was as described in Example 3 and paste was stored frozen.

Example 25

Fc-L-wGVIA bacterial expression

Bacterial expression of Fc-L-wGVIA. The methods to clone and express the peptibody in bacteria are described in Example 3. The vector used was pAMG21ampR-Fc-Pep and the oligos listed below were used to generate a duplex (see below) for cloning and expression in bacteria of Fc-L-wGVIA.

Oligos used to form duplex are shown below:

TGGTTCCGGTGGTGGTGGTTCCTGCAAATCCCCGGGTT //SEQ ID NO:829;

CCTCCTGCTCCCCGACCTCCTACAACTGCTGCCGTTCCTGCAACCCGTACACCAAACGTTGCTACGGT SEQ ID NO:830;

CTTAACCGTAGCAACGTTTGGTGTACGGGTTGCAGGAA //SEQ ID NO:831;

CGGCAGCAGTTGTAGGAGGTCGGGGAGCAGGAGGAACCCGGGGATTTGCAGGAACCACCACCACCGGA //SEQ ID NO:832;

The oligos above were used to form the duplex below:

```
   TGGTTCCGGTGGTGGTGGTTCCTGCAAATCCCCGGGTTCCTCCTGCTCCCCGACCTCCTA
 1 ---------+---------+---------+---------+---------+---------+ 60
     AGGCCACCACCACCAAGGACGTTTAGGGGCCCAAGGAGGACGAGGGGCTGGAGGAT
```

```
    G  S  G  G  G  G  S  C  K  S  P  G  S  S  C  S  P  T  S  Y  -
```

```
   CAACTGCTGCCGTTCCTGCAACCCGTACACCAAACGTTGCTACGGT SEQ ID NO:833
61 ---------+---------+---------+---------+------
   GTTGACGACGGCAAGGACGTTGGGCATGTGGTTTGCAACGATGCCAATTC SEQ ID NO:835
```

```
    N  C  C  R  S  C  N  P  Y  T  K  R  C  Y  G  SEQ ID NO:834
```

Bacterial expression of the peptibody was as described in Example 3 and paste was stored frozen.

Example 26

Fc-L-ωMVIIA bacterial expression

Bacterial expression of Fc-L-ωMVIIA. The methods to clone and express the peptibody in bacteria are described in Example 3. The vector used was pAMG21ampR-Fc-Pep and the oligos listed below were used to generate a duplex (see below) for cloning and expression in bacteria of Fc-L-ωMVIIA.

Oligos used to form duplex are shown below:

TGGTTCCGGTGGTGGTGGTTCCTGCAAAGGTAAA //SEQ ID NO:836;

GGTGCTAAATGCTCCCGTCTGATGTACGACTGCTGCACCGGTTCCTGCCGTTCCGGTAAATGCGGT //SEQ ID NO:837;

CTTAACCGCATTTACCGGAACGGCAGGAACCGGT //SEQ ID NO:838;

GCAGCAGTCGTACATCAGACGGGAGCATTTAGCACCTTTACCTTTGCAGGAACCACCACCACCGGA //SEQ ID NO:839;

The oligos above were used to form the duplex below:

```
   TGGTTCCGGTGGTGGTGGTTCCTGCAAAGGTAAAGGTGCTAAATGCTCCCGTCTGATGTA
 1 ---------+---------+---------+---------+---------+---------+ 60
     AGGCCACCACCACCAAGGACGTTTCCATTTCCACGATTTACGAGGGCAGACTACAT

    G  S  G  G  G  G  S  C  K  G  K  G  A  K  C  S  R  L  M  Y  -

   CGACTGCTGCACCGGTTCCTGCCGTTCCGGTAAATGCGGT SEQ ID NO:840
61 ---------+---------+---------+---------+
   GCTGACGACGTGGCCAAGGACGGCAAGGCCATTTACGCCAATTC SEQ ID NO:842

    D  C  C  T  G  S  C  R  S  G  K  C  G   - SEQ ID NO:841
```

Bacterial expression of the peptibody was as described in Example 3 and paste was stored frozen.

Example 27

Fc-L-Ptu1 bacterial expression

Bacterial expression of Fc-L-Ptu1. The methods to clone and express the peptibody in bacteria are described in Example 3. The vector used was pAMG21ampR-Fc-Pep and the oligos listed below were used to generate a duplex (see below) for cloning and expression in bacteria of Fc-L-Ptu1.

Oligos used to form duplex are shown below:

TGGTTCCGGTGGTGGTGGTTCCGCTGAAAAAGACTGCATC //SEQ ID NO:843;

GCTCCGGGTGCTCCGTGCTTCGGTACCGACAAACCGTGCTGCAACCCGCGTGCTTGGTGCTCCTCCTACGCTA ACAAATGCCTG //SEQ ID NO:844;

CTTACAGGCATTTGTTAGCGTAGGAGGAGCACCAAGCACG //SEQ ID NO:845;

CGGGTTGCAGCACGGTTTGTCGGTACCGAAGCACGGAGCACCCGGAGCGATGCAGTCTTTTTCAGCGGAACCA CCACCACCGGA //SEQ ID NO:846;

The oligos above were used to form the duplex below:

```
   TGGTTCCGGTGGTGGTGGTTCCGCTGAAAAAGACTGCATCGCTCCGGGTGCTCCGTGCTT
 1 ---------+---------+---------+---------+---------+---------+ 60
     AGGCCACCACCACCAAGGCGACTTTTTCTGACGTAGCGAGGCCCACGAGGCACGAA

    G  S  G  G  G  G  S  A  E  K  D  C  I  A  P  G  A  P  C  F  -

   CGGTACCGACAAACCGTGCTGCAACCCGCGTGCTTGGTGCTCCTCCTACGCTAACAAATG
61 ---------+---------+---------+---------+---------+---------+ 120
   GCCATGGCTGTTTGGCACGACGTTGGGCGCACGAACCACGAGGAGGATGCGATTGTTTAC

    G  T  D  K  P  C  C  N  P  R  A  W  C  S  S  Y  A  N  K  C  -

   CCTG SEQ ID NO:847
121 ----
```

```
GGACATTC SEQ ID NO:849

 L   - SEQ ID NO:848
```

Bacterial expression of the peptibody was as described in Example 3 and paste was stored frozen.

Example 28

Fc-L-ProTx1 bacterial expression

Bacterial expression of Fc-L-ProTx1. The methods to clone and express the peptibody in bacteria are described in Example 3. The vector used was pAMG21ampR-Fc-Pep and the oligos listed below were used to generate a duplex (see below) for cloning and expression in bacteria of Fc-L-ProTx1.

Oligos used to form duplex are shown below:

```
TGGTTCCGGTGGTGGTGGTTCCGAATGCCGTTACTGGCTGG //SEQ ID NO:850;

GTGGTTGCTCCGCTGGTCAGACCTGCTGCAAACACCTGGTTTGCTCCCGTCGTCACGGTTGGTGCGTTTGGGA
CGGTACCTTCTCC //SEQ ID NO:851;

CTTAGGAGAAGGTACCGTCCCAAACGCACCAACCGTGACGA //SEQ ID NO:852;

CGGGAGCAAACCAGGTGTTTGCAGCAGGTCTGACCAGCGGAGCAACCACCCAGCCAGTAACGGCATTCGGAAC
CACCACCACCGGA //SEQ ID NO:853;
```

The oligos above were used to form the duplex below:

```
    TGGTTCCGGTGGTGGTGGTTCCGAATGCCGTTACTGGCTGGGTGGTTGCTCCGCTGGTCA
  1 ---------+---------+---------+---------+---------+---------+ 60
      AGGCCACCACCACCAAGGCTTACGGCAATGACCGACCCACCAACGAGGCGACCAGT

     G  S  G  G  G  G  S  E  C  R  Y  W  L  G  G  C  S  A  G  Q  -

    GACCTGCTGCAAACACCTGGTTTGCTCCCGTCGTCACGGTTGGTGCGTTTGGGACGGTAC
 61 ---------+---------+---------+---------+---------+---------+ 120
    CTGGACGACGTTTGTGGACCAAACGAGGGCAGCAGTGCCAACCACGCAAACCCTGCCATG

     T  C  C  K  H  L  V  C  S  R  R  H  G  W  C  V  W  D  G  T  -

    CTTCTCC SEQ ID NO:854
121 -------
    GAAGAGGATTC SEQ ID NO:856

     F  S   - SEQ ID NO:855
```

Bacterial expression of the peptibody was as described in Example 3 and paste was stored frozen.

Example 29

Fc-L-BeKM1 bacterial expression

Bacterial expression of Fc-L-BeKM1. The methods to clone and express the peptibody in bacteria are described in Example 3. The vector used was pAMG21ampR-Fc-Pep and the oligos listed below were used to generate a duplex (see below) for cloning and expression in bacteria of Fc-L-BeKM1.

Oligos used to form duplex are shown below:

TGGTTCCGGTGGTGGTGGTTCCCGTCCGACCGACATCAAATG //SEQ ID NO:857;

CTCCGAATCCTACCAGTGCTTCCCGGTTTGCAAATCCCGTTTCGGTAAAACCAACGGTCGTTGCGTTAACGGT TTCTGCGACTGCTTC //SEQ ID NO:858;

CTTAGAAGCAGTCGCAGAAACCGTTAACGCAACGACCGTTGG //SEQ ID NO:859;

TTTTACCGAAACGGGATTTGCAAACCGGGAAGCACTGGTAGGATTCGGAGCATTTGATGTCGGTCGGACGGGA ACCACCACCACCGGA //SEQ ID NO:860;

The oligos above were used to form the duplex below:

```
   TGGTTCCGGTGGTGGTGGTTCCCGTCCGACCGACATCAAATGCTCCGAATCCTACCAGTG
 1 ----------+---------+---------+---------+---------+---------+ 60
     AGGCCACCACCACCAAGGGCAGGCTGGCTGTAGTTTACGAGGCTTAGGATGGTCAC

     G  S  G  G  G  G  S  R  P  T  D  I  K  C  S  E  S  Y  Q  C  -

   CTTCCCGGTTTGCAAATCCCGTTTCGGTAAAACCAACGGTCGTTGCGTTAACGGTTTCTG
61 ----------+---------+---------+---------+---------+---------+ 120
   GAAGGGCCAAACGTTTAGGGCAAAGCCATTTTGGTTGCCAGCAACGCAATTGCCAAAGAC

     F  P  V  C  K  S  R  F  G  K  T  N  G  R  C  V  N  G  F  C  -

   CGACTGCTTC SEQ ID NO:861
121 ----------+
   GCTGACGAAGATTC SEQ ID NO:863

     D  C  F   - SEQ ID NO:862
```

Bacterial expression of the peptibody was as described in Example 3 and paste was stored frozen.

Example 30

Fc-L-CTX bacterial expression

Bacterial expression of Fc-L-CTX. The methods to clone and express the peptibody in bacteria are described in Example 3. The vector used was pAMG21ampR-Fc-Pep and the oligos listed below were used to generate a duplex (see below) for cloning and expression in bacteria of Fc-L-CTX.

Oligos used to form duplex are shown below:

TGGTTCCGGTGGTGGTGGTTCCATGTGCATGCCGTGCTTCAC //SEQ ID NO:864;

CACCGACCACCAGATGGCTCGTAAATGCGACGACTGCTGCGGTGGTAAAGGTCGTGGTAAATGCTACGGTCCG CAGTGCCTGTGCCGT //SEQ ID NO:865;

CTTAACGGCACAGGCACTGCGGACCGTAGCATTTACCACGAC //SEQ ID NO:866;

CTTTACCACCGCAGCAGTCGTCGCATTTACGAGCCATCTGGTGGTCGGTGGTGAAGCACGGCATGCACATGGA ACCACCACCACCGGA //SEQ ID NO:867;

The oligos above were used to form the duplex below:

```
   TGGTTCCGGTGGTGGTGGTTCCATGTGCATGCCGTGCTTCACCACCGACCACCAGATGGC
 1 ----------+----------+----------+----------+----------+----------+ 60
     AGGCCACCACCACCAAGGTACACGTACGGCACGAAGTGGTGGCTGGTGGTCTACCG
5
     G  S  G  G  G  G  S  M  C  M  P  C  F  T  T  D  H  Q  M  A  -

   TCGTAAATGCGACGACTGCTGCGGTGGTAAAGGTCGTGGTAAATGCTACGGTCCGCAGTG
61 ----------+----------+----------+----------+----------+----------+ 120
10   AGCATTTACGCTGCTGACGACGCCACCATTTCCAGCACCATTTACGATGCCAGGCGTCAC

     R  K  C  D  D  C  C  G  G  K  G  R  G  K  C  Y  G  P  Q  C  -

   CCTGTGCCGT SEQ ID NO:868
15 121 ----------+
   GGACACGGCACCAC SEQ ID NO:870

     L  C  R   - SEQ ID NO:869
```

20 Bacterial expression of the peptibody was as described in Example 3 and paste was stored frozen.

Example 31

N-Terminally PEGylated-Des-Arg1-ShK

Peptide Synthesis of reduced Des-Arg1-ShK. Des-Arg1-ShK, having the sequence

25 SCIDTIPKSRCTAFQCKHSMKYRLSFCRKTCGTC

(Peptide 1, SEQ ID NO: 92)

was synthesized in a stepwise manner on a Symphony™ multi-peptide synthesizer by solid-phase peptide synthesis (SPPS) using 2-(1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HBTU)/ N-methyl morpholine (NMM)/N,N-dimethyl-formamide (DMF) 30 coupling chemistry at 0.1 mmol equivalent resin scale on Tentagel™-S PHB Fmoc-Cys(Trt)-resin. N-alpha-(9-fluorenylmethyloxycarbonyl)- and side-chain protected amino acids were purchased from Midwest Biotech Incorporated. Fmoc-Cys(Trt)-Tentagel™ resin was purchased from Fluka. The following side-chain protection strategy was employed: Asp(O^{t}Bu), Arg(Pbf), Cys(Trt), Gln(Trt), His(Trt), Lys(N$^\varepsilon$-Boc), Ser(O^{t}Bu), Thr(O^{t}Bu) and Tyr(O^{t}Bu). Two Oxazolidine dipeptides, Fmoc-Gly-35 Thr($^{\psi Me,Me}$Pro)-OH and Fmoc-Leu-Ser($^{\psi Me,Me}$Pro)-OH, were used in the chain assembly and were obtained from NovaBiochem and used in the synthesis of the sequence. The protected amino acid derivatives (20mmol) were dissolved in 100 ml 20% dimethyl sulfoxide (DMSO) in DMF (*v/v*). Protected amino acids were activated with 20 mM HBTU, 400 mM NMM in 20%DMSO in DMF, and coupling were carried out using two treatments with 0.5mmol protected amino acid, 0.5mmol 40 HBTU, 1 mmol NMM in 20% DMF/DMSO for 25 minutes and then 40 minutes. Fmoc deprotection reactions were carried out with two treatments using a 20% piperidine in DMF (v/v) solution for 10 minutes and then 15 minutes. Following synthesis, the resin was then drained, and washed with DCM, DMF, DCM, and then dried in vacuo. The peptide-resin was deprotected and released from the resin by treatment with a TFA/EDT/TIS/H_2O (92.5:2.5:2.5:2.5 (v/v)) solution at room

temperature for 1 hour. The volatiles were then removed with a stream of nitrogen gas, the crude peptide precipitated twice with cold diethyl ether and collected by centrifugation. The crude peptide was then analyzed on a Waters 2795 analytical RP-HPLC system using a linear gradient (0-60% buffer B in 12 minutes, A:0.1% TFA in water, B: 0.1% TFA in acetonitrile) on a Jupiter 4µm Proteo™ 90Å column. A PE-Sciex™ API Electro-spray mass spectrometer was used to confirm correct peptide product mass. Crude peptide was obtained in 143 mg yield at approximately 70% pure based as estimated by analytical RP-HPLC analysis. Reduced Des-Arg1-ShK (Peptide 1) Retention time (Rt) = 5.31 minutes, calculated molecular weight = 3904.6917 Da (average); Experimental observed molecular weight 3907.0 Da.

Folding of Des-Arg1-ShK (Disulphide bond formation). Following TFA cleavage and peptide precipitation, reduced Des-Arg1-ShK was then air-oxidized to give the folded peptide. The crude cleaved peptide was extracted using 20% AcOH in water (v/v) and then diluted with water to a concentration of approximately 0.15 mg reduced Des-Arg1-ShK per mL, the pH adjusted to about 8.0 using NH_4OH (28-30%), and gently stirred at room temperature for 36 hours. Folding process was monitored by LC-MS analysis. Following this, folded Des-Arg1-ShK peptide was purified using reversed phase HPLC using a 1" Luna 5 µm C18 100 Å Proteo™ column with a linear gradient 0-40% buffer B in 120 min (A=0.1% TFA in water, B=0.1% TFA in acetonitrile). Folded Des-Arg1-ShK crude peptide eluted earlier (when compared to the elution time in its reduced form) at approximately 25% buffer B. Folded Des-Arg1-ShK (Peptide 2) was obtained in 23.2 mg yield in >97% purity as estimated by analytical RP-HPLC analysis (Figure 20). Calculated molecular weight = 3895.7693 Da (monoisotopic), experimental observed molecular weight = 3896.5 Da(analyzed on a Waters LCT Premier Micromass MS Technologies). Des-Arg1-ShK disulfide connectivity was C1-C6, C2-C4, C3-C5.



(Peptide 2, SEQ ID NO: 58)

N-terminal PEGylation of Folded Des-Arg1-ShK. Folded Des-Arg1-ShK, (Peptide 2) was dissolved in water at 1 mg/ml concentration. A 2 M MeO-PEG-Aldehyde, CH_3O-[CH_2CH_2O]n-CH_2CH_2CHO (average molecular weight 20 kDa), solution in 50 mM NaOAc, pH 4.5, and a separate 1 M solution of $NaCNBH_3$ were freshly prepared. The peptide solution was then added to the MeO-PEG-Aldehyde containing solution and was followed by the addition of the $NaCNBH_3$

solution. The reaction stoichiometry was peptide:PEG:NaCNBH3 (1:2:0.02), respectively. The reaction was left for 48 hours, and was analyzed on an Agilent 1100 RP-HPLC system using Zorbax™ 300SB-C8 5 μm column at 40 °C with a linear gradient (6-60% B in 16 minutes, A: 0.1% TFA in water, B: 0.1% TFA/90% ACN in water). Mono-pegylated folded Des-Arg1-ShK constituted approximately 58% of the crude product by analytical RP-HPLC. Mono Pegylated Des-Arg1-ShK was then isolated using a HiTrap™ 5 ml SP HP cation exchange column on AKTA FPLC system at 4 °C at 1 mL/min using a gradient of 0-50% B in 25 column volumes (Buffers: A = 20 mM sodium acetate pH 4.0, B = 1 M NaCl, 20 mM sodium acetate, pH 4.0). The fractions were analyzed using a 4-20 tris-Gly SDS-PAGE gel and RP-HPLC (as described for the crude). SDS-PAGE gels were run for 1.5 hours at 125 V, 35 mA, 5 W. Pooled product was then dialyzed at 4 °C in 3 changes of 1 L of A4S buffer(10 mM NaOAc, 5% sorbitol, pH 4.0). The dialyzed product was then concentrated in 10 K microCentrifuge filter to 2 mL volume and sterile-filtered using 0.2 μM syringe filter to give the final product. N-Terminally PEGylated-Des-Arg1-ShK (Peptide 3) was isolated in 1.7 mg yield with 85% purity as estimated by analytical RP-HPLC analysis (Figure 23).

The N-Terminally PEGylated-Des-Arg1-ShK, also referred to as "PEG-ShK[2-35]", was active in blocking human Kv1.3 (Figure 38A and Figure 38B) as determined by patch clamp electrophysiology (Example 36).

Example 32

N-Terminally PEGylated ShK

The experimental procedures of this working example correspond to the results shown in Figure 17.

Peptide Synthesis of reduced ShK. ShK, having the amino acid sequence

RSCIDTIPKSRCTAFQCKHSMKYRLSFCRKTCGTC

(Peptide 4, SEQ ID NO:5)

was synthesized in a stepwise manner on a Symphony™ multi-peptide synthesizer by solid-phase peptide synthesis (SPPS) using 2-(1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HBTU)/ N-methyl morpholine (NMM)/N,N-dimethyl-formamide (DMF) coupling chemistry at 0.1 mmol equivalent resin scale on Tentagel™-S PHB Fmoc-Cys(Trt)-resin. N-alpha-9-fluorenylmethyloxycarbonyl) and side-chain protected amino acids were purchased from Midwest Biotech Incorporated. Fmoc-Cys(Trt)-Tentagel™ resin was purchased from Fluka. The following side-chain protection strategy was employed: Asp(O^{t}Bu), Arg(Pbf), Cys(Trt), Gln(Trt), His(Trt), Lys(N$^\varepsilon$-Boc), Ser(O^{t}Bu), Thr(O^{t}Bu) and Tyr(O^{t}Bu). Two Oxazolidine dipeptides, Fmoc-Gly-Thr($^{\psi Me,Me}$Pro)-OH and Fmoc-Leu-Ser($^{\psi Me,Me}$Pro)-OH, were used in the chain assembly and were

obtained from NovaBiochem and used in the synthesis of the sequence. The protected amino acid derivatives (20 mmol) were dissolved in 100 ml 20% dimethyl sulfoxide (DMSO) in DMF (*v/v*). Protected amino acids were activated with 200 mM HBTU, 400 mM NMM in 20%DMSO in DMF, and coupling were carried out using two treatments with 0.5 mmol protected amino acid, 0.5 mmol HBTU, 1 mmol NMM in 20%DMF/DMSO for 25 minutes and then 40 minutes. Fmoc deprotections were carried out with two treatments using a 20% piperidine in DMF (v/v) solution for 10 minutes and then 15 minutes. Following synthesis, the resin was then drained, and washed with DCM, DMF, DCM, and then dried in vacuo. The peptide-resin was deprotected and released from the resin by treatment with a TFA/EDT/TIS/H_2O (92.5:2.5:2.5:2.5 (v/v)) solution at room temperature for 1 hour. The volatiles were then removed with a stream of nitrogen gas, the crude peptide precipitated twice with cold diethyl ether and collected by centrifugation. The crude peptide was then analyzed on a Waters 2795 analytical RP-HPLC system using a linear gradient (0-60% buffer B in 12 minutes, A:0.1% TFA in water, B: 0.1% TFA in acetonitrile) on a Jupiter 4µm Proteo™ 90 Å column. A PE-Sciex API Electro-spray mass spectrometer was used to confirm correct peptide product mass. Crude peptide was approximately was obtained 170 mg yield at about 45% purity as estimated by analytical RP-HPLC analysis. Reduced ShK (Peptide 4) Retention time (Rt) = 5.054 minutes, calculated molecular weight = 4060.8793 Da (average); experimental observed molecular weight = 4063.0 Da.

Folding of ShK (Disulphide bond formation). Following TFA cleavage and peptide precipitation, reduced ShK was then air oxidized to give the folded peptide. The crude cleaved peptide was extracted using 20% AcOH in water (v/v) and then diluted with water to a concentration of approximately 0.15 mg reduced ShK per mL, the pH adjusted to about 8.0 using NH_4OH (28-30%), and gently stirred at room temperature for 36 hours. Folding process was monitored by LC-MS analysis. Following this, folded ShK peptide was purified by reversed phase HPLC using a 1" Luna 5 µm C18 100 Å Proteo™ column with a linear gradient 0-40% buffer B in 120 min (A=0.1% TFA in water, B=0.1% TFA in acetonitrile). Folded ShK crude peptide eluted earlier (when compared to the elution time in its reduced form) at approximately 25% buffer B. Folded ShK (Peptide 5) was obtained in 25.5 mg yield in >97% purity as estimated by analytical RP-HPLC analysis. See Figure 60. Calculated molecular weight = 4051.8764 Da (monoisotopic); experimental observed molecular weight = 4052.5 Da (analyzed on Waters LCT Premier

Micromass MS Technologies). ShK disulfide connectivity was C1-C6, C2-C4, and C3-C5.



(Peptide 5, SEQ ID NO:10)

N-terminal PEGylation of Folded ShK. Folded ShK, having the amino acid sequence

RSCIDTIPKSRCTAFQCKHSMKYRLSFCRKTCGTC

(SEQ ID NO:5)

can be dissolved in water at 1 mg/ml concentration. A 2 M MeO-PEG-Aldehyde, CH_3O-$CH_2CH_2O]n$-CH_2CH_2CHO (average molecular weight 20 kDa), solution in 50 mM NaOAc, pH 4.5 and a separate 1 M solution of $NaCNBH_3$ can be freshly prepared. The peptide solution can be then added to the MeO-PEG-Aldehyde containing solution and can be followed by the addition of the $NaCNBH_3$ solution. The reaction stoichiometry can be peptide:PEG:NaCNBH3 (1:2:0.02), respectively. The reaction can be left for 48 hours, and can be analyzed on an Agilent™ 1100 RP-HPLC system using Zorbax™ 300SB-C8 5 μm column at 40 °C with a linear gradient (6-60% B in 16 minutes, A: 0.1% TFA in water, B: 0.1% TFA/90% ACN in water). Mono-pegylated Shk (Peptide 6) can be then isolated using a HiTrap™ 5 mL SP HP cation exchange column on AKTA FPLC system at 4 °C at 1 mL/min using a gradient of 0-50 % B in 25 column volumes (Buffers: A = 20 mM sodium acetate pH 4.0, B = 1 M NaCl, 20 mM sodium acetate, pH 4.0). The fractions can be analyzed using a 4-20 tris-Gly SDS-PAGE gel and RP-HPLC. SDS-PAGE gels can be run for 1.5 hours at 125 V, 35 mA, 5 W. Pooled product can be then dialyzed at 4 °C in 3 changes of 1 L of A4S buffer (10 mM sodium acetate, 5% sorbitol, pH 4.0). The dialyzed product can be then concentrated in 10 K microCentrifuge filter to 2 mL volume and sterile-filtered using 0.2 μM syringe filter to give the final product.

Example 33

N-Terminally PEGylated ShK by oxime formation

Peptide Synthesis of reduced ShK. ShK, having the sequence

RSCIDTIPKSRCTAFQCKHSMKYRLSFCRKTCGTC

(SEQ ID NO: 5)

can be synthesized in a stepwise manner on a Symphony™ multi-peptide synthesizer by solid-phase peptide synthesis (SPPS) using 2-(1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HBTU)/ N-methyl morpholine (NMM)/N,N-dimethyl-formamide (DMF) coupling chemistry at 0.1 mmol equivalent resin scale on Tentagel™-S PHB Fmoc-Cys(Trt)-resin.

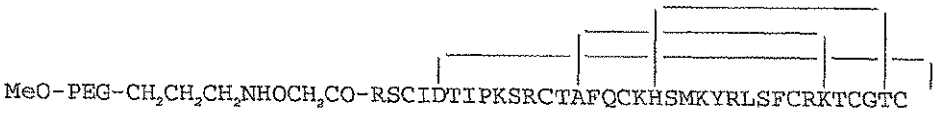
N-alpha-(9-fluorenylmethyloxycarbonyl)- and side-chain protected amino acids can be purchased from Midwest Biotech Incorporated. Fmoc-Cys(Trt)-Tentagel™ resin can be purchased from Fluka. The following side-chain protection strategy can be employed: Asp(O^{t}Bu), Arg(Pbf), Cys(Trt), Gln(Trt), His(Trt), Lys(N$^\varepsilon$-Boc), Ser(O^{t}Bu), Thr(O^{t}Bu) and Tyr(O^{t}Bu). Two Oxazolidine dipeptides, Fmoc-Gly-Thr($\Psi^{Me,Me}$Pro)-OH and Fmoc-Leu-Ser($\psi^{Me,Me}$Pro)-OH, can be used in the chain assembly and can be obtained from NovaBiochem and used in the synthesis of the sequence. The protected amino acid derivatives (20 mmol) can be dissolved in 100 ml 20% dimethyl sulfoxide (DMSO) in DMF (*v/v*). Protected amino acids can be activated with 200 mM HBTU, 400 mM NMM in 20% DMSO in DMF, and coupling can be carried out using two treatments with 0.5 mmol protected amino acid, 0.5 mmol HBTU, 1 mmol NMM in 20% DMF/DMSO for 25 minutes and then 40 minutes. Fmoc deprotection reactions can be carried out with two treatments using a 20% piperidine in DMF (v/v) solution for 10 minutes and then 15 minutes. Following the chain-assembly of the Shk peptide, Boc-amionooxyacetic acid (1.2 equiv) can be coupled at the N-terminus using 0.5 M HBTU in DMF with 4 equiv collidine for 5 minutes. Following synthesis, the resin can be then drained, and washed with DCM, DMF, DCM, and then dried in vacuo. The peptide-resin can be deprotected and released from the resin by treatment with a TFA/amionooxyacetic acid/TIS/EDT/H2O (90:2.5:2.5:2.5:2.5) solution at room temperature for 1 hour. The volatiles can be then removed with a stream of nitrogen gas, the crude peptide precipitated twice with cold diethyl ether and collected by centrifugation. The aminooxy-Shk peptide (Peptide 7) can be then analyzed on a Waters 2795 analytical RP-HPLC system using a linear gradient (0-60% buffer B in 12 minutes, A: 0.1% TFA in water also containing 0.1% aminooxyacetic acid, B: 0.1% TFA in acetonitrile) on a Jupiter 4 μm Proteo™ 90 Å column.

Reversed-Phase HPLC Purification. Preparative Reversed-phase high-performance liquid chromatography can be performed on C18, 5 μm, 2.2 cm × 25 cm) column. Chromatographic separations can be achieved using linear gradients of buffer B in A (A = 0.1% aqueous TFA; B = 90% aq. ACN containing 0.09% TFA and 0.1% aminooxyacetic acid), typically 5-95% over 90 minutes at 15 mL/min. Preparative HPLC fractions can be characterized by ESMS and photodiode array (PDA) HPLC, combined and lyophilized.

N-Terminal PEGylation of Shk by Oxime Formation. Lyophilized aminooxy-Shk (Peptide 7) can be dissolved in 50% HPLC buffer A/B (5 mg/mL) and added to a two-fold molar excess of MeO-PEG-Aldehyde, CH_3O-[CH_2CH_2O]$_n$-CH_2CH_2CHO (average molecular weight 20 kDa). The reaction can be left for 24 hours, and can be analyzed on an Agilent™ 1100 RP-HPLC system using Zorbax™ 300SB-C8 5 μm column at 40 °C with a linear gradient (6-60 % B in 16 minutes, A:

0.1% TFA in water, B: 0.1% TFA/90% ACN in water). Mono-pegylated reduced Shk constituted approximately 58% of the crude product by analytical RP-HPLC. Mono PEGylated (oximated) Shk (Peptide 8) can be then isolated using a HiTrap™ 5 mL SP HP cation exchange column on AKTA FPLC system at 4 °C at 1 mL/min using a gradient of 0-50 % B in 25 column volumes (Buffers: A = 20 mM sodium acetate pH 4.0, B = 1 M NaCl, 20 mM sodium acetate, pH 4.0). The fractions can be analyzed using a 4-20 tris-Gly SDS-PAGE gel and RP-HPLC. SDS-PAGE gels can be run for 1.5 hours at 125 V, 35 mA, 5 W. Pooled product can be then dialyzed at 4 °C in 3 changes of 1 L of A4S buffer (10 mM NaOAc, 5% sorbitol, pH 4.0). The dialyzed product can be then concentrated in 10 K microCentrifuge filter to 2 mL volume and sterile-filtered using 0.2 μM syringe filter to give the final product.

Folding of ShK (Disulphide bond formation). The mono-PEGylated (oximated) Shk can be dissolved in 20% AcOH in water (v/v) and can be then diluted with water to a concentration of approximately 0.15 mg peptide mL, the pH adjusted to about 8.0 using NH_4OH (28-30%), and gently stirred at room temperature for 36 hours. Folding process can be monitored by LC-MS analysis. Following this, folded mono-PEGylated (oximated) Shk (Peptide 9) can be purified using by reversed phase HPLC using a 1" Luna 5 μm C18 100 Å Proteo™ column with a linear gradient 0-40% buffer B in 120 min (A=0.1% TFA in water, B=0.1% TFA in acetonitrile). Mono-PEGylated (oximated) ShK disulfide connectivity can be C1-C6, C2-C4, and C3-C5.



(Peptide 9, SEQ ID NO:10)

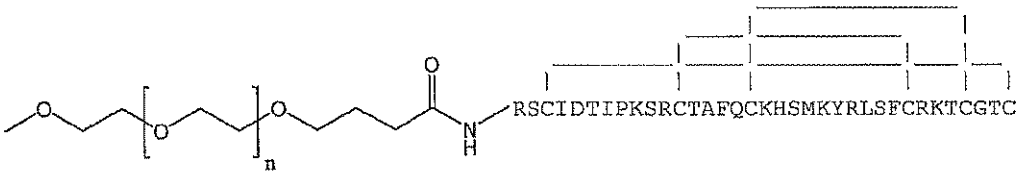
Example 34

N-Terminally PEGylated ShK (amidation)

The experimental procedures of this working example correspond to the results shown in Figure 18.

N-Terminal PEGylation of Shk by Amide Formation. A 10 mg/mL solution of folded Shk (Peptide 5), in 100 mM Bicine pH 8.0, can be added to solid succinimidyl ester of 20 kDa PEG propionic acid (mPEG-SPA; CH_3O-[CH_2CH_2O]n-CH_2CH_2CO-NHS) at room temperature using a 1.5 molar excess of the mPEG-SPA to Shk. After one hour with gentle stirring, the mixture can be diluted to 2 mg/mL with water, and the pH can be adjusted to 4.0 with dilute HCl. The extent of mono-pegylated Shk (Peptide 10), some di-PEGylated Shk or tri-PEGylated Shk, unmodified Shk

and succinimidyl ester hydrolysis can be determined by SEC HPLC using a Superdex™ 75 HR 10/30 column (Amersham) eluted with 0.05 M NaH_2PO_4, 0.05 M Na_2HPO_4, 0.15 M NaCl, 0.01 M NaN_3, pH 6.8, at 1 mL/min. The fractions can be analyzed using a 4-20 tris-Gly SDS-PAGE gel and RP-HPLC. SDS-PAGE gels can be run for 1.5 hours at 125 V, 35 mA, 5 W. Pooled product can be then dialyzed at 4 °C in 3 changes of 1 L of A4S buffer (10 mM NaOAc, 5% sorbitol, pH 4.0). The dialyzed N-terminally PEGylated (amidated) ShK (Peptide 10) can be then concentrated in 10 K microCentrifuge filter to 2 mL volume and sterile-filtered using 0.2 μM syringe filter to give the final product.



PEG 20kDa



(Peptide 10, SEQ ID NO:10)

Example 35

Fc-L-SmIIIA

Fc-SmIIIA expression vector. A 104 bp BamHI-NotI fragment containing partial linker sequence and SmIIIA peptide encoded with human high frequency codons was assembled by PCR with overlapping primers 3654-50 and 3654-51 and cloned into to the 7.1 kb NotI-BamHI back bone to generate pcDNA3.1(+)CMVi-hFc-SmIIIA as described in Example 1.

```
  BamHI
5'GGATCCGGAGGAGGAGGAAGCTGCTGCAACGGCCGCCGCGGCTGCAGCAGCCGCTGG
                        C  C  N  G  R  R  G  C  S  S  R  W
TGCCGCGACCACAGCCGCTGCTGCTGAGCGGCCGC3' //SEQ ID NO:872
C  R  D  H  S  R  C  C       NotI
SEQ ID NO:873

Forward 5'-3':
GGAGGAGGATCCGGAGGAGGAGGAAGCTGCTGCAACGGCCGCCGCGGCTGCAGCAGC CGC //SEQ ID
NO:874

Reverse 5'-3':
ATTATTGCGGCCGCTCAGCAGCAGCGGCTGTGGTCGCGGCACCAGCGGCTGCTGCAG CCGC SEQ ID
NO:875
```

The sequences of the BamHI to NotI fragments in the final constructs were verified by sequencing.

Transient expression of Fc-L-SmIIIa. 7.5 ug of the toxin peptide Fc fusion construct pcDNA3.1(+)CMVi-hFc-SmIIIA were transfected into 293-T cells in 10 cm tissue culture plate with FuGENE 6 as transfection reagent. Culture medium was replaced with serum-free medium at 24 hours post-transfection and the conditioned medium was harvested at day 5 post-transfection. Transient expression of Fc-SmIIIA from 293-T cells was analyzed by Western blot probed with anti-hFc antibody (Figure 25A and Figure 25B). Single band of expressed protein with estimated MW was shown in both reduced and non-reduced samples. Transient expression level of Fc-SmIIIA was further determined to be 73.4 μg/ml according to ELISA.

Example 36

Electrophysiology experiments

Cell Culture. Stable cell line expressing human $K_v1.3$ channel was licensed from Biofocus. Cells were kept at 37 °C in 5% CO_2 environment. Culture medium contains DMEM with GlutaMax™ (Invitrogen), 1X non-essential amino acid, 10% fetal bovine serum and 500 μg/mL geneticin. Cells were plated and grown at low confluence on 35 mm culture dishes for at least 24 hours prior to electrophysiology experiments.

Electrophysiology Recording by Patch Clamping. Whole-cell currents were recorded from single cells by using tight seal configuration of the patch-clamp technique. A 35 mm culture dish was transferred to the recording stage after rinsing and replacing the culture medium with recording buffer containing 135 mM NaCl, 5 mM KCl, 1.8 mM $CaCl_2$, 10 mM HEPES, and 5 mM Glucose. pH was adjusted to 7.4 with NaOH and the osmolarity was set at 300 mOsm. Cells were perfused continuously with the recording buffer via one of the glass capillaries arranged in parallel and attached to a motorized rod, which places the glass capillary directly on top of the cell being recorded. Recording pipette solution contained 90 mM K-gluconate, 20 mM KF, 10 mM NaCl, 1 mM $MgCl_2$-$6H_2O$, 10 mM EGTA, 5 mM K_2-ATP, and 10 mM HEPES. The pH for the internal solution was adjusted to 7.4 with KOH and the osmolarity was set at 280 mOsm. Experiments were performed at room temperature (20-22 °C) and recorded using Multiclamp™ 700A amplifier (Molecular Devices Inc.). Pipette resistances were typically 2-3 MΩ.

Protein toxin potency determination on Kv1.3 current: HEK293 cells stably expressing human Kv1.3 channel were voltage clamped at -80 mV holding potential. Outward $K_v1.3$ currents were activated by giving 200 msec long depolarizing steps to +30 mV from the holding potential of -80 mV and filtered at 3 kHz. Each depolarizing step was separated from the subsequent one with

a 10 s interval. Analogue signals were digitized by Digidata™ 1322A digitizer (Molecular Devices) and subsequently stored on computer disk for offline analyses using Clampfit™ 9 (Molecular Devices Inc.). In all studies, stable baseline $K_V1.3$ current amplitudes were established for 4 minutes before starting the perfusion of the protein toxin at incremental concentrations. A steady state block was always achieved before starting the perfusion of the subsequent concentration of the protein toxin.

Data analysis. Percent of control (POC) is calculated based on the following equation: ($K_V1.3$ current after protein toxin addition/$K_V1.3$ current in control)* 100. At least 5 concentrations of the protein toxin (e.g. 0.003, 0.01, 0.03, 0.1, 0.3, 100 nM) were used to calculate the IC_{50} value. IC_{50} values and curve fits were estimated using the four parameter logistic fit of XLfit software (Microsoft Corp.). IC_{50} values are presented as mean value ± s.e.m. (standard error of the mean).

Drug preparations. Protein toxins (typically 10 -100 µM) were dissolved in distilled water and kept frozen at ~80 °C. Serial dilutions of the stock protein toxins were mixed into the recording buffer containing 0.1% bovine serum albumin (BSA) and subsequently transferred to glass perfusion reservoirs. Electronic pinch valves controlled the flow of the protein toxin from the reservoirs onto the cell being recorded.

Example 37

Immunobiology and Channel Binding

Inhibition of T cell cytokine production following PMA and anti-CD3 antibody stimulation of PBMCs. PBMC's were previously isolated from normal human donor Leukophoresis packs, purified by density gradient centrifugation (Ficoll Hypaque), cryopreserved in CPZ Cryopreservation Medium Complete (INCELL, MCPZF-100 plus 10% DMSO final). PBMC's were thawed (95% viability), washed, and seeded at $2x10^5$ cells per well in culture medium (RPMI medium 1640; GIBCO) supplemented with 10% fetal calf serum, 100U/ml penicillin, 100mg/ml streptomycin 2mM L-glutamine, 100uM non-essential amino acids, and 20uM 2-ME) in 96-well flat-bottom tissue culture plates. Cells were pre-incubated with serially diluted (100nM-0.001nM final) ShK[1-35], Fc-L10-ShK[1-35] or fc control for 90 min before stimulating for 48hr with PMA/anti-CD3 (1ng/ml and 50ng/ml, respectively) in a final assay volume of 200 ul. Analysis of the assay samples was performed using the Meso Scale Discovery (MSD) SECTOR™ Imager 6000 (Meso Scale Discovery, Gaithersbury, MD) to measure the IL-2 and IFNg protein levels by utilizing electrochemiluminescence (ECL). The conditioned medium (50ul) was added to the MSD Multi-spot 96-well plates (each well containing three capture antibodies; IL-2, TNF, IFNγ). The plates

were sealed, wrapped in tin foil, and incubated at room temperature on a plate shaker for 2 hr. The wells were washed 1X with 200ul PBST (BIOTEK, Elx405 Auto Plate Washer). For each well, 20 ul of Ruthenium–labeled detection antibodies (1ug/ml final in Antibody Dilution Buffer; IL-1, TNF, IFNγ) and 130 ul of 2X MSD Read Buffer added, final volume 150ul. The plates were sealed, wrapped in tin foil, and incubated at room temperature on a plate shaker for 1 hr. The plates were then read on the SECTOR™ Imager 6000. Figure 35A & 35B shows the CHO-derived Fc-L10-ShK[1-35] peptibody potently inhibits IL-2 and IFNg production from T cells in a dose-dependent manner. Compared to native ShK[1-35] peptide, the peptibody produces a greater extent of inhibition (POC = Percent Of Control of response in the absence of inhibitor).

Inhibition of T cell cytokine production following anti-CD3 and anti-CD28 antibody stimulation of PBMCs. PBMCs were previously isolated from normal human donor Leukopheresis packs, purified by density gradient centrifugation (Ficoll Hypaque), and cryopreserved using INCELL Freezing Medium. PBMCs were thawed (95% viability), washed, and seeded (in RPMI complete medium containing serum replacement, PSG) at 2x105 cells per well into 96-well flat bottom plates. Cells were pre-incubated with serially diluted (100nM-0.003nM final) ShK[1-35], Fc-L10-ShK[1-35], or Fc control for 1 hour before the addition of aCD3 and aCD28 (2.5 ng/mL and 100 ng/mL respectively) in a final assay volume of 200 mL. Supernatants were collected after 48 hours, and analyzed using the Meso Scale Discovery (MSD) SECTOR™ Imager 6000 (Meso Scale Discovery, Gaithersbury, MD) to measure the IL-2 and IFNg protein levels by utilizing electrochemiluminescence (ECL). 20 mL of supernatant was added to the MSD multi-spot 96-well plates (each well containing IL-2, TNFa, and IFNg capture antibodies). The plates were sealed and incubated at room temperature on a plate shaker for 1 hour. Then 20 mL of Ruthenium–labeled detection antibodies (1ug/ml final of IL-2, TNFα, and IFNγ in Antibody Dilution Buffer) and 110 mL of 2X MSD Read Buffer were added. The plates were sealed, covered with tin foil, and incubated at room temperature on a plate shaker for 1 hour. The plates were then read on the SECTOR™ Imager 6000. Figure 37A & 37B shows the CHO-derived Fc-L10-ShK[1-35] peptibody potently inhibits IL-2 and IFNg production from T cells in a dose-dependent manner. Compared to native ShK[1-35] peptide which shows only partial inhibtion, the peptibody produces nearly complete inhibitiono of the inflammatory cytokine response. (POC = Percent Of Control of response in the absence of inhibitor).

Inhibition of T cell proliferation following anti-CD3 and anti-CD28 antibody stimulation of PBMCs. PBMC's were previously isolated from normal human donor Leukophoresis packs, purified by density gradient centrifugation (Ficoll Hypaque), cryopreserved in CPZ

Cryopreservation Medium Complete (INCELL, MCPZF-100 plus 10% DMSO final). PBMC's were thawed (95% viability), washed, and seeded at $2x10^5$ cells per well in culture medium (RPMI medium 1640; GIBCO) supplemented with 10% fetal calf serum, 100U/ml penicillin, 100mg/ml streptomycin, 2mM L-glutamine, 100 μM non-essential amino acids, and 20 μM 2-ME) in 96-well flat-bottom tissue culture plates. Cells were pre-incubated with either anti-human CD32 (FcγRII) blocking antibody (per manufacturers instructions EASY SEP Human Biotin Selection Kit #18553, StemCell Technologies Vancouver, BC) or Fc-L10-ShK (100nM-0.001nM final) for 45 min. Fc-L10-ShK (100nM-0.001nM final) was then added to the cells containing anti-human CD32 blocking antibody while medium was added to the cells containing Fc-L10-ShK. Both sets were incubated for an additional 45 min before stimulating for 48hr with aCD3/aCD28 (0.2 ng/ml and 100 ng/ml, respectively). Final assay volume was 200 ul. [3H]TdR (1uCi per well) was added and the plates were incubated for an additional 16 hrs. Cells were then harvested onto glass fiber filters and radioactivity was measured in a B-scintillation counter. Figure 36A & 36B shows the CHO-derived Fc-L10-ShK[1-35] peptibody potently inhibits proliferation of T cells in a dose-dependent manner. Pre-blocking with the anti-CD32 (FcR) blocking antibody has little effect on the peptibodies ability to inhibit T cell proliferation suggesting Kv1.3 inhibition and not FcR binding is the mechanism for the inhibition observed (POC = Percent Of Control of response in the absence of inhibitor).

Immunohistochemistry analysis of Fc-L10-ShK[1-35] binding to HEK 293 cells overexpressing human Kv1.3. HEK 293 cells overexpressing human Kv1.3 (HEK Kv1.3) were obtained from BioFocus plc (Cambridge, UK) and maintained per manufacturer's recommendation. The parental HEK 293 cell line was used as a control. Cells were plated on Poly-D-Lysine 24 well plates (#35-4414; Becton-Dickinson, Bedford, MA) and allowed to grow to approximately 70% confluence. HEK KV1.3 were plated at 0.5 x 10e5 cells/well in 1ml/well of medium. HEK 293 cells were plated at a density of 1.5 x 10e5 cells/well in 1ml/well of medium. Before staining, cells were fixed with formalin (Sigma HT50-1-1 Formalin solution, diluted 1:1 with PBS/0.5% BSA before use) by removing cell growth medium, adding 0.2ml/well formalin solution and incubating at room temperature for ten minutes. Cells were stained by incubating with 0.2ml/well of 5ug/ml Fc-L10-ShK[1-35] in PBS/BSA for 30' at room temperature. Fc-L10-ShK[1-35] was aspirated and then the cells were washed one time with PBS/0.5% BSA. Detection antibody (Goat F(ab)2 anti-human IgG-phycoerythrin; Southern Biotech Associates, Birmingham, AL) was added to the wells at 5ug/ml in PBS/0.5% BSA and incubated for 30' at room temperature. Wash cells once with PBS/0.5% BSA and examine using confocal microscopy (LSM 510 Meta Confocal Microscope; Carl Zeiss AG, Germany). Figure 33B shows the Fc-L10-ShK[1-35] peptibody retains binds to

Kv1.3 overexpressing HEK 293 cells but shows little binding to untransfected cells(Figure 33A) indicating the Fc-L10-ShK[1-35] peptibody can be used as a reagent to detect cells overexpressing the Kv1.3 channel. In disease settings where activated T effector memory cells have been reported to overproduce Kv1.3, this reagent can find utility in both targeting these cells and in their detection.

An ELISA assay demonstrating Fc-L10-ShK[1-35] binding to fixed HEK 293 cells overexpressing Kv1.3. Figure 34A shows a dose-dependent increase in the peptibody binding to fixed cells that overexpress Kv1.3, demonstrating that the peptibody shows high affinity binding to its target and the utility of the Fc-L10-ShK[1-35] molecule in detection of cells expressing the channel. Antigen specific T cells that cause disease in patients with multiple sclerosis have been shown to overexpress Kv1.3 by whole cell patch clamp electrophysiology, - a laborius approach. Our peptibody reagent can be a useful and convenient tool for monitoring Kv1.3 channel expression in patients and have utility in diagnostic applications. The procedure shown in Figure 34A and Figure 34B follows.

Figure 34A. A whole cell immunoassay was performed to show binding of intact Fc-L10-ShK[1-35] to Kv1.3 transfected HEK 293 cells (BioFocus plc, Cambridge, UK). Parent HEK 293 cells or HEK Kv1.3 cells were plated at 3 x 10e4 cells/well in poly-D-Lysine coated ninety-six well plates (#35-4461; Becton-Dickinson, Bedford, MA). Cells were fixed with formalin (Sigma HT50-1-1 Formalin solution, diluted 1:1 with PBS/0.5% BSA before use) by removing cell growth medium, adding 0.2ml/well formalin solution and incubating at room temperature for 25 minutes and then washing one time with 100 ul/well of PBS/0.5% BSA. Wells were blocked by addition of 0.3ml/well of BSA blocker (50-61-00; KPL 10% BSA Diluent/Blocking Solution, diluted 1:1 with PBS; KPL, Gaithersburg, MD) followed by incubation at room temperature, with shaking, for 3hr. Plates were washed 2 times with 1x KP Wash Buffer (50-63-00; KPL). Samples were diluted in Dilution Buffer (PBS/0.5% Tween-20) or Dilution Buffer with 1% Male Lewis Rat Serum (RATSRM-M; Bioreclamation Inc., Hicksville, NY) and 0.1ml/well was added to blocked plates, incubating for 1hr at room temperature with shaking. Plates were washed 3 times with 1xKP Wash Buffer and then incubated with HRP-Goat anti-human IgG Fc (#31416; Pierce, Rockford, IL) diluted 1:5000 in PBS/0.1% Tween-20 for 1hr at room temperature, with shaking. Plates were washed plates 3 times with 1xKP Wash Buffer, and then 0.1ml/well TMB substrate (52-00-01; KPL) was added. The reactions were stopped by addition of 0.1 ml/well 2 N Sulfuric Acid. Absorbance was read at 450nm on a Molecular Devices SpectroMax 340 (Sunnyvale, CA).

Figure 34B. Whole cell immunoassay was performed as above with the following modifications. HEK 293 cells were plated at 1 x 10e5 cells/well and HEK Kv1.3 cells were plated at 6 x 10e4 cells/well in poly-D-Lysine coated 96 well plates. Fc Control was added at 500ng/ml in a volume of 0.05ml/well. HRP-Goat anti-human IgG Fc (#31416; Pierce, Rockford, IL) was diluted 1:10,000 in PBS/0.1% Tween-20. ABTS (50-66-00, KPL) was used as the substrate. Absorbances were read at 405nm after stopping reactions by addition of 0.1ml/well of 1% SDS.

Example 38

Purification of Fc-L10-ShK(1-35)

Expression of Fc-L10-ShK[1-35] was as described in Example 3 herein above. Frozen, E. coli paste (18 g) was combined with 200 ml of room temperature 50 mM tris HCl, 5 mM EDTA, pH 8.0 and was brought to about 0.1 mg/ml hen egg white lysozyme. The suspended paste was passed through a chilled microfluidizer twice at 12,000 PSI. The cell lysate was then centrifuged at 22,000 g for 15 min at 4 °C. The pellet was then resuspended in 200 ml 1% deoxycholic acid using a tissue grinder and then centrifuged at 22,000 g for 15 min at 4 °C. The pellet was then resuspended in 200 ml water using a tissue grinder and then centrifuged at 22,000 g for 15 min at 4 °C. The pellet (3.2 g) was then dissolved in 32 ml 8 M guanidine HCl, 50 mM tris HCl, pH 8.0. The pellet solution was then centrifuged at 27,000 g for 15 min at room temperature, and then 5 ml of the supernatant was transferred to 500 ml of the refolding buffer (3 M urea, 20% glycerol, 50 mM tris, 160 mM arginine HCl, 5 mM EDTA, 1 mM cystamine HCl, 4 mM cysteine, pH 9.5) at 4 °C with vigorous stirring. The stirring rate was then slowed and the incubation was continued for 2 days at 4 °C. The refolding solution was then stored at -70 °C.

The stored refold was defrosted and then diluted with 2 L of water and the pH was adjusted to 7.3 using 1 M H_3PO_4. The pH adjusted material was then filtered through a 0.22 µm cellulose acetate filter and loaded on to a 60 ml Amersham SP-FF (2.6 cm I.D.) column at 20 ml/min in S-Buffer A (20 mM NaH2PO4, pH 7.3) at 7 °C. The column was then washed with several column volumes of S-Buffer A, followed by elution with a linear gradient from 0% to 60% S-Buffer B (20 mM NaH2PO4, 1 M NaCl, pH 7.3) followed by a step to 100% S-Buffer B at 10 ml/min 7 °C. Fractions were then analyzed using a Coomassie brilliant blue stained tris-glycine 4-20% SDS-PAGE, and the fractions containing the desired product were pooled based on these data. The pool was then loaded on to a 1 ml Amersham rProtein A HiTrap column in PBS at 1 ml/min 7 °C. Then column was then washed with several column volumes of 20 mM NaH_2PO_4 pH 6.5, 1 M NaCl and eluted with 100 mM glycine pH 3.0. To the elution peak, 0.0125 volumes (25 ml) of 3 M sodium acetate was added.

A spectral scan was then conducted on 50 µl of the combined pool diluted in 700 µl water using a Hewlett Packard 8453 spectrophotometer (Figure 46A). The concentration of the filtered material was determined to be 2.56 mg/ml using a calculated molecular mass of 30,410 g/mol and extinction coefficient of 36,900 M-1 cm-1. The purity of the filtered material was then assessed using a Coomassie brilliant blue stained tris-glycine 4-20% SDS-PAGE (Figure 46B). The macromolecular state of the product was then determined using size exclusion chromatography on 20 µg of the product injected on to a Phenomenex BioSep SEC 3000 column (7.8 x 300 mm) in 50 mM NaH_2PO_4, 250 mM NaCl, pH 6.9 at 1 ml/min observing the absorbance at 280 nm (Figure 46C). The product was then subject to mass spectral analysis by diluting 1 µl of the sample into 10 µl of sinapinic acid (10 mg per ml in 0.05% trifluroacetic acid, 50% acetonitrile) . One milliliter of the resultant solution was spotted onto a MALDI sample plate. The sample was allowed to dry before being analyzed using a Voyager DE-RP time-of-flight mass spectrometer equipped with a nitrogen laser (337 nm, 3 ns pulse). The positive ion/linear mode was used, with an accelerating voltage of 25 kV. Each spectrum was produced by accumulating data from ~ 200 laser shots. External mass calibration was accomplished using purified proteins of known molecular masses. The product was then stored at -80 °C.

The IC_{50} for blockade of human Kv1.3 by purified *E.coli*-derived Fc-L10-ShK[1-35], also referred to as "Fc-L-ShK[1-35]", is shown in Table 35 (in Example 50 herein below).

Example 39

Purification of bacterially expressed Fc-L10-ShK(2-35)

Expression of Fc-L10-ShK[2-35] was as described in Example 4 herein above. Frozen, E. coli paste (16.5 g) was combined with 200 ml of room temperature 50 mM tris HCl, 5 mM EDTA, pH 8.0 and was brought to about 0.1 mg/ml hen egg white lysozyme. The suspended paste was passed through a chilled microfluidizer twice at 12,000 PSI. The cell lysate was then centrifuged at 22,000 g for 15 min at 4 °C. The pellet was then resuspended in 200 ml 1% deoxycholic acid using a tissue grinder and then centrifuged at 22,000 g for 15 min at 4 °C. The pellet was then resuspended in 200 ml water using a tissue grinder and then centrifuged at 22,000 g for 15 min at 4 °C. The pellet (3.9 g) was then dissolved in 39 ml 8 M guanidine HCl, 50 mM tris HCl, pH 8.0. The pellet solution was then centrifuged at 27,000 g for 15 min at room temperature, and then 5 ml of the supernatant was transferred to 500 ml of the refolding buffer (3 M urea, 20% glycerol, 50 mM tris, 160 mM arginine HCl, 5 mM EDTA, 1 mM cystamine HCl, 4 mM cysteine, pH 9.5) at 4 °C with

vigorous stirring. The stirring rate was then slowed and the incubation was continued for 2 days at 4 °C. The refolding solution was then stored at -70 °C.

The stored refold was defrosted and then diluted with 2 L of water and the pH was adjusted to 7.3 using 1 M H_3PO_4. The pH adjusted material was then filtered through a 0.22 µm cellulose acetate filter and loaded on to a 60 ml Amersham SP-FF (2.6 cm I.D.) column at 20 ml/min in S-Buffer A (20 mM NaH_2PO_4, pH 7.3) at 7 °C. The column was then washed with several column volumes of S-Buffer A, followed by elution with a linear gradient from 0% to 60% S-Buffer B (20 mM NaH2PO4, 1 M NaCl, pH 7.3) followed by a step to 100% S-Buffer B at 10 ml/min 7 °C. The fractions containing the desired product were pooled and filtered through a 0.22 µm cellulose acetate filter. The pool was then loaded on to a 1 ml Amersham rProtein A HiTrap column in PBS at 2 ml/min 7 °C. Then column was then washed with several column volumes of 20 mM NaH_2PO_4 pH 6.5, 1 M NaCl and eluted with 100 mM glycine pH 3.0. To the elution peak, 0.0125 volumes (18 ml) of 3 M sodium acetate was added, and the sample was filtered through a 0.22 µm cellulose acetate filter.

A spectral scan was then conducted on 20 µl of the combined pool diluted in 700 µl water using a Hewlett Packard 8453 spectrophotometer (Figure 40A). The concentration of the filtered material was determined to be 3.20 mg/ml using a calculated molecular mass of 29,282 g/mol and extinction coefficient of 36,900 M^{-1} cm^{-1}. The purity of the filtered material was then assessed using a Coomassie brilliant blue stained tris-glycine 4-20% SDS-PAGE (Figure 40B). The macromolecular state of the product was then determined using size exclusion chromatography on 50 µg of the product injected on to a Phenomenex BioSep SEC 3000 column (7.8 x 300 mm) in 50 mM NaH_2PO_4, 250 mM NaCl, pH 6.9 at 1 ml/min observing the absorbance at 280 nm (Figure 40C). The product was then subject to mass spectral analysis by diluting 1 µl of the sample into 10 µl of sinapinic acid (10 mg per ml in 0.05% trifluroacetic acid, 50% acetonitrile) . One milliliter of the resultant solution was spotted onto a MALDI sample plate. The sample was allowed to dry before being analyzed using a Voyager DE-RP time-of-flight mass spectrometer equipped with a nitrogen laser (337 nm, 3 ns pulse). The positive ion/linear mode was used, with an accelerating voltage of 25 kV. Each spectrum was produced by accumulating data from ~ 200 laser shots. External mass calibration was accomplished using purified proteins of known molecular masses (Figure 40D). The product was then stored at –80 °C.

The IC_{50} for blockade of human Kv1.3 by purified *E.coli*-derived Fc-L10-ShK[2-35], also referred to as "Fc-L-ShK[2-35]", is shown in Table 35 (in Example 50 herein below).

Example 40

Purification of bacterially expressed Fc-L10-OsK1

Frozen, *E. coli* paste (129 g; see Example 10) was combined with 1290 ml of room temperature 50 mM tris HCl, 5 mM EDTA, pH 7.8 and was brought to about 0.1 mg/ml hen egg white lysozyme. The suspended paste was passed through a chilled microfluidizer twice at 12,000 PSI. The cell lysate was then centrifuged at 17,700 g for 15 min at 4°C. The pellet was then resuspended in 1290 ml 1% deoxycholic acid using a tissue grinder and then centrifuged at 17,700 g for 15 min at 4°C. The pellet was then resuspended in 1290 ml water using a tissue grinder and then centrifuged at 17,700 g for 15 min at 4 °C. 8 g of the pellet (16.3 g total) was then dissolved in 160 ml 8 M guanidine HCl, 50 mM tris HCl, pH 8.0. 100 ml of the pellet solution was then incubated with 1 ml of 1 M DTT for 60 min at 37 °C. The reduced material was transferred to 5000 ml of the refolding buffer (1 M urea, 50 mM tris, 160 mM arginine HCl, 2.5 mM EDTA, 1.2 mM cystamine HCl, 4 mM cysteine, pH 10.5) at 2 ml/min , 4°C with vigorous stirring. The stirring rate was then slowed and the incubation was continued for 3 days at 4°C.

The pH of the refold was adjusted to 8.0 using acetic acid. The pH adjusted material was then filtered through a 0.22 μm cellulose acetate filter and loaded on to a 50 ml Amersham Q Sepharose-FF (2.6 cm I.D.) column at 10 ml/min in Q-Buffer A (20 mM Tris, pH 8.5) at 8 °C with an inline 50 Amersham Protein A column (2.6 cm I.D.). After loading, the Q Sepharose column was removed from the circuit, and the remaining chromatography was carried out on the protein A column. The column was washed with several column volumes of Q-Buffer A, followed by elution using a step to 100 mM glycine pH 3.0. The fractions containing the desired product were pooled and immediately loaded on to a 50 ml Amersham SP-Sepharose HP column (2.6 cm I.D.) at 20 ml/min in S-Buffer A (20 mM NaH_2PO_4, pH 7.0) at 8 °C. The column was then washed with several column volumes of S-Buffer A followed by a linear gradient from 5% to 60% S-Buffer B (20 mM NaH_2PO_4, 1 M NaCl, pH 7.0) followed by a step to 100% S-Buffer B. Fractions were then analyzed using a Coomassie brilliant blue stained tris-glycine 4-20% SDS-PAGE. The fractions containing the bulk of the desired product were pooled and then applied to a 75 ml MEP Hypercel column (2.6 cm I.D.) at 5 ml/min in MEP Buffer A (20 mM tris, 200 mM NaCl, pH 8.0) at 8 °C. Column was eluted with a linear gradient from 5% to 50% MEP Buffer B(50 mM sodium citrate pH 4.0) followed by a step to 100% MEP Buffer B. Fractions were then analyzed using a Coomassie brilliant blue stained tris-glycine 4-20% SDS-PAGE, and the fractions containing the bulk of the desired product were pooled.

The MEP pool was then concentrated to about 20 ml using a Pall Jumbo-Sep with a 10 kDa membrane followed by buffer exchange with Formulation Buffer (20 mM NaH_2PO_4, 200 mM NaCl, pH 7.0) using the same membrane. A spectral scan was then conducted on 50 µl of the combined pool diluted in 700 µl Formulation Buffer using a Hewlett Packard 8453 spectrophotometer (Figure 41A). The concentration of the material was determined to be 4.12 mg/ml using a calculated molecular mass of 30,558 g/mol and extinction coefficient of 35,720 M^{-1} cm^{-1}. The purity of the material was then assessed using a Coomassie brilliant blue stained tris-glycine 4-20% SDS-PAGE (Figure 41B). The macromolecular state of the product was then determined using size exclusion chromatography on 123 µg of the product injected on to a Phenomenex BioSep SEC 3000 column (7.8 x 300 mm) in 50 mM NaH_2PO_4, 250 mM NaCl, pH 6.9 at 1 ml/min observing the absorbance at 280 nm (Figure 41C). The product was then subject to mass spectral analysis by chromatographing approximately 4 µg of the sample through a RP-HPLC column (Vydac C_4, 1 x 150 mm). Solvent A was 0.1 % trifluoroacetic acid in water and solvent B was 0.1 % trifluoroacetic acid in 90 % acetonitrile, 10 % water. The column was pre-equilibrated in 10 % solvent B at a flow rate of 80 µl per min. The protein was eluted using a linear gradient of 10 % to 90% solvent B over 30 min. Part of the effluent was directed into a LCQ ion trap mass spectrometer. The mass spectrum was deconvoluted using the Bioworks software provided by the mass spectrometer manufacturer. (Figure 41D). The product was filtered through a 0.22 µm cellulose acetate filter and then stored at –80 °C.

The yield for the E. coli –expressed Fc-L10-OSK1 prep was 81 mg from 40 g of cell paste (129 g x (8g / 16.3g) x (100 ml / 160 ml) = 39.6 g which was rounded to 40 g), the purity was greater than 80% judging by SDS-PAGE, it is running as the expected dimer judging by SEC-HPLC, and the mass was within the expected molecular weight range judging by MS.

The IC_{50} for blockade of human Kv1.3 by purified *E.coli*-derived Fc-L10-OSK1, also referred to as "Fc-L-OSK1", is shown in Table 35 (in Example 50 herein below).

Example 41

Fc-L10-OSK1, Fc-L10-OSK1[K7S], Fc-L10-OSK1[E16K,K20D], and Fc-L10-OSK1 [K7S,E16K,K20D] expressed by mammalian cells

Fc-L10-OSK1, Fc-L10-OSK1[K7S], Fc-L10-OSK1[E16K,K20D], and Fc-L10-OSK1 [K7S,E16K,K20D], inhibitors of Kv1.3, were expressed in mammalian cells. A DNA sequence coding for the Fc region of human IgG1 fused in-frame to a linker sequence and a monomer of the Kv1.3 inhibitor peptide OSK1, OSK1[K7S], OSK1[E16K,K20D], or OSK1[K7S,E16K,K20D] was

constructed as described below. Methods for expressing and purifying the peptibody from mammalian cells (HEK 293 and Chinese Hamster Ovary cells) are disclosed herein.

For construction of Fc-L10-OSK1, Fc-L10-OSK1[K7S], Fc-L10-OSK1[E16K,K20D], and Fc-L10-OSK1[K7S,E16K,K20D] expression vectors, a PCR strategy was employed to generate the full length genes, OSK1, OSK1[K7S], OSK1[E16K,K20D], and OSK1[K7S,E16K,K20D], each linked to a four glycine and one serine amino acid linker with two stop codons and flanked by BamHI and NotI restriction sites as shown below.

Two oligos for each of OSK1, OSK1[K7S], OSK1[E16K,K20D], and [K7S,E16K,K20D]OSK1 with the sequence as depicted below were used in a PCR reaction with PfuTurbo HotStart DNA polymerase (Stratagene) at 95°C-30sec, 55°C-30sec, 75°C-45sec for 35 cycles; BamHI (ggatcc) and NotI (gcggccgc) restriction sites are underlined.

OSK1:

Forward primer: cat gga tcc gga gga gga gga agc ggc gtg atc atc aac gtg aag tgc aag atc agc cgc cag tgc ctg gag ccc tgc aag aag gcc g (SEQ ID NO: 876);

Reverse primer: cat gcg gcc gct tac tac ttg ggg gtg cag tgg cac ttg ccg ttc atg cac ttg ccg aag cgc atg ccg gcc ttc ttg cag ggc tcc a (SEQ ID NO:877);

OSK1[K7S]:

Forward primer: cat gga tcc gga gga gga gga agc ggc gtg atc atc aac gtg agc tgc aag atc agc cgc cag tgc ctg gag ccc tgc aag aag gcc g (SEQ ID NO:878);

Reverse primer: cat gcg gcc gct tac tac ttg ggg gtg cag tgg cac ttg ccg ttc atg cac ttg ccg aag cgc atg ccg gcc ttc ttg cag ggc tcc a (SEQ ID NO:879);

OSK1[E16K,K20D]:

Forward primer: cat gga tcc gga gga gga gga agc ggc gtg atc atc aac gtg aag tgc aag atc agc cgc cag tgc ctg aag ccc tgc aag gac gcc g (SEQ ID NO:880);

Reverse primer: cat gcg gcc gct tac tac ttg ggg gtg cag tgg cac ttg ccg ttc atg cac ttg ccg aag cgc atg ccg gcg tcc ttg cag ggc ttc a (SEQ ID NO:881);

OSK1[K7S,E16K,K20D]:

Forward primer: cat gga tcc gga gga gga gga agc ggc gtg atc atc aac gtg agc tgc aag atc agc cgc cag tgc ctg aag ccc tgc aag gac gcc g (SEQ ID NO:882);

Reverse primer: cat gcg gcc gct tac tac ttg ggg gtg cag tgg cac ttg ccg ttc atg cac ttg ccg aag cgc atg ccg gcg tcc ttg cag ggc ttc a (SEQ ID NO:883).

The resulting PCR products were resolved as the 155bp bands on a four percent agarose gel. The 155bp PCR product was purified using PCR Purification Kit (Qiagen), then digested with BamHI and NotI (Roche) restriction enzymes, and agarose gel was purified by Gel Extraction Kit (Qiagen). At the same time, the pcDNA3.1(+)CMVi-hFc-Shk[2-35] vector was digested with BamHI and NotI restriction enzymes and the large fragment was purified by Gel Extraction Kit. The gel purified PCR fragment was ligated to the purified large fragment and transformed into One Shot® Top10F' (Invitrogen). DNAs from transformed bacterial colonies were isolated and digested with BamHI and NotI restriction enzymes and resolved on a two percent agarose gel. DNAs resulting in an expected pattern were submitted for sequencing. Although, analysis of several sequences of clones yielded a 100% percent match with the above sequences, only one clone from each gene was selected for large scaled plasmid purification. The DNA of Fc-L10-OSK1, Fc-L10-OSK1[K7S], Fc-L10-OSK1[E16K,K20D], and Fc-L10-OSK1[K7S,E16K,K20D] in pCMVi vector was resequenced to confirm the Fc and linker regions and the sequence was 100% identical to the above sequences. The sequences and pictorial representations of Fc-L10-OSK1, Fc-L10-OSK1[K7S], Fc-L10-OSK1[E16K,K20D], and Fc-L10-OSK1[K7S,E16K,K20D] are depicted in Figure 42A-B, Figure 43A-B, Figure 44A-B and Figure 45A-B, respectively.

HEK-293 cells used in transient transfection expression of Fc-L10-OSK1, Fc-L10-OSK1[K7S], Fc-L10-OSK1[E16K,K20D], and Fc-L10-OSK1[K7S,E16K,K20D] in pCMVi protein were cultured in growth medium containing DMEM High Glucose (Gibco), 10% fetal bovine serum (FBS from Gibco), 1X non-essential amino acid (NEAA from Gibco)and 1X Penicillin/Streptomycine/Glutamine (Pen/Strep/Glu from Gibco). 5.6 μg each of Fc-L10-OSK1, Fc-L10-OSK1[K7S], Fc-L10-OSK1[E16K,K20D], and Fc-L10-OSK1[K7S,E16K,K20D] in pCMVi plasmid that had been phenol/chloroform extracted was transfected into HEK-293 cells using FuGENE 6 (Roche). The cells were recovered for 24 hours, and then placed in DMEM High Glucose, 1x NEAA and 1X Pen/Strep/Glu medium for 48 hours. Fc-L10-OSK1[K7S], Fc-L10-OSK1[E16K,K20D], and Fc-L10-OSK1[K7S,E16K,K20D] were purified from medium

conditioned by these transfected HEK-293 cells using a protocol described in Example 50 herein below.

Fifteen µl of conditioned medium was mixed with an in-house 4x Loading Buffer (without β-mercaptoethanol) and electrophoresed on a Novex 4-20% tris-glycine gel using a Novex Xcell II apparatus at 101V/46mA for 2 hours in a 1x Gel Running solution (25mM Tris Base, 192mM Glycine, 3.5mM SDS) along with 20µl of BenchMark Pre-Stained Protein ladder (Invitrogen). The gel was then soaked in Electroblot buffer (25mM Tris base, 192mM glycine, 20%methanol,) for 5 minutes. A nitrocellulose membrane from Invitrogen (Cat. No. LC200, 0.2 µm pores size) was soaked in Electroblot buffer. The pre-soaked gel was blotted to the nitrocellulose membrane using the Mini Trans-Blot Cell module according to the manufacturer instructions (Bio-Rad Laboratories) at 300mA for 2 hours. The blot was rinsed in Tris buffered saline solution pH7.5 with 0.1% Tween20 (TBST). Then, the blot was first soaked in a 5% milk (Carnation) in TBST for 1 hour at room temperature, followed by washing three times in TBST for 10 minutes per wash. Then, incubated with 1:1000 dilution of the HRP-conjugated Goat anti-human IgG, (Fcγ) antibody (Pierece Biotechnology Cat. no. 31413) in TBST with 5% milk buffer for 1 hour with shaking at room temperature. The blot was then washed three times in TBST for 15 minutes per wash at room temperature. The primary antibody was detected using Amersham Pharmacia Biotech's ECL western blotting detection reagents according to manufacturer's instructions. Upon ECL detection, the western blot analysis displayed the expected size of 66kDa under non-reducing gel conditions (Figure 46).

Plasmids containing the Fc-L10-OSK1, Fc-L10-OSK1[K7S], Fc-L10-OSK1[E16K,K20D], and Fc-L10-OSK1[K7S,E16K,K20D] inserts in pCMVi vector were digested with XbaI and NotI (Roche) restriction enzymes and gel purified. The inserts were individually ligated into SpeI and NotI (Roche) digested pDSRα24 (Amgen Proprietary) expression vector. Integrity of the resulting constructs were confirmed by DNA sequencing. Although, analysis of several sequences of clones yielded a 100% percent match with the above sequence, only one clone was selected for large scaled plasmid purification.

AM1 CHOd- (Amgen Proprietary) cells used in the stable expression of Fc-L10-OSK1 protein were cultured in AM1 CHOd- growth medium containing DMEM High Glucose, 10% fetal bovine serum, 1x hypoxantine/thymidine (HT from Gibco), 1X NEAA and 1X Pen/Strep/Glu. 5.6 µg of pDSRα-24-Fc-L10-OSK1 plasmid was transfected into AM1 CHOd- cells using FuGene 6. Twenty-four hours post transfection, the cells were split 1:11 into DHFR selection medium (DMEM High Glucose plus 10% Dialyzed Fetal Bovine Serum (dFBS), 1x NEAA and 1X Pen/Strep/Glu)

and at 1:50 dilution for colony selection. The cells were selected in DHFR selection medium for thirteen days. The ten 10-cm^2 pools of the resulting colonies were expanded to ten T-175 flasks, then were scaled up ten roller bottles and cultured under AM1 CHOd- production medium (DMEM/F12 (1:1), 1X NEAA, 1X Sodium Pyruvate (Na Pyruvate), 1X Pen/Strep/Glu and 1.5% DMSO). The conditioned medium was harvested and replaced at one-week intervals. The resulting six liters of conditioned medium were filtered through a 0.45 μm cellulose acetate filter (Corning, Acton, MA), and characterized by SDS-PAGE analysis as shown in Figure 47. Then, transferred to Protein Chemistry for purification.

Twelve colonies were selected after 13 days on DHFR selection medium and picked into one 24-well plate. The plate was allowed to grow up for one week, and then was transferred to AM1 CHOd- production medium for 48-72 hours and the conditioned medium was harvested. The expression levels were evaluated by Western blotting similar to the transient Western blot analysis with detection by the same HRP-conjugated Goat anti-human IgG, (Fcγ) antibody to screen 5μl of conditioned medium. All 12 stable clones exhibited expression at the expected size of 66 kDa. Two clones, A3 and C2 were selected and expanded to T175 flask for freezing with A3 as a backup to the primary clone C2 (Figure 48).

The C2 clone was scaled up into fifty roller bottles (Corning) using selection medium and grown to confluency. Then, the medium was exchanged with a production medium, and let incubate for one week. The conditioned medium was harvested and replaced at the one-week interval. The resulting fifty liters of conditioned medium were filtered through a 0.45 μm cellulose acetate filter (Corning, Acton, MA), and characterized by SDS-PAGE analysis (data not shown). Further purification was accomplished as described in Example 42 herein below.

Example 42

Purification of Fc-L10-OSK1, Fc-L10-OSK1(K7S), Fc-L10-OSK1(E16K,K20D), and Fc-L10-OSK1(K7S,E16K,K20D) expressed by mammalian cells

Purification of Fc-L10-OSK1. Approximately 6 L of CHO (AM1 CHOd-) cell-conditioned medium (see, Example 41 above) was loaded on to a 35 ml MAb Select column (GE Healthcare) at 10 ml/min 7°C, and the column was washed with several column volumes of Dulbecco's phosphate buffered saline without divalent cations (PBS) and sample was eluted with a step to 100 mM glycine pH 3.0. The MAb Select elution was directly loaded on to an inline 65 ml SP-HP column (GE Healthcare) in S-Buffer A (20 mM NaH_2PO_4, pH 7.0) at 10 ml/min 7°C. After disconnecting the MAb select column, the SP-HP column was then washed with several column

volumes S-Buffer A, and then developed using a linear gradient from 5% to 60% S-Buffer B (20 mM NaH_2PO_4, 1 M NaCl, pH 7.0) at 10 ml/min followed by a step to 100% S-Buffer B at 7 °C. Fractions were then analyzed using a Coomassie brilliant blue stained tris-glycine 4-20% SDS-PAGE, and the fractions containing the desired product were pooled based on these data. The pooled material was then concentrated to about 20 ml using a Pall Life Sciences Jumbosep 10K Omega centrifugal ultra-filtration device. The concentrated material was then buffer exchanged by diluting with 20 ml of 20 mM NaH_2PO_4, pH 7.0 and reconcentrated to 20 ml using the Jumbosep 10K Omega filter. The material was then diluted with 20 ml 20 mM NaH_2PO_4, 200 mM NaCl, pH 7.0 and then reconcentrated to 22 ml. The buffer exchanged material was then filtered though a Pall Life Sciences Acrodisc with a 0.22 µm, 25 mm Mustang E membrane at 1 ml/min room temperature. A spectral scan was then conducted on 50 µl of the filtered material diluted in 700 µl PBS using a Hewlett Packard 8453 spectrophotometer (Figure 49A, black trace). The concentration of the filtered material was determined to be 4.96 mg/ml using a calculated molecular mass of 30,371 g/mol and extinction coefficient of 35,410 M^{-1} cm^{-1}. The purity of the filtered material was then assessed using a Coomassie brilliant blue stained tris-glycine 4-20% SDS-PAGE (Figure 49B). The endotoxin level was then determined using a Charles River Laboratories Endosafe-PTS system (0.05 – 5 EU/ml sensitivity) using a 30-fold dilution of the sample in Charles Rivers Laboratories Endotoxin Specific Buffer yielding a result of 1.8 EU/mg protein. The macromolecular state of the product was then determined using size exclusion chromatography on 149 µg of the product injected on to a Phenomenex BioSep SEC 3000 column (7.8 x 300 mm) in 50 mM NaH_2PO_4, 250 mM NaCl, pH 6.9 at 1 ml/min observing the absorbance at 280 nm (Figure 49C). The product was then subject to mass spectral analysis by diluting 1 µl of the sample into 10 µl of sinapinic acid (10 mg per ml in 0.05% trifluroacetic acid, 50% acetonitrile) . One milliliter of the resultant solution was spotted onto a MALDI sample plate. The sample was allowed to dry before being analyzed using a Voyager DE-RP time-of-flight mass spectrometer equipped with a nitrogen laser (337 nm, 3 ns pulse). The positive ion/linear mode was used, with an accelerating voltage of 25 kV. Each spectrum was produced by accumulating data from about 200 laser shots. External mass calibration was accomplished using purified proteins of known molecular masses. (Figure 49D). The product was then stored at –80°C.

The yield for the mammalian Fc-L10-OSK1 prep was 115 mg from 6 L, the purity was >90% judging by SDS-PAGE; Fc-L10-OSK1 ran as the expected dimer judging by SEC-HPLC, and the mass is with the expected range judging by MS.

The activity of purified Fc-L10-OSK1 in blocking human Kv1.3 and human Kv1.1 is described in Example 43 herein below.

Purification of Fc-L10-OSK1(K7S), Fc-L10-OSK1(E16K,K20D), and Fc-L10-OSK1(K7S,E16K,K20D). Approximately 500 mL of medium conditioned by transfected HEK-293 (see, Example 41 above) was combined with a 65 % slurry of MAb Select resin (1.5 ml) (GE Healthcare) and 500 µl 20% NaN_3. The slurry was then gently agitated for 3 days at 4 °C followed by centrifugation at 1000 g for 5 minutes at 4 °C using no brake. The majority of the supernatant was then aspirated and the remaining slurry in the pellet was transferred to a 14 ml conical tube and combined with 12 ml of Dulbecco's phosphate buffered saline without divalent cations (PBS). The slurry was centrifuged at 2000 g for 1 minute at 4 °C using a low brake and the supernatant was aspirated. The PBS wash cycle was repeated an additional 3 times. The bound protein was then eluted by adding 1 ml of 100 mM glycine pH 3.0 and gently agitating for 5 min at room temperature. The slurry was then centrifuged at 2000 g for 1 minute at 4 °C using a low brake and the supernatant was aspirated as the first elution. The elution cycle was repeated 2 more times, and all 3 supernatants were combined into a single pool. Sodium acetate (37.5 µl of a 3 M solution) was added to the elution pool to raise the pH, which was then dialyzed against 10 mM acetic acid, 5% sorbitol, pH 5.0 for 2 hours at room temperature using a 10 kDa SlideAlyzer (Pierce). The dialysis buffer was changed, and the dialysis continued over night at 4°C. The dialyzed material was then filtered through a 0.22 µm cellulose acetate filter syringe filter. Then concentration of the filtered material was determined to be 1.27 mg/ml using a calculated molecular mass of 30,330 and extinction coefficient of 35,410 M^{-1} cm^{-1} (Figure 50A). The purity of the filtered material was then assessed using a Coomassie brilliant blue stained tris-glycine 4-20% SDS-PAGE (Figure 50B). The endotoxin level was then determined using a Charles River Laboratories Endosafe-PTS system (0.05 – 5 EU/ml sensitivity) using a 25-fold dilution of the sample in Charles Rivers Laboratories Endotoxin Specific Buffer yielding a result of <1 EU/mg protein. The macromolecular state of the product was then determined using size exclusion chromatography on 50 µg of the product injected on to a Phenomenex BioSep SEC 3000 column (7.8 x 300 mm) in 50 mM NaH_2PO_4, 250 mM NaCl, pH 6.9 at 1 ml/min observing the absorbance at 280 nm (Figure 50C). The product was then subject to mass spectral analysis by diluting 1 µl of the sample into 10 µl of sinapinic acid (10 mg per ml in 0.05% trifluroacetic acid, 50% acetonitrile). One milliter of the resultant solution was spotted onto a MALDI sample plate. The sample was allowed to dry before being analyzed using a Voyager DE-RP time-of-flight mass spectrometer equipped with a nitrogen laser (337 nm, 3 ns pulse). The positive ion/linear mode was used, with

an accelerating voltage of 25 kV. Each spectrum was produced by accumulating data from ~ 200 laser shots. External mass calibration was accomplished using purified proteins of known molecular masses. (Figure 50D). The product was then stored at –80 °C.

Figures 51A-D show results from the purification and analysis for Fc-L10-OsK1(E16K, K20D), which was conducted using the same protocol as that for the Fc-L10-OsK1(K7S) molecule (described above) with the following exceptions: the concentration was found to be 1.59 mg/ml using a calculated molecular mass of 30,357 g/mol and a calculated extinction coefficient of 35,410; the pyrogen level was found to be < 1 EU/mg using a 32-fold dilution.

Figures 52A-D show results from the purification and analysis for Fc-L10-OsK1(K7S,E16K, K20D), which was conducted using the same protocol as that for the Fc-L10-OsK1(K7S) molecule (described above) with the following exceptions: the concentration was found to be 0.81 mg/ml using a calculated molecular mass of 30,316 g/mol and a calculated extinction coefficient of 35,410; the pyrogen level was found to be < 1 EU/mg using a 16-fold dilution.

The activity of purified Fc-L10-OSK1[K7S], Fc-L10-OSK1[E16K, K20D] and Fc-L10-OSK1[K7S, E16K, K20D] in blocking human Kv1.3 and human Kv1.1 is described in Example 43 herein below.

Example 43

Electrophysiology of OSK1 and OSK1 peptibody analogs

A 38-residue peptide toxin of the Asian scorpion Orthochirus scrobiculosus venom (OSK1) was synthesized (see, Examples 41) to evaluate its impact on the human Kv1.1 and Kv1.3 channels, subtypes of the potassium channel family. The potency and selectivity of synthetic OSK1 in inhibiting the human Kv1.1 and Kv1.3 channels was evaluated by the use of HEK293 cell expression system and electrophysiology (Figure 53). Whole cell patch clamp recording of stably expressed Kv1.3 channels revealed that the synthetic OSK1 peptide is more potent in inhibiting human Kv1.3 when compared to Kv1.1 (Table 33).

Fusion of OSK1 peptide toxin to antibody to generate OSK1 peptibody. To improve plasma half-life and prevent OSK1 peptide toxin from penetrating the CNS, the OSK1 peptide toxin was fused to the Fc-fragment of a human antibody IgG1 via a linker chain length of 10 amino acid residues (Fc-L10-OSK1), as described in Example 41 herein. This fusion resulted in a decrease in the potency of Kv1.3 by 5-fold when compared to the synthetic OSK1 peptide. However, it

significantly improved the selectivity of OSK1 against Kv1.1 by 210-fold when compared to that of the synthetic peptide alone (4-fold; Table 33 and Figure 54).

Modification of OSK1-peptibody (Fc-L10-OSK1). OSK1 shares 60 to 80% sequence homology to other members of scorpion toxins, which are collectively termed α-KTx3. Sequence alignment of OSK1 and other members of α-KTx3 family revealed 4 distinct structural differences at positions 12, 16, 20, and 36. These structural differences of OSK1 have been postulated to play an important role in its wide range of activities against other potassium channels, which is not observed with other members of α-KTx3 family. Hence, two amino acid residues at position 16 and 20 were restored to the more conserved amino acid residues within the OSK1 sequence in order to evaluate their impact on selectivity against other potassium channels such as Kv1.1, which is predominantly found in the CNS as a heterotetromer with Kv1.2. By substituting for glutamic acid at position 16, and for lysine at position 20, the conserved lysine and aspartic acid residues, respectively (i.e., Fc-L10-OSK1[E16K, K20D]), we did not observe a significant change in potency when compared to that of Fc-L10-OSK1 (1.3-fold difference; Figure 56 and Table 33). However, this double mutation removed the blocking activity against Kv1.1. The selectivity ratio of Kv1.1/Kv1.3 was 403-fold, which was a significant improvement over the selectivity ratio for Fc-L10-OSK1 (210-fold). A single amino acid mutation at position 7 from lysine to serine (Fc-L10-OSK1[K7S]) produced a slight change in potency and selectivity by 2- and 1.3-fold, respectively, when compared to those of Fc-L10-OSK1 (Figure 55 and Table 33). There was a significant decrease in potency as well as selectivity when all three residues were mutated to generate Fc-L10-OSK1[K7S, E16K, K20D] (Figure 57 and Table 33).

As demonstrated by the results in Table 33, we dramatically improved selectivity against Kv1.1 by fusing the OSK1 peptide toxin to the Fc-fragment of the human antibody IgG1, but reduced target potency against Kv1.3. The selectivity against Kv1.1 was further improved when 2 residues at two key positions were restored to the conserved residues found in other members of the α-KTx3 family.

Table 33 shows a summary of IC50 values for OSK1 and OSK1 analogues against hKv1.3 and hKv1.1 channels. All analogues are ranked based on their potency against hKv1.3. Also shown in the table is the selectivity ratio of hKv1.1/hKv1.3 for all OSK1 analogues.

Compound	hKv1.3: IC_{50} [pM]	hKv1.1: IC_{50} [pM]	hKv1.1/hKv1.3
Synthetic OSK1	39	160	4
Fc-L10-OSK1	198	41600	210
Fc-L10-OSK1[E16K,K20D]	248	100000	403
Fc-L10-OSK1[K7S]	372	100000	269
Fc-L10-OSK1[K7S, E16K, K20D]	812	10000	12

Example 44

Pharmacokinetic Study of PEG-ShK[1-35] molecule in Rats

The intravenous (IV) pharmacokinetic profile was determined of a about 24-kDa 20K PEG-ShK[1-35] molecule and the about 4-kDa small native ShK peptide was determined in Spraque Dawley rats. The IV dose for the native ShK peptide and our novel 20K PEG-ShK[1-35] molecule was 1 mg/kg. This dose represented equal molar amounts of these two molecules. The average weight of the rats was about 0.3 kg and two rats were used for each dose & molecule. At various times following IV injection, blood was drawn and about 0.1 ml of serum was collected. Serum samples were stored frozen at –80°C until analysis.

Assay Plate preparation for electrophysiology. Rat serum samples containing the 20K PEG-ShK[1-35] molecule or the native ShK peptide from pharmacokinetic studies were received frozen. Before experiments, each sample was thawed at room temperature and an aliquot (70 to 80 µl) was transferred to a well in a 96-well polypropylene plate. In order to prepare the Assay Plate, several dilutions were made from the pharmacokinetic serum samples to give rise to Test Solutions. Dilutions of serum samples from the pharmacokinetic study were into 10% Phosphate Buffered Saline (PBS, with Ca^{2+} and Mg^{2+}). For determination of the amount of our novel 20K PEG-ShK[1-35] molecule in serum samples from the pharmacokinetic study, the final serum concentrations in the Test Solutions were 90%, 30%, 10%, 3.3% and 1.1%. Purified 20K PEG-Shk[1-35] Standard inhibition curves were also prepared in the Assay Plate. To do this, 8-point serial dilutions of the purified 20K PEG-ShK[1-35] molecule (Standard) were prepared in either 90%, 30%, 10%, 3.3% or 1.1% rat serum and the final concentration of standard was 50, 16.7, 5.5, 1.85, 0.62, 0.21, 0.068 and 0.023 nM.

Cell preparation for electrophysiology. CHO cells stably expressing the voltage-activated K^+ channel, $K_V1.3$ were plated in T-175 tissue culture flasks (at a density of $5x10^6$) 2 days before experimentation and allowed to grow to around 95% confluence. Immediately prior to the

experiment, the cells were washed with PBS and then detached with a 2 ml mixture (1:1 volume ratio) of trypsin (0.25%) and versene (1:5000) at 37°C (for 3 minutes). Subsequently, the cells were re-suspended in the flask in 10 ml of tissue culture medium (HAM's F-12 with Glutamax, InVitrogen, Cat#31765) with 10% FBS, 1x NEAA and 750 µg/ml of G418) and centrifuged at about 1000 rpm for 1½ minutes. The resultant cell pellet was re-suspended in PBS at 3-5x10^6cells/ ml. IonWorks electrophysiology and data analysis. The ability of Test solutions or Standards in serum to inhibit K^+ currents in the CHO-K_V1.3 cells was investigated using the automated electrophysiology system, IonWorks Quattro. Re-suspended cells, the Assay Plate, a Population Patch Clamp (PPC) PatchPlate as well as appropriate intracellular (90mMK-Gluconate, 20mMKF, 2 mM NaCl, 1mM MgCl2, 10mM EGTA, 10mM HEPES, pH 7.35) and extracellular (PBS, with Ca^{2+} and Mg^{2+}) buffers were positioned on IonWorks Quattro. Electrophysiology recordings were made from the CHO-K_V1.3 cells using an amphotericin-based perforated patch-clamp method. Using the voltage-clamp circuitry of the IonWorks Quattro, cells were held at a membrane potential of –80 mV and voltage-activated K^+ currents were evoked by stepping the membrane potential to +30 mV for 400 ms. K^+ currents were evoked under control conditions i.e., in the absence of inhibitor at the beginning of the experiment and after 10-minute incubation in the presence of the Test Solution or Standard. The mean K^+ current amplitude was measured between 430 and 440ms and the data were exported to a Microsoft Excel spreadsheet. The amplitude of the K^+ current in the presence of each concentration of the Test Solution or Standard was expressed as a percentage of the K^+ current in control conditions in the same well.

Standard inhibition curves were generated for each standard in various levels of rat serum and expressed as current percent of control (POC) versus log of nM concentration. Percent of control (POC) is inversely related to inhibition, where 100 POC is no inhibition and 0 POC is 100% inhibition. Linear regression over a selected region of the curve was used to derive an equation to enable calculation of drug concentrations within Test solutions. Only current values within the linear portion of the Standard curve were used to calculate the concentration of drug in Test solutions. The corresponding Standard curve in a given level of serum, was always compared to the same level of serum of Test solution when calculating drug level. The Standard curves for ShK and 20K PEG-ShK[1-35] are shown in Figure 58A and Figure 58B, respectively, and each figure contains linear regression equations for each Standard at a given percentage of serum. For the 20K PEG-ShK[1-35] standard curve the linear portion of the Standard curve was from 20 POC to 70 POC and only current values derived from the Test solution which fell within this range were used to calculate drug concentration within the Test solution.

The pharmacokinetic profile of our novel 20K PEG ShK[1-35] molecule after IV injection is shown in Figure 59. The terminal half-life ($t_{1/2}$b) of this molecule is estimated from this curve to be between 6 to 12 hours long. Beyond 48 hours, the level of drug falls outside the linear range of the Standard curve and is not calculated. The calculated 6 to 12 hour half-life of our novel 20K PEG-ShK[1-35] molecule was substantially longer than the approximately 0.33 hour (or 20 min) half-life of the native ShK molecule reported earlier by C. Beeton et al. [C. Beeton et al. (2001) Proc. Natl Acad. Sci. 98, 13942-13947], and is a desirable feature of a therapeutic molecule. A comparison of the relative levels of Kv1.3 inhibitor after an equal molar IV injection of ShK versus 20K PEG-ShK[1-35] is shown in Figure 60. As can be seen from this figure examining 5% serum Test solutions, the 20K PEG-ShK[1-35] molecule showed significant suppression of Kv1.3 current (<70 POC) for more than 24 hours, whereas the native ShK peptide only showed a significant level of inhibition of Kv1.3 current for the first hour and beyond 1 hour showed no significant blockade. These data again demonstrate a desirable feature of the 20K PEG ShK[1-35] molecule as a therapeutic for treatment of autoimmune disease.

Example 45

PEGylated Toxin Peptide suppressed severe autoimmune encephalomyelitis in animal model

The 20KPEG-ShK inhibitor of Kv1.3 shows improved efficacy in suppressing severe autoimmune encephalomyelitis in rats. Using an adoptive transfer experimental autoimmune encephalomyelitis (AT-EAE) model of multiple sclerosis described earlier [C. Beeton et al. (2001) J. Immunol. 166, 936], we examined the activity in vivo of our novel 20KPEG-ShK molecule and compared its efficacy to that of the ShK toxin peptide alone. The study design is illustrated in Figure 61. The results from this in vivo study are provided in Figure 62 and Figure 63. The 20KPEG-ShK molecule delivered subcutaneously (SC) at 10 µg/kg daily from day –1 to day 3 significantly reduced disease severity and increased survival, whereas animals treated with an equal molar dose (10 µg/kg) of the small ShK peptide developed severe disease and died.

The 35-amino acid toxin peptide ShK (Stichodactyla helianthus neurotoxin) was purchased from Bachem Bioscience Inc and confirmed by electrophysiology to potently block Kv1.3 (see Example 36 herein). The synthesis, PEGylation and purification of the 20KPEG ShK molecule was as described herein above. The encephalomyelogenic CD4+ rat T cell line, PAS, specific for myelin-basic protein (MBP) originated from Dr. Evelyne Beraud. The maintenance of these cells in vitro and their use in the AT-EAE model has been described earlier [C. Beeton et al.

(2001) PNAS 98, 13942]. PAS T cells were maintained in vitro by alternating rounds of antigen stimulation or activation with MBP and irradiated thymocytes (2 days), and propagation with T cell growth factors (5 days). Activation of PAS T cells (3×10^5/ml) involved incubating the cells for 2 days with 10 µg/ml MBP and 15×10^6/ml syngeneic irradiated (3500 rad) thymocytes. On day 2 after in vitro activation, $10\text{-}15 \times 10^6$ viable PAS T cells were injected into 6-12 week old female Lewis rats (Charles River Laboratories) by tail IV. Daily subcutaneous injections of vehicle (2% Lewis rat serum in PBS), 20KPEG-ShK or ShK were given from days –1 to 3 (Figure 61), where day –1 represent 1 day prior to injection of PAS T cells (day 0). In vehicle treated rats, acute EAE developed 4 to 5 days after injection of PAS T cells (Figure 62). Serum was collected by retro-orbital bleeding at day 4 and by cardiac puncture at day 8 (end of the study) for analysis of levels of inhibitor. Rats were weighed on days –1, 4, 6, and 8. Animals were scored blinded once a day from the day of cell transfer (day 0) to day 3, and twice a day from day 4 to day 8. Clinical signs were evaluated as the total score of the degree of paresis of each limb and tail. Clinical scoring: 0 = No signs, 0.5 = distal limp tail, 1.0 = limp tail, 2.0 = mild paraparesis, ataxia, 3.0 = moderate paraparesis, 3.5 = one hind leg paralysis, 4.0 = complete hind leg paralysis, 5.0 = complete hind leg paralysis and incontinence, 5.5 = tetraplegia, 6.0 = moribund state or death. Rats reaching a score of 5.5 were euthanized.

Treatment of rats with the Kv1.3 blocker PEG-ShK prior to the onset of EAE caused a lag in the onset of disease, inhibited the progression of disease, and prevented death in a dose-dependent manner (Figure 62). Onset of disease in rats that were treated with the vehicle alone, 10 µg/kg ShK or 1 µg/kg of PEG-ShK was observed on day 4, compared to day 4.5 in rats treated with 10 µg/kg PEG-ShK or 100 µg/kg PEG-ShK. In addition, rats treated with vehicle alone, 10 µg/kg ShK or 1 µg/kg of PEG-ShK all developed severe disease by the end of the study with an EAE score of 5.5 or above. In contrast, rats treated with 10 µg/kg PEG-ShK or 100 µg/kg PEG-ShK, reached a peak clinical severity score average of < 2, and all but one rat survived to the end of the study. Furthermore, we found that rat body weight correlated with disease severity (Figure 63). Rats treated with vehicle alone, 10 µg/kg ShK or 1 ug/kg of PEG-ShK all lost an average of 31g, 30g, and 30g, respectively, while rats treated with 10 µg/kg PEG-ShK or 100 µg/kg PEG-ShK lost 18g and 11g, respectively. Rats in the latter two groups also appeared to be gaining weight by the end of the study, a sign of recovery. It should be noted that rats treated with 10 µg/kg ShK and 10 µg/kg PEG-ShK received molar equivalents of the ShK peptide. The significantly greater efficacy of the PEG-ShK molecule relative to unconjugated ShK, is likely due to the PEG-ShK molecule's greater stability and prolonged half-life in vivo (see, Example 44).

Example 46

Compositions including Kv1.3 Antagonist Peptides Block Inflammation in Human Whole Blood

Ex vivo assay to examine impact of Kv1.3 inhibitors on secretion of IL-2 and IFN-g.

Human whole blood was obtained from healthy, non-medicated donors in a heparin vacutainer. DMEM complete media was Iscoves DMEM (with L-glutamine and 25 mM Hepes buffer) containg 0.1% human albumin (Bayer #68471), 55 µM 2-mercaptoethanol (Gibco), and 1X Pen-Strep-Gln (PSG, Gibco, Cat#10378-016). Thapsigargin was obtained from Alomone Labs (Israel). A 10 mM stock solution of thapsigargin in 100% DMSO was diluted with DMEM complete media to a 40 µM, 4X solution to provide the 4X thapsigargin stimulus for calcium mobilization. The Kv1.3 inhibitor peptide ShK (Stichodacytla helianthus toxin, Cat# H2358) and the BKCa1 inhibitor peptide IbTx (Iberiotoxin, Cat# H9940) were purchased from Bachem Biosciences, whereas the Kv1.1 inhibitor peptide DTX-k (Dendrotoxin-K) was from Alomone Labs (Israel). The CHO-derived Fc-L10-ShK[2-35] peptibody inhibitor of Kv1.3 was obtained as described herein at Example 4 and Example 39. The calcineurin inhibitor cyclosporin A was obtained from the Amgen sample bank, but is also available commercially from a variety of vendors. Ten 3-fold serial dilutions of inhibitors were prepared in DMEM complete media at 4X final concentration and 50 µl of each were added to wells of a 96-well Falcon 3075 flat-bottom microtiter plate. Whereas columns 1-5 and 7-11 of the microtiter plate contained inhibitors (each row with a separate inhibitor dilution series), 50 µl of DMEM complete media alone was added to the 8 wells in column 6 and 100 µl of DMEM complete media alone was added to the 8 wells in column 12. To initiate the experiment, 100 µl of whole blood was added to each well of the microtiter plate. The plate was then incubated at 37°C, 5% CO_2 for one hour. After one hour, the plate was removed and 50 µl of the 4X thapsigargin stimulus (40 µM) was added to all wells of the plate, except the 8 wells in column 12. The plates were placed back at 37°C, 5% CO_2 for 48 hours. To determine the amount of IL-2 and IFN-g secreted in whole blood, 100 µl of the supernatant (conditioned media) from each well of the 96-well plate was transferred to a storage plate. For MSD electrochemilluminesence analysis of cytokine production, 20 µl of the supernatants (conditioned media) were added to MSD Multi-Spot Custom Coated plates (www.meso-scale.com). The working electrodes on these plates were coated with four Capture Antibodies (hIL-5, hIL-2, hIFNg and hIL-4) in advance. After addition of 20 µl of conditioned media to the MSD plate, 150 µl of a cocktail of Detection Antibodies and P4 Buffer were added to each well. The 150 µl cocktail contained 20 ul of four Detection Antibodies (hIL-5,

hIL-2, hIFNg and hIL-4) at 1 µg/ml each and 130 ul of 2X P4 Buffer. The plates were covered and placed on a shaking platform overnight (in the dark). The next morning the plates were read on the MSD Sector Imager. Since the 8 wells in column 6 of each plate received only the thapsigargin stimulus and no inhibitor, the average MSD response here was used to calculate the "High" value for a plate. The calculate "Low" value for the plate was derived from the average MSD response from the 8 wells in column 12 which contained no thapsigargin stimulus and no inhibitor. Percent of control (POC) is a measure of the response relative to the unstimulated versus stimulated controls, where 100 POC is equivalent to the average response of thapsigargin stimulus alone or the "High" value. Therefore, 100 POC represents 0% inhibition of the response. In contrast, 0 POC represents 100% inhibition of the response and would be equivalent to the response where no stimulus is given or the "Low" value. To calculate percent of control (POC), the following formula is used: [(MSD response of well) – ("Low")] / [("High") – ("Low")] x 100. The potency of the molecules in whole blood was calculated after curve fitting from the inhibition curve (IC) and IC50 was derived using standard curve fitting software. Although we describe here measurement of cytokine production using a high throughput MSD electrochemillumenescence assay, one of skill in the art can readily envision lower throughput ELISA assays are equally applicable for measuring cytokine production.

Ex vivo assay demonstrating Kv1.3 inhibitors block cell surface activation of CD40L & IL-2R. Human whole blood was obtained from healthy, non-medicated donors in a heparin vacutainer. DMEM complete media was Iscoves DMEM (with L-glutamine and 25 mM Hepes buffer) containing 0.1% human albumin (Bayer #68471), 55 µM 2-mercaptoethanol (Gibco), and 1X Pen-Strep-Gln (PSG, Gibco, Cat#10378-016). Thapsigargin was obtained from Alomone Labs (Israel). A 10 mM stock solution of thapsigargin in 100% DMSO was diluted with DMEM complete media to a 40 µM, 4X solution to provide the 4X thapsigargin stimulus for calcium mobilization. The Kv1.3 inhibitor peptide peptide ShK (Stichodacytla helianthus toxin, Cat# H2358) and the BKCa1 inhibitor peptide IbTx (Iberiotoxin, Cat# H9940) were purchased from Bachem Biosciences, whereas the Kv1.1 inhibitor peptide DTX-k (Dendrotoxin-K) was from Alomone Labs (Israel). The CHO-derived Fc-L10-ShK[2-35] peptibody inhibitor of Kv1.3 was obtained as described in Example 4 and Example 39. The calcineurin inhibitor cyclosporin A was obtained from the Amgen sample bank, but is also available commercially from a variety of vendors. The ion channel inhibitors ShK, IbTx or DTK-k were diluted into DMEM complete media to 4X of the final concentration desired (final = 50 or 100 nM). The calcineurin inhibitor cyclosporin A was also diluted into DMEM complete media to 4X final concentration (final = 10 µM). To appropriate wells of a 96-well Falcon

3075 flat-bottom microtiter plate, 50 µl of either DMEM complete media or the 4X inhibitor solutions were added. Then, 100 µl of human whole blood was added and the plate was incubated for 1 hour at 37°C, 5% CO_2. After one hour, the plate was removed and 50 µl of the 4X thapsigargin stimulus (40 µM) was added to all wells of the plate containing inhibitor. To some wells containing no inhibitor but just DMEM complete media, thapsigargin was also added whereas others wells with just DMEM complete media had an additional 50 µl of DMEM complete media added. The wells with no inhibitor and no thapsigargin stimulus represented the untreated "Low" control. The wells with no inhibitor but which received thapsigargin stimulus represented the control for maximum stimulation or "High" control. Plates were placed back at 37°C, 5% CO_2 for 24 hours. After 24 hours, plates were removed and wells were process for FACS analysis. Cells were removed from the wells and washed in staining buffer (phosphate buffered saline containing 2% heat-inactivated fetal calf serum). Red blood cells were lysed using BD FACS Lysing Solution containing 1.5% formaldehyde (BD Biosciences) as directed by the manufacturer. Cells were distributed at a concentration of 1 million cells per 100 microliters of staining buffer per tube. Cells were first stained with 1 microliter of biotin-labeled anti-human CD4, washed, then stained simultaneously 1 microliter each of streptavidin-APC, FITC-labeled anti-human CD45RA, and phycoerythrin (PE)-labeled anti-human CD25 (IL-2Ra) or PE-labeled anti-human CD40L. Cells were washed with staining buffer between antibody addition steps. All antibodies were obtained from BD Biosciences (San Diego, CA). Twenty to fifty thousand live events were collected for each sample on a Becton Dickinson FACSCaliber (Mountain View, CA) flow cytometer and analyzed using FlowJo software (Tree Star Inc., San Carlos, CA). Dead cells, monocytes, and granulocytes were excluded from the analysis on the basis of forward and side scatter properties.

Figure 64 and Figure 67 demonstrate that Kv1.3 inhibitors ShK and Fc-L10-ShK[2-35] potently blocked IL-2 secretion in human whole blood, in addition to suppressing activation of the IL-2R on CD4+ T cells. The Kv1.3 inhibitor Fc-L10-ShK[2-35] was more than 200 times more potent in blocking IL-2 production in human whole blood than cyclosporine A (Figure 64) as reflected by the IC50. Figure 65 shows that Kv1.3 inhibitors also potently blocked secretion of IFNg in human whole blood, and Figure 66 demonstrates that upregulation of CD40L on T cells was additionally blocked. The data in Figures 64-67 show that the Fc-L10-ShK[2-35] molecule was stable in whole blood at 37°C for up to 48 hours, providing potent blockade of inflammatory responses. Toxin peptide therapeutic agents that target Kv1.3 and have prolonged half-life, are sought to provide sustained blockade of these responses *in vivo* over time. In contrast, despite the fact the Kv1.3 inhibitor peptide ShK also showed potent blockade in whole blood, the ShK peptide

has a short (~20 min) half-life in vivo (C. Beeton et al. (2001) Proc. Natl. Acad. Sci. 98, 13942), and cannot, therefore, provide prolonged blockade. Whole blood represents a physiologically relevant assay to predict the response in animals. The whole blood assays described here can also be used as a pharmacodynamic (PD) assay to measure target coverage and drug exposure following dosing of patients. These human whole blood data support the therapeutic usefulness of the compositions of the present invention for treatment of a variety immune disorders, such as multiple sclerosis, type 1 diabetes, psoriasis, inflammatory bowel disease, contact-mediated dermatitis, rheumatoid arthritis, psoriatic arthritis, asthma, allergy, restinosis, systemic sclerosis, fibrosis, scleroderma, glomerulonephritis, Sjogren syndrome, inflammatory bone resorption, transplant rejection, graft-versus-host disease, and lupus.

Example 47

PEGylated Peptibodies

By way of example, PEGylated peptibodies of the present invention were made by the following method. CHO-expressed FcL10-OsK1(19.2 mg; MW 30,371 Da, 0.63 micromole) in 19.2 ml A5S, 20mM $NaBH_3CN$, pH 5, was treated with 38 mg PEG aldehyde (MW 20 kDa; 3x, Lot 104086). The sealed reaction mixture was stirred in a cold room overnight. The extent of the protein modification during the course of the reaction was monitored by SEC HPLC using a Superose 6 HR 10/30 column (Amersham Pharmacia Biotech) eluted with a 0.05 M phosphate buffer, 0.5 M NaCl, pH 7.0 at 0.4 ml/min. The reaction mixture was dialyzed with A5S, pH 5 overnight. The dialyzed material was then loaded onto an SP HP FPLC column (16/10) in A5S pH 5 and eluted with a 1 M NaCl gradient. The collected fractions were analyzed by SEC HPLC, pooled into 3 pools, exchanged into DPBS, concentrated and submitted for functional testing (Table 34).

In another example, FcL10-ShK1 (16.5 mg; MW 30,065 Da, 0.55 micro mole) in 16.5 ml A5S, 20mM $NaBH_3CN$, pH 5 was treated with 44 mg PEG aldehyde (MW 20 kDa; 4x, Lot 104086). The sealed reaction mixture was stirred in a cold room overnight. The extent of the protein modification during the course of the reaction was monitored by SEC HPLC using a Superose 6 HR 10/30 column (Amersham Pharmacia Biotech) eluted with a 0.05 M phosphate buffer, 0.5 M NaCl, pH 7.0 at 0.4 ml/min. The reaction mixture was dialyzed with A5S, pH 5 overnight. The dialyzed material was loaded onto an SP HP FPLC column (16/10) in A5S pH 5 and was eluted with a 1 M NaCl gradient. The collected fractions were analyzed by SEC HPLC, pooled into 3 pools, exchanged into DPBS, concentrated and submitted for functional testing (Table 34).

The data in Table 34 demonstrate potency of the PEGylated peptibody molecules as Kv1.3 inhibitors.

Table 34 shows determinations of IC50 made by whole cell patch clamp electrophysiology with HEK 293 as described in Example 36 herein above. The sustained IC50 was derived from the current 400 msecs after voltage ramp from -80mV to +30 mV. Pool #2 samples comprised di-PEGylated peptibodies and Pool #3 samples comprised mono-PEGylated peptibodies.

PEGylated Peptibody	Pool #	IC50 Sustained (nM)
PEG-Fc-L10-SHK(2-35)	3	0.175(n=4)
PEG-Fc-L10-SHK(2-35)	2	0.158(n=4)
PEG-Fc-L10-OSK1	3	0.256(n=3)
PEG-Fc-L10-OSK1	2	0.332(n=3)

Example 48

PEGylated Toxin Peptides

Shk and Osk-1 PEGylation, purification and analysis. Synthetic Shk or OSK1-1 toxin peptides were selectively PEGylated by reductive alkylation at their N-termini. Conjugation was achieved, with either Shk or OSK-1 toxin peptides, at 2 mg/ml in 50mM NaH_2PO_4, pH 4.5 reaction buffer containing 20mM sodium cyanoborohydride and a 2 molar excess of 20 kDa monomethoxy-PEG-aldehyde (Nektar Therapeutics, Huntsville, AL). Conjugation reactions were stirred overnight at room temperature, and their progress was monitored by RP-HPLC. Completed reactions were quenched by 4-fold dilution with 20mM NaOAc, pH 4, adjusted to pH 3.5 and chilled to 4°C. The PEG-peptides were then purified chromatographically at 4°C; using SP Sepharose HP columns (GE Healthcare, Piscataway, NJ) eluted with linear 0-1M NaCl gradients in 20mM NaOAc, pH 4.0. (Figure 68A and Figure 68B) Eluted peak fractions were analyzed by SDS-PAGE and RP-HPLC and pooling determined by purity >97%. Principle contaminants observed were di-PEGylated toxin peptide and unmodified toxin peptide. Selected pools were concentrated to 2-5 mg/ml by centrifugal filtration against 3kDa MWCO membranes and dialyzed into 10mM NaOAc, pH 4 with 5% sorbitol. Dialyzed pools were then sterile filtered through 0.2 micron filters and purity determined to be >97% by SDS-PAGE and RP-HPLC (Figure 69A and Figure 69B). Reverse-phase HPLC was performed on an Agilent 1100 model HPLC running a Zorbax 5µm 300SB-C8 4.6 x 50 mm column (Phenomenex) in 0.1% TFA/H_20 at 1 ml/min and column temperature maintained

at 40°C. Samples of PEG-peptide (20 µg) were injected and eluted in a linear 6-60% gradient while monitoring wavelengths 215 nm and 280 nm.

Electrophysiology performed by patch clamp on whole cells (see, Example 36) yielded a peak IC50 of 1.285 nM for PEG-OSK1 and 0.169 nM for PEG-ShK[1-35] (Figure 74), in a concentration dependent block of the outward potassium current recorded from HEK293 cells stably expressing human Kv1.3 channel. The purified PEG-ShK[1-35] molecule, also referred to as "20K PEG-ShK[1-35]" and "PEG-ShK", had a much longer half-life in vivo than the small ShK peptide (Figure 59 and Figure 60). PEG-ShK[1-35] suppressed severe autoimmune encephalomyelitis in rats (Example 45, Figures 61 – 63) and showed greater efficacy than the small native ShK peptide.

Example 49

Fc loop insertions of ShK and OSK1 toxin peptides

As exemplified in Figure 70, Figure 71, Figure 72, and Figure 73, disulphide-constrained toxin peptides were inserted into the human IgG1 Fc–loop domain, defined as the sequence $D_{137}E_{138}L_{139}T_{140}K_{141}$, according to the method published in Example 1 in Gegg et al., Modified Fc molecules, WO 2006/036834 A2 [PCT/US2005/034273]). Exemplary FcLoop-L2-OsK1-L2, FcLoop-L2-ShK-L2, FcLoop-L2-ShK-L4, and FcLoop-L4-OsK1-L2 were made having three linked domains. These were collected, purified and submitted for functional testing.

The peptide insertion for these examples was between Fc residues Leu_{139} and Thr_{140} and included 2-4 Gly residues as linkers flanking either side of the inserted peptide. However, alternate insertion sites for the human IgG1 Fc sequence, or different linkers, are also useful in the practice of the present invention, as is known in the art, e.g., as described in Example 13 of Gegg et al., Modified Fc molecules, WO 2006/036834 A2 [PCT/US2005/034273]).

Example 50

Purification of ShK(2-35)-L-Fc from E. coli

Frozen, *E. coli* paste (117 g), obtained as described in Example 16 herein above, was combined with 1200 ml of room temperature 50 mM tris HCl, 5 mM EDTA, pH 7.5 and was brought to about 0.1 mg/ml hen egg white lysozyme. The suspended paste was passed through a chilled microfluidizer twice at 12,000 PSI. The cell lysate was then centrifuged at 17,700 g for 30 min at 4 °C. The pellet was then resuspended in 1200 ml 1% deoxycholic acid using a tissue grinder and then centrifuged at 17,700 g for 30 min at 4 °C. The pellet was then resuspended in 1200 ml water

using a tissue grinder and then centrifuged at 17,700 g for 30 min at 4 °C. 6.4 g of the pellet (total 14.2g) was then dissolved in 128 ml 8 M guanidine HCl, 50 mM tris HCl, pH 8.0. 120 ml of the pellet solution was then incubated with 0.67 ml of 1 M DTT for 60 min at 37°C The reduced material was transferred to 5500 ml of the refolding buffer (3 M urea, 50 mM tris, 160 mM arginine HCl, 2.5 mM EDTA, 2.5 mM cystamine HCl, 4 mM cysteine, pH 9.5) at 2 ml/min , 4 °C with vigorous stirring. The stirring rate was then slowed and the incubation was continued for 3 days at 4°C.

The refold was diluted with 5.5L of water, and the pH was adjusted to 8.0 using acetic acid, then the solution was filtered through a 0.22 μm cellulose acetate filter and loaded on to a 35 ml Amersham Q Sepharose-FF (2.6 cm I.D.) column at 10 ml/min in Q-Buffer A (20 mM Tris, pH 8.5) at 8 °C with an inline 35 ml Amersham Mab Select column (2.6 cm I.D.). After loading, the Q Sepharose column was removed from the circuit, and the remaining chromatography was carried out on the Mab Select column. The column was washed with several column volumes of Q-Buffer A, followed by elution using a step to 100 mM glycine pH 3.0. The fractions containing the desired product immediately loaded on to a 5.0 ml Amersham SP-Sepharose HP column at 5.0 ml/min in S-Buffer A (10 mM NaH_2PO_4, pH 7.0) at 8 °C. The column was then washed with several column volumes of S-Buffer A followed by a linear gradient from 5% to 60% S-Buffer B (10 mM NaH_2PO_4, 1 M NaCl, pH 7.0) followed by a step to 100% S-Buffer B. Fractions were then analyzed using a Coomassie brilliant blue stained tris-glycine 4-20% SDS-PAGE. The fractions containing the bulk of the desired product were pooled and then applied to a 50 ml MEP Hypercel column (2.6 cm I.D.) at 10 ml/min in MEP Buffer A (20 mM tris, 200 mM NaCl, pH 8.0) at 8°C. Column was eluted with a linear gradient from 5% to 50% MEP Buffer B(50 mM sodium citrate pH 4.0) followed by a step to 100% MEP Buffer B. Fractions were then analyzed using a Coomassie brilliant blue stained tris-glycine 4-20% SDS-PAGE, and the fractions containing the bulk of the desired product were pooled.

The MEP-pool was then concentrated to about 10 ml using a Pall Jumbo-Sep with a 10 kDa membrane. A spectral scan was then conducted on 50 μl of the combined pool diluted in 700 μl PBS using a Hewlett Packard 8453 spectrophotometer (Figure 76A). Then concentration of the material was determined to be 3.7 mg/ml using a calculated molecular mass of 30,253 and extinction coefficient of 36,900 M^{-1} cm^{-1}. The purity of the material was then assessed using a Coomassie brilliant blue stained tris-glycine 4-20% SDS-PAGE (Figure 76B). The macromolecular state of the product was then determined using size exclusion chromatography on 70 μg of the product injected on to a Phenomenex BioSep SEC 3000 column (7.8 x 300 mm) in 50 mM

NaH_2PO_4, 250 mM NaCl, pH 6.9 at 1 ml/min observing the absorbance at 280 nm (Figure 76C). The product was then subject to mass spectral analysis by chromatographing approximately 4 μg of the sample through a RP-HPLC column (Vydac C_4, 1 x 150 mm). Solvent A was 0.1 % trifluoroacetic acid in water and solvent B was 0.1 % trifluoroacetic acid in 90 % acetonitrile, 10 % water. The column was pre-equilibrated in 10 % solvent B at a flow rate of 80 μl per min. The protein was eluted using a linear gradient of 10 % to 90% solvent B over 30 min. Part of the effluent was directed into a LCQ ion trap mass spectrometer. The mass spectrum was deconvoluted using the Bioworks software provided by the mass spectrometer manufacturer. (Figure 76D). The product was filtered through a 0.22 μm cellulose acetate filter and then stored at –80 °C.

In Table 35, IC50 data for the purified E. coli-derived ShK[2-35]-L-Fc are compared to some other embodiments of the inventive composition of matter.

Table 35. *E.coli-derived* recombinant Fc-L-ShK[1-35], Fc-L-ShK[2-35], Fc-L-OSK1, Shk[1-35]-L-Fc and ShK[2-35]-L-Fc peptibodies containing Fc at either the N-terminus or C-terminus show potent blockade of human Kv1.3. The activity of the *CHO-derived* Fc-L10-ShK[1-35] R1Q mutant is also shown. Whole cell patch clamp electrophysiology (WCVC), by methods described in Example 36, was performed using HEK293 / Kv1.3 cells and the IC50 shown is the average from dose-response curves from 3 or more cells. IonWorks™ (IWQ) planar patch clamp electrophysiology by methods described in Example 44 was on CHO / Kv1.3 cells and the average IC50 is shown. The inventive molecules were obtained by methods as described in the indicated Example: E.coli-derived Fc-L-ShK[1-35] (Example 3 and Example 38), E.coli-derived Fc-L-ShK[2-35] (Example 4 and Example 39), E.coli Fc-L-OSK1 (Example 10 and Example 40), ShK[1-35]-L-Fc (Example 15 and Example 51), and ShK[2-35]-L-Fc (Example 16 and this Example 50). CHO-derived Fc-L10-ShK[1-35] R1Q molecule was generated using methods similar to those described for CHO-derived Fc-L10-ShK[1-35].

Molecule	Kv1.3 IC_{50} by WCVC (nM)	Kv1.3 IC_{50} by IWQ (nM)
E.coli-derived Fc-L-ShK[1-35]	1.4	
E.coli-derived Fc-L-ShK[2-35]	1.3	2.8
E.coli-derived Fc-L-OSK1	3.2	
***E.coli-derived* Shk[1-35]-L-Fc**		2.4
E.coli-derived ShK[2-35]-L-Fc		4.9
CHO-derived Fc-L10-ShK[1-35] R1Q		2.2

Example 51
Purification of Met-ShK(1-35)-Fc from E. coli

Frozen, *E. coli* paste (65 g), obtained as described in Example 15 herein above was combined with 660 ml of room temperature 50 mM tris HCl, 5 mM EDTA, pH 7.5 and was brought to about 0.1 mg/ml hen egg white lysozyme. The suspended paste was passed through a chilled

microfluidizer twice at 12,000 PSI. The cell lysate was then centrifuged at 17,700 g for 30 min at 4 °C. The pellet was then resuspended in 660 ml 1% deoxycholic acid using a tissue grinder and then centrifuged at 17,700 g for 30 min at 4 °C. The pellet was then resuspended in 660 ml water using a tissue grinder and then centrifuged at 17,700 g for 30 min at 4 °C. 13 g of the pellet was then dissolved in 130 ml 8 M guanidine HCl, 50 mM tris HCl, pH 8.0. 10 ml of the pellet solution was then incubated with 0.1 ml of 1 M DTT for 60 min at 37 °C The reduced material was transferred to 1000 ml of the refolding buffer (2 M urea, 50 mM tris, 160 mM arginine HCl, 2.5 mM EDTA, 1.2 mM cystamine HCl, 4 mM cysteine, pH 8.5) at 2 ml/min , 4°C with vigorous stirring. The stirring rate was then slowed and the incubation was continued for 3 days at 4°C.

The refold was diluted with 1L of water, and filtered through a 0.22 μm cellulose acetate filter then loaded on to a 35 ml Amersham Q Sepharose-FF (2.6 cm I.D.) column at 10 ml/min in Q-Buffer A (20 mM Tris, pH 8.5) at 8 °C with an inline 35 ml Amersham Mab Select column (2.6 cm I.D.). After loading, the Q Sepharose column was removed from the circuit, and the remaining chromatography was carried out on the Mab Select column. The column was washed with several column volumes of Q-Buffer A, followed by elution using a step to 100 mM glycine pH 3.0. The fractions containing the desired product immediately loaded on to a 5.0 ml Amersham SP-Sepharose HP column at 5.0 ml/min in S-Buffer A (20 mM NaH_2PO_4, pH 7.0) at 8 °C. The column was then washed with several column volumes of S-Buffer A followed by a linear gradient from 5% to 60% S-Buffer B (20 mM NaH_2PO_4, 1 M NaCl, pH 7.0) followed by a step to 100% S-Buffer B. Fractions were then analyzed using a Coomassie brilliant blue stained tris-glycine 4-20% SDS-PAGE. The fractions containing the bulk of the desired product were pooled.

The S-pool was then concentrated to about 10 ml using a Pall Jumbo-Sep with a 10 kDa membrane. A spectral scan was then conducted on 20 μl of the combined pool diluted in 700 μl PBS using a Hewlett Packard 8453 spectrophotometer (Figure 77A). Then concentration of the material was determined to be 3.1 mg/ml using a calculated molecular mass of 30,409 and extinction coefficient of 36,900 M^{-1} cm^{-1}. The purity of the material was then assessed using a Coomassie brilliant blue stained tris-glycine 4-20% SDS-PAGE (Figure 77B). The macromolecular state of the product was then determined using size exclusion chromatography on 93 μg of the product injected on to a Phenomenex BioSep SEC 3000 column (7.8 x 300 mm) in 50 mM NaH_2PO_4, 250 mM NaCl, pH 6.9 at 1 ml/min observing the absorbance at 280 nm (Figure 77C). The product was then subject to mass spectral analysis by MALDI mass spectrometry.
An aliquot of the sample was spotted with the MALDI matrix sinapinic acid on sample plate. A Voyager DE-RP time-of-flight mass spectrometer equipped with a nitrogen laser (337 nm, 3 ns

pulse) was used to collect spectra. The positive ion/linear mode was used, with an accelerating voltage of 25 kV. Each spectrum was produced by accumulating data from ~ 200 laser shots (Figure 77D). External mass calibration was accomplished using purified proteins of known molecular masses.

The IC_{50} for blockade of human Kv1.3 by purified *E.coli*-derived Met-ShK(1-35)-Fc, also referred to as "ShK[1-35]-L-Fc", is shown in Table 35 herein above.

Example 52
Bacterial expression of OsK1-L-Fc inhibitor of Kv1.3

The methods to clone and express the peptibody in bacteria were as described in Example 3. The vector used was pAMG21amgR-pep-Fc and the oligos listed below were used to generate a duplex (see below) for cloning and expression in bacteria of OsK1-L-Fc.

Oligos used to form duplex are shown below:

```
GGGTGTTATCATCAACGTTAAATGCAAAATCTCCCGTCAGTGCCTGGAACCGTGCAAAAAAGCTGGTATGCGT
//SEQ ID NO:1347;

TTCGGTAAATGCATGAACGGTAAATGCCACTGCACCCCGAAATCTGGTGGTGGTGGTTCT  //SEQ ID
NO:1348;

CACCAGAACCACCACCACCACCAGATTTCGGGGTGCAGTGGCATTTACCGTTCATGCATTTACCGAAACGCAT
//SEQ ID NO:1349;

ACCAGCTTTTTTGCACGGTTCCAGGCACTGACGGGAGATTTTGCATTTAACGTTGATGATAAC  //SEQ ID
NO:1310;
```

The oligos shown above were used to form the duplex shown below:

```
    GGGTGTTATCATCAACGTTAAATGCAAAATCTCCCGTCAGTGCCTGGAACCGTGCAAAAA
  1 ---------+---------+---------+---------+---------+---------+ 60
      CAATAGTAGTTGCAATTTACGTTTTAGAGGGCAGTCACGGACCTTGGCACGTTTTT

     G  V  I  I  N  V  K  C  K  I  S  R  Q  C  L  E  P  C  K  K  -

    AGCTGGTATGCGTTTCGGTAAATGCATGAACGGTAAATGCCACTGCACCCCGAAATCTGG
 61 ---------+---------+---------+---------+---------+---------+ 120
    TCGACCATACGCAAAGCCATTTACGTACTTGCCATTTACGGTGACGTGGGGCTTTAGACC

     A  G  M  R  F  G  K  C  M  N  G  K  C  H  C  T  P  K  S  G  -

    TGGTGGTGGTTCT   //SEQ ID NO:1350
121 ---------+------- 137
    ACCACCACCAAGACCAC     //SEQ ID NO:1352

     G  G  G  S  G    -  //SEQ ID NO:1351
```

Bacterial expression of the peptibody was as described in Example 3 and paste was stored frozen.

Example 53

Bacterial expression of Gly-ShK(1-35)-L-Fc inhibitor of Kv1.3

The methods to clone and express the peptibody in bacteria were as described in Example 3. The vector used was pAMG21amgR-pep-Fc and the oligos listed below were used to generate a duplex (see below) for cloning and expression in bacteria of Gly-ShK(1-35) -L-Fc.

Oligos used to form duplex are shown below:

GGGTCGTTCTTGTATTGATACTATTCCAAAATCTCGTTGTACTGCTTTTCAATGTAAACATTCTA TGAAATATCGTCTTTCTT //SEQ ID NO:1313;

TTTGTCGTAAAACTTGTGGTACTTGTTCTGGTGGTGGTGGTTCT //SEQ ID NO:1314;

CACCAGAACCACCACCACCAGAACAAGTACCACAAGTTTTACGACAAAAAGAAAGACGATATTT CATAGAATGTTTACATTGA //SEQ ID NO:1353;

AAAGCAGTACAACGAGATTTTGGAATAGTATCAATACAAGAACG //SEQ ID NO:1354

The oligos shown above were used to form the duplex shown below:

```
   GGGTCGTTCTTGTATTGATACTATTCCAAAATCTCGTTGTACTGCTTTTCAATGTAAACA
 1 ---------+---------+---------+---------+---------+---------+ 60
     GCAAGAACATAACTATGATAAGGTTTTAGAGCAACATGACGAAAAGTTACATTTGT

    G  R  S  C  I  D  T  I  P  K  S  R  C  T  A  F  Q  C  K  H  -

   TTCTATGAAATATCGTCTTTCTTTTTGTCGTAAAACTTGTGGTACTTGTTCTGGTGGTGG
61 ---------+---------+---------+---------+---------+---------+ 120
   AAGATACTTTATAGCAGAAAGAAAAACAGCATTTTGAACACCATGAACAAGACCACCACC

    S  M  K  Y  R  L  S  F  C  R  K  T  C  G  T  C  S  G  G  G  -

   TGGTTCT    //SEQ ID NO:1355
121 ---------+- 131
   ACCAAGACCAC   //SEQ ID NO:1357

    G  S  G   -   //SEQ ID NO:1356
```

Bacterial expression of the peptibody was as described in Example 3 and paste was stored frozen.

Abbreviations

Abbreviations used throughout this specification are as defined below, unless otherwise defined in specific circumstances.

Ac	acetyl (used to refer to acetylated residues)
AcBpa	acetylated p-benzoyl-L-phenylalanine
ADCC	antibody-dependent cellular cytotoxicity
Aib	aminoisobutyric acid

bA	beta-alanine
Bpa	p-benzoyl-L-phenylalanine
BrAc	bromoacetyl ($BrCH_2C(O)$
BSA	Bovine serum albumin
Bzl	Benzyl
Cap	Caproic acid
COPD	Chronic obstructive pulmonary disease
CTL	Cytotoxic T lymphocytes
DCC	Dicylcohexylcarbodiimide
Dde	1-(4,4-dimethyl-2,6-dioxo-cyclohexylidene)ethyl
ESI-MS	Electron spray ionization mass spectrometry
Fmoc	fluorenylmethoxycarbonyl
HOBt	1-Hydroxybenzotriazole
HPLC	high performance liquid chromatography
HSL	homoserine lactone
IB	inclusion bodies
KCa	calcium-activated potassium channel (including IKCa, BKCa, SKCa)
Kv	voltage-gated potassium channel
Lau	Lauric acid
LPS	lipopolysaccharide
LYMPH	lymphocytes
MALDI-MS	Matrix-assisted laser desorption ionization mass spectrometry
Me	methyl
MeO	methoxy
MHC	major histocompatibility complex
MMP	matrix metalloproteinase
1-Nap	1-napthylalanine
NEUT	neutrophils
Nle	norleucine
NMP	N-methyl-2-pyrrolidinone
PAGE	polyacrylamide gel electrophoresis
PBMC	*peripheral blood mononuclear cell*
PBS	Phosphate-buffered saline

Pbf	2,2,4,6,7-pendamethyldihydrobenzofuran-5-sulfonyl
PCR	polymerase chain reaction
Pec	pipecolic acid
PEG	Poly(ethylene glycol)
pGlu	pyroglutamic acid
Pic	picolinic acid
pY	phosphotyrosine
RBS	ribosome binding site
RT	room temperature (25 °C)
Sar	sarcosine
SDS	sodium dodecyl sulfate
STK	serine-threonine kinases
t-Boc	tert-Butoxycarbonyl
tBu	tert-Butyl
THF	thymic humoral factor
Trt	trityl

CLAIMS

1. A composition of matter of the formula

$$(X^1)_a\text{-}(F^1)_d\text{-}(X^2)_b\text{-}(F^2)_e\text{-}(X^3)_c$$

or multimers thereof, wherein:

F^1 and F^2 are half-life extending moieties, and d and e are each independently 0 or 1, provided that at least one of d and e is 1;

X^1, X^2, and X^3 are each independently $\text{-}(L)_f\text{-}P\text{-}(L)_g\text{-}$, and f and g are each independently 0 or 1;

P is a ShK toxin peptide or a ShK peptide analog of no more than about 80 amino acid residues in length, comprising at least two intrapeptide disulfide bonds;

L is a linker; and

a, b, and c are each independently 0 or 1, provided that at least one of a, b and c is 1; or

a physiologically acceptable salt thereof.

2. The composition of matter of claim 1 of a formula selected from

$P\text{-}(L)_g\text{-}F^1$,

$F^1\text{-}(L)_f\text{-}P$,

$P\text{-}(L)_g\text{-}F^1\text{-}(L)_f\text{-}P$,

$F^1\text{-}(L)_f\text{-}P\text{-}(L)_g\text{-}F^2$,

$F^1\text{-}(L)_f\text{-}P\text{-}(L)_g\text{-}F^2\text{-}(L)_f\text{-}P$,

$F^1\text{-}F^2\text{-}(L)_f\text{-}P$,

$P\text{-}(L)_g\text{-}F^1\text{-}F^2$, and

$P\text{-}(L)_g\text{-}F^1\text{-}F^2\text{-}(L)_f\text{-}P$.

3. The composition of matter of Claim 1, wherein F^1 or F^2, or both, is a copolymer of ethylene glycol, a polypropylene glycol, a copolymer of propylene glycol, a carboxymethylcellulose, a polyvinyl pyrrolidone, a poly-1,3-dioxolane, a poly-1,3,6-

trioxane, an ethylene/maleic anhydride copolymer, a polyaminoacid, a dextran n-vinyl pyrrolidone, a poly n-vinyl pyrrolidone, a propylene glycol homopolymer, a propylene oxide polymer, an ethylene oxide polymer, a polyoxyethylated polyol, a polyvinyl alcohol, a linear or branched glycosylated chain, a polyacetal, a long chain fatty acid, a long chain hydrophobic aliphatic group, an immunoglobulin F_c domain or portion thereof, a CH2 domain of Fc, an Fc domain loop, an albumin, an albumin-binding protein, a transthyretin, a thyroxine-binding globulin, or a ligand that has an affinity for a long half-life serum protein, said ligand being selected from the group consisting of peptide ligands and small molecule ligands; or a combination of any of these members.

4. The composition of matter of claim 1 wherein F^1 or F^2, or both, comprises a human IgG Fc domain or a portion thereof.

5. The composition of matter of claim 4, wherein the human IgG Fc domain comprises a human IgG1 Fc domain.

6. The composition of matter of claim 5, wherein the human IgG Fc domain comprises a human IgG2 Fc domain.

7. The composition of matter of Claim 1, wherein F^1 and F^2 are different half-life extending moieties.

8. The composition of matter of claim 1, wherein F^1 or F^2, or both, comprises a sequence selected from the group consisting of SEQ ID NOS: 2, 4, 70, 72, 74, 76, 1340 through 1342, 1359, 1360, 1362, and 1363.

9. The composition of matter of claim 1, wherein F^1 or F^2, or both, comprises a human serum albumin protein domain, or a transthyretin protein domain, or a biologically suitable polymer or copolymer.

10. The composition of matter of claim 9, wherein the biologically suitable polymer is polyethylene glycol (PEG) of molecular mass about 1,000 Da to about 100,000 Da.

11. The composition of matter of claim 10, wherein the PEG is selected from the group consisting of 5 kD and 20 kD PEG.

12. The composition of matter of Claim 1 of a formula selected from

F^1-$(L)_f$-P-$(L)_g$-F^2,

F^1-$(L)_f$-P-$(L)_g$-F^2-$(L)_f$-P,

P-$(L)_g$-F^1-F^2 ,

and P-$(L)_g$-F^1-F^2-$(L)_f$-P, wherein F^1 is an human IgG Fc domain or HSA, and F^2 is PEG, or a formula selected from

F^1-$(L)_f$-P-$(L)_g$-F^2,

F^1-$(L)_f$-P-$(L)_g$-F^2-$(L)_f$-P,

F^1-F^2-$(L)_f$-P ,

and P-$(L)_g$-F^1-F^2-$(L)_f$-P, wherein F^2 is an human IgG Fc domain or HSA and F^1 is PEG.

13. The composition of matter of Claim 1, further comprising one or more PEG moieties conjugated to a non-PEG F^1 or non-PEG F^2, or to P, or to any combination of any of these.

14. The composition of matter of Claim 1, in which the toxin peptide is inserted into a human IgG1 Fc domain loop.

15. The composition of matter of claim 1, wherein the ShK peptide analog comprises an amino acid sequence selected from the group consisting of SEQ ID NOS: 88, 89, 92, 148 through 200, 548 through 561, 884 through 950, and 1295 through 1300 as set forth in Table 2.

16. A DNA encoding a composition of matter of claim 1.

17. An expression vector comprising the DNA of claim 16.

18. A host cell comprising the expression vector of claim 17.

19. The host cell of claim 18, wherein the cell is a eukaryotic cell.

20. The host cell of claim 18, wherein the cell is a mammalian cell.

21. The host cell of claim 18, wherein the cell is a CHO cell.

22. The host cell of claim 18, wherein the cell is a prokaryotic cell.

23. The host cell of claim 18, wherein the cell is an E. coli cell.

24. The composition of matter of claim 1, further comprising an additional pharmacologically active, covalently bound peptide.

25. The composition of matter of claim 24, wherein the additional peptide is bound to F^1 or F^2 or to P.

26. The composition of matter Claim 1, further comprising an agonistic peptide or an antagonistic peptide, in relation to the activity of the toxin peptide, or a targeting peptide.

27. A composition of matter, comprising a ShK peptide analog that comprises an amino acid sequence selected from the group consisting of SEQ ID NOS: 88, 89, 92, 148 through 200, 548 through 561, 884 through 949, and 1295 through 1300 as set forth in Table 2, or a physiologically acceptable salt thereof.

28. A pharmaceutical composition, comprising the composition of any of Claims 1 or 27 and a pharmaceutically acceptable carrier.

29. Use of composition of matter for the preparation of a medicament for preventing or mitigating a relapse of a symptom of multiple sclerosis in a patient, wherein the composition of matter is selected from:

a composition according to claim 1; and

a composition of matter comprising a ShK peptide analog that comprises an amino acid sequence selected from the group consisting of SEQ ID NOS: 88, 89, 92, 148 through 200, 548 through 561, 884 through 949, and 1295 through 1300 as set forth in Table 2, or a physiologically acceptable salt thereof.

30. Use of composition of matter for the preparation of a medicament for treating an autoimmune disorder in a patient selected from the group consisting of multiple sclerosis, type 1 diabetes, psoriasis, inflammatory bowel disease, contact-mediated dermatitis, rheumatoid arthritis, psoriatic arthritis, asthma, allergy, restinosis, systemic sclerosis, fibrosis, scleroderma, glomerulonephritis, Sjogren syndrome, inflammatory

bone resorption, transplant rejection, graft-versus-host disease, and lupus, a therapeutically effective amount of a composition of matter whereby at least one symptom of the disorder is alleviated in the patient, wherein the composition of matter is selected from:

a composition according to claim 1; and

a composition of matter comprising a ShK peptide analog that comprises an amino acid sequence selected from the group consisting of SEQ ID NOS: 88, 89, 92, 148 through 200, 548 through 561, 884 through 949, and 1295 through 1300 as set forth in Table 2, or a physiologically acceptable salt thereof.

31. The composition of matter of Claim 1, wherein any f or any g is 1, and L is a peptide linker comprising an amino acid sequence selected from the group consisting of SEQ ID NOS: 79, 84, and 637 through 656.

32. The composition of Claim 1 or Claim 27, comprising a ShK peptide analog that comprises an amino acid sequence of SEQ ID NOS: 914.

33. The composition of Claim 1 or Claim 27, comprising a ShK peptide analog that comprises an amino acid sequence of SEQ ID NOS: 915.

34. The composition of Claim 1 or Claim 27, comprising a ShK peptide analog that comprises an amino acid sequence of SEQ ID NOS: 916.

35. The composition of Claim 1 or Claim 27, comprising a ShK peptide analog that comprises an amino acid sequence of SEQ ID NOS: 917.

SEQUENCE LISTING

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<120> Toxin Peptide Therapeutic Agents

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<140> WO 2006/116156
<141> 2006-04-18

<150> 60/674,342
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Val His Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
            20                  25                  30

ctc ctg ggg gga ccg tca gtc ttc ctc ttc ccc cca aaa ccc aag gac       144
Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
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gcc gtg gag tgg gag agc aat ggg cag ccg gag aac aac tac aag acc      576
Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
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acg cct ccc gtg ctg gac tcc gac ggc tcc ttc ttc ctc tac agc aag      624
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            20                  25                  30

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

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
    50                  55                  60

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
65                  70                  75                  80

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
                85                  90                  95

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
            100                 105                 110

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
        115                 120                 125
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130 135 140

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
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Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
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Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
195 200 205

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
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Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
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atc gag aaa acc atc tcc aaa gcc aaa ggg cag ccc cga gaa cca cag      384
Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
        115                 120                 125

gtg tac acc ctg ccc cca tcc cgg gat gag ctg acc aag aac cag gtc      432
Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val
    130                 135                 140

agc ctg acc tgc ctg gtc aaa ggc ttc tat ccc agc gac atc gcc gtg      480
Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
145                 150                 155                 160

gag tgg gag agc aat ggg cag ccg gag aac aac tac aag acc acg cct      528
Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
                165                 170                 175

ccc gtg ctg gac tcc gac ggc tcc ttc ttc ctc tac agc aag ctc acc      576
Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
            180                 185                 190

gtg gac aag agc agg tgg cag cag ggg aac gtc ttc tca tgc tcc gtg      624
Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
        195                 200                 205

atg cat gag gct ctg cac aac cac tac acg cag aag agc ctc tcc ctg      672
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His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
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Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
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Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
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Gly Val Pro Ile Asn Val Ser Cys Thr Gly Ser Pro Gln Cys Ile Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Arg Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 24
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Kaliotoxin 1 (KTX1) peptide sequence

<400> 24

Gly Val Glu Ile Asn Val Lys Cys Ser Gly Ser Pro Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Arg Lys
20 25 30

Cys His Cys Thr Pro Lys

35

<210> 25
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Kv1.3 peptide inhibitor sequence - OSK1

<400> 25

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Glu
1 5 10 15

Pro Cys Lys Lys Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 26
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Kvt1.3 peptide inhibitor sequence - BmKTX

<400> 26

Val Gly Ile Asn Val Lys Cys Lys His Ser Gly Gln Cys Leu Lys Pro
1 5 10 15

Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Ile Asn Gly Lys Cys
20 25 30

Asp Cys Thr Pro Lys Gly
35

<210> 27
<211> 39
<212> PRT
<213> Artificial Sequence

<220>
<223> Kvt1.3 peptide inhibitor sequence - HgTx1

<400> 27

Thr Val Ile Asp Val Lys Cys Thr Ser Pro Lys Gln Cys Leu Pro Pro
1 5 10 15

Cys Lys Ala Gln Phe Gly Ile Arg Ala Gly Ala Lys Cys Met Asn Gly
20 25 30

Lys Cys Lys Cys Tyr Pro His
35

<210> 28
<211> 39
<212> PRT
<213> Artificial Sequence

<220>
<223> MgTx peptide sequence - MgTx

<400> 28

Thr Ile Ile Asn Val Lys Cys Thr Ser Pro Lys Gln Cys Leu Pro Pro
1 5 10 15

Cys Lys Ala Gln Phe Gly Gln Ser Ala Gly Ala Lys Cys Met Asn Gly
20 25 30

Lys Cys Lys Cys Tyr Pro His
35

<210> 29
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> BKCa peptide inhibitor sequence - BlITx1

<400> 29

Ile Thr Ile Asn Val Lys Cys Thr Ser Pro Gln Gln Cys Leu Arg Pro
1 5 10 15

Cys Lys Asp Arg Phe Gly Gln His Ala Gly Gly Lys Cys Ile Asn Gly
20 25 30

Lys Cys Lys Cys Tyr Pro
35

<210> 30
<211> 39
<212> PRT
<213> Artificial Sequence

<220>
<223> Noxiustoxin peptide sequence - NTX

<400> 30

Thr Ile Ile Asn Val Lys Cys Thr Ser Pro Lys Gln Cys Ser Lys Pro
1 5 10 15

Cys Lys Glu Leu Tyr Gly Ser Ser Ala Gly Ala Lys Cys Met Asn Gly
20 25 30

Lys Cys Lys Cys Tyr Asn Asn
35

<210> 31

<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Tc30

<400> 31

Val Phe Ile Asn Val Lys Cys Arg Gly Ser Lys Glu Cys Leu Pro Ala
1 5 10 15

Cys Lys Ala Ala Val Gly Lys Ala Ala Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Lys Cys Tyr Pro
35

<210> 32
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> TsTX-Ka

<400> 32

Val Phe Ile Asn Ala Lys Cys Arg Gly Ser Pro Glu Cys Leu Pro Lys
1 5 10 15

Cys Lys Glu Ala Ile Gly Lys Ala Ala Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Lys Cys Tyr Pro
35

<210> 33
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> PBTx3

<400> 33

Glu Val Asp Met Arg Cys Lys Ser Ser Lys Glu Cys Leu Val Lys Cys
1 5 10 15

Lys Gln Ala Thr Gly Arg Pro Asn Gly Lys Cys Met Asn Arg Lys Cys
20 25 30

Lys Cys Tyr Pro Arg
35

<210> 34
<211> 36
<212> PRT

<213> Artificial Sequence

<220>
<223> Lgh 15-1

<400> 34

Gly Leu Ile Asp Val Arg Cys Tyr Asp Ser Arg Gln Cys Trp Ile Ala
1 5 10 15

Cys Lys Lys Val Thr Gly Ser Thr Gln Gly Lys Cys Gln Asn Lys Gln
20 25 30

Cys Arg Cys Tyr
35

<210> 35
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> BKCa peptide inhibitor sequence - MartenTx

<400> 35

Phe Gly Leu Ile Asp Val Lys Cys Phe Ala Ser Ser Glu Cys Trp Thr
1 5 10 15

Ala Cys Lys Lys Val Thr Gly Ser Gly Gln Gly Lys Cys Gln Asn Asn
20 25 30

Gln Cys Arg Cys Tyr
35

<210> 36
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Kvt1.3 peptide inhibitor sequence - ChTx

<400> 36

Gln Phe Thr Asn Val Ser Cys Thr Thr Ser Lys Glu Cys Trp Ser Val
1 5 10 15

Cys Gln Arg Leu His Asn Thr Ser Arg Gly Lys Cys Met Asn Lys Lys
20 25 30

Cys Arg Cys Tyr Ser
35

<210> 37
<211> 59
<212> PRT
<213> Artificial Sequence

<220>
<223> MartenTx-precursor

<400> 37

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

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

Ser Ser Glu Cys Trp Thr Ala Cys Lys Lys Val Thr Gly Ser Gly Gln
35 40 45

Gly Lys Cys Gln Asn Asn Gln Cys Arg Cys Tyr
50 55

<210> 38
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> BKCa peptide inhibitor sequence - IbTx

<400> 38

Gln Phe Thr Asp Val Asp Cys Ser Val Ser Lys Glu Cys Trp Ser Val
1 5 10 15

Cys Lys Asp Leu Phe Gly Val Asp Arg Gly Lys Cys Met Gly Lys Lys
20 25 30

Cys Arg Cys Tyr Gln
35

<210> 39
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> BKCa peptide inhibitor sequence - Slotoxin (SloTx)

<400> 39

Thr Phe Ile Asp Val Asp Cys Thr Val Ser Lys Glu Cys Trp Ala Pro
1 5 10 15

Cys Lys Ala Ala Phe Gly Val Asp Arg Gly Lys Cys Met Gly Lys Lys
20 25 30

Cys Lys Cys Tyr Val
35

<210> 40
<211> 37
<212> PRT

<213> Artificial Sequence

<220>
<223> Kvt1.3 peptide inhibitor sequence - BmTx1

<400> 40

Gln Phe Thr Asp Val Lys Cys Thr Gly Ser Lys Gln Cys Trp Pro Val
1 5 10 15

Cys Lys Gln Met Phe Gly Lys Pro Asn Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Arg Cys Tyr Ser
35

<210> 41
<211> 41
<212> PRT
<213> Artificial Sequence

<220>
<223> BKCa peptide inhibitor sequence - BuTx

<400> 41

Trp Cys Ser Thr Cys Leu Asp Leu Ala Cys Gly Ala Ser Arg Glu Cys
1 5 10 15

Tyr Asp Pro Cys Phe Lys Ala Phe Gly Arg Ala His Gly Lys Cys Met
20 25 30

Asn Asn Lys Cys Arg Cys Tyr Thr Asn
35 40

<210> 42
<211> 59
<212> PRT
<213> Artificial Sequence

<220>
<223> ChTx-Lg2

<400> 42

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

Val Gly Trp Ser Glu Ala Gln Phe Thr Asn Val Ser Cys Thr Thr Ser
20 25 30

Lys Glu Cys Trp Ser Val Cys Gln Arg Leu His Asn Thr Ser Arg Gly
35 40 45

Lys Cys Met Asn Lys Lys Cys Arg Cys Tyr Ser
50 55

<210> 43

<211> 57
<212> PRT
<213> Artificial Sequence

<220>
<223> BmTx1-precursor

<400> 43

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

Trp Ser Glu Ala Gln Phe Thr Asp Val Lys Cys Thr Gly Ser Lys Gln
20 25 30

Cys Trp Pro Val Cys Lys Gln Met Phe Gly Lys Pro Asn Gly Lys Cys
35 40 45

Met Asn Gly Lys Cys Arg Cys Tyr Ser
50 55

<210> 44
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> AmmTX3

<400> 44

Gln Ile Glu Thr Asn Lys Lys Cys Gln Gly Gly Ser Cys Ala Ser Val
1 5 10 15

Cys Arg Lys Val Ile Gly Val Ala Ala Gly Lys Cys Ile Asn Gly Arg
20 25 30

Cys Val Cys Tyr Pro
35

<210> 45
<211> 59
<212> PRT
<213> Artificial Sequence

<220>
<223> AaTX1

<400> 45

Met Lys Phe Ser Ser Ile Ile Leu Leu Thr Leu Leu Ile Cys Ser Met
1 5 10 15

Ser Ile Phe Gly Asn Cys Gln Ile Glu Thr Asn Lys Lys Cys Gln Gly
20 25 30

Gly Ser Cys Ala Ser Val Cys Arg Arg Val Ile Gly Val Ala Ala Gly
35 40 45

Lys Cys Ile Asn Gly Arg Cys Val Cys Tyr Pro
50 55

<210> 46
<211> 59
<212> PRT
<213> Artificial Sequence

<220>
<223> BmTX3

<400> 46

Met Lys Phe Ser Ser Ile Ile Leu Leu Thr Leu Leu Ile Cys Ser Met
1 5 10 15

Ser Lys Phe Gly Asn Cys Gln Val Glu Thr Asn Val Lys Cys Gln Gly
20 25 30

Gly Ser Cys Ala Ser Val Cys Arg Lys Ala Ile Gly Val Ala Ala Gly
35 40 45

Lys Cys Ile Asn Gly Arg Cys Val Cys Tyr Pro
50 55

<210> 47
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> SKCa peptide inhibitor sequence - TsK

<400> 47

Val Val Ile Gly Gln Arg Cys Tyr Arg Ser Pro Asp Cys Tyr Ser Ala
1 5 10 15

Cys Lys Lys Leu Val Gly Lys Ala Thr Gly Lys Cys Thr Asn Gly Arg
20 25 30

Cys Asp Cys
35

<210> 48
<211> 23
<212> PRT
<213> Artificial Sequence

<220>
<223> Tc1

<400> 48

Ala Cys Gly Ser Cys Arg Lys Lys Cys Lys Gly Ser Gly Lys Cys Ile
1 5 10 15

Asn Gly Arg Cys Lys Cys Tyr

20

<210> 49
<211> 28
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK2

<400> 49

Ala Cys Gly Pro Gly Cys Ser Gly Ser Cys Arg Gln Lys Gly Asp Arg
1 5 10 15

Ile Lys Cys Ile Asn Gly Ser Cys His Cys Tyr Pro
20 25

<210> 50
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> SKCa peptide inhibitor sequence - BmP05

<400> 50

Ala Val Cys Asn Leu Lys Arg Cys Gln Leu Ser Cys Arg Ser Leu Gly
1 5 10 15

Leu Leu Gly Lys Cys Ile Gly Asp Lys Cys Glu Cys Val Lys His Gly
20 25 30

<210> 51
<211> 31
<212> PRT
<213> Artificial Sequence

<220>
<223> SKCa peptide inhibitor sequence - ScyTx

<400> 51

Ala Phe Cys Asn Leu Arg Met Cys Gln Leu Ser Cys Arg Ser Leu Gly
1 5 10 15

Leu Leu Gly Lys Cys Ile Gly Asp Lys Cys Glu Cys Val Lys His
20 25 30

<210> 52
<211> 31
<212> PRT
<213> Artificial Sequence

<220>
<223> SKCa peptide inhibitor sequence - P05

<400> 52

Thr Val Cys Asn Leu Arg Arg Cys Gln Leu Ser Cys Arg Ser Leu Gly

1 5 10 15

Leu Leu Gly Lys Cys Ile Gly Val Lys Cys Glu Cys Val Lys His
20 25 30

<210> 53
<211> 31
<212> PRT
<213> Artificial Sequence

<220>
<223> SKCa peptide inhibitor sequence - Tamapin

<400> 53

Ala Phe Cys Asn Leu Arg Arg Cys Glu Leu Ser Cys Arg Ser Leu Gly
1 5 10 15

Leu Leu Gly Lys Cys Ile Gly Glu Glu Cys Lys Cys Val Pro Tyr
20 25 30

<210> 54
<211> 57
<212> PRT
<213> Artificial Sequence

<220>
<223> TsK-precursor

<400> 54

Met Lys Val Leu Tyr Gly Ile Leu Ile Ile Phe Ile Leu Cys Ser Met
1 5 10 15

Phe Tyr Leu Ser Gln Glu Val Val Ile Gly Gln Arg Cys Tyr Arg Ser
20 25 30

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

Lys Cys Thr Asn Gly Arg Cys Asp Cys
50 55

<210> 55
<211> 62
<212> PRT
<213> Artificial Sequence

<220>
<223> CoTx1

<400> 55

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

Thr Met His Thr Phe Ala Asn Trp Asn Thr Glu Ala Ala Val Cys Val
20 25 30

Tyr Arg Thr Cys Asp Lys Asp Cys Lys Arg Arg Gly Tyr Arg Ser Gly
35 40 45

Lys Cys Ile Asn Asn Ala Cys Lys Cys Tyr Pro Tyr Gly Lys
50 55 60

<210> 56
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> T type Ca channel peptide inhibitor sequence - ProTx1

<400> 56

Glu Cys Arg Tyr Trp Leu Gly Gly Cys Ser Ala Gly Gln Thr Cys Cys
1 5 10 15

Lys His Leu Val Cys Ser Arg Arg His Gly Trp Cys Val Trp Asp Gly
20 25 30

Thr Phe Ser
35

<210> 57
<211> 31
<212> PRT
<213> Artificial Sequence

<220>
<223> Kv4.3 & Kv4.2 peptide inhibitor sequence - PaTx2

<400> 57

Tyr Cys Gln Lys Trp Met Trp Thr Cys Asp Glu Glu Arg Lys Cys Cys
1 5 10 15

Glu Gly Leu Val Cys Arg Leu Trp Cys Lys Arg Ile Ile Asn Met
20 25 30

<210> 58
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Folded Des-Arg1-ShK.

<220>
<221> DISULFID
<222> (2)..(34)
<223> Folded Des-Arg1-Shk with disulfide bonds between 2-34, 51-67, and 56-71.

<220>
<221> DISULFID
<222> (11)..(27)
<223> Folded Des-Arg1-Shk with disulfide bonds between 2-34, 11-27, and

16-31.

<220>
<221> DISULFID
<222> (16)..(31)
<223> Folded Des-Arg1-Shk with disulfide bonds between 2-34, 11-27, and 16-31.

<400> 58

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 59
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Charybdotoxin (ChTx)peptide sequence - ChTx-E32

<400> 59

Gln Phe Thr Asn Val Ser Cys Thr Thr Ser Lys Glu Cys Trp Ser Val
1 5 10 15

Cys Gln Arg Leu His Asn Thr Ser Arg Gly Lys Cys Met Asn Lys Glu
20 25 30

Cys Arg Cys Tyr Ser
35

<210> 60
<211> 61
<212> PRT
<213> Artificial Sequence

<220>
<223> BmPo5-precursor

<400> 60

Met His Asn Tyr Tyr Lys Ile Val Leu Ile Met Val Ala Phe Phe Ala
1 5 10 15

Val Ile Ile Thr Phe Ser Asn Ile Gln Val Glu Gly Ala Val Cys Asn
20 25 30

Leu Lys Arg Cys Gln Leu Ser Cys Arg Ser Leu Gly Leu Leu Gly Lys
35 40 45

Cys Ile Gly Asp Lys Cys Glu Cys Val Lys His Gly Lys
50 55 60

<210> 61
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Heteromitrus spinnifer peptide sequence - HsTx1.

<400> 61

Ala Ser Cys Arg Thr Pro Lys Asp Cys Ala Asp Pro Cys Arg Lys Glu
1 5 10 15

Thr Gly Cys Pro Tyr Gly Lys Cys Met Asn Arg Lys Cys Lys Cys Asn
20 25 30

Arg Cys

<210> 62
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Kv1.3 peptide inhibitor sequence - Anuroctoxin

<400> 62

Glx Lys Glu Cys Thr Gly Pro Gln His Cys Thr Asn Phe Cys Arg Lys
1 5 10 15

Asn Lys Cys Thr His Gly Lys Cys Met Asn Arg Lys Cys Lys Cys Phe
20 25 30

Asn Cys Lys
35

<210> 63
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> M current peptide inhibitor sequence - BeKm1

<400> 63

Arg Pro Thr Asp Ile Lys Cys Ser Glu Ser Tyr Gln Cys Phe Pro Val
1 5 10 15

Cys Lys Ser Arg Phe Gly Lys Thr Asn Gly Arg Cys Val Asn Gly Phe
20 25 30

Cys Asp Cys Phe
35

<210> 64
<211> 27
<212> PRT
<213> Artificial Sequence

<220>
<223> N type Ca channel peptide inhibitor sequence - GVIA

<400> 64

Cys Lys Ser Pro Gly Ser Ser Cys Ser Pro Thr Ser Tyr Asn Cys Cys
1 5 10 15

Arg Ser Cys Asn Pro Tyr Thr Lys Arg Cys Tyr
20 25

<210> 65
<211> 25
<212> PRT
<213> Artificial Sequence

<220>
<223> N type Ca channel peptide inhibitor sequence - MVIIA

<400> 65

Cys Lys Gly Lys Gly Ala Lys Cys Ser Arg Leu Met Tyr Asp Cys Cys
1 5 10 15

Thr Gly Ser Cys Arg Ser Gly Lys Cys
20 25

<210> 66
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> N type Ca channel peptide inhibitor sequence - Ptu1

<400> 66

Ala Glu Lys Asp Cys Ile Ala Pro Gly Ala Pro Cys Phe Gly Thr Asp
1 5 10 15

Lys Pro Cys Cys Asn Pro Arg Ala Trp Cys Ser Ser Tyr Ala Asn Lys
20 25 30

Cys Leu

<210> 67
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> CI channel peptide inhibitor sequence - CTX

<400> 67

Met Cys Met Pro Cys Phe Thr Thr Asp His Gln Met Ala Arg Lys Cys
1 5 10 15

Asp Asp Cys Cys Gly Gly Lys Gly Arg Gly Lys Cys Tyr Gly Pro Gln
20 25 30

Cys Leu Cys Arg
35

<210> 68
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> SKCa peptide inhibitor sequence - Apamin

<400> 68

Cys Asn Cys Lys Ala Pro Glu Thr Ala Leu Cys Ala Arg Arg Cys Gln
1 5 10 15

Gln His Gly

<210> 69
<211> 720
<212> DNA
<213> Artificial Sequence

<220>
<223> Nucleic acid and amino acid sequences of pAMG21ampR-Fc-pep

<220>
<221> CDS
<222> (4)..(702)

<400> 69

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cat atg gac aaa act cac aca tgt cca cct tgt cca gct ccg gaa ctc       48
    Met Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
    1               5                  10                  15

ctg ggg gga ccg tca gtc ttc ctc ttc ccc cca aaa ccc aag gac acc       96
Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
                20                  25                  30

ctc atg atc tcc cgg acc cct gag gtc aca tgc gtg gtg gtg gac gtg      144
Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
            35                  40                  45

agc cac gaa gac cct gag gtc aag ttc aac tgg tac gtg gac ggc gtg      192
Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
        50                  55                  60

gag gtg cat aat gcc aag aca aag ccg cgg gag gag cag tac aac agc      240
Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
    65                  70                  75

acg tac cgt gtg gtc agc gtc ctc acc gtc ctg cac cag gac tgg ctg      288
Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
80                  85                  90                  95
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aat ggc aag gag tac aag tgc aag gtc tcc aac aaa gcc ctc cca gcc      336
Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
                100                 105                 110

ccc atc gag aaa acc atc tcc aaa gcc aaa ggg cag ccc cga gaa cca      384
Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
            115                 120                 125

cag gtg tac acc ctg ccc cca tcc cgg gat gag ctg acc aag aac cag      432
Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
        130                 135                 140

gtc agc ctg acc tgc ctg gtc aaa ggc ttc tat ccc agc gac atc gcc      480
Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
    145                 150                 155

gtg gag tgg gag agc aat ggg cag ccg gag aac aac tac aag acc acg      528
Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
160                 165                 170                 175

cct ccc gtg ctg gac tcc gac ggc tcc ttc ttc ctc tac agc aag ctc      576
Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
                180                 185                 190

acc gtg gac aag agc agg tgg cag cag ggg aac gtc ttc tca tgc tcc      624
Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
            195                 200                 205

gtg atg cat gag gct ctg cac aac cac tac acg cag aag agc ctc tcc      672
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
        210                 215                 220

ctg tct ccg ggt aaa ggt gga ggt ggt ggt tgagacgctg caggacgt          720
Leu Ser Pro Gly Lys Gly Gly Gly Gly Gly
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<210> 70
<211> 233
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 70

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1               5                   10                  15

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
            20                  25                  30

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
        35                  40                  45

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
    50                  55                  60

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
65                  70                  75                  80

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
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85 90 95

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
100 105 110

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
115 120 125

Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val
130 135 140

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
145 150 155 160

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
165 170 175

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
180 185 190

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
195 200 205

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

Ser Pro Gly Lys Gly Gly Gly Gly Gly
225 230

<210> 71
<211> 687
<212> DNA
<213> Artificial Sequence

<220>
<223> Nucleic acid and amino acid sequences of pAMG21ampR-Fc-pep. Fc domain sequences exclude the five C-terminal glycine residues.

<220>
<221> CDS
<222> (4)..(687)

<400> 71
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1 5 10 15

ctg ggg gga ccg tca gtc ttc ctc ttc ccc cca aaa ccc aag gac acc 96
Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
20 25 30

ctc atg atc tcc cgg acc cct gag gtc aca tgc gtg gtg gtg gac gtg 144
Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
35 40 45

agc cac gaa gac cct gag gtc aag ttc aac tgg tac gtg gac ggc gtg 192
Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val

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        50                  55                  60

gag gtg cat aat gcc aag aca aag ccg cgg gag gag cag tac aac agc      240
Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
    65                  70                  75

acg tac cgt gtg gtc agc gtc ctc acc gtc ctg cac cag gac tgg ctg      288
Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
80                  85                  90                  95

aat ggc aag gag tac aag tgc aag gtc tcc aac aaa gcc ctc cca gcc      336
Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
                100                 105                 110

ccc atc gag aaa acc atc tcc aaa gcc aaa ggg cag ccc cga gaa cca      384
Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
            115                 120                 125

cag gtg tac acc ctg ccc cca tcc cgg gat gag ctg acc aag aac cag      432
Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
        130                 135                 140

gtc agc ctg acc tgc ctg gtc aaa ggc ttc tat ccc agc gac atc gcc      480
Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
    145                 150                 155

gtg gag tgg gag agc aat ggg cag ccg gag aac aac tac aag acc acg      528
Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
160                 165                 170                 175

cct ccc gtg ctg gac tcc gac ggc tcc ttc ttc ctc tac agc aag ctc      576
Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
                180                 185                 190

acc gtg gac aag agc agg tgg cag cag ggg aac gtc ttc tca tgc tcc      624
Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
            195                 200                 205

gtg atg cat gag gct ctg cac aac cac tac acg cag aag agc ctc tcc      672
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
        210                 215                 220

ctg tct ccg ggt aaa                                                 687
Leu Ser Pro Gly Lys
    225
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<210> 72
<211> 228
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 72

```
Met Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
1               5                   10                  15

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
            20                  25                  30

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
        35                  40                  45
```

```
His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
    50                  55                  60

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
65                  70                  75                  80

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
                85                  90                  95

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
            100                 105                 110

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
        115                 120                 125

Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val
    130                 135                 140

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
145                 150                 155                 160

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
                165                 170                 175

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
            180                 185                 190

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
        195                 200                 205

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

Ser Pro Gly Lys
225
```

<210> 73
<211> 709
<212> DNA
<213> Artificial Sequence

<220>
<223> Nucleic acid and amino acid sequences of pAMG21ampR-Pep-Fc.

<220>
<221> CDS
<222> (4)..(699)

<400> 73

```
tca ggt ggt ggt ggt ggt gac aaa act cac aca tgc cca ccg tgc cca      48
    Gly Gly Gly Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro
    1               5                   10                  15

gca cct gaa ctc ctg ggg gga ccg tca gtc ttc ctc ttc ccc cca aaa      96
```

```
Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
                20                  25                  30

ccc aag gac acc ctc atg atc tcc cgg acc cct gag gtc aca tgc gtg      144
Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
            35                  40                  45

gtg gtg gac gtg agc cac gaa gac cct gag gtc aag ttc aac tgg tac      192
Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
        50                  55                  60

gtg gac ggc gtg gag gtg cat aat gcc aag aca aag ccg cgg gag gag      240
Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
    65                  70                  75

cag tac aac agc acg tac cgt gtg gtc agc gtc ctc acc gtc ctg cac      288
Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
80                  85                  90                  95

cag gac tgg ctg aat ggc aag gag tac aag tgc aag gtc tcc aac aaa      336
Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
                100                 105                 110

gcc ctc cca gcc ccc atc gag aaa acc atc tcc aaa gcc aaa ggg cag      384
Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
            115                 120                 125

ccc cga gaa cca cag gtg tac acc ctg ccc cca tcc cgg gat gag ctg      432
Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu
        130                 135                 140

acc aag aac cag gtc agc ctg acc tgc ctg gtc aaa ggc ttc tat ccc      480
Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
    145                 150                 155

agc gac atc gcc gtg gag tgg gag agc aat ggg cag ccg gag aac aac      528
Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
160                 165                 170                 175

tac aag acc acg cct ccc gtg ctg gac tcc gac ggc tcc ttc ttc ctc      576
Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
                180                 185                 190

tac agc aag ctc acc gtg gac aag agc agg tgg cag cag ggg aac gtc      624
Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
            195                 200                 205

ttc tca tgc tcc gtg atg cat gag gct ctg cac aac cac tac acg cag      672
Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
        210                 215                 220

aag agc ctc tcc ctg tct ccg ggt aaa taatggatcc                      709
Lys Ser Leu Ser Leu Ser Pro Gly Lys
    225                 230
```

<210> 74
<211> 232
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 74

```
Gly Gly Gly Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
1               5                   10                  15
```

```
Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
            20                  25                  30

Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
        35                  40                  45

Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
    50                  55                  60

Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
65                  70                  75                  80

Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
                85                  90                  95

Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
            100                 105                 110

Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
        115                 120                 125

Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr
    130                 135                 140

Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
145                 150                 155                 160

Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
                165                 170                 175

Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
            180                 185                 190

Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
        195                 200                 205

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

Ser Leu Ser Leu Ser Pro Gly Lys
225                 230
```

<210> 75
<211> 691
<212> DNA
<213> Artificial Sequence

<220>
<223> Nucleic acid and amino acid sequences of pAMG21ampR-Pep-Fc. The Fc domain sequences exclude the five N-terminal glycine residues.

<220>
<221> CDS
<222> (1)..(681)

<400> 75

```
gac aaa act cac aca tgc cca ccg tgc cca gca cct gaa ctc ctg ggg        48
Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
1               5                  10                  15

gga ccg tca gtc ttc ctc ttc ccc cca aaa ccc aag gac acc ctc atg        96
Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
            20                  25                  30

atc tcc cgg acc cct gag gtc aca tgc gtg gtg gtg gac gtg agc cac       144
Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
        35                  40                  45

gaa gac cct gag gtc aag ttc aac tgg tac gtg gac ggc gtg gag gtg       192
Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
    50                  55                  60

cat aat gcc aag aca aag ccg cgg gag gag cag tac aac agc acg tac       240
His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
65                  70                  75                  80

cgt gtg gtc agc gtc ctc acc gtc ctg cac cag gac tgg ctg aat ggc       288
Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
                85                  90                  95

aag gag tac aag tgc aag gtc tcc aac aaa gcc ctc cca gcc ccc atc       336
Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
            100                 105                 110

gag aaa acc atc tcc aaa gcc aaa ggg cag ccc cga gaa cca cag gtg       384
Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
        115                 120                 125

tac acc ctg ccc cca tcc cgg gat gag ctg acc aag aac cag gtc agc       432
Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
    130                 135                 140

ctg acc tgc ctg gtc aaa ggc ttc tat ccc agc gac atc gcc gtg gag       480
Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
145                 150                 155                 160

tgg gag agc aat ggg cag ccg gag aac aac tac aag acc acg cct ccc       528
Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
                165                 170                 175

gtg ctg gac tcc gac ggc tcc ttc ttc ctc tac agc aag ctc acc gtg       576
Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
            180                 185                 190

gac aag agc agg tgg cag cag ggg aac gtc ttc tca tgc tcc gtg atg       624
Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
        195                 200                 205

cat gag gct ctg cac aac cac tac acg cag aag agc ctc tcc ctg tct       672
His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
    210                 215                 220

ccg ggt aaa taatggatcc                                                691
Pro Gly Lys
225
```

<210> 76
<211> 227

<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 76

```
Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
1               5                  10                  15

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
            20                  25                  30

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
        35                  40                  45

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
    50                  55                  60

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
65                  70                  75                  80

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
                85                  90                  95

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
            100                 105                 110

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
        115                 120                 125

Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
    130                 135                 140

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
145                 150                 155                 160

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
                165                 170                 175

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
            180                 185                 190

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
        195                 200                 205

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
    210                 215                 220

Pro Gly Lys
225
```

<210> 77
<211> 879
<212> DNA
<213> Artificial Sequence

<220>
<223> Nucleotide and amino acid sequences of molecule Fc-L10-ShK [1-35].

<220>
<221> CDS
<222> (1)..(879)

<400> 77

```
atg gaa tgg agc tgg gtc ttt ctc ttc ttc ctg tca gta acg act ggt        48
Met Glu Trp Ser Trp Val Phe Leu Phe Phe Leu Ser Val Thr Thr Gly
1               5                  10                  15

gtc cac tcc gac aaa act cac aca tgc cca ccg tgc cca gca cct gaa        96
Val His Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
            20                  25                  30

ctc ctg ggg gga ccg tca gtc ttc ctc ttc ccc cca aaa ccc aag gac       144
Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
        35                  40                  45

acc ctc atg atc tcc cgg acc cct gag gtc aca tgc gtg gtg gtg gac       192
Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
    50                  55                  60

gtg agc cac gaa gac cct gag gtc aag ttc aac tgg tac gtg gac ggc       240
Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
65                  70                  75                  80

gtg gag gtg cat aat gcc aag aca aag ccg cgg gag gag cag tac aac       288
Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
                85                  90                  95

agc acg tac cgt gtg gtc agc gtc ctc acc gtc ctg cac cag gac tgg       336
Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
            100                 105                 110

ctg aat ggc aag gag tac aag tgc aag gtc tcc aac aaa gcc ctc cca       384
Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
        115                 120                 125

gcc ccc atc gag aaa acc atc tcc aaa gcc aaa ggg cag ccc cga gaa       432
Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
    130                 135                 140

cca cag gtg tac acc ctg ccc cca tcc cgg gat gag ctg acc aag aac       480
Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
145                 150                 155                 160

cag gtc agc ctg acc tgc ctg gtc aaa ggc ttc tat ccc agc gac atc       528
Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
                165                 170                 175

gcc gtg gag tgg gag agc aat ggg cag ccg gag aac aac tac aag acc       576
Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
            180                 185                 190

acg cct ccc gtg ctg gac tcc gac ggc tcc ttc ttc ctc tac agc aag       624
Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
        195                 200                 205

ctc acc gtg gac aag agc agg tgg cag cag ggg aac gtc ttc tca tgc       672
```

```
Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
    210                 215                 220

tcc gtg atg cat gag gct ctg cac aac cac tac acg cag aag agc ctc      720
Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
225                 230                 235                 240

tcc ctg tct ccg ggt aaa gga gga gga gga tcc gga gga gga gga agc      768
Ser Leu Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
                245                 250                 255

cgc agc tgc atc gac acc atc ccc aag agc cgc tgc acc gcc ttc cag      816
Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
            260                 265                 270

tgc aag cac agc atg aag tac cgc ctg agc ttc tgc cgc aag acc tgc      864
Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
        275                 280                 285

ggc acc tgc taa tga                                                  879
Gly Thr Cys
    290
```

<210> 78
<211> 291
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 78

```
Met Glu Trp Ser Trp Val Phe Leu Phe Phe Leu Ser Val Thr Thr Gly
1               5                   10                  15

Val His Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
            20                  25                  30

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

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
    50                  55                  60

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
65                  70                  75                  80

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
                85                  90                  95

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
            100                 105                 110

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

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
    130                 135                 140
```

```
Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
145                 150                 155                 160

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
                165                 170                 175

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
            180                 185                 190

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
        195                 200                 205

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
    210                 215                 220

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
225                 230                 235                 240

Ser Leu Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
                245                 250                 255

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
            260                 265                 270

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
        275                 280                 285

Gly Thr Cys
    290
```

<210> 79
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> L10 linker amino acid sequence used in Fc-L10-ShK [1-35].

<400> 79

```
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
1               5                   10
```

<210> 80
<211> 873
<212> DNA
<213> Artificial Sequence

<220>
<223> Nucleotide and amino acid sequences of molecule Fc-L10-ShK [2-35].

<220>
<221> CDS

<222> (1)..(873)

<400> 80

```
atg gaa tgg agc tgg gtc ttt ctc ttc ttc ctg tca gta acg act ggt       48
Met Glu Trp Ser Trp Val Phe Leu Phe Phe Leu Ser Val Thr Thr Gly
1               5                  10                  15

gtc cac tcc gac aaa act cac aca tgc cca ccg tgc cca gca cct gaa       96
Val His Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
            20                  25                  30

ctc ctg ggg gga ccg tca gtc ttc ctc ttc ccc cca aaa ccc aag gac      144
Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
        35                  40                  45

acc ctc atg atc tcc cgg acc cct gag gtc aca tgc gtg gtg gtg gac      192
Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
    50                  55                  60

gtg agc cac gaa gac cct gag gtc aag ttc aac tgg tac gtg gac ggc      240
Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
65                  70                  75                  80

gtg gag gtg cat aat gcc aag aca aag ccg cgg gag gag cag tac aac      288
Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
                85                  90                  95

agc acg tac cgt gtg gtc agc gtc ctc acc gtc ctg cac cag gac tgg      336
Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
            100                 105                 110

ctg aat ggc aag gag tac aag tgc aag gtc tcc aac aaa gcc ctc cca      384
Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
        115                 120                 125

gcc ccc atc gag aaa acc atc tcc aaa gcc aaa ggg cag ccc cga gaa      432
Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
    130                 135                 140

cca cag gtg tac acc ctg ccc cca tcc cgg gat gag ctg acc aag aac      480
Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
145                 150                 155                 160

cag gtc agc ctg acc tgc ctg gtc aaa ggc ttc tat ccc agc gac atc      528
Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
                165                 170                 175

gcc gtg gag tgg gag agc aat ggg cag ccg gag aac aac tac aag acc      576
Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
            180                 185                 190

acg cct ccc gtg ctg gac tcc gac ggc tcc ttc ttc ctc tac agc aag      624
Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
        195                 200                 205

ctc acc gtg gac aag agc agg tgg cag cag ggg aac gtc ttc tca tgc      672
Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
    210                 215                 220

tcc gtg atg cat gag gct ctg cac aac cac tac acg cag aag agc ctc      720
Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
225                 230                 235                 240

tcc ctg tct ccg ggt aaa gga gga gga gga tcc gga gga gga gga agc      768
Ser Leu Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
                245                 250                 255

agc tgc atc gac acc atc ccc aag agc cgc tgc acc gcc ttc cag tgc      816
```

```
Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys
            260                 265                 270

aag cac agc atg aag tac cgc ctg agc ttc tgc cgc aag acc tgc ggc      864
Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
        275                 280                 285

acc tgc taa                                                          873
Thr Cys
    290
```

<210> 81
<211> 290
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 81

```
Met Glu Trp Ser Trp Val Phe Leu Phe Phe Leu Ser Val Thr Thr Gly
1               5                  10                  15

Val His Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
            20                  25                  30

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

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
    50                  55                  60

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
65                  70                  75                  80

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
                85                  90                  95

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
            100                 105                 110

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

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
    130                 135                 140

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

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
                165                 170                 175

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
            180                 185                 190
```

```
Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
        195                 200                 205

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
    210                 215                 220

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
225                 230                 235                 240

Ser Leu Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
                245                 250                 255

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys
            260                 265                 270

Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
        275                 280                 285

Thr Cys
    290
```

<210> 82
<211> 918
<212> DNA
<213> Artificial Sequence

<220>
<223> Nucleotide and amino acid sequences of molecule Fc-L25-ShK [2-35].

<220>
<221> CDS
<222> (1)..(918)

<400> 82

```
atg gaa tgg agc tgg gtc ttt ctc ttc ttc ctg tca gta acg act ggt       48
Met Glu Trp Ser Trp Val Phe Leu Phe Phe Leu Ser Val Thr Thr Gly
1               5                   10                  15

gtc cac tcc gac aaa act cac aca tgc cca ccg tgc cca gca cct gaa       96
Val His Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
            20                  25                  30

ctc ctg ggg gga ccg tca gtc ttc ctc ttc ccc cca aaa ccc aag gac      144
Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
        35                  40                  45

acc ctc atg atc tcc cgg acc cct gag gtc aca tgc gtg gtg gtg gac      192
Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
    50                  55                  60

gtg agc cac gaa gac cct gag gtc aag ttc aac tgg tac gtg gac ggc      240
Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
65                  70                  75                  80

gtg gag gtg cat aat gcc aag aca aag ccg cgg gag gag cag tac aac      288
Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
                85                  90                  95
```

```
agc acg tac cgt gtg gtc agc gtc ctc acc gtc ctg cac cag gac tgg      336
Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
            100                 105                 110

ctg aat ggc aag gag tac aag tgc aag gtc tcc aac aaa gcc ctc cca      384
Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
        115                 120                 125

gcc ccc atc gag aaa acc atc tcc aaa gcc aaa ggg cag ccc cga gaa      432
Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
    130                 135                 140

cca cag gtg tac acc ctg ccc cca tcc cgg gat gag ctg acc aag aac      480
Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
145                 150                 155                 160

cag gtc agc ctg acc tgc ctg gtc aaa ggc ttc tat ccc agc gac atc      528
Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
                165                 170                 175

gcc gtg gag tgg gag agc aat ggg cag ccg gag aac aac tac aag acc      576
Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
            180                 185                 190

acg cct ccc gtg ctg gac tcc gac ggc tcc ttc ttc ctc tac agc aag      624
Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
        195                 200                 205

ctc acc gtg gac aag agc agg tgg cag cag ggg aac gtc ttc tca tgc      672
Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
    210                 215                 220

tcc gtg atg cat gag gct ctg cac aac cac tac acg cag aag agc ctc      720
Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
225                 230                 235                 240

tcc ctg tct ccg ggt aaa gga gga gga gga tcc ggg ggt ggg ggt tct      768
Ser Leu Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
                245                 250                 255

ggg ggt ggg ggt tct gga gga gga gga agc gga gga gga gga agc agc      816
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ser
            260                 265                 270

tgc atc gac acc atc ccc aag agc cgc tgc acc gcc ttc cag tgc aag      864
Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys Lys
        275                 280                 285

cac agc atg aag tac cgc ctg agc ttc tgc cgc aag acc tgc ggc acc      912
His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly Thr
    290                 295                 300

tgc taa                                                             918
Cys
305
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<210> 83
<211> 305
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 83

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Met Glu Trp Ser Trp Val Phe Leu Phe Phe Leu Ser Val Thr Thr Gly
1               5                  10                  15

Val His Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
            20                  25                  30

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

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
    50                  55                  60

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
65                  70                  75                  80

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
                85                  90                  95

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
            100                 105                 110

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

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
    130                 135                 140

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

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
                165                 170                 175

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
            180                 185                 190

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
        195                 200                 205

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
    210                 215                 220

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
225                 230                 235                 240

Ser Leu Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
                245                 250                 255

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ser
            260                 265                 270
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Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys Lys
275 280 285

His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly Thr
290 295 300

Cys
305

<210> 84
<211> 25
<212> PRT
<213> Artificial Sequence

<220>
<223> L-25 linker amino acid sequence used in Fc-L25-ShK [2-35].

<400> 84

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser Gly Gly Gly Gly Ser
20 25

<210> 85
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Kv1.3 peptide inhibitor sequence - AgTx1

<400> 85

Gly Val Pro Ile Asn Val Lys Cys Thr Gly Ser Pro Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Ile Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 86
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Kvt1.3 peptide inhibitor sequence - Titystoxin-Ka

<400> 86

Val Phe Ile Asn Ala Lys Cys Arg Gly Ser Pro Glu Cys Leu Pro Lys
1 5 10 15

Cys Lys Glu Ala Ile Gly Lys Ala Ala Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Lys Cys Tyr Pro
35

<210> 87
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Kvt1.3 peptide inhibitor sequence - Tc30

<400> 87

Val Phe Ile Asn Val Lys Cys Arg Gly Ser Lys Glu Cys Leu Pro Ala
1 5 10 15

Cys Lys Ala Ala Val Gly Lys Ala Ala Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Lys Cys Tyr Pro
35

<210> 88
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-S17/S32

<400> 88

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Ser Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Ser
20 25 30

Gly Thr Cys
35

<210> 89
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-S3/S35

<400> 89

Arg Ser Ser Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Ser
35

<210> 90
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-S1

<400> 90

Ser Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 91
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-N-acetylarg1

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> N-acetylarginine

<400> 91

Xaa Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 92
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-d1

<400> 92

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 93
<211> 33
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-d2

<400> 93

Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys Lys
1 5 10 15

His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly Thr
20 25 30

Cys

<210> 94
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A1

<400> 94

Ala Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 95
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A4

<400> 95

Arg Ser Cys Ala Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 96
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A4/A15

<400> 96

Arg Ser Cys Ala Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Ala Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 97
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A4/A15/A25

<400> 97

Arg Ser Cys Ala Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Ala Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Ala Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 98
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A6

<400> 98

Arg Ser Cys Ile Asp Ala Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 99
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A7

<400> 99

Arg Ser Cys Ile Asp Thr Ala Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 100
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - Shk-A8

<400> 100

Arg Ser Cys Ile Asp Thr Ile Ala Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 101
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A9

<400> 101

Arg Ser Cys Ile Asp Thr Ile Pro Ala Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 102
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-E9

<400> 102

Arg Ser Cys Ile Asp Thr Ile Pro Glu Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 103
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-Q9

<400> 103

Arg Ser Cys Ile Asp Thr Ile Pro Gln Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 104
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A10

<400> 104

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ala Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 105
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A11

<400> 105

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Ala Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 106
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-E11

<400> 106

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Glu Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 107
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-Q11

<400> 107

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Gln Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 108
<211> 35

<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A13

<400> 108

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Ala Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 109
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A15

<400> 109

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Ala Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 110
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-W15

<400> 110

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Trp Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 111
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-X15

<220>
<221> MISC_FEATURE
<222> (15)..(15)
<223> Any nonfunctional amino acid residue

<400> 111

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Xaa Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 112
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A15/A25

<400> 112

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Ala Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Ala Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 113
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A16

<400> 113

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Ala
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 114
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-E16

<400> 114

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Glu
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 115
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A18

<400> 115

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Ala His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 116
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-E18

<400> 116

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Glu His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 117
<211> 35

<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A19

<400> 117

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys Ala Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 118
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-K19

<400> 118

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys Lys Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 119
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A20

<400> 119

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ala Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 120
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A21

<400> 120

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Ala Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 121
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-X21

<220>
<221> MISC_FEATURE
<222> (21)..(21)
<223> Any nonfunctional amino acid residue.

<400> 121

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Xaa Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 122
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-Nle21

<220>
<221> MISC_FEATURE
<222> (21)..(21)
<223> Xaa is norleucine.

<400> 122

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Xaa Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 123
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A22

<400> 123

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 124
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-E22

<400> 124

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Glu Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 125
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-R22

<400> 125

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Arg Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 126
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-X22

<220>
<221> MISC_FEATURE
<222> (22)..(22)
<223> Any nonfunctional amino acid residue

<400> 126

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Xaa Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 127
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-Nle22

<220>
<221> MISC_FEATURE
<222> (22)..(22)
<223> Xaa is Norleucine.

<400> 127

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Xaa Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 128
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-Orn22

<220>
<221> MISC_FEATURE
<222> (22)..(22)
<223> Xaa is Ornithine.

<400> 128

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Xaa Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 129
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-Homocit22

<220>
<221> MISC_FEATURE
<222> (22)..(22)
<223> Xaa is homocitrulline.

<400> 129

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Xaa Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 130
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-Diaminopropionic22

<220>
<221> MISC_FEATURE
<222> (22)..(22)
<223> Xaa is diaminopropionic acid.

<400> 130

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Xaa Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 131
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A23

<400> 131

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Lys Ala Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 132
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-S23

<400> 132

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Lys Ser Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 133
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-F23

<400> 133

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Lys Phe Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 134
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-X23

<220>
<221> MISC_FEATURE
<222> (23)..(23)
<223> Any nonfunctional amino acid residue.

<400> 134

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Lys Xaa Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 135
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-Nitrophe23

<220>
<221> MISC_FEATURE
<222> (23)..(23)
<223> Nitrophenylalanine

<400> 135

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Lys Xaa Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 136
<211> 35
<212> PRT
<213> Artificial Sequence

<220>

<223> ShK peptide sequence - ShK-aminopheala23

<220>
<221> MISC_FEATURE
<222> (23)..(23)
<223> Xaa is aminophenylalanine.

<400> 136

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Lys Xaa Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 137
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence -ShK-Benzoylpheala23

<220>
<221> MISC_FEATURE
<222> (23)..(23)
<223> Xaa is benzoylphenylalanine.

<400> 137

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Lys Xaa Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 138
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A24

<400> 138

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Ala Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 139
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-E24

<400> 139

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Glu Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 140
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A25

<400> 140

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Ala Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 141
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A26

<400> 141

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ala Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 142
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A27

<400> 142

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Ala Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 143
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-X27

<220>
<221> MISC_FEATURE
<222> (27)..(27)
<223> Xaa is any nonfunctional amino acid residue.

<400> 143

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Xaa Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 144
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A29

<400> 144

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Ala Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 145
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A30

<400> 145

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Ala Thr Cys
20 25 30

Gly Thr Cys
35

<210> 146
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A31

<400> 146

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Ala Cys
20 25 30

Gly Thr Cys
35

<210> 147
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A34

<400> 147

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Ala Cys
35

<210> 148
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A4d1

<400> 148

Ser Cys Ala Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 149
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A4/A15d1

<400> 149

Ser Cys Ala Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Ala Gln Cys
1 5 10 15

Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 150
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A4/A15/A25 d1

<400> 150

Ser Cys Ala Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Ala Gln Cys
1 5 10 15

Lys His Ser Met Lys Tyr Arg Ala Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 151
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A6 d1

<400> 151

Ser Cys Ile Asp Ala Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 152
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A7 d1

<400> 152

Ser Cys Ile Asp Thr Ala Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 153
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A8 d1

<400> 153

Ser Cys Ile Asp Thr Ile Ala Lys Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 154
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A9 d1

<400> 154

Ser Cys Ile Asp Thr Ile Pro Ala Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 155
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-E9 d1

<400> 155

Ser Cys Ile Asp Thr Ile Pro Glu Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 156
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-Q9 d1

<400> 156

Ser Cys Ile Asp Thr Ile Pro Gln Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 157
<211> 34

<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A10 d1

<400> 157

Ser Cys Ile Asp Thr Ile Pro Lys Ala Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 158
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A11 d1

<400> 158

Ser Cys Ile Asp Thr Ile Pro Lys Ser Ala Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 159
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-E11 d1

<400> 159

Ser Cys Ile Asp Thr Ile Pro Lys Ser Glu Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 160
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-Q11 d1

<400> 160

Ser Cys Ile Asp Thr Ile Pro Lys Ser Gln Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 161
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A13 d1

<400> 161

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Ala Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 162
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A15 d1

<400> 162

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Ala Gln Cys
1 5 10 15

Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 163
<211> 34
<212> PRT
<213> Artificial Sequence

<220>

<223> ShK peptide sequence - ShK-W15 d1

<400> 163

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Trp Gln Cys
1 5 10 15

Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 164
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-X15 d1

<220>
<221> MISC_FEATURE
<222> (14)..(14)
<223> Xaa is any nonfunctional amino acid residue.

<400> 164

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Xaa Gln Cys
1 5 10 15

Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 165
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A15/A25 d1

<400> 165

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Ala Gln Cys
1 5 10 15

Lys His Ser Met Lys Tyr Arg Ala Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 166
<211> 34

<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A16 d1

<400> 166

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Ala Cys
1 5 10 15

Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 167
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-E16 d1

<400> 167

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Glu Cys
1 5 10 15

Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 168
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A18 d1

<400> 168

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Ala His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 169
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-E18 d1

<400> 169

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Glu His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 170
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A19 d1

<400> 170

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys Ala Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 171
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-K19 d1

<400> 171

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys Lys Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 172
<211> 34
<212> PRT
<213> Artificial Sequence

<220>

<223> ShK peptide sequence - ShK-A20 d1

<400> 172

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ala Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 173
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A21 d1

<400> 173

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Ala Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 174
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-X21 d1

<220>
<221> MISC_FEATURE
<222> (20)..(20)
<223> Xaa is any nonfunctional amino acid residue.

<400> 174

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Xaa Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 175
<211> 34

<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-Nle21 d1

<220>
<221> MISC_FEATURE
<222> (20)..(20)
<223> Xaa is norleucine.

<400> 175

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Xaa Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 176
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A22 d1

<400> 176

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 177
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-E22 d1

<400> 177

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Glu Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 178
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-R22 d1

<400> 178

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Arg Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 179
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-X22 d1

<220>
<221> MISC_FEATURE
<222> (21)..(21)
<223> Xaa is any nonfunctional amino acid residue.

<400> 179

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Xaa Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 180
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-Nle22 d1

<220>
<221> MISC_FEATURE
<222> (21)..(21)
<223> Xaa is norleucine.

<400> 180

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Xaa Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 181
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-Orn22 d1

<220>
<221> MISC_FEATURE
<222> (21)..(21)
<223> Xaa is ornithine.

<400> 181

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Xaa Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 182
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-Homocit22 d1

<220>
<221> MISC_FEATURE
<222> (21)..(21)
<223> Xaa is homocitrulline.

<400> 182

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Xaa Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 183
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-Diaminopropionic22 d1

<220>
<221> MISC_FEATURE
<222> (21)..(21)
<223> Xaa is diaminopropionic acid.

<400> 183

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Xaa Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 184
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A23 d1

<400> 184

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Lys Ala Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 185
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-S23 d1

<400> 185

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Lys Ser Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 186
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-F23 d1

<400> 186

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Lys Phe Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 187
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-X23 d1

<220>
<221> MISC_FEATURE
<222> (22)..(22)
<223> Xaa is any nonfunctional amino acid residue.

<400> 187

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Lys Xaa Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 188
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - - ShK-Nitrophe23 d1

<220>
<221> MISC_FEATURE
<222> (22)..(22)
<223> Xaa is nitrophenaylalanine.

<400> 188

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Lys Xaa Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 189
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-Aminopheala23 d1

<220>
<221> MISC_FEATURE
<222> (22)..(22)
<223> Xaa is aminophenylalanine.

<400> 189

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Lys Xaa Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 190
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-Benzoylpheala23 d1

<220>
<221> MISC_FEATURE
<222> (22)..(22)
<223> Xaa is benzoylphenylalanine.

<400> 190

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Lys Xaa Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 191
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A24 d1

<400> 191

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Lys Tyr Ala Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 192
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-E24 d1

<400> 192

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Lys Tyr Glu Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 193
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - - ShK-A25 d1

<400> 193

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Lys Tyr Arg Ala Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 194
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A26 d1

<400> 194

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Lys Tyr Arg Leu Ala Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 195
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A27 d1

<400> 195

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Lys Tyr Arg Leu Ser Ala Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 196
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-X27 d1

<220>
<221> MISC_FEATURE
<222> (26)..(26)
<223> Xaa is any nonfunctional amino acid residue.

<400> 196

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Lys Tyr Arg Leu Ser Xaa Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 197
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A29 d1

<400> 197

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Ala Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 198
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A30 d1

<400> 198

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Ala Thr Cys Gly
20 25 30

Thr Cys

<210> 199
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A31 d1

<400> 199

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Ala Cys Gly
20 25 30

Thr Cys

<210> 200
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-A34 d1

<400> 200

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Ala Cys

<210> 201
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> HmK peptide sequence - HmK-A1

<400> 201

Ala Thr Cys Lys Asp Leu Ile Pro Val Ser Glu Cys Thr Asp Ile Arg
1 5 10 15

Cys Arg Thr Ser Met Lys Tyr Arg Leu Asn Leu Cys Arg Lys Thr Cys
20 25 30

Gly Ser Cys
35

<210> 202
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> HmK peptide sequence - HmK-S1

<400> 202

Ser Thr Cys Lys Asp Leu Ile Pro Val Ser Glu Cys Thr Asp Ile Arg
1 5 10 15

Cys Arg Thr Ser Met Lys Tyr Arg Leu Asn Leu Cys Arg Lys Thr Cys
20 25 30

Gly Ser Cys
35

<210> 203
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> HmK peptide sequence - HmK-d1

<400> 203

Thr Cys Lys Asp Leu Ile Pro Val Ser Glu Cys Thr Asp Ile Arg Cys
1 5 10 15

Arg Thr Ser Met Lys Tyr Arg Leu Asn Leu Cys Arg Lys Thr Cys Gly
20 25 30

Ser Cys

<210> 204
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> HmK peptide sequence - HmK-d1/S2

<400> 204

Ser Cys Lys Asp Leu Ile Pro Val Ser Glu Cys Thr Asp Ile Arg Cys
1 5 10 15

Arg Thr Ser Met Lys Tyr Arg Leu Asn Leu Cys Arg Lys Thr Cys Gly
20 25 30

Ser Cys

<210> 205
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> HmK peptide sequence - HmK-d1/I4

<400> 205

Thr Cys Ile Asp Leu Ile Pro Val Ser Glu Cys Thr Asp Ile Arg Cys
1 5 10 15

Arg Thr Ser Met Lys Tyr Arg Leu Asn Leu Cys Arg Lys Thr Cys Gly
20 25 30

Ser Cys

<210> 206
<211> 34

<212> PRT
<213> Artificial Sequence

<220>
<223> HmK peptide sequence - HmK-d1T6

<400> 206

Thr Cys Lys Asp Thr Ile Pro Val Ser Glu Cys Thr Asp Ile Arg Cys
1 5 10 15

Arg Thr Ser Met Lys Tyr Arg Leu Asn Leu Cys Arg Lys Thr Cys Gly
20 25 30

Ser Cys

<210> 207
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> HmK peptide sequence - HmK-d1/K9

<400> 207

Thr Cys Lys Asp Leu Ile Pro Lys Ser Glu Cys Thr Asp Ile Arg Cys
1 5 10 15

Arg Thr Ser Met Lys Tyr Arg Leu Asn Leu Cys Arg Lys Thr Cys Gly
20 25 30

Ser Cys

<210> 208
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> HmK peptide sequence - HmK-d1/R11

<400> 208

Thr Cys Lys Asp Leu Ile Pro Val Ser Arg Cys Thr Asp Ile Arg Cys
1 5 10 15

Arg Thr Ser Met Lys Tyr Arg Leu Asn Leu Cys Arg Lys Thr Cys Gly
20 25 30

Ser Cys

<210> 209
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> HmK peptide sequence - HmK-d1/A14

<400> 209

Thr Cys Lys Asp Leu Ile Pro Val Ser Glu Cys Thr Ala Ile Arg Cys
1 5 10 15

Arg Thr Ser Met Lys Tyr Arg Leu Asn Leu Cys Arg Lys Thr Cys Gly
20 25 30

Ser Cys

<210> 210
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> HmK peptide sequence - HmK-d1/F15

<400> 210

Thr Cys Lys Asp Leu Ile Pro Val Ser Glu Cys Thr Asp Phe Arg Cys
1 5 10 15

Arg Thr Ser Met Lys Tyr Arg Leu Asn Leu Cys Arg Lys Thr Cys Gly
20 25 30

Ser Cys

<210> 211
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> HmK peptide sequence - HmK-d1/Q16

<400> 211

Thr Cys Lys Asp Leu Ile Pro Val Ser Glu Cys Thr Asp Ile Gln Cys
1 5 10 15

Arg Thr Ser Met Lys Tyr Arg Leu Asn Leu Cys Arg Lys Thr Cys Gly
20 25 30

Ser Cys

<210> 212
<211> 34
<212> PRT
<213> Artificial Sequence

<220>

<223> HmK peptide sequence - HmK-d1/K18

<400> 212

Thr Cys Lys Asp Leu Ile Pro Val Ser Glu Cys Thr Asp Ile Arg Cys
1 5 10 15

Lys Thr Ser Met Lys Tyr Arg Leu Asn Leu Cys Arg Lys Thr Cys Gly
20 25 30

Ser Cys

<210> 213
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> HmK peptide sequence - HmK-d1/H19

<400> 213

Thr Cys Lys Asp Leu Ile Pro Val Ser Glu Cys Thr Asp Ile Arg Cys
1 5 10 15

Arg His Ser Met Lys Tyr Arg Leu Asn Leu Cys Arg Lys Thr Cys Gly
20 25 30

Ser Cys

<210> 214
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> HmK peptide sequence - HmK-d1/S26

<400> 214

Thr Cys Lys Asp Leu Ile Pro Val Ser Glu Cys Thr Asp Ile Arg Cys
1 5 10 15

Arg Thr Ser Met Lys Tyr Arg Leu Ser Leu Cys Arg Lys Thr Cys Gly
20 25 30

Ser Cys

<210> 215
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> HmK peptide sequence - HmK-d1/F27

<400> 215

Thr Cys Lys Asp Leu Ile Pro Val Ser Glu Cys Thr Asp Ile Arg Cys
1 5 10 15

Arg Thr Ser Met Lys Tyr Arg Leu Asn Phe Cys Arg Lys Thr Cys Gly
20 25 30

Ser Cys

<210> 216
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> HmK peptide sequence - HmK-d1/T34

<400> 216

Thr Cys Lys Asp Leu Ile Pro Val Ser Glu Cys Thr Asp Ile Arg Cys
1 5 10 15

Arg Thr Ser Met Lys Tyr Arg Leu Asn Leu Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 217
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> HmK peptide sequence - HmK-d1/R11/F27

<400> 217

Thr Cys Lys Asp Leu Ile Pro Val Ser Arg Cys Thr Asp Ile Arg Cys
1 5 10 15

Arg Thr Ser Met Lys Tyr Arg Leu Asn Phe Cys Arg Lys Thr Cys Gly
20 25 30

Ser Cys

<210> 218
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> HmK peptide sequence - HmK-A1/R11/F27

<400> 218

Ala Thr Cys Lys Asp Leu Ile Pro Val Ser Arg Cys Thr Asp Ile Arg
1 5 10 15

Cys Arg Thr Ser Met Lys Tyr Arg Leu Asn Phe Cys Arg Lys Thr Cys
20 25 30

Gly Ser Cys
35

<210> 219
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> HmK peptide sequence - HmK-d1/Z1

<400> 219

Thr Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Ser Cys

<210> 220
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> HmK peptide sequence - HmK-d1/Z2

<400> 220

Thr Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Arg Thr Ser Met Lys Tyr Arg Leu Asn Phe Cys Arg Lys Thr Cys Gly
20 25 30

Ser Cys

<210> 221
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> HmK peptide sequence - HmK-d1Z3

<400> 221

Thr Cys Ala Asp Leu Ile Pro Ala Ser Arg Cys Thr Ala Ile Ala Cys
1 5 10 15

Arg Thr Ser Met Lys Tyr Arg Leu Asn Phe Cys Arg Lys Thr Cys Gly
20 25 30

Ser Cys

<210> 222
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> HmK peptide sequence - HmK-d1/Z4

<400> 222

Thr Cys Ala Asp Leu Ile Pro Ala Ser Arg Cys Thr Ala Ile Ala Cys
1 5 10 15

Lys His Ser Met Lys Tyr Arg Leu Asn Phe Cys Arg Lys Thr Cys Gly
20 25 30

Ser Cys

<210> 223
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> HmK peptide sequence - HmK-d1/Z5

<400> 223

Thr Cys Ala Asp Leu Ile Pro Ala Ser Arg Cys Thr Ala Ile Ala Cys
1 5 10 15

Ala His Ser Met Lys Tyr Arg Leu Asn Phe Cys Arg Lys Thr Cys Gly
20 25 30

Ser Cys

<210> 224
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> HmK peptide sequence - HmK-X22

<220>
<221> MISC_FEATURE
<222> (22)..(22)
<223> Xaa is a nonfunctional amino acid residue.

<400> 224

Arg Thr Cys Lys Asp Leu Ile Pro Val Ser Glu Cys Thr Asp Ile Arg
1 5 10 15

Cys Arg Thr Ser Met Xaa Tyr Arg Leu Asn Leu Cys Arg Lys Thr Cys
20 25 30

Gly Ser Cys
35

<210> 225
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> HmK peptide sequence - HmK-X6,22,26

<220>
<221> MISC_FEATURE
<222> (7)..(7)
<223> Xaa in positions 7, 23, and 27 are each independently nonfunctional amino acid residues.

<220>
<221> MISC_FEATURE
<222> (23)..(23)
<223> Xaa in positions 7, 23, and 27 are each independently nonfunctional amino acid residues.

<220>
<221> MISC_FEATURE
<222> (27)..(27)
<223> Xaa in positions 7, 23, and 27 are each independently nonfunctional amino acid residues.

<400> 225

Ala Thr Cys Lys Asp Leu Xaa Pro Val Ser Arg Cys Thr Asp Ile Arg
1 5 10 15

Cys Arg Thr Ser Met Lys Xaa Arg Leu Asn Xaa Cys Arg Lys Thr Cys
20 25 30

Gly Ser Cys
35

<210> 226
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> BgK peptide sequence - BhK-A1

<400> 226

Ala Cys Arg Asp Trp Phe Lys Glu Thr Ala Cys Arg His Ala Lys Ser
1 5 10 15

Leu Gly Asn Cys Arg Thr Ser Gln Lys Tyr Arg Ala Asn Cys Ala Lys
20 25 30

Thr Cys Glu Leu Cys
35

<210> 227
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> BgK peptide sequence - BgK-A3

<400> 227

Val Cys Ala Asp Trp Phe Lys Glu Thr Ala Cys Arg His Ala Lys Ser
1 5 10 15

Leu Gly Asn Cys Arg Thr Ser Gln Lys Tyr Arg Ala Asn Cys Ala Lys
20 25 30

Thr Cys Glu Leu Cys
35

<210> 228
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> BgK peptide sequence - BgK-A5

<400> 228

Val Cys Arg Asp Ala Phe Lys Glu Thr Ala Cys Arg His Ala Lys Ser
1 5 10 15

Leu Gly Asn Cys Arg Thr Ser Gln Lys Tyr Arg Ala Asn Cys Ala Lys
20 25 30

Thr Cys Glu Leu Cys
35

<210> 229
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> BgK peptide sequence - BgK-A8

<400> 229

Val Cys Arg Asp Trp Phe Lys Ala Thr Ala Cys Arg His Ala Lys Ser
1 5 10 15

Leu Gly Asn Cys Arg Thr Ser Gln Lys Tyr Arg Ala Asn Cys Ala Lys

20 25 30

Thr Cys Glu Leu Cys
35

<210> 230
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> BgK peptide sequence - BgK-A9

<400> 230

Val Cys Arg Asp Trp Phe Lys Glu Ala Ala Cys Arg His Ala Lys Ser
1 5 10 15

Leu Gly Asn Cys Arg Thr Ser Gln Lys Tyr Arg Ala Asn Cys Ala Lys
20 25 30

Thr Cys Glu Leu Cys
35

<210> 231
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> BgK peptide sequence - BgK-A12

<400> 231

Val Cys Arg Asp Trp Phe Lys Glu Thr Ala Cys Ala His Ala Lys Ser
1 5 10 15

Leu Gly Asn Cys Arg Thr Ser Gln Lys Tyr Arg Ala Asn Cys Ala Lys
20 25 30

Thr Cys Glu Leu Cys
35

<210> 232
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> BgK peptide sequence - BgK-A15

<400> 232

Val Cys Arg Asp Trp Phe Lys Glu Thr Ala Cys Arg His Ala Ala Ser
1 5 10 15

Leu Gly Asn Cys Arg Thr Ser Gln Lys Tyr Arg Ala Asn Cys Ala Lys
20 25 30

Thr Cys Glu Leu Cys
35

<210> 233
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> BgK peptide sequence - BgK-A16

<400> 233

Val Cys Arg Asp Trp Phe Lys Glu Thr Ala Cys Arg His Ala Lys Ala
1 5 10 15

Leu Gly Asn Cys Arg Thr Ser Gln Lys Tyr Arg Ala Asn Cys Ala Lys
20 25 30

Thr Cys Glu Leu Cys
35

<210> 234
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> BgK peptide sequence - BgK-A17

<400> 234

Val Cys Arg Asp Trp Phe Lys Glu Thr Ala Cys Arg His Ala Lys Ser
1 5 10 15

Ala Gly Asn Cys Arg Thr Ser Gln Lys Tyr Arg Ala Asn Cys Ala Lys
20 25 30

Thr Cys Glu Leu Cys
35

<210> 235
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> BgK peptide sequence - BgK-A21

<400> 235

Val Cys Arg Asp Trp Phe Lys Glu Thr Ala Cys Arg His Ala Lys Ser
1 5 10 15

Leu Gly Asn Cys Ala Thr Ser Gln Lys Tyr Arg Ala Asn Cys Ala Lys
20 25 30

Thr Cys Glu Leu Cys

35

<210> 236
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> BgK peptide sequence - BgK-A22

<400> 236

Val Cys Arg Asp Trp Phe Lys Glu Thr Ala Cys Arg His Ala Lys Ser
1 5 10 15

Leu Gly Asn Cys Arg Ala Ser Gln Lys Tyr Arg Ala Asn Cys Ala Lys
20 25 30

Thr Cys Glu Leu Cys
35

<210> 237
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> BgK peptide sequence - BgK-A27

<400> 237

Val Cys Arg Asp Trp Phe Lys Glu Thr Ala Cys Arg His Ala Lys Ser
1 5 10 15

Leu Gly Asn Cys Arg Thr Ser Gln Lys Tyr Ala Ala Asn Cys Ala Lys
20 25 30

Thr Cys Glu Leu Cys
35

<210> 238
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> BgK peptide sequence - BgK-A32

<400> 238

Val Cys Arg Asp Trp Phe Lys Glu Thr Ala Cys Arg His Ala Lys Ser
1 5 10 15

Leu Gly Asn Cys Arg Thr Ser Gln Lys Tyr Arg Ala Asn Cys Ala Ala
20 25 30

Thr Cys Glu Leu Cys
35

<210> 239
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> BgK peptide sequence - BgK-A33

<400> 239

Val Cys Arg Asp Trp Phe Lys Glu Thr Ala Cys Arg His Ala Lys Ser
1 5 10 15

Leu Gly Asn Cys Arg Thr Ser Gln Lys Tyr Arg Ala Asn Cys Ala Lys
20 25 30

Ala Cys Glu Leu Cys
35

<210> 240
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> BgK peptide sequence - BgK-A35

<400> 240

Val Cys Arg Asp Trp Phe Lys Glu Thr Ala Cys Arg His Ala Lys Ser
1 5 10 15

Leu Gly Asn Cys Arg Thr Ser Gln Lys Tyr Arg Ala Asn Cys Ala Lys
20 25 30

Thr Cys Ala Leu Cys
35

<210> 241
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> BgK peptide sequence - BgK-A37

<400> 241

Val Cys Arg Asp Trp Phe Lys Glu Thr Ala Cys Arg His Ala Lys Ser
1 5 10 15

Leu Gly Asn Cys Arg Thr Ser Gln Lys Tyr Arg Ala Asn Cys Ala Lys
20 25 30

Thr Cys Glu Ala Cys
35

<210> 242

<211> 39
<212> PRT
<213> Artificial Sequence

<220>
<223> MgTx peptide sequence - MgTx-A6

<400> 242

Thr Ile Ile Asn Val Ala Cys Thr Ser Pro Lys Gln Cys Leu Pro Pro
1 5 10 15

Cys Lys Ala Gln Phe Gly Gln Ser Ala Gly Ala Lys Cys Met Asn Gly
20 25 30

Lys Cys Lys Cys Tyr Pro His
35

<210> 243
<211> 39
<212> PRT
<213> Artificial Sequence

<220>
<223> MgTx peptide sequence - MgTx-S6

<400> 243

Thr Ile Ile Asn Val Ser Cys Thr Ser Pro Lys Gln Cys Leu Pro Pro
1 5 10 15

Cys Lys Ala Gln Phe Gly Gln Ser Ala Gly Ala Lys Cys Met Asn Gly
20 25 30

Lys Cys Lys Cys Tyr Pro His
35

<210> 244
<211> 39
<212> PRT
<213> Artificial Sequence

<220>
<223> MgTx peptide sequence - MgTx-A11

<400> 244

Thr Ile Ile Asn Val Lys Cys Thr Ser Pro Ala Gln Cys Leu Pro Pro
1 5 10 15

Cys Lys Ala Gln Phe Gly Gln Ser Ala Gly Ala Lys Cys Met Asn Gly
20 25 30

Lys Cys Lys Cys Tyr Pro His
35

<210> 245
<211> 39
<212> PRT

<213> Artificial Sequence

<220>
<223> MgTx peptide sequence - MgTx-A18

<400> 245

Thr Ile Ile Asn Val Lys Cys Thr Ser Pro Lys Gln Cys Leu Pro Pro
1 5 10 15

Cys Ala Ala Gln Phe Gly Gln Ser Ala Gly Ala Lys Cys Met Asn Gly
20 25 30

Lys Cys Lys Cys Tyr Pro His
35

<210> 246
<211> 39
<212> PRT
<213> Artificial Sequence

<220>
<223> MgTx peptide sequence - MgTx-A28

<400> 246

Thr Ile Ile Asn Val Lys Cys Thr Ser Pro Lys Gln Cys Leu Pro Pro
1 5 10 15

Cys Lys Ala Gln Phe Gly Gln Ser Ala Gly Ala Ala Cys Met Asn Gly
20 25 30

Lys Cys Lys Cys Tyr Pro His
35

<210> 247
<211> 39
<212> PRT
<213> Artificial Sequence

<220>
<223> MgTx peptide sequence - MgTx-A33

<400> 247

Thr Ile Ile Asn Val Lys Cys Thr Ser Pro Lys Gln Cys Leu Pro Pro
1 5 10 15

Cys Lys Ala Gln Phe Gly Gln Ser Ala Gly Ala Lys Cys Met Asn Gly
20 25 30

Ala Cys Lys Cys Tyr Pro His
35

<210> 248
<211> 39
<212> PRT
<213> Artificial Sequence

<220>
<223> MgTx peptide sequence - MgTx-A35

<400> 248

Thr Ile Ile Asn Val Lys Cys Thr Ser Pro Lys Gln Cys Leu Pro Pro
1 5 10 15

Cys Lys Ala Gln Phe Gly Gln Ser Ala Gly Ala Lys Cys Met Asn Gly
20 25 30

Lys Cys Ala Cys Tyr Pro His
35

<210> 249
<211> 39
<212> PRT
<213> Artificial Sequence

<220>
<223> MgTx peptide sequence - MgTx-H39N

<400> 249

Thr Ile Ile Asn Val Lys Cys Thr Ser Pro Lys Gln Cys Leu Pro Pro
1 5 10 15

Cys Lys Ala Gln Phe Gly Gln Ser Ala Gly Ala Lys Cys Met Asn Gly
20 25 30

Lys Cys Lys Cys Tyr Pro Asn
35

<210> 250
<211> 39
<212> PRT
<213> Artificial Sequence

<220>
<223> MgTx peptide sequence - MgTx-A6/H39N

<400> 250

Thr Ile Ile Asn Val Ala Cys Thr Ser Pro Lys Gln Cys Leu Pro Pro
1 5 10 15

Cys Lys Ala Gln Phe Gly Gln Ser Ala Gly Ala Lys Cys Met Asn Gly
20 25 30

Lys Cys Lys Cys Tyr Pro Asn
35

<210> 251
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> MgTx peptide sequence - MgTxS6/38/d39

<400> 251

Thr Ile Ile Asn Val Ser Cys Thr Ser Pro Lys Gln Cys Leu Pro Pro
1 5 10 15

Cys Lys Ala Gln Phe Gly Gln Ser Ala Gly Ala Lys Cys Met Asn Gly
20 25 30

Lys Cys Lys Cys Tyr Ser
35

<210> 252
<211> 39
<212> PRT
<213> Artificial Sequence

<220>
<223> MgTx peptide sequence - MgTx-T4/15/S6

<400> 252

Thr Ile Ile Thr Ile Ser Cys Thr Ser Pro Lys Gln Cys Leu Pro Pro
1 5 10 15

Cys Lys Ala Gln Phe Gly Gln Ser Ala Gly Ala Lys Cys Met Asn Gly
20 25 30

Lys Cys Lys Cys Tyr Pro His
35

<210> 253
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> MgTx peptide sequence - MgTx-d3/T4/15/S6

<400> 253

Thr Ile Ser Cys Thr Ser Pro Lys Gln Cys Leu Pro Pro Cys Lys Ala
1 5 10 15

Gln Phe Gly Gln Ser Ala Gly Ala Lys Cys Met Asn Gly Lys Cys Lys
20 25 30

Cys Tyr Pro His
35

<210> 254
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> MgTx peptide sequence - MgTx-Pi2

<400> 254

Thr Ile Ser Cys Thr Ser Pro Lys Gln Cys Leu Pro Pro Cys Lys Ala
1 5 10 15

Gln Phe Gly Gln Ser Ala Gly Ala Lys Cys Met Asn Gly Lys Cys Lys
20 25 30

Cys Phe Gly Arg
35

<210> 255
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> MgTx peptide sequence - MgTx-d3/A6

<400> 255

Asn Val Ala Cys Thr Ser Pro Lys Gln Cys Leu Pro Pro Cys Lys Ala
1 5 10 15

Gln Phe Gly Gln Ser Ala Gly Ala Lys Cys Met Asn Gly Lys Cys Lys
20 25 30

Cys Tyr Pro His
35

<210> 256
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> MgTx peptide sequence - MgTx-ChTx

<400> 256

Gln Phe Thr Asn Val Ser Cys Thr Ser Pro Lys Gln Cys Leu Pro Pro
1 5 10 15

Cys Lys Ala Gln Phe Gly Gln Ser Ala Gly Ala Lys Cys Met Asn Gly
20 25 30

Lys Cys Lys Cys Tyr Ser
35

<210> 257
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> MgTx peptide sequence - MgTx-1bTx

<400> 257

Gln Phe Thr Asp Val Asp Cys Thr Ser Pro Lys Gln Cys Leu Pro Pro

1 5 10 15

Cys Lys Ala Gln Phe Gly Gln Ser Ala Gly Ala Lys Cys Met Asn Gly
20 25 30

Lys Cys Lys Cys Tyr Gln
35

<210> 258
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> MgTx peptide sequence - MgTx-Z1

<400> 258

Ile Ile Asn Val Ser Cys Thr Ser Pro Lys Gln Cys Leu Pro Pro Cys
1 5 10 15

Lys Ala Gln Phe Gly Gln Ser Ala Gly Ala Lys Cys Met Asn Gly Lys
20 25 30

Cys Lys Cys Tyr Pro His
35

<210> 259
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> MgTx peptide sequence - MgTx-Z2

<400> 259

Ile Ile Thr Ile Ser Cys Thr Ser Pro Lys Gln Cys Leu Pro Pro Cys
1 5 10 15

Lys Ala Gln Phe Gly Gln Ser Ala Gly Ala Lys Cys Met Asn Gly Lys
20 25 30

Cys Lys Cys Tyr Pro His
35

<210> 260
<211> 40
<212> PRT
<213> Artificial Sequence

<220>
<223> MgTx peptide sequence - MgTx-Z3

<400> 260

Gly Val Ile Ile Asn Val Ser Cys Thr Ser Pro Lys Gln Cys Leu Pro
1 5 10 15

Pro Cys Lys Ala Gln Phe Gly Gln Ser Ala Gly Ala Lys Cys Met Asn
20 25 30

Gly Lys Cys Lys Cys Tyr Pro His
35 40

<210> 261
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> AgTx2 peptide sequence - AgTx2-A5

<400> 261

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

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Arg Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 262
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> AgTx2 peptide sequence - AgTx2-A16

<400> 262

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

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Arg Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 263
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> AgTx2 peptide sequence - AgTx2-A19

<400> 263

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

Pro Cys Ala Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Arg Lys

20 25 30

Cys His Cys Thr Pro Lys
35

<210> 264
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> AgTx2 peptide sequence - AgTx2-A24

<400> 264

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

Pro Cys Lys Asp Ala Gly Met Ala Phe Gly Lys Cys Met Asn Arg Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 265
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> AgTx2 peptide sequence - AgTx2-A27

<400> 265

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

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Ala Cys Met Asn Arg Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 266
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> AgTx2 peptide sequence - AgTx2-A31

<400> 266

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

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Ala Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 267
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> AgTx2 peptide sequence - AgTx2-A32

<400> 267

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

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Arg Ala
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 268
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> AgTx2 peptide sequence - AgTx2-A38

<400> 268

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

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Arg Lys
20 25 30

Cys His Cys Thr Pro Ala
35

<210> 269
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> AgTx2 peptide sequence - AgTx2-A5/A38

<400> 269

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

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Arg Lys
20 25 30

Cys His Cys Thr Pro Ala

35

<210> 270
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> AgTx2 peptide sequence - AgTx2-G31

<400> 270

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

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 271
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> AgTx2 peptide sequence - AgTx2-OSK_z1

<400> 271

Gly Val Pro Ile Ile Val Ser Cys Lys Gly Ser Arg Gln Cys Ile Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 272
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> AgTx2 peptide sequence - AgTx2-OSK_z2

<400> 272

Gly Val Pro Ile Ile Val Ser Cys Lys Ile Ser Arg Gln Cys Ile Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 273
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> AgTx2 peptide sequence - AgTx2-OSK_z3

<400> 273

Gly Val Pro Ile Ile Val Lys Cys Lys Gly Ser Arg Gln Cys Ile Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 274
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> AgTx2 peptide sequence - AgTx2-OSK_z4

<400> 274

Gly Val Pro Ile Ile Val Lys Cys Lys Ile Ser Arg Gln Cys Ile Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 275
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> AgTx2 peptide sequence - AgTx2-OSK_z5

<400> 275

Gly Val Pro Ile Ile Val Lys Cys Lys Ile Ser Arg Gln Cys Ile Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 276

<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Heteromitrus spinnifer peptide sequence - HsTx1-X4

<220>
<221> MISC_FEATURE
<222> (4)..(4)
<223> Xaa is any amino acid residue.

<400> 276

Ala Ser Cys Xaa Thr Pro Lys Asp Cys Ala Asp Pro Cys Arg Lys Glu
1 5 10 15

Thr Gly Cys Pro Tyr Gly Lys Cys Met Asn Arg Lys Cys Lys Cys Asn
20 25 30

Arg Cys

<210> 277
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Heteromitrus spinnifer peptide sequence - HsTx1-A4

<400> 277

Ala Ser Cys Ala Thr Pro Lys Asp Cys Ala Asp Pro Cys Arg Lys Glu
1 5 10 15

Thr Gly Cys Pro Tyr Gly Lys Cys Met Asn Arg Lys Cys Lys Cys Asn
20 25 30

Arg Cys

<210> 278
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Heteromitrus spinnifer peptide sequence - HsTx1-X7

<220>
<221> MISC_FEATURE
<222> (7)..(7)
<223> Xaa is any amino acid residue.

<400> 278

Ala Ser Cys Arg Thr Pro Xaa Asp Cys Ala Asp Pro Cys Arg Lys Glu
1 5 10 15

Thr Gly Cys Pro Tyr Gly Lys Cys Met Asn Arg Lys Cys Lys Cys Asn
20 25 30

Arg Cys

<210> 279
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Heteromitrus spinnifer peptide sequence - HsTx1-A7

<400> 279

Ala Ser Cys Arg Thr Pro Ala Asp Cys Ala Asp Pro Cys Arg Lys Glu
1 5 10 15

Thr Gly Cys Pro Tyr Gly Lys Cys Met Asn Arg Lys Cys Lys Cys Asn
20 25 30

Arg Cys

<210> 280
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Heteromitrus spinnifer peptide sequence - HsTx1-X14

<220>
<221> MISC_FEATURE
<222> (14)..(14)
<223> Xaa is any amino acid residue.

<400> 280

Ala Ser Cys Arg Thr Pro Lys Asp Cys Ala Asp Pro Cys Xaa Lys Glu
1 5 10 15

Thr Gly Cys Pro Tyr Gly Lys Cys Met Asn Arg Lys Cys Lys Cys Asn
20 25 30

Arg Cys

<210> 281
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Heteromitrus spinnifer peptide sequence - HsTx1-A14

<400> 281

Ala Ser Cys Arg Thr Pro Lys Asp Cys Ala Asp Pro Cys Ala Lys Glu
1 5 10 15

Thr Gly Cys Pro Tyr Gly Lys Cys Met Asn Arg Lys Cys Lys Cys Asn
20 25 30

Arg Cys

<210> 282
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Heteromitrus spinnifer peptide sequence - HsTx1-X15

<220>
<221> MISC_FEATURE
<222> (15)..(15)
<223> Xaa is any amino acid residue.

<400> 282

Ala Ser Cys Arg Thr Pro Lys Asp Cys Ala Asp Pro Cys Arg Xaa Glu
1 5 10 15

Thr Gly Cys Pro Tyr Gly Lys Cys Met Asn Arg Lys Cys Lys Cys Asn
20 25 30

Arg Cys

<210> 283
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Heteromitrus spinnifer peptide sequence - HsTx1-A15

<400> 283

Ala Ser Cys Arg Thr Pro Lys Asp Cys Ala Asp Pro Cys Arg Ala Glu
1 5 10 15

Thr Gly Cys Pro Tyr Gly Lys Cys Met Asn Arg Lys Cys Lys Cys Asn
20 25 30

Arg Cys

<210> 284
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Heteromitrus spinnifer peptide sequence - HsTx1-X23

<220>
<221> MISC_FEATURE
<222> (23)..(23)
<223> Xaa is any amino acid residue.

<400> 284

Ala Ser Cys Arg Thr Pro Lys Asp Cys Ala Asp Pro Cys Arg Lys Glu
1 5 10 15

Thr Gly Cys Pro Tyr Gly Xaa Cys Met Asn Arg Lys Cys Lys Cys Asn
20 25 30

Arg Cys

<210> 285
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Heteromitrus spinnifer peptide sequence - HsTx1-A23

<400> 285

Ala Ser Cys Arg Thr Pro Lys Asp Cys Ala Asp Pro Cys Arg Lys Glu
1 5 10 15

Thr Gly Cys Pro Tyr Gly Ala Cys Met Asn Arg Lys Cys Lys Cys Asn
20 25 30

Arg Cys

<210> 286
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Heteromitrus spinnifer peptide sequence - HsTx1-X27

<220>
<221> MISC_FEATURE
<222> (27)..(27)
<223> Xaa is any amino acid residue.

<400> 286

Ala Ser Cys Arg Thr Pro Lys Asp Cys Ala Asp Pro Cys Arg Lys Glu
1 5 10 15

Thr Gly Cys Pro Tyr Gly Lys Cys Met Asn Xaa Lys Cys Lys Cys Asn
20 25 30

Arg Cys

<210> 287
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Heteromitrus spinnifer peptide sequence - HsTx1-A27

<400> 287

Ala Ser Cys Arg Thr Pro Lys Asp Cys Ala Asp Pro Cys Arg Lys Glu
1 5 10 15

Thr Gly Cys Pro Tyr Gly Lys Cys Met Asn Ala Lys Cys Lys Cys Asn
20 25 30

Arg Cys

<210> 288
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Heteromitrus spinnifer peptide sequence - HsTx1-X28

<220>
<221> MISC_FEATURE
<222> (28)..(28)
<223> Xaa is any amino acid residue.

<400> 288

Ala Ser Cys Arg Thr Pro Lys Asp Cys Ala Asp Pro Cys Arg Lys Glu
1 5 10 15

Thr Gly Cys Pro Tyr Gly Lys Cys Met Asn Arg Xaa Cys Lys Cys Asn
20 25 30

Arg Cys

<210> 289
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Heteromitrus spinnifer peptide sequence - HsTx1-A28

<400> 289

Ala Ser Cys Arg Thr Pro Lys Asp Cys Ala Asp Pro Cys Arg Lys Glu
1 5 10 15

Thr Gly Cys Pro Tyr Gly Lys Cys Met Asn Arg Ala Cys Lys Cys Asn
20 25 30

Arg Cys

<210> 290
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Heteromitrus spinnifer peptide sequence - HsTx1-X30

<220>
<221> MISC_FEATURE
<222> (30)..(30)
<223> Xaa can be any amino acid residue.

<400> 290

Ala Ser Cys Arg Thr Pro Lys Asp Cys Ala Asp Pro Cys Arg Lys Glu
1 5 10 15

Thr Gly Cys Pro Tyr Gly Lys Cys Met Asn Arg Lys Cys Xaa Cys Asn
20 25 30

Arg Cys

<210> 291
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Heteromitrus spinnifer peptide sequence - HxTx1-A30

<400> 291

Ala Ser Cys Arg Thr Pro Lys Asp Cys Ala Asp Pro Cys Arg Lys Glu
1 5 10 15

Thr Gly Cys Pro Tyr Gly Lys Cys Met Asn Arg Lys Cys Ala Cys Asn
20 25 30

Arg Cys

<210> 292
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Heteromitrus spinnifer peptide sequence - HsTx1-X33

<220>
<221> MISC_FEATURE
<222> (33)..(33)
<223> Xaa can be any amino acid residue.

<400> 292

Ala Ser Cys Arg Thr Pro Lys Asp Cys Ala Asp Pro Cys Arg Lys Glu
1 5 10 15

Thr Gly Cys Pro Tyr Gly Lys Cys Met Asn Arg Lys Cys Lys Cys Asn
20 25 30

Xaa Cys

<210> 293
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Heteromitrus spinnifer peptide sequence - HsTx1-A33

<400> 293

Ala Ser Cys Arg Thr Pro Lys Asp Cys Ala Asp Pro Cys Arg Lys Glu
1 5 10 15

Thr Gly Cys Pro Tyr Gly Lys Cys Met Asn Arg Lys Cys Lys Cys Asn
20 25 30

Ala Cys

<210> 294
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - OSK1-K16

<400> 294

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Lys Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 295
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - OSK1-D20

<400> 295

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Glu
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 296
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - OSK1-K16,D20

<400> 296

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 297
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - PSL1-P12,K16,D20

<400> 297

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Pro Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 298
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-K16,D20,Y36

<400> 298

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Pro Lys
35

<210> 299
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Pi2 peptide sequence - Pi2-X8

<220>
<221> MISC_FEATURE
<222> (8)..(8)
<223> Xaa can be any amino acid residue.

<400> 299

Thr Ile Ser Cys Thr Asn Pro Xaa Gln Cys Tyr Pro His Cys Lys Lys
1 5 10 15

Glu Thr Gly Tyr Pro Asn Ala Lys Cys Met Asn Arg Lys Cys Lys Cys
20 25 30

Phe Gly Arg
35

<210> 300
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Pi2 peptide sequence - Pi2-A8

<400> 300

Thr Ile Ser Cys Thr Asn Pro Ala Gln Cys Tyr Pro His Cys Lys Lys
1 5 10 15

Glu Thr Gly Tyr Pro Asn Ala Lys Cys Met Asn Arg Lys Cys Lys Cys
20 25 30

Phe Gly Arg
35

<210> 301
<211> 35
<212> PRT

<213> Artificial Sequence

<220>
<223> Pi2 peptide sequence - Pi2-X15

<220>
<221> MISC_FEATURE
<222> (15)..(15)
<223> Xaa can be any amino acid residue.

<400> 301

Thr Ile Ser Cys Thr Asn Pro Lys Gln Cys Tyr Pro His Cys Xaa Lys
1 5 10 15

Glu Thr Gly Tyr Pro Asn Ala Lys Cys Met Asn Arg Lys Cys Lys Cys
20 25 30

Phe Gly Arg
35

<210> 302
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Pi2 peptide sequence - Pi2-A15

<400> 302

Thr Ile Ser Cys Thr Asn Pro Lys Gln Cys Tyr Pro His Cys Ala Lys
1 5 10 15

Glu Thr Gly Tyr Pro Asn Ala Lys Cys Met Asn Arg Lys Cys Lys Cys
20 25 30

Phe Gly Arg
35

<210> 303
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Pi2 peptide sequence - Pi2-X16

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Xaa can be any amino acid residue.

<400> 303

Thr Ile Ser Cys Thr Asn Pro Lys Gln Cys Tyr Pro His Cys Lys Xaa
1 5 10 15

Glu Thr Gly Tyr Pro Asn Ala Lys Cys Met Asn Arg Lys Cys Lys Cys

20 25 30

Phe Gly Arg
35

<210> 304
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Pi2 peptide sequence - Pi2-A16

<400> 304

Thr Ile Ser Cys Thr Asn Pro Lys Gln Cys Tyr Pro His Cys Lys Ala
1 5 10 15

Glu Thr Gly Tyr Pro Asn Ala Lys Cys Met Asn Arg Lys Cys Lys Cys
20 25 30

Phe Gly Arg
35

<210> 305
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Pi2 peptide sequence - Pi2-X24

<220>
<221> MISC_FEATURE
<222> (24)..(24)
<223> Xaa can be any amino acid residue.

<400> 305

Thr Ile Ser Cys Thr Asn Pro Lys Gln Cys Tyr Pro His Cys Lys Lys
1 5 10 15

Glu Thr Gly Tyr Pro Asn Ala Xaa Cys Met Asn Arg Lys Cys Lys Cys
20 25 30

Phe Gly Arg
35

<210> 306
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Pi2 peptide sequence - Pi2-A24

<400> 306

Thr Ile Ser Cys Thr Asn Pro Lys Gln Cys Tyr Pro His Cys Lys Lys

1 5 10 15

Glu Thr Gly Tyr Pro Asn Ala Ala Cys Met Asn Arg Lys Cys Lys Cys
20 25 30

Phe Gly Arg
35

<210> 307
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Pi2 peptide sequence - Pi2-X28

<220>
<221> MISC_FEATURE
<222> (28)..(28)
<223> Xaa can be any amino acid residue.

<400> 307

Thr Ile Ser Cys Thr Asn Pro Lys Gln Cys Tyr Pro His Cys Lys Lys
1 5 10 15

Glu Thr Gly Tyr Pro Asn Ala Lys Cys Met Asn Xaa Lys Cys Lys Cys
20 25 30

Phe Gly Arg
35

<210> 308
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Pi2 peptide sequence - Pi2-A28

<400> 308

Thr Ile Ser Cys Thr Asn Pro Lys Gln Cys Tyr Pro His Cys Lys Lys
1 5 10 15

Glu Thr Gly Tyr Pro Asn Ala Lys Cys Met Asn Ala Lys Cys Lys Cys
20 25 30

Phe Gly Arg
35

<210> 309
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Pi2 peptide sequence - Pi2-X29

<220>
<221> MISC_FEATURE
<222> (29)..(29)
<223> Xaa can be any amino acid residue.

<400> 309

Thr Ile Ser Cys Thr Asn Pro Lys Gln Cys Tyr Pro His Cys Lys Lys
1 5 10 15

Glu Thr Gly Tyr Pro Asn Ala Lys Cys Met Asn Arg Xaa Cys Lys Cys
20 25 30

Phe Gly Arg
35

<210> 310
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Pi2 peptide sequence - Pi2-A29

<400> 310

Thr Ile Ser Cys Thr Asn Pro Lys Gln Cys Tyr Pro His Cys Lys Lys
1 5 10 15

Glu Thr Gly Tyr Pro Asn Ala Lys Cys Met Asn Arg Ala Cys Lys Cys
20 25 30

Phe Gly Arg
35

<210> 311
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Pi2 peptide sequence - Pi2-X31

<220>
<221> MISC_FEATURE
<222> (31)..(31)
<223> Xaa can be any amino acid residue.

<400> 311

Thr Ile Ser Cys Thr Asn Pro Lys Gln Cys Tyr Pro His Cys Lys Lys
1 5 10 15

Glu Thr Gly Tyr Pro Asn Ala Lys Cys Met Asn Arg Lys Cys Xaa Cys
20 25 30

Phe Gly Arg

35

<210> 312
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Pi2 peptide sequence - Pi2-A31

<400> 312

Thr Ile Ser Cys Thr Asn Pro Lys Gln Cys Tyr Pro His Cys Lys Lys
1 5 10 15

Glu Thr Gly Tyr Pro Asn Ala Lys Cys Met Asn Arg Lys Cys Ala Cys
20 25 30

Phe Gly Arg
35

<210> 313
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Pi2 peptide sequence - Pi2-X35

<220>
<221> MISC_FEATURE
<222> (35)..(35)
<223> Xaa can be any amino acid residue.

<400> 313

Thr Ile Ser Cys Thr Asn Pro Lys Gln Cys Tyr Pro His Cys Lys Lys
1 5 10 15

Glu Thr Gly Tyr Pro Asn Ala Lys Cys Met Asn Arg Lys Cys Lys Cys
20 25 30

Phe Gly Xaa
35

<210> 314
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Pi2 peptide sequence - Pi2-A35

<400> 314

Thr Ile Ser Cys Thr Asn Pro Lys Gln Cys Tyr Pro His Cys Lys Lys
1 5 10 15

Glu Thr Gly Tyr Pro Asn Ala Lys Cys Met Asn Arg Lys Cys Lys Cys

20 25 30

Phe Gly Ala
35

<210> 315
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Pi2 peptide sequence - Pi2-d35

<400> 315

Thr Ile Ser Cys Thr Asn Pro Lys Gln Cys Tyr Pro His Cys Lys Lys
1 5 10 15

Glu Thr Gly Tyr Pro Asn Ala Lys Cys Met Asn Arg Lys Cys Lys Cys
20 25 30

Phe Gly

<210> 316
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Anuroctoxin peptide sequence - AnTx-d1

<400> 316

Lys Glu Cys Thr Gly Pro Gln His Cys Thr Asn Phe Cys Arg Lys Asn
1 5 10 15

Lys Cys Thr His Gly Lys Cys Met Asn Arg Lys Cys Lys Cys Phe Asn
20 25 30

Cys Lys

<210> 317
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Anuroctoxin peptide sequence - AnTx-d1, X2

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa can be any amino acid residue.

<400> 317

Xaa Glu Cys Thr Gly Pro Gln His Cys Thr Asn Phe Cys Arg Lys Asn

1 5 10 15

Lys Cys Thr His Gly Lys Cys Met Asn Arg Lys Cys Lys Cys Phe Asn
20 25 30

Cys Lys

<210> 318
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Anuroctoxin peptide sequence - AnTxd1,A2

<400> 318

Ala Glu Cys Thr Gly Pro Gln His Cys Thr Asn Phe Cys Arg Lys Asn
1 5 10 15

Lys Cys Thr His Gly Lys Cys Met Asn Arg Lys Cys Lys Cys Phe Asn
20 25 30

Cys Lys

<210> 319
<211> 39
<212> PRT
<213> Artificial Sequence

<220>
<223> Noxiustoxin (NTX) peptide sequence - NTX-A6

<400> 319

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

Cys Lys Glu Leu Tyr Gly Ser Ser Ala Gly Ala Lys Cys Met Asn Gly
20 25 30

Lys Cys Lys Cys Tyr Asn Asn
35

<210> 320
<211> 39
<212> PRT
<213> Artificial Sequence

<220>
<223> Noxiustoxin (NTX) peptide sequence - NTX-R25

<400> 320

Thr Ile Ile Asn Val Lys Cys Thr Ser Pro Lys Gln Cys Ser Lys Pro
1 5 10 15

Cys Lys Glu Leu Tyr Gly Ser Ser Arg Gly Ala Lys Cys Met Asn Gly
20 25 30

Lys Cys Lys Cys Tyr Asn Asn
35

<210> 321
<211> 39
<212> PRT
<213> Artificial Sequence

<220>
<223> Noxiustoxin (NTX) peptide sequence - NTX-S10

<400> 321

Thr Ile Ile Asn Val Lys Cys Thr Ser Ser Lys Gln Cys Ser Lys Pro
1 5 10 15

Cys Lys Glu Leu Tyr Gly Ser Ser Ala Gly Ala Lys Cys Met Asn Gly
20 25 30

Lys Cys Lys Cys Tyr Asn Asn
35

<210> 322
<211> 39
<212> PRT
<213> Artificial Sequence

<220>
<223> Noxiustoxin (NTX) peptide sequence - NTX-W14

<400> 322

Thr Ile Ile Asn Val Lys Cys Thr Ser Pro Lys Gln Cys Trp Lys Pro
1 5 10 15

Cys Lys Glu Leu Tyr Gly Ser Ser Ala Gly Ala Lys Cys Met Asn Gly
20 25 30

Lys Cys Lys Cys Tyr Asn Asn
35

<210> 323
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Noxiustoxin (NTX) peptide sequence - NTX-A25d

<400> 323

Thr Ile Ile Asn Val Lys Cys Thr Ser Pro Lys Gln Cys Ser Lys Pro
1 5 10 15

Cys Lys Glu Leu Tyr Gly Ser Ser Gly Ala Lys Cys Met Asn Gly Lys

20 25 30

Cys Lys Cys Tyr Asn Asn
35

<210> 324
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Noxiustoxin (NTX) peptide sequence - NTX-1bTx1

<400> 324

Thr Ile Ile Asn Val Lys Cys Thr Ser Pro Lys Gln Cys Ser Lys Pro
1 5 10 15

Cys Lys Glu Leu Phe Gly Val Asp Arg Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Lys Cys Tyr Asn Asn
35

<210> 325
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Noxiustoxin (NTX) peptide sequence - NTX-1BTX2

<400> 325

Thr Ile Ile Asn Val Lys Cys Thr Ser Pro Lys Gln Cys Trp Lys Pro
1 5 10 15

Cys Lys Glu Leu Phe Gly Val Asp Arg Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Lys Cys Tyr Asn
35

<210> 326
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Kaliotoxin 1 (KTX1) peptide sequence - KTX2

<400> 326

Val Arg Ile Pro Val Ser Cys Lys His Ser Gly Gln Cys Leu Lys Pro
1 5 10 15

Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys Cys
20 25 30

Asp Cys Thr Pro Lys
35

<210> 327
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Kaliotoxin 1 (KTX1) peptide sequence - KTX1-S7

<400> 327

Gly Val Glu Ile Asn Val Ser Cys Ser Gly Ser Pro Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Arg Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 328
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Kaliotoxin 1 (KTX1) peptide sequence - KTX1-A7

<400> 328

Gly Val Glu Ile Asn Val Ala Cys Ser Gly Ser Pro Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Arg Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 329
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> IKCa1 peptide inhibitor sequence - ChTx-Lq2

<400> 329

Gln Phe Thr Gln Glu Ser Cys Thr Ala Ser Asn Gln Cys Trp Ser Ile
1 5 10 15

Cys Lys Arg Leu His Asn Thr Asn Arg Gly Lys Cys Met Asn Lys Lys
20 25 30

Cys Arg Cys Tyr Ser

35

<210> 330
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Maurotoxin (MTx) peptide sequence - MTX-A4

<400> 330

Val Ser Cys Ala Gly Ser Lys Asp Cys Tyr Ala Pro Cys Arg Lys Gln
1 5 10 15

Thr Gly Cys Pro Asn Ala Lys Cys Ile Asn Lys Ser Cys Lys Cys Tyr
20 25 30

Gly Cys

<210> 331
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Maurotoxin (MTx) peptide sequence - MTX-A6

<400> 331

Val Ser Cys Thr Gly Ala Lys Asp Cys Tyr Ala Pro Cys Arg Lys Gln
1 5 10 15

Thr Gly Cys Pro Asn Ala Lys Cys Ile Asn Lys Ser Cys Lys Cys Tyr
20 25 30

Gly Cys

<210> 332
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Maurotoxin (MTx) peptide sequence - MTX-A7

<400> 332

Val Ser Cys Thr Gly Ser Ala Asp Cys Tyr Ala Pro Cys Arg Lys Gln
1 5 10 15

Thr Gly Cys Pro Asn Ala Lys Cys Ile Asn Lys Ser Cys Lys Cys Tyr
20 25 30

Gly Cys

<210> 333
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Maurotoxin (MTx) peptide sequence - MTX-A10

<400> 333

Val Ser Cys Thr Gly Ser Lys Asp Cys Ala Ala Pro Cys Arg Lys Gln
1 5 10 15

Thr Gly Cys Pro Asn Ala Lys Cys Ile Asn Lys Ser Cys Lys Cys Tyr
20 25 30

Gly Cys

<210> 334
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Maurotoxin (MTx) peptide sequence - MTX-Q14

<400> 334

Val Ser Cys Thr Gly Ser Lys Asp Cys Tyr Ala Pro Cys Gln Lys Gln
1 5 10 15

Thr Gly Cys Pro Asn Ala Lys Cys Ile Asn Lys Ser Cys Lys Cys Tyr
20 25 30

Gly Cys

<210> 335
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Maurotoxin (MTx) peptide sequence - MTX-Q15

<400> 335

Val Ser Cys Thr Gly Ser Lys Asp Cys Tyr Ala Pro Cys Arg Gln Gln
1 5 10 15

Thr Gly Cys Pro Asn Ala Lys Cys Ile Asn Lys Ser Cys Lys Cys Tyr
20 25 30

Gly Cys

<210> 336

<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Maurotoxin (MTx) peptide sequence - MTX-Q14,15

<400> 336

Val Ser Cys Thr Gly Ser Lys Asp Cys Tyr Ala Pro Cys Gln Gln Gln
1 5 10 15

Thr Gly Cys Pro Asn Ala Lys Cys Ile Asn Lys Ser Cys Lys Cys Tyr
20 25 30

Gly Cys

<210> 337
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Maurotoxin (MTx) peptide sequence - MTX-A33

<400> 337

Val Ser Cys Thr Gly Ser Lys Asp Cys Tyr Ala Pro Cys Arg Lys Gln
1 5 10 15

Thr Gly Cys Pro Asn Ala Lys Cys Ile Asn Lys Ser Cys Lys Cys Tyr
20 25 30

Ala Cys

<210> 338
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Maurotoxin (MTx) peptide sequence - MTX-HsTx1

<400> 338

Val Ser Cys Thr Gly Ser Lys Asp Cys Tyr Ala Pro Cys Arg Lys Gln
1 5 10 15

Thr Gly Cys Pro Tyr Gly Lys Cys Met Asn Arg Lys Cys Lys Cys Asn
20 25 30

Arg Cys

<210> 339
<211> 34
<212> PRT

<213> Artificial Sequence

<220>
<223> Maurotoxin (MTx) peptide sequence - MTX-A12,20

<400> 339

Val Ser Cys Thr Gly Ser Lys Asp Cys Tyr Ala Ala Cys Arg Lys Gln
1 5 10 15

Thr Gly Cys Ala Asn Ala Lys Cys Ile Asn Lys Ser Cys Lys Cys Tyr
20 25 30

Gly Cys

<210> 340
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Maurotoxin (MTx) peptide sequence - MTX-X19,34

<220>
<221> MISC_FEATURE
<222> (19)..(19)
<223> Xaa in positions 19 and 34 are each independently nonfuctional residues.

<220>
<221> MISC_FEATURE
<222> (34)..(34)
<223> Xaa in positions 19 and 34 are each independently nonfuctional residues.

<400> 340

Val Ser Cys Thr Gly Ser Lys Asp Cys Tyr Ala Pro Cys Arg Lys Gln
1 5 10 15

Thr Gly Xaa Pro Asn Ala Lys Cys Ile Asn Lys Ser Cys Lys Cys Tyr
20 25 30

Gly Xaa

<210> 341
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Maurotoxin (MTx) peptide sequence - MTX-S19,34

<400> 341

Val Ser Cys Thr Gly Ser Lys Asp Cys Tyr Ala Pro Cys Arg Lys Gln
1 5 10 15

Thr Gly Ser Pro Asn Ala Lys Cys Ile Asn Lys Ser Cys Lys Cys Tyr
20 25 30

Gly Ser

<210> 342
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Maurotoxin (MTx) peptide sequence - MTX-A7

<400> 342

Val Ser Cys Thr Gly Ser Ala Asp Cys Tyr Ala Pro Cys Arg Lys Gln
1 5 10 15

Thr Gly Cys Pro Asn Ala Lys Cys Ile Asn Lys Ser Cys Lys Cys Tyr
20 25 30

Gly Cys

<210> 343
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Maurotoxin (MTx) peptide sequence - Tsk-MTX

<400> 343

Val Val Ile Gly Gln Arg Cys Thr Gly Ser Lys Asp Cys Tyr Ala Pro
1 5 10 15

Cys Arg Lys Gln Thr Gly Cys Pro Asn Ala Lys Cys Ile Asn Lys Ser
20 25 30

Cys Lys Cys Tyr Gly Cys
35

<210> 344
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Charybdotoxin (ChTx)peptide sequence - ChTx-D32

<400> 344

Gln Phe Thr Asn Val Ser Cys Thr Thr Ser Lys Glu Cys Trp Ser Val
1 5 10 15

Cys Gln Arg Leu His Asn Thr Ser Arg Gly Lys Cys Met Asn Lys Asp
20 25 30

Cys Arg Cys Tyr Ser
35

<210> 345
<211> 31
<212> PRT
<213> Artificial Sequence

<220>
<223> Charybdotoxin (ChTx)peptide sequence - ChTx_d1-d6

<400> 345

Cys Thr Thr Ser Lys Glu Cys Trp Ser Val Cys Gln Arg Leu His Asn
1 5 10 15

Thr Ser Arg Gly Lys Cys Met Asn Lys Lys Cys Arg Cys Tyr Ser
20 25 30

<210> 346
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Charybdotoxin (ChTx)peptide sequence - ChTx-lbTx

<400> 346

Gln Phe Thr Asn Val Ser Cys Thr Thr Ser Lys Glu Cys Trp Ser Val
1 5 10 15

Cys Gln Arg Leu Phe Gly Val Asp Arg Gly Lys Cys Met Gly Lys Lys
20 25 30

Cys Arg Cys Tyr Gln
35

<210> 347
<211> 26
<212> PRT
<213> Artificial Sequence

<220>
<223> N type Ca channel peptide inhibitor sequence - SVIB

<400> 347

Cys Lys Leu Lys Gly Gln Ser Cys Arg Lys Thr Ser Tyr Asp Cys Cys
1 5 10 15

Ser Gly Ser Cys Gly Arg Ser Gly Lys Cys
20 25

<210> 348
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> Apamin peptide inhibitor sequence - Ap-X4

<220>
<221> MISC_FEATURE
<222> (4)..(4)
<223> Xaa can be any amino acid residue.

<400> 348

Cys Asn Cys Xaa Ala Pro Glu Thr Ala Leu Cys Ala Arg Arg Cys Gln
1 5 10 15

Gln His Gly

<210> 349
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> Apamin peptide inhibitor sequence - Ap-A4

<400> 349

Cys Asn Cys Ala Ala Pro Glu Thr Ala Leu Cys Ala Arg Arg Cys Gln
1 5 10 15

Gln His Gly

<210> 350
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> Apamin peptide inhibitor sequence - Ap-X13

<220>
<221> MISC_FEATURE
<222> (13)..(13)
<223> Xaa can be any amino acid residue.

<400> 350

Cys Asn Cys Lys Ala Pro Glu Thr Ala Leu Cys Ala Xaa Arg Cys Gln
1 5 10 15

Gln His Gly

<210> 351
<211> 19
<212> PRT
<213> Artificial Sequence

<220>

<223> Apamin peptide inhibitor sequence - Ap-A13

<400> 351

Cys Asn Cys Lys Ala Pro Glu Thr Ala Leu Cys Ala Ala Arg Cys Gln
1 5 10 15

Gln His Gly

<210> 352
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> Apamin peptide inhibitor sequence - Ap-X14

<220>
<221> MISC_FEATURE
<222> (14)..(14)
<223> Xaa can be any amino acid residue.

<400> 352

Cys Asn Cys Lys Ala Pro Glu Thr Ala Leu Cys Ala Arg Xaa Cys Gln
1 5 10 15

Gln His Gly

<210> 353
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> Apamin peptide inhibitor sequence - Ap-A14

<400> 353

Cys Asn Cys Lys Ala Pro Glu Thr Ala Leu Cys Ala Arg Ala Cys Gln
1 5 10 15

Gln His Gly

<210> 354
<211> 31
<212> PRT
<213> Artificial Sequence

<220>
<223> Scyllatoxin (ScyTx), BMP05, P05, Tamapin, P01 peptide inhibitor sequence - ScyTx-R7

<400> 354

Ala Phe Cys Asn Leu Arg Arg Cys Gln Leu Ser Cys Arg Ser Leu Gly
1 5 10 15

Leu Leu Gly Lys Cys Ile Gly Asp Lys Cys Glu Cys Val Lys His
20 25 30

<210> 355
<211> 31
<212> PRT
<213> Artificial Sequence

<220>
<223> Scyllatoxin (ScyTx), BMP05, P05, Tamapin, P01 peptide inhibitor sequence - ScyTx-IbTx

<400> 355

Ala Phe Cys Asn Leu Arg Met Cys Gln Leu Ser Cys Arg Ser Leu Gly
1 5 10 15

Leu Leu Gly Lys Cys Met Gly Lys Lys Cys Arg Cys Val Lys His
20 25 30

<210> 356
<211> 31
<212> PRT
<213> Artificial Sequence

<220>
<223> Scyllatoxin (ScyTx), BMP05, P05, Tamapin, P01 peptide inhibitor sequence - ScyTx-C/S

<400> 356

Ala Phe Ser Asn Leu Arg Met Cys Gln Leu Ser Cys Arg Ser Leu Gly
1 5 10 15

Leu Leu Gly Lys Ser Ile Gly Asp Lys Cys Glu Cys Val Lys His
20 25 30

<210> 357
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> IbTx (Slotoxin family) peptide inhibitor sequence - IbTx-X11

<220>
<221> MISC_FEATURE
<222> (11)..(11)
<223> Xaa can be any amino acid residue.

<400> 357

Gln Phe Thr Asp Val Asp Cys Ser Val Ser Xaa Glu Cys Trp Ser Val
1 5 10 15

Cys Lys Asp Leu Phe Gly Val Asp Arg Gly Lys Cys Met Gly Lys Lys
20 25 30

Cys Arg Cys Tyr Gln

35

<210> 358
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> IbTx (Slotoxin family) peptide inhibitor sequence - IbTx-A11

<400> 358

Gln Phe Thr Asp Val Asp Cys Ser Val Ser Ala Glu Cys Trp Ser Val
1 5 10 15

Cys Lys Asp Leu Phe Gly Val Asp Arg Gly Lys Cys Met Gly Lys Lys
20 25 30

Cys Arg Cys Tyr Gln
35

<210> 359
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> IbTx (Slotoxin family) peptide inhibitor sequence - IbTx-X18

<220>
<221> MISC_FEATURE
<222> (18)..(18)
<223> Xaa can be any amino acid residue.

<400> 359

Gln Phe Thr Asp Val Asp Cys Ser Val Ser Lys Glu Cys Trp Ser Val
1 5 10 15

Cys Xaa Asp Leu Phe Gly Val Asp Arg Gly Lys Cys Met Gly Lys Lys
20 25 30

Cys Arg Cys Tyr Gln
35

<210> 360
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> IbTx (Slotoxin family) peptide inhibitor sequence - IbTx-A18

<400> 360

Gln Phe Thr Asp Val Asp Cys Ser Val Ser Lys Glu Cys Trp Ser Val
1 5 10 15

Cys Ala Asp Leu Phe Gly Val Asp Arg Gly Lys Cys Met Gly Lys Lys

20 25 30

Cys Arg Cys Tyr Gln
35

<210> 361
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> IbTx (Slotoxin family) peptide inhibitor sequence - IbTx-X25

<220>
<221> MISC_FEATURE
<222> (25)..(25)
<223> Xaa can be any amino acid residue.

<400> 361

Gln Phe Thr Asp Val Asp Cys Ser Val Ser Lys Glu Cys Trp Ser Val
1 5 10 15

Cys Lys Asp Leu Phe Gly Val Asp Xaa Gly Lys Cys Met Gly Lys Lys
20 25 30

Cys Arg Cys Tyr Gln
35

<210> 362
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> IbTx (Slotoxin family) peptide inhibitor sequence - IbTx-A25

<400> 362

Gln Phe Thr Asp Val Asp Cys Ser Val Ser Lys Glu Cys Trp Ser Val
1 5 10 15

Cys Lys Asp Leu Phe Gly Val Asp Ala Gly Lys Cys Met Gly Lys Lys
20 25 30

Cys Arg Cys Tyr Gln
35

<210> 363
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> IbTx (Slotoxin family) peptide inhibitor sequence - IbTx-X27

<220>
<221> MISC_FEATURE

<222> (27)..(27)
<223> Xaa can be any amino acid residue.

<400> 363

Gln Phe Thr Asp Val Asp Cys Ser Val Ser Lys Glu Cys Trp Ser Val
1 5 10 15

Cys Lys Asp Leu Phe Gly Val Asp Arg Gly Xaa Cys Met Gly Lys Lys
20 25 30

Cys Arg Cys Tyr Gln
35

<210> 364
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> IbTx, (Slotoxin family) peptide inhibitor sequence - IbTx-A27

<400> 364

Gln Phe Thr Asp Val Asp Cys Ser Val Ser Lys Glu Cys Trp Ser Val
1 5 10 15

Cys Lys Asp Leu Phe Gly Val Asp Arg Gly Ala Cys Met Gly Lys Lys
20 25 30

Cys Arg Cys Tyr Gln
35

<210> 365
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> IbTx (Slotoxin family) peptide inhibitor sequence - IbTx-X31

<220>
<221> MISC_FEATURE
<222> (31)..(31)
<223> Xaa can be any amino acid residue.

<400> 365

Gln Phe Thr Asp Val Asp Cys Ser Val Ser Lys Glu Cys Trp Ser Val
1 5 10 15

Cys Lys Asp Leu Phe Gly Val Asp Arg Gly Lys Cys Met Gly Xaa Lys
20 25 30

Cys Arg Cys Tyr Gln
35

<210> 366

<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> IbTx (Slotoxin family) peptide inhibitor sequence - IbTx-A31

<400> 366

Gln Phe Thr Asp Val Asp Cys Ser Val Ser Lys Glu Cys Trp Ser Val
1 5 10 15

Cys Lys Asp Leu Phe Gly Val Asp Arg Gly Lys Cys Met Gly Ala Lys
20 25 30

Cys Arg Cys Tyr Gln
35

<210> 367
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> IbTx (Slotoxin family) peptide inhibitor sequence - IbTx-X32

<220>
<221> MISC_FEATURE
<222> (32)..(32)
<223> Xaa can be any amino acid residue.

<400> 367

Gln Phe Thr Asp Val Asp Cys Ser Val Ser Lys Glu Cys Trp Ser Val
1 5 10 15

Cys Lys Asp Leu Phe Gly Val Asp Arg Gly Lys Cys Met Gly Lys Xaa
20 25 30

Cys Arg Cys Tyr Gln
35

<210> 368
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> IbTx (Slotoxin family) peptide inhibitor sequence - IbTx-A32

<400> 368

Gln Phe Thr Asp Val Asp Cys Ser Val Ser Lys Glu Cys Trp Ser Val
1 5 10 15

Cys Lys Asp Leu Phe Gly Val Asp Arg Gly Lys Cys Met Gly Lys Ala
20 25 30

Cys Arg Cys Tyr Gln

35

<210> 369
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> IbTx peptide inhibitor sequence - IbTx-X34

<220>
<221> MISC_FEATURE
<222> (34)..(34)
<223> Xaa can be any amino acid residue.

<400> 369

Gln Phe Thr Asp Val Asp Cys Ser Val Ser Lys Glu Cys Trp Ser Val
1 5 10 15

Cys Lys Asp Leu Phe Gly Val Asp Arg Gly Lys Cys Met Gly Lys Lys
20 25 30

Cys Xaa Cys Tyr Gln
35

<210> 370
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> IbTx (Slotoxin family) peptide inhibitor sequence - IbTx-A34

<400> 370

Gln Phe Thr Asp Val Asp Cys Ser Val Ser Lys Glu Cys Trp Ser Val
1 5 10 15

Cys Lys Asp Leu Phe Gly Val Asp Arg Gly Lys Cys Met Gly Lys Lys
20 25 30

Cys Ala Cys Tyr Gln
35

<210> 371
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Slotoxin peptide inhibitor sequence - SloTx

<400> 371

Gln Phe Thr Asp Val Lys Cys Thr Gly Ser Lys Gln Cys Trp Pro Val
1 5 10 15

Cys Lys Gln Met Phe Gly Lys Pro Asn Gly Lys Cys Met Asn Gly Lys

20 25 30

Cys Arg Cys Tyr Ser
35

<210> 372
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Slotoxin peptide inhibitor sequence - SloTx-X6

<220>
<221> MISC_FEATURE
<222> (6)..(6)
<223> Xaa can be any amino acid residue.

<400> 372

Gln Phe Thr Asp Val Xaa Cys Thr Gly Ser Lys Gln Cys Trp Pro Val
1 5 10 15

Cys Lys Gln Met Phe Gly Lys Pro Asn Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Arg Cys Tyr Ser
35

<210> 373
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Slotoxin peptide inhibitor sequence - SloTx-A6

<400> 373

Gln Phe Thr Asp Val Ala Cys Thr Gly Ser Lys Gln Cys Trp Pro Val
1 5 10 15

Cys Lys Gln Met Phe Gly Lys Pro Asn Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Arg Cys Tyr Ser
35

<210> 374
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Slotoxin peptide inhibitor sequence - SloTx-X11

<220>
<221> MISC_FEATURE

<222> (11)..(11)
<223> Xaa can be any amino acid residue.

<400> 374

Gln Phe Thr Asp Val Lys Cys Thr Gly Ser Xaa Gln Cys Trp Pro Val
1 5 10 15

Cys Lys Gln Met Phe Gly Lys Pro Asn Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Arg Cys Tyr Ser
35

<210> 375
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Slotoxin peptide inhibitor sequence - SloTx-A11

<400> 375

Gln Phe Thr Asp Val Lys Cys Thr Gly Ser Ala Gln Cys Trp Pro Val
1 5 10 15

Cys Lys Gln Met Phe Gly Lys Pro Asn Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Arg Cys Tyr Ser
35

<210> 376
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Slotoxin peptide inhibitor sequence - SloTx-X18

<220>
<221> MISC_FEATURE
<222> (18)..(18)
<223> Xaa can be any amino acid residue.

<400> 376

Gln Phe Thr Asp Val Lys Cys Thr Gly Ser Lys Gln Cys Trp Pro Val
1 5 10 15

Cys Xaa Gln Met Phe Gly Lys Pro Asn Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Arg Cys Tyr Ser
35

<210> 377

<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Slotoxin peptide inhibitor sequence - SloTx-A18

<400> 377

Gln Phe Thr Asp Val Lys Cys Thr Gly Ser Lys Gln Cys Trp Pro Val
1 5 10 15

Cys Ala Gln Met Phe Gly Lys Pro Asn Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Arg Cys Tyr Ser
35

<210> 378
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Slotoxin peptide inhibitor sequence - SloTx-X23

<220>
<221> MISC_FEATURE
<222> (23)..(23)
<223> Xaa can be any amino acid residue.

<400> 378

Gln Phe Thr Asp Val Lys Cys Thr Gly Ser Lys Gln Cys Trp Pro Val
1 5 10 15

Cys Lys Gln Met Phe Gly Xaa Pro Asn Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Arg Cys Tyr Ser
35

<210> 379
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Slotoxin peptide inhibitor sequence - SloTx-A23

<400> 379

Gln Phe Thr Asp Val Lys Cys Thr Gly Ser Lys Gln Cys Trp Pro Val
1 5 10 15

Cys Lys Gln Met Phe Gly Ala Pro Asn Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Arg Cys Tyr Ser

35

<210> 380
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Slotoxin peptide inhibitor sequence - SloTx-X27

<220>
<221> MISC_FEATURE
<222> (27)..(27)
<223> Xaa can be any amino acid residue.

<400> 380

Gln Phe Thr Asp Val Lys Cys Thr Gly Ser Lys Gln Cys Trp Pro Val
1 5 10 15

Cys Lys Gln Met Phe Gly Lys Pro Asn Gly Xaa Cys Met Asn Gly Lys
20 25 30

Cys Arg Cys Tyr Ser
35

<210> 381
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Slotoxin peptide inhibitor sequence - SloTx-A27

<400> 381

Gln Phe Thr Asp Val Lys Cys Thr Gly Ser Lys Gln Cys Trp Pro Val
1 5 10 15

Cys Lys Gln Met Phe Gly Lys Pro Asn Gly Ala Cys Met Asn Gly Lys
20 25 30

Cys Arg Cys Tyr Ser
35

<210> 382
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Slotoxin peptide inhibitor sequence - SloTx-X32

<220>
<221> MISC_FEATURE
<222> (32)..(32)
<223> Xaa can be any amino acid residue.

<400> 382

Gln Phe Thr Asp Val Lys Cys Thr Gly Ser Lys Gln Cys Trp Pro Val
1 5 10 15

Cys Lys Gln Met Phe Gly Lys Pro Asn Gly Lys Cys Met Asn Gly Xaa
20 25 30

Cys Arg Cys Tyr Ser
35

<210> 383
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> Slotoxin peptide inhibitor sequence - SloTx-A32

<400> 383

Gln Phe Thr Asp Val Lys Cys Thr Gly Ser Lys Gln Cys Trp Pro Val
1 5 10 15

Cys Lys Gln Met Phe Gly Lys Pro Asn Gly Lys Cys Met Asn Gly Ala
20 25 30

Arg Cys Tyr Ser
35

<210> 384
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> Slotoxin peptide inhibitor sequence - SloTx-X34

<220>
<221> MISC_FEATURE
<222> (34)..(34)
<223> Xaa can be any amino acid residue.

<400> 384

Gln Phe Thr Asp Val Lys Cys Thr Gly Ser Lys Gln Cys Trp Pro Val
1 5 10 15

Cys Lys Gln Met Phe Gly Lys Pro Asn Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Xaa Tyr Ser
35

<210> 385
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> Slotoxin peptide inhibitor sequence - SloTx-A34

<400> 385

Gln Phe Thr Asp Val Lys Cys Thr Gly Ser Lys Gln Cys Trp Pro Val
1 5 10 15

Cys Lys Gln Met Phe Gly Lys Pro Asn Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Tyr Ser
35

<210> 386
<211> 41
<212> PRT
<213> Artificial Sequence

<220>
<223> BuTX (Slotoxin family) peptide inhibitor sequence - BuTx

<400> 386

Trp Cys Ser Thr Cys Leu Asp Leu Ala Cys Gly Ala Ser Arg Glu Cys
1 5 10 15

Tyr Asp Pro Cys Phe Lys Ala Phe Gly Arg Ala His Gly Lys Cys Met
20 25 30

Asn Asn Lys Cys Arg Cys Tyr Thr Asn
35 40

<210> 387
<211> 40
<212> PRT
<213> Artificial Sequence

<220>
<223> BuTX (Slotoxin family) peptide inhibitor sequence - BuTx-X14

<220>
<221> MISC_FEATURE
<222> (14)..(14)
<223> Xaa can be any amino acid residue.

<400> 387

Trp Cys Ser Thr Cys Leu Asp Leu Ala Cys Gly Ala Ser Xaa Cys Tyr
1 5 10 15

Asp Pro Cys Phe Lys Ala Phe Gly Arg Ala His Gly Lys Cys Met Asn
20 25 30

Asn Lys Cys Arg Cys Tyr Thr Asn
35 40

<210> 388

<211> 40
<212> PRT
<213> Artificial Sequence

<220>
<223> BuTX (Slotoxin family) peptide inhibitor sequence - BuTx-A14

<400> 388

Trp Cys Ser Thr Cys Leu Asp Leu Ala Cys Gly Ala Ser Ala Cys Tyr
1 5 10 15

Asp Pro Cys Phe Lys Ala Phe Gly Arg Ala His Gly Lys Cys Met Asn
20 25 30

Asn Lys Cys Arg Cys Tyr Thr Asn
35 40

<210> 389
<211> 40
<212> PRT
<213> Artificial Sequence

<220>
<223> BuTX (Slotoxin family) peptide inhibitor sequence - BiTx-X22

<220>
<221> MISC_FEATURE
<222> (22)..(22)
<223> Xaa can be any amino acid residue.

<400> 389

Trp Cys Ser Thr Cys Leu Asp Leu Ala Cys Gly Ala Ser Arg Glu Cys
1 5 10 15

Tyr Asp Pro Cys Phe Xaa Phe Gly Arg Ala His Gly Lys Cys Met Asn
20 25 30

Asn Lys Cys Arg Cys Tyr Thr Asn
35 40

<210> 390
<211> 39
<212> PRT
<213> Artificial Sequence

<220>
<223> BuTX (Slotoxin family) peptide inhibitor sequence - BuTx-A22

<400> 390

Trp Cys Ser Thr Cys Leu Asp Leu Ala Cys Gly Ala Ser Arg Glu Cys
1 5 10 15

Tyr Asp Pro Cys Phe Ala Gly Arg Ala His Gly Lys Cys Met Asn Asn
20 25 30

Lys Cys Arg Cys Tyr Thr Asn

35

<210> 391
<211> 40
<212> PRT
<213> Artificial Sequence

<220>
<223> BuTX (Slotoxin family) peptide inhibitor sequence - BuTx-X26

<220>
<221> MISC_FEATURE
<222> (26)..(26)
<223> Xaa can be any amino acid residue.

<400> 391

Trp Cys Ser Thr Cys Leu Asp Leu Ala Cys Gly Ala Ser Arg Glu Cys
1 5 10 15

Tyr Asp Pro Cys Phe Lys Ala Phe Gly Xaa His Gly Lys Cys Met Asn
20 25 30

Asn Lys Cys Arg Cys Tyr Thr Asn
35 40

<210> 392
<211> 40
<212> PRT
<213> Artificial Sequence

<220>
<223> BuTX (Slotoxin family) peptide inhibitor sequence - BuTx-A26

<400> 392

Trp Cys Ser Thr Cys Leu Asp Leu Ala Cys Gly Ala Ser Arg Glu Cys
1 5 10 15

Tyr Asp Pro Cys Phe Lys Ala Phe Gly Ala His Gly Lys Cys Met Asn
20 25 30

Asn Lys Cys Arg Cys Tyr Thr Asn
35 40

<210> 393
<211> 40
<212> PRT
<213> Artificial Sequence

<220>
<223> BuTX (Slotoxin family) peptide inhibitor sequence - BuTx-X30

<220>
<221> MISC_FEATURE
<222> (30)..(30)
<223> Xaa can be any amino acid residue.

<400> 393

Trp Cys Ser Thr Cys Leu Asp Leu Ala Cys Gly Ala Ser Arg Glu Cys
1 5 10 15

Tyr Asp Pro Cys Phe Lys Ala Phe Gly Arg Ala His Gly Xaa Met Asn
20 25 30

Asn Lys Cys Arg Cys Tyr Thr Asn
35 40

<210> 394
<211> 40
<212> PRT
<213> Artificial Sequence

<220>
<223> BuTX (Slotoxin family) peptide inhibitor sequence - BuTx-A30

<400> 394

Trp Cys Ser Thr Cys Leu Asp Leu Ala Cys Gly Ala Ser Arg Glu Cys
1 5 10 15

Tyr Asp Pro Cys Phe Lys Ala Phe Gly Arg Ala His Gly Ala Met Asn
20 25 30

Asn Lys Cys Arg Cys Tyr Thr Asn
35 40

<210> 395
<211> 40
<212> PRT
<213> Artificial Sequence

<220>
<223> BuTX (Slotoxin family) peptide inhibitor sequence - BuTx-X35

<220>
<221> MISC_FEATURE
<222> (35)..(35)
<223> Xaa can be any amino acid residue.

<400> 395

Trp Cys Ser Thr Cys Leu Asp Leu Ala Cys Gly Ala Ser Arg Glu Cys
1 5 10 15

Tyr Asp Pro Cys Phe Lys Ala Phe Gly Arg Ala His Gly Lys Cys Met
20 25 30

Asn Asn Xaa Arg Cys Tyr Thr Asn
35 40

<210> 396
<211> 40
<212> PRT
<213> Artificial Sequence

<220>
<223> BuTX (Slotoxin family) peptide inhibitor sequence - BuTx-A35

<400> 396

Trp Cys Ser Thr Cys Leu Asp Leu Ala Cys Gly Ala Ser Arg Glu Cys
1 5 10 15

Tyr Asp Pro Cys Phe Lys Ala Phe Gly Arg Ala His Gly Lys Cys Met
20 25 30

Asn Asn Ala Arg Cys Tyr Thr Asn
35 40

<210> 397
<211> 40
<212> PRT
<213> Artificial Sequence

<220>
<223> BuTX (Slotoxin family) peptide inhibitor sequence - BuTx-X37

<220>
<221> MISC_FEATURE
<222> (37)..(37)
<223> Xaa can be any amino acid residue.

<400> 397

Trp Cys Ser Thr Cys Leu Asp Leu Ala Cys Gly Ala Ser Arg Glu Cys
1 5 10 15

Tyr Asp Pro Cys Phe Lys Ala Phe Gly Arg Ala His Gly Lys Cys Met
20 25 30

Asn Asn Lys Cys Xaa Tyr Thr Asn
35 40

<210> 398
<211> 40
<212> PRT
<213> Artificial Sequence

<220>
<223> BuTX (Slotoxin family) peptide inhibitor sequence - BuTx-A37

<400> 398

Trp Cys Ser Thr Cys Leu Asp Leu Ala Cys Gly Ala Ser Arg Glu Cys
1 5 10 15

Tyr Asp Pro Cys Phe Lys Ala Phe Gly Arg Ala His Gly Lys Cys Met
20 25 30

Asn Asn Lys Cys Ala Tyr Thr Asn
35 40

<210> 399

<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Martentoxin peptide inhibitor sequence - Marten Tx-X7

<220>
<221> MISC_FEATURE
<222> (7)..(7)
<223> Xaa can be any amino acid residue.

<400> 399

Phe Gly Leu Ile Asp Val Xaa Cys Phe Ala Ser Ser Glu Cys Trp Thr
1 5 10 15

Ala Cys Lys Lys Val Thr Gly Ser Gly Gln Gly Lys Cys Gln Asn Asn
20 25 30

Gln Cys Arg Cys Tyr
35

<210> 400
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Martentoxin peptide inhibitor sequence - Marten Tx-A7

<400> 400

Phe Gly Leu Ile Asp Val Ala Cys Phe Ala Ser Ser Glu Cys Trp Thr
1 5 10 15

Ala Cys Lys Lys Val Thr Gly Ser Gly Gln Gly Lys Cys Gln Asn Asn
20 25 30

Gln Cys Arg Cys Tyr
35

<210> 401
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Martentoxin peptide inhibitor sequence - Marten Tx-X19

<220>
<221> MISC_FEATURE
<222> (19)..(19)
<223> Xaa can be any amino acid residue.

<400> 401

Phe Gly Leu Ile Asp Val Lys Cys Phe Ala Ser Ser Glu Cys Trp Thr
1 5 10 15

Ala Cys Xaa Lys Val Thr Gly Ser Gly Gln Gly Lys Cys Gln Asn Asn
20 25 30

Gln Cys Arg Cys Tyr
35

<210> 402
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Martentoxin peptide inhibitor sequence - MartenTx-A19

<400> 402

Phe Gly Leu Ile Asp Val Lys Cys Phe Ala Ser Ser Glu Cys Trp Thr
1 5 10 15

Ala Cys Ala Lys Val Thr Gly Ser Gly Gln Gly Lys Cys Gln Asn Asn
20 25 30

Gln Cys Arg Cys Tyr
35

<210> 403
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Martentoxin peptide inhibitor sequence - MartenTx-X20

<220>
<221> MISC_FEATURE
<222> (20)..(20)
<223> Xaa can be any amino acid residue.

<400> 403

Phe Gly Leu Ile Asp Val Lys Cys Phe Ala Ser Ser Glu Cys Trp Thr
1 5 10 15

Ala Cys Lys Xaa Val Thr Gly Ser Gly Gln Gly Lys Cys Gln Asn Asn
20 25 30

Gln Cys Arg Cys Tyr
35

<210> 404
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Martentoxin peptide inhibitor sequence - Marten Tx-A20

<400> 404

Phe Gly Leu Ile Asp Val Lys Cys Phe Ala Ser Ser Glu Cys Trp Thr
1 5 10 15

Ala Cys Lys Ala Val Thr Gly Ser Gly Gln Gly Lys Cys Gln Asn Asn
20 25 30

Gln Cys Arg Cys Tyr
35

<210> 405
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Martentoxin peptide inhibitor sequence - MartenTx-X28

<220>
<221> MISC_FEATURE
<222> (28)..(28)
<223> Xaa can be any amino acid residue.

<400> 405

Phe Gly Leu Ile Asp Val Lys Cys Phe Ala Ser Ser Glu Cys Trp Thr
1 5 10 15

Ala Cys Lys Lys Val Thr Gly Ser Gly Gln Gly Xaa Cys Gln Asn Asn
20 25 30

Gln Cys Arg Cys Tyr
35

<210> 406
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Martentoxin peptide inhibitor sequence - MartenTx-A28

<400> 406

Phe Gly Leu Ile Asp Val Lys Cys Phe Ala Ser Ser Glu Cys Trp Thr
1 5 10 15

Ala Cys Lys Lys Val Thr Gly Ser Gly Gln Gly Ala Cys Gln Asn Asn
20 25 30

Gln Cys Arg Cys Tyr
35

<210> 407
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Martentoxin peptide inhibitor sequence - MartenTx-X35

<220>
<221> MISC_FEATURE
<222> (35)..(35)
<223> Xaa can be any amino acid residue.

<400> 407

Phe Gly Leu Ile Asp Val Lys Cys Phe Ala Ser Ser Glu Cys Trp Thr
1 5 10 15

Ala Cys Lys Lys Val Thr Gly Ser Gly Gln Gly Lys Cys Gln Asn Asn
20 25 30

Gln Cys Xaa Cys Tyr
35

<210> 408
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Martentoxin peptide inhibitor sequence - MartenTx-A35

<400> 408

Phe Gly Leu Ile Asp Val Lys Cys Phe Ala Ser Ser Glu Cys Trp Thr
1 5 10 15

Ala Cys Lys Lys Val Thr Gly Ser Gly Gln Gly Lys Cys Gln Asn Asn
20 25 30

Gln Cys Ala Cys Tyr
35

<210> 409
<211> 27
<212> PRT
<213> Artificial Sequence

<220>
<223> N type Ca channel peptide inhibitor sequence - CVIA

<400> 409

Cys Lys Ser Lys Gly Ala Lys Cys Ser Lys Leu Met Tyr Asp Cys Cys
1 5 10 15

Thr Gly Ser Cys Ser Gly Thr Val Gly Arg Cys
20 25

<210> 410
<211> 25
<212> PRT
<213> Artificial Sequence

<220>
<223> wMVIIA peptide inhibitor sequence - MVIIA-X2

<220>
<221> MISC_FEATURE
<222> (2)..(2)
<223> Xaa can be any amino acid residue.

<400> 410

Cys Xaa Gly Lys Gly Ala Lys Cys Ser Arg Leu Met Tyr Asp Cys Cys
1 5 10 15

Thr Gly Ser Cys Arg Ser Gly Lys Cys
20 25

<210> 411
<211> 25
<212> PRT
<213> Artificial Sequence

<220>
<223> wMVIIA peptide inhibitor sequence - MVIIA-A2

<400> 411

Cys Ala Gly Lys Gly Ala Lys Cys Ser Arg Leu Met Tyr Asp Cys Cys
1 5 10 15

Thr Gly Ser Cys Arg Ser Gly Lys Cys
20 25

<210> 412
<211> 25
<212> PRT
<213> Artificial Sequence

<220>
<223> wMVIIA peptide inhibitor sequence - MVIIA-X4

<220>
<221> MISC_FEATURE
<222> (4)..(4)
<223> Xaa can be any amino acid residue.

<400> 412

Cys Lys Gly Xaa Gly Ala Lys Cys Ser Arg Leu Met Tyr Asp Cys Cys
1 5 10 15

Thr Gly Ser Cys Arg Ser Gly Lys Cys
20 25

<210> 413
<211> 25
<212> PRT
<213> Artificial Sequence

<220>
<223> wMVIIA peptide inhibitor sequence - MVIIA-A4

<400> 413

Cys Lys Gly Ala Gly Ala Lys Cys Ser Arg Leu Met Tyr Asp Cys Cys
1 5 10 15

Thr Gly Ser Cys Arg Ser Gly Lys Cys
20 25

<210> 414
<211> 25
<212> PRT
<213> Artificial Sequence

<220>
<223> wMVIIA peptide inhibitor sequence - MVIIA-X7

<220>
<221> MISC_FEATURE
<222> (7)..(7)
<223> Xaa can be any amino acid residue.

<400> 414

Cys Lys Gly Lys Gly Ala Xaa Cys Ser Arg Leu Met Tyr Asp Cys Cys
1 5 10 15

Thr Gly Ser Cys Arg Ser Gly Lys Cys
20 25

<210> 415
<211> 25
<212> PRT
<213> Artificial Sequence

<220>
<223> wMVIIA peptide inhibitor sequence - MVIIA-A7

<400> 415

Cys Lys Gly Lys Gly Ala Ala Cys Ser Arg Leu Met Tyr Asp Cys Cys
1 5 10 15

Thr Gly Ser Cys Arg Ser Gly Lys Cys
20 25

<210> 416
<211> 25
<212> PRT
<213> Artificial Sequence

<220>
<223> wMVIIA peptide inhibitor sequence - MVIIA-X10

<220>
<221> MISC_FEATURE
<222> (10)..(10)
<223> Xaa can be any amino acid residue.

<400> 416

Cys Lys Gly Lys Gly Ala Lys Cys Ser Xaa Leu Met Tyr Asp Cys Cys
1 5 10 15

Thr Gly Ser Cys Arg Ser Gly Lys Cys
20 25

<210> 417
<211> 25
<212> PRT
<213> Artificial Sequence

<220>
<223> wMVIIA peptide inhibitor sequence - MVIIA-A10

<400> 417

Cys Lys Gly Lys Gly Ala Lys Cys Ser Ala Leu Met Tyr Asp Cys Cys
1 5 10 15

Thr Gly Ser Cys Arg Ser Gly Lys Cys
20 25

<210> 418
<211> 25
<212> PRT
<213> Artificial Sequence

<220>
<223> wMVIIA peptide inhibitor sequence - MVIIA-X21

<220>
<221> MISC_FEATURE
<222> (21)..(21)
<223> Xaa can be any amino acid residue.

<400> 418

Cys Lys Gly Lys Gly Ala Lys Cys Ser Arg Leu Met Tyr Asp Cys Cys
1 5 10 15

Thr Gly Ser Cys Xaa Ser Gly Lys Cys
20 25

<210> 419
<211> 25
<212> PRT
<213> Artificial Sequence

<220>
<223> wMVIIA peptide inhibitor sequence - MVIIA-A21

<400> 419

Cys Lys Gly Lys Gly Ala Lys Cys Ser Arg Leu Met Tyr Asp Cys Cys
1 5 10 15

Thr Gly Ser Cys Ala Ser Gly Lys Cys
20 25

<210> 420
<211> 25
<212> PRT
<213> Artificial Sequence

<220>
<223> wMVIIA peptide inhibitor sequence - MVIIA-X24

<220>
<221> MISC_FEATURE
<222> (24)..(24)
<223> Xaa can be any amino acid residue.

<400> 420

Cys Lys Gly Lys Gly Ala Lys Cys Ser Arg Leu Met Tyr Asp Cys Cys
1 5 10 15

Thr Gly Ser Cys Arg Ser Gly Xaa Cys
20 25

<210> 421
<211> 25
<212> PRT
<213> Artificial Sequence

<220>
<223> wMVIIA peptide inhibitor sequence - MVIIA-A24

<400> 421

Cys Lys Gly Lys Gly Ala Lys Cys Ser Arg Leu Met Tyr Asp Cys Cys
1 5 10 15

Thr Gly Ser Cys Arg Ser Gly Ala Cys
20 25

<210> 422
<211> 27
<212> PRT
<213> Artificial Sequence

<220>
<223> wGVIA peptide inhibitor sequence - GVIA-X2

<220>
<221> MISC_FEATURE
<222> (2)..(2)
<223> Xaa can be any amino acid residue.

<400> 422

Cys Xaa Ser Pro Gly Ser Ser Cys Ser Pro Thr Ser Tyr Asn Cys Cys
1 5 10 15

Arg Ser Cys Asn Pro Tyr Thr Lys Arg Cys Tyr
20 25

<210> 423

<211> 27
<212> PRT
<213> Artificial Sequence

<220>
<223> wGVIA peptide inhibitor sequence - GVIA-A2

<400> 423

Cys Ala Ser Pro Gly Ser Ser Cys Ser Pro Thr Ser Tyr Asn Cys Cys
1 5 10 15

Arg Ser Cys Asn Pro Tyr Thr Lys Arg Cys Tyr
20 25

<210> 424
<211> 27
<212> PRT
<213> Artificial Sequence

<220>
<223> wGVIA peptide inhibitor sequence - GVIA-X17

<220>
<221> MISC_FEATURE
<222> (17)..(17)
<223> Xaa can be any amino acid residue.

<400> 424

Cys Lys Ser Pro Gly Ser Ser Cys Ser Pro Thr Ser Tyr Asn Cys Cys
1 5 10 15

Xaa Ser Cys Asn Pro Tyr Thr Lys Arg Cys Tyr
20 25

<210> 425
<211> 27
<212> PRT
<213> Artificial Sequence

<220>
<223> wGVIA peptide inhibitor sequence - GVIA-A17

<400> 425

Cys Lys Ser Pro Gly Ser Ser Cys Ser Pro Thr Ser Tyr Asn Cys Cys
1 5 10 15

Ala Ser Cys Asn Pro Tyr Thr Lys Arg Cys Tyr
20 25

<210> 426
<211> 27
<212> PRT
<213> Artificial Sequence

<220>
<223> wGVIA peptide inhibitor sequence - GVIA-X24

<220>
<221> MISC_FEATURE
<222> (24)..(24)
<223> Xaa can be any amino acid residue.

<400> 426

Cys Lys Ser Pro Gly Ser Ser Cys Ser Pro Thr Ser Tyr Asn Cys Cys
1 5 10 15

Arg Ser Cys Asn Pro Tyr Thr Xaa Arg Cys Tyr
20 25

<210> 427
<211> 27
<212> PRT
<213> Artificial Sequence

<220>
<223> wGVIA peptide inhibitor sequence - GVIA-A24

<400> 427

Cys Lys Ser Pro Gly Ser Ser Cys Ser Pro Thr Ser Tyr Asn Cys Cys
1 5 10 15

Arg Ser Cys Asn Pro Tyr Thr Ala Arg Cys Tyr
20 25

<210> 428
<211> 27
<212> PRT
<213> Artificial Sequence

<220>
<223> wGVIA peptide inhibitor sequence - GVIA-X25

<220>
<221> MISC_FEATURE
<222> (25)..(25)
<223> Xaa can be any amino acid residue.

<400> 428

Cys Lys Ser Pro Gly Ser Ser Cys Ser Pro Thr Ser Tyr Asn Cys Cys
1 5 10 15

Arg Ser Cys Asn Pro Tyr Thr Lys Xaa Cys Tyr
20 25

<210> 429
<211> 27
<212> PRT
<213> Artificial Sequence

<220>
<223> wGVIA peptide inhibitor sequence - GVIA-A25

<400> 429

Cys Lys Ser Pro Gly Ser Ser Cys Ser Pro Thr Ser Tyr Asn Cys Cys

1 5 10 15

Arg Ser Cys Asn Pro Tyr Thr Lys Ala Cys Tyr
20 25

<210> 430
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Ptu1 peptide inhibitor sequence - Ptu1-X3

<220>
<221> MISC_FEATURE
<222> (3)..(3)
<223> Xaa can be any amino acid residue.

<400> 430

Ala Glu Xaa Asp Cys Ile Ala Pro Gly Ala Pro Cys Phe Gly Thr Asp
1 5 10 15

Lys Pro Cys Cys Asn Pro Arg Ala Trp Cys Ser Ser Tyr Ala Asn Lys
20 25 30

Cys Leu

<210> 431
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Ptu1 peptide inhibitor sequence - Ptu1-A3

<400> 431

Ala Glu Ala Asp Cys Ile Ala Pro Gly Ala Pro Cys Phe Gly Thr Asp
1 5 10 15

Lys Pro Cys Cys Asn Pro Arg Ala Trp Cys Ser Ser Tyr Ala Asn Lys
20 25 30

Cys Leu

<210> 432
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Ptu1 peptide inhibitor sequence - Ptu1-X17

<220>
<221> MISC_FEATURE

<222> (17)..(17)
<223> Xaa can be any amino acid residue.

<400> 432

Ala Glu Lys Asp Cys Ile Ala Pro Gly Ala Pro Cys Phe Gly Thr Asp
1 5 10 15

Xaa Pro Cys Cys Asn Pro Arg Ala Trp Cys Ser Ser Tyr Ala Asn Lys
20 25 30

Cys Leu

<210> 433
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Ptu1 peptide inhibitor sequence - Ptu1-A17

<400> 433

Ala Glu Lys Asp Cys Ile Ala Pro Gly Ala Pro Cys Phe Gly Thr Asp
1 5 10 15

Ala Pro Cys Cys Asn Pro Arg Ala Trp Cys Ser Ser Tyr Ala Asn Lys
20 25 30

Cys Leu

<210> 434
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Ptu1 peptide inhibitor sequence - Ptu1-X23

<220>
<221> MISC_FEATURE
<222> (23)..(23)
<223> Xaa can be any amino acid residue.

<400> 434

Ala Glu Lys Asp Cys Ile Ala Pro Gly Ala Pro Cys Phe Gly Thr Asp
1 5 10 15

Lys Pro Cys Cys Asn Pro Xaa Ala Trp Cys Ser Ser Tyr Ala Asn Lys
20 25 30

Cys Leu

<210> 435

<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Ptu1 peptide inhibitor sequence - Ptu1-A23

<400> 435

Ala Glu Lys Asp Cys Ile Ala Pro Gly Ala Pro Cys Phe Gly Thr Asp
1 5 10 15

Lys Pro Cys Cys Asn Pro Ala Ala Trp Cys Ser Ser Tyr Ala Asn Lys
20 25 30

Cys Leu

<210> 436
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Ptu1 peptide inhibitor sequence - Ptu1-X32

<220>
<221> MISC_FEATURE
<222> (32)..(32)
<223> Xaa can be any amino acid residue.

<400> 436

Ala Glu Lys Asp Cys Ile Ala Pro Gly Ala Pro Cys Phe Gly Thr Asp
1 5 10 15

Lys Pro Cys Cys Asn Pro Arg Ala Trp Cys Ser Ser Tyr Ala Asn Xaa
20 25 30

Cys Leu

<210> 437
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Ptu1 peptide inhibitor sequence - Ptu1-A32

<400> 437

Ala Glu Lys Asp Cys Ile Ala Pro Gly Ala Pro Cys Phe Gly Thr Asp
1 5 10 15

Lys Pro Cys Cys Asn Pro Arg Ala Trp Cys Ser Ser Tyr Ala Asn Ala
20 25 30

Cys Leu

<210> 438
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> T type Ca channel peptide inhibitor sequence - ProTx1-X3

<220>
<221> MISC_FEATURE
<222> (3)..(3)
<223> Xaa can be any amino acid residue.

<400> 438

Glu Cys Xaa Tyr Trp Leu Gly Gly Cys Ser Ala Gly Gln Thr Cys Cys
1 5 10 15

Lys His Leu Val Cys Ser Arg Arg His Gly Trp Cys Val Trp Asp Gly
20 25 30

Thr Phe Ser
35

<210> 439
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> T type Ca channel peptide inhibitor sequence - ProTx1-A3

<400> 439

Glu Cys Ala Tyr Trp Leu Gly Gly Cys Ser Ala Gly Gln Thr Cys Cys
1 5 10 15

Lys His Leu Val Cys Ser Arg Arg His Gly Trp Cys Val Trp Asp Gly
20 25 30

Thr Phe Ser
35

<210> 440
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> T type Ca channel peptide inhibitor sequence - ProTx1-X17

<220>
<221> MISC_FEATURE
<222> (17)..(17)
<223> Xaa can be any amino acid residue.

<400> 440

Glu Cys Arg Tyr Trp Leu Gly Gly Cys Ser Ala Gly Gln Thr Cys Cys
1 5 10 15

Xaa His Leu Val Cys Ser Arg Arg His Gly Trp Cys Val Trp Asp Gly
20 25 30

Thr Phe Ser
35

<210> 441
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> T type Ca channel peptide inhibitor sequence - ProTx1-A17

<400> 441

Glu Cys Arg Tyr Trp Leu Gly Gly Cys Ser Ala Gly Gln Thr Cys Cys
1 5 10 15

Ala His Leu Val Cys Ser Arg Arg His Gly Trp Cys Val Trp Asp Gly
20 25 30

Thr Phe Ser
35

<210> 442
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> T type Ca channel peptide inhibitor sequence - ProTx1-X23

<220>
<221> MISC_FEATURE
<222> (23)..(23)
<223> Xaa can be any amino acid residue.

<400> 442

Glu Cys Arg Tyr Trp Leu Gly Gly Cys Ser Ala Gly Gln Thr Cys Cys
1 5 10 15

Lys His Leu Val Cys Ser Xaa Arg His Gly Trp Cys Val Trp Asp Gly
20 25 30

Thr Phe Ser
35

<210> 443
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> T type Ca channel peptide inhibitor sequence - ProTx1-A23

<400> 443

Glu Cys Arg Tyr Trp Leu Gly Gly Cys Ser Ala Gly Gln Thr Cys Cys
1 5 10 15

Lys His Leu Val Cys Ser Ala Arg His Gly Trp Cys Val Trp Asp Gly
20 25 30

Thr Phe Ser
35

<210> 444
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> T type Ca channel peptide inhibitor sequence - ProTx1-X24

<220>
<221> MISC_FEATURE
<222> (24)..(24)
<223> Xaa can be any amino acid residue.

<400> 444

Glu Cys Arg Tyr Trp Leu Gly Gly Cys Ser Ala Gly Gln Thr Cys Cys
1 5 10 15

Lys His Leu Val Cys Ser Arg Xaa His Gly Trp Cys Val Trp Asp Gly
20 25 30

Thr Phe Ser
35

<210> 445
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> T type Ca channel peptide inhibitor sequence - ProTx1-A24

<400> 445

Glu Cys Arg Tyr Trp Leu Gly Gly Cys Ser Ala Gly Gln Thr Cys Cys
1 5 10 15

Lys His Leu Val Cys Ser Arg Ala His Gly Trp Cys Val Trp Asp Gly
20 25 30

Thr Phe Ser
35

<210> 446

<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> M current peptide inhibitor sequence - BeKM1-d1

<400> 446

Pro Thr Asp Ile Lys Cys Ser Glu Ser Tyr Gln Cys Phe Pro Val Cys
1 5 10 15

Lys Ser Arg Phe Gly Lys Thr Asn Gly Arg Cys Val Asn Gly Phe Cys
20 25 30

Asp Cys Phe
35

<210> 447
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> M current peptide inhibitor sequence - BeKM1-X1

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa can be any amino acid residue.

<400> 447

Xaa Pro Thr Asp Ile Lys Cys Ser Glu Ser Tyr Gln Cys Phe Pro Val
1 5 10 15

Cys Lys Ser Arg Phe Gly Lys Thr Asn Gly Arg Cys Val Asn Gly Phe
20 25 30

Cys Asp Cys Phe
35

<210> 448
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> M current peptide inhibitor sequence - BeKM1-A1

<400> 448

Ala Pro Thr Asp Ile Lys Cys Ser Glu Ser Tyr Gln Cys Phe Pro Val
1 5 10 15

Cys Lys Ser Arg Phe Gly Lys Thr Asn Gly Arg Cys Val Asn Gly Phe
20 25 30

Cys Asp Cys Phe

35

<210> 449
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> M current peptide inhibitor sequence - BeKM1-X6

<220>
<221> MISC_FEATURE
<222> (6)..(6)
<223> Xaa can be any amino acid residue.

<400> 449

Arg Pro Thr Asp Ile Xaa Cys Ser Glu Ser Tyr Gln Cys Phe Pro Val
1 5 10 15

Cys Lys Ser Arg Phe Gly Lys Thr Asn Gly Arg Cys Val Asn Gly Phe
20 25 30

Cys Asp Cys Phe
35

<210> 450
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> M current peptide inhibitor sequence - BeKM1-A6

<400> 450

Arg Pro Thr Asp Ile Ala Cys Ser Glu Ser Tyr Gln Cys Phe Pro Val
1 5 10 15

Cys Lys Ser Arg Phe Gly Lys Thr Asn Gly Arg Cys Val Asn Gly Phe
20 25 30

Cys Asp Cys Phe
35

<210> 451
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> M current peptide inhibitor sequence - BeKM1-X18

<220>
<221> MISC_FEATURE
<222> (18)..(18)
<223> Xaa can be any amino acid residue.

<400> 451

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Arg Pro Thr Asp Ile Lys Cys Ser Glu Ser Tyr Gln Cys Phe Pro Val
1               5                   10                  15

Cys Xaa Ser Arg Phe Gly Lys Thr Asn Gly Arg Cys Val Asn Gly Phe
            20                  25                  30

Cys Asp Cys Phe
        35


<210>  452
<211>  36
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  M current peptide inhibitor sequence - BeKM1-A18

<400>  452

Arg Pro Thr Asp Ile Lys Cys Ser Glu Ser Tyr Gln Cys Phe Pro Val
1               5                   10                  15

Cys Ala Ser Arg Phe Gly Lys Thr Asn Gly Arg Cys Val Asn Gly Phe
            20                  25                  30

Cys Asp Cys Phe
        35


<210>  453
<211>  36
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  M current peptide inhibitor sequence - BeKM1-X20


<220>
<221>  MISC_FEATURE
<222>  (20)..(20)
<223>  Xaa can be any amino acid residue.

<400>  453

Arg Pro Thr Asp Ile Lys Cys Ser Glu Ser Tyr Gln Cys Phe Pro Val
1               5                   10                  15

Cys Lys Ser Xaa Phe Gly Lys Thr Asn Gly Arg Cys Val Asn Gly Phe
            20                  25                  30

Cys Asp Cys Phe
        35


<210>  454
<211>  36
<212>  PRT
<213>  Artificial Sequence
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<220>
<223> M current peptide inhibitor sequence - BeKM1-A20

<400> 454

Arg Pro Thr Asp Ile Lys Cys Ser Glu Ser Tyr Gln Cys Phe Pro Val
1 5 10 15

Cys Lys Ser Ala Phe Gly Lys Thr Asn Gly Arg Cys Val Asn Gly Phe
20 25 30

Cys Asp Cys Phe
35

<210> 455
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> M current peptide inhibitor sequence - BeKm1-X23

<220>
<221> MISC_FEATURE
<222> (23)..(23)
<223> Xaa can be any amino acid residue.

<400> 455

Arg Pro Thr Asp Ile Lys Cys Ser Glu Ser Tyr Gln Cys Phe Pro Val
1 5 10 15

Cys Lys Ser Arg Phe Gly Xaa Thr Asn Gly Arg Cys Val Asn Gly Phe
20 25 30

Cys Asp Cys Phe
35

<210> 456
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> M current peptide inhibitor sequence - BeKM1-A23

<400> 456

Arg Pro Thr Asp Ile Lys Cys Ser Glu Ser Tyr Gln Cys Phe Pro Val
1 5 10 15

Cys Lys Ser Arg Phe Gly Ala Thr Asn Gly Arg Cys Val Asn Gly Phe
20 25 30

Cys Asp Cys Phe
35

<210> 457

<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> M current peptide inhibitor sequence - BeKM1-X27

<220>
<221> MISC_FEATURE
<222> (27)..(27)
<223> Xaa can be any amino acid residue.

<400> 457

Arg Pro Thr Asp Ile Lys Cys Ser Glu Ser Tyr Gln Cys Phe Pro Val
1 5 10 15

Cys Lys Ser Arg Phe Gly Lys Thr Asn Gly Xaa Cys Val Asn Gly Phe
20 25 30

Cys Asp Cys Phe
35

<210> 458
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> M current peptide inhibitor sequence - BeKM1-A27

<400> 458

Arg Pro Thr Asp Ile Lys Cys Ser Glu Ser Tyr Gln Cys Phe Pro Val
1 5 10 15

Cys Lys Ser Arg Phe Gly Lys Thr Asn Gly Ala Cys Val Asn Gly Phe
20 25 30

Cys Asp Cys Phe
35

<210> 459
<211> 22
<212> PRT
<213> Artificial Sequence

<220>
<223> Na channel peptide inhibitor sequence - Sm1la

<400> 459

Gln Arg Cys Cys Asn Gly Arg Arg Gly Cys Ser Ser Arg Trp Cys Arg
1 5 10 15

Asp His Ser Arg Cys Cys
20

<210> 460

<211> 22
<212> PRT
<213> Artificial Sequence

<220>
<223> Na channel peptide inhibitor sequence - mu-GIIIA

<220>
<221> MISC_FEATURE
<222> (6)..(6)
<223> Xaa is hydroxyproline in positions 6, 7, and 17.

<220>
<221> MISC_FEATURE
<222> (7)..(7)
<223> Xaa is hydroxyproline in positions 6, 7, and 17.

<220>
<221> MISC_FEATURE
<222> (17)..(17)
<223> Xaa is hydroxyproline in positions 6, 7, and 17.

<400> 460

Arg Asp Cys Cys Thr Xaa Xaa Lys Lys Cys Lys Asp Arg Gln Cys Lys
1 5 10 15

Xaa Gln Arg Cys Cys Ala
20

<210> 461
<211> 22
<212> PRT
<213> Artificial Sequence

<220>
<223> Na channel peptide inhibitor sequence - mu-GIIIB

<220>
<221> MISC_FEATURE
<222> (6)..(6)
<223> Xaa is hydroxyproline in positions 6, 7, and 17.

<220>
<221> MISC_FEATURE
<222> (7)..(7)
<223> Xaa is hydroxyproline in positions 6, 7, and 17.

<220>
<221> MISC_FEATURE
<222> (17)..(17)
<223> Xaa is hydroxyproline in positions 6, 7, and 17.

<400> 461

Arg Asp Cys Cys Thr Xaa Xaa Arg Lys Cys Lys Asp Arg Arg Cys Lys
1 5 10 15

Xaa Met Arg Cys Cys Ala
20

<210> 462

<211> 22
<212> PRT
<213> Artificial Sequence

<220>
<223> Na channel peptide inhibitor sequence - mu-PIIIA

<220>
<221> MISC_FEATURE
<222> (8)..(8)
<223> Xaa is hydroxyproline in positions 8 and 18.

<220>
<221> MISC_FEATURE
<222> (18)..(18)
<223> Xaa is hydroxyproline in positions 8 and 18.

<400> 462

Glx Arg Leu Cys Cys Gly Phe Xaa Lys Ser Cys Arg Ser Arg Gln Cys
1 5 10 15

Lys Xaa His Arg Cys Cys
20

<210> 463
<211> 22
<212> PRT
<213> Artificial Sequence

<220>
<223> Na channel peptide inhibitor sequence - mu-SmIIIA

<400> 463

Glx Arg Cys Cys Asn Gly Arg Arg Gly Cys Ser Ser Arg Trp Cys Arg
1 5 10 15

Asp His Ser Arg Cys Cys
20

<210> 464
<211> 31
<212> PRT
<213> Artificial Sequence

<220>
<223> Na channel peptide inhibitor sequence - muO-MrVIA

<400> 464

Ala Cys Arg Lys Lys Trp Glu Tyr Cys Ile Val Pro Ile Ile Gly Phe
1 5 10 15

Ile Tyr Cys Cys Pro Gly Leu Ile Cys Gly Pro Phe Val Cys Val
20 25 30

<210> 465
<211> 31
<212> PRT
<213> Artificial Sequence

<220>
<223> Na channel peptide inhibitor sequence - muO-MrVIB

<400> 465

Ala Cys Ser Lys Lys Trp Glu Tyr Cys Ile Val Pro Ile Ile Gly Phe
1 5 10 15

Ile Tyr Cys Cys Pro Gly Leu Ile Cys Gly Pro Phe Val Cys Val
20 25 30

<210> 466
<211> 29
<212> PRT
<213> Artificial Sequence

<220>
<223> Na channel peptide inhibitor sequence - delta-PVIA

<220>
<221> MISC_FEATURE
<222> (6)..(6)
<223> Xaa is hydroxyproline in positions 6 and 14.

<220>
<221> MISC_FEATURE
<222> (14)..(14)
<223> Xaa is hydroxyproline in positions 6 and 14.

<400> 466

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

Cys Cys Ser Glu Phe Cys Leu Pro Gly Val Cys Phe Gly
20 25

<210> 467
<211> 31
<212> PRT
<213> Artificial Sequence

<220>
<223> Na channel peptide inhibitor sequence - delta-SVIE

<220>
<221> MISC_FEATURE
<222> (14)..(14)
<223> Xaa is hydroxyproline.

<400> 467

Asp Gly Cys Ser Ser Gly Gly Thr Phe Cys Gly Ile His Xaa Gly Leu
1 5 10 15

Cys Cys Ser Glu Phe Cys Phe Leu Trp Cys Ile Thr Phe Ile Asp
20 25 30

<210> 468

<211> 27
<212> PRT
<213> Artificial Sequence

<220>
<223> Na channel peptide inhibitor sequence - delta-TxVIA

<400> 468

Trp Cys Lys Gln Ser Gly Glu Met Cys Asn Leu Leu Asp Gln Asn Cys
1 5 10 15

Cys Asp Gly Tyr Cys Ile Val Leu Val Cys Thr
20 25

<210> 469
<211> 29
<212> PRT
<213> Artificial Sequence

<220>
<223> Na channel peptide inhibitor sequence - delta-GmVIA

<400> 469

Val Lys Pro Cys Arg Lys Glu Gly Gln Leu Cys Asp Pro Ile Phe Gln
1 5 10 15

Asn Cys Cys Arg Gly Trp Asn Cys Val Leu Phe Cys Val
20 25

<210> 470
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> CI channel peptide inhibitor sequence - CTX-X14

<220>
<221> MISC_FEATURE
<222> (14)..(14)
<223> Xaa can be any amino acid residue.

<400> 470

Met Cys Met Pro Cys Phe Thr Thr Asp His Gln Met Ala Xaa Lys Cys
1 5 10 15

Asp Asp Cys Cys Gly Gly Lys Gly Arg Gly Lys Cys Tyr Gly Pro Gln
20 25 30

Cys Leu Cys Arg
35

<210> 471
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> CI channel peptide inhibitor sequence - CTX-A14

<400> 471

Met Cys Met Pro Cys Phe Thr Thr Asp His Gln Met Ala Ala Lys Cys
1 5 10 15

Asp Asp Cys Cys Gly Gly Lys Gly Arg Gly Lys Cys Tyr Gly Pro Gln
20 25 30

Cys Leu Cys Arg
35

<210> 472
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> CI channel peptide inhibitor sequence - CTX-X15

<220>
<221> MISC_FEATURE
<222> (15)..(15)
<223> Xaa can be any amino acid residue.

<400> 472

Met Cys Met Pro Cys Phe Thr Thr Asp His Gln Met Ala Arg Xaa Cys
1 5 10 15

Asp Asp Cys Cys Gly Gly Lys Gly Arg Gly Lys Cys Tyr Gly Pro Gln
20 25 30

Cys Leu Cys Arg
35

<210> 473
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> CI channel peptide inhibitor sequence - CTX-A15

<400> 473

Met Cys Met Pro Cys Phe Thr Thr Asp His Gln Met Ala Arg Ala Cys
1 5 10 15

Asp Asp Cys Cys Gly Gly Lys Gly Arg Gly Lys Cys Tyr Gly Pro Gln
20 25 30

Cys Leu Cys Arg
35

<210> 474

<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> CI channel peptide inhibitor sequence - CTX-X23

<220>
<221> MISC_FEATURE
<222> (23)..(23)
<223> Xaa can be any amino acid residue.

<400> 474

Met Cys Met Pro Cys Phe Thr Thr Asp His Gln Met Ala Arg Lys Cys
1 5 10 15

Asp Asp Cys Cys Gly Gly Xaa Gly Arg Gly Lys Cys Tyr Gly Pro Gln
20 25 30

Cys Leu Cys Arg
35

<210> 475
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> CI channel peptide inhibitor sequence - CTX-A23

<400> 475

Met Cys Met Pro Cys Phe Thr Thr Asp His Gln Met Ala Arg Lys Cys
1 5 10 15

Asp Asp Cys Cys Gly Gly Ala Gly Arg Gly Lys Cys Tyr Gly Pro Gln
20 25 30

Cys Leu Cys Arg
35

<210> 476
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> CI channel peptide inhibitor sequence - CTX-X25

<220>
<221> MISC_FEATURE
<222> (25)..(25)
<223> Xaa can be any amino acid residue.

<400> 476

Met Cys Met Pro Cys Phe Thr Thr Asp His Gln Met Ala Arg Lys Cys
1 5 10 15

Asp Asp Cys Cys Gly Gly Lys Gly Xaa Gly Lys Cys Tyr Gly Pro Gln
20 25 30

Cys Leu Cys Arg
35

<210> 477
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> CI channel peptide inhibitor sequence - CTX-A25

<400> 477

Met Cys Met Pro Cys Phe Thr Thr Asp His Gln Met Ala Arg Lys Cys
1 5 10 15

Asp Asp Cys Cys Gly Gly Lys Gly Ala Gly Lys Cys Tyr Gly Pro Gln
20 25 30

Cys Leu Cys Arg
35

<210> 478
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> CI channel peptide inhibitor sequence - CTX-X27

<220>
<221> MISC_FEATURE
<222> (27)..(27)
<223> Xaa can be any amino acid residue.

<400> 478

Met Cys Met Pro Cys Phe Thr Thr Asp His Gln Met Ala Arg Lys Cys
1 5 10 15

Asp Asp Cys Cys Gly Gly Lys Gly Arg Gly Xaa Cys Tyr Gly Pro Gln
20 25 30

Cys Leu Cys Arg
35

<210> 479
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> CI channel peptide inhibitor sequence - CTX-A27

<400> 479

Met Cys Met Pro Cys Phe Thr Thr Asp His Gln Met Ala Arg Lys Cys
1 5 10 15

Asp Asp Cys Cys Gly Gly Lys Gly Arg Gly Ala Cys Tyr Gly Pro Gln
20 25 30

Cys Leu Cys Arg
35

<210> 480
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> CI channel peptide inhibitor sequence - CTX-X36

<220>
<221> MISC_FEATURE
<222> (36)..(36)
<223> Xaa in position 36 is any amino acid.

<400> 480

Met Cys Met Pro Cys Phe Thr Thr Asp His Gln Met Ala Arg Lys Cys
1 5 10 15

Asp Asp Cys Cys Gly Gly Lys Gly Arg Gly Lys Cys Tyr Gly Pro Gln
20 25 30

Cys Leu Cys Xaa
35

<210> 481
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> CI channel peptide inhibitor sequence - CTX-A36

<400> 481

Met Cys Met Pro Cys Phe Thr Thr Asp His Gln Met Ala Arg Lys Cys
1 5 10 15

Asp Asp Cys Cys Gly Gly Lys Gly Arg Gly Lys Cys Tyr Gly Pro Gln
20 25 30

Cys Leu Cys Ala
35

<210> 482
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> CI channel peptide inhibitor sequence - CTX-d36

<400> 482

Met Cys Met Pro Cys Phe Thr Thr Asp His Gln Met Ala Arg Lys Cys
1 5 10 15

Asp Asp Cys Cys Gly Gly Lys Gly Arg Gly Lys Cys Tyr Gly Pro Gln
20 25 30

Cys Leu Cys
35

<210> 483
<211> 39
<212> PRT
<213> Artificial Sequence

<220>
<223> CI channel peptide inhibitor sequence - Bm-12b

<400> 483

Gln Thr Asp Gly Cys Gly Pro Cys Phe Thr Thr Asp Ala Asn Met Ala
1 5 10 15

Arg Lys Cys Arg Glu Cys Cys Gly Gly Asn Gly Lys Cys Phe Gly Pro
20 25 30

Gln Cys Leu Cys Asn Arg Glu
35

<210> 484
<211> 39
<212> PRT
<213> Artificial Sequence

<220>
<223> CI channel peptide inhibitor sequence - Bm-12b-X17

<220>
<221> MISC_FEATURE
<222> (17)..(17)
<223> Xaa can be any amino acid residue.

<400> 484

Gln Thr Asp Gly Cys Gly Pro Cys Phe Thr Thr Asp Ala Asn Met Ala
1 5 10 15

Xaa Lys Cys Arg Glu Cys Cys Gly Gly Asn Gly Lys Cys Phe Gly Pro
20 25 30

Gln Cys Leu Cys Asn Arg Glu
35

<210> 485

<211> 39
<212> PRT
<213> Artificial Sequence

<220>
<223> CI channel peptide inhibitor sequence - Bm-12b-A17

<400> 485

Gln Thr Asp Gly Cys Gly Pro Cys Phe Thr Thr Asp Ala Asn Met Ala
1 5 10 15

Ala Lys Cys Arg Glu Cys Cys Gly Gly Asn Gly Lys Cys Phe Gly Pro
20 25 30

Gln Cys Leu Cys Asn Arg Glu
35

<210> 486
<211> 39
<212> PRT
<213> Artificial Sequence

<220>
<223> CI channel peptide inhibitor sequence - Bm-12b-X18

<220>
<221> MISC_FEATURE
<222> (18)..(18)
<223> Xaa can be any amino acid residue.

<400> 486

Gln Thr Asp Gly Cys Gly Pro Cys Phe Thr Thr Asp Ala Asn Met Ala
1 5 10 15

Arg Xaa Cys Arg Glu Cys Cys Gly Gly Asn Gly Lys Cys Phe Gly Pro
20 25 30

Gln Cys Leu Cys Asn Arg Glu
35

<210> 487
<211> 39
<212> PRT
<213> Artificial Sequence

<220>
<223> CI channel peptide inhibitor sequence - Bm-12b-A18

<400> 487

Gln Thr Asp Gly Cys Gly Pro Cys Phe Thr Thr Asp Ala Asn Met Ala
1 5 10 15

Arg Ala Cys Arg Glu Cys Cys Gly Gly Asn Gly Lys Cys Phe Gly Pro
20 25 30

Gln Cys Leu Cys Asn Arg Glu

35

<210> 488
<211> 39
<212> PRT
<213> Artificial Sequence

<220>
<223> CI channel peptide inhibitor sequence - Bm-12b-X20

<220>
<221> MISC_FEATURE
<222> (20)..(20)
<223> Xaa can be any amino acid residue.

<400> 488

Gln Thr Asp Gly Cys Gly Pro Cys Phe Thr Thr Asp Ala Asn Met Ala
1 5 10 15

Arg Lys Cys Xaa Glu Cys Cys Gly Gly Asn Gly Lys Cys Phe Gly Pro
20 25 30

Gln Cys Leu Cys Asn Arg Glu
35

<210> 489
<211> 39
<212> PRT
<213> Artificial Sequence

<220>
<223> CI channel peptide inhibitor sequence - Bm12b-A20

<400> 489

Gln Thr Asp Gly Cys Gly Pro Cys Phe Thr Thr Asp Ala Asn Met Ala
1 5 10 15

Arg Lys Cys Ala Glu Cys Cys Gly Gly Asn Gly Lys Cys Phe Gly Pro
20 25 30

Gln Cys Leu Cys Asn Arg Glu
35

<210> 490
<211> 39
<212> PRT
<213> Artificial Sequence

<220>
<223> CI channel peptide inhibitor sequence - Bm-12b-X28

<220>
<221> MISC_FEATURE
<222> (28)..(28)
<223> Xaa can be any amino acid residue.

<400> 490

Gln Thr Asp Gly Cys Gly Pro Cys Phe Thr Thr Asp Ala Asn Met Ala
1 5 10 15

Arg Lys Cys Arg Glu Cys Cys Gly Gly Asn Gly Xaa Cys Phe Gly Pro
20 25 30

Gln Cys Leu Cys Asn Arg Glu
35

<210> 491
<211> 39
<212> PRT
<213> Artificial Sequence

<220>
<223> CI channel peptide inhibitor sequence - Bm-12b-A28

<400> 491

Gln Thr Asp Gly Cys Gly Pro Cys Phe Thr Thr Asp Ala Asn Met Ala
1 5 10 15

Arg Lys Cys Arg Glu Cys Cys Gly Gly Asn Gly Ala Cys Phe Gly Pro
20 25 30

Gln Cys Leu Cys Asn Arg Glu
35

<210> 492
<211> 39
<212> PRT
<213> Artificial Sequence

<220>
<223> CI channel peptide inhibitor sequence - Bm-12b-X38

<220>
<221> MISC_FEATURE
<222> (38)..(38)
<223> Xaa can be any amino acid residue.

<400> 492

Gln Thr Asp Gly Cys Gly Pro Cys Phe Thr Thr Asp Ala Asn Met Ala
1 5 10 15

Arg Lys Cys Arg Glu Cys Cys Gly Gly Asn Gly Lys Cys Phe Gly Pro
20 25 30

Gln Cys Leu Cys Asn Xaa Glu
35

<210> 493
<211> 39
<212> PRT
<213> Artificial Sequence

<220>
<223> CI channel peptide inhibitor sequence - Bm-12b-A38

<400> 493

Gln Thr Asp Gly Cys Gly Pro Cys Phe Thr Thr Asp Ala Asn Met Ala
1 5 10 15

Arg Lys Cys Arg Glu Cys Cys Gly Gly Asn Gly Lys Cys Phe Gly Pro
20 25 30

Gln Cys Leu Cys Asn Ala Glu
35

<210> 494
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Kv2.1 peptide inhibitor sequence - HaTx1

<400> 494

Glu Cys Arg Tyr Leu Phe Gly Gly Cys Lys Thr Thr Ser Asp Cys Cys
1 5 10 15

Lys His Leu Gly Cys Lys Phe Arg Asp Lys Tyr Cys Ala Trp Asp Phe
20 25 30

Thr Phe Ser
35

<210> 495
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Kv2.1 peptide inhibitor sequence - HaTx1-X3

<220>
<221> MISC_FEATURE
<222> (3)..(3)
<223> Xaa can be any amino acid residue.

<400> 495

Glu Cys Xaa Tyr Leu Phe Gly Gly Cys Lys Thr Thr Ser Asp Cys Cys
1 5 10 15

Lys His Leu Gly Cys Lys Phe Arg Asp Lys Tyr Cys Ala Trp Asp Phe
20 25 30

Thr Phe Ser
35

<210> 496

<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Kv2.1 peptide inhibitor sequence - HaTx1-A3

<400> 496

Glu Cys Ala Tyr Leu Phe Gly Gly Cys Lys Thr Thr Ser Asp Cys Cys
1 5 10 15

Lys His Leu Gly Cys Lys Phe Arg Asp Lys Tyr Cys Ala Trp Asp Phe
20 25 30

Thr Phe Ser
35

<210> 497
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Kv2.1 peptide inhibitor sequence - HaTx1-X10

<220>
<221> MISC_FEATURE
<222> (10)..(10)
<223> Xaa can be any amino acid residue.

<400> 497

Glu Cys Arg Tyr Leu Phe Gly Gly Cys Xaa Thr Thr Ser Asp Cys Cys
1 5 10 15

Lys His Leu Gly Cys Lys Phe Arg Asp Lys Tyr Cys Ala Trp Asp Phe
20 25 30

Thr Phe Ser
35

<210> 498
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Kv2.1 peptide inhibitor sequence - HaTx1-A10

<400> 498

Glu Cys Arg Tyr Leu Phe Gly Gly Cys Ala Thr Thr Ser Asp Cys Cys
1 5 10 15

Lys His Leu Gly Cys Lys Phe Arg Asp Lys Tyr Cys Ala Trp Asp Phe
20 25 30

Thr Phe Ser

35

<210> 499
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Kv2.1 peptide inhibitor sequence - HaTx1-X17

<220>
<221> MISC_FEATURE
<222> (17)..(17)
<223> Xaa can be any amino acid residue.

<400> 499

Glu Cys Arg Tyr Leu Phe Gly Gly Cys Lys Thr Thr Ser Asp Cys Cys
1 5 10 15

Xaa His Leu Gly Cys Lys Phe Arg Asp Lys Tyr Cys Ala Trp Asp Phe
20 25 30

Thr Phe Ser
35

<210> 500
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Kv2.1 peptide inhibitor sequence - HaTx1-A17

<400> 500

Glu Cys Arg Tyr Leu Phe Gly Gly Cys Lys Thr Thr Ser Asp Cys Cys
1 5 10 15

Ala His Leu Gly Cys Lys Phe Arg Asp Lys Tyr Cys Ala Trp Asp Phe
20 25 30

Thr Phe Ser
35

<210> 501
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Kv2.1 peptide inhibitor sequence - HaTx1-X22

<220>
<221> MISC_FEATURE
<222> (22)..(22)
<223> Xaa can be any amino acid residue.

<400> 501

Glu Cys Arg Tyr Leu Phe Gly Gly Cys Lys Thr Thr Ser Asp Cys Cys
1 5 10 15

Lys His Leu Gly Cys Xaa Phe Arg Asp Lys Tyr Cys Ala Trp Asp Phe
20 25 30

Thr Phe Ser
35

<210> 502
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Kv2.1 peptide inhibitor sequence - HaTx1-A22

<400> 502

Glu Cys Arg Tyr Leu Phe Gly Gly Cys Lys Thr Thr Ser Asp Cys Cys
1 5 10 15

Lys His Leu Gly Cys Ala Phe Arg Asp Lys Tyr Cys Ala Trp Asp Phe
20 25 30

Thr Phe Ser
35

<210> 503
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Kv2.1 peptide inhibitor sequence - HaTx1-X24

<220>
<221> MISC_FEATURE
<222> (24)..(24)
<223> Xaa can be any amino acid residue.

<400> 503

Glu Cys Arg Tyr Leu Phe Gly Gly Cys Lys Thr Thr Ser Asp Cys Cys
1 5 10 15

Lys His Leu Gly Cys Lys Phe Xaa Asp Lys Tyr Cys Ala Trp Asp Phe
20 25 30

Thr Phe Ser
35

<210> 504
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Kv2.1 peptide inhibitor sequence - HaTx1-A24

<400> 504

Glu Cys Arg Tyr Leu Phe Gly Gly Cys Lys Thr Thr Ser Asp Cys Cys
1 5 10 15

Lys His Leu Gly Cys Lys Phe Ala Asp Lys Tyr Cys Ala Trp Asp Phe
20 25 30

Thr Phe Ser
35

<210> 505
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Kv2.1 peptide inhibitor sequence - HaTx1-X26

<220>
<221> MISC_FEATURE
<222> (26)..(26)
<223> Xaa can be any amino acid residue.

<400> 505

Glu Cys Arg Tyr Leu Phe Gly Gly Cys Lys Thr Thr Ser Asp Cys Cys
1 5 10 15

Lys His Leu Gly Cys Lys Phe Arg Asp Xaa Tyr Cys Ala Trp Asp Phe
20 25 30

Thr Phe Ser
35

<210> 506
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Kv2.1 peptide inhibitor sequence - HaTx1-A26

<400> 506

Glu Cys Arg Tyr Leu Phe Gly Gly Cys Lys Thr Thr Ser Asp Cys Cys
1 5 10 15

Lys His Leu Gly Cys Lys Phe Arg Asp Ala Tyr Cys Ala Trp Asp Phe
20 25 30

Thr Phe Ser
35

<210> 507

<211> 31
<212> PRT
<213> Artificial Sequence

<220>
<223> Kv4.3 & Kv4.2 peptide inhibitor sequence - PaTx2-X4

<220>
<221> MISC_FEATURE
<222> (4)..(4)
<223> Xaa can be any amino acid residue.

<400> 507

Tyr Cys Gln Xaa Trp Met Trp Thr Cys Asp Glu Glu Arg Lys Cys Cys
1 5 10 15

Glu Gly Leu Val Cys Arg Leu Trp Cys Lys Arg Ile Ile Asn Met
20 25 30

<210> 508
<211> 31
<212> PRT
<213> Artificial Sequence

<220>
<223> Kv4.3 & Kv4.2 peptide inhibitor sequence - PaTx2-A4

<400> 508

Tyr Cys Gln Ala Trp Met Trp Thr Cys Asp Glu Glu Arg Lys Cys Cys
1 5 10 15

Glu Gly Leu Val Cys Arg Leu Trp Cys Lys Arg Ile Ile Asn Met
20 25 30

<210> 509
<211> 31
<212> PRT
<213> Artificial Sequence

<220>
<223> Kv4.3 & Kv4.2 peptide inhibitor sequence - PaTx2-X13

<220>
<221> MISC_FEATURE
<222> (13)..(13)
<223> Xaa can be any amino acid residue.

<400> 509

Tyr Cys Gln Lys Trp Met Trp Thr Cys Asp Glu Glu Xaa Lys Cys Cys
1 5 10 15

Glu Gly Leu Val Cys Arg Leu Trp Cys Lys Arg Ile Ile Asn Met
20 25 30

<210> 510
<211> 31
<212> PRT

<213> Artificial Sequence

<220>
<223> Kv4.3 & Kv4.2 peptide inhibitor sequence - PaTx2-A13

<400> 510

Tyr Cys Gln Lys Trp Met Trp Thr Cys Asp Glu Glu Ala Lys Cys Cys
1 5 10 15

Glu Gly Leu Val Cys Arg Leu Trp Cys Lys Arg Ile Ile Asn Met
20 25 30

<210> 511
<211> 31
<212> PRT
<213> Artificial Sequence

<220>
<223> Kv4.3 & Kv4.2 peptide inhibitor sequence - PaTx2-X14

<220>
<221> MISC_FEATURE
<222> (14)..(14)
<223> Xaa can be any amino acid residue.

<400> 511

Tyr Cys Gln Lys Trp Met Trp Thr Cys Asp Glu Glu Arg Xaa Cys Cys
1 5 10 15

Glu Gly Leu Val Cys Arg Leu Trp Cys Lys Arg Ile Ile Asn Met
20 25 30

<210> 512
<211> 31
<212> PRT
<213> Artificial Sequence

<220>
<223> Kv4.3 & Kv4.2 peptide inhibitor sequence - PaTx2-A14

<400> 512

Tyr Cys Gln Lys Trp Met Trp Thr Cys Asp Glu Glu Arg Ala Cys Cys
1 5 10 15

Glu Gly Leu Val Cys Arg Leu Trp Cys Lys Arg Ile Ile Asn Met
20 25 30

<210> 513
<211> 31
<212> PRT
<213> Artificial Sequence

<220>
<223> Kv4.3 & Kv4.2 peptide inhibitor sequence - PaTx2-X22

<220>
<221> MISC_FEATURE

<222> (22)..(22)
<223> Xaa can be any amino acid residue.

<400> 513

Tyr Cys Gln Lys Trp Met Trp Thr Cys Asp Glu Glu Arg Lys Cys Cys
1 5 10 15

Glu Gly Leu Val Cys Xaa Leu Trp Cys Lys Arg Ile Ile Asn Met
20 25 30

<210> 514
<211> 31
<212> PRT
<213> Artificial Sequence

<220>
<223> Kv4.3 & Kv4.2 peptide inhibitor sequence - PaTx2-A22

<400> 514

Tyr Cys Gln Lys Trp Met Trp Thr Cys Asp Glu Glu Arg Lys Cys Cys
1 5 10 15

Glu Gly Leu Val Cys Ala Leu Trp Cys Lys Arg Ile Ile Asn Met
20 25 30

<210> 515
<211> 31
<212> PRT
<213> Artificial Sequence

<220>
<223> Kv4.3 & Kv4.2 peptide inhibitor sequence - PaTx2-X26

<220>
<221> MISC_FEATURE
<222> (26)..(26)
<223> Xaa can be any amino acid residue.

<400> 515

Tyr Cys Gln Lys Trp Met Trp Thr Cys Asp Glu Glu Arg Lys Cys Cys
1 5 10 15

Glu Gly Leu Val Cys Arg Leu Trp Cys Xaa Arg Ile Ile Asn Met
20 25 30

<210> 516
<211> 31
<212> PRT
<213> Artificial Sequence

<220>
<223> Kv4.3 & Kv4.2 peptide inhibitor sequence - PaTx2-A26

<400> 516

Tyr Cys Gln Lys Trp Met Trp Thr Cys Asp Glu Glu Arg Lys Cys Cys
1 5 10 15

Glu Gly Leu Val Cys Arg Leu Trp Cys Ala Arg Ile Ile Asn Met
20 25 30

<210> 517
<211> 31
<212> PRT
<213> Artificial Sequence

<220>
<223> Kv4.3 & Kv4.2 peptide inhibitor sequence - PaTx2-X27

<220>
<221> MISC_FEATURE
<222> (27)..(27)
<223> Xaa can be any amino acid residue.

<400> 517

Tyr Cys Gln Lys Trp Met Trp Thr Cys Asp Glu Glu Arg Lys Cys Cys
1 5 10 15

Glu Gly Leu Val Cys Arg Leu Trp Cys Lys Xaa Ile Ile Asn Met
20 25 30

<210> 518
<211> 31
<212> PRT
<213> Artificial Sequence

<220>
<223> Kv4.3 & Kv4.2 peptide inhibitor sequence - PaTx2-A27

<400> 518

Tyr Cys Gln Lys Trp Met Trp Thr Cys Asp Glu Glu Arg Lys Cys Cys
1 5 10 15

Glu Gly Leu Val Cys Arg Leu Trp Cys Lys Ala Ile Ile Asn Met
20 25 30

<210> 519
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> nACHR channel peptide inhibitor sequence - PnIA

<400> 519

Gly Cys Cys Ser Leu Pro Pro Cys Ala Ala Asn Asn Pro Asp Tyr Cys
1 5 10 15

<210> 520
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> nACHR channel peptide inhibitor sequence - PnIA-L10

<400> 520

Gly Cys Cys Ser Leu Pro Pro Cys Ala Leu Asn Asn Pro Asp Tyr Cys
1 5 10 15

<210> 521
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> nACHR channel peptide inhibitor sequence - PnIA-S11

<400> 521

Gly Cys Cys Ser Leu Pro Pro Cys Ala Ala Ser Asn Pro Asp Tyr Cys
1 5 10 15

<210> 522
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> nACHR channel peptide inhibitor sequence - PnIB

<400> 522

Gly Cys Cys Ser Leu Pro Pro Cys Ala Leu Ser Asn Pro Asp Tyr Cys
1 5 10 15

<210> 523
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> nACHR channel peptide inhibitor sequence - PnIB-A10

<400> 523

Gly Cys Cys Ser Leu Pro Pro Cys Ala Ala Ser Asn Pro Asp Tyr Cys
1 5 10 15

<210> 524
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> nACHR channel peptide inhibitor sequence - PnIB-N11

<400> 524

Gly Cys Cys Ser Leu Pro Pro Cys Ala Leu Asn Asn Pro Asp Tyr Cys
1 5 10 15

<210> 525
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> nACHR channel peptide inhibitor sequence - MII

<400> 525

Gly Cys Cys Ser Asn Pro Val Cys His Leu Glu His Ser Asn Leu Cys
1 5 10 15

<210> 526
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> nACHR channel peptide inhibitor sequence - alpha-MI

<400> 526

Gly Arg Cys Cys His Pro Ala Cys Gly Lys Asn Tyr Ser Cys
1 5 10

<210> 527
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<223> nACHR channel peptide inhibitor sequence - alpha-EI

<220>
<221> MISC_FEATURE
<222> (3)..(3)
<223> Xaa is hydroxyproline.

<400> 527

Arg Asp Xaa Cys Cys Tyr His Pro Thr Cys Asn Met Ser Asn Pro Gln
1 5 10 15

Ile Cys

<210> 528
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> nACHR channel peptide inhibitor sequence - alpha-AuIB

<400> 528

Gly Cys Cys Ser Tyr Pro Pro Cys Phe Ala Thr Asn Pro Asp Cys
1 5 10 15

<210> 529
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<223> nACHR channel peptide inhibitor sequence - alpha-PIA

<400> 529

Arg Asp Pro Cys Cys Ser Asn Pro Val Cys Thr Val His Asn Pro Gln
1 5 10 15

Ile Cys

<210> 530
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> nACHR channel peptide inhibitor sequence - alpha-ImI

<400> 530

Gly Cys Cys Ser Asp Pro Arg Cys Ala Trp Arg Cys
1 5 10

<210> 531
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> nACHR channel peptide inhibitor sequence - alpha-ImII

<400> 531

Ala Cys Cys Ser Asp Arg Arg Cys Arg Trp Arg Cys
1 5 10

<210> 532
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> nACHR channel peptide inhibitor sequence - alpha-GI

<400> 532

Glu Cys Cys Asn Pro Ala Cys Gly Arg His Tyr Ser Cys
1 5 10

<210> 533
<211> 25
<212> PRT
<213> Artificial Sequence

<220>
<223> nACHR channel peptide inhibitor sequence - alphaA-PIVA

<220>
<221> MISC_FEATURE
<222> (7)..(7)
<223> Xaa is hydroxyproline in positions 7, 13, and 20.

<220>

<221> MISC_FEATURE
<222> (13)..(13)
<223> Xaa is hydroxyproline in positions 7, 13, and 20.

<220>
<221> MISC_FEATURE
<222> (20)..(20)
<223> Xaa is hydroxyproline in positions 7, 13, and 20.

<400> 533

Gly Cys Cys Gly Ser Tyr Xaa Asn Ala Ala Cys His Xaa Cys Ser Cys
1 5 10 15

Lys Asp Arg Xaa Ser Tyr Cys Gly Gln
20 25

<210> 534
<211> 29
<212> PRT
<213> Artificial Sequence

<220>
<223> nACHR channel peptide inhibitor sequence - alphaA-EIVA

<220>
<221> MISC_FEATURE
<222> (6)..(6)
<223> Xaa is hydroxyproline in positons 6, 12, 20, 21, and 26.

<220>
<221> MISC_FEATURE
<222> (12)..(12)
<223> Xaa is hydroxyproline in positons 6, 12, 20, 21, and 26.

<220>
<221> MISC_FEATURE
<222> (20)..(20)
<223> Xaa is hydroxyproline in positons 6, 12, 20, 21, and 26.

<220>
<221> MISC_FEATURE
<222> (21)..(21)
<223> Xaa is hydroxyproline in positons 6, 12, 20, 21, and 26.

<220>
<221> MISC_FEATURE
<222> (26)..(26)
<223> Xaa is hydroxyproline in positons 6, 12, 20, 21, and 26.

<400> 534

Gly Cys Cys Pro Tyr Xaa Asn Ala Ala Cys His Xaa Cys Gly Cys Lys
1 5 10 15

Val Gly Arg Xaa Xaa Tyr Cys Asp Arg Xaa Ser Gly Gly
20 25

<210> 535
<211> 24
<212> PRT
<213> Artificial Sequence

<220>
<223> nACHR channel peptide inhibitor sequence - psi-PIIIE

<220>
<221> MISC_FEATURE
<222> (2)..(2)
<223> Xaa is hydroxyproline in positions 2, 3, and 14.

<220>
<221> MISC_FEATURE
<222> (3)..(3)
<223> Xaa is hydroxyproline in positions 2, 3, and 14.

<220>
<221> MISC_FEATURE
<222> (14)..(14)
<223> Xaa is hydroxyproline in positions 2, 3, and 14.

<400> 535

His Xaa Xaa Cys Cys Leu Tyr Gly Lys Cys Arg Arg Tyr Xaa Gly Cys
1 5 10 15

Ser Ser Ala Ser Cys Cys Gln Arg
20

<210> 536
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> nACHR channel peptide inhibitor sequence - EpI

<400> 536

Gly Cys Cys Ser Asp Pro Arg Cys Asn Met Asn Asn Pro Asp Tyr Cys
1 5 10 15

<210> 537
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> nACHR channel peptide inhibitor sequence - GIC

<400> 537

Gly Cys Cys Ser His Pro Ala Cys Ala Gly Asn Asn Gln His Ile Cys
1 5 10 15

<210> 538
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> nACHR channel peptide inhibitor sequence - GID

<220>
<221> MISC_FEATURE

<222> (4)..(4)
<223> Xaa in position 4 is gamma carboxy glutamic acid.

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Xaa in position 16 is hydroxyproline.

<400> 538

Ile Arg Asp Xaa Cys Cys Ser Asn Pro Ala Cys Arg Val Asn Asn Xaa
1 5 10 15

His Val Cys

<210> 539
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> nACHR channel peptide inhibitor sequence - AnIB

<400> 539

Gly Gly Cys Cys Ser His Pro Ala Cys Ala Ala Asn Asn Gln Asp Tyr
1 5 10 15

Cys

<210> 540
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> nACHR channel peptide inhibitor sequence - AuIA

<400> 540

Gly Cys Cys Ser Tyr Pro Pro Cys Phe Ala Thr Asn Ser Asp Tyr Cys
1 5 10 15

<210> 541
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> nACHR channel peptide inhibitor sequence - AuIC

<400> 541

Gly Cys Cys Ser Tyr Pro Pro Cys Phe Ala Thr Asn Ser Gly Tyr Cys
1 5 10 15

<210> 542
<211> 74
<212> PRT
<213> Heteractis magnifica

<220>
<221> MISC_FEATURE
<223> The HmK peptide toxin sequence shows the immature precursor peptide. The mature HmK peptide toxin would be predicted to be 35 amino acids in length and span residues 40 through 74.

<400> 542

Met Lys Ser Gln Met Ile Ala Ala Val Leu Leu Ile Ala Phe Cys Leu
1 5 10 15

Cys Val Val Val Thr Ala Arg Met Glu Leu Gln Asp Val Glu Asp Met
20 25 30

Glu Asn Gly Phe Gln Lys Arg Arg Thr Cys Lys Asp Leu Ile Pro Val
35 40 45

Ser Glu Cys Thr Asp Ile Arg Cys Arg Thr Ser Met Lys Tyr Arg Leu
50 55 60

Asn Leu Cys Arg Lys Thr Cys Gly Ser Cys
65 70

<210> 543
<211> 74
<212> PRT
<213> Heteractis magnifica

<220>
<221> DISULFID
<222> (42)..(74)
<223> With predicted disulfide linkages between 47-74, 51-67, and 56-71.

<220>
<221> DISULFID
<222> (51)..(67)
<223> With predicted disulfide linkages between 47-74, 51-67, and 56-71.

<220>
<221> DISULFID
<222> (56)..(71)
<223> With predicted disulfide linkages between 47-74, 51-67, and 56-71.

<400> 543

Met Lys Ser Gln Met Ile Ala Ala Val Leu Leu Ile Ala Phe Cys Leu
1 5 10 15

Cys Val Val Val Thr Ala Arg Met Glu Leu Gln Asp Val Glu Asp Met
20 25 30

Glu Asn Gly Phe Gln Lys Arg Arg Thr Cys Lys Asp Leu Ile Pro Val
35 40 45

Ser Glu Cys Thr Asp Ile Arg Cys Arg Thr Ser Met Lys Tyr Arg Leu
50 55 60

Asn Leu Cys Arg Lys Thr Cys Gly Ser Cys
65 70

<210> 544
<211> 36
<212> PRT
<213> Actinia equina

<220>
<221> DISULFID
<222> (2)..(36)
<223> With predicted disulfide linkages between 2-36, 11-29, and 20-33.

<220>
<221> DISULFID
<222> (11)..(29)
<223> With predicted disulfide linkages between 2-36, 11-29, and 20-33.

<220>
<221> DISULFID
<222> (20)..(33)
<223> With predicted disulfide linkages between 2-36, 11-29, and 20-33.

<400> 544

Gly Cys Lys Asp Asn Phe Ser Ala Asn Thr Cys Lys His Val Lys Ala
1 5 10 15

Asn Asn Asn Cys Gly Ser Gln Lys Tyr Ala Thr Asn Cys Ala Lys Thr
20 25 30

Cys Gly Lys Cys
35

<210> 545
<211> 36
<212> PRT
<213> Anemonia sulcata

<220>
<221> DISULFID
<222> (2)..(36)
<223> With predicted disulfide linkages between 2-36, 11-29, and 20-33.

<220>
<221> DISULFID
<222> (11)..(29)
<223> With predicted disulfide linkages between 2-36, 11-29, and 20-33.

<220>
<221> DISULFID
<222> (20)..(33)
<223> With predicted disulfide linkages between 2-36, 11-29, and 20-33.

<400> 545

Ala Cys Lys Asp Asn Phe Ala Ala Ala Thr Cys Lys His Val Lys Glu
1 5 10 15

Asn Lys Asn Cys Gly Ser Gln Lys Tyr Ala Thr Asn Cys Ala Lys Thr
20 25 30

Cys Gly Lys Cys
35

<210> 546
<211> 37
<212> PRT
<213> Bunodosoma granulifera

<220>
<221> DISULFID
<222> (2)..(37)
<223> With predicted disulfide linkages between 2-37, 11-30, and 20-34.

<220>
<221> DISULFID
<222> (11)..(30)
<223> With predicted disulfide linkages between 2-37, 11-30, and 20-34.

<220>
<221> DISULFID
<222> (20)..(34)
<223> With predicted disulfide linkages between 2-37, 11-30, and 20-34.

<400> 546

Val Cys Arg Asp Trp Phe Lys Glu Thr Ala Cys Arg His Ala Lys Ser
1 5 10 15

Leu Gly Asn Cys Arg Thr Ser Gln Lys Tyr Arg Ala Asn Cys Ala Lys
20 25 30

Thr Cys Glu Leu Cys
35

<210> 547
<211> 59
<212> PRT
<213> Artificial Sequence

<220>
<223> Modified form of the peptide ChTx-Lg2

<220>
<221> MISC_FEATURE
<223> The CHTx-Lg2 sequence shows the immature or modified form of the peptide.

<400> 547

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

Ile Asp Trp Ser Glu Gly Gln Phe Thr Gln Glu Ser Cys Thr Ala Ser
20 25 30

Asn Gln Cys Trp Ser Ile Cys Lys Arg Leu His Asn Thr Asn Arg Gly
35 40 45

Lys Cys Met Asn Lys Lys Cys Arg Cys Tyr Ser
50 55

<210> 548
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-Y1

<400> 548

Tyr Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 549
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-K1

<400> 549

Lys Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 550
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-H1.

<400> 550

His Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys

20 25 30

Gly Thr Cys
35

<210> 551
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-Q1.

<400> 551

Gln Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 552
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - PP-ShK.

<400> 552

Pro Pro Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala
1 5 10 15

Phe Gln Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys
20 25 30

Thr Cys Gly Thr Cys
35

<210> 553
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - M-ShK.

<400> 553

Met Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe
1 5 10 15

Gln Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr
20 25 30

Cys Gly Thr Cys
35

<210> 554
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - G-ShK.

<400> 554

Gly Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe
1 5 10 15

Gln Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr
20 25 30

Cys Gly Thr Cys
35

<210> 555
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-K1/A22.

<400> 555

Tyr Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 556
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-K1/A22.

<400> 556

Lys Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys

35

<210> 557
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-H1/A22

<400> 557

His Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 558
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - ShK-Q1/A22.

<400> 558

Gln Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 559
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - PP-ShK-A22.

<400> 559

Pro Pro Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala
1 5 10 15

Phe Gln Cys Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys
20 25 30

Thr Cys Gly Thr Cys
35

<210> 560
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - M-ShK-A22.

<400> 560

Met Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe
1 5 10 15

Gln Cys Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr
20 25 30

Cys Gly Thr Cys
35

<210> 561
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK peptide sequence - G-ShK-A22.

<400> 561

Gly Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe
1 5 10 15

Gln Cys Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr
20 25 30

Cys Gly Thr Cys
35

<210> 562
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - Ac-OSK1-P12,K16,D20

<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLATION

<400> 562

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Pro Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 563
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - OSK1-P12,K16,D20-NH2

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 563

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Pro Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 564
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - Ac-OSK1-P12,K16,D20-NH2.

<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLATION

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 564

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Pro Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 565
<211> 38

<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - OSK1-K16,D20,Y36-NH2.

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 565

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Pro Lys
35

<210> 566
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - Ac-OSK1-K16,D20,Y36

<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLATION

<400> 566

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Pro Lys
35

<210> 567
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - Ac-OSK1-K16,D20,Y36-NH2

<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLATION

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 567

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Pro Lys
35

<210> 568
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - OSK1-K16-NH2

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 568

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Lys Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 569
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - Ac-OSK1-K16.

<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLATION

<400> 569

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Lys Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys

20 25 30

Cys His Cys Thr Pro Lys
35

<210> 570
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - Ac-OSK1-K16-NH2

<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLATION

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 570

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Lys Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 571
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - Ac-OSK1-D20.

<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLATION

<400> 571

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Glu
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 572
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - OSK1-D20-NH2

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 572

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Glu
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 573
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - Ac-OSK1-D20-NH2

<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLATION

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 573

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Glu
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 574
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - OSK1-NH2

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 574

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Glu
1 5 10 15

Pro Cys Lys Lys Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 575
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - Ac-OSK1

<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLATION

<400> 575

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Glu
1 5 10 15

Pro Cys Lys Lys Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 576
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - Ac-OSK1-NH2

<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLATION

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 576

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Glu
1 5 10 15

Pro Cys Lys Lys Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 577
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-peptide sequence - OSK1-K16,D20-NH2

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 577

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 578
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - Ac-OSK1-K16,D20

<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLATION

<400> 578

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 579
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLATION

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 579

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 580
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - Delta1-OSK1.

<400> 580

Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Glu Pro
1 5 10 15

Cys Lys Lys Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys Cys
20 25 30

His Cys Thr Pro Lys
35

<210> 581
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - Ac-Delta1-OSK1.

<220>
<221> MOD_RES

<222> (1)..(1)
<223> ACETYLATION

<400> 581

Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Glu Pro
1 5 10 15

Cys Lys Lys Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys Cys
20 25 30

His Cys Thr Pro Lys
35

<210> 582
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - Delta1-OSK1-NH2.

<220>
<221> MOD_RES
<222> (37)..(37)
<223> AMIDATION

<400> 582

Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Glu Pro
1 5 10 15

Cys Lys Lys Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys Cys
20 25 30

His Cys Thr Pro Lys
35

<210> 583
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - Ac-Delta1-OsK1-NH2

<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLATION

<220>
<221> MOD_RES
<222> (37)..(37)
<223> AMIDATION

<400> 583

Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Glu Pro
1 5 10 15

Cys Lys Lys Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys Cys
20 25 30

His Cys Thr Pro Lys
35

<210> 584
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - OSK1-A34.

<400> 584

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Glu
1 5 10 15

Pro Cys Lys Lys Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Thr Pro Lys
35

<210> 585
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - Ac-OSK1-A34.

<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLATION

<400> 585

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Glu
1 5 10 15

Pro Cys Lys Lys Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Thr Pro Lys
35

<210> 586
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - OSK1-A34-NH2

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 586

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Glu
1 5 10 15

Pro Cys Lys Lys Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Thr Pro Lys
35

<210> 587
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - Ac-OSK1-A34-NH2

<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLATION

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 587

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Glu
1 5 10 15

Pro Cys Lys Lys Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Thr Pro Lys
35

<210> 588
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - Delta1-OSK1-K16,D20

<400> 588

Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys Pro
1 5 10 15

Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys Cys

20 25 30

His Cys Thr Pro Lys
35

<210> 589
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - Ac-Delta1-OSK1-K16,D20

<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLATION

<400> 589

Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys Pro
1 5 10 15

Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys Cys
20 25 30

His Cys Thr Pro Lys
35

<210> 590
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - Delta1-OSK1-K16,D20-NH2

<220>
<221> MOD_RES
<222> (37)..(37)
<223> AMIDATION

<400> 590

Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys Pro
1 5 10 15

Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys Cys
20 25 30

His Cys Thr Pro Lys
35

<210> 591
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - Ac-Delta1-OSK1-K16,D20-NH2

<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLATION

<220>
<221> MOD_RES
<222> (37)..(37)
<223> AMIDATION

<400> 591

Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys Pro
1 5 10 15

Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys Cys
20 25 30

His Cys Thr Pro Lys
35

<210> 592
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - (Delta1-4)-OSD1-K16,D20.

<400> 592

Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys Pro Cys Lys Asp
1 5 10 15

Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys Cys His Cys Thr
20 25 30

Pro Lys

<210> 593
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - Ac-(Delta1-4)-OSK1-K16,D20.

<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLATION

<400> 593

Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys Pro Cys Lys Asp
1 5 10 15

Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys Cys His Cys Thr
20 25 30

Pro Lys

<210> 594
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - (Delta1-4)-OSK1-K16,D20-NH2.

<220>
<221> MOD_RES
<222> (34)..(34)
<223> AMIDATION

<400> 594

Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys Pro Cys Lys Asp
1 5 10 15

Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys Cys His Cys Thr
20 25 30

Pro Lys

<210> 595
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequences - Ac-(Delta1-4)-OSK1-K16,D20-NH2

<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLATION

<220>
<221> MOD_RES
<222> (34)..(34)
<223> AMIDATION

<400> 595

Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys Pro Cys Lys Asp
1 5 10 15

Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys Cys His Cys Thr
20 25 30

Pro Lys

<210> 596
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - (Delta1-6)-OSK1-K16,D20.

<400> 596

Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys Pro Cys Lys Asp Ala Gly
1 5 10 15

Met Arg Phe Gly Lys Cys Met Asn Gly Lys Cys His Cys Thr Pro Lys
20 25 30

<210> 597
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-peptide sequence - Ac-(Delta1-6)-OSK1-K16,D20.

<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLATION

<400> 597

Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys Pro Cys Lys Asp Ala Gly
1 5 10 15

Met Arg Phe Gly Lys Cys Met Asn Gly Lys Cys His Cys Thr Pro Lys
20 25 30

<210> 598
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - (Delta1-6)-OSK1-K16,D20-NH2

<220>
<221> MOD_RES
<222> (32)..(32)
<223> AMIDATION

<400> 598

Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys Pro Cys Lys Asp Ala Gly
1 5 10 15

Met Arg Phe Gly Lys Cys Met Asn Gly Lys Cys His Cys Thr Pro Lys
20 25 30

<210> 599
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - Ac-(Delta1-6)-OSK1-K16,D20-NH2

<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLATION

<220>
<221> MOD_RES
<222> (32)..(32)
<223> AMIDATION

<400> 599

Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys Pro Cys Lys Asp Ala Gly
1 5 10 15

Met Arg Phe Gly Lys Cys Met Asn Gly Lys Cys His Cys Thr Pro Lys
20 25 30

<210> 600
<211> 31
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - (Delta1-7)-OSK1-K16,D20

<400> 600

Cys Lys Ile Ser Arg Gln Cys Leu Lys Pro Cys Lys Asp Ala Gly Met
1 5 10 15

Arg Phe Gly Lys Cys Met Asn Gly Lys Cys His Cys Thr Pro Lys
20 25 30

<210> 601
<211> 31
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - Ac-(Delta1-7)-OSK1-K16,D20

<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLATION

<400> 601

Cys Lys Ile Ser Arg Gln Cys Leu Lys Pro Cys Lys Asp Ala Gly Met
1 5 10 15

Arg Phe Gly Lys Cys Met Asn Gly Lys Cys His Cys Thr Pro Lys
20 25 30

<210> 602
<211> 31
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - (Delta1-7)-OSK1-K16,D20-NH2

<220>
<221> MOD_RES
<222> (31)..(31)
<223> AMIDATION

<400> 602

Cys Lys Ile Ser Arg Gln Cys Leu Lys Pro Cys Lys Asp Ala Gly Met
1 5 10 15

Arg Phe Gly Lys Cys Met Asn Gly Lys Cys His Cys Thr Pro Lys
20 25 30

<210> 603
<211> 31
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - Ac-(Delta1-7)-OSK1-K16,D20-NH2

<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLATION

<220>
<221> MOD_RES
<222> (31)..(31)
<223> AMIDATION

<400> 603

Cys Lys Ile Ser Arg Gln Cys Leu Lys Pro Cys Lys Asp Ala Gly Met
1 5 10 15

Arg Phe Gly Lys Cys Met Asn Gly Lys Cys His Cys Thr Pro Lys
20 25 30

<210> 604
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequences - OSK1-K16,D20,N25

<400> 604

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys

1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Asn Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 605
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - OSK1-K16,D20,N25-NH2

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 605

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Asn Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 606
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - Ac-OSK1-K16,D20,N25

<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLATION

<400> 606

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Asn Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 607

<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - Ac-OSK1-K16,D20,N25-NH2

<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLATION

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 607

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Asn Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 608
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - OSK1-K16,D20,R31

<400> 608

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Arg Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 609
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequences - OsK1-K16,D20,R31-NH2

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 609

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Arg Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 610
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - Ac-OSK1-K16,D20,R31

<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLATION

<400> 610

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Arg Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 611
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - Ac-OSK1-K16,D20,R31-NH2

<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLATION

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 611

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Arg Lys

20 25 30

Cys His Cys Thr Pro Lys
35

<210> 612
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - OSK1-K12,K16,R19,D20

<400> 612

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Lys Gln Cys Leu Lys
1 5 10 15

Pro Cys Arg Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 613
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - Ac-OSK1-K12,K16,R19,D20

<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLATION

<400> 613

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Lys Gln Cys Leu Lys
1 5 10 15

Pro Cys Arg Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 614
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequences - OSK1-K12,K16,R19,D20,NH2

<220>
<221> MOD_RES

<222> (38)..(38)
<223> AMIDATION

<400> 614

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Lys Gln Cys Leu Lys
1 5 10 15

Pro Cys Arg Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 615
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - Ac-OSK1-K12,K16,R19, D20-NH2

<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLATION

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 615

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Lys Gln Cys Leu Lys
1 5 10 15

Pro Cys Arg Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 616
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - Delta1-OSK1-T2,K16,D20

<400> 616

Thr Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys Pro
1 5 10 15

Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys Cys
20 25 30

His Cys Thr Pro Lys
35

<210> 617
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - Ac-Delta1-OSK1-T2,K16,D20

<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLATION

<400> 617

Thr Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys Pro
1 5 10 15

Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys Cys
20 25 30

His Cys Thr Pro Lys
35

<210> 618
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - Delta1-OSK1-T2,K16,D20-NH2

<220>
<221> MOD_RES
<222> (37)..(37)
<223> AMIDATION

<400> 618

Thr Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys Pro
1 5 10 15

Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys Cys
20 25 30

His Cys Thr Pro Lys
35

<210> 619
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - Ac-Delta1-OSK1-T2,K16,D20-NH2

<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLATION

<220>
<221> MOD_RES
<222> (37)..(37)
<223> AMIDATION

<400> 619

Thr Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys Pro
1 5 10 15

Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys Cys
20 25 30

His Cys Thr Pro Lys
35

<210> 620
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequences - OSK1-K3

<400> 620

Gly Val Lys Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Glu
1 5 10 15

Pro Cys Lys Lys Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 621
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - Ac-OSK1-K3

<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLATION

<400> 621

Gly Val Lys Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Glu
1 5 10 15

Pro Cys Lys Lys Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys

20 25 30

Cys His Cys Thr Pro Lys
35

<210> 622
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - OSK1-K3-NH2

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 622

Gly Val Lys Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Glu
1 5 10 15

Pro Cys Lys Lys Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 623
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - AC-OSK1-K3-NH2

<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLATION

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 623

Gly Val Lys Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Glu
1 5 10 15

Pro Cys Lys Lys Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 624
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - OSK1-K3, A34

<400> 624

Gly Val Lys Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Glu
1 5 10 15

Pro Cys Lys Lys Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Thr Pro Lys
35

<210> 625
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - OSK1-K3, K16,D20

<400> 625

Gly Val Lys Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 626
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - OSK1-K3,K16,D20,A34

<400> 626

Gly Val Lys Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Thr Pro Lys
35

<210> 627
<211> 38

<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - Ac-OSK1-K3,A34

<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLATION

<400> 627

Gly Val Lys Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Glu
1 5 10 15

Pro Cys Lys Lys Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Thr Pro Lys
35

<210> 628
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - OSK1-K3,A34-NH2

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 628

Gly Val Lys Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Glu
1 5 10 15

Pro Cys Lys Lys Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Thr Pro Lys
35

<210> 629
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - Ac-OSK1-K3,A34,NH2

<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLATION

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 629

Gly Val Lys Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Glu
1 5 10 15

Pro Cys Lys Lys Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Thr Pro Lys
35

<210> 630
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - Ac-OSK1-K3,K16,D20,A34

<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLATION

<400> 630

Gly Val Lys Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Thr Pro Lys
35

<210> 631
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - OSK1-K3,K16,D20,A34-NH2

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 631

Gly Val Lys Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys

20 25 30

Cys Ala Cys Thr Pro Lys
35

<210> 632
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - Ac-OSK1-K3,K16,D20,A34-NH2

<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLATION

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 632

Gly Val Lys Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Thr Pro Lys
35

<210> 633
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - Ac-OSK1-K3,K16,D20

<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLATION

<400> 633

Gly Val Lys Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 634
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - OSK1-K3,K16,D20-NH2

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 634

Gly Val Lys Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 635
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - Ac-OSK1-K3,K16,D20-NH2

<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLATION

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 635

Gly Val Lys Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 636
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1 peptide sequence - Delta36-38-OSK1-K16,D20

<400> 636

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr
35

<210> 637
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino acid linker sequence.

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa in positions 1, 2, 4, and 5 are each independently any amino acid residue.

<220>
<221> MISC_FEATURE
<222> (2)..(2)
<223> Xaa in positions 1, 2, 4, and 5 are each independently any amino acid residue.

<220>
<221> MISC_FEATURE
<222> (4)..(4)
<223> Xaa in positions 1, 2, 4, and 5 are each independently any amino acid residue.

<220>
<221> MISC_FEATURE
<222> (5)..(5)
<223> Xaa in positions 1, 2, 4, and 5 are each independently any amino acid residue.

<400> 637

Xaa Xaa Asn Xaa Xaa Gly
1 5

<210> 638
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> L5 linker amino acid sequence.

<400> 638

Gly Gly Gly Gly Ser
1 5

<210> 639
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Peptide linker sequence.

<400> 639

Gly Gly Glu Gly Gly Gly
1 5

<210> 640
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Peptide linker sequence.

<400> 640

Gly Gly Glu Glu Glu Gly Gly Gly
1 5

<210> 641
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Peptide linker sequence.

<400> 641

Gly Glu Glu Glu Gly
1 5

<210> 642
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Peptide linker sequence.

<400> 642

Gly Glu Glu Glu
1

<210> 643
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Peptide linker sequence.

<400> 643

Gly Gly Asp Gly Gly Gly
1 5

<210> 644
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Peptide linker sequence.

<400> 644

Gly Gly Asp Asp Asp Gly Gly
1 5

<210> 645
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Peptide linker sequence.

<400> 645

Gly Asp Asp Asp Gly
1 5

<210> 646
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Peptide linker sequence.

<400> 646

Gly Asp Asp Asp
1

<210> 647
<211> 21
<212> PRT
<213> Artificial Sequence

<220>
<223> Peptide linker sequence.

<400> 647

Gly Gly Gly Gly Ser Asp Asp Ser Asp Glu Gly Ser Asp Gly Glu Asp
1 5 10 15

Gly Gly Gly Gly Ser
20

<210> 648
<211> 5
<212> PRT
<213> Artificial Sequence

<220>

<223> Peptide linker sequence.

<400> 648

Trp Glu Trp Glu Trp
1 5

<210> 649
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Peptide linker sequence.

<400> 649

Phe Glu Phe Glu Phe
1 5

<210> 650
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Peptide linker sequence.

<400> 650

Glu Glu Glu Trp Trp Trp
1 5

<210> 651
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Peptide linker sequence.

<400> 651

Glu Glu Glu Phe Phe Phe
1 5

<210> 652
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Peptide linker sequence.

<400> 652

Trp Trp Glu Glu Glu Trp Trp
1 5

<210> 653
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Peptide linker sequence.

<400> 653

Phe Phe Glu Glu Glu Phe Phe
1 5

<210> 654
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Peptide linker sequence.

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa in positions 1, 2, 4, and 5 are each independently any amino acid residue.

<220>
<221> MISC_FEATURE
<222> (2)..(2)
<223> Xaa in positions 1, 2, 4, and 5 are each independently any amino acid residue.

<220>
<221> MISC_FEATURE
<222> (4)..(4)
<223> Xaa in positions 1, 2, 4, and 5 are each independently any amino acid residue.

<220>
<221> MISC_FEATURE
<222> (5)..(5)
<223> Xaa in positions 1, 2, 4, and 5 are each independently any amino acid residue.

<400> 654

Xaa Xaa Tyr Xaa Xaa Gly
1 5

<210> 655
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Peptide linker sequence.

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa in positions 1, 2, 4, and 5 are each independently any amino acid residue.

<220>
<221> MISC_FEATURE
<222> (2)..(2)
<223> Xaa in positions 1, 2, 4, and 5 are each independently any amino

acid residue.

<220>
<221> MISC_FEATURE
<222> (4)..(4)
<223> Xaa in positions 1, 2, 4, and 5 are each independently any amino acid residue.

<220>
<221> MISC_FEATURE
<222> (5)..(5)
<223> Xaa in positions 1, 2, 4, and 5 are each independently any amino acid residue.

<400> 655

Xaa Xaa Ser Xaa Xaa Gly
1 5

<210> 656
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Peptide linker sequence.

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa in positions 1, 2, 4, and 5 are each independently any amino acid residue.

<220>
<221> MISC_FEATURE
<222> (2)..(2)
<223> Xaa in positions 1, 2, 4, and 5 are each independently any amino acid residue.

<220>
<221> MISC_FEATURE
<222> (4)..(4)
<223> Xaa in positions 1, 2, 4, and 5 are each independently any amino acid residue.

<220>
<221> MISC_FEATURE
<222> (5)..(5)
<223> Xaa in positions 1, 2, 4, and 5 are each independently any amino acid residue.

<400> 656

Xaa Xaa Thr Xaa Xaa Gly
1 5

<210> 657
<211> 140
<212> DNA
<213> Artificial Sequence

<220>
<223> Amino acid linker

<220>
<221> misc_feature
<223> Full length ShK gene linked to four glycine and one serine amino acid linker in positions 7, 8, 9, 10, and 11.

<220>
<221> CDS
<222> (7)..(132)

<400> 657
ggatcc gga gga gga gga agc cgc agc tgc atc gac acc atc ccc aag 48
Gly Gly Gly Gly Ser Arg Ser Cys Ile Asp Thr Ile Pro Lys
1 5 10

agc cgc tgc acc gcc ttc cag tgc aag cac agc atg aag tac cgc ctg 96
Ser Arg Cys Thr Ala Phe Gln Cys Lys His Ser Met Lys Tyr Arg Leu
15 20 25 30

agc ttc tgc cgc aag acc tgc ggc acc tgc taa tga gcggccgc 140
Ser Phe Cys Arg Lys Thr Cys Gly Thr Cys
35 40

<210> 658
<211> 40
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 658

Gly Gly Gly Gly Ser Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg
1 5 10 15

Cys Thr Ala Phe Gln Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe
20 25 30

Cys Arg Lys Thr Cys Gly Thr Cys
35 40

<210> 659
<211> 81
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide (3632-93)

<400> 659
catggatccg gaggaggagg aagccgcagc tgcatcgaca ccatccccaa gagccgctgc 60

accgccttcc agtgcaagca c 81

<210> 660
<211> 82
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide (3632-95)

<400> 660

catgcggccg ctcattagca ggtgccgcag gtcttgcggc agaagctcag gcggtacttc 60

atgctgtgct tgcactggaa gg 82

<210> 661
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer sequence [4101-57]

<400> 661
catggatcca gctgcatcga caccatc 27

<210> 662
<211> 19
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer sequence [3632-96]

<400> 662
catgcggccg ctcattagc 19

<210> 663
<211> 31
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer sequence [4101-58]

<400> 663
catggatccg gaggaggagg aagcagctgc a 31

<210> 664
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer sequence [4101-61]

<400> 664
catgcggccg ctcattagca ggtgc 25

<210> 665
<211> 76
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer sequence [4101-59]

<400> 665
catggatccg ggggtggggg ttctgggggt gggggttctg gaggaggagg aagcggagga 60

ggaggaagca gctgca 76

<210> 666

<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer Sequence [4101-61]

<400> 666
catgcggccg ctcattagca ggtgc 25

<210> 667
<211> 31
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer 3008-05.

<400> 667
ccaacacact tcgaaagacg ttgatcggca c 31

<210> 668
<211> 34
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer 3008-06.

<400> 668
cacccaacaa tgcatcctta aaaaaattac gccc 34

<210> 669
<211> 42
<212> DNA
<213> Artificial Sequence

<220>
<223> 4142-87: Oligonucleotide.

<400> 669
tggttccggt ggtggtggtt cccgttcctg catcgacacc at 42

<210> 670
<211> 85
<212> DNA
<213> Artificial Sequence

<220>
<223> 4142-88: Oligonucleotide.

<400> 670
cccgaaatcc cgttgcaccg ctttccagtg caaacactcc atgaaatacc gtctgtcctt 60

ctgccgtaaa acctgcggta cctgc 85

<210> 671
<211> 42
<212> DNA
<213> Artificial Sequence

<220>
<223> 4142-89: Oligonucleotide.

<400> 671
cttagcaggt accgcaggtt ttacggcaga aggacagacg gt 42

<210> 672
<211> 85
<212> DNA
<213> Artificial Sequence

<220>
<223> 4142-90: Oligonucleotide.

<400> 672
atttcatgga gtgtttgcac tggaaagcgg tgcaacggga tttcgggatg gtgtcgatgc 60

aggaacggga accaccacca ccgga 85

<210> 673
<211> 127
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex.

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in position 1-4.

<220>
<221> CDS
<222> (2)..(127)

<400> 673
t ggt tcc ggt ggt ggt ggt tcc cgt tcc tgc atc gac acc atc ccg aaa 49
Gly Ser Gly Gly Gly Gly Ser Arg Ser Cys Ile Asp Thr Ile Pro Lys
1 5 10 15

tcc cgt tgc acc gct ttc cag tgc aaa cac tcc atg aaa tac cgt ctg 97
Ser Arg Cys Thr Ala Phe Gln Cys Lys His Ser Met Lys Tyr Arg Leu
20 25 30

tcc ttc tgc cgt aaa acc tgc ggt acc tgc 127
Ser Phe Cys Arg Lys Thr Cys Gly Thr Cys
35 40

<210> 674
<211> 42
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 674

Gly Ser Gly Gly Gly Gly Ser Arg Ser Cys Ile Asp Thr Ile Pro Lys
1 5 10 15

Ser Arg Cys Thr Ala Phe Gln Cys Lys His Ser Met Lys Tyr Arg Leu
20 25 30

Ser Phe Cys Arg Lys Thr Cys Gly Thr Cys
35 40

<210> 675
<211> 127
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex.

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in position 1-4.

<400> 675
cttagcaggt accgcaggtt ttacggcaga aggacagacg gtatttcatg gagtgtttgc 60

actggaaagc ggtgcaacgg gatttcggga tggtgtcgat gcaggaacgg gaaccaccac 120

caccgga 127

<210> 676
<211> 83
<212> DNA
<213> Artificial Sequence

<220>
<223> 4154-78: Oligonucleotide duplex.

<400> 676
tggttccggt ggtggtggtt cctgcatcga caccatcccg aaatcccgtt gcaccgcttt 60

ccagtgcaaa cactccatga aat 83

<210> 677
<211> 38
<212> DNA
<213> Artificial Sequence

<220>
<223> 4154-79: Oglionucleotide duplex.

<400> 677
accgtctgtc cttctgccgt aaaacctgcg gtacctgc 38

<210> 678
<211> 82
<212> DNA
<213> Artificial Sequence

<220>
<223> 4154-80: Oligonucleotide duplex.

<400> 678
cttagcaggt accgcaggtt ttacggcaga aggacagacg gtatttcatg gagtgtttgc 60

actggaaagc ggtgcaacgg ga 82

<210> 679

<211> 39
<212> DNA
<213> Artificial Sequence

<220>
<223> 4154-81: Oligonucleotide duplex.

<400> 679
tttcgggatg gtgtcgatgc aggaaccacc accaccgga 39

<210> 680
<211> 121
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex.

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<220>
<221> CDS
<222> (2)..(121)

<400> 680
t ggt tcc ggt ggt ggt ggt tcc tgc atc gac acc atc ccg aaa tcc cgt 49
Gly Ser Gly Gly Gly Gly Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg
1 5 10 15

tgc acc gct ttc cag tgc aaa cac tcc atg aaa tac cgt ctg tcc ttc 97
Cys Thr Ala Phe Gln Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe
20 25 30

tgc cgt aaa acc tgc ggt acc tgc 121
Cys Arg Lys Thr Cys Gly Thr Cys
35 40

<210> 681
<211> 40
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 681

Gly Ser Gly Gly Gly Gly Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg
1 5 10 15

Cys Thr Ala Phe Gln Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe
20 25 30

Cys Arg Lys Thr Cys Gly Thr Cys
35 40

<210> 682
<211> 116
<212> DNA

<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex.

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded in positions 1-4.

<400> 682
caggtaccgc aggttttacg gcagaaggac agacggtatt tcatggagtg tttgcactgg 60

aaagcggtgc aacgggattt cgggatggtg tcgatgcagg aaccaccacc accgga 116

<210> 683
<211> 11
<212> DNA
<213> Artificial Sequence

<220>
<223> Peptide duplex

<400> 683
tggttgagac g 11

<210> 684
<211> 10
<212> DNA
<213> Artificial Sequence

<220>
<223> Peptide duplex

<400> 684
tccaccacca 10

<210> 685
<211> 10
<212> DNA
<213> Artificial Sequence

<220>
<223> Peptide duplex

<400> 685
taaggatccg 10

<210> 686
<211> 11
<212> DNA
<213> Artificial Sequence

<220>
<223> Peptide duplex

<400> 686
gcagagaatt c 11

<210> 687
<211> 11
<212> DNA

<213> Artificial Sequence

<220>
<223> Peptide duplex

<400> 687
tatgcgagac g 11

<210> 688
<211> 11
<212> DNA
<213> Artificial Sequence

<220>
<223> Peptide duplex

<400> 688
ttattgtata c 11

<210> 689
<211> 11
<212> DNA
<213> Artificial Sequence

<220>
<223> Peptide duplex

<400> 689
gcagagtcca c 11

<210> 690
<211> 42
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide [4142-91]

<400> 690
tggttccggt ggtggtggtt cccgtacctg caaagacctg at 42

<210> 691
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> TmTx

<400> 691

Arg Cys His Phe Val Val Cys Thr Thr Asp Cys Arg Arg Asn Ser Pro
1 5 10 15

Gly Thr Tyr Gly Glu Cys Val Lys Lys Glu Lys Gly Lys Glu Cys Val
20 25 30

Cys Lys Ser
35

<210> 692

<211> 85
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide [nt 4142-92]

<400> 692
cccggtttcc gaatgcaccg acatccgttg ccgtacctcc atgaaatacc gtctgaacct 60

gtgccgtaaa acctgcggtt cctgc 85

<210> 693
<211> 42
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide [nt 4142-93]

<400> 693
cttagcagga accgcaggtt ttacggcaca ggttcagacg gt 42

<210> 694
<211> 85
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide [nt 4142-94]

<400> 694
atttcatgga ggtacggcaa cggatgtcgg tgcattcgga aaccgggatc aggtctttgc 60

aggtacggga accaccacca ccgga 85

<210> 695
<211> 127
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4 on both strands.

<220>
<221> CDS
<222> (2)..(127)

<400> 695
t ggt tcc ggt ggt ggt ggt tcc cgt acc tgc aaa gac ctg atc ccg gtt 49
  Gly Ser Gly Gly Gly Gly Ser Arg Thr Cys Lys Asp Leu Ile Pro Val
  1   5   10   15

tcc gaa tgc acc gac atc cgt tgc cgt acc tcc atg aaa tac cgt ctg 97
Ser Glu Cys Thr Asp Ile Arg Cys Arg Thr Ser Met Lys Tyr Arg Leu
            20   25   30

aac ctg tgc cgt aaa acc tgc ggt tcc tgc 127
Asn Leu Cys Arg Lys Thr Cys Gly Ser Cys

35 40

<210> 696
<211> 42
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 696

Gly Ser Gly Gly Gly Gly Ser Arg Thr Cys Lys Asp Leu Ile Pro Val
1 5 10 15

Ser Glu Cys Thr Asp Ile Arg Cys Arg Thr Ser Met Lys Tyr Arg Leu
20 25 30

Asn Leu Cys Arg Lys Thr Cys Gly Ser Cys
35 40

<210> 697
<211> 127
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex.

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<400> 697
cttagcagga accgcaggtt ttacggcaca ggttcagacg gtatttcatg gaggtacggc 60

aacggatgtc ggtgcattcg gaaaccggga tcaggtcttt gcaggtacgg gaaccaccac 120

caccgga 127

<210> 698
<211> 47
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4128-77]

<400> 698
tggttccggt ggtggtggtt ccggtgttga aatcaacgtt aaatgct 47

<210> 699
<211> 89
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4128-78]

<400> 699

ccggttcccc gcagtgcctg aaaccgtgca aagacgctgg tatgcgtttc ggtaaatgca 60

tgaaccgtaa atgccactgc accccgaaa 89

<210> 700
<211> 47
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4128-79]

<400> 700
cttatttcgg ggtgcagtgg catttacggt tcatgcattt accgaaa 47

<210> 701
<211> 89
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4128-80]

<400> 701
cgcataccag cgtctttgca cggtttcagg cactgcgggg aaccggagca tttaacgttg 60

atttcaacac cggaaccacc accaccgga 89

<210> 702
<211> 136
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<220>
<221> CDS
<222> (2)..(136)

<400> 702
t ggt tcc ggt ggt ggt ggt tcc ggt gtt gaa atc aac gtt aaa tgc tcc 49
  Gly Ser Gly Gly Gly Gly Ser Gly Val Glu Ile Asn Val Lys Cys Ser
  1   5   10   15

ggt tcc ccg cag tgc ctg aaa ccg tgc aaa gac gct ggt atg cgt ttc 97
Gly Ser Pro Gln Cys Leu Lys Pro Cys Lys Asp Ala Gly Met Arg Phe
            20   25   30

ggt aaa tgc atg aac cgt aaa tgc cac tgc acc ccg aaa 136
Gly Lys Cys Met Asn Arg Lys Cys His Cys Thr Pro Lys
        35   40   45

<210> 703
<211> 45
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 703

Gly Ser Gly Gly Gly Gly Ser Gly Val Glu Ile Asn Val Lys Cys Ser
1 5 10 15

Gly Ser Pro Gln Cys Leu Lys Pro Cys Lys Asp Ala Gly Met Arg Phe
20 25 30

Gly Lys Cys Met Asn Arg Lys Cys His Cys Thr Pro Lys
35 40 45

<210> 704
<211> 136
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<400> 704
cttatttcgg ggtgcagtgg catttacggt tcatgcattt accgaaacgc ataccagcgt 60

ctttgcacgg tttcaggcac tgcggggaac cggagcattt aacgttgatt tcaacaccgg 120

aaccaccacc accgga 136

<210> 705
<211> 46
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4128-85]

<400> 705
tggttccggt ggtggtggtt ccgcttcctg ccgtaccccg aaagac 46

<210> 706
<211> 78
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4128-86]

<400> 706
tgcgctgacc cgtgccgtaa agaaaccggt tgcccgtacg gtaaatgcat gaaccgtaaa 60

tgcaaatgca accgttgc 78

<210> 707
<211> 48
<212> DNA

<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4128-87]

<400> 707
cttagcaacg gttgcatttg catttacggt tcatgcattt accgtacg 48

<210> 708
<211> 76
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4128-88]

<400> 708
ggcaaccggt ttctttacgg cacgggtcag cgcagtcttt cggggtacgg caggaagcgg 60

aaccaccacc accgga 76

<210> 709
<211> 124
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<220>
<221> CDS
<222> (2)..(124)

<400> 709
t ggt tcc ggt ggt ggt ggt tcc gct tcc tgc cgt acc ccg aaa gac tgc 49
Gly Ser Gly Gly Gly Gly Ser Ala Ser Cys Arg Thr Pro Lys Asp Cys
1 5 10 15

gct gac ccg tgc cgt aaa gaa acc ggt tgc ccg tac ggt aaa tgc atg 97
Ala Asp Pro Cys Arg Lys Glu Thr Gly Cys Pro Tyr Gly Lys Cys Met
20 25 30

aac cgt aaa tgc aaa tgc aac cgt tgc 124
Asn Arg Lys Cys Lys Cys Asn Arg Cys
35 40

<210> 710
<211> 41
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 710

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

Ala Asp Pro Cys Arg Lys Glu Thr Gly Cys Pro Tyr Gly Lys Cys Met
20 25 30

Asn Arg Lys Cys Lys Cys Asn Arg Cys
35 40

<210> 711
<211> 124
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<400> 711
cttagcaacg gttgcatttg catttacggt tcatgcattt accgtacggg caaccggttt 60

ctttacggca cgggtcagcg cagtctttcg gggtacggca ggaagcggaa ccaccaccac 120

cgga 124

<210> 712
<211> 48
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4128-59]

<400> 712
tggttccggt ggtggtggtt ccaccatcat caacgttaaa tgcacctc 48

<210> 713
<211> 91
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4128-60]

<400> 713
cccgaaacag tgcctgccgc cgtgcaaagc tcagttcggt cagtccgctg gtgctaaatg 60

catgaacggt aaatgcaaat gctacccgca c 91

<210> 714
<211> 48
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4128-61]

<400> 714
cttagtgcgg gtagcatttg catttaccgt tcatgcattt agcaccag 48

<210> 715
<211> 91
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4128-62]

<400> 715
cggactgacc gaactgagct ttgcacggcg gcaggcactg tttcggggag gtgcatttaa 60

cgttgatgat ggtggaacca ccaccaccgg a 91

<210> 716
<211> 139
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<220>
<221> CDS
<222> (2)..(139)

<400> 716
t ggt tcc ggt ggt ggt ggt tcc acc atc atc aac gtt aaa tgc acc tcc 49
  Gly Ser Gly Gly Gly Gly Ser Thr Ile Ile Asn Val Lys Cys Thr Ser
  1   5   10   15

ccg aaa cag tgc ctg ccg ccg tgc aaa gct cag ttc ggt cag tcc gct 97
Pro Lys Gln Cys Leu Pro Pro Cys Lys Ala Gln Phe Gly Gln Ser Ala
            20   25   30

ggt gct aaa tgc atg aac ggt aaa tgc aaa tgc tac ccg cac 139
Gly Ala Lys Cys Met Asn Gly Lys Cys Lys Cys Tyr Pro His
        35   40   45

<210> 717
<211> 46
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 717

Gly Ser Gly Gly Gly Gly Ser Thr Ile Ile Asn Val Lys Cys Thr Ser
1   5   10   15

Pro Lys Gln Cys Leu Pro Pro Cys Lys Ala Gln Phe Gly Gln Ser Ala
            20   25   30

Gly Ala Lys Cys Met Asn Gly Lys Cys Lys Cys Tyr Pro His
        35   40   45

<210> 718
<211> 139
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<400> 718
cttagtgcgg gtagcatttg catttaccgt tcatgcattt agcaccagcg gactgaccga 60

actgagcttt gcacggcggc aggcactgtt tcggggaggt gcatttaacg ttgatgatgg 120

tggaaccacc accaccgga 139

<210> 719
<211> 52
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4128-89]

<400> 719
tggttccggt ggtggtggtt ccggtgttcc gatcaacgtt tcctgcaccg gt 52

<210> 720
<211> 84
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4128-90]

<400> 720
tccccgcagt gcatcaaacc gtgcaaagac gctggtatgc gtttcggtaa atgcatgaac 60

cgtaaatgcc actgcacccc gaaa 84

<210> 721
<211> 53
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4128-91]

<400> 721
cttatttcgg ggtgcagtgg catttacggt tcatgcattt accgaaacgc ata 53

<210> 722
<211> 83
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4128-92]

<400> 722
ccagcgtctt tgcacggttt gatgcactgc ggggaaccgg tgcaggaaac gttgatcgga 60

acaccggaac caccaccacc gga 83

<210> 723
<211> 136
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<220>
<221> CDS
<222> (2)..(136)

<400> 723
t ggt tcc ggt ggt ggt ggt tcc ggt gtt ccg atc aac gtt tcc tgc acc 49
Gly Ser Gly Gly Gly Gly Ser Gly Val Pro Ile Asn Val Ser Cys Thr
1 5 10 15

ggt tcc ccg cag tgc atc aaa ccg tgc aaa gac gct ggt atg cgt ttc 97
Gly Ser Pro Gln Cys Ile Lys Pro Cys Lys Asp Ala Gly Met Arg Phe
20 25 30

ggt aaa tgc atg aac cgt aaa tgc cac tgc acc ccg aaa 136
Gly Lys Cys Met Asn Arg Lys Cys His Cys Thr Pro Lys
35 40 45

<210> 724
<211> 45
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 724

Gly Ser Gly Gly Gly Gly Ser Gly Val Pro Ile Asn Val Ser Cys Thr
1 5 10 15

Gly Ser Pro Gln Cys Ile Lys Pro Cys Lys Asp Ala Gly Met Arg Phe
20 25 30

Gly Lys Cys Met Asn Arg Lys Cys His Cys Thr Pro Lys
35 40 45

<210> 725
<211> 136
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<400> 725
cttatttcgg ggtgcagtgg catttacggt tcatgcattt accgaaacgc ataccagcgt 60

ctttgcacgg tttgatgcac tgcggggaac cggtgcagga aacgttgatc ggaacaccgg 120

aaccaccacc accgga 136

<210> 726
<211> 83
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4154-82]

<400> 726
tggttccggt ggtggtggtt ccggtgttat catcaacgtt aaatgcaaaa tctcccgtca 60

gtgcctggaa ccgtgcaaaa aag 83

<210> 727
<211> 53
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4154-83]

<400> 727
ctggtatgcg tttcggtaaa tgcatgaacg gtaaatgcca ctgcaccccg aaa 53

<210> 728
<211> 83
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4154-84]

<400> 728
cttatttcgg ggtgcagtgg catttaccgt tcatgcattt accgaaacgc ataccagctt 60

ttttgcacgg ttccaggcac tga 83

<210> 729
<211> 53
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4154-85]

<400> 729
cgggagattt tgcatttaac gttgatgata acaccggaac caccaccacc gga 53

<210> 730

<211> 136
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<220>
<221> CDS
<222> (2)..(136)

<400> 730
t ggt tcc ggt ggt ggt ggt tcc ggt gtt atc atc aac gtt aaa tgc aaa 49
Gly Ser Gly Gly Gly Gly Ser Gly Val Ile Ile Asn Val Lys Cys Lys
1 5 10 15

atc tcc cgt cag tgc ctg gaa ccg tgc aaa aaa gct ggt atg cgt ttc 97
Ile Ser Arg Gln Cys Leu Glu Pro Cys Lys Lys Ala Gly Met Arg Phe
20 25 30

ggt aaa tgc atg aac ggt aaa tgc cac tgc acc ccg aaa 136
Gly Lys Cys Met Asn Gly Lys Cys His Cys Thr Pro Lys
35 40 45

<210> 731
<211> 45
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 731

Gly Ser Gly Gly Gly Gly Ser Gly Val Ile Ile Asn Val Lys Cys Lys
1 5 10 15

Ile Ser Arg Gln Cys Leu Glu Pro Cys Lys Lys Ala Gly Met Arg Phe
20 25 30

Gly Lys Cys Met Asn Gly Lys Cys His Cys Thr Pro Lys
35 40 45

<210> 732
<211> 136
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<400> 732

cttatttcgg ggtgcagtgg catttaccgt tcatgcattt accgaaacgc ataccagctt 60

ttttgcacgg ttccaggcac tgacgggaga ttttgcattt aacgttgatg ataacaccgg 120

aaccaccacc accgga 136

<210> 733
<211> 83
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4154-86]

<400> 733
tggttccggt ggtggtggtt ccggtgttat catcaacgtt aaatgcaaaa tctcccgtca 60

gtgcctgaaa ccgtgcaaag acg 83

<210> 734
<211> 53
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4154-83]

<400> 734
ctggtatgcg tttcggtaaa tgcatgaacg gtaaatgcca ctgcaccccg aaa 53

<210> 735
<211> 83
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4154-87]

<400> 735
cttatttcgg ggtgcagtgg catttaccgt tcatgcattt accgaaacgc ataccagcgt 60

ctttgcacgg tttcaggcac tga 83

<210> 736
<211> 53
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4154-85]

<400> 736
cgggagattt tgcatttaac gttgatgata acaccggaac caccaccacc gga 53

<210> 737
<211> 136
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA strand in position 1-4.

<220>
<221> CDS
<222> (2)..(136)

<400> 737
t ggt tcc ggt ggt ggt ggt tcc ggt gtt atc atc aac gtt aaa tgc aaa 49
Gly Ser Gly Gly Gly Gly Ser Gly Val Ile Ile Asn Val Lys Cys Lys
1 5 10 15

atc tcc cgt cag tgc ctg aaa ccg tgc aaa gac gct ggt atg cgt ttc 97
Ile Ser Arg Gln Cys Leu Lys Pro Cys Lys Asp Ala Gly Met Arg Phe
20 25 30

ggt aaa tgc atg aac ggt aaa tgc cac tgc acc ccg aaa 136
Gly Lys Cys Met Asn Gly Lys Cys His Cys Thr Pro Lys
35 40 45

<210> 738
<211> 45
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 738

Gly Ser Gly Gly Gly Gly Ser Gly Val Ile Ile Asn Val Lys Cys Lys
1 5 10 15

Ile Ser Arg Gln Cys Leu Lys Pro Cys Lys Asp Ala Gly Met Arg Phe
20 25 30

Gly Lys Cys Met Asn Gly Lys Cys His Cys Thr Pro Lys
35 40 45

<210> 739
<211> 136
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<400> 739
cttatttcgg ggtgcagtgg catttaccgt tcatgcattt accgaaacgc ataccagcgt 60

ctttgcacgg tttcaggcac tgacgggaga ttttgcattt aacgttgatg ataacaccgg 120

aaccaccacc accgga 136

<210> 740

<211> 83
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4154-88]

<400> 740
tggttccggt ggtggtggtt ccaaagaatg caccggtccg cagcactgca ccaacttctg 60

ccgtaaaaac aaatgcaccc acg 83

<210> 741
<211> 41
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4154-89]

<400> 741
gtaaatgcat gaaccgtaaa tgcaaatgct tcaactgcaa a 41

<210> 742
<211> 83
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4154-90]

<400> 742
cttatttgca gttgaagcat ttgcatttac ggttcatgca tttaccgtgg gtgcatttgt 60

ttttacggca gaagttggtg cag 83

<210> 743
<211> 41
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4154-91]

<400> 743
tgctgcggac cggtgcattc tttggaacca ccaccaccgg a 41

<210> 744
<211> 124
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<220>
<221> CDS
<222> (2)..(124)

<400> 744
t ggt tcc ggt ggt ggt ggt tcc aaa gaa tgc acc ggt ccg cag cac tgc 49
Gly Ser Gly Gly Gly Gly Ser Lys Glu Cys Thr Gly Pro Gln His Cys
1 5 10 15

acc aac ttc tgc cgt aaa aac aaa tgc acc cac ggt aaa tgc atg aac 97
Thr Asn Phe Cys Arg Lys Asn Lys Cys Thr His Gly Lys Cys Met Asn
20 25 30

cgt aaa tgc aaa tgc ttc aac tgc aaa 124
Arg Lys Cys Lys Cys Phe Asn Cys Lys
35 40

<210> 745
<211> 41
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 745

Gly Ser Gly Gly Gly Gly Ser Lys Glu Cys Thr Gly Pro Gln His Cys
1 5 10 15

Thr Asn Phe Cys Arg Lys Asn Lys Cys Thr His Gly Lys Cys Met Asn
20 25 30

Arg Lys Cys Lys Cys Phe Asn Cys Lys
35 40

<210> 746
<211> 124
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(1)
<223> Single-stranded DNA in positions 1-4

<400> 746
cttatttgca gttgaagcat ttgcatttac ggttcatgca tttaccgtgg gtgcatttgt 60

ttttacggca gaagttggtg cagtgctgcg gaccggtgca ttctttggaa ccaccaccac 120

cgga 124

<210> 747
<211> 83
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4154-92]

<400> 747

tggttccggt ggtggtggtt ccaccatcat caacgttaaa tgcacctccc cgaaacagtg 60

ctccaaaccg tgcaaagaac tgt 83

<210> 748
<211> 56
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4154-93]

<400> 748
acggttcctc cgctggtgct aaatgcatga acggtaaatg caaatgctac aacaac 56

<210> 749
<211> 83
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4154-94]

<400> 749
cttagttgtt gtagcatttg catttaccgt tcatgcattt agcaccagcg gaggaaccgt 60

acagttcttt gcacggtttg gag 83

<210> 750
<211> 56
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4154-95]

<400> 750
cactgtttcg gggaggtgca tttaacgttg atgatggtgg aaccaccacc accgga 56

<210> 751
<211> 139
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<220>
<221> CDS
<222> (2)..(139)

<400> 751
t ggt tcc ggt ggt ggt ggt tcc acc atc atc aac gtt aaa tgc acc tcc 49
  Gly Ser Gly Gly Gly Gly Ser Thr Ile Ile Asn Val Lys Cys Thr Ser
  1   5   10   15

ccg aaa cag tgc tcc aaa ccg tgc aaa gaa ctg tac ggt tcc tcc gct 97
Pro Lys Gln Cys Ser Lys Pro Cys Lys Glu Leu Tyr Gly Ser Ser Ala

20 25 30

ggt gct aaa tgc atg aac ggt aaa tgc aaa tgc tac aac aac 139
Gly Ala Lys Cys Met Asn Gly Lys Cys Lys Cys Tyr Asn Asn
35 40 45

<210> 752
<211> 46
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 752

Gly Ser Gly Gly Gly Gly Ser Thr Ile Ile Asn Val Lys Cys Thr Ser
1 5 10 15

Pro Lys Gln Cys Ser Lys Pro Cys Lys Glu Leu Tyr Gly Ser Ser Ala
20 25 30

Gly Ala Lys Cys Met Asn Gly Lys Cys Lys Cys Tyr Asn Asn
35 40 45

<210> 753
<211> 139
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<400> 753
cttagttgtt gtagcatttg catttaccgt tcatgcattt agcaccagcg gaggaaccgt 60

acagttcttt gcacggtttg gagcactgtt tcggggaggt gcatttaacg ttgatgatgg 120

tggaaccacc accaccgga 139

<210> 754
<211> 43
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4128-81]

<400> 754
tggttccggt ggtggtggtt ccaccatctc ctgcaccaac ccg 43

<210> 755
<211> 84
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4128-82]

<400> 755
aaacagtgct acccgcactg caaaaaagaa accggttacc cgaacgctaa atgcatgaac 60

cgtaaatgca aatgcttcgg tcgt 84

<210> 756
<211> 44
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4128-83]

<400> 756
cttaacgacc gaagcatttg catttacggt tcatgcattt agcg 44

<210> 757
<211> 83
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<400> 757
ttcgggtaac cggtttcttt tttgcagtgc gggtagcact gtttcgggtt ggtgcaggag 60

atggtggaac caccaccacc gga 83

<210> 758
<211> 127
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in postions 1-4.

<220>
<221> CDS
<222> (2)..(127)

<400> 758
t ggt tcc ggt ggt ggt ggt tcc acc atc tcc tgc acc aac ccg aaa cag 49
  Gly Ser Gly Gly Gly Gly Ser Thr Ile Ser Cys Thr Asn Pro Lys Gln
  1   5   10   15

tgc tac ccg cac tgc aaa aaa gaa acc ggt tac ccg aac gct aaa tgc 97
Cys Tyr Pro His Cys Lys Lys Glu Thr Gly Tyr Pro Asn Ala Lys Cys
            20   25   30

atg aac cgt aaa tgc aaa tgc ttc ggt cgt 127
Met Asn Arg Lys Cys Lys Cys Phe Gly Arg
        35   40

<210> 759

<211> 42
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 759

Gly Ser Gly Gly Gly Gly Ser Thr Ile Ser Cys Thr Asn Pro Lys Gln
1 5 10 15

Cys Tyr Pro His Cys Lys Lys Glu Thr Gly Tyr Pro Asn Ala Lys Cys
20 25 30

Met Asn Arg Lys Cys Lys Cys Phe Gly Arg
35 40

<210> 760
<211> 127
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<400> 760
cttaacgacc gaagcatttg catttacggt tcatgcattt agcgttcggg taaccggttt 60

ctttttgca gtgcgggtag cactgtttcg ggttggtgca ggagatggtg gaaccaccac 120

caccgga 127

<210> 761
<211> 83
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide [4154-96]

<400> 761
tatgcgttct tgtattgata ctattccaaa atctcgttgt actgcttttc aatgtaaaca 60

ttctatgaaa tatcgtcttt ctt 83

<210> 762
<211> 44
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligo nucleotide [4154-97]

<400> 762
tttgtcgtaa aacttgtggt acttgttctg gtggtggtgg ttct 44

<210> 763
<211> 83
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<400> 763
caccagaacc accaccacca gaacaagtac cacaagtttt acgacaaaaa gaaagacgat 60

atttcataga atgtttacat tga 83

<210> 764
<211> 44
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4154-99]

<400> 764
aaagcagtac aacgagattt tggaatagta tcaatacaag aacg 44

<210> 765
<211> 127
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<220>
<221> CDS
<222> (2)..(127)

<400> 765
t atg cgt tct tgt att gat act att cca aaa tct cgt tgt act gct ttt 49
Met Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe
1 5 10 15

caa tgt aaa cat tct atg aaa tat cgt ctt tct ttt tgt cgt aaa act 97
Gln Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr
20 25 30

tgt ggt act tgt tct ggt ggt ggt ggt tct 127
Cys Gly Thr Cys Ser Gly Gly Gly Gly Ser
35 40

<210> 766
<211> 42
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 766

Met Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe
1 5 10 15

Gln Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr
20 25 30

Cys Gly Thr Cys Ser Gly Gly Gly Gly Ser
35 40

<210> 767
<211> 127
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<400> 767
caccagaacc accaccacca gaacaagtac cacaagtttt acgacaaaaa gaaagacgat 60

atttcataga atgtttacat tgaaaagcag tacaacgaga ttttggaata gtatcaatac 120

aagaacg 127

<210> 768
<211> 80
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4155-01]

<400> 768
tatgtcttgt attgatacta ttccaaaatc tcgttgtact gcttttcaat gtaaacattc 60

tatgaaatat cgtctttctt 80

<210> 769
<211> 44
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4154-97]

<400> 769
tttgtcgtaa aacttgtggt acttgttctg gtggtggtgg ttct 44

<210> 770
<211> 83
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4154-98]

<400> 770
caccagaacc accaccacca gaacaagtac cacaagtttt acgacaaaaa gaaagacgat 60

atttcataga atgtttacat tga 83

<210> 771
<211> 41
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4155-02]

<400> 771
aaagcagtac aacgagattt tggaatagta tcaatacaag a 41

<210> 772
<211> 124
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<220>
<221> CDS
<222> (2)..(124)

<400> 772
t atg tct tgt att gat act att cca aaa tct cgt tgt act gct ttt caa 49
Met Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

tgt aaa cat tct atg aaa tat cgt ctt tct ttt tgt cgt aaa act tgt 97
Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

ggt act tgt tct ggt ggt ggt ggt tct 124
Gly Thr Cys Ser Gly Gly Gly Gly Ser
35 40

<210> 773
<211> 41
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 773

Met Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys Ser Gly Gly Gly Gly Ser
35 40

<210> 774
<211> 124
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<400> 774
caccagaacc accaccacca gaacaagtac cacaagtttt acgacaaaaa gaaagacgat 60

atttcataga atgtttacat tgaaaagcag tacaacgaga ttttggaata gtatcaatac 120

aaga 124

<210> 775
<211> 37
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4128-69]

<400> 775
tggttccggt ggtggtggtt cccagttcac caacgtt 37

<210> 776
<211> 96
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4128-70]

<400> 776
tcctgcacca cctccaaaga atgctggtcc gtttgccagc gtctgcacaa cacctcccgt 60

ggtaaatgca tgaacaaaaa atgccgttgc tactcc 96

<210> 777
<211> 38
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4128-71]

<400> 777
cttaggagta gcaacggcat tttttgttca tgcattta 38

<210> 778
<211> 95
<212> DNA

<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4128-72]

<400> 778
ccacgggagg tgttgtgcag acgctggcaa acggaccagc attctttgga ggtggtgcag 60

gaaacgttgg tgaactggga accaccacca ccgga 95

<210> 779
<211> 133
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<220>
<221> CDS
<222> (2)..(133)

<400> 779
t ggt tcc ggt ggt ggt ggt tcc cag ttc acc aac gtt tcc tgc acc acc 49
  Gly Ser Gly Gly Gly Gly Ser Gln Phe Thr Asn Val Ser Cys Thr Thr
  1   5   10   15

tcc aaa gaa tgc tgg tcc gtt tgc cag cgt ctg cac aac acc tcc cgt 97
Ser Lys Glu Cys Trp Ser Val Cys Gln Arg Leu His Asn Thr Ser Arg
            20   25   30

ggt aaa tgc atg aac aaa aaa tgc cgt tgc tac tcc 133
Gly Lys Cys Met Asn Lys Lys Cys Arg Cys Tyr Ser
        35   40

<210> 780
<211> 44
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 780

Gly Ser Gly Gly Gly Gly Ser Gln Phe Thr Asn Val Ser Cys Thr Thr
1   5   10   15

Ser Lys Glu Cys Trp Ser Val Cys Gln Arg Leu His Asn Thr Ser Arg
            20   25   30

Gly Lys Cys Met Asn Lys Lys Cys Arg Cys Tyr Ser
        35   40

<210> 781
<211> 133
<212> DNA

<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<400> 781
cttaggagta gcaacggcat tttttgttca tgcatttacc acgggaggtg ttgtgcagac 60

gctggcaaac ggaccagcat tctttggagg tggtgcagga aacgttggtg aactgggaac 120

caccaccacc gga 133

<210> 782
<211> 37
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4128-65]

<400> 782
tggttccggt ggtggtggtt ccgtttcctg caccggt 37

<210> 783
<211> 87
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4128-66]

<400> 783
tccaaagact gctacgctcc gtgccgtaaa cagaccggtt gcccgaacgc taaatgcatc 60

aacaaatcct gcaaatgcta cggttgc 87

<210> 784
<211> 38
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4128-67]

<400> 784
cttagcaacc gtagcatttg caggatttgt tgatgcat 38

<210> 785
<211> 86
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4128-68]

<400> 785
ttagcgttcg ggcaaccggt ctgtttacgg cacggagcgt agcagtcttt ggaaccggtg 60

caggaaacgg aaccaccacc accgga 86

<210> 786
<211> 124
<212> DNA

<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<220>
<221> CDS
<222> (2)..(124)

<400> 786
t ggt tcc ggt ggt ggt ggt tcc gtt tcc tgc acc ggt tcc aaa gac tgc 49
Gly Ser Gly Gly Gly Gly Ser Val Ser Cys Thr Gly Ser Lys Asp Cys
1 5 10 15

tac gct ccg tgc cgt aaa cag acc ggt tgc ccg aac gct aaa tgc atc 97
Tyr Ala Pro Cys Arg Lys Gln Thr Gly Cys Pro Asn Ala Lys Cys Ile
20 25 30

aac aaa tcc tgc aaa tgc tac ggt tgc 124
Asn Lys Ser Cys Lys Cys Tyr Gly Cys
35 40

<210> 787
<211> 41
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 787

Gly Ser Gly Gly Gly Gly Ser Val Ser Cys Thr Gly Ser Lys Asp Cys
1 5 10 15

Tyr Ala Pro Cys Arg Lys Gln Thr Gly Cys Pro Asn Ala Lys Cys Ile
20 25 30

Asn Lys Ser Cys Lys Cys Tyr Gly Cys
35 40

<210> 788
<211> 124
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<400> 788
cttagcaacc gtagcatttg caggatttgt tgatgcattt agcgttcggg caaccggtct 60

gtttacggca cggagcgtag cagtctttgg aaccggtgca ggaaacggaa ccaccaccac 120

cgga 124

<210> 789
<211> 42
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4128-73]

<400> 789
tggttccggt ggtggtggtt cccagttcac caacgtttcc tg 42

<210> 790
<211> 91
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4128-74]

<400> 790
caccacctcc aaagaatgct ggtccgtttg ccagcgtctg cacaacacct cccgtggtaa 60

atgcatgaac aaagaatgcc gttgctactc c 91

<210> 791
<211> 43
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4128-75]

<400> 791
cttaggagta gcaacggcat tctttgttca tgcatttacc acg 43

<210> 792
<211> 90
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4128-76]

<400> 792
ggaggtgttg tgcagacgct ggcaaacgga ccagcattct ttggaggtgg tgcaggaaac 60

gttggtgaac tgggaaccac caccaccgga 90

<210> 793
<211> 133
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature

<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<220>
<221> CDS
<222> (2)..(133)

<400> 793
t ggt tcc ggt ggt ggt ggt tcc cag ttc acc aac gtt tcc tgc acc acc 49
Gly Ser Gly Gly Gly Gly Ser Gln Phe Thr Asn Val Ser Cys Thr Thr
1 5 10 15

tcc aaa gaa tgc tgg tcc gtt tgc cag cgt ctg cac aac acc tcc cgt 97
Ser Lys Glu Cys Trp Ser Val Cys Gln Arg Leu His Asn Thr Ser Arg
20 25 30

ggt aaa tgc atg aac aaa gaa tgc cgt tgc tac tcc 133
Gly Lys Cys Met Asn Lys Glu Cys Arg Cys Tyr Ser
35 40

<210> 794
<211> 44
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 794

Gly Ser Gly Gly Gly Gly Ser Gln Phe Thr Asn Val Ser Cys Thr Thr
1 5 10 15

Ser Lys Glu Cys Trp Ser Val Cys Gln Arg Leu His Asn Thr Ser Arg
20 25 30

Gly Lys Cys Met Asn Lys Glu Cys Arg Cys Tyr Ser
35 40

<210> 795
<211> 133
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<400> 795
cttaggagta gcaacggcat tctttgttca tgcatttacc acgggaggtg ttgtgcagac 60

gctggcaaac ggaccagcat tctttggagg tggtgcagga aacgttggtg aactgggaac 120

caccaccacc gga 133

<210> 796
<211> 79
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4128-63]

<400> 796

tggttccggt ggtggtggtt cctgcaactg caaagctccg gaaaccgctc tgtgcgctcg 60

tcgttgccag cagcacggt 79

<210> 797
<211> 79
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4128-64]

<400> 797
cttaaccgtg ctgctggcaa cgacgagcgc acagagcggt ttccggagct ttgcagttgc 60

aggaaccacc accaccgga 79

<210> 798
<211> 79
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<220>
<221> CDS
<222> (2)..(79)

<400> 798
t ggt tcc ggt ggt ggt ggt tcc tgc aac tgc aaa gct ccg gaa acc gct 49
Gly Ser Gly Gly Gly Gly Ser Cys Asn Cys Lys Ala Pro Glu Thr Ala
1 5 10 15

ctg tgc gct cgt cgt tgc cag cag cac ggt 79
Leu Cys Ala Arg Arg Cys Gln Gln His Gly
20 25

<210> 799
<211> 26
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 799

Gly Ser Gly Gly Gly Gly Ser Cys Asn Cys Lys Ala Pro Glu Thr Ala
1 5 10 15

Leu Cys Ala Arg Arg Cys Gln Gln His Gly
20 25

<210> 800
<211> 79
<212> DNA

<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<400> 800
cttaaccgtg ctgctggcaa cgacgagcgc acagagcggt ttccggagct ttgcagttgc 60

aggaaccacc accaccgga 79

<210> 801
<211> 39
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4129-18]

<400> 801
tggttccggt ggtggtggtt ccgctttctg caacctgcg 39

<210> 802
<211> 76
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4129-19]

<400> 802
tatgtgccag ctgtcctgcc gttccctggg tctgctgggt aaatgcatcg gtgacaaatg 60

cgaatgcgtt aaacac 76

<210> 803
<211> 40
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4129-20]

<400> 803
cttagtgttt aacgcattcg catttgtcac cgatgcattt 40

<210> 804
<211> 75
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4129-21]

<400> 804
acccagcaga cccagggaac ggcaggacag ctggcacata cgcaggttgc agaaagcgga 60

accaccacca ccgga 75

<210> 805
<211> 115
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<220>
<221> CDS
<222> (2)..(115)

<400> 805
t ggt tcc ggt ggt ggt ggt tcc gct ttc tgc aac ctg cgt atg tgc cag 49
Gly Ser Gly Gly Gly Gly Ser Ala Phe Cys Asn Leu Arg Met Cys Gln
1 5 10 15

ctg tcc tgc cgt tcc ctg ggt ctg ctg ggt aaa tgc atc ggt gac aaa 97
Leu Ser Cys Arg Ser Leu Gly Leu Leu Gly Lys Cys Ile Gly Asp Lys
20 25 30

tgc gaa tgc gtt aaa cac 115
Cys Glu Cys Val Lys His
35

<210> 806
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 806

Gly Ser Gly Gly Gly Gly Ser Ala Phe Cys Asn Leu Arg Met Cys Gln
1 5 10 15

Leu Ser Cys Arg Ser Leu Gly Leu Leu Gly Lys Cys Ile Gly Asp Lys
20 25 30

Cys Glu Cys Val Lys His
35

<210> 807
<211> 115
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<400> 807
cttagtgttt aacgcattcg catttgtcac cgatgcattt acccagcaga cccagggaac 60

ggcaggacag ctggcacata cgcaggttgc agaaagcgga accaccacca ccgga 115

<210> 808
<211> 48
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4194-44]

<400> 808
tggttccggt ggtggtggtt cccagttcac cgacgttgac tgctccgt 48

<210> 809
<211> 85
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4194-45]

<400> 809
ttccaaagaa tgctggtccg tttgcaaaga cctgttcggt gttgaccgtg gtaaatgcat 60

gggtaaaaaa tgccgttgct accag 85

<210> 810
<211> 48
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4194-46]

<400> 810
cttactggta gcaacggcat tttttaccca tgcatttacc acggtcaa 48

<210> 811
<211> 85
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4194-47]

<400> 811
caccgaacag gtctttgcaa acggaccagc attctttgga aacggagcag tcaacgtcgg 60

tgaactggga accaccacca ccgga 85

<210> 812
<211> 133
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<220>
<221> CDS
<222> (2)..(133)

<400> 812
t ggt tcc ggt ggt ggt ggt tcc cag ttc acc gac gtt gac tgc tcc gtt 49
Gly Ser Gly Gly Gly Gly Ser Gln Phe Thr Asp Val Asp Cys Ser Val
1 5 10 15

tcc aaa gaa tgc tgg tcc gtt tgc aaa gac ctg ttc ggt gtt gac cgt 97
Ser Lys Glu Cys Trp Ser Val Cys Lys Asp Leu Phe Gly Val Asp Arg
20 25 30

ggt aaa tgc atg ggt aaa aaa tgc cgt tgc tac cag 133
Gly Lys Cys Met Gly Lys Lys Cys Arg Cys Tyr Gln
35 40

<210> 813
<211> 44
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 813

Gly Ser Gly Gly Gly Gly Ser Gln Phe Thr Asp Val Asp Cys Ser Val
1 5 10 15

Ser Lys Glu Cys Trp Ser Val Cys Lys Asp Leu Phe Gly Val Asp Arg
20 25 30

Gly Lys Cys Met Gly Lys Lys Cys Arg Cys Tyr Gln
35 40

<210> 814
<211> 133
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<400> 814
cttactggta gcaacggcat tttttaccca tgcatttacc acggtcaaca ccgaacaggt 60

ctttgcaaac ggaccagcat tctttggaaa cggagcagtc aacgtcggtg aactgggaac 120

caccaccacc gga 133

<210> 815

<211> 48
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4129-06]

<400> 815
tggttccggt ggtggtggtt ccgaatgccg ttacctgttc ggtggttg 48

<210> 816
<211> 79
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4129-07]

<400> 816
caaaaccacc tccgactgct gcaaacacct gggttgcaaa ttccgtgaca aatactgcgc 60

ttgggacttc accttctcc 79

<210> 817
<211> 48
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4129-08]

<400> 817
cttaggagaa ggtgaagtcc caagcgcagt atttgtcacg gaatttgc 48

<210> 818
<211> 79
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4129-09]

<400> 818
aacccaggtg tttgcagcag tcggaggtgg ttttgcaacc accgaacagg taacggcatt 60

cggaaccacc accaccgga 79

<210> 819
<211> 127
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<220>
<221> CDS
<222> (2)..(127)

<400> 819
t ggt tcc ggt ggt ggt ggt tcc gaa tgc cgt tac ctg ttc ggt ggt tgc 49
Gly Ser Gly Gly Gly Gly Ser Glu Cys Arg Tyr Leu Phe Gly Gly Cys
1 5 10 15

aaa acc acc tcc gac tgc tgc aaa cac ctg ggt tgc aaa ttc cgt gac 97
Lys Thr Thr Ser Asp Cys Cys Lys His Leu Gly Cys Lys Phe Arg Asp
20 25 30

aaa tac tgc gct tgg gac ttc acc ttc tcc 127
Lys Tyr Cys Ala Trp Asp Phe Thr Phe Ser
35 40

<210> 820
<211> 42
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 820

Gly Ser Gly Gly Gly Gly Ser Glu Cys Arg Tyr Leu Phe Gly Gly Cys
1 5 10 15

Lys Thr Thr Ser Asp Cys Cys Lys His Leu Gly Cys Lys Phe Arg Asp
20 25 30

Lys Tyr Cys Ala Trp Asp Phe Thr Phe Ser
35 40

<210> 821
<211> 127
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<400> 821
cttaggagaa ggtgaagtcc caagcgcagt atttgtcacg gaatttgcaa cccaggtgtt 60

tgcagcagtc ggaggtggtt ttgcaaccac cgaacaggta acggcattcg gaaccaccac 120

caccgga 127

<210> 822
<211> 38
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4129-14]

<400> 822

tggttccggt ggtggtggtt cctactgcca gaaatgga 38

<210> 823
<211> 77
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4129-15]

<400> 823
tgtggacctg cgacgaagaa cgtaaatgct gcgaaggtct ggtttgccgt ctgtggtgca 60

aacgtatcat caacatg 77

<210> 824
<211> 39
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4129-16]

<400> 824
cttacatgtt gatgatacgt ttgcaccaca gacggcaaa 39

<210> 825
<211> 76
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4129-17]

<400> 825
ccagaccttc gcagcattta cgttcttcgt cgcaggtcca catccatttc tggcagtagg 60

aaccaccacc accgga 76

<210> 826
<211> 115
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<220>
<221> CDS
<222> (2)..(115)

<400> 826
t ggt tcc ggt ggt ggt ggt tcc tac tgc cag aaa tgg atg tgg acc tgc 49
  Gly Ser Gly Gly Gly Gly Ser Tyr Cys Gln Lys Trp Met Trp Thr Cys
  1   5   10   15

gac gaa gaa cgt aaa tgc tgc gaa ggt ctg gtt tgc cgt ctg tgg tgc 97
Asp Glu Glu Arg Lys Cys Cys Glu Gly Leu Val Cys Arg Leu Trp Cys

20 25 30

aaa cgt atc atc aac atg 115
Lys Arg Ile Ile Asn Met
35

<210> 827
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 827

Gly Ser Gly Gly Gly Gly Ser Tyr Cys Gln Lys Trp Met Trp Thr Cys
1 5 10 15

Asp Glu Glu Arg Lys Cys Cys Glu Gly Leu Val Cys Arg Leu Trp Cys
20 25 30

Lys Arg Ile Ile Asn Met
35

<210> 828
<211> 115
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<400> 828
cttacatgtt gatgatacgt ttgcaccaca gacggcaaac cagaccttcg cagcatttac 60

gttcttcgtc gcaggtccac atccatttct ggcagtagga accaccacca ccgga 115

<210> 829
<211> 38
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4128-93]

<400> 829
tggttccggt ggtggtggtt cctgcaaatc cccgggtt 38

<210> 830
<211> 68
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4128-94]

<400> 830
cctcctgctc cccgacctcc tacaactgct gccgttcctg caacccgtac accaaacgtt 60

gctacggt 68

<210> 831
<211> 38
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4128-95]

<400> 831
cttaaccgta gcaacgtttg gtgtacgggt tgcaggaa 38

<210> 832
<211> 68
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4128-96]

<400> 832
cggcagcagt tgtaggaggt cggggagcag gaggaacccg gggatttgca ggaaccacca 60

ccaccgga 68

<210> 833
<211> 106
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<220>
<221> CDS
<222> (2)..(106)

<400> 833
t ggt tcc ggt ggt ggt ggt tcc tgc aaa tcc ccg ggt tcc tcc tgc tcc 49
Gly Ser Gly Gly Gly Gly Ser Cys Lys Ser Pro Gly Ser Ser Cys Ser
1 5 10 15

ccg acc tcc tac aac tgc tgc cgt tcc tgc aac ccg tac acc aaa cgt 97
Pro Thr Ser Tyr Asn Cys Cys Arg Ser Cys Asn Pro Tyr Thr Lys Arg
20 25 30

tgc tac ggt 106
Cys Tyr Gly
35

<210> 834
<211> 35
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 834

Gly Ser Gly Gly Gly Gly Ser Cys Lys Ser Pro Gly Ser Ser Cys Ser
1 5 10 15

Pro Thr Ser Tyr Asn Cys Cys Arg Ser Cys Asn Pro Tyr Thr Lys Arg
20 25 30

Cys Tyr Gly
35

<210> 835
<211> 106
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<400> 835
cttaaccgta gcaacgtttg gtgtacgggt tgcaggaacg gcagcagttg taggaggtcg 60

gggagcagga ggaacccggg gatttgcagg aaccaccacc accgga 106

<210> 836
<211> 34
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4129-02]

<400> 836
tggttccggt ggtggtggtt cctgcaaagg taaa 34

<210> 837
<211> 66
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4129-03]

<400> 837
ggtgctaaat gctcccgtct gatgtacgac tgctgcaccg gttcctgccg ttccggtaaa 60

tgcggt 66

<210> 838
<211> 34
<212> DNA

<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4129-04]

<400> 838
cttaaccgca tttaccggaa cggcaggaac cggt 34

<210> 839
<211> 66
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4129-05]

<400> 839
gcagcagtcg tacatcagac gggagcattt agcaccttta cctttgcagg aaccaccacc 60

accgga 66

<210> 840
<211> 100
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<220>
<221> CDS
<222> (2)..(100)

<400> 840
t ggt tcc ggt ggt ggt ggt tcc tgc aaa ggt aaa ggt gct aaa tgc tcc 49
Gly Ser Gly Gly Gly Gly Ser Cys Lys Gly Lys Gly Ala Lys Cys Ser
1 5 10 15

cgt ctg atg tac gac tgc tgc acc ggt tcc tgc cgt tcc ggt aaa tgc 97
Arg Leu Met Tyr Asp Cys Cys Thr Gly Ser Cys Arg Ser Gly Lys Cys
20 25 30

ggt 100
Gly

<210> 841
<211> 33
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 841

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

Arg Leu Met Tyr Asp Cys Cys Thr Gly Ser Cys Arg Ser Gly Lys Cys
20 25 30

Gly

<210> 842
<211> 100
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<400> 842
cttaaccgca tttaccggaa cggcaggaac cggtgcagca gtcgtacatc agacgggagc 60

atttagcacc tttacctttg caggaaccac caccaccgga 100

<210> 843
<211> 40
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4128-97]

<400> 843
tggttccggt ggtggtggtt ccgctgaaaa agactgcatc 40

<210> 844
<211> 84
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4128-98]

<400> 844
gctccgggtg ctccgtgctt cggtaccgac aaaccgtgct gcaacccgcg tgcttggtgc 60

tcctcctacg ctaacaaatg cctg 84

<210> 845
<211> 40
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4128-99]

<400> 845
cttacaggca tttgttagcg taggaggagc accaagcacg 40

<210> 846

<211> 84
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4129-01]

<400> 846
cgggttgcag cacggtttgt cggtaccgaa gcacggagca cccggagcga tgcagtcttt 60

ttcagcggaa ccaccaccac cgga 84

<210> 847
<211> 124
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<220>
<221> CDS
<222> (2)..(124)

<400> 847
t ggt tcc ggt ggt ggt ggt tcc gct gaa aaa gac tgc atc gct ccg ggt 49
Gly Ser Gly Gly Gly Gly Ser Ala Glu Lys Asp Cys Ile Ala Pro Gly
1 5 10 15

gct ccg tgc ttc ggt acc gac aaa ccg tgc tgc aac ccg cgt gct tgg 97
Ala Pro Cys Phe Gly Thr Asp Lys Pro Cys Cys Asn Pro Arg Ala Trp
20 25 30

tgc tcc tcc tac gct aac aaa tgc ctg 124
Cys Ser Ser Tyr Ala Asn Lys Cys Leu
35 40

<210> 848
<211> 41
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 848

Gly Ser Gly Gly Gly Gly Ser Ala Glu Lys Asp Cys Ile Ala Pro Gly
1 5 10 15

Ala Pro Cys Phe Gly Thr Asp Lys Pro Cys Cys Asn Pro Arg Ala Trp
20 25 30

Cys Ser Ser Tyr Ala Asn Lys Cys Leu
35 40

<210> 849

<211> 124
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<400> 849
cttacaggca tttgttagcg taggaggagc accaagcacg cgggttgcag cacggtttgt 60

cggtaccgaa gcacggagca cccggagcga tgcagtcttt ttcagcggaa ccaccaccac 120

cgga 124

<210> 850
<211> 41
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4129-22]

<400> 850
tggttccggt ggtggtggtt ccgaatgccg ttactggctg g 41

<210> 851
<211> 86
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4129-23]

<400> 851
gtggttgctc cgctggtcag acctgctgca aacacctggt ttgctcccgt cgtcacggtt 60

ggtgcgtttg ggacggtacc ttctcc 86

<210> 852
<211> 41
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4129-24]

<400> 852
cttaggagaa ggtaccgtcc caaacgcacc aaccgtgacg a 41

<210> 853
<211> 86
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4129-25]

<400> 853

cgggagcaaa ccaggtgttt gcagcaggtc tgaccagcgg agcaaccacc cagccagtaa 60

cggcattcgg aaccaccacc accgga 86

<210> 854
<211> 127
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<220>
<221> CDS
<222> (2)..(127)

<400> 854
t ggt tcc ggt ggt ggt ggt tcc gaa tgc cgt tac tgg ctg ggt ggt tgc 49
Gly Ser Gly Gly Gly Gly Ser Glu Cys Arg Tyr Trp Leu Gly Gly Cys
1 5 10 15

tcc gct ggt cag acc tgc tgc aaa cac ctg gtt tgc tcc cgt cgt cac 97
Ser Ala Gly Gln Thr Cys Cys Lys His Leu Val Cys Ser Arg Arg His
20 25 30

ggt tgg tgc gtt tgg gac ggt acc ttc tcc 127
Gly Trp Cys Val Trp Asp Gly Thr Phe Ser
35 40

<210> 855
<211> 42
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 855

Gly Ser Gly Gly Gly Gly Ser Glu Cys Arg Tyr Trp Leu Gly Gly Cys
1 5 10 15

Ser Ala Gly Gln Thr Cys Cys Lys His Leu Val Cys Ser Arg Arg His
20 25 30

Gly Trp Cys Val Trp Asp Gly Thr Phe Ser
35 40

<210> 856
<211> 127
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4

<400> 856
cttaggagaa ggtaccgtcc caaacgcacc aaccgtgacg acgggagcaa accaggtgtt 60

tgcagcaggt ctgaccagcg gagcaaccac ccagccagta acggcattcg gaaccaccac 120

caccgga 127

<210> 857
<211> 42
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4129-10]

<400> 857
tggttccggt ggtggtggtt cccgtccgac cgacatcaaa tg 42

<210> 858
<211> 88
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4129-11]

<400> 858
ctccgaatcc taccagtgct tcccggtttg caaatcccgt ttcggtaaaa ccaacggtcg 60

ttgcgttaac ggtttctgcg actgcttc 88

<210> 859
<211> 42
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4129-12]

<400> 859
cttagaagca gtcgcagaaa ccgttaacgc aacgaccgtt gg 42

<210> 860
<211> 88
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4129-13]

<400> 860
ttttaccgaa acgggatttg caaaccggga agcactggta ggattcggag catttgatgt 60

cggtcggacg ggaaccacca ccaccgga 88

<210> 861
<211> 130
<212> DNA

<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<220>
<221> CDS
<222> (2)..(130)

<400> 861
t ggt tcc ggt ggt ggt ggt tcc cgt ccg acc gac atc aaa tgc tcc gaa 49
Gly Ser Gly Gly Gly Gly Ser Arg Pro Thr Asp Ile Lys Cys Ser Glu
1 5 10 15

tcc tac cag tgc ttc ccg gtt tgc aaa tcc cgt ttc ggt aaa acc aac 97
Ser Tyr Gln Cys Phe Pro Val Cys Lys Ser Arg Phe Gly Lys Thr Asn
20 25 30

ggt cgt tgc gtt aac ggt ttc tgc gac tgc ttc 130
Gly Arg Cys Val Asn Gly Phe Cys Asp Cys Phe
35 40

<210> 862
<211> 43
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 862

Gly Ser Gly Gly Gly Gly Ser Arg Pro Thr Asp Ile Lys Cys Ser Glu
1 5 10 15

Ser Tyr Gln Cys Phe Pro Val Cys Lys Ser Arg Phe Gly Lys Thr Asn
20 25 30

Gly Arg Cys Val Asn Gly Phe Cys Asp Cys Phe
35 40

<210> 863
<211> 130
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<400> 863
cttagaagca gtcgcagaaa ccgttaacgc aacgaccgtt ggttttaccg aaacgggatt 60

tgcaaaccgg gaagcactgg taggattcgg agcatttgat gtcggtcgga cgggaaccac 120

caccaccgga 130

<210> 864
<211> 42
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4129-26]

<400> 864
tggttccggt ggtggtggtt ccatgtgcat gccgtgcttc ac 42

<210> 865
<211> 88
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4129-27]

<400> 865
caccgaccac cagatggctc gtaaatgcga cgactgctgc ggtggtaaag gtcgtggtaa 60

atgctacggt ccgcagtgcc tgtgccgt 88

<210> 866
<211> 42
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4129-28]

<400> 866
cttaacggca caggcactgc ggaccgtagc atttaccacg ac 42

<210> 867
<211> 88
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex [4129-29]

<400> 867
ctttaccacc gcagcagtcg tcgcatttac gagccatctg gtggtcggtg gtgaagcacg 60

gcatgcacat ggaaccacca ccaccgga 88

<210> 868
<211> 130
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature

<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<220>
<221> CDS
<222> (2)..(130)

<400> 868
t ggt tcc ggt ggt ggt ggt tcc atg tgc atg ccg tgc ttc acc acc gac 49
Gly Ser Gly Gly Gly Gly Ser Met Cys Met Pro Cys Phe Thr Thr Asp
1 5 10 15

cac cag atg gct cgt aaa tgc gac gac tgc tgc ggt ggt aaa ggt cgt 97
His Gln Met Ala Arg Lys Cys Asp Asp Cys Cys Gly Gly Lys Gly Arg
20 25 30

ggt aaa tgc tac ggt ccg cag tgc ctg tgc cgt 130
Gly Lys Cys Tyr Gly Pro Gln Cys Leu Cys Arg
35 40

<210> 869
<211> 43
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 869

Gly Ser Gly Gly Gly Gly Ser Met Cys Met Pro Cys Phe Thr Thr Asp
1 5 10 15

His Gln Met Ala Arg Lys Cys Asp Asp Cys Cys Gly Gly Lys Gly Arg
20 25 30

Gly Lys Cys Tyr Gly Pro Gln Cys Leu Cys Arg
35 40

<210> 870
<211> 130
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<400> 870
caccacggca caggcactgc ggaccgtagc atttaccacg acctttacca ccgcagcagt 60

cgtcgcattt acgagccatc tggtggtcgg tggtgaagca cggcatgcac atggaaccac 120

caccaccgga 130

<210> 871
<211> 32
<212> PRT

<213> Artificial Sequence

<220>
<223> CoTx2

<400> 871

Val Ala Cys Val Tyr Arg Thr Cys Asp Lys Asp Cys Thr Ser Arg Lys
1 5 10 15

Tyr Arg Ser Gly Lys Cys Ile Asn Asn Ala Cys Lys Cys Tyr Pro Tyr
20 25 30

<210> 872
<211> 92
<212> DNA
<213> Artificial Sequence

<220>
<223> BamHI-NotI fragment containing partial linker sequence and SmIIIA peptide.

<220>
<221> misc_feature
<222> (1)..(6)
<223> BamHI site

<220>
<221> CDS
<222> (22)..(81)

<220>
<221> misc_feature
<222> (85)..(92)
<223> NotI site

<400> 872
ggatccggag gaggaggaag c tgc tgc aac ggc cgc cgc ggc tgc agc agc 51
Cys Cys Asn Gly Arg Arg Gly Cys Ser Ser
1 5 10

cgc tgg tgc cgc gac cac agc cgc tgc tgc tgagcggccg c 92
Arg Trp Cys Arg Asp His Ser Arg Cys Cys
15 20

<210> 873
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 873

Cys Cys Asn Gly Arg Arg Gly Cys Ser Ser Arg Trp Cys Arg Asp His
1 5 10 15

Ser Arg Cys Cys
20

<210> 874

<211> 60
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer Sequence [3654-50]

<400> 874
ggaggaggat ccggaggagg aggaagctgc tgcaacggcc gccgcggctg cagcagccgc 60

<210> 875
<211> 61
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer Sequence [3654-51]

<400> 875
attattgcgg ccgctcagca gcagcggctg tggtcgcggc accagcggct gctgcagccg 60

c 61

<210> 876
<211> 88
<212> DNA
<213> Artificial Sequence

<220>
<223> OSK1 - Primer Sequence [4210-35]

<400> 876
catggatccg gaggaggagg aagcggcgtg atcatcaacg tgaagtgcaa gatcagccgc 60

cagtgcctgg agccctgcaa gaaggccg 88

<210> 877
<211> 88
<212> DNA
<213> Artificial Sequence

<220>
<223> OSK1 - Primer Sequence [4210-36]

<400> 877
catgcggccg cttactactt gggggtgcag tggcacttgc cgttcatgca cttgccgaag 60

cgcatgccgg ccttcttgca gggctcca 88

<210> 878
<211> 88
<212> DNA
<213> Artificial Sequence

<220>
<223> OSK1[K7S] - Primer Sequence [4210-37]

<400> 878
catggatccg gaggaggagg aagcggcgtg atcatcaacg tgagctgcaa gatcagccgc 60

cagtgcctgg agccctgcaa gaaggccg 88

<210> 879

<211> 88
<212> DNA
<213> Artificial Sequence

<220>
<223> OSK1[K7S] - Primer Sequence [4210-36]

<400> 879
catgcggccg cttactactt gggggtgcag tggcacttgc cgttcatgca cttgccgaag 60

cgcatgccgg ccttcttgca gggctcca 88

<210> 880
<211> 88
<212> DNA
<213> Artificial Sequence

<220>
<223> OSK1[E16K,K20D] - Primer Sequence [4210-38]

<400> 880
catggatccg gaggaggagg aagcggcgtg atcatcaacg tgaagtgcaa gatcagccgc 60

cagtgcctga agccctgcaa ggacgccg 88

<210> 881
<211> 88
<212> DNA
<213> Artificial Sequence

<220>
<223> OSK1[E16K,K20D] - Primer Sequence [4210-39]

<400> 881
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cgcatgccgg cgtccttgca gggcttca 88

<210> 882
<211> 88
<212> DNA
<213> Artificial Sequence

<220>
<223> OSK1[K7S,E16K,K20D] - Primer Sequence [4210-40]

<400> 882
catggatccg gaggaggagg aagcggcgtg atcatcaacg tgagctgcaa gatcagccgc 60

cagtgcctga agccctgcaa ggacgccg 88

<210> 883
<211> 88
<212> DNA
<213> Artificial Sequence

<220>
<223> OSK1[K7S,E16K,K20D] - Primer Sequence [4210-39]

<400> 883
catgcggccg cttactactt gggggtgcag tggcacttgc cgttcatgca cttgccgaag 60

cgcatgccgg cgtccttgca gggcttca 88

<210> 884
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-A9/A22

<400> 884

Arg Ser Cys Ile Asp Thr Ile Pro Ala Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 885
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-A9/A22 d1

<400> 885

Ser Cys Ile Asp Thr Ile Pro Ala Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 886
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-V9

<400> 886

Arg Ser Cys Ile Asp Thr Ile Pro Val Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 887

<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-V9/A22

<400> 887

Arg Ser Cys Ile Asp Thr Ile Pro Val Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 888
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-V9 d1

<400> 888

Ser Cys Ile Asp Thr Ile Pro Val Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 889
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-V9/A22 d1

<400> 889

Ser Cys Ile Asp Thr Ile Pro Val Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 890
<211> 35
<212> PRT

<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-E9/A22

<400> 890

Arg Ser Cys Ile Asp Thr Ile Pro Glu Ser Arg Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 891
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-E9/A22 d1

<400> 891

Ser Cys Ile Asp Thr Ile Pro Glu Ser Arg Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 892
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-A11/A22

<400> 892

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Ala Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 893
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-A11/A22 d1

<400> 893

Ser Cys Ile Asp Thr Ile Pro Lys Ser Ala Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 894
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-E11/A22

<400> 894

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Glu Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 895
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-E11/A22 d1

<400> 895

Ser Cys Ile Asp Thr Ile Pro Lys Ser Glu Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 896
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-D14

<400> 896

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Asp Phe Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 897
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-D14/A22

<400> 897

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Asp Phe Gln
1 5 10 15

Cys Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 898
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-D14 d1

<400> 898

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Asp Phe Gln Cys
1 5 10 15

Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 899
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-D14/A22 d1

<400> 899

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Asp Phe Gln Cys
1 5 10 15

Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 900
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-A15/A22

<400> 900

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Ala Gln
1 5 10 15

Cys Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 901
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-A15/A22 d1

<400> 901

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Ala Gln Cys
1 5 10 15

Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 902
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-I15

<400> 902

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Ile Gln

1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 903
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-I15/A22

<400> 903

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Ile Gln
1 5 10 15

Cys Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 904
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-I15 d1

<400> 904

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Ile Gln Cys
1 5 10 15

Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 905
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-I15/A22 d1

<400> 905

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Ile Gln Cys
1 5 10 15

Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 906
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-V15

<400> 906

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Val Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 907
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-V15/A22

<400> 907

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Val Gln
1 5 10 15

Cys Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 908
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-V15 d1

<400> 908

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Val Gln Cys
1 5 10 15

Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly

20 25 30

Thr Cys

<210> 909
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-V15/A22 d1

<400> 909

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Val Gln Cys
1 5 10 15

Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 910
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-R16

<400> 910

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Arg
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 911
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-R16/A22

<400> 911

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Arg
1 5 10 15

Cys Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 912
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-R16 d1

<400> 912

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Arg Cys
1 5 10 15

Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 913
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-R16/A22 d1

<400> 913

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Arg Cys
1 5 10 15

Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 914
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-K16

<400> 914

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Lys
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys

35

<210> 915
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-K16/A22

<400> 915

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Lys
1 5 10 15

Cys Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 916
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-K16 d1

<400> 916

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Lys Cys
1 5 10 15

Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 917
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-K16/A22 d1

<400> 917

Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Lys Cys
1 5 10 15

Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 918
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-A9/E11

<400> 918

Arg Ser Cys Ile Asp Thr Ile Pro Ala Ser Glu Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 919
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-A9/E11/A22

<400> 919

Arg Ser Cys Ile Asp Thr Ile Pro Ala Ser Glu Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 920
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-A9/E11 d1

<400> 920

Ser Cys Ile Asp Thr Ile Pro Ala Ser Glu Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 921

<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-A9/E11/A22 d1

<400> 921

Ser Cys Ile Asp Thr Ile Pro Ala Ser Glu Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 922
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-V9/E11

<400> 922

Arg Ser Cys Ile Asp Thr Ile Pro Val Ser Glu Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 923
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-V9/E11/A22

<400> 923

Arg Ser Cys Ile Asp Thr Ile Pro Val Ser Glu Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 924
<211> 34
<212> PRT

<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-V9/E11 d1

<400> 924

Ser Cys Ile Asp Thr Ile Pro Val Ser Glu Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 925
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-V9/E11/A22 d1

<400> 925

Ser Cys Ile Asp Thr Ile Pro Val Ser Glu Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 926
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-V9/A11

<400> 926

Arg Ser Cys Ile Asp Thr Ile Pro Val Ser Ala Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 927
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-V9/A11/A22

<400> 927

Arg Ser Cys Ile Asp Thr Ile Pro Val Ser Ala Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 928
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-V9/A11 d1

<400> 928

Ser Cys Ile Asp Thr Ile Pro Val Ser Ala Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 929
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-V9/A11/A22 d1

<400> 929

Ser Cys Ile Asp Thr Ile Pro Val Ser Ala Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 930
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-A9/A11

<400> 930

Arg Ser Cys Ile Asp Thr Ile Pro Ala Ser Ala Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 931
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-A9/A11/A22

<400> 931

Arg Ser Cys Ile Asp Thr Ile Pro Ala Ser Ala Cys Thr Ala Phe Gln
1 5 10 15

Cys Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 932
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-A9/A11 d1

<400> 932

Ser Cys Ile Asp Thr Ile Pro Ala Ser Ala Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 933
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-A9/A11/A22 d1

<400> 933

Ser Cys Ile Asp Thr Ile Pro Ala Ser Ala Cys Thr Ala Phe Gln Cys
1 5 10 15

Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 934
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-E11/D14/I15/R16

<400> 934

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Glu Cys Thr Asp Ile Arg
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 935
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-E11/D14/I15/R16/A22

<400> 935

Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Glu Cys Thr Asp Ile Arg
1 5 10 15

Cys Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 936
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-E11/D14/I15/R16 d1

<400> 936

Ser Cys Ile Asp Thr Ile Pro Lys Ser Glu Cys Thr Asp Ile Arg Cys

1 5 10 15

Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 937
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-E11/D14/I15/R16/A22 d1

<400> 937

Ser Cys Ile Asp Thr Ile Pro Lys Ser Glu Cys Thr Asp Ile Arg Cys
1 5 10 15

Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 938
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-V9/E11/D14/I15/R16

<400> 938

Arg Ser Cys Ile Asp Thr Ile Pro Val Ser Glu Cys Thr Asp Ile Arg
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 939
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-V9/E11/D14/I15/R16/A22

<400> 939

Arg Ser Cys Ile Asp Thr Ile Pro Val Ser Glu Cys Thr Asp Ile Arg
1 5 10 15

Cys Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 940
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-V9/E11/D14/I15/R16 d1

<400> 940

Ser Cys Ile Asp Thr Ile Pro Val Ser Glu Cys Thr Asp Ile Arg Cys
1 5 10 15

Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 941
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-V9/E11/D14/I15/R16/A22 d1

<400> 941

Ser Cys Ile Asp Thr Ile Pro Val Ser Glu Cys Thr Asp Ile Arg Cys
1 5 10 15

Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 942
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-V9/E11/D14/I15

<400> 942

Arg Ser Cys Ile Asp Thr Ile Pro Val Ser Glu Cys Thr Asp Ile Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys

20 25 30

Gly Thr Cys
35

<210> 943
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-V9/E11/D14/I15/A22

<400> 943

Arg Ser Cys Ile Asp Thr Ile Pro Val Ser Glu Cys Thr Asp Ile Gln
1 5 10 15

Cys Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 944
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-V9/E11/D14/I15 d1

<400> 944

Ser Cys Ile Asp Thr Ile Pro Val Ser Glu Cys Thr Asp Ile Gln Cys
1 5 10 15

Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 945
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-V9/E11/D14/I15/A22 d1

<400> 945

Ser Cys Ile Asp Thr Ile Pro Val Ser Glu Cys Thr Asp Ile Gln Cys
1 5 10 15

Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 946
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-T2/K4/L6/V9/E11/D14/I15/R16

<400> 946

Arg Thr Cys Lys Asp Leu Ile Pro Val Ser Glu Cys Thr Asp Ile Arg
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 947
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-T2/K4/L6/V9/E11/D14/I15/R16/A22

<400> 947

Arg Thr Cys Lys Asp Leu Ile Pro Val Ser Glu Cys Thr Asp Ile Arg
1 5 10 15

Cys Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 948
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-T2/K4/L6/V9/E11/D14/I15/R16 d1

<400> 948

Thr Cys Lys Asp Leu Ile Pro Val Ser Glu Cys Thr Asp Ile Arg Cys
1 5 10 15

Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 949
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk Peptide Sequence - ShK-T2/K4/L6/V9/E11/D14/I15/R16/A22 d1

<400> 949

Thr Cys Lys Asp Leu Ile Pro Val Ser Glu Cys Thr Asp Ile Arg Cys
1 5 10 15

Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly
20 25 30

Thr Cys

<210> 950
<211> 40
<212> PRT
<213> Artificial Sequence

<220>
<223> Shk (L5)

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> X in position 1 is phosphotyrosine.

<400> 950

Xaa Ala Glu Glu Ala Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg
1 5 10 15

Cys Thr Ala Phe Gln Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe
20 25 30

Cys Arg Lys Thr Cys Gly Thr Cys
35 40

<210> 951
<211> 888
<212> DNA
<213> Artificial Sequence

<220>
<223> Fc-L10-OSK1

<220>
<221> CDS
<222> (1)..(888)

<400> 951
atg gaa tgg agc tgg gtc ttt ctc ttc ttc ctg tca gta acg act ggt 48

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Met Glu Trp Ser Trp Val Phe Leu Phe Phe Leu Ser Val Thr Thr Gly
1               5                  10                  15

gtc cac tcc gac aaa act cac aca tgc cca ccg tgc cca gca cct gaa      96
Val His Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
            20                  25                  30

ctc ctg ggg gga ccg tca gtc ttc ctc ttc ccc cca aaa ccc aag gac     144
Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
        35                  40                  45

acc ctc atg atc tcc cgg acc cct gag gtc aca tgc gtg gtg gtg gac     192
Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
    50                  55                  60

gtg agc cac gaa gac cct gag gtc aag ttc aac tgg tac gtg gac ggc     240
Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
65                  70                  75                  80

gtg gag gtg cat aat gcc aag aca aag ccg cgg gag gag cag tac aac     288
Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
                85                  90                  95

agc acg tac cgt gtg gtc agc gtc ctc acc gtc ctg cac cag gac tgg     336
Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
            100                 105                 110

ctg aat ggc aag gag tac aag tgc aag gtc tcc aac aaa gcc ctc cca     384
Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
        115                 120                 125

gcc ccc atc gag aaa acc atc tcc aaa gcc aaa ggg cag ccc cga gaa     432
Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
    130                 135                 140

cca cag gtg tac acc ctg ccc cca tcc cgg gat gag ctg acc aag aac     480
Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
145                 150                 155                 160

cag gtc agc ctg acc tgc ctg gtc aaa ggc ttc tat ccc agc gac atc     528
Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
                165                 170                 175

gcc gtg gag tgg gag agc aat ggg cag ccg gag aac aac tac aag acc     576
Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
            180                 185                 190

acg cct ccc gtg ctg gac tcc gac ggc tcc ttc ttc ctc tac agc aag     624
Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
        195                 200                 205

ctc acc gtg gac aag agc agg tgg cag cag ggg aac gtc ttc tca tgc     672
Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
    210                 215                 220

tcc gtg atg cat gag gct ctg cac aac cac tac acg cag aag agc ctc     720
Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
225                 230                 235                 240

tcc ctg tct ccg ggt aaa gga gga gga gga tcc gga gga gga gga agc     768
Ser Leu Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
                245                 250                 255

ggc gtg atc atc aac gtg aag tgc aag atc agc cgc cag tgc ctg gag     816
Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Glu
            260                 265                 270

ccc tgc aag aag gcc ggc atg cgc ttc ggc aag tgc atg aac ggc aag     864
```

Pro Cys Lys Lys Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
275 280 285

tgc cac tgc acc ccc aag tag taa 888
Cys His Cys Thr Pro Lys
290

<210> 952
<211> 294
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 952

Met Glu Trp Ser Trp Val Phe Leu Phe Phe Leu Ser Val Thr Thr Gly
1 5 10 15

Val His Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
20 25 30

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

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
50 55 60

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
65 70 75 80

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
85 90 95

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
100 105 110

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

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
130 135 140

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

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
165 170 175

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
180 185 190

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
195 200 205

```
Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
    210                 215                 220

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
225                 230                 235                 240

Ser Leu Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
                245                 250                 255

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Glu
            260                 265                 270

Pro Cys Lys Lys Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
        275                 280                 285

Cys His Cys Thr Pro Lys
    290
```

<210> 953
<211> 888
<212> DNA
<213> Artificial Sequence

<220>
<223> Fc-L10-OSK1 [K7S]

<220>
<221> CDS
<222> (1)..(888)

<400> 953

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atg gaa tgg agc tgg gtc ttt ctc ttc ttc ctg tca gta acg act ggt      48
Met Glu Trp Ser Trp Val Phe Leu Phe Phe Leu Ser Val Thr Thr Gly
1               5                   10                  15

gtc cac tcc gac aaa act cac aca tgc cca ccg tgc cca gca cct gaa      96
Val His Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
            20                  25                  30

ctc ctg ggg gga ccg tca gtc ttc ctc ttc ccc cca aaa ccc aag gac     144
Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
        35                  40                  45

acc ctc atg atc tcc cgg acc cct gag gtc aca tgc gtg gtg gtg gac     192
Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
    50                  55                  60

gtg agc cac gaa gac cct gag gtc aag ttc aac tgg tac gtg gac ggc     240
Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
65                  70                  75                  80

gtg gag gtg cat aat gcc aag aca aag ccg cgg gag gag cag tac aac     288
Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
                85                  90                  95

agc acg tac cgt gtg gtc agc gtc ctc acc gtc ctg cac cag gac tgg     336
Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
            100                 105                 110
```

```
ctg aat ggc aag gag tac aag tgc aag gtc tcc aac aaa gcc ctc cca      384
Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
        115                 120                 125

gcc ccc atc gag aaa acc atc tcc aaa gcc aaa ggg cag ccc cga gaa      432
Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
    130                 135                 140

cca cag gtg tac acc ctg ccc cca tcc cgg gat gag ctg acc aag aac      480
Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
145                 150                 155                 160

cag gtc agc ctg acc tgc ctg gtc aaa ggc ttc tat ccc agc gac atc      528
Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
                165                 170                 175

gcc gtg gag tgg gag agc aat ggg cag ccg gag aac aac tac aag acc      576
Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
            180                 185                 190

acg cct ccc gtg ctg gac tcc gac ggc tcc ttc ttc ctc tac agc aag      624
Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
        195                 200                 205

ctc acc gtg gac aag agc agg tgg cag cag ggg aac gtc ttc tca tgc      672
Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
    210                 215                 220

tcc gtg atg cat gag gct ctg cac aac cac tac acg cag aag agc ctc      720
Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
225                 230                 235                 240

tcc ctg tct ccg ggt aaa gga gga gga gga tcc gga gga gga gga agc      768
Ser Leu Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
                245                 250                 255

ggc gtg atc atc aac gtg agc tgc aag atc agc cgc cag tgc ctg gag      816
Gly Val Ile Ile Asn Val Ser Cys Lys Ile Ser Arg Gln Cys Leu Glu
            260                 265                 270

ccc tgc aag aag gcc ggc atg cgc ttc ggc aag tgc atg aac ggc aag      864
Pro Cys Lys Lys Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
        275                 280                 285

tgc cac tgc acc ccc aag tag taa                                      888
Cys His Cys Thr Pro Lys
    290
```

<210> 954
<211> 294
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 954

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Met Glu Trp Ser Trp Val Phe Leu Phe Phe Leu Ser Val Thr Thr Gly
1               5                   10                  15

Val His Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
            20                  25                  30

Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
```

35 40 45

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
50 55 60

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
65 70 75 80

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
85 90 95

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
100 105 110

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

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
130 135 140

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

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
165 170 175

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
180 185 190

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
195 200 205

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
210 215 220

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
225 230 235 240

Ser Leu Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
245 250 255

Gly Val Ile Ile Asn Val Ser Cys Lys Ile Ser Arg Gln Cys Leu Glu
260 265 270

Pro Cys Lys Lys Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
275 280 285

Cys His Cys Thr Pro Lys
290

<210> 955

<211> 888
<212> DNA
<213> Artificial Sequence

<220>
<223> Fc-L10-OSK1 [E16K, K20D]

<220>
<221> CDS
<222> (1)..(888)

<400> 955

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atg gaa tgg agc tgg gtc ttt ctc ttc ttc ctg tca gta acg act ggt        48
Met Glu Trp Ser Trp Val Phe Leu Phe Phe Leu Ser Val Thr Thr Gly
1               5                  10                  15

gtc cac tcc gac aaa act cac aca tgc cca ccg tgc cca gca cct gaa        96
Val His Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
            20                  25                  30

ctc ctg ggg gga ccg tca gtc ttc ctc ttc ccc cca aaa ccc aag gac       144
Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
        35                  40                  45

acc ctc atg atc tcc cgg acc cct gag gtc aca tgc gtg gtg gtg gac       192
Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
    50                  55                  60

gtg agc cac gaa gac cct gag gtc aag ttc aac tgg tac gtg gac ggc       240
Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
65                  70                  75                  80

gtg gag gtg cat aat gcc aag aca aag ccg cgg gag gag cag tac aac       288
Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
                85                  90                  95

agc acg tac cgt gtg gtc agc gtc ctc acc gtc ctg cac cag gac tgg       336
Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
            100                 105                 110

ctg aat ggc aag gag tac aag tgc aag gtc tcc aac aaa gcc ctc cca       384
Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
        115                 120                 125

gcc ccc atc gag aaa acc atc tcc aaa gcc aaa ggg cag ccc cga gaa       432
Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
    130                 135                 140

cca cag gtg tac acc ctg ccc cca tcc cgg gat gag ctg acc aag aac       480
Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
145                 150                 155                 160

cag gtc agc ctg acc tgc ctg gtc aaa ggc ttc tat ccc agc gac atc       528
Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
                165                 170                 175

gcc gtg gag tgg gag agc aat ggg cag ccg gag aac aac tac aag acc       576
Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
            180                 185                 190

acg cct ccc gtg ctg gac tcc gac ggc tcc ttc ttc ctc tac agc aag       624
Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
        195                 200                 205

ctc acc gtg gac aag agc agg tgg cag cag ggg aac gtc ttc tca tgc       672
Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
    210                 215                 220
```

```
tcc gtg atg cat gag gct ctg cac aac cac tac acg cag aag agc ctc      720
Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
225                 230                 235                 240

tcc ctg tct ccg ggt aaa gga gga gga gga tcc gga gga gga gga agc      768
Ser Leu Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
                245                 250                 255

ggc gtg atc atc aac gtg aag tgc aag atc agc cgc cag tgc ctg aag      816
Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
            260                 265                 270

ccc tgc aag gac gcc ggc atg cgc ttc ggc aag tgc atg aac ggc aag      864
Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
        275                 280                 285

tgc cac tgc acc ccc aag tag taa                                     888
Cys His Cys Thr Pro Lys
    290
```

<210> 956
<211> 294
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 956

```
Met Glu Trp Ser Trp Val Phe Leu Phe Phe Leu Ser Val Thr Thr Gly
1               5                   10                  15

Val His Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
            20                  25                  30

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

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
    50                  55                  60

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
65                  70                  75                  80

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
                85                  90                  95

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
            100                 105                 110

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

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
    130                 135                 140
```

```
Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
145                 150                 155                 160

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
                165                 170                 175

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
            180                 185                 190

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
        195                 200                 205

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
    210                 215                 220

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
225                 230                 235                 240

Ser Leu Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
                245                 250                 255

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
            260                 265                 270

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
        275                 280                 285

Cys His Cys Thr Pro Lys
    290
```

<210> 957
<211> 888
<212> DNA
<213> Artificial Sequence

<220>
<223> Fc-L10-OSK1 [K7S, E16K, K20D]

<220>
<221> CDS
<222> (1)..(888)

<400> 957

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atg gaa tgg agc tgg gtc ttt ctc ttc ttc ctg tca gta acg act ggt       48
Met Glu Trp Ser Trp Val Phe Leu Phe Phe Leu Ser Val Thr Thr Gly
1               5                   10                  15

gtc cac tcc gac aaa act cac aca tgc cca ccg tgc cca gca cct gaa       96
Val His Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
            20                  25                  30

ctc ctg ggg gga ccg tca gtc ttc ctc ttc ccc cca aaa ccc aag gac      144
Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
        35                  40                  45

acc ctc atg atc tcc cgg acc cct gag gtc aca tgc gtg gtg gtg gac      192
Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
```

50 55 60

gtg agc cac gaa gac cct gag gtc aag ttc aac tgg tac gtg gac ggc 240
Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
65 70 75 80

gtg gag gtg cat aat gcc aag aca aag ccg cgg gag gag cag tac aac 288
Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
85 90 95

agc acg tac cgt gtg gtc agc gtc ctc acc gtc ctg cac cag gac tgg 336
Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
100 105 110

ctg aat ggc aag gag tac aag tgc aag gtc tcc aac aaa gcc ctc cca 384
Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
115 120 125

gcc ccc atc gag aaa acc atc tcc aaa gcc aaa ggg cag ccc cga gaa 432
Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
130 135 140

cca cag gtg tac acc ctg ccc cca tcc cgg gat gag ctg acc aag aac 480
Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
145 150 155 160

cag gtc agc ctg acc tgc ctg gtc aaa ggc ttc tat ccc agc gac atc 528
Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
165 170 175

gcc gtg gag tgg gag agc aat ggg cag ccg gag aac aac tac aag acc 576
Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
180 185 190

acg cct ccc gtg ctg gac tcc gac ggc tcc ttc ttc ctc tac agc aag 624
Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
195 200 205

ctc acc gtg gac aag agc agg tgg cag cag ggg aac gtc ttc tca tgc 672
Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
210 215 220

tcc gtg atg cat gag gct ctg cac aac cac tac acg cag aag agc ctc 720
Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
225 230 235 240

tcc ctg tct ccg ggt aaa gga gga gga gga tcc gga gga gga gga agc 768
Ser Leu Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
245 250 255

ggc gtg atc atc aac gtg agc tgc aag atc agc cgc cag tgc ctg aag 816
Gly Val Ile Ile Asn Val Ser Cys Lys Ile Ser Arg Gln Cys Leu Lys
260 265 270

ccc tgc aag gac gcc ggc atg cgc ttc ggc aag tgc atg aac ggc aag 864
Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
275 280 285

tgc cac tgc acc ccc aag tag taa 888
Cys His Cys Thr Pro Lys
290

<210> 958
<211> 294
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 958

```
Met Glu Trp Ser Trp Val Phe Leu Phe Phe Leu Ser Val Thr Thr Gly
1               5                  10                  15

Val His Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
            20                  25                  30

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

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
    50                  55                  60

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
65                  70                  75                  80

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
                85                  90                  95

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
            100                 105                 110

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

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
    130                 135                 140

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

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
                165                 170                 175

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
            180                 185                 190

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
        195                 200                 205

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
    210                 215                 220

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
225                 230                 235                 240

Ser Leu Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
                245                 250                 255
```

Gly Val Ile Ile Asn Val Ser Cys Lys Ile Ser Arg Gln Cys Leu Lys
260 265 270

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
275 280 285

Cys His Cys Thr Pro Lys
290

<210> 959
<211> 48
<212> PRT
<213> Artificial Sequence

<220>
<223> Agelenopsis aperta (Agatoxin) toxin peptide sequence - Omega-Aga-IVA

<400> 959

Lys Lys Lys Cys Ile Ala Lys Asp Tyr Gly Arg Cys Lys Trp Gly Gly
1 5 10 15

Thr Pro Cys Cys Arg Gly Arg Gly Cys Ile Cys Ser Ile Met Gly Thr
20 25 30

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

<210> 960
<211> 48
<212> PRT
<213> Artificial Sequence

<220>
<223> Agelenopsis aperta (Agatoxin) toxin peptide sequence - Omega-Aga-IVB

<400> 960

Glu Asp Asn Cys Ile Ala Glu Asp Tyr Gly Lys Cys Thr Trp Gly Gly
1 5 10 15

Thr Lys Cys Cys Arg Gly Arg Pro Cys Arg Cys Ser Met Ile Gly Thr
20 25 30

Asn Cys Glu Cys Thr Pro Arg Leu Ile Met Glu Gly Leu Ser Phe Ala
35 40 45

<210> 961
<211> 76
<212> PRT
<213> Artificial Sequence

<220>
<223> Agelenopsis aperta (Agatoxin) toxin peptide sequence - Omega-Aga-IIIA

<400> 961

Ser Cys Ile Asp Ile Gly Gly Asp Cys Asp Gly Glu Lys Asp Asp Cys
1 5 10 15

Gln Cys Cys Arg Arg Asn Gly Tyr Cys Ser Cys Tyr Ser Leu Phe Gly
20 25 30

Tyr Leu Lys Ser Gly Cys Lys Cys Val Val Gly Thr Ser Ala Glu Phe
35 40 45

Gln Gly Ile Cys Arg Arg Lys Ala Arg Gln Cys Tyr Asn Ser Asp Pro
50 55 60

Asp Lys Cys Glu Ser His Asn Lys Pro Lys Arg Arg
65 70 75

<210> 962
<211> 76
<212> PRT
<213> Artificial Sequence

<220>
<223> Agelenopsis aperta (Agatoxin) toxin peptide sequence - Omega-Aga-IIIA-T58

<400> 962

Ser Cys Ile Asp Ile Gly Gly Asp Cys Asp Gly Glu Lys Asp Asp Cys
1 5 10 15

Gln Cys Cys Arg Arg Asn Gly Tyr Cys Ser Cys Tyr Ser Leu Phe Gly
20 25 30

Tyr Leu Lys Ser Gly Cys Lys Cys Val Val Gly Thr Ser Ala Glu Phe
35 40 45

Gln Gly Ile Cys Arg Arg Lys Ala Arg Thr Cys Tyr Asn Ser Asp Pro
50 55 60

Asp Lys Cys Glu Ser His Asn Lys Pro Lys Arg Arg
65 70 75

<210> 963
<211> 76
<212> PRT
<213> Artificial Sequence

<220>
<223> Agelenopsis aperta (Agatoxin) toxin peptide sequence - Omega-Aga-IIIB

<400> 963

Ser Cys Ile Asp Phe Gly Gly Asp Cys Asp Gly Glu Lys Asp Asp Cys
1 5 10 15

Gln Cys Cys Arg Ser Asn Gly Tyr Cys Ser Cys Tyr Ser Leu Phe Gly
20 25 30

Tyr Leu Lys Ser Gly Cys Lys Cys Glu Val Gly Thr Ser Ala Glu Phe
35 40 45

Arg Arg Ile Cys Arg Arg Lys Ala Lys Gln Cys Tyr Asn Ser Asp Pro
50 55 60

Asp Lys Cys Val Ser Val Tyr Lys Pro Lys Arg Arg
65 70 75

<210> 964
<211> 76
<212> PRT
<213> Artificial Sequence

<220>
<223> Agelenopsis aperta (Agatoxin) toxin peptide sequence - Omega-Aga-IIIB-N29

<400> 964

Ser Cys Ile Asp Phe Gly Gly Asp Cys Asp Gly Glu Lys Asp Asp Cys
1 5 10 15

Gln Cys Cys Arg Ser Asn Gly Tyr Cys Ser Cys Tyr Asn Leu Phe Gly
20 25 30

Tyr Leu Lys Ser Gly Cys Lys Cys Glu Val Gly Thr Ser Ala Glu Phe
35 40 45

Arg Arg Ile Cys Arg Arg Lys Ala Lys Gln Cys Tyr Asn Ser Asp Pro
50 55 60

Asp Lys Cys Val Ser Val Tyr Lys Pro Lys Arg Arg
65 70 75

<210> 965
<211> 76
<212> PRT
<213> Artificial Sequence

<220>
<223> Agelenopsis aperta (Agatoxin) toxin peptide sequence - Omega-Aga-IIIB-N29/R35

<400> 965

Ser Cys Ile Asp Phe Gly Gly Asp Cys Asp Gly Glu Lys Asp Asp Cys
1 5 10 15

Gln Cys Cys Arg Ser Asn Gly Tyr Cys Ser Cys Tyr Asn Leu Phe Gly
20 25 30

Tyr Leu Arg Ser Gly Cys Lys Cys Glu Val Gly Thr Ser Ala Glu Phe
35 40 45

Arg Arg Ile Cys Arg Arg Lys Ala Lys Gln Cys Tyr Asn Ser Asp Pro
50 55 60

Asp Lys Cys Val Ser Val Tyr Lys Pro Lys Arg Arg
65 70 75

<210> 966
<211> 43
<212> PRT
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<220>
<223> Agelenopsis aperta (Agatoxin) toxin peptide sequence - Omega-Aga-IIIC

<220>
<221> misc_feature
<222> (20)..(20)
<223> Xaa can be any naturally occurring amino acid

<220>
<221> misc_feature
<222> (40)..(40)
<223> Xaa can be any naturally occurring amino acid

<400> 966

Asn Cys Ile Asp Phe Gly Gly Asp Cys Asp Gly Glu Lys Asp Asp Cys
1 5 10 15

Gln Cys Cys Xaa Arg Asn Gly Tyr Cys Ser Cys Tyr Asn Leu Phe Gly
20 25 30

Tyr Leu Lys Arg Gly Cys Lys Xaa Glu Val Gly
35 40

<210> 967
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Agelenopsis aperta (Agatoxin) toxin peptide sequence - Omega-Aga-IIID

<220>
<221> misc_feature
<222> (27)..(27)
<223> Xaa can be any naturally occurring amino acid

<220>
<221> misc_feature
<222> (29)..(29)
<223> Xaa can be any naturally occurring amino acid

<400> 967

Ser Cys Ile Lys Ile Gly Glu Asp Cys Asp Gly Asp Lys Asp Asp Cys
1 5 10 15

Gln Cys Cys Arg Thr Asn Gly Tyr Cys Ser Xaa Tyr Xaa Leu Phe Gly
20 25 30

Tyr Leu Lys Ser Gly
35

<210> 968
<211> 28
<212> PRT
<213> Artificial Sequence

<220>
<223> Agelenopsis aperta (Agatoxin) toxin peptide sequence - Omega-Aga-IIA

<400> 968

Gly Cys Ile Glu Ile Gly Gly Asp Cys Asp Gly Tyr Gln Glu Lys Ser
1 5 10 15

Tyr Cys Gln Cys Cys Arg Asn Asn Gly Phe Cys Ser
20 25

<210> 969
<211> 66
<212> PRT
<213> Artificial Sequence

<220>
<223> Agelenopsis aperta (Agatoxin) toxin peptide sequence - Omega-Aga-IA (major chain)

<400> 969

Ala Lys Ala Leu Pro Pro Gly Ser Val Cys Asp Gly Asn Glu Ser Asp
1 5 10 15

Cys Lys Cys Tyr Gly Lys Trp His Lys Cys Arg Cys Pro Trp Lys Trp
20 25 30

His Phe Thr Gly Glu Gly Pro Cys Thr Cys Glu Lys Gly Met Lys His
35 40 45

Thr Cys Ile Thr Lys Leu His Cys Pro Asn Lys Ala Glu Trp Gly Leu
50 55 60

Asp Trp
65

<210> 970
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Agelenopsis aperta (Agatoxin) toxin peptide sequence - mu-Aga

<220>
<221> misc_feature
<222> (37)..(37)
<223> Xaa can be any naturally occurring amino acid

<400> 970

Glu Cys Val Pro Glu Asn Gly His Cys Arg Asp Trp Tyr Asp Glu Cys
1 5 10 15

Cys Glu Gly Phe Tyr Cys Ser Cys Arg Gln Pro Pro Lys Cys Ile Cys
20 25 30

Arg Asn Asn Asn Xaa
35

<210> 971
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Agelenopsis aperta (Agatoxin) toxin peptide sequence - mu-Aga-6

<400> 971

Asp Cys Val Gly Glu Ser Gln Gln Cys Ala Asp Trp Ala Gly Pro His
1 5 10 15

Cys Cys Asp Gly Tyr Tyr Cys Thr Cys Arg Tyr Phe Pro Lys Cys Ile
20 25 30

Cys Val Asn Asn Asn
35

<210> 972
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Agelenopsis aperta (Agatoxin) toxin peptide sequence - mu-Aga-5

<400> 972

Ala Cys Val Gly Glu Asn Lys Gln Cys Ala Asp Trp Ala Gly Pro His
1 5 10 15

Cys Cys Asp Gly Tyr Tyr Cys Thr Cys Arg Tyr Phe Pro Lys Cys Ile
20 25 30

Cys Arg Asn Asn Asn
35

<210> 973
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Agelenopsis aperta (Agatoxin) toxin peptide sequence - mu-Aga-4

<400> 973

Ala Cys Val Gly Glu Asn Gln Gln Cys Ala Asp Trp Ala Gly Pro His
1 5 10 15

Cys Cys Asp Gly Tyr Tyr Cys Thr Cys Arg Tyr Phe Pro Lys Cys Ile
20 25 30

Cys Arg Asn Asn Asn
35

<210> 974
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Agelenopsis aperta (Agatoxin) toxin peptide sequence - mu-Aga-2

<400> 974

Glu Cys Ala Thr Lys Asn Lys Arg Cys Ala Asp Trp Ala Gly Pro Trp
1 5 10 15

Cys Cys Asp Gly Leu Tyr Cys Ser Cys Arg Ser Tyr Pro Gly Cys Met
20 25 30

Cys Arg Pro Ser Ser
35

<210> 975
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> Agelenopsis aperta (Agatoxin) toxin peptide sequence - mu-Aga-1

<400> 975

Glu Cys Val Pro Glu Asn Gly His Cys Arg Asp Trp Tyr Asp Glu Cys
1 5 10 15

Cys Glu Gly Phe Tyr Cys Ser Cys Arg Gln Pro Pro Lys Cys Ile Cys
20 25 30

Arg Asn Asn Asn
35

<210> 976
<211> 270
<212> PRT
<213> Artificial Sequence

<220>

<223> FcLoop-L2-OsK1-L2

<220>
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<222> (1)..(139)
<223> Fc(N-term)

<220>
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<222> (142)..(179)
<223> OsK1

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<222> (182)..(270)
<223> Fc(C-term)

<400> 976

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Met Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
1               5                  10                  15

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
            20                  25                  30

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
        35                  40                  45

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
    50                  55                  60

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
65                  70                  75                  80

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
                85                  90                  95

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
            100                 105                 110

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
        115                 120                 125

Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Gly Gly Gly Val Ile
    130                 135                 140

Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Glu Pro Cys Lys
145                 150                 155                 160

Lys Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys Cys His Cys
                165                 170                 175

Thr Pro Lys Gly Gly Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val
            180                 185                 190
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Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
195 200 205

Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp
210 215 220

Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp
225 230 235 240

Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His
245 250 255

Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
260 265 270

<210> 977
<211> 267
<212> PRT
<213> Artificial Sequence

<220>
<223> FcLoop-L2-ShK-L2

<220>
<221> MISC_FEATURE
<222> (1)..(139)
<223> Fc(N-term)

<220>
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<222> (142)..(176)
<223> ShK

<220>
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<222> (179)..(267)
<223> Fc(C-term)

<400> 977

Met Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
1 5 10 15

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
20 25 30

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
35 40 45

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
50 55 60

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
65 70 75 80

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
85 90 95

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Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
            100                 105                 110

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
        115                 120                 125

Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Gly Gly Arg Ser Cys
    130                 135                 140

Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys Lys His
145                 150                 155                 160

Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly Thr Cys
                165                 170                 175

Gly Gly Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
            180                 185                 190

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
        195                 200                 205

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

Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
225                 230                 235                 240

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
                245                 250                 255

Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
            260                 265
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<210> 978
<211> 269
<212> PRT
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<220>
<223> FcLoop-L2-ShK-L4

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<223> Fc(N-term)

<220>
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<223> ShK

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<223> Fc(C-term)

<400> 978

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Met Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
1               5                  10                  15

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
            20                  25                  30

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
        35                  40                  45

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
    50                  55                  60

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
65                  70                  75                  80

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
                85                  90                  95

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
            100                 105                 110

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
        115                 120                 125

Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Gly Gly Arg Ser Cys
    130                 135                 140

Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe Gln Cys Lys His
145                 150                 155                 160

Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys Gly Thr Cys
                165                 170                 175

Gly Gly Gly Gly Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
            180                 185                 190

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
        195                 200                 205

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
    210                 215                 220

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
225                 230                 235                 240

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
                245                 250                 255
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His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
260 265

<210> 979
<211> 272
<212> PRT
<213> Artificial Sequence

<220>
<223> FcLoop-L4-OsK1-L2

<220>
<221> MISC_FEATURE
<222> (1)..(139)
<223> Fc(N-term)

<220>
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<222> (144)..(181)
<223> OsK1

<220>
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<222> (184)..(272)
<223> Fc(C-term)

<400> 979

Met Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
1 5 10 15

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
20 25 30

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
35 40 45

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
50 55 60

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
65 70 75 80

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
85 90 95

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
100 105 110

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
115 120 125

Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Gly Gly Gly Gly Gly
130 135 140

Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Glu Pro
145 150 155 160

Cys Lys Lys Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys Cys
165 170 175

His Cys Thr Pro Lys Gly Gly Thr Lys Asn Gln Val Ser Leu Thr Cys
180 185 190

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
195 200 205

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

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
225 230 235 240

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
245 250 255

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
260 265 270

<210> 980
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-O16,D20

<220>
<221> MOD_RES
<222> (16)..(16)
<223> Ornithine

<400> 980

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 981
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-hLys 16,D20

<220>

<221> MISC_FEATURE
<222> (16)..(16)
<223> Homolysine

<400> 981

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 982
<211> 38
<212> PRT
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<220>
<223> OSK1-hArg 16,D20

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homoarginine

<400> 982

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 983
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-Cit 16,D20

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Citrulline

<400> 983

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 984
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-hCit 16,D20

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homocitrulline

<400> 984

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 985
<211> 38
<212> PRT
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<220>
<223> OSK1-Dpr 16,D20

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Alpha,beta-diaminopropionoic acid

<400> 985

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 986
<211> 38
<212> PRT
<213> Artificial Sequence

<220>

<223> OSK1-Dab 16,D20

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Alpha,gamma-diaminobutyric acid

<400> 986

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 987
<211> 38
<212> PRT
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<220>
<223> OSK1-O16,D20,Y36

<220>
<221> MOD_RES
<222> (16)..(16)
<223> Ornithine

<400> 987

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Pro Lys
35

<210> 988
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-hLys 16,D20,Y36

<220>
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<222> (16)..(16)
<223> Homolysine

<400> 988

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Pro Lys
35

<210> 989
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-hArg 16,D20,Y36

<220>
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<222> (16)..(16)
<223> Homoarginine

<400> 989

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Pro Lys
35

<210> 990
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-Cit 16,D20,Y36

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Citrulline

<400> 990

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Pro Lys
35

<210> 991
<211> 38

<212> PRT
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<220>
<223> OSK1-hCit 16,D20,Y36

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homocitrulline

<400> 991

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Pro Lys
35

<210> 992
<211> 38
<212> PRT
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<220>
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<220>
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<222> (16)..(16)
<223> Alpha,beta-diaminopropionoic acid

<400> 992

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Pro Lys
35

<210> 993
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-Dab 16,D20,Y36

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Alpha,gamma-diaminobutyric acid

<400> 993

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Pro Lys
35

<210> 994
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-K16,D20,A34,Y36

<400> 994

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Tyr Pro Lys
35

<210> 995
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-K16,D20,G34,Y36

<400> 995

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Gly Cys Tyr Pro Lys
35

<210> 996
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-K16,D20,A34,F36

<400> 996

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Phe Pro Lys
35

<210> 997
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-K16,D20,A34,W36

<400> 997

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Trp Pro Lys
35

<210> 998
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-K16,E20,A34,Y36

<400> 998

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Tyr Pro Lys
35

<210> 999
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-O16,D20,A34

<220>
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<222> (16)..(16)

<223> Ornithine

<400> 999

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Thr Pro Lys
35

<210> 1000
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-hLys 16,D20,A34

<220>
<221> MISC_FEATURE
<222> (16)..(16)
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<400> 1000

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Thr Pro Lys
35

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<220>
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<400> 1001

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Thr Pro Lys
35

<210> 1002
<211> 38
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<223> Citrulline

<400> 1002

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Thr Pro Lys
35

<210> 1003
<211> 38
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<223> Homocitrulline

<400> 1003

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 1004
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<220>
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<223> Alpha,beta-diaminopropionoic acid

<400> 1004

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Arg Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn
20 25 30

Gly Lys Cys Ala Cys Thr Pro Lys
35 40

<210> 1005
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<400> 1005

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Thr Pro Lys
35

<210> 1006
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<220>
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<220>
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<223> Ornithine

<400> 1006

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys
35

<210> 1007
<211> 35
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<223> Homolysine

<400> 1007

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys
35

<210> 1008
<211> 35
<212> PRT
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<220>
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<400> 1008

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys
35

<210> 1009
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Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys
35

<210> 1010
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<400> 1010

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys
35

<210> 1011
<211> 35
<212> PRT
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Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys
35

<210> 1012
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<220>
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<400> 1012

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

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20 25 30

Cys His Cys
35

<210> 1013
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<220>
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Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys
35

<210> 1014
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Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys
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<210> 1015
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Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys
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<223> Citrulline

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Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys
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1 5 10 15

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20 25 30

Cys Ala Cys
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<223> Alpha,gamma-diaminobutyric acid

<400> 1019

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys
35

<210> 1020
<211> 38
<212> PRT
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<220>
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<400> 1020

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
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Cys Gly Cys Tyr Gly Gly
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<210> 1021
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-O16,D20,Y36,G37,G38

<220>
<221> MISC_FEATURE
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<223> Ornithine

<400> 1021

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Gly Gly
35

<210> 1022
<211> 38
<212> PRT
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<220>
<223> OSK1-hLys 16,D20,Y36,G37,G38

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homolysine

<400> 1022

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Gly Gly
35

<210> 1023
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<220>
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<220>
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<222> (16)..(16)
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<400> 1023

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Gly Gly
35

<210> 1024
<211> 38
<212> PRT
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<220>
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<222> (16)..(16)
<223> Citrulline

<400> 1024

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Gly Gly
35

<210> 1025
<211> 38
<212> PRT
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<220>
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<222> (16)..(16)
<223> Homocitrulline

<400> 1025

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Gly Gly
35

<210> 1026
<211> 38
<212> PRT
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<220>
<223> OSK1-Dpr 16,D20,Y36,G37,G38

<220>

<221> MISC_FEATURE
<222> (16)..(16)
<223> Alpha,beta-diaminopropionoic acid

<400> 1026

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Gly Gly
35

<210> 1027
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-K16,D20,A34,Y36,G37,G38

<400> 1027

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Tyr Gly Gly
35

<210> 1028
<211> 38
<212> PRT
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<220>
<223> OSK1-O16,D20,A34,Y36,G37,G38

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Ornithine

<400> 1028

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Tyr Gly Gly
35

<210> 1029
<211> 38
<212> PRT
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<220>
<223> OSK1-hLys 16,D20,A34,Y36,G37,G38

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homolysine

<400> 1029

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Tyr Gly Gly
35

<210> 1030
<211> 38
<212> PRT
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<220>
<223> OSK1-hArg 16,D20,A34,Y36,G37,G38

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homoarginine

<400> 1030

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Tyr Gly Gly
35

<210> 1031
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-Cit 16,D20,A34,Y36,G37,G38

<220>
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<222> (16)..(16)

<223> Citrulline

<400> 1031

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Tyr Gly Gly
35

<210> 1032
<211> 38
<212> PRT
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<220>
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<220>
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<222> (16)..(16)
<223> Homocitrulline

<400> 1032

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Gly Gly
35

<210> 1033
<211> 38
<212> PRT
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<220>
<223> OSK1-Dpr 16,D20,A34,Y36,G37,G38

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Alpha,beta-diaminopropionoic acid

<400> 1033

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Tyr Gly Gly
35

<210> 1034
<211> 38
<212> PRT
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<220>
<223> OSK1-Dab 16,D20,A34,Y36,G37,G38

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Alpha,gamma-diaminobutyric acid

<400> 1034

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Tyr Gly Gly
35

<210> 1035
<211> 37
<212> PRT
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<220>
<223> Delta38, OSK1-K16,D20,A34,Y36,G37

<400> 1035

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Tyr Gly
35

<210> 1036
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-O16,D20,G36-38

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Ornithine

<400> 1036

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Gly Gly Gly
35

<210> 1037
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-hLys 16,D20,G36-38

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homolysine

<400> 1037

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Gly Gly Gly
35

<210> 1038
<211> 38
<212> PRT
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<220>
<223> OSK1-hArg 16,D20,G36-38

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homoarginine

<400> 1038

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Gly Gly Gly
35

<210> 1039
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-Cit 16,D20,G36-38

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Citrulline

<400> 1039

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Gly Gly Gly
35

<210> 1040
<211> 38
<212> PRT
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<220>
<223> OSK1-hCit 16,D20,G36-38

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homocitrulline

<400> 1040

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Gly Gly Gly
35

<210> 1041
<211> 38
<212> PRT
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<220>
<223> OSK1-Dpr 16,D20,G36-38

<220>

<221> MISC_FEATURE
<222> (16)..(16)
<223> Alpha,beta-diaminopropionoic acid

<400> 1041

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Gly Gly Gly
35

<210> 1042
<211> 38
<212> PRT
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<220>
<223> OSK1-K16,D20,A34,F36,G37,G38

<400> 1042

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Phe Gly Gly
35

<210> 1043
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-O16,D20,A34,G36-38

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Ornithine

<400> 1043

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Gly Gly Gly
35

<210> 1044
<211> 38
<212> PRT
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<220>
<223> OSK1-hLys 16,D20,A34,G36-38

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homolysine

<400> 1044

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Gly Gly Gly
35

<210> 1045
<211> 38
<212> PRT
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<220>
<223> OSK1-hArg 16,D20,A34,G36-38

<220>
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<222> (16)..(16)
<223> Homoarginine

<400> 1045

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Gly Gly Gly
35

<210> 1046
<211> 38
<212> PRT
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<220>
<223> OSK1-Cit 16,D20,A34,G36-38

<220>
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<222> (16)..(16)

<223> Citrulline

<400> 1046

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Gly Gly Gly
35

<210> 1047
<211> 38
<212> PRT
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<220>
<223> OSK1-hCit 16,D20,A34,G36-38

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homocitrulline

<400> 1047

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Gly Gly Gly
35

<210> 1048
<211> 38
<212> PRT
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<220>
<223> OSK1-Dpr 16,D20,A34,G36-38

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Alpha,beta-diaminopropionoic acid

<400> 1048

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Gly Gly Gly
35

<210> 1049
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-Dab 16,D20,A34,G36-38

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Alpha,gamma-diaminobutyric acid

<400> 1049

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Gly Gly Gly
35

<210> 1050
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Delta38, OSK1-K16,D20,A34,G36-37

<400> 1050

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Gly Gly
35

<210> 1051
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Delta38, OSK1-K16,D20,A35,Y36,G37

<400> 1051

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Tyr Gly
35

<210> 1052
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Delta38, OSK1-O16,D20,A35,Y36,G37

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Ornithine

<400> 1052

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Gly Gly
35

<210> 1053
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-hLys 16,E20

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homolysine

<400> 1053

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 1054
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-hArg 16,E20

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homoarginine

<400> 1054

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 1055
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-Cit 16,E20

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Citrulline

<400> 1055

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 1056
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-hCit 16,E20

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homocitrulline

<400> 1056

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 1057
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-Dpr 16,E20

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Alpha,beta-diaminopropionoic acid

<400> 1057

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 1058
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-Dab 16,E20

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Alpha,gamma-diaminobutyric acid

<400> 1058

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 1059
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-O16,E20,Y36

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Ornithine

<400> 1059

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Pro Lys
35

<210> 1060
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-hLys 16,E20,Y36

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homolysine

<400> 1060

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Pro Lys
35

<210> 1061
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-hArg 16,E20,Y36

<220>
<221> MISC_FEATURE
<222> (16)..(16)

<223> Homoarginine

<400> 1061

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Pro Lys
35

<210> 1062
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-Cit 16,E20,Y36

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Citrulline

<400> 1062

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Pro Lys
35

<210> 1063
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-hCit 16,E20,Y36

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homocitrulline

<400> 1063

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Pro Lys
35

<210> 1064
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-Dpr 16,E20,Y36

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Alpha,beta-diaminopropionoic acid

<400> 1064

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Pro Lys
35

<210> 1065
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-Dab 16,E20,Y36

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Alpha,gamma-diaminobutyric acid

<400> 1065

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Pro Lys
35

<210> 1066
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-O16,E20,A34

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Ornithine

<400> 1066

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Thr Pro Lys
35

<210> 1067
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-hLys 16,E20,A34

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homolysine

<400> 1067

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Thr Pro Lys
35

<210> 1068
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-hArg 16,E20,A34

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homoarginine

<400> 1068

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Thr Pro Lys
35

<210> 1069
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-Cit 16,E20,A34

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Citrulline

<400> 1069

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Thr Pro Lys
35

<210> 1070
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-hCit 16,E20,A34

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homocitrulline

<400> 1070

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 1071
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-Dpr 16,E20,A34

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Alpha,beta-diaminopropionoic acid

<400> 1071

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Thr Pro Lys
35

<210> 1072
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-Dab 16,E20,A34

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Alpha,gamma-diaminobutyric acid

<400> 1072

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Thr Pro Lys
35

<210> 1073
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Delta36-38, OSK1-O16,E20,

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Ornithine

<400> 1073

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys
35

<210> 1074
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Delta36-38, OSK1-hLys 16,E20

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homolysine

<400> 1074

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys
35

<210> 1075
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Delta36-38, OSK1-hArg 16,E20

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homoarginine

<400> 1075

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys
35

<210> 1076
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Delta36-38, OSK1-Cit 16,E20

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Citrulline

<400> 1076

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys
35

<210> 1077
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Delta36-38, OSK1-hCit16,E20

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homocitrulline

<400> 1077

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys
35

<210> 1078
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Delta36-38, OSK1-Dpr 16,E20

<220>
<221> MISC_FEATURE
<222> (16)..(16)

<223> Alpha,beta-diaminopropionoic acid

<400> 1078

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys
35

<210> 1079
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Delta36-38, OSK1-016,E20,A34

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Ornithine

<400> 1079

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys
35

<210> 1080
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Delta36-38, OSK1-hLys 16,E20,A34

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homolysine

<400> 1080

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys
35

<210> 1081
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Delta36-38, OSK1-hArg 16,E20,A34

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homoarginine

<400> 1081

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys
35

<210> 1082
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Delta36-38, OSK1-Cit 16,E20,A34

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Citrulline

<400> 1082

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys
35

<210> 1083
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Delta36-38, OSK1-hCit 16,E20,A34

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homocitrulline

<400> 1083

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys
35

<210> 1084
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Delta36-38, OSK1-Dpr 16,E20,A34

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Alpha,beta-diaminopropionoic acid

<400> 1084

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys
35

<210> 1085
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Delta36-38, OSK1-Dab 16,E20,A34

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Alpha,gamma-diaminobutyric acid

<400> 1085

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys
35

<210> 1086
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-K16,E20,Y36,G37,G38

<400> 1086

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Gly Gly
35

<210> 1087
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-O16,E20,Y36,G37,G38

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Ornithine

<400> 1087

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Gly Gly
35

<210> 1088
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Delta38 OSK1-K16,E20,Y36,G37

<400> 1088

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Gly
35

<210> 1089
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Delta38 OSK1-K16,E20,A34, Y36,G37

<400> 1089

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Tyr Gly
35

<210> 1090
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-hLys 16,E20,Y36,G37,G38

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homolysine

<400> 1090

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Gly Gly
35

<210> 1091
<211> 38
<212> PRT
<213> Artificial Sequence

<220>

<223> OSK1-hArg 16,E20,Y36,G37,G38

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homoarginine

<400> 1091

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Gly Gly
35

<210> 1092
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-Cit 16,E20,Y36,G37,G38

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Citrulline

<400> 1092

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Gly Gly
35

<210> 1093
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Delta37-38, OSK1-hCit 16,E20,Y36,G37,G38

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homocitrulline

<400> 1093

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Gly Gly
35

<210> 1094
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-Dpr 16,E20,Y36,G37,G38

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Alpha,beta-diaminopropionoic acid

<400> 1094

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Gly Gly
35

<210> 1095
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-Dab 16,E20,Y36,G37,G38

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Alpha,gamma-diaminobutyric acid

<400> 1095

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Gly Gly
35

<210> 1096
<211> 37

<212> PRT
<213> Artificial Sequence

<220>
<223> Delta38, OSK1-K16,E20,A34,Y36,G37

<400> 1096

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Tyr Gly
35

<210> 1097
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-O16,E20,A34,Y36,G37,G38

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Ornithine

<400> 1097

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Tyr Gly Gly
35

<210> 1098
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-hLys 16,E20,A34,Y36,G37,G38

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homolysine

<400> 1098

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Tyr Gly Gly
35

<210> 1099
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-hArg 16,E20,A34,Y36,G37,G38

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homoarginine

<400> 1099

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Tyr Gly Gly
35

<210> 1100
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-Cit 16,E20,A34,Y36,G37,G38

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Citrulline

<400> 1100

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Tyr Gly Gly
35

<210> 1101
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-hCit 16,E20,A34,Y3,G37,G38

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homocitrulline

<400> 1101

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Gly Gly
35

<210> 1102
<211> 38
<212> PRT
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<220>
<223> OSK1-Dpr 16,E20,A34,Y36,G37,G38

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Alpha,beta-diaminopropionoic acid

<400> 1102

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Tyr Gly Gly
35

<210> 1103
<211> 38
<212> PRT
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<220>
<223> OSK1-Dab 16,E20,A34,Y36,G37,G38

<220>
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<222> (16)..(16)
<223> Alpha,gamma-diaminobutyric acid

<400> 1103

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Tyr Gly Gly
35

<210> 1104
<211> 38
<212> PRT
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<220>
<223> OSK1-K16,D20,A34,F36,G37,G38

<400> 1104

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Phe Gly Gly
35

<210> 1105
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-O16,E20,G36-38

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Ornithine

<400> 1105

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Gly Gly Gly
35

<210> 1106
<211> 38
<212> PRT
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<220>

<223> OSK1-hLys 16,E20,G36-38

<220>
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<222> (16)..(16)
<223> Homolysine

<400> 1106

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Gly Gly Gly
35

<210> 1107
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-hArg 16,E20,G36-38

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homoarginine

<400> 1107

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Gly Gly Gly
35

<210> 1108
<211> 38
<212> PRT
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<220>
<223> OSK1-Cit 16,E20,G36-38

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Citrulline

<400> 1108

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Gly Gly Gly
35

<210> 1109
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-hCit 16,E20,G36-38

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homocitrulline

<400> 1109

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Gly Gly Gly
35

<210> 1110
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-Dpr 16,E20,G36-38

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Alpha,beta-diaminopropionoic acid

<400> 1110

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Gly Gly Gly
35

<210> 1111
<211> 38

<212> PRT
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<220>
<223> OSK1-O16,E20,A34,G36-38

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Ornithine

<400> 1111

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Gly Gly Gly
35

<210> 1112
<211> 38
<212> PRT
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<220>
<223> OSK1-hLys 16,E20,A34,G36-38

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homolysine

<400> 1112

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Gly Gly Gly
35

<210> 1113
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-hArg 16,E20,A34,G36-38

<220>
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<222> (16)..(16)
<223> Homoarginine

<400> 1113

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Gly Gly Gly
35

<210> 1114
<211> 38
<212> PRT
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<220>
<223> OSK1-Cit 16,E20,A34,G36-38

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Citrulline

<400> 1114

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Gly Gly Gly
35

<210> 1115
<211> 37
<212> PRT
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<220>
<223> OSK1-hCit 16,E20,A34,G36-38

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homocitrulline

<400> 1115

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Thr Pro
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<210> 1116
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Alpha,beta-diaminopropionoic acid

<400> 1116

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Thr Pro
35

<210> 1117
<211> 37
<212> PRT
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<220>
<223> OSK1-Dab 16,E20,A34,G36-38

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Alpha,gamma-diaminobutyric acid

<400> 1117

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Thr Pro
35

<210> 1118
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-O16,D20-amide

<220>

<221> MISC_FEATURE
<222> (16)..(16)
<223> Ornithine

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1118

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 1119
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homolysine

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1119

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 1120
<211> 38
<212> PRT
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<220>
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<220>
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<222> (16)..(16)

<223> Homoarginine

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1120

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 1121
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-Cit 16,D20-amide

<220>
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<222> (16)..(16)
<223> Citrulline

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1121

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 1122
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-hCit 16,D20-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homocitrulline

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1122

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 1123
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<223> Alpha,beta-diaminopropionoic acid

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1123

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 1124
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-Dab 16,D20-amide

<220>
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<222> (16)..(16)
<223> Alpha,gamma-diaminobutyric acid

<220>
<221> MOD_RES

<222> (38)..(38)
<223> AMIDATION

<400> 1124

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 1125
<211> 38
<212> PRT
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<220>
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<220>
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<222> (16)..(16)
<223> Ornithine

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1125

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Pro Lys
35

<210> 1126
<211> 38
<212> PRT
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<220>
<223> OSK1-hLys 16,D20,Y36-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homolysine

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1126

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Pro Lys
35

<210> 1127
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-hArg 16,D20,Y36-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homoarginine

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1127

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Pro Lys
35

<210> 1128
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-Cit 16,D20,Y36-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Citrulline

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1128

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Pro Lys
35

<210> 1129
<211> 38
<212> PRT
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<220>
<223> OSK1-hCit 16,D20,Y36-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homocitrulline

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1129

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Pro Lys
35

<210> 1130
<211> 38
<212> PRT
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<220>
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<220>
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<222> (16)..(16)
<223> Alpha,beta-diaminopropionoic acid

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1130

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa

1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Pro Lys
35

<210> 1131
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-Dab 16,D20,Y36-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Alpha,gamma-diaminobutyric acid

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1131

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Pro Lys
35

<210> 1132
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-O16,D20,A34-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Ornithine

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1132

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Thr Pro Lys
35

<210> 1133
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-hLys 16,D20,A34-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homolysine

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1133

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Thr Pro Lys
35

<210> 1134
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-hArg 16,D20,A34-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homoarginine

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1134

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys

20 25 30

Cys Ala Cys Thr Pro Lys
35

<210> 1135
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-Cit 16,D20,A34-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Citrulline

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1135

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Thr Pro Lys
35

<210> 1136
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-hCit 16,D20,A34-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homocitrulline

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1136

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Thr Pro Lys
35

<210> 1137
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-Dpr 16,D20,A34-amide

<220>
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<222> (16)..(16)
<223> Alpha,beta-diaminopropionoic acid

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1137

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Thr Pro Lys
35

<210> 1138
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<222> (16)..(16)
<223> Alpha,gamma-diaminobutyric acid

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1138

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Thr Pro Lys

35

<210> 1139
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Delta36-38, OSK1-O16,D20-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Ornithine

<220>
<221> MOD_RES
<222> (35)..(35)
<223> AMIDATION

<400> 1139

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys
35

<210> 1140
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Delta36-38, OSK1-hLys 16,D20-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homolysine

<220>
<221> MOD_RES
<222> (35)..(35)
<223> AMIDATION

<400> 1140

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys
35

<210> 1141
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Delta36-38, OSK1-hArg 16,D20-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homoarginine

<220>
<221> MOD_RES
<222> (35)..(35)
<223> AMIDATION

<400> 1141

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys
35

<210> 1142
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Delta36-38, OSK1-Cit 16,D20-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Citrulline

<220>
<221> MOD_RES
<222> (35)..(35)
<223> AMIDATION

<400> 1142

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys
35

<210> 1143

<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Delta36-38, OSK1- hCit16,D20-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homocitrulline

<220>
<221> MOD_RES
<222> (35)..(35)
<223> AMIDATION

<400> 1143

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys
35

<210> 1144
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Delta36-38, OSK1-Dpr 16,D20-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Alpha,beta-diaminopropionoic acid

<220>
<221> MOD_RES
<222> (35)..(35)
<223> AMIDATION

<400> 1144

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys
35

<210> 1145
<211> 35
<212> PRT

<213> Artificial Sequence

<220>
<223> Delta36-38, OSK1-O16,D20,A34-amide

<220>
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<222> (16)..(16)
<223> Ornithine

<220>
<221> MOD_RES
<222> (35)..(35)
<223> AMIDATION

<400> 1145

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys
35

<210> 1146
<211> 35
<212> PRT
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<220>
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<220>
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<223> Homolysine

<220>
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<222> (35)..(35)
<223> AMIDATION

<400> 1146

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys
35

<210> 1147
<211> 35
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<220>
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<223> Homoaginine

<220>
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<222> (35)..(35)
<223> AMIDATION

<400> 1147

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys
35

<210> 1148
<211> 35
<212> PRT
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<220>
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<220>
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<223> Citrulline

<220>
<221> MOD_RES
<222> (35)..(35)
<223> AMIDATION

<400> 1148

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys
35

<210> 1149
<211> 35
<212> PRT
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<220>
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<220>
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<222> (16)..(16)
<223> Homocitrulline

<220>
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<222> (35)..(35)
<223> AMIDATION

<400> 1149

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys
35

<210> 1150
<211> 35
<212> PRT
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<220>
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<220>
<221> MOD_RES
<222> (35)..(35)
<223> AMIDATION

<400> 1150

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys
35

<210> 1151
<211> 35
<212> PRT
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<220>
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<223> Alpha,gamma-diaminobutyric acid

<220>
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<222> (35)..(35)
<223> AMIDATION

<400> 1151

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys
35

<210> 1152
<211> 38
<212> PRT
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<220>
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<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1152

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Gly Gly
35

<210> 1153
<211> 38
<212> PRT
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<220>
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<223> Ornithine

<220>
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<222> (38)..(38)
<223> AMIDATION

<400> 1153

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Gly Gly
35

<210> 1154
<211> 38
<212> PRT
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<220>
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<220>
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<222> (16)..(16)
<223> Homolysine

<220>
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<222> (38)..(38)
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<400> 1154

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Gly Gly
35

<210> 1155
<211> 38
<212> PRT
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<220>
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<220>
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<222> (16)..(16)
<223> Homoarginine

<220>
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<222> (38)..(38)
<223> AMIDATION

<400> 1155

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Gly Gly
35

<210> 1156
<211> 38
<212> PRT
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<220>
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<220>
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<222> (16)..(16)
<223> Citrulline

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1156

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Gly Gly
35

<210> 1157
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1- hCit16,D20,Y36,G37,G38-amide

<220>
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<222> (16)..(16)
<223> Homocitrulline

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1157

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Gly Gly
35

<210> 1158
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<223> Alpha,beta-diaminopropionoic acid

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1158

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Gly Gly
35

<210> 1159
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1159

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Phe Gly Gly
35

<210> 1160
<211> 37
<212> PRT
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<220>
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<221> MOD_RES
<222> (37)..(37)
<223> AMIDATION

<400> 1160

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Gly
35

<210> 1161
<211> 37
<212> PRT
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<220>
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<222> (37)..(37)
<223> AMIDATION

<400> 1161

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Tyr Gly
35

<210> 1162
<211> 38
<212> PRT
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<220>

<223> OSK1-O16,D20,A34,Y36,G37,G38-amide

<220>
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<223> Ornithine

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1162

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Tyr Gly Gly
35

<210> 1163
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-hLys 16,D20,A34,Y36,G37,G38-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homolysine

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1163

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Tyr Gly Gly
35

<210> 1164
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-hArg 16,D20,A34,Y36,G37,G38-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homoarginine

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1164

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Tyr Gly Gly
35

<210> 1165
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-Cit 16,D20,A34,Y36,G37,G38

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Citrulline

<220>
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<222> (38)..(38)
<223> AMIDATION

<400> 1165

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Tyr Gly Gly
35

<210> 1166
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1- hCit16,D20,A34,Y3,G37,G38-amide

<220>

<221> MISC_FEATURE
<222> (16)..(16)
<223> Homocitrulline

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1166

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Tyr Gly Gly
35

<210> 1167
<211> 38
<212> PRT
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<220>
<223> OSK1-Dpr 16,D20,A34,Y36,G37,G38-amide

<220>
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<222> (16)..(16)
<223> Alpha,beta-diaminopropionoic acid

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1167

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Tyr Gly Gly
35

<210> 1168
<211> 38
<212> PRT
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<220>
<223> OSK1-Dab 16,D20,A34,Y36,G37,G38-amide

<220>
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<223> Alpha,gamma-diaminobutyric acid

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1168

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Tyr Gly Gly
35

<210> 1169
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-K16,D20,A34,Y36,G37,G38-amide

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1169

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Tyr Gly Gly
35

<210> 1170
<211> 38
<212> PRT
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<220>
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<220>
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<223> Ornithine

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1170

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Gly Gly Gly
35

<210> 1171
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-hLys 16,D20,G36-38-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homolysine

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1171

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Gly Gly Gly
35

<210> 1172
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-hArg 16,D20,G36-38-amide

<220>
<221> MISC_FEATURE
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<223> Homoarginine

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1172

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Gly Gly Gly
35

<210> 1173
<211> 38
<212> PRT
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<220>
<223> OSK1-Cit 16,D20,G36-38-amide

<220>
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<222> (16)..(16)
<223> Citrulline

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1173

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Gly Gly Gly
35

<210> 1174
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1- hCit16,D20,G36-38-amide

<220>
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<222> (16)..(16)
<223> Homocitrulline

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1174

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Gly Gly Gly
35

<210> 1175
<211> 38
<212> PRT
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<220>
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<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Alpha,beta-diaminopropionoic acid

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1175

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Gly Gly Gly
35

<210> 1176
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1176

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Gly Gly Gly

35

<210> 1177
<211> 38
<212> PRT
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<220>
<223> OSK1-O16,D20,A34,F36, G37-38-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Ornithine

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1177

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Phe Gly Gly
35

<210> 1178
<211> 38
<212> PRT
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<220>
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<220>
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<222> (16)..(16)
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<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1178

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Gly Gly Gly
35

<210> 1179
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-hLys 16,D20,A34,G36-38-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homolysine

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1179

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Gly Gly Gly
35

<210> 1180
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-hArg 16,D20,A34,G36-38-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homoarginine

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1180

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Gly Gly Gly
35

<210> 1181

<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-Cit 16,D20,A34,G36-38-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Citrulline

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1181

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Gly Gly Gly
35

<210> 1182
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1- hCit16,D20,A34,G36-38-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homocitrulline

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1182

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Gly Gly Gly
35

<210> 1183
<211> 38
<212> PRT

<213> Artificial Sequence

<220>
<223> OSK1-Dpr 16,D20,A34,G36-38-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Alpha,beta-diaminopropionoic acid

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1183

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Gly Gly Gly
35

<210> 1184
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<222> (16)..(16)
<223> Alpha,gamma-diaminobutyric acid

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1184

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Gly Gly Gly
35

<210> 1185
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-O16,E20-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Ornithine

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1185

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 1186
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Hmolysine

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1186

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 1187
<211> 38
<212> PRT
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<220>
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<400> 1187

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
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<210> 1188
<211> 38
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<220>
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<223> AMIDATION

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Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
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<210> 1189
<211> 38
<212> PRT
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<220>
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<220>
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<223> Homocitrulline

<220>
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<222> (38)..(38)
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Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
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<210> 1190
<211> 38
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Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 1191
<211> 38
<212> PRT
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<220>
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Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 1192
<211> 38
<212> PRT
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<220>
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<223> Ornithine

<220>
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Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Pro Lys
35

<210> 1193
<211> 38
<212> PRT
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<220>
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<222> (16)..(16)
<223> Homolysine

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

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Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Pro Lys
35

<210> 1194
<211> 38
<212> PRT
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<220>
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<223> Homoarginine

<220>
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<223> AMIDATION

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Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Pro Lys
35

<210> 1195
<211> 38
<212> PRT
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<220>
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<220>
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<220>

<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

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Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Pro Lys
35

<210> 1196
<211> 38
<212> PRT
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<220>
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<220>
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<220>
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<222> (38)..(38)
<223> AMIDATION

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Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Pro Lys
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<210> 1197
<211> 38
<212> PRT
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<220>
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<220>
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<223> AMIDATION

<400> 1197

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Pro Lys
35

<210> 1198
<211> 38
<212> PRT
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<220>
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<220>
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<220>
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Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Pro Lys
35

<210> 1199
<211> 38
<212> PRT
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<220>
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<220>
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<223> Ornithine

<220>
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Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Thr Pro Lys
35

<210> 1200
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<220>
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<220>
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<223> Homolysine

<220>
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Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Thr Pro Lys
35

<210> 1201
<211> 38
<212> PRT
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<220>
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<220>
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<223> Homoarginine

<220>
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<222> (38)..(38)
<223> AMIDATION

<400> 1201

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Thr Pro Lys
35

<210> 1202
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<212> PRT
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<220>
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<220>
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<222> (16)..(16)
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<223> AMIDATION

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Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Thr Pro Lys
35

<210> 1203
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<220>
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<220>
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Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Thr Pro Lys
35

<210> 1204
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<212> PRT
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<223> AMIDATION

<400> 1204

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Thr Pro Lys
35

<210> 1205
<211> 38
<212> PRT
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<220>
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<220>
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<221> MOD_RES
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<223> AMIDATION

<400> 1205

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Thr Pro Lys
35

<210> 1206
<211> 35
<212> PRT
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<220>
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<220>
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<223> Ornithine

<220>
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<223> AMIDATION

<400> 1206

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys
35

<210> 1207
<211> 35
<212> PRT
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<220>
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<220>
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<223> Homolysine

<220>
<221> MOD_RES
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<223> AMIDATION

<400> 1207

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys
35

<210> 1208
<211> 35
<212> PRT
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<220>
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<223> Homoarginine

<220>
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<222> (35)..(35)
<223> AMIDATION

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Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys
35

<210> 1209
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<212> PRT
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<220>
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<220>
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<223> Citrulline

<220>
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<223> AMIDATION

<400> 1209

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys
35

<210> 1210
<211> 35
<212> PRT
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<220>
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<220>
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<222> (16)..(16)
<223> Homocitrulline

<220>
<221> MOD_RES
<222> (35)..(35)
<223> AMIDATION

<400> 1210

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys
35

<210> 1211
<211> 35
<212> PRT
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<220>
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<220>
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<223> Alpha,beta-diaminopropionoic acid

<220>
<221> MOD_RES
<222> (35)..(35)
<223> AMIDATION

<400> 1211

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys
35

<210> 1212
<211> 35
<212> PRT
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<220>
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<222> (16)..(16)
<223> Ornithine

<220>
<221> MOD_RES
<222> (35)..(35)
<223> AMIDATION

<400> 1212

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys
35

<210> 1213
<211> 35
<212> PRT
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<220>
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<220>
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<222> (16)..(16)
<223> Homolysine

<220>
<221> MOD_RES
<222> (35)..(35)
<223> AMIDATION

<400> 1213

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys
35

<210> 1214
<211> 35
<212> PRT
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<220>
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<220>
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<222> (16)..(16)
<223> Homoarginine

<220>
<221> MOD_RES
<222> (35)..(35)
<223> AMIDATION

<400> 1214

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys
35

<210> 1215
<211> 35
<212> PRT
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<220>
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<220>
<221> MISC_FEATURE
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<223> Citrulline

<220>
<221> MOD_RES
<222> (35)..(35)
<223> AMIDATION

<400> 1215

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys
35

<210> 1216
<211> 35

<212> PRT
<213> Artificial Sequence

<220>
<223> Delta36-38, OSK1- hCit16,E20,A34-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homocitrulline

<220>
<221> MOD_RES
<222> (35)..(35)
<223> AMIDATION

<400> 1216

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys
35

<210> 1217
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<222> (16)..(16)
<223> Alpha,beta-diaminopropionoic acid

<220>
<221> MOD_RES
<222> (35)..(35)
<223> AMIDATION

<400> 1217

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys
35

<210> 1218
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<222> (16)..(16)
<223> Alpha,gamma-diaminobutyric acid

<220>
<221> MOD_RES
<222> (35)..(35)
<223> AMIDATION

<400> 1218

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys
35

<210> 1219
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-016,E20,W36,G37,G38-amide

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1219

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Trp Gly Gly
35

<210> 1220
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-016,E20,Y36,G37,G38-amide

<220>
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<222> (16)..(16)
<223> Ornithine

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1220

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Gly Gly
35

<210> 1221
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-hLys 16,E20,Y36,G37,G38-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homolysine

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1221

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Gly Gly
35

<210> 1222
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-hArg 16,E20,Y36,G37,G38-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homoarginine

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1222

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Gly Gly
35

<210> 1223
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-Cit 16,E20,Y36,G37,G38-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Citrulline

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1223

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Gly Gly
35

<210> 1224
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-hCit 16,E20,Y36,G37,G38-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homocitrulline

<220>

<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1224

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Gly Gly
35

<210> 1225
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-Dpr 16,E20,Y36,G37,G38-amide

<220>
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<222> (16)..(16)
<223> Alpha,beta-diaminopropionoic acid

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1225

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Gly Gly
35

<210> 1226
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-Dpr 16,E20,Y36,G37,G38-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Alpha,gamma-diaminobutyric acid

<220>
<221> MOD_RES
<222> (38)..(38)

<223> AMIDATION

<400> 1226

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Gly Gly
35

<210> 1227
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-K16,E20,A34,Y36,G37,G38-amide

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1227

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Tyr Gly Gly
35

<210> 1228
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-O16,E20,A34,Y36,G37,G38-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Ornithine

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1228

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Tyr Gly Gly
35

<210> 1229
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-hLys 16,E20,A34,Y36,G37,G38-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homolysine

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1229

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Tyr Gly Gly
35

<210> 1230
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-hArg 16,E20,A34,Y36,G37,G38-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homoarginine

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1230

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys

20 25 30

Cys Ala Cys Tyr Gly Gly
35

<210> 1231
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-Cit 16,E20,A34,Y36,G37,G38-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Citrulline

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1231

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Tyr Gly Gly
35

<210> 1232
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1- hCit 16,E20,A34,Y3,G37,G38-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homocitrulline

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1232

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Gly Gly
35

<210> 1233
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-Dpr 16,E20,A34,Y36,G37,G38-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Alpha,beta-diaminopropionoic acid

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1233

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Tyr Gly Gly
35

<210> 1234
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-Dab 16,E20,A34,Y36,G37,G38-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Alpha,gamma-diaminobutyric acid

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1234

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Tyr Gly Gly

35

<210> 1235
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-O16,E20,G36-38-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Ornithine

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1235

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Gly Gly Gly
35

<210> 1236
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-hLys 16,E20,G36-38-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homolysine

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1236

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Gly Gly Gly
35

<210> 1237
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-hArg 16,E20,G36-38-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homoarginine

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1237

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Gly Gly Gly
35

<210> 1238
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-Cit 16,E20,G36-38-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Citrulline

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1238

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Gly Gly Gly
35

<210> 1239

<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-hCit 16,E20,G36-38-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homocitrulline

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1239

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Gly Gly Gly
35

<210> 1240
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-Dpr 16,E20,G36-38-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Alpha,beta-diaminopropionoic acid

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1240

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Gly Gly Gly
35

<210> 1241
<211> 38
<212> PRT

<213> Artificial Sequence

<220>
<223> OSK1-O16,E20,A34,G36-38-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Ornithine

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1241

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Gly Gly Gly
35

<210> 1242
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-hLys 16,E20,A34,G36-38-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homolysine

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1242

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Gly Gly Gly
35

<210> 1243
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-hArg 16,E20,A34,G36-38-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homoarginine

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1243

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Gly Gly Gly
35

<210> 1244
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-Cit 16,E20,A34,G36-38-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Citrulline

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1244

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Gly Gly Gly
35

<210> 1245
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Delta38 OSK1-hCit 16,E20,A34-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Homocitrulline

<220>
<221> MOD_RES
<222> (37)..(37)
<223> AMIDATION

<400> 1245

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Thr Pro
35

<210> 1246
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-Dpr 16,E20,A34,G36-38-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Alpha,beta-diaminopropionoic acid

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1246

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Gly Gly Gly
35

<210> 1247
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-Dab 16,E20,A34,G36-38-amide

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> Alpha,gamma-diaminobutyric acid

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1247

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Xaa
1 5 10 15

Pro Cys Lys Glu Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Gly Gly Gly
35

<210> 1248
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-K 16,CPA20,A34,Y36,G37,G38-amide

<220>
<221> MISC_FEATURE
<222> (20)..(20)
<223> p-carboxyl-phenylalanine

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1248

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Xaa Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Tyr Gly Gly
35

<210> 1249
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-K 16,CPA20,A34,G36-38-amide

<220>
<221> MISC_FEATURE

<222> (20)..(20)
<223> p-carboxyl-phenylalanine

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1249

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Xaa Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Gly Gly Gly
35

<210> 1250
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> Delta37-38OSK1-K 16,CPA20,A34,Y36-amide

<220>
<221> MISC_FEATURE
<222> (20)..(20)
<223> p-carboxyl-phenylalanine

<220>
<221> MOD_RES
<222> (36)..(36)
<223> AMIDATION

<400> 1250

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Xaa Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Tyr
35

<210> 1251
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> Acetyl-OSK1-K 16,D20,A34,Y36,G37,G38-amide

<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLATION

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1251

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Tyr Gly Gly
35

<210> 1252
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-K 16, Aad20,A34,Y36,G37,G38-amide

<220>
<221> MISC_FEATURE
<222> (20)..(20)
<223> Alpha-aminoadipic acid

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1252

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Xaa Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Tyr Gly Gly
35

<210> 1253
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-K 16, Aad20,Y36,G37,G38-amide

<220>
<221> MISC_FEATURE
<222> (20)..(20)
<223> Alpha-aminoadipic acid

<220>

<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1253

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Xaa Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Gly Gly
35

<210> 1254
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-K 16, Aad20,A34,Y36,G37,G38

<220>
<221> MISC_FEATURE
<222> (20)..(20)
<223> Alpha-aminoadipic acid

<400> 1254

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Xaa Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Tyr Gly Gly
35

<210> 1255
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-H 16,D20,A34,Y36,G37,G38-amide

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1255

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu His
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Tyr Gly Gly
35

<210> 1256
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-H 16,D20,A34,Y36,G37,G38

<400> 1256

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu His
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Tyr Gly Gly
35

<210> 1257
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> Delta37-38-OSK1-H 16,D20,A34,Y36-amide

<220>
<221> MOD_RES
<222> (36)..(36)
<223> AMIDATION

<400> 1257

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu His
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Tyr
35

<210> 1258
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-H 16,D20,A34,Y36,G37,G38-amide

<220>
<221> MOD_RES
<222> (38)..(38)

<223> AMIDATION

<400> 1258

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu His
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Gly Gly
35

<210> 1259
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-H 16,D20,A34,Y36,G37,G38

<400> 1259

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu His
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Gly Gly
35

<210> 1260
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-H 16,D20,A34,Y36,

<400> 1260

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu His
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Tyr Pro Lys
35

<210> 1261
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Delta36-38 OSK1-H 16,D20,A34,Y36,

<400> 1261

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu His
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys
35

<210> 1262
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-K 16,D20,A34,1Nal36,G37,G38-amide

<220>
<221> MISC_FEATURE
<222> (36)..(36)
<223> Beta-(1-Naphthyl)-alanine

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1262

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Xaa Gly Gly
35

<210> 1263
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-K 16,D20,A34,1Nal36-amide

<220>
<221> MISC_FEATURE
<222> (36)..(36)
<223> Beta-(1-Naphthyl)-alanine

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1263

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Xaa Pro Lys
35

<210> 1264
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-K 16,D20,A34,2Nal36,G37,G38-amide

<220>
<221> MISC_FEATURE
<222> (36)..(36)
<223> Beta-(2-Naphthyl)-alanine

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1264

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Xaa Gly Gly
35

<210> 1265
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-K 16,D20,A34,Cha36,G37,G38-amide

<220>
<221> MISC_FEATURE
<222> (36)..(36)
<223> Cyclohexylalanine

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1265

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Xaa Gly Gly
35

<210> 1266
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-K 16,D20,A34, MePhe36,G37,G38-amide

<220>
<221> MISC_FEATURE
<222> (36)..(36)
<223> 4-methyl-phenylalanine

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1266

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Xaa Gly Gly
35

<210> 1267
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-K 16,D20,A34, BiPhA36,G37,G38-amide

<220>
<221> MISC_FEATURE
<222> (36)..(36)
<223> Beta,beta-diphenyl-alanine

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1267

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Xaa Gly Gly
35

<210> 1268
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-K 16,D20, Aib34,Y36,G37,G38-amide

<220>
<221> MISC_FEATURE
<222> (34)..(34)
<223> Alpha-amino-isobutyric acid

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1268

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Xaa Cys Tyr Gly Gly
35

<210> 1269
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-K 16,D20, Abu34,Y36,G37,G38-amide

<220>
<221> MISC_FEATURE
<222> (34)..(34)
<223> Aminobutyric acid

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1269

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Xaa Cys Tyr Gly Gly
35

<210> 1270
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> Delta37-38 OSK1-H 16,D20,A34,1Nal36, -amide

<220>
<221> MISC_FEATURE
<222> (36)..(36)
<223> Beta-(1-Naphthyl)-alanine

<400> 1270

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Xaa
35

<210> 1271
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-H 16,D20,A34, 1Nal36,G37,G38-amide

<220>
<221> MISC_FEATURE
<222> (36)..(36)
<223> Beta-(1-Naphthyl)-alanine

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1271

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu His
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Xaa Gly Gly
35

<210> 1272

<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> Delta37-38 OSK1-H 16,D20,A34, 4Bip 36,-amide

<220>
<221> MISC_FEATURE
<222> (36)..(36)
<223> 4-phenyl-phenylalanine

<220>
<221> MOD_RES
<222> (36)..(36)
<223> AMIDATION

<400> 1272

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Xaa
35

<210> 1273
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-H 16,D20,A34, 4Bip 36,G37,G38-amide

<220>
<221> MISC_FEATURE
<222> (36)..(36)
<223> 4-phenyl-phenylalanine

<220>
<221> MOD_RES
<222> (38)..(38)
<223> AMIDATION

<400> 1273

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu His
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys Ala Cys Xaa Gly Gly
35

<210> 1274
<211> 38
<212> PRT

<213> Artificial Sequence

<220>
<223> OSK1-K16,E20,G36-38

<400> 1274

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Gly Gly Gly
35

<210> 1275
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> μ-Aga-3

<400> 1275

Ala Asp Cys Val Gly Asp Gly Gln Arg Cys Ala Asp Trp Ala Gly Pro
1 5 10 15

Tyr Cys Cys Ser Gly Tyr Tyr Cys Ser Cys Arg Ser Met Pro Tyr Cys
20 25 30

Arg Cys Arg Ser Asp Ser
35

<210> 1276
<211> 63
<212> PRT
<213> Parabuthus transvaalicus

<220>
<221> MISC_FEATURE
<223> Kurtoxin

<400> 1276

Lys Ile Asp Gly Tyr Pro Val Asp Tyr Trp Asn Cys Lys Arg Ile Cys
1 5 10 15

Trp Tyr Asn Asn Lys Tyr Cys Asn Asp Leu Cys Lys Gly Leu Lys Ala
20 25 30

Asp Ser Gly Tyr Cys Trp Gly Trp Thr Leu Ser Cys Tyr Cys Gln Gly
35 40 45

Leu Pro Asp Asn Ala Arg Ile Lys Arg Ser Gly Arg Cys Arg Ala
50 55 60

<210> 1277
<211> 77
<212> PRT
<213> Artificial Sequence

<220>
<223> Tx-1

<400> 1277

Ala Glu Leu Thr Ser Cys Phe Pro Val Gly His Glu Cys Asp Gly Asp
1 5 10 15

Ala Ser Asn Cys Asn Cys Cys Gly Asp Asp Val Tyr Cys Gly Cys Gly
20 25 30

Trp Gly Arg Trp Asn Cys Lys Cys Lys Val Ala Asp Gln Ser Tyr Ala
35 40 45

Tyr Gly Ile Cys Lys Asp Lys Val Asn Cys Pro Asn Arg His Leu Trp
50 55 60

Pro Ala Lys Val Cys Lys Lys Pro Cys Arg Arg Glu Cys
65 70 75

<210> 1278
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Tx3-3

<220>
<221> misc_feature
<222> (31)..(31)
<223> Xaa can be any naturally occurring amino acid

<400> 1278

Gly Cys Ala Asn Ala Tyr Lys Ser Cys Asn Gly Pro His Thr Cys Cys
1 5 10 15

Trp Gly Tyr Asn Gly Tyr Lys Lys Ala Cys Ile Cys Ser Gly Xaa Asn
20 25 30

Trp Lys

<210> 1279
<211> 40
<212> PRT
<213> Artificial Sequence

<220>
<223> Tx3-4

<400> 1279

Ser Cys Ile Asn Val Gly Asp Phe Cys Asp Gly Lys Lys Asp Cys Cys
1 5 10 15

Gln Cys Asp Arg Asp Asn Ala Phe Cys Ser Cys Ser Val Ile Phe Gly
20 25 30

Tyr Lys Thr Asn Cys Arg Cys Glu
35 40

<210> 1280
<211> 76
<212> PRT
<213> Artificial Sequence

<220>
<223> omega-PtXIIA

<400> 1280

Ser Cys Ile Asn Val Gly Asp Phe Cys Asp Gly Lys Lys Asp Asp Cys
1 5 10 15

Gln Cys Cys Arg Asp Asn Ala Phe Cys Ser Cys Ser Val Ile Phe Gly
20 25 30

Tyr Lys Thr Asn Cys Arg Cys Glu Val Gly Thr Thr Ala Thr Ser Tyr
35 40 45

Gly Ile Cys Met Ala Lys His Lys Cys Gly Arg Gln Thr Thr Cys Thr
50 55 60

Lys Pro Cys Leu Ser Lys Arg Cys Lys Lys Asn His
65 70 75

<210> 1281
<211> 74
<212> PRT
<213> Artificial Sequence

<220>
<223> Dw13.3

<400> 1281

Ala Glu Cys Leu Met Ile Gly Asp Thr Ser Cys Val Pro Arg Leu Gly
1 5 10 15

Arg Arg Cys Cys Tyr Gly Ala Trp Cys Tyr Cys Asp Gln Gln Leu Ser
20 25 30

Cys Arg Arg Val Gly Arg Lys Arg Glu Cys Gly Trp Val Glu Val Asn
35 40 45

Cys Lys Cys Gly Trp Ser Trp Ser Gln Arg Ile Asp Asp Trp Arg Ala
50 55 60

Asp Tyr Ser Cys Lys Cys Pro Glu Asp Gln
65 70

<210> 1282
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Agelenin

<400> 1282

Gly Gly Cys Leu Pro His Asn Arg Phe Cys Asn Ala Leu Ser Gly Pro
1 5 10 15

Arg Cys Cys Ser Gly Leu Lys Cys Lys Glu Leu Ser Ile Trp Asp Ser
20 25 30

Arg Cys Leu
35

<210> 1283
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> omega-GTx-SIA

<400> 1283

Asp Cys Val Arg Phe Trp Gly Lys Cys Ser Gln Thr Ser Asp Cys Cys
1 5 10 15

Pro His Leu Ala Cys Lys Ser Lys Trp Pro Arg Asn Ile Cys Val Trp
20 25 30

Asp Gly Ser Val
35

<210> 1284
<211> 31
<212> PRT
<213> Conus pennaceus

<220>
<221> MISC_FEATURE
<223> omega-conotoxin PnVIA

<400> 1284

Gly Cys Leu Glu Val Asp Tyr Phe Cys Gly Ile Pro Phe Ala Asn Asn
1 5 10 15

Gly Leu Cys Cys Ser Gly Asn Cys Val Phe Val Cys Thr Pro Gln
20 25 30

<210> 1285
<211> 30
<212> PRT
<213> Conus pennaceus

<220>
<221> MISC_FEATURE
<223> omega-conotoxin PnVIB

<400> 1285

Asp Asp Asp Cys Glu Pro Pro Gly Asn Phe Cys Gly Met Ile Lys Ile
1 5 10 15

Gly Pro Pro Cys Cys Ser Gly Trp Cys Phe Phe Ala Cys Ala
20 25 30

<210> 1286
<211> 11
<212> PRT
<213> Conus marmoreus

<220>
<221> MISC_FEATURE
<223> Lambda-conotoxin CMrVIA

<400> 1286

Val Cys Cys Gly Tyr Lys Leu Cys His Pro Cys
1 5 10

<210> 1287
<211> 61
<212> PRT
<213> Conus marmoreus

<220>
<221> MISC_FEATURE
<223> Lambda-conotoxin CMrVIB

<400> 1287

Met Arg Cys Leu Pro Val Leu Ile Ile Leu Leu Leu Leu Thr Ala Ser
1 5 10 15

Ala Pro Gly Val Val Val Leu Pro Lys Thr Glu Asp Asp Val Pro Met
20 25 30

Ser Ser Val Tyr Gly Asn Gly Lys Ser Ile Leu Arg Gly Ile Leu Arg
35 40 45

Asn Gly Val Cys Cys Gly Tyr Lys Leu Cys His Pro Cys
50 55 60

<210> 1288
<211> 77
<212> PRT

<213> Phoneutria nigriventer

<220>
<221> MISC_FEATURE
<223> Tx1

<400> 1288

Ala Glu Leu Thr Ser Cys Phe Pro Val Gly His Glu Cys Asp Gly Asp
1 5 10 15

Ala Ser Asn Cys Asn Cys Cys Gly Asp Asp Val Tyr Cys Gly Cys Gly
20 25 30

Trp Gly Arg Trp Asn Cys Lys Cys Lys Val Ala Asp Gln Ser Tyr Ala
35 40 45

Tyr Gly Ile Cys Lys Asp Lys Val Asn Cys Pro Asn Arg His Leu Trp
50 55 60

Pro Ala Lys Val Cys Lys Lys Pro Cys Arg Arg Glu Cys
65 70 75

<210> 1289
<211> 34
<212> PRT
<213> Phoneutria nigriventer

<220>
<221> MISC_FEATURE
<223> Tx3-3

<220>
<221> misc_feature
<222> (31)..(31)
<223> Xaa can be any naturally occurring amino acid

<400> 1289

Gly Cys Ala Asn Ala Tyr Lys Ser Cys Asn Gly Pro His Thr Cys Cys
1 5 10 15

Trp Gly Tyr Asn Gly Tyr Lys Lys Ala Cys Ile Cys Ser Gly Xaa Asn
20 25 30

Trp Lys

<210> 1290
<211> 40
<212> PRT
<213> Phoneutria nigriventer

<220>
<221> MISC_FEATURE
<223> Tx3-4

<400> 1290

Ser Cys Ile Asn Val Gly Asp Phe Cys Asp Gly Lys Lys Asp Cys Cys
1 5 10 15

Gln Cys Asp Arg Asp Asn Ala Phe Cys Ser Cys Ser Val Ile Phe Gly
20 25 30

Tyr Lys Thr Asn Cys Arg Cys Glu
35 40

<210> 1291
<211> 76
<212> PRT
<213> Phoneutria nigriventer

<220>
<221> MISC_FEATURE
<223> omega-PtXIIA

<400> 1291

Ser Cys Ile Asn Val Gly Asp Phe Cys Asp Gly Lys Lys Asp Asp Cys
1 5 10 15

Gln Cys Cys Arg Asp Asn Ala Phe Cys Ser Cys Ser Val Ile Phe Gly
20 25 30

Tyr Lys Thr Asn Cys Arg Cys Glu Val Gly Thr Thr Ala Thr Ser Tyr
35 40 45

Gly Ile Cys Met Ala Lys His Lys Cys Gly Arg Gln Thr Thr Cys Thr
50 55 60

Lys Pro Cys Leu Ser Lys Arg Cys Lys Lys Asn His
65 70 75

<210> 1292
<211> 74
<212> PRT
<213> Filistata hibernalis

<220>
<221> MISC_FEATURE
<223> Dw13.3

<400> 1292

Ala Glu Cys Leu Met Ile Gly Asp Thr Ser Cys Val Pro Arg Leu Gly
1 5 10 15

Arg Arg Cys Cys Tyr Gly Ala Trp Cys Tyr Cys Asp Gln Gln Leu Ser
20 25 30

Cys Arg Arg Val Gly Arg Lys Arg Glu Cys Gly Trp Val Glu Val Asn
35 40 45

Cys Lys Cys Gly Trp Ser Trp Ser Gln Arg Ile Asp Asp Trp Arg Ala
50 55 60

Asp Tyr Ser Cys Lys Cys Pro Glu Asp Gln
65 70

<210> 1293
<211> 35
<212> PRT
<213> Agelena opulenta

<220>
<221> MISC_FEATURE
<223> Agelenin

<400> 1293

Gly Gly Cys Leu Pro His Asn Arg Phe Cys Asn Ala Leu Ser Gly Pro
1 5 10 15

Arg Cys Cys Ser Gly Leu Lys Cys Lys Glu Leu Ser Ile Trp Asp Ser
20 25 30

Arg Cys Leu
35

<210> 1294
<211> 36
<212> PRT
<213> Grammostola spatulata

<220>
<221> MISC_FEATURE
<223> omega-GTx-SIA

<400> 1294

Asp Cys Val Arg Phe Trp Gly Lys Cys Ser Gln Thr Ser Asp Cys Cys
1 5 10 15

Pro His Leu Ala Cys Lys Ser Lys Trp Pro Arg Asn Ile Cys Val Trp
20 25 30

Asp Gly Ser Val
35

<210> 1295
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK Q1/A4/A15

<400> 1295

Gln Ser Cys Ala Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Ala Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 1296
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK Q1/A4/A15/A22

<400> 1296

Gln Ser Cys Ala Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Ala Gln
1 5 10 15

Cys Lys His Ser Met Ala Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 1297
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK Q1/A4/A15/Dap22

<220>
<221> MISC_FEATURE
<222> (22)..(22)
<223> Diaminopropionic acid

<400> 1297

Gln Ser Cys Ala Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Ala Gln
1 5 10 15

Cys Lys His Ser Met Xaa Tyr Arg Leu Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 1298
<211> 35
<212> PRT
<213> Artificial Sequence

<220>

<223> ShK Q1/A4/A15/A25

<400> 1298

Gln Ser Cys Ala Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Ala Gln
1 5 10 15

Cys Lys His Ser Met Lys Tyr Arg Ala Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 1299
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK Q1/A4/A15/A22/A25

<400> 1299

Gln Ser Cys Ala Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Ala Gln
1 5 10 15

Cys Lys His Ser Met Ala Tyr Arg Ala Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 1300
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> ShK Q1/A4/A15/Dap22/A25

<220>
<221> MISC_FEATURE
<222> (22)..(22)
<223> Diaminopropionic acid

<400> 1300

Gln Ser Cys Ala Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Ala Gln
1 5 10 15

Cys Lys His Ser Met Xaa Tyr Arg Ala Ser Phe Cys Arg Lys Thr Cys
20 25 30

Gly Thr Cys
35

<210> 1301
<211> 34

<212> PRT
<213> Artificial Sequence

<220>
<223> MTX-R4

<400> 1301

Val Ser Cys Arg Gly Ser Lys Asp Cys Tyr Ala Pro Cys Arg Lys Gln
1 5 10 15

Thr Gly Cys Pro Asn Ala Lys Cys Ile Asn Lys Ser Cys Lys Cys Tyr
20 25 30

Gly Cys

<210> 1302
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> MTX-G4

<400> 1302

Val Ser Cys Gly Gly Ser Lys Asp Cys Tyr Ala Pro Cys Arg Lys Gln
1 5 10 15

Thr Gly Cys Pro Asn Ala Lys Cys Ile Asn Lys Ser Cys Lys Cys Tyr
20 25 30

Gly Cys

<210> 1303
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-S7

<400> 1303

Gly Val Ile Ile Asn Val Ser Cys Lys Ile Ser Arg Gln Cys Leu Glu
1 5 10 15

Pro Cys Lys Lys Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 1304
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> MTX-T5

<400> 1304

Val Ser Cys Thr Thr Ser Lys Asp Cys Tyr Ala Pro Cys Arg Lys Gln
1 5 10 15

Thr Gly Cys Pro Asn Ala Lys Cys Ile Asn Lys Ser Cys Lys Cys Tyr
20 25 30

Gly Cys

<210> 1305
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> MTX-A5

<400> 1305

Val Ser Cys Thr Ala Ser Lys Asp Cys Tyr Ala Pro Cys Arg Lys Gln
1 5 10 15

Thr Gly Cys Pro Asn Ala Lys Cys Ile Asn Lys Ser Cys Lys Cys Tyr
20 25 30

Gly Cys

<210> 1306
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> MTX-T6

<400> 1306

Val Ser Cys Thr Gly Thr Lys Asp Cys Tyr Ala Pro Cys Arg Lys Gln
1 5 10 15

Thr Gly Cys Pro Asn Ala Lys Cys Ile Asn Lys Ser Cys Lys Cys Tyr
20 25 30

Gly Cys

<210> 1307
<211> 34
<212> PRT
<213> Artificial Sequence

<220>

<223> MTX-P6

<400> 1307

Val Ser Cys Thr Gly Pro Lys Asp Cys Tyr Ala Pro Cys Arg Lys Gln
1 5 10 15

Thr Gly Cys Pro Asn Ala Lys Cys Ile Asn Lys Ser Cys Lys Cys Tyr
20 25 30

Gly Cys

<210> 1308
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> OSK1-S7,K16,D20

<400> 1308

Gly Val Ile Ile Asn Val Ser Cys Lys Ile Ser Arg Gln Cys Leu Lys
1 5 10 15

Pro Cys Lys Asp Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys
35

<210> 1309
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> MTX-G10

<400> 1309

Val Ser Cys Thr Gly Ser Lys Asp Cys Gly Ala Pro Cys Arg Lys Gln
1 5 10 15

Thr Gly Cys Pro Asn Ala Lys Cys Ile Asn Lys Ser Cys Lys Cys Tyr
20 25 30

Gly Cys

<210> 1310
<211> 63
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<400> 1310
accagctttt ttgcacggtt ccaggcactg acgggagatt ttgcatttaa cgttgatgat 60

aac 63

<210> 1311
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> MTX-R11

<400> 1311

Val Ser Cys Thr Gly Ser Lys Asp Cys Tyr Arg Pro Cys Arg Lys Gln
1 5 10 15

Thr Gly Cys Pro Asn Ala Lys Cys Ile Asn Lys Ser Cys Lys Cys Tyr
20 25 30

Gly Cys

<210> 1312
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> MTX-D11

<400> 1312

Val Ser Cys Thr Gly Ser Lys Asp Cys Tyr Asp Pro Cys Arg Lys Gln
1 5 10 15

Thr Gly Cys Pro Asn Ala Lys Cys Ile Asn Lys Ser Cys Lys Cys Tyr
20 25 30

Gly Cys

<210> 1313
<211> 83
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<400> 1313
gggtcgttct tgtattgata ctattccaaa atctcgttgt actgcttttc aatgtaaaca 60

ttctatgaaa tatcgtcttt ctt 83

<210> 1314
<211> 44
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<400> 1314
tttgtcgtaa aacttgtggt acttgttctg gtggtggtgg ttct 44

<210> 1315
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> MTX-R16

<400> 1315

Val Ser Cys Thr Gly Ser Lys Asp Cys Tyr Ala Pro Cys Arg Lys Arg
1 5 10 15

Thr Gly Cys Pro Asn Ala Lys Cys Ile Asn Lys Ser Cys Lys Cys Tyr
20 25 30

Gly Cys

<210> 1316
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> MTX-E16

<400> 1316

Val Ser Cys Thr Gly Ser Lys Asp Cys Tyr Ala Pro Cys Arg Lys Glu
1 5 10 15

Thr Gly Cys Pro Asn Ala Lys Cys Ile Asn Lys Ser Cys Lys Cys Tyr
20 25 30

Gly Cys

<210> 1317
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> MTX-Y21

<400> 1317

Val Ser Cys Thr Gly Ser Lys Asp Cys Tyr Ala Pro Cys Arg Lys Gln
1 5 10 15

Thr Gly Cys Pro Tyr Ala Lys Cys Ile Asn Lys Ser Cys Lys Cys Tyr
20 25 30

Gly Cys

<210> 1318
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> MTX-S22

<400> 1318

Val Ser Cys Thr Gly Ser Lys Asp Cys Tyr Ala Pro Cys Arg Lys Gln
1 5 10 15

Thr Gly Cys Pro Asn Ser Lys Cys Ile Asn Lys Ser Cys Lys Cys Tyr
20 25 30

Gly Cys

<210> 1319
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> MTX-G22

<400> 1319

Val Ser Cys Thr Gly Ser Lys Asp Cys Tyr Ala Pro Cys Arg Lys Gln
1 5 10 15

Thr Gly Cys Pro Asn Gly Lys Cys Ile Asn Lys Ser Cys Lys Cys Tyr
20 25 30

Gly Cys

<210> 1320
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> MTX-R27

<400> 1320

Val Ser Cys Thr Gly Ser Lys Asp Cys Tyr Ala Pro Cys Arg Lys Gln
1 5 10 15

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

Gly Cys

<210> 1321
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> MTX-T28

<400> 1321

Val Ser Cys Thr Gly Ser Lys Asp Cys Tyr Ala Pro Cys Arg Lys Gln
1 5 10 15

Thr Gly Cys Pro Asn Ala Lys Cys Ile Asn Lys Thr Cys Lys Cys Tyr
20 25 30

Gly Cys

<210> 1322
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> MTX-M28

<400> 1322

Val Ser Cys Thr Gly Ser Lys Asp Cys Tyr Ala Pro Cys Arg Lys Gln
1 5 10 15

Thr Gly Cys Pro Asn Ala Lys Cys Ile Asn Lys Met Cys Lys Cys Tyr
20 25 30

Gly Cys

<210> 1323
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> MTX-K28

<400> 1323

Val Ser Cys Thr Gly Ser Lys Asp Cys Tyr Ala Pro Cys Arg Lys Gln
1 5 10 15

Thr Gly Cys Pro Asn Ala Lys Cys Ile Asn Lys Lys Cys Lys Cys Tyr
20 25 30

Gly Cys

<210> 1324
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> MTX-N32

<400> 1324

Val Ser Cys Thr Gly Ser Lys Asp Cys Tyr Ala Pro Cys Arg Lys Gln
1 5 10 15

Thr Gly Cys Pro Asn Ala Lys Cys Ile Asn Lys Ser Cys Lys Cys Asn
20 25 30

Gly Cys

<210> 1325
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> MTX-R33

<400> 1325

Val Ser Cys Thr Gly Ser Lys Asp Cys Tyr Ala Pro Cys Arg Lys Gln
1 5 10 15

Thr Gly Cys Pro Asn Ala Lys Cys Ile Asn Lys Ser Cys Lys Cys Tyr
20 25 30

Arg Cys

<210> 1326
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> MTX-S35

<400> 1326

Val Ser Cys Thr Gly Ser Lys Asp Cys Tyr Ala Pro Cys Arg Lys Gln
1 5 10 15

Thr Gly Cys Pro Asn Ala Lys Cys Ile Asn Lys Ser Cys Lys Cys Tyr
20 25 30

Gly Cys Ser
35

<210> 1327
<211> 33
<212> PRT
<213> Artificial Sequence

<220>
<223> MTX-d1

<400> 1327

Ser Cys Thr Gly Ser Lys Asp Cys Tyr Ala Pro Cys Arg Lys Gln Thr
1 5 10 15

Gly Cys Pro Asn Ala Lys Cys Ile Asn Lys Ser Cys Lys Cys Tyr Gly
20 25 30

Cys

<210> 1328
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> MTX-S35 d1

<400> 1328

Ser Cys Thr Gly Ser Lys Asp Cys Tyr Ala Pro Cys Arg Lys Gln Thr
1 5 10 15

Gly Cys Pro Asn Ala Lys Cys Ile Asn Lys Ser Cys Lys Cys Tyr Gly
20 25 30

Cys Ser

<210> 1329
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> MTX-A14

<400> 1329

Val Ser Cys Thr Gly Ser Lys Asp Cys Tyr Ala Pro Cys Ala Lys Gln
1 5 10 15

Thr Gly Cys Pro Asn Ala Lys Cys Ile Asn Lys Ser Cys Lys Cys Tyr
20 25 30

Gly Cys

<210> 1330
<211> 34

<212> PRT
<213> Artificial Sequence

<220>
<223> MTX-A15

<400> 1330

Val Ser Cys Thr Gly Ser Lys Asp Cys Tyr Ala Pro Cys Arg Ala Gln
1 5 10 15

Thr Gly Cys Pro Asn Ala Lys Cys Ile Asn Lys Ser Cys Lys Cys Tyr
20 25 30

Gly Cys

<210> 1331
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> MTX-A23

<400> 1331

Val Ser Cys Thr Gly Ser Lys Asp Cys Tyr Ala Pro Cys Arg Lys Gln
1 5 10 15

Thr Gly Cys Pro Asn Ala Ala Cys Ile Asn Lys Ser Cys Lys Cys Tyr
20 25 30

Gly Cys

<210> 1332
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> MTX-A27

<400> 1332

Val Ser Cys Thr Gly Ser Lys Asp Cys Tyr Ala Pro Cys Arg Lys Gln
1 5 10 15

Thr Gly Cys Pro Asn Ala Lys Cys Ile Asn Ala Ser Cys Lys Cys Tyr
20 25 30

Gly Cys

<210> 1333
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> MTX-A30

<400> 1333

Val Ser Cys Thr Gly Ser Lys Asp Cys Tyr Ala Pro Cys Arg Lys Gln
1 5 10 15

Thr Gly Cys Pro Asn Ala Lys Cys Ile Asn Lys Ser Cys Ala Cys Tyr
20 25 30

Gly Cys

<210> 1334
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> MTX-A32

<400> 1334

Val Ser Cys Thr Gly Ser Lys Asp Cys Tyr Ala Pro Cys Arg Lys Gln
1 5 10 15

Thr Gly Cys Pro Asn Ala Lys Cys Ile Asn Lys Ser Cys Lys Cys Ala
20 25 30

Gly Cys

<210> 1335
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> MTX-A1

<400> 1335

Ala Ser Cys Thr Gly Ser Lys Asp Cys Tyr Ala Pro Cys Arg Lys Gln
1 5 10 15

Thr Gly Cys Pro Asn Ala Lys Cys Ile Asn Lys Ser Cys Lys Cys Tyr
20 25 30

Gly Cys

<210> 1336
<211> 34
<212> PRT
<213> Artificial Sequence

<220>

<223> MTX-M1

<400> 1336

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

Thr Gly Cys Pro Asn Ala Lys Cys Ile Asn Lys Ser Cys Lys Cys Tyr
20 25 30

Gly Cys

<210> 1337
<211> 219
<212> PRT
<213> Artificial Sequence

<220>
<223> Chloramphenicol Acetyltransferase (product of the cat gene)

<400> 1337

Met Glu Lys Lys Ile Thr Gly Tyr Thr Thr Val Asp Ile Ser Gln Trp
1 5 10 15

His Arg Lys Glu His Phe Glu Ala Phe Gln Ser Val Ala Gln Cys Thr
20 25 30

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

Lys Lys Asn Lys His Lys Phe Tyr Pro Ala Phe Ile His Ile Leu Ala
50 55 60

Arg Leu Met Asn Ala His Pro Glu Phe Arg Met Ala Met Lys Asp Gly
65 70 75 80

Glu Leu Val Ile Trp Asp Ser Val His Pro Cys Tyr Thr Val Phe His
85 90 95

Glu Gln Thr Glu Thr Phe Ser Ser Leu Trp Ser Glu Tyr His Asp Asp
100 105 110

Phe Arg Gln Phe Leu His Ile Tyr Ser Gln Asp Val Ala Cys Tyr Gly
115 120 125

Glu Asn Leu Ala Tyr Phe Pro Lys Gly Phe Ile Glu Asn Met Phe Phe
130 135 140

Val Ser Ala Asn Pro Trp Val Ser Phe Thr Ser Phe Asp Leu Asn Val
145 150 155 160

Ala Asn Met Asp Asn Phe Phe Ala Pro Val Phe Thr Met Gly Lys Tyr
165 170 175

Tyr Thr Gln Gly Asp Lys Val Leu Met Pro Leu Ala Ile Gln Val His
180 185 190

His Ala Val Cys Asp Gly Phe His Val Gly Arg Met Leu Asn Glu Leu
195 200 205

Gln Gln Tyr Cys Asp Glu Trp Gln Gly Gly Ala
210 215

<210> 1338
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<223> Zeocin Resistance Protein (product of the ble gene)

<400> 1338

Met Ala Lys Leu Thr Ser Ala Val Pro Val Leu Thr Ala Arg Asp Val
1 5 10 15

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

Phe Val Glu Asp Asp Phe Ala Gly Val Val Arg Asp Asp Val Thr Leu
35 40 45

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

Trp Val Trp Val Arg Gly Leu Asp Glu Leu Tyr Ala Glu Trp Ser Glu
65 70 75 80

Val Val Ser Thr Asn Phe Arg Asp Ala Ser Gly Pro Ala Met Thr Glu
85 90 95

Ile Gly Glu Gln Pro Trp Gly Arg Glu Phe Ala Leu Arg Asp Pro Ala
100 105 110

Gly Asn Cys Val His Phe Val Ala Glu Glu Gln Asp
115 120

<210> 1339
<211> 1192
<212> DNA
<213> Artificial Sequence

<220>
<223> Cloning vector pAMG21ampR-Pep-Fc

<220>
<221> CDS
<222> (4)..(9)

<220>
<221> CDS
<222> (66)..(83)

<220>
<221> CDS
<222> (87)..(461)

<220>
<221> CDS
<222> (487)..(1182)

<400> 1339
cat atg ggt cgagacgggg cggtgttgac aattaatcat cggcatagta 49
Met Gly
1

tatcggcata gtataa tac gac aag gtg agg aac taa acc atg gcc aag ttg 101
Tyr Asp Lys Val Arg Asn Thr Met Ala Lys Leu
5 10

acc agt gcc gtt ccg gtg ctc acc gcg cgc gac gtc gcc gga gcg gtc 149
Thr Ser Ala Val Pro Val Leu Thr Ala Arg Asp Val Ala Gly Ala Val
15 20 25

gag ttc tgg acc gac cgg ctc ggg ttc tcc cgg gac ttc gtg gag gac 197
Glu Phe Trp Thr Asp Arg Leu Gly Phe Ser Arg Asp Phe Val Glu Asp
30 35 40 45

gac ttc gcc ggt gtg gtc cgg gac gac gtg acc ctg ttc atc agc gcg 245
Asp Phe Ala Gly Val Val Arg Asp Asp Val Thr Leu Phe Ile Ser Ala
50 55 60

gtc cag gac cag gtg gtg ccg gac aac acc ctg gcc tgg gtg tgg gtg 293
Val Gln Asp Gln Val Val Pro Asp Asn Thr Leu Ala Trp Val Trp Val
65 70 75

cgc ggc ctg gac gag ctg tac gcc gag tgg tcg gag gtc gtg tcc acg 341
Arg Gly Leu Asp Glu Leu Tyr Ala Glu Trp Ser Glu Val Val Ser Thr
80 85 90

aac ttc cgg gac gcc tcc ggg ccg gcc atg acc gag atc ggc gag cag 389
Asn Phe Arg Asp Ala Ser Gly Pro Ala Met Thr Glu Ile Gly Glu Gln
95 100 105

ccg tgg ggg cgg gag ttc gcc ctg cgc gac ccg gcc ggc aac tgc gtg 437
Pro Trp Gly Arg Glu Phe Ala Leu Arg Asp Pro Ala Gly Asn Cys Val
110 115 120 125

cac ttc gtg gcc gag gag cag gac tgacacgtcc gacggcggcg tctca ggt 489
His Phe Val Ala Glu Glu Gln Asp Gly
130

ggt ggt ggt ggt gac aaa act cac aca tgc cca ccg tgc cca gca cct 537
Gly Gly Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
135 140 145 150

gaa ctc ctg ggg gga ccg tca gtc ttc ctc ttc ccc cca aaa ccc aag 585
Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
155 160 165

gac acc ctc atg atc tcc cgg acc cct gag gtc aca tgc gtg gtg gtg 633
Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
170 175 180

gac gtg agc cac gaa gac cct gag gtc aag ttc aac tgg tac gtg gac 681
Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp

185 190 195

ggc gtg gag gtg cat aat gcc aag aca aag ccg cgg gag gag cag tac 729
Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
200 205 210

aac agc acg tac cgt gtg gtc agc gtc ctc acc gtc ctg cac cag gac 777
Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
215 220 225 230

tgg ctg aat ggc aag gag tac aag tgc aag gtc tcc aac aaa gcc ctc 825
Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
235 240 245

cca gcc ccc atc gag aaa acc atc tcc aaa gcc aaa ggg cag ccc cga 873
Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
250 255 260

gaa cca cag gtg tac acc ctg ccc cca tcc cgg gat gag ctg acc aag 921
Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys
265 270 275

aac cag gtc agc ctg acc tgc ctg gtc aaa ggc ttc tat ccc agc gac 969
Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
280 285 290

atc gcc gtg gag tgg gag agc aat ggg cag ccg gag aac aac tac aag 1017
Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
295 300 305 310

acc acg cct ccc gtg ctg gac tcc gac ggc tcc ttc ttc ctc tac agc 1065
Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
315 320 325

aag ctc acc gtg gac aag agc agg tgg cag cag ggg aac gtc ttc tca 1113
Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
330 335 340

tgc tcc gtg atg cat gag gct ctg cac aac cac tac acg cag aag agc 1161
Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
345 350 355

ctc tcc ctg tct ccg ggt aaa taatggatcc 1192
Leu Ser Leu Ser Pro Gly Lys
360 365

<210> 1340
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 1340

Tyr Asp Lys Val Arg Asn
1 5

<210> 1341
<211> 125
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 1341

Thr Met Ala Lys Leu Thr Ser Ala Val Pro Val Leu Thr Ala Arg Asp
1 5 10 15

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

Asp Phe Val Glu Asp Asp Phe Ala Gly Val Val Arg Asp Asp Val Thr
35 40 45

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

Ala Trp Val Trp Val Arg Gly Leu Asp Glu Leu Tyr Ala Glu Trp Ser
65 70 75 80

Glu Val Val Ser Thr Asn Phe Arg Asp Ala Ser Gly Pro Ala Met Thr
85 90 95

Glu Ile Gly Glu Gln Pro Trp Gly Arg Glu Phe Ala Leu Arg Asp Pro
100 105 110

Ala Gly Asn Cys Val His Phe Val Ala Glu Glu Gln Asp
115 120 125

<210> 1342
<211> 232
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 1342

Gly Gly Gly Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
1 5 10 15

Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
20 25 30

Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
35 40 45

Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
50 55 60

Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
65 70 75 80

Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
85 90 95

Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
100 105 110

Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
115 120 125

Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr
130 135 140

Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
145 150 155 160

Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
165 170 175

Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
180 185 190

Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
195 200 205

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

Ser Leu Ser Leu Ser Pro Gly Lys
225 230

<210> 1343
<211> 10
<212> DNA
<213> Artificial Sequence

<220>
<223> Peptide duplex

<400> 1343
aataacatat 10

<210> 1344
<211> 11
<212> DNA
<213> Artificial Sequence

<220>
<223> Peptide duplex

<400> 1344
gggtcgagac g 11

<210> 1345
<211> 14
<212> DNA
<213> Artificial Sequence

<220>
<223> Peptide duplex

<400> 1345
ttattgtata ccca 14

<210> 1346
<211> 11
<212> DNA
<213> Artificial Sequence

<220>
<223> Peptide duplex

<400> 1346
gcagagtcca c 11

<210> 1347
<211> 73
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<400> 1347
gggtgttatc atcaacgtta aatgcaaaat ctcccgtcag tgcctggaac cgtgcaaaaa 60

agctggtatg cgt 73

<210> 1348
<211> 60
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<400> 1348
ttcggtaaat gcatgaacgg taaatgccac tgcaccccga aatctggtgg tggtggttct 60

<210> 1349
<211> 73
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<400> 1349
caccagaacc accaccacca ccagatttcg gggtgcagtg gcatttaccg ttcatgcatt 60

taccgaaacg cat 73

<210> 1350
<211> 133
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature

<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<220>
<221> CDS
<222> (2)..(133)

<400> 1350
g ggt gtt atc atc aac gtt aaa tgc aaa atc tcc cgt cag tgc ctg gaa 49
Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Glu
1 5 10 15

ccg tgc aaa aaa gct ggt atg cgt ttc ggt aaa tgc atg aac ggt aaa 97
Pro Cys Lys Lys Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

tgc cac tgc acc ccg aaa tct ggt ggt ggt ggt tct 133
Cys His Cys Thr Pro Lys Ser Gly Gly Gly Gly Ser
35 40

<210> 1351
<211> 44
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 1351

Gly Val Ile Ile Asn Val Lys Cys Lys Ile Ser Arg Gln Cys Leu Glu
1 5 10 15

Pro Cys Lys Lys Ala Gly Met Arg Phe Gly Lys Cys Met Asn Gly Lys
20 25 30

Cys His Cys Thr Pro Lys Ser Gly Gly Gly Gly Ser
35 40

<210> 1352
<211> 133
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<400> 1352
caccagaacc accaccacca gatttcgggg tgcagtggca tttaccgttc atgcatttac 60

cgaaacgcat accagctttt ttgcacggtt ccaggcactg acgggagatt ttgcatttaa 120

cgttgatgat aac 133

<210> 1353
<211> 83
<212> DNA

<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<400> 1353
caccagaacc accaccacca gaacaagtac cacaagtttt acgacaaaaa gaaagacgat 60

atttcataga atgtttacat tga 83

<210> 1354
<211> 44
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<400> 1354
aaagcagtac aacgagattt tggaatagta tcaatacaag aacg 44

<210> 1355
<211> 127
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<220>
<221> CDS
<222> (2)..(127)

<400> 1355
g ggt cgt tct tgt att gat act att cca aaa tct cgt tgt act gct ttt 49
Gly Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe
1 5 10 15

caa tgt aaa cat tct atg aaa tat cgt ctt tct ttt tgt cgt aaa act 97
Gln Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr
20 25 30

tgt ggt act tgt tct ggt ggt ggt ggt tct 127
Cys Gly Thr Cys Ser Gly Gly Gly Gly Ser
35 40

<210> 1356
<211> 42
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 1356

Gly Arg Ser Cys Ile Asp Thr Ile Pro Lys Ser Arg Cys Thr Ala Phe
1 5 10 15

Gln Cys Lys His Ser Met Lys Tyr Arg Leu Ser Phe Cys Arg Lys Thr
20 25 30

Cys Gly Thr Cys Ser Gly Gly Gly Gly Ser
35 40

<210> 1357
<211> 127
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide duplex

<220>
<221> misc_feature
<222> (1)..(4)
<223> Single-stranded DNA in positions 1-4.

<400> 1357
caccagaacc accaccacca gaacaagtac cacaagtttt acgacaaaaa gaaagacgat 60

atttcataga atgtttacat tgaaaagcag tacaacgaga ttttggaata gtatcaatac 120

aagaacg 127

<210> 1358
<211> 1530
<212> DNA
<213> Artificial Sequence

<220>
<223> Nucleic acid and amino acid sequences of pAMG21ampR-Fc-pep

<220>
<221> CDS
<222> (4)..(702)

<220>
<221> CDS
<222> (824)..(1480)

<400> 1358
cat atg gac aaa act cac aca tgt cca cct tgt cca gct ccg gaa ctc 48
Met Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
1 5 10 15

ctg ggg gga ccg tca gtc ttc ctc ttc ccc cca aaa ccc aag gac acc 96
Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
20 25 30

ctc atg atc tcc cgg acc cct gag gtc aca tgc gtg gtg gtg gac gtg 144
Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
35 40 45

agc cac gaa gac cct gag gtc aag ttc aac tgg tac gtg gac ggc gtg 192
Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
50 55 60

gag gtg cat aat gcc aag aca aag ccg cgg gag gag cag tac aac agc 240
Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
65 70 75

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acg tac cgt gtg gtc agc gtc ctc acc gtc ctg cac cag gac tgg ctg      288
Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
80                  85                  90                  95

aat ggc aag gag tac aag tgc aag gtc tcc aac aaa gcc ctc cca gcc      336
Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
                100                 105                 110

ccc atc gag aaa acc atc tcc aaa gcc aaa ggg cag ccc cga gaa cca      384
Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
            115                 120                 125

cag gtg tac acc ctg ccc cca tcc cgg gat gag ctg acc aag aac cag      432
Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
        130                 135                 140

gtc agc ctg acc tgc ctg gtc aaa ggc ttc tat ccc agc gac atc gcc      480
Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
    145                 150                 155

gtg gag tgg gag agc aat ggg cag ccg gag aac aac tac aag acc acg      528
Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
160                 165                 170                 175

cct ccc gtg ctg gac tcc gac ggc tcc ttc ttc ctc tac agc aag ctc      576
Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
                180                 185                 190

acc gtg gac aag agc agg tgg cag cag ggg aac gtc ttc tca tgc tcc      624
Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
            195                 200                 205

gtg atg cat gag gct ctg cac aac cac tac acg cag aag agc ctc tcc      672
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
        210                 215                 220

ctg tct ccg ggt aaa ggt gga ggt ggt ggt tgagacgctg caggacgttg      722
Leu Ser Pro Gly Lys Gly Gly Gly Gly Gly
    225                 230

atcggcacgt aagaggttcc aactttcacc ataatgaaat aagatcacta ccgggcgtat    782

tttttgagtt atcgagattt tcaggagcta aggaagccaa a atg gag aaa aaa atc    838
                                              Met Glu Lys Lys Ile
                                                  235

act gga tat acc acc gtt gat ata tcc caa tgg cat cgt aaa gaa cat      886
Thr Gly Tyr Thr Thr Val Asp Ile Ser Gln Trp His Arg Lys Glu His
    240                 245                 250

ttt gag gca ttt cag tca gtt gct caa tgt acc tat aac cag acc gtt      934
Phe Glu Ala Phe Gln Ser Val Ala Gln Cys Thr Tyr Asn Gln Thr Val
255                 260                 265                 270

cag ctg gat att acg gcc ttt tta aag acc gta aag aaa aat aag cac      982
Gln Leu Asp Ile Thr Ala Phe Leu Lys Thr Val Lys Lys Asn Lys His
                275                 280                 285

aag ttt tat ccg gcc ttt att cac att ctt gcc cgc ctg atg aat gct     1030
Lys Phe Tyr Pro Ala Phe Ile His Ile Leu Ala Arg Leu Met Asn Ala
            290                 295                 300

cat ccg gaa ttc cgt atg gca atg aaa gac ggt gag ctg gtg ata tgg     1078
His Pro Glu Phe Arg Met Ala Met Lys Asp Gly Glu Leu Val Ile Trp
        305                 310                 315

gat agt gtt cac cct tgt tac acc gtt ttc cat gag caa act gaa acg     1126
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Asp Ser Val His Pro Cys Tyr Thr Val Phe His Glu Gln Thr Glu Thr
    320                 325                 330

ttt tca tcg cta tgg agt gaa tac cac gac gat tcc cgg cag ttt cta     1174
Phe Ser Ser Leu Trp Ser Glu Tyr His Asp Asp Ser Arg Gln Phe Leu
335                 340                 345                 350

cac ata tat tcg caa gat gtg gcg tgt tac ggt gaa aac ctg gcc tat     1222
His Ile Tyr Ser Gln Asp Val Ala Cys Tyr Gly Glu Asn Leu Ala Tyr
                355                 360                 365

ttc cct aaa ggg ttt att gag aat atg ttt ttc gtt tca gcc aat ccc     1270
Phe Pro Lys Gly Phe Ile Glu Asn Met Phe Phe Val Ser Ala Asn Pro
            370                 375                 380

tgg gtg agt ttc acc agt ttt gat tta aac gtg gcc aat atg gac aac     1318
Trp Val Ser Phe Thr Ser Phe Asp Leu Asn Val Ala Asn Met Asp Asn
        385                 390                 395

ttc ttc gcc ccc gtt ttc acc atg ggc aaa tat tat acg caa ggc gac     1366
Phe Phe Ala Pro Val Phe Thr Met Gly Lys Tyr Tyr Thr Gln Gly Asp
    400                 405                 410

aag gtg ctg atg ccg ctg gcg att cag gtt cat cat gcc gtt tgt gat     1414
Lys Val Leu Met Pro Leu Ala Ile Gln Val His His Ala Val Cys Asp
415                 420                 425                 430

ggc ttc cat gtc ggc aga atg ctt aat gaa tta caa cag tac tgc gat     1462
Gly Phe His Val Gly Arg Met Leu Asn Glu Leu Gln Gln Tyr Cys Asp
                435                 440                 445

gag tgg cgg ggc ggg gcg taatttttt aaggcagtta ttggtggcgc             1510
Glu Trp Arg Gly Gly Ala
            450

gcccgtctct taaggatccg                                               1530


<210>  1359
<211>  233
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  Synthetic Construct

<400>  1359

Met Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
1               5                   10                  15


Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
            20                  25                  30


Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
        35                  40                  45


His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
    50                  55                  60


Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
65                  70                  75                  80
```

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
85 90 95

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
100 105 110

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
115 120 125

Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val
130 135 140

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
145 150 155 160

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
165 170 175

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
180 185 190

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
195 200 205

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

Ser Pro Gly Lys Gly Gly Gly Gly Gly
225 230

<210> 1360
<211> 219
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 1360

Met Glu Lys Lys Ile Thr Gly Tyr Thr Thr Val Asp Ile Ser Gln Trp
1 5 10 15

His Arg Lys Glu His Phe Glu Ala Phe Gln Ser Val Ala Gln Cys Thr
20 25 30

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

Lys Lys Asn Lys His Lys Phe Tyr Pro Ala Phe Ile His Ile Leu Ala
50 55 60

Arg Leu Met Asn Ala His Pro Glu Phe Arg Met Ala Met Lys Asp Gly
65 70 75 80

```
Glu Leu Val Ile Trp Asp Ser Val His Pro Cys Tyr Thr Val Phe His
                85                  90                  95

Glu Gln Thr Glu Thr Phe Ser Ser Leu Trp Ser Glu Tyr His Asp Asp
            100                 105                 110

Ser Arg Gln Phe Leu His Ile Tyr Ser Gln Asp Val Ala Cys Tyr Gly
        115                 120                 125

Glu Asn Leu Ala Tyr Phe Pro Lys Gly Phe Ile Glu Asn Met Phe Phe
    130                 135                 140

Val Ser Ala Asn Pro Trp Val Ser Phe Thr Ser Phe Asp Leu Asn Val
145                 150                 155                 160

Ala Asn Met Asp Asn Phe Phe Ala Pro Val Phe Thr Met Gly Lys Tyr
                165                 170                 175

Tyr Thr Gln Gly Asp Lys Val Leu Met Pro Leu Ala Ile Gln Val His
            180                 185                 190

His Ala Val Cys Asp Gly Phe His Val Gly Arg Met Leu Asn Glu Leu
        195                 200                 205

Gln Gln Tyr Cys Asp Glu Trp Arg Gly Gly Ala
    210                 215
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<210> 1361
<211> 1189
<212> DNA
<213> Artificial Sequence

<220>
<223> Nucleic acid and amino acid sequences of pAMG21ampR-pep-Fc

<220>
<221> CDS
<222> (4)..(6)

<220>
<221> CDS
<222> (87)..(458)

<220>
<221> CDS
<222> (484)..(1179)

<400> 1361

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cat atg cgagacgggg cggtgttgac aattaatcat cggcatagta tatcggcata        56
    Met
    1

gtataatacg acaaggtgag gaactaaacc atg gcc aag ttg acc agt gcc gtt     110
                                Met Ala Lys Leu Thr Ser Ala Val
                                    5
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ccg gtg ctc acc gcg cgc gac gtc gcc gga gcg gtc gag ttc tgg acc        158
Pro Val Leu Thr Ala Arg Asp Val Ala Gly Ala Val Glu Phe Trp Thr
10                  15                  20                  25

gac cgg ctc ggg ttc tcc cgg gac ttc gtg gag gac gac ttc gcc ggt        206
Asp Arg Leu Gly Phe Ser Arg Asp Phe Val Glu Asp Asp Phe Ala Gly
                30                  35                  40

gtg gtc cgg gac gac gtg acc ctg ttc atc agc gcg gtc cag gac cag        254
Val Val Arg Asp Asp Val Thr Leu Phe Ile Ser Ala Val Gln Asp Gln
            45                  50                  55

gtg gtg ccg gac aac acc ctg gcc tgg gtg tgg gtg cgc ggc ctg gac        302
Val Val Pro Asp Asn Thr Leu Ala Trp Val Trp Val Arg Gly Leu Asp
        60                  65                  70

gag ctg tac gcc gag tgg tcg gag gtc gtg tcc acg aac ttc cgg gac        350
Glu Leu Tyr Ala Glu Trp Ser Glu Val Val Ser Thr Asn Phe Arg Asp
    75                  80                  85

gcc tcc ggg ccg gcc atg acc gag atc ggc gag cag ccg tgg ggg cgg        398
Ala Ser Gly Pro Ala Met Thr Glu Ile Gly Glu Gln Pro Trp Gly Arg
90                  95                  100                 105

gag ttc gcc ctg cgc gac ccg gcc ggc aac tgc gtg cac ttc gtg gcc        446
Glu Phe Ala Leu Arg Asp Pro Ala Gly Asn Cys Val His Phe Val Ala
                110                 115                 120

gag gag cag gac tgacacgtcc gacggcggcg tctca ggt ggt ggt ggt ggt        498
Glu Glu Gln Asp                                 Gly Gly Gly Gly Gly
            125                                                 130

gac aaa act cac aca tgc cca ccg tgc cca gca cct gaa ctc ctg ggg        546
Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
                135                 140                 145

gga ccg tca gtc ttc ctc ttc ccc cca aaa ccc aag gac acc ctc atg        594
Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
            150                 155                 160

atc tcc cgg acc cct gag gtc aca tgc gtg gtg gtg gac gtg agc cac        642
Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
        165                 170                 175

gaa gac cct gag gtc aag ttc aac tgg tac gtg gac ggc gtg gag gtg        690
Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
    180                 185                 190

cat aat gcc aag aca aag ccg cgg gag gag cag tac aac agc acg tac        738
His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
195                 200                 205                 210

cgt gtg gtc agc gtc ctc acc gtc ctg cac cag gac tgg ctg aat ggc        786
Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
                215                 220                 225

aag gag tac aag tgc aag gtc tcc aac aaa gcc ctc cca gcc ccc atc        834
Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
            230                 235                 240

gag aaa acc atc tcc aaa gcc aaa ggg cag ccc cga gaa cca cag gtg        882
Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
        245                 250                 255

tac acc ctg ccc cca tcc cgg gat gag ctg acc aag aac cag gtc agc        930
Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
    260                 265                 270
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ctg acc tgc ctg gtc aaa ggc ttc tat ccc agc gac atc gcc gtg gag      978
Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
275                 280                 285                 290

tgg gag agc aat ggg cag ccg gag aac aac tac aag acc acg cct ccc     1026
Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
                295                 300                 305

gtg ctg gac tcc gac ggc tcc ttc ttc ctc tac agc aag ctc acc gtg     1074
Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
            310                 315                 320

gac aag agc agg tgg cag cag ggg aac gtc ttc tca tgc tcc gtg atg     1122
Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
        325                 330                 335

cat gag gct ctg cac aac cac tac acg cag aag agc ctc tcc ctg tct     1170
His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
    340                 345                 350

ccg ggt aaa taatggatcc                                              1189
Pro Gly Lys
355
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<210> 1362
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 1362

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Met Ala Lys Leu Thr Ser Ala Val Pro Val Leu Thr Ala Arg Asp Val
1               5                   10                  15

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

Phe Val Glu Asp Asp Phe Ala Gly Val Val Arg Asp Asp Val Thr Leu
        35                  40                  45

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

Trp Val Trp Val Arg Gly Leu Asp Glu Leu Tyr Ala Glu Trp Ser Glu
65                  70                  75                  80

Val Val Ser Thr Asn Phe Arg Asp Ala Ser Gly Pro Ala Met Thr Glu
                85                  90                  95

Ile Gly Glu Gln Pro Trp Gly Arg Glu Phe Ala Leu Arg Asp Pro Ala
            100                 105                 110

Gly Asn Cys Val His Phe Val Ala Glu Glu Gln Asp
        115                 120
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<210> 1363

<211> 232
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 1363

Gly Gly Gly Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
1 5 10 15

Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
20 25 30

Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
35 40 45

Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
50 55 60

Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
65 70 75 80

Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
85 90 95

Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
100 105 110

Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
115 120 125

Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr
130 135 140

Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
145 150 155 160

Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
165 170 175

Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
180 185 190

Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
195 200 205

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

Ser Leu Ser Leu Ser Pro Gly Lys
225 230

<210> 1364
<211> 25
<212> PRT
<213> Conus catus

<220>
<221> MOD_RES
<222> (25)..(25)
<223> AMIDATION

<400> 1364

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

Arg Gly Ser Cys Arg Ser Gly Arg Cys
20 25

<210> 1365
<211> 26
<212> PRT
<213> Conus catus

<220>
<221> MOD_RES
<222> (26)..(26)
<223> AMIDATION

<400> 1365

Cys Lys Gly Lys Gly Gln Ser Cys Ser Lys Leu Met Tyr Asp Cys Cys
1 5 10 15

Thr Gly Ser Cys Ser Arg Arg Gly Lys Cys
20 25

<210> 1366
<211> 27
<212> PRT
<213> Conus catus

<220>
<221> MOD_RES
<222> (27)..(27)
<223> AMIDATION

<400> 1366

Cys Lys Ser Lys Gly Ala Lys Cys Ser Lys Leu Met Tyr Asp Cys Cys
1 5 10 15

Ser Gly Ser Cys Ser Gly Thr Val Gly Arg Cys
20 25

<210> 1367
<211> 27
<212> PRT
<213> Conus tulipa

<220>
<221> MISC_FEATURE
<222> (4)..(4)
<223> Ornithine

<220>
<221> MISC_FEATURE
<222> (10)..(10)
<223> Ornithine

<220>
<221> MISC_FEATURE
<222> (21)..(21)
<223> Ornithine

<220>
<221> MOD_RES
<222> (27)..(27)
<223> AMIDATION

<400> 1367

Cys Leu Ser Xaa Gly Ser Ser Cys Ser Xaa Thr Ser Tyr Asn Cys Cys
1 5 10 15

Arg Ser Cys Asn Xaa Tyr Ser Arg Lys Cys Tyr
20 25

<210> 1368
<211> 26
<212> PRT
<213> Conus magus

<220>
<221> MOD_RES
<222> (26)..(26)
<223> AMIDATION

<400> 1368

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

Ser Gly Ser Cys Gly Arg Arg Gly Lys Cys
20 25

<210> 1369
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> ChTx-G31

<400> 1369

Gln Phe Thr Asn Val Ser Cys Thr Thr Ser Lys Glu Cys Trp Ser Val
1 5 10 15

Cys Gln Arg Leu His Asn Thr Ser Arg Gly Lys Cys Met Asn Gly Lys

20 25 30

Cys Arg Cys Tyr Ser
35

<210> 1370
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> ChTx-L14

<400> 1370

Gln Phe Thr Asn Val Ser Cys Thr Thr Ser Lys Glu Cys Leu Ser Val
1 5 10 15

Cys Gln Arg Leu His Asn Thr Ser Arg Gly Lys Cys Met Asn Lys Lys
20 25 30

Cys Arg Cys Tyr Ser
35

<210> 1371
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> ChTx-A14

<400> 1371

Gln Phe Thr Asn Val Ser Cys Thr Thr Ser Lys Glu Cys Ala Ser Val
1 5 10 15

Cys Gln Arg Leu His Asn Thr Ser Arg Gly Lys Cys Met Asn Lys Lys
20 25 30

Cys Arg Cys Tyr Ser
35

<210> 1372
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> ChTx-A15

<400> 1372

Gln Phe Thr Asn Val Ser Cys Thr Thr Ser Lys Glu Cys Trp Ala Val
1 5 10 15

Cys Gln Arg Leu His Asn Thr Ser Arg Gly Lys Cys Met Asn Lys Lys
20 25 30

Cys Arg Cys Tyr Ser
35

<210> 1373
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> ChTx-P15

<400> 1373

Gln Phe Thr Asn Val Ser Cys Thr Thr Ser Lys Glu Cys Trp Pro Val
1 5 10 15

Cys Gln Arg Leu His Asn Thr Ser Arg Gly Lys Cys Met Asn Lys Lys
20 25 30

Cys Arg Cys Tyr Ser
35

<210> 1374
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> ChTx-A16

<400> 1374

Gln Phe Thr Asn Val Ser Cys Thr Thr Ser Lys Glu Cys Trp Ser Ala
1 5 10 15

Cys Gln Arg Leu His Asn Thr Ser Arg Gly Lys Cys Met Asn Lys Lys
20 25 30

Cys Arg Cys Tyr Ser
35

<210> 1375
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> ChTx-P16

<400> 1375

Gln Phe Thr Asn Val Ser Cys Thr Thr Ser Lys Glu Cys Trp Ser Pro
1 5 10 15

Cys Gln Arg Leu His Asn Thr Ser Arg Gly Lys Cys Met Asn Lys Lys
20 25 30

Cys Arg Cys Tyr Ser

35

<210> 1376
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> ChTx-A25

<400> 1376

Gln Phe Thr Asn Val Ser Cys Thr Thr Ser Lys Glu Cys Trp Ser Val
1 5 10 15

Cys Gln Arg Leu His Asn Thr Ser Ala Gly Lys Cys Met Asn Lys Lys
20 25 30

Cys Arg Cys Tyr Ser
35

<210> 1377
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> ChTx-A6

<400> 1377

Gln Phe Thr Asn Val Ala Cys Thr Thr Ser Lys Glu Cys Trp Ser Val
1 5 10 15

Cys Gln Arg Leu His Asn Thr Ser Arg Gly Lys Cys Met Asn Lys Lys
20 25 30

Cys Arg Cys Tyr Ser
35

<210> 1378
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> ChTx-K6

<400> 1378

Gln Phe Thr Asn Val Lys Cys Thr Thr Ser Lys Glu Cys Trp Ser Val
1 5 10 15

Cys Gln Arg Leu His Asn Thr Ser Arg Gly Lys Cys Met Asn Lys Lys
20 25 30

Cys Arg Cys Tyr Ser
35

<210> 1379
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> ChTx-A10

<400> 1379

Gln Phe Thr Asn Val Ser Cys Thr Thr Ala Lys Glu Cys Trp Ser Val
1 5 10 15

Cys Gln Arg Leu His Asn Thr Ser Arg Gly Lys Cys Met Asn Lys Lys
20 25 30

Cys Arg Cys Tyr Ser
35

<210> 1380
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> ChTx-P10

<400> 1380

Gln Phe Thr Asn Val Ser Cys Thr Thr Pro Lys Glu Cys Trp Ser Val
1 5 10 15

Cys Gln Arg Leu His Asn Thr Ser Arg Gly Lys Cys Met Asn Lys Lys
20 25 30

Cys Arg Cys Tyr Ser
35

<210> 1381
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> ChTx-A12

<400> 1381

Gln Phe Thr Asn Val Ser Cys Thr Thr Ser Lys Ala Cys Trp Ser Val
1 5 10 15

Cys Gln Arg Leu His Asn Thr Ser Arg Gly Lys Cys Met Asn Lys Lys
20 25 30

Cys Arg Cys Tyr Ser
35

<210> 1382

<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> ChTx-Q12

<400> 1382

Gln Phe Thr Asn Val Ser Cys Thr Thr Ser Lys Gln Cys Trp Ser Val
1 5 10 15

Cys Gln Arg Leu His Asn Thr Ser Arg Gly Lys Cys Met Asn Lys Lys
20 25 30

Cys Arg Cys Tyr Ser
35

<210> 1383
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> ChTx-A1

<400> 1383

Ala Phe Thr Asn Val Ser Cys Thr Thr Ser Lys Glu Cys Trp Ser Val
1 5 10 15

Cys Gln Arg Leu His Asn Thr Ser Arg Gly Lys Cys Met Asn Lys Lys
20 25 30

Cys Arg Cys Tyr Ser
35

<210> 1384
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> ChTx-T1

<400> 1384

Thr Phe Thr Asn Val Ser Cys Thr Thr Ser Lys Glu Cys Trp Ser Val
1 5 10 15

Cys Gln Arg Leu His Asn Thr Ser Arg Gly Lys Cys Met Asn Lys Lys
20 25 30

Cys Arg Cys Tyr Ser
35

<210> 1385
<211> 37
<212> PRT

<213> Artificial Sequence

<220>
<223> ChTx-A2

<400> 1385

Gln Ala Thr Asn Val Ser Cys Thr Thr Ser Lys Glu Cys Trp Ser Val
1 5 10 15

Cys Gln Arg Leu His Asn Thr Ser Arg Gly Lys Cys Met Asn Lys Lys
20 25 30

Cys Arg Cys Tyr Ser
35

<210> 1386
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> ChTx-I2

<400> 1386

Gln Ile Thr Asn Val Ser Cys Thr Thr Ser Lys Glu Cys Trp Ser Val
1 5 10 15

Cys Gln Arg Leu His Asn Thr Ser Arg Gly Lys Cys Met Asn Lys Lys
20 25 30

Cys Arg Cys Tyr Ser
35

<210> 1387
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> ChTx-A3

<400> 1387

Gln Phe Ala Asn Val Ser Cys Thr Thr Ser Lys Glu Cys Trp Ser Val
1 5 10 15

Cys Gln Arg Leu His Asn Thr Ser Arg Gly Lys Cys Met Asn Lys Lys
20 25 30

Cys Arg Cys Tyr Ser
35

<210> 1388
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> ChTx-I3

<400> 1388

Gln Phe Ile Asn Val Ser Cys Thr Thr Ser Lys Glu Cys Trp Ser Val
1 5 10 15

Cys Gln Arg Leu His Asn Thr Ser Arg Gly Lys Cys Met Asn Lys Lys
20 25 30

Cys Arg Cys Tyr Ser
35

<210> 1389
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> ChTx-MgTx

<400> 1389

Thr Ile Ile Asn Val Lys Cys Thr Ser Pro Lys Gln Cys Leu Pro Pro
1 5 10 15

Cys Lys Ala Gln Phe Gly Thr Ser Arg Gly Lys Cys Met Asn Lys Lys
20 25 30

Cys Arg Cys Tyr Ser Pro
35

<210> 1390
<211> 38
<212> PRT
<213> Artificial Sequence

<220>
<223> ChTx-MgTx-b

<400> 1390

Thr Ile Ile Asn Val Ser Cys Thr Ser Pro Lys Gln Cys Leu Pro Pro
1 5 10 15

Cys Lys Ala Gln Phe Gly Thr Ser Arg Gly Lys Cys Met Asn Lys Lys
20 25 30

Cys Arg Cys Tyr Ser Pro
35