

REPUBLIC OF SOUTH AFRICA  
PATENTS ACT, 1978**PUBLICATION PARTICULARS AND ABSTRACT**

(Section 32(3)(a) – Regulation 22(1)(g) and 31)

OFFICIAL APPLICATION NO.

|    |           |
|----|-----------|
| 04 | 2003/9863 |
|----|-----------|

LODGING DATE

|    |             |
|----|-------------|
| 22 | 14 JUN 2002 |
|----|-------------|

ACCEPTANCE DATE

|    |         |
|----|---------|
| 43 | 24-4-06 |
|----|---------|

INTERNATIONAL CLASSIFICATION

|    |      |
|----|------|
| 51 | A61K |
|----|------|

NOT FOR PUBLICATION

CLASSIFIED BY: WIPO

FULL NAMES OF APPLICANT

|    |                       |
|----|-----------------------|
| 71 | PHARMACIA CORPORATION |
|----|-----------------------|

FULL NAMES OF INVENTORS

|    |                                                           |
|----|-----------------------------------------------------------|
| 72 | 1. SIEGEL, NED R<br>2. FINN, RORY F<br>3. HILLS, ROBERT L |
|----|-----------------------------------------------------------|

EARLIEST PRIORITY CLAIMED

|    |               |
|----|---------------|
| 33 | COUNTRY<br>US |
|----|---------------|

|    |                      |
|----|----------------------|
| 31 | NUMBER<br>60/300,362 |
|----|----------------------|

|    |                     |
|----|---------------------|
| 32 | DATE<br>22 JUN 2001 |
|----|---------------------|

TITLE OF INVENTION

|    |                                               |
|----|-----------------------------------------------|
| 54 | CHEMICALLY-MODIFIED PROGENIPOIETIN CONJUGATES |
|----|-----------------------------------------------|

|    |                                    |
|----|------------------------------------|
| 57 | ABSTRACT (NOT MORE THAN 150 WORDS) |
|----|------------------------------------|

|                  |     |
|------------------|-----|
| NUMBER OF SHEETS | 307 |
|------------------|-----|

If no classification is finished, Form P.9 should accompany this form.  
The figure of the drawing to which the abstract refers is attached.

### Abstract

The present invention provides a chemically modified Progenipointins (ProGPs) prepared by binding a water soluble polymer to the protein. The chemically-modified protein according to the present invention may have a much longer lasting neutrophil-increasing activity than that of the un-modified ProGP, enabling reduced dose and scheduling opportunities.

## CHEMICALLY-MODIFIED PROGENIPOIETIN CONJUGATES

5

FIELD OF THE INVENTION

The present invention relates to a chemical modification of Progenipoietins (ProGPs), a family of recombinant proteins, which are multifunctional agonists of flt3 ligand and another hematopoietic growth factor receptor, including but not limited to G-CSF, by which the chemical and/or physiological properties of ProGP can be changed. The PEGylated ProGPs may have a decreased clearance rate, improved stability, decreased antigenicity, or a combination thereof. The family of ProGP proteins is defined as the multifunctional proteins comprising a flt3 receptor agonist and a second hematopoietic growth factor or colony stimulating factor receptor agonist described in WO98/17810, which is incorporated herein in its entirety. The present invention also relates to processes for the modification of ProGP. In addition, the present invention relates to pharmaceutical compositions comprising the modified ProGP. A further embodiment is the use of the modified ProGP to treat hematopoietic disorders.

BACKGROUND OF THE INVENTION

Progenipoietin may be useful in the treatment of general haematopoietic disorders, including those arising from chemotherapy or from radiation therapy (Mac Vittie, T. J.; *et al.*, *Exp. Hematol.* (1999), 27(10), 1557-1568). ProGP may also be useful in bone

marrow transplantation, wound healing, burn treatment, and the treatment of parasite, bacterial or viral infection.

It is generally observed that physiologically  
5 active proteins administered into a body can show their pharmacological activity only for a short period due to their high clearance rate in the body. Furthermore, the relative hydrophobicity of these proteins may limit their stability.

10 For the purpose of decreasing the clearance rate, improving stability or abolishing antigenicity of therapeutic proteins, some methods have been proposed wherein the proteins are chemically modified with water-soluble polymers. Chemical modification of this  
15 type may block effectively a proteolytic enzyme from physical contact with the protein backbone itself, thus preventing degradation. Chemical attachment may effectively reduce renal clearance. Additional advantages include, under certain circumstances,  
20 increasing the stability and circulation time of the therapeutic protein, increasing solubility, and decreasing immunogenicity. A review article describing protein modification and fusion proteins is Francis, Focus on Growth Factors 3: 4-10 (May 1992) (published  
25 by Mediscript, Mountview Court, Friern Barnet Lane, London N20, OLD, UK).

Poly(alkylene oxide), notably poly(ethylene glycol) (PEG), is one such chemical moiety, which has been used in the preparation of therapeutic protein  
30 products (the verb "pegylate" meaning to attach at least one PEG molecule). The attachment of poly(ethylene glycol) has been shown to protect against proteolysis, Sada, et al., *J. Fermentation Bioengineering* 71: 137-139 (1991), and methods for

attachment of certain poly(ethylene glycol) moieties are available. See U.S. Pat. No. 4,179,337, Davis et al., "Non-Immunogenic Polypeptides," issued Dec. 18, 1979; and U.S. Pat. No. 4,002,531, Royer, "Modifying enzymes with Polyethylene Glycol and Product Produced  
5 Thereby," issued Jan. 11, 1977. For a review, see Abuchowski et al., in Enzymes as Drugs. (J. S. Holcerberg and J. Roberts, eds. pp. 367-383 (1981)).

Other water-soluble polymers have been used, such  
10 as copolymers of ethylene glycol/propylene glycol, carboxymethylcellulose, dextran, poly(vinyl alcohol), poly(vinyl pyrrolidone), poly(-1,3-dioxolane), poly(-1,3,6-trioxane), ethylene/maleic anhydride copolymer, and poly- amino acids (either homopolymers or random  
15 copolymers).

A number of examples of pegylated therapeutic proteins have been described. ADAGEN®, a pegylated formulation of adenosine deaminase, is approved for treating severe combined immunodeficiency disease.  
20 ONCASPAR®, a pegylated L-asparaginase has been approved for treating hypersensitive ALL patients. Pegylated superoxide dismutase has been in clinical trials for treating head injury. Pegylated  $\alpha$ -interferon (U.S. 5,738,846, 5,382,657) has been tested in phase III  
25 clinical trials for treating hepatitis with PEG-Intron (pegitron alfa-2b) approved for the treatment of chronic hepatitis C while another molecule, PEGASYS™, still awaits regulatory approval; pegylated glucocerebrosidase and pegylated hemoglobin are  
30 reported to have been in preclinical testing. Another example is pegylated IL-6, EF 0 442 724, entitled, "Modified hIL-6," which discloses poly(ethylene glycol) molecules added to IL-6.

Another specific therapeutic protein, which has been chemically modified, is granulocyte colony stimulating factor, (G-CSF). G-CSF induces the rapid proliferation and release of neutrophilic granulocytes to the blood stream, and thereby provides therapeutic effect in fighting infection. European patent publication EP 0 401 384, published Dec. 12, 1990, entitled, "Chemically Modified Granulocyte Colony Stimulating Factor," describes materials and methods for preparing G-CSF to which poly(ethylene glycol) molecules are attached. Modified G-CSF and analogs thereof are also reported in EP 0 473 268, published Mar. 4, 1992, entitled "Continuous Release Pharmaceutical Compositions Comprising a Polypeptide Covalently Conjugated To A Water Soluble Polymer," stating the use of various G-CSF and derivatives covalently conjugated to a water soluble particle polymer, such as poly(ethylene glycol). A modified polypeptide having human granulocyte colony stimulating factor activity is reported in EP 0 335 423 published Oct. 4, 1989. Provided in U.S. 5,824,784 are methods for N-terminally modifying proteins, including N-terminally chemically modified G-CSF compositions. U.S. 5,824,778 discloses chemically modified G-CSF.

Japanese patent application Hei2 (1990)-30555 discloses chemically modified human IL-3 having decreased antigenicity.

The family of ProGP proteins is disclosed in WO 98/17810.

For poly(ethylene glycol), a variety of means has been used to attach the poly(ethylene glycol) molecules to the protein. Generally, poly(ethylene glycol) molecules are connected to the protein via a reactive group found on the protein.

Amino groups, such as those on lysine residues or at the N-terminus, are convenient for such attachment. For example, Royer (U.S. Pat. No. 4,002,531, above) states that reductive alkylation was used for  
5 attachment of poly(ethylene glycol) molecules to an enzyme. EP 0 539 167, published Apr. 28, 1993, Wright, "Peg Imidates and Protein Derivatives Thereof" states that peptides and organic compounds with free amino group(s) are modified with an imidate derivative of PEG  
10 or related water-soluble organic polymers. Chamow et al., *Bioconjugate Chem.* 5: 133-140 (1994) report the modification of CD4 immunoadhesin with monomethoxypoly(ethylene glycol)aldehyde via reductive alkylation. The authors report that 50% of the CD4-Ig  
15 was MePEG-modified under conditions allowing control over the extent of pegylation. *Ibid.* at page 137. The authors also report that the *in vitro* binding capability of the modified CD4-Ig (to the protein gp 120) decreased at a rate correlated to the extent of  
20 MePEGylation *Ibid.* U.S. Pat. No. 4,904,584, Shaw, issued Feb. 27, 1990, relates to the modification of the number of lysine residues in proteins for the attachment of poly(ethylene glycol) molecules via reactive amine groups.

25 Many methods of attaching a polymer to a protein involve using a moiety to act as a linking group. However, such moieties may be antigenic. A tresyl chloride method involving no linking group is available, but this method may be difficult to use to  
30 produce therapeutic products as the use of tresyl chloride may produce toxic by-products. See Francis et al., In: Stability of protein pharmaceuticals: in vivo pathways of degradation and strategies for protein stabilization (Eds. Ahern. T. and Manning, M. C.)

Plenum, New York, 1991) Also, Delgado et al., "Coupling of PEG to Protein By Activation With Tresyl Chloride, Applications In Immunoaffinity Cell Preparation", in Separations Using Aqueous Phase Systems, Applications  
5 In Cell Biology and Biotechnology, Fisher et al., eds. Plenum Press, New York, N.Y., 1989 pp. 211-213.

See also, Rose et al., *Bioconjugate Chemistry 2*: 154-159 (1991) which reports the selective attachment of the linker group carbonylhydrazide to the C-terminal  
10 carboxyl group of a protein substrate (insulin).

The present invention provides chemically modified ProGP molecules having decreased clearance rate, increased stability, decreased antigenicity, or combinations thereof.

15

#### SUMMARY OF THE INVENTION

The present invention relates to chemically modified ProGPs, which have at least one improved  
20 chemical or physiological property selected from but not limited to decreased clearance rate, increased stability, and decreased antigenicity. Thus, as described below in more detail, the present invention has a number of aspects relating to chemically  
25 modifying ProGPs as well as specific modifications using a variety of poly(ethylene glycol) moieties.

The present invention also relates to methods of producing the chemically modified ProGPs.

The present invention also relates to compositions  
30 comprising the chemically modified ProGPs.

The modified ProGP of the present invention may be useful in the treatment of, but not limited to, neutropenia, thrombocytopenia, mobilization of hematopoietic progenitors and stem cells into

peripheral blood, bone marrow suppression or hematopoietic deficiencies, and immunodeficiencies.

BRIEF DESCRIPTION OF THE DRAWINGS

5

FIG. 1 is a reproduction of the ion-exchange chromatography elution profile of a 30,000 MW PEG-ALD ProGP-4 reaction.

10 FIG. 2a is an SEC HPLC profile of recombinant ProGP-4.

FIG. 2b is an SEC HPLC profile of the 30,000 MW PEG-ALD ProGP-4 Reaction mix.

15 FIG. 2c is an SEC HPLC profile of ion exchange purified N-terminally mono-pegylated 30,000 MW PEG-ALD ProGP-4.

FIG. 3 is an SDS-PAGE of 30000 MW PEG-ALD ProGP-4. Lane 1. MW Protein standards; Lane 2. Blank; Lane 3. ProGP-4; Lane 4. 30,000 MW PEG-ALD ProGP-4.  
20

FIG. 4 is an SDS-SEC HPLC profile of ion exchange purified N-terminally mono-pegylated 30,000 MW PEG-ALD ProGP-4.

25

FIG. 5 shows a reversed phase HPLC profile for N-terminally mono-PEGylated 30,000 MW PEG-ALD ProGP-4.

FIG. 6 shows a MALDI-TOF spectrum of reversed phase purified monomeric mono-PEGylated 30,000 MW PEG-ALD ProGP-4 monomer.

5 FIG. 7 shows a SEC HPLC profile of a mono-PEGylated 30,000 MW PEG-ALD ProGP-4 trypsin digest.

FIG. 8 illustrates a comparison of response curves for a flt3 receptor agonist, a G-CSF receptor agonist,  
10 co-addition of a flt3 receptor agonist and a G-CSF receptor agonist, un-PEGylated ProGP-4 and mono-PEGylated 30,000 MW PEG-ALD ProGP-4 in a colony forming unit granulocyte/macrophage (CFU-GM) assay which measures expansion and differentiation of a human bone  
15 marrow-derived CD34+ cells.

FIG. 9 illustrates a comparison of murine plasma concentration curves for ProGP-4 and mono-PEGylated 30,000 MW PEG-ALD ProGP-4.

20

FIG. 10 compares the *in vivo* bioactivity of un-PEGylated ProGP-4 dosed daily in mice to N-terminally mono-PEGylated 30,000 MW PEG-ALD ProGP-4 dosed every three days by illustrating the total white blood cell  
25 (WBC) and dendritic cell (DC) counts in peripheral blood and spleen obtained 24 hours following dosing.

FIG 11 compares the *kinetics of the in vivo* DC response for un-PEGylated ProGP-4 dosed daily in mice to N-

terminally mono-PEGylated 30,000 MW PEG-ALD ProGP-4  
 dosed every three days by illustrating the total white  
 blood cell (WBC) and dendritic cell (DC) counts in  
 peripheral blood and spleen obtained 24,48 and 72 hours  
 5 following dosing.

FIG 12 shows the amino acid sequence of ProGP-4.

### DETAILED DESCRIPTION OF THE INVENTION

10 Progenipoietin (ProGP) proteins are members of a  
 family of recombinant proteins, which are  
 multifunctional agonists of flt3 ligand and another  
 hematopoietic growth factor. Their recombinant  
 production and methods of use are detailed in WO  
 15 98/17810.

Progenipoietin proteins are of the formula

$R_1-L_1-R_2$ ,  $R_2-L_1-R_1$ ,  $R_1-R_2$ , or  $R_2-R_1$

20 wherein  $R_1$  is a polypeptide comprising; a modified  
 flt-3 ligand amino acid sequence of the Formula:

|    |                                                              |             |
|----|--------------------------------------------------------------|-------------|
|    | ThrGlnAspCysSerPheGlnHisSerProIleSerSerAspPheAlaValLysIleArg |             |
|    | 10                                                           | 20          |
| 25 | GluLeuSerAspTyrLeuLeuGlnAspTyrProValThrValAlaSerAsnLeuGlnAsp |             |
|    | 30                                                           | 40          |
| 30 | GluGluLeuCysGlyGlyLeuTrpArgLeuValLeuAlaGlnArgTrpMetGluArgLeu |             |
|    | 50                                                           | 60          |
|    | LysThrValAlaGlySerLysMetGlnGlyLeuLeuGluArgValAsnThrGluIleHis |             |
|    | 70                                                           | 80          |
| 35 | PheValThrLysCysAlaPheGlnProProProSerCysLeuArgPheValGlnThrAsn |             |
|    | 90                                                           | 100         |
|    | IleSerArgLeuLeuGlnGluThrSerGluGlnLeuValAlaLeuLysProTrpIleThr |             |
|    | 110                                                          | 120         |
| 40 | ArgGlnAsnPheSerArgCysLeuGluLeuGlnCysGlnProAsrSerSerThrLeu    |             |
|    | 130                                                          | SEQ ID NO:1 |

wherein the N-terminus is joined to the C-terminus directly or through a linker (L<sub>2</sub>) capable of joining the N-terminus to the C-terminus and having new C- and N-termini at amino acids;

5

|       |       |               |
|-------|-------|---------------|
| 28-29 | 42-43 | 93-94         |
| 29-30 | 64-65 | 94-95         |
| 30-31 | 65-66 | 95-96         |
| 31-32 | 66-67 | 96-97         |
| 32-33 | 86-87 | 97-98         |
| 34-35 | 87-88 | 98-99         |
| 36-37 | 88-89 | 99-100        |
| 37-38 | 89-90 | 100-101       |
| 38-39 | 90-91 | 101-102       |
| 39-40 | 91-92 | 102-103       |
| 40-41 | 92-93 | respectively; |
| 41-42 |       |               |

wherein R<sub>2</sub> is a factor selected from the group consisting of: a colony stimulating factor, a cytokine, a lymphokine, an interleukin, and a hematopoietic growth factor;

10

wherein L<sub>1</sub> is a linker capable of linking R<sub>1</sub> to R<sub>2</sub>.

The Progenipoietin protein can optionally be immediately preceded by (methionine<sup>-1</sup>), (alanine<sup>-1</sup>) or (methionine<sup>-2</sup>, alanine<sup>-1</sup>).

15

In a preferred embodiment the Progenipoietin proteins are of the formula:

20

$$R_1-L_1-R_2, R_2-L_1-R_1, R_1-R_2, \text{ or } R_2-R_1$$

wherein R<sub>1</sub> is a polypeptide comprising; a modified flt-3 ligand amino acid sequence of the Formula:

25

ThrGlnAspCysSerPheGlnHisSerProIleSerSerAspPheAlaValLysIleArg  
10 20

GluLeuSerAspTyrLeuLeuGlnAspTyrProValThrValAlaSerAsnLeuGlnAsp

30

```

                                30                                40
GluGluLeuCysGlyGlyLeuTrpArgLeuValLeuAlaGlnArgTrpMetGluArgLeu
                                50                                60
5  LysThrValAlaGlySerLysMetGlnGlyLeuLeuGluArgValAsnThrGluIleHis
                                70                                80
PheValThrLysCysAlaPheGlnProProProSerCysLeuArgPheValGlnThrAsn
10                                90                                100
IleSerArgLeuLeuGlnGluThrSerGluGlnLeuValAlaLeuLysProTrpIleThr
                                110                                120
15 ArgGlnAsnPheSerArgCysLeuGluLeuGlnCysGlnProAsrSerSerThrLeu
                                130                                SEQ ID NO:1

```

wherein the N-terminus is joined to the C-terminus directly or through a linker (L<sub>2</sub>) capable of joining the N-terminus to the C-terminus and having new C- and N-termini at amino acids;

|       |       |               |
|-------|-------|---------------|
| 28-29 | 42-43 | 93-94         |
| 29-30 | 64-65 | 94-95         |
| 30-31 | 65-66 | 95-96         |
| 31-32 | 66-67 | 96-97         |
| 32-33 | 86-87 | 97-98         |
| 34-35 | 87-88 | 98-99         |
| 36-37 | 88-89 | 99-100        |
| 37-38 | 89-90 | 100-101       |
| 38-39 | 90-91 | 101-102       |
| 39-40 | 91-92 | 102-103       |
| 40-41 | 92-93 | respectively; |
| 41-42 |       |               |

wherein R<sub>2</sub> is a polypeptide, comprising; a modified human G-CSF amino acid sequence of the formula:

```

1                                10
Xaa Xaa Xaa Gly Pro Ala Ser Ser Leu Pro Gln Ser Xaa
30
                                20
Leu Leu Xaa Xaa Xaa Glu Gln Val Xaa Lys Xaa Gln Gly Xaa Gly
                                30                                40
35 Ala Xaa Leu Gln Glu Xaa Leu Xaa Ala Thr Tyr Lys Leu Xaa Xaa
                                50
Xaa Glu Xaa Xaa Val Xaa Xaa Gly His Ser Xaa Gly Ile Pro Trp
40                                60                                70

```

Ala Pro Leu Ser Ser Xaa Pro Ser Xaa Ala Leu Xaa Leu Ala Gly  
 80  
 5 Xaa Leu Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu  
 90 100  
 Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu  
 110  
 10 Xaa Thr Leu Gln Xaa Asp Val Ala Asp Phe Ala Xaa Thr Ile Trp  
 120 130  
 Gln Gln Met Glu Xaa Xaa Gly Met Ala Pro Ala Leu Gln Pro Thr  
 140  
 15 Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Xaa Gln Xaa Xaa Ala  
 150 160  
 20 Gly Gly Val Leu Val Ala Ser Xaa Leu Gln Xaa Phe Leu Xaa Xaa  
 170  
 Ser Tyr Arg Val Leu Xaa Xaa Leu Ala Gln Pro SEQ ID NO:260

wherein  
 25 Xaa at position 1 is Thr, Ser, Arg, Tyr or Gly;  
 Xaa at position 2 is Pro or Leu;  
 Xaa at position 3 is Leu, Arg, Tyr or Ser;  
 Xaa at position 13 is Phe, Ser, His, Thr or Pro;  
 30 Xaa at position 16 is Lys, Pro, Ser, Thr or His;  
 Xaa at position 17 is Cys, Ser, Gly, Ala, Ile, Tyr or  
 Arg;  
 Xaa at position 18 is Leu, Thr, Pro, His, Ile or Cys;  
 Xaa at position 22 is Arg, Tyr, Ser, Thr or Ala;  
 35 Xaa at position 24 is Ile, Pro, Tyr or Leu;  
 Xaa at position 27 is Asp, or Gly;  
 Xaa at position 30 is Ala, Ile, Leu or Gly;  
 Xaa at position 34 is Lys or Ser;  
 Xaa at position 36 is Cys or Ser;  
 40 Xaa at position 42 is Cys or Ser;  
 Xaa at position 43 is His, Thr, Gly, Val, Lys, Trp,  
 Ala, Arg, Cys, or Leu;  
 Xaa at position 44 is Pro, Gly, Arg, Asp, Val, Ala,  
 His, Trp, Gln, or Thr;  
 45 Xaa at position 46 is Glu, Arg, Phe, Arg, Ile or Ala;  
 Xaa at position 47 is Leu or Thr;  
 Xaa at position 49 is Leu, Phe, Arg or Ser;  
 Xaa at position 50 is Leu, Ile, His, Pro or Tyr;  
 Xaa at position 54 is Leu or His;  
 50 Xaa at position 64 is Cys or Ser;  
 Xaa at position 67 is Gln, Lys, Leu or Cys;  
 Xaa at position 70 is Gln, Pro, Leu, Arg or Ser;  
 Xaa at position 74 is Cys or Ser;  
 Xaa at position 104 is Asp, Gly or Val;

- Xaa at position 108 is Leu, Ala, Val, Arg, Trp, Gln or Gly;  
 Xaa at position 115 is Thr, His, Leu or Ala;  
 Xaa at position 120 is Gln, Gly, Arg, Lys or His  
 5 Xaa at position 123 is Glu, Arg, Phe or Thr  
 Xaa at position 144 is Phe, His, Arg, Pro, Leu, Gln or Glu;  
 Xaa at position 146 is Arg or Gln;  
 Xaa at position 147 is Arg or Gln;  
 10 Xaa at position 156 is His, Gly or Ser;  
 Xaa at position 159 is Ser, Arg, Thr, Tyr, Val or Gly;  
 Xaa at position 162 is Glu, Leu, Gly or Trp;  
 Xaa at position 163 is Val, Gly, Arg or Ala;  
 Xaa at position 169 is Arg, Ser, Leu, Arg or Cys;  
 15 Xaa at position 170 is His, Arg or Ser;

wherein 1-11 amino acids from the N-terminus and/or 1-5 amino acids from the C-terminus are optionally deleted from said modified human G-CSF amino acid sequence; and  
 20

wherein the N-terminus is joined to the C-terminus directly or through a linker (L<sub>2</sub>) capable of joining the N-terminus to the C-terminus and having new C- and N-termini at amino acids;  
 25

|    |       |        |               |
|----|-------|--------|---------------|
|    | 38-39 | 62-63  | 123-124       |
|    | 39-40 | 63-64  | 124-125       |
|    | 40-41 | 64-65  | 125-126       |
| 30 | 41-42 | 65-66  | 126-127       |
|    | 42-43 | 66-67  | 128-129       |
|    | 43-44 | 67-68  | 128-129       |
|    | 45-46 | 68-69  | 129-130       |
|    | 48-49 | 69-70  | 130-131       |
| 35 | 49-50 | 70-71  | 131-132       |
|    | 52-53 | 71-72  | 132-133       |
|    | 53-54 | 91-92  | 133-134       |
|    | 54-55 | 92-93  | 134-135       |
|    | 55-56 | 93-94  | 135-136       |
| 40 | 56-57 | 94-95  | 136-137       |
|    | 57-58 | 95-96  | 137-138       |
|    | 58-59 | 96-97  | 138-139       |
|    | 59-60 | 97-98  | 139-140       |
|    | 60-61 | 98-99  | 140-141       |
| 45 | 61-62 | 99-100 | 141-142       |
|    |       |        | or 142-143    |
|    |       |        | respectively; |

wherein  $L_1$  is a linker capable of linking  $R_1$  to  $R_2$ .

In another embodiment the progenipoietin can  
5 optionally be immediately preceded by (methionine<sup>-1</sup>),  
(alanine<sup>-1</sup>) or (methionine<sup>-2</sup>, alanine<sup>-1</sup>).

In a preferred embodiment  $R_1$  is selected from SEQ  
ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID  
10 NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID  
NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID  
NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID  
NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID  
NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID  
15 NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID  
NO:30, SEQ ID NO:31, SEQ ID NO:169, SEQ ID NO:170, SEQ  
ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174,  
and SEQ ID NO:175.

20 In a preferred embodiment  $R_2$  is GM-CSF, G-CSF, G-  
CSF Ser<sup>17</sup>, c-mpl ligand (TPO), M-CSF, erythropoietin  
(EPO), IL-1, IL-4, IL-2, IL-3, IL-3 variant, IL-5, IL  
6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, IL-15,  
LIF, flt3/flk2 ligand, human growth hormone, B-cell  
25 growth factor, B-cell differentiation factor,  
eosinophil differentiation factor and stem cell factor  
(SCF).

In a preferred embodiment the Progenipoietin  
30 protein is selected from SEQ ID NO:32, SEQ ID NO:33,  
SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37,  
38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID  
NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID  
NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID  
35 NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID

NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID  
NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID  
NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID  
NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID  
5 NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID  
NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID  
NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID  
NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID  
NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID  
10 NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID  
NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID  
NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ  
ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105,  
SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID  
15 NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112,  
SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID  
NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119,  
SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID  
NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126,  
20 SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID  
NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133,  
SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID  
NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140,  
SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID  
25 NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147,  
SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID  
NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154,  
SEQ ID NO:155, SEQ ID NO:1556, SEQ ID NO:157, SEQ ID  
NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161,  
30 SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID  
NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168,  
SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID  
NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182,  
SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID

NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189,  
 SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID  
 NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196,  
 SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID  
 5 NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203,  
 SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID  
 NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210,  
 SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID  
 NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217,  
 10 SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID  
 NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224,  
 SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID  
 NO:228, SEQ ID NO:229, and SEQ ID NO:230. More  
 preferably the Progenipoiectin protein is SEQ ID NO:165.

15

In a preferred embodiment  $R_2$  is selected from the  
 group consisting of G-CSF, G-CSF Ser<sup>17</sup>, G-CSF Ala<sup>17</sup> and  
 c-mpl ligand (TPO).

20 In a preferred embodiment  $R_2$  is an IL-3 variant of  
 SEQ ID 261. In a preferred embodiment  $R_2$  is the IL-3  
 variant of SEQ ID NO:256, SEQ ID NO:257, SEQ ID NO:258,  
 or SEQ ID NO:259.

25 In preferred embodiment the linker ( $L_2$ ) is selected  
 from the group consisting of;

Ser;  
 Asn;  
 Gly;  
 30 Thr;  
 GlySer;  
 AlaAla;  
 GlySerGly;  
 GlyGlyGly;  
 35 GlyAsnGly;  
 GlyAlaGly;  
 GlyThrGly;

AlaSerAla;  
AlaAlaAla;  
GlyGlyGlySer SEQ ID NO:231;  
GlyGlyGlySerGlyGlyGlySer SEQ ID NO:232;  
5 GlyGlyGlySerGlyGlyGlySerGlyGlyGlySer SEQ ID NO:233;  
SerGlyGlySerGlyGlySer SEQ ID NO:234;  
GluPheGlyAsnMet SEQ ID NO:235;  
GluPheGlyGlyAsnMet SEQ ID NO:236;  
GluPheGlyGlyAsnGlyGlyAsnMet SEQ ID NO:237;  
10 GlyGlySerAspMetAlaGly SEQ ID NO:238;  
SerGlyGlyAsnGly SEQ ID NO:239;  
SerGlyGlyAsnGlySerGlyGlyAsnGly SEQ ID NO:240;  
SerGlyGlyAsnGlySerGlyGlyAsnGlySerGlyGlyAsnGly  
SEQ ID NO:241;  
15 SerGlyGlySerGlySerGlyGlySerGly SEQ ID NO:242;  
SerGlyGlySerGlySerGlyGlySerGlySerGlyGlySerGly  
SEQ ID NO:243;  
GlyGlyGlySerGlyGly SEQ ID NO:244;  
GlyGlyGlySerGlyGlyGly SEQ ID NO:245;  
20 GlyGlyGlySerGlyGlyGlySerGlyGly SEQ ID NO:246;  
GlyGlyGlySerGlyGlyGlySerGlyGlyGlySerGly  
SEQ ID NO:247;  
GlyGlyGlySerGlyGlyGlySerGlyGlyGlySerGlyGlyGly  
SEQ ID NO:248;  
25 GlyGlyGlySerGlyGlyGlySerGlyGlyGlySerGlyGlyGlySer  
GlyGlyGlySerGly SEQ ID NO:249;  
ProProProTrpSerProArgProLeuGlyAlaThrAlaProThrAla  
GlyGlnProProLeu SEQ ID NO:250;  
ProProProTrpSerProArgProLeuGlyAlaThrAlaProThr  
30 SEQ ID NO:251;  
ValGluThrValPheHisArgValSerGlnAspGlyLeuLeuThrSer  
SEQ ID NO:252;  
GlyGlyGlySerGlyGlyGlySerGlyGlyGlySerGluGlyGlyGly  
SerGluGlyGlyGlySerGluGlyGlyGlySerGluGlyGlyGlySer  
35 GlyGlyGlySer SEQ ID NO:253;  
IleSerGluProSerGlyProIleSerThrIleAsnProSerProPro  
SerLysGluSerHisLysSerPro; SEQ ID NO:254, and  
IleGluGlyArgIleSerGluProSerGlyProIleSerThrIleAsn  
ProSerProProSerLysGluSerHisLysSerPro SEQ ID NO:255.  
40

Any purified and isolated ProGP, which is produced by host cells such as *E. coli* and animal cells transformed or transfected by using recombinant genetic techniques, may be used in the present invention. Among  
5 them, ProGP, which is produced by the transformed *E. coli*, is particularly preferable. Such ProGP may be obtained in large quantities with high purity and homogeneity. For example, the above ProGP may be prepared according to a method disclosed in WO  
10 98/17810. The term "substantially has the following amino acid sequence" means that the above amino acid sequence may include one or more amino-acid changes (deletion, addition, insertion or replacement) as long as such changes will not cause any disadvantageous non-  
15 similarity in function to ProGP. It is more preferable to use the ProGP substantially having an amino acid sequence, in which at least one lysine, aspartic acid, glutamic acid, or unpaired cysteine residue is included.

20 According to the present invention, poly(ethylene glycol) is covalently bound through amino acid residues of ProGP. The amino acid residue may be any reactive one(s) having, for example, free amino, carboxyl or sulfhydryl (thiol) groups, to which a terminal reactive  
25 group of an activated poly(ethylene glycol) may be bound. The amino acid residues having the free amino groups may include lysine residues and/or N-terminal amino acid residue, those having a free carboxyl group may include aspartic acid, glutamic acid and/or C-  
30 terminal amino acid residues, and having a sulfhydryl (thiol) such as cysteine.

In another embodiment, oxime chemistries (Lemieux & Bertozzi *Tib Tech* 16:506-513, 1998) are used to target N-terminal serine residues.

The poly(ethylene glycol) used in the present invention is not restricted to any particular form or molecular weight range. Normally a molecular weight of 500-60,000 is used and preferably of from 1,000-40,000.

5 The poly(ethylene glycol) can also be a branched PEG as described in U.S. 5,932,462, U.S. 5,342,940, U.S. 5,643,575, U.S. 5,919,455, U.S. 6,113,906, and U.S. 5,183,660.

Poly(alkylene oxides), notably poly(ethylene glycol)s, is bound to ProGP via a terminal reactive group, which may or may not leave a linking moiety (spacer) between the PEG and the protein. In order to form the ProGP conjugates of the present invention, polymers such as poly(alkylene oxide) are converted

10 into "activated" forms. The reactive group, for example, is a terminal reactive group, which mediates a bond between chemical moieties on the protein, such as amino, carboxyl or thiol groups, and poly(ethylene glycol). Typically, one or both of the terminal polymer

20 hydroxyl end-groups, (i.e. the alpha and omega terminal hydroxyl groups) are converted into reactive functional groups, which allows covalent conjugation. This process is frequently referred to as "activation" and the poly(ethylene glycol) product having the reactive group

25 is hereinafter referred to as "an activated poly(ethylene glycol)". Polymers containing both  $\alpha$  and  $\omega$  linking groups are referred to as "bis-activated poly(alkylene oxides)" and are referred to as "bifunctional". Polymers containing the same reactive

30 group on  $\alpha$  and  $\omega$  terminal hydroxyls are sometimes referred to as "homobifunctional" or "homobis-activated". Polymers containing different reactive groups on  $\alpha$  and  $\omega$  terminal hydroxyls are sometimes

referred to as "heterobifunctional" or "heterobis-activated". Polymers containing a single reactive group are referred to as "mono-activated" polyalkylene oxides or "mono-functional". Other substantially non-  
5 antigenic polymers are similarly "activated" or "functionalized".

The activated polymers are thus suitable for mediating a bond between chemical moieties on the protein, such as  $\alpha$ -amino, carboxyl or thiol groups, and  
10 poly(ethylene glycol). Bis-activated polymers can react in this manner with two protein molecules or one protein molecule and a reactive small molecule in another embodiment to effectively form protein polymers or protein-small molecule conjugates through cross  
15 linkages. Functional groups capable of reacting with either the amino terminal  $\alpha$ -amino group or  $\epsilon$ -amino groups of lysines found on the ProGP include: carbonates such as the p-nitrophenyl, or succinimidyl; carbonyl imidazole; azlactones; cyclic imide thiones;  
20 isocyanates or isothiocyanates and aldehydes. Functional groups capable of reacting with carboxylic acid groups, reactive carbonyl groups and oxidized carbohydrate moieties on ProGP include; primary amines; and hydrazine and hydrazide functional groups such as  
25 the acyl hydrazides, carbazates, semicarbamates, thiocarbazates, etc. Mercapto groups, if available on the ProGP, can also be used as attachment sites for suitably activated polymers with reactive groups such as thiols; maleimides, sulfones, and phenyl glyoxals;  
30 see, for example, U.S. Pat. No. 5,093,531, the disclosure of which is hereby incorporated by reference. Other nucleophiles capable of reacting with an electrophilic center include, but are not limited

to, for example, hydroxyl, amino, carboxyl, thiol, active methylene and the like.

In one preferred embodiment of the invention secondary amine or amide linkages are formed using the  
5 ProGP N-terminal amino groups or  $\epsilon$ -amino groups of lysine and the activated PEG. In another preferred aspect of the invention, a secondary amine linkage is formed between the N-terminal primary amino group of ProGP and single or branched chain PEG aldehyde by  
10 reduction with a suitable reducing agent such as  $\text{NaCNBH}_3$ ,  $\text{NaBH}_3$ , Pyridine Borane etc. as described in Chamow *et al.*, *Bioconjugate Chem.* 5: 133-140 (1994) and US Pat. No 5,824,784.

In another preferred embodiment of the invention,  
15 polymers activated with amide-forming linkers such as succinimidyl esters, cyclic imide thiones, or the like are used to effect the linkage between the ProGP and polymer, see for example, U.S. Pat. No. 5,349,001; U.S. Pat. No. 5,405,877; and Greenwald, *et al.*, *Crit. Rev.*  
20 *Ther. Drug Carrier Syst.* 17:101-161, 2000, which are incorporated herein by reference. One preferred activated poly(ethylene glycol), which may be bound to the free amino groups of ProGP includes single or branched chain N-hydroxysuccinylimide poly(ethylene  
25 glycol) may be prepared by activating succinic acid esters of poly(ethylene glycol) with N-hydroxysuccinylimide.

Other preferred embodiments of the invention include using other activated polymers to form covalent  
30 linkages of the polymer with the ProGP via  $\epsilon$ -amino or other groups. For example, isocyanate or isothiocyanate forms of terminally activated polymers can be used to form urea or thiourea-based linkages with the lysine amino groups.

In another preferred aspect of the invention, carbamate (urethane) linkages are formed with protein amino groups as described in U.S. Pat. Nos. 5,122,614, 5,324,844, and 5,612,640, which are hereby incorporated  
5 by reference. Examples include N-succinimidyl carbonate, para-nitrophenyl carbonate, and carbonyl imidazole activated polymers. In another preferred embodiment of this invention, a benzotriazole carbonate derivative of PEG is linked to amino groups on ProGP.

10 Another aspect of the invention represents a prodrug or sustained release form of ProGP, comprised of a water soluble polymer, such as poly(ethylene glycol), attached to an ProGP molecule by a functional linker that can predictably break down by enzymatic or  
15 pH directed hydrolysis to release free ProGP or other ProGP derivative. The prodrug can also be a "double prodrug" (Bundgaard in *Advanced Drug Delivery Reviews* 3:39-65, 1989) involving the use of a cascade latentiation. In such systems, the hydrolytic reaction  
20 involves an initial rate-limiting (slow) enzymatic or pH directed step and a second step involving a rapid non-enzymatic hydrolysis that occurs only after the first has taken place. Such a releasable polymer provides protein conjugates, which are impermanent and  
25 could act as a reservoir, that continually discharge ProGP. Such functional linkers are described in US 5,614,549; US 5,840,900; US 5,880,131; US 5,965,119; US 6,011,042; US 6,180,095 B1; Greenwald R.B. et al., *J. Med. Chem.* **42**:3657-3667, 1999; Lee, S. et al.,  
30 *Bioconjugate Chem* **12**:163-169, 2001; Garman A.J. et al., *FEBS Lett.* **223**:361-365, 1987; Woghiren C. et al., *Bioconjugate Chem.* **4**:314-318, 1993; Roberts M.J. et al., *J. Pharm. Sci.* **87**:1440-1445, 1998; Zhao X., in *Ninth Int. Symp. Recent Adv. Drug Delivery Syst.* 199;

Greenwald R.B. et al., *J. Med. Chem.* **43**:475-487, 2000;  
and Greenwald R.B. *Crit. Rev. Ther. Drug Carrier Syst.*  
**17**:101-161, 2000.

Another embodiment of the present invention is a  
5 method of conjugating a PEG to a nucleophile where the  
conjugation is carried out in the presence of an  
inorganic solvent. A "nucleophile" is defined as  
proteins including but not limited to antibodies and  
hematopoietic growth factors, peptides, enzymes,  
10 medicinal chemicals or organic moieties. Preferably the  
inorganic solvent is acetonitrile, methanol, or  
ethanol. More preferably the inorganic solvent is  
acetonitrile. Preferably the inorganic concentration is  
between about 1% and about 25%, more preferably between  
15 about 3% and about 13%, and more preferably about 8%.

Conjugation reactions, referred to as pegylation  
reactions, were historically carried out in solution  
with molar excess of polymer and without regard to  
where the polymer will attach to the protein. Such  
20 general techniques, however, have typically been proven  
inadequate for conjugating bioactive proteins to non-  
antigenic polymers while retaining sufficient  
bioactivity. One way to maintain the ProGP bioactivity  
is to substantially avoid the conjugation of those  
25 ProGP reactive groups associated with the receptor  
binding site(s) in the polymer coupling process.  
Another aspect of the present invention is to provide a  
process of conjugating poly(ethylene glycol) to ProGP  
maintaining high levels of retained activity.

30 The chemical modification through a covalent bond  
may be performed under any suitable condition generally  
adopted in a reaction of a biologically active  
substance with the activated poly(ethylene glycol). The  
conjugation reaction is carried out under relatively

mild conditions to avoid inactivating the ProGP. Mild conditions include maintaining the pH of the reaction solution in the range of 3 to 10 and the reaction temperatures within the range of from about 0°-37°C. In the cases where the reactive amino acid residues in ProGP have free amino groups, the above modification is preferably carried out in a non-limiting list of suitable buffers (pH 3 to 10), including phosphate, citrate, acetate, succinate or HEPES, for 1-48 hrs at 4°-37°C. In targeting N-terminal amino groups with reagents such as PEG aldehydes pH 4-7 is preferably maintained. The activated poly(ethylene glycol) may be used in 0.05-100 times, preferably 0.05-0.5 times, the molar amount of the number of free amino groups of ProGP. On the other hand, where reactive amino acid residues in ProGP have the free carboxyl groups, the above modification is preferably carried out in pH from about 3.5 to about 5.5, for example, the modification with poly(oxyethylenediamine) is carried out in the presence of carbodiimide (pH 4-5) for 1-24 hrs at 4°-37°C. The activated poly(ethylene glycol) may be used in 0.05-300 times the molar amount of the number of free carboxyl groups of ProGP.

In separate embodiments, the upper limit for the amount of polymer included in the conjugation reactions exceeds about 1:1 to the extent that it is possible to react the activated polymer and ProGP without forming a substantial amount of high molecular weight species, i.e. more than about 20% of the conjugates containing more than about one strand of polymer per molecule of ProGP. For example, it is contemplated in this aspect of the invention that ratios of up to about 6:1 can be employed to form significant amounts of the desired

conjugates which can thereafter be isolated from any high molecular weight species.

In another aspect of this invention, bifunctionally activated PEG derivatives may be used to generate polymeric ProGP-PEG molecules in which multiple ProGP molecules are crosslinked via PEG. Although the reaction conditions described herein can result in significant amounts of unmodified ProGP, the unmodified ProGP can be readily recycled into future batches for additional conjugation reactions. The processes of the present invention generate surprisingly very little, i.e. less than about 30% and more preferably, less than about 10%, of high molecular weight species and species containing more than one polymer strand per ProGP. These reaction conditions are to be contrasted with those typically used for polymeric conjugation reactions wherein the activated polymer is present in several-fold molar excesses with respect to the target. In other aspects of the invention, the polymer is present in amounts of from about 0.1 to about 50 equivalents per equivalent of ProGP. In other aspects of the invention, the polymer is present in amounts of from about 1 to about 10 equivalents per equivalent of ProGP.

The conjugation reactions of the present invention initially provide a reaction mixture or pool containing mono- and di-PEG-ProGP conjugates, unreacted ProGP, unreacted polymer and usually less than about 20% high molecular weight species. The high molecular weight species include conjugates containing more than one polymer strand and/or polymerized PEG-ProGP species. After the unreacted species and high molecular weight species have been removed, compositions containing primarily mono- and di-polymer-ProGP conjugates are

recovered. Given the fact that the conjugates for the most part include a single polymer strand, the conjugates are substantially homogeneous. These modified ProGPs have at least about 5% of the *in vitro* biological activity associated with the native or unmodified ProGP as measured using standard cell proliferation assays, such as AML, TF1 and colony forming unit assays (U.S. Patent 6,030,812 which is incorporated by reference herein). In preferred aspects of the invention, the modified ProGPs have about 25% of the *in vitro* biological activity, more preferably, the modified ProGPs have about 50% of the *in vitro* biological activity, more preferably, the modified ProGPs have about 75% of the *in vitro* biological activity, and most preferably the modified ProGPs have equivalent or improved *in vitro* biological activity.

The processes of the present invention preferably include rather limited ratios of polymer to ProGP. Thus, the ProGP conjugates have been found to be predominantly limited to species containing only one strand of polymer. Furthermore, the attachment of the polymer to the ProGP reactive groups is substantially less random than when higher molar excesses of polymer linker are used. The unmodified ProGP present in the reaction pool, after the conjugation reaction has been quenched, can be recycled into future reactions using ion exchange or size exclusion chromatography or similar separation techniques.

A poly(ethylene glycol)-modified ProGP, namely chemically modified protein according to the present invention, may be purified from a reaction mixture by conventional methods which are used for purification of proteins, such as dialysis, salting-out, ultrafiltration, ion-exchange chromatography, gel

chromatography and electrophoresis. Ion-exchange chromatography is particularly effective in removing unreacted poly(ethylene glycol) and ProGP. In a further embodiment of the invention, the mono- and di-polymer-  
5 ProGP species are isolated from the reaction mixture to remove high molecular weight species, and unmodified ProGP. Separation is effected by placing the mixed species in a buffer solution containing from about 0.5-10 mg/mL of the ProGP-polymer conjugates. Suitable  
10 solutions have a pH from about 4 to about 10. The solutions preferably contain one or more buffer salts selected from KCl, NaCl,  $K_2HPO_4$ ,  $KH_2PO_4$ ,  $Na_2HPO_4$ ,  $NaH_2PO_4$ ,  $NaHCO_3$ ,  $NaBO_4$ ,  $CH_3CO_2H$ , and NaOH.

Depending upon the reaction buffer, the ProGP  
15 polymer conjugate solution may first have to undergo buffer exchange/ultrafiltration to remove any unreacted polymer. For example, the PEG-ProGP conjugate solution can be ultrafiltered across a low molecular weight cut-off (10,000 to 30,000 Dalton) membrane to remove most  
20 unwanted materials such as unreacted polymer, surfactants, if present, or the like.

The fractionation of the conjugates into a pool containing the desired species is preferably carried out using an ion exchange chromatography medium. Such  
25 media are capable of selectively binding PEG-ProGP conjugates via differences in charge, which vary in a somewhat predictable fashion. For example, the surface charge of ProGP is determined by the number of available charged groups on the surface of the protein.  
30 These charged groups typically serve as the point of potential attachment of poly(alkylene oxide) conjugates. Therefore, ProGP conjugates will have a different charge from the other species to allow selective isolation.

Strongly polar anion or cation exchange resins such as quaternary amine or sulfopropyl resins, respectively, are used for the method of the present invention. Cation exchange resins are especially preferred. A non-limiting list of included commercially available cation exchange resins suitable for use with the present invention are SP-hitrap®, SP Sepharose HP® and SP Sepharose® fast flow. Other suitable cation exchange resins e.g. S and CM resins can also be used.

10 A non-limiting list of anion exchange resins, including commercially available anion exchange resins, suitable for use with the present invention are Q-hitrap®, Q Sepharose HP®, and Q sepharose® fast flow. Other suitable anion exchange resins, e.g. DEAE resins, can

15 also be used.

For example, the cation exchange resin is preferably packed in a column and equilibrated by conventional means. A buffer having the same pH and osmolality as the polymer conjugated ProGP solution is

20 used. The elution buffer preferably contains one or more salts selected from KCl, NaCl,  $K_2HPO_4$ ,  $KH_2PO_4$ ,  $Na_2HPO_4$ ,  $NaH_2PO_4$ ,  $NaHCO_3$ ,  $NaBO_4$ , and  $(NH_4)_2CO_3$ . The conjugate-containing solution is then adsorbed onto the column with unreacted polymer and some high molecular

25 weight species not being retained. At the completion of the loading, a gradient flow of an elution buffer with increasing salt concentrations is applied to the column to elute the desired fraction of polyalkylene oxide-conjugated ProGP. The eluted pooled fractions are

30 preferably limited to uniform polymer conjugates after the cation exchange separation step. Any unconjugated ProGP species can then be back washed from the column by conventional techniques. If desired, mono and multiply pegylated ProGP species can be further

separated from each other via additional ion exchange chromatography or size exclusion chromatography.

Techniques utilizing multiple isocratic steps of increasing concentration can also be used. Multiple  
5 isocratic elution steps of increasing concentration will result in the sequential elution of di- and then mono-ProGP-polymer conjugates.

The temperature range for elution is between about 4°C and about 25°C. Preferably, elution is carried out  
10 at a temperature of from about 6°C to about 22°C. For example, the elution of the PEG-ProGP fraction is detected by UV absorbance at 280 nm. Fraction collection may be achieved through simple time elution profiles.

15 A surfactant can be used in the processes of conjugating the poly(ethylene glycol) polymer with the ProGP moiety. Suitable surfactants include ionic-type agents such as sodium dodecyl sulfate (SDS). Other ionic surfactants such as lithium dodecyl sulfate,  
20 quaternary ammonium compounds, taurocholic acid, caprylic acid, decane sulfonic acid, etc. can also be used. Non-ionic surfactants can also be used. For example, materials such as poly(oxyethylene) sorbitans (Tweens), poly(oxyethylene) ethers (Tritons) can be  
25 used. See also Neugebauer, A Guide to the Properties and Uses of Detergents in Biology and Biochemistry (1992) Calbiochem Corp. The only limitations on the surfactants used in the processes of the invention are that they are used under conditions and at  
30 concentrations that do not cause substantial irreversible denaturation of the ProGP and do not completely inhibit polymer conjugation. The surfactants are present in the reaction mixtures in amounts from about 0.01-0.5%; preferably from 0.05-0.5%; and most

preferably from about 0.075-0.25%. Mixtures of the surfactants are also contemplated.

It is thought that the surfactants provide a temporary, reversible protecting system during the polymer conjugation process. Surfactants have been shown to be effective in selectively discouraging polymer conjugation while allowing lysine-based or amino terminal-based conjugation to proceed.

The present poly(ethylene glycol)-modified ProGP has a more enduring pharmacological effect, which may be possibly attributed to its prolonged half-life in vivo.

An intended use of the PEG-ProGP of the present invention is for the generation of larger numbers of dendritic cells, from precursors, to be used as adjuvants for immunization. Dendritic cells play a crucial role in the immune system. They are the professional antigen-presenting cells most efficient in the activation of resting T cells and are the major antigen-presenting cells for activation of naïve T cells *in vivo* and, thus, for initiation of primary immune responses. They efficiently internalize, process and present soluble tumor-specific antigens (Ag). Dendritic cells have the unique capacity to cluster naïve T cells and to respond to Ag encounter by rapid up-regulation of the expression of major histocompatibility complex (MHC) and co-stimulatory molecules, the production of cytokines and migration towards lymphatic organs. Since dendritic cells are of central importance for sensitizing the host against a neoantigen for CD4-dependent immune responses, they may also play a crucial role in the generation and regulation of tumor immunity.

Dendritic cells originate from a bone marrow CD34+ precursor common to granulocytes and macrophages, and the existence of a separate dendritic cell colony-forming unit (CFU-DC) that give rise to pure dendritic cell colonies has been established in humans. In addition, a post-CFU CD14+ intermediate has been described with the potential to differentiate along the dendritic cell or the macrophage pathway under distinct cytokine conditions. This bipotential precursor is present in the bone marrow, cord blood, and peripheral blood. Dendritic cells can be isolated based on specific cell surface markers, such as CD1a+, CD3-, CD4-, CD20-, CD40+, CD80+, and CD83+, to delineate the maturation of cultured dendritic cells.

15

Dendritic cells based strategies provide a method for enhancing immune response against tumors and infectious agents. AIDS is another disease for which dendritic cell based therapies can be used, since dendritic cells can play a major role in promoting HIV-1 replication. An immunotherapy requires the generation of dendritic cells from cancer patients, their *in vitro* exposure to tumor Ag, derived from surgically removed tumor masses, and reinjection of these cells into the tumor patients. Relatively crude membrane preparations of tumor cells will suffice as sources of tumor antigen, avoiding the necessity for molecular identification of the tumor antigen. The tumor antigen may also be synthetic peptides, carbohydrates, or nucleic acid sequences. In addition, concomitant administration of cytokines such as the PEG-ProGP of the present invention may further facilitate the induction of tumor immunity. It is foreseen that the immunotherapy can be in an *in vivo*

setting, wherein the PEG-ProGP of the present invention is administered to a patient, having a tumor, alone or with other hematopoietic growth factors to increase the number of dendritic cells and endogenous tumor antigen is presented on the dendritic cells. It is also envisioned that *in vivo* immunotherapy can be with exogenous antigen. It is also envisioned that the immunotherapy treatment may include the mobilization of dendritic cell precursors or mature dendritic, by administering the PEG-ProGP of the present invention alone or with other hematopoietic growth factors to the patient, removing the dendritic cell precursors or mature dendritic cells from the patient, exposing the dendritic cells to antigen and returning the dendritic cells to the patient. Furthermore, the dendritic cells that have been removed can be cultured *ex vivo* with the PEG-ProGP of the present invention alone or with other hematopoietic growth factors to increase the number of dendritic cells prior to exposure to antigen. Dendritic cells based strategies also provide a method for reducing the immune response in autoimmune diseases.

Studies on dendritic cells have been greatly hampered by difficulties in preparing the cells in sufficient numbers and in a reasonably pure form. In an ex-vivo cell expansion setting, granulocyte-macrophage colony-stimulating factor (GM-CSF) and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) cooperate in the *ex vivo* generation of dendritic cells from hematopoietic progenitors (CD34+ cells) retrieved from bone marrow, cord blood, or peripheral blood and flk-2/flt-3 ligand and c-kit ligand (stem cell factor [SCF]) synergize to enhance the GM-CSF plus TNF- $\alpha$  induced generation of dendritic cells (Siena, S. et al. *Experimental Hematology*

23:1463-1471, 1995). Also provide is a method of ex vivo expansion of dendritic cell precursors or mature dendritic cells using the PEG-ProGP of the present invention to provide sufficient quantities of dendritic  
5 cells for immunotherapy.

Furthermore, it is observed that the present poly(ethylene glycol)-modified ProGP may accelerate recovery from neutropenia. The present poly(ethylene  
10 glycol)-modified ProGP may have essentially the same biological activity as an intact ProGP and may accordingly be used in the same applications. The poly(ethylene glycol)-modified ProGP has an activity for increasing the number of neutrophils, and it is  
15 useful therefore in the treatment of general hematopoietic disorders including those arising from chemotherapy or from radiation therapy. It may be also useful in the treatment of infection and in bone marrow transplantation. The modified ProGP of the present  
20 invention may be useful in the treatment of diseases characterized by decreased levels of either myeloid, erythroid, lymphoid, or megakaryocyte cells of the hematopoietic system or combinations thereof. In addition, they may be used to activate mature myeloid  
25 and/or lymphoid cells. Among conditions susceptible to treatment with the polypeptides of the present invention is leukopenia, a reduction in the number of circulating leukocytes (white cells) in the peripheral blood. Leukopenia may be induced by exposure to  
30 certain viruses or to radiation. It is often a side effect of various forms of cancer therapy, e.g., exposure to chemotherapeutic drugs, radiation and of infection or hemorrhage. Therapeutic treatment of leukopenia with these modified ProGP of the present

invention may avoid undesirable side effects caused by treatment with presently available drugs.

The modified ProGP of the present invention may be useful in the treatment or prevention of neutropenia and, for example, in the treatment of such conditions as aplastic anemia, cyclic neutropenia, idiopathic neutropenia, Chediak-Higashi syndrome, systemic lupus erythematosus (SLE), leukemia, myelodysplastic syndrome and myelofibrosis.

10       The modified ProGP of the present invention may be useful in the treatment or prevention of thrombocytopenia. Currently the only therapies for thrombocytopenia are platelet transfusions, which are costly and carry the significant risks of infection  
15       (HIV, HBV) and alloimmunization, and IL-11 (Neumega™) that is approved for certain thrombocytopenia. The modified ProGP may alleviate or diminish the need for platelet transfusions. Severe thrombocytopenia may result from genetic defects such as Fanconi's Anemia,  
20       Wiscott-Aldrich, or May-Hegglin syndromes. Acquired thrombocytopenia may result from auto- or allo-antibodies as in Immune Thrombocytopenia Purpura, Systemic Lupus Erythematosus, hemolytic anemia, or fetal maternal incompatibility. In addition,  
25       splenomegaly, disseminated intravascular coagulation, thrombotic thrombocytopenic purpura, infection, or prosthetic heart valves may result in thrombocytopenia. Severe thrombocytopenia may also result from chemotherapy and/or radiation therapy or cancer.  
30       Thrombocytopenia may also result from marrow invasion by carcinoma, lymphoma, leukemia, or fibrosis.

The modified ProGP of the present invention may be useful in the mobilization of hematopoietic progenitors and stem cells into peripheral blood. Peripheral blood

derived progenitors have been shown to be effective in reconstituting patients in the setting of autologous marrow transplantation. Hematopoietic growth factors including G-CSF and GM-CSF have been shown to enhance  
5 the number of circulating progenitors and stem cells in the peripheral blood. This has simplified the procedure for peripheral stem cell collection and dramatically decreased the cost of the procedure by decreasing the number of phereses required. The modified ProGP may be  
10 useful in mobilization of stem cells and further enhance the efficacy of peripheral stem cell transplantation.

Another projected clinical use of growth factors has been in the *in vitro* activation of hematopoietic  
15 progenitors and stem cells for gene therapy. In order to have the gene of interest incorporated into the genome of the hematopoietic progenitor or stem cell one needs to stimulate cell division and DNA replication. Hematopoietic stem cells cycle at a very low frequency,  
20 which means that growth factors may be useful to promote gene transduction and thereby enhance the clinical prospects for gene therapy.

Many drugs may cause bone marrow suppression or hematopoietic deficiencies. Examples of such drugs are  
25 AZT, DDI, alkylating agents and anti-metabolites used in chemotherapy, antibiotics such as chloramphenicol, penicillin, gancyclovir, daunomycin and sulfa drugs, phenothiazones, tranquilizers such as meprobamate, analgesics such as aminopyrine and dipyrone, anti-  
30 convulsants such as phenytoin or carbamazepine, antithyroids such as propylthiouracil and methimazole and diuretics. The modified ProGP of the present invention may be useful in preventing or treating the bone marrow suppression or hematopoietic deficiencies,

which often occur in patients treated with these drugs.

Hematopoietic deficiencies may also occur because of viral, microbial, or parasitic infections and as a result of treatment for renal disease or renal failure, e.g., dialysis. The modified ProGP of the present invention may be useful in treating such hematopoietic deficiency.

The treatment of hematopoietic deficiency may include administration of a pharmaceutical composition containing the modified ProGP to a patient. The modified ProGP of the present invention may also be useful for the activation and amplification of hematopoietic precursor cells by treating these cells *in vitro* with the modified ProGP of the present invention prior to injecting the cells into a patient.

Various immunodeficiencies e.g., in T and/or B-lymphocytes, or immune disorders, e.g., rheumatoid arthritis, may also be beneficially affected by treatment with the modified ProGP of the present invention. Immunodeficiencies may be the result of viral infections e.g. HTLV-I, HTLV-II, HTLV-III, severe exposure to radiation, cancer therapy or the result of other medical treatment. The modified ProGP of the present invention may also be employed, alone or in combination with other hematopoietins, in the treatment of other blood cell deficiencies, including thrombocytopenia (platelet deficiency), or anemia. Other uses for these novel polypeptides are in the treatment of patients recovering from bone marrow transplants *in vivo* and *ex vivo*, and in the development of monoclonal and polyclonal antibodies generated by standard methods for diagnostic or therapeutic use.

The present poly(ethylene glycol)-modified ProGP may be formulated into pharmaceuticals containing also a pharmaceutically acceptable diluent, an agent for preparing an isotonic solution, a pH-conditioner and the like in order to administer them into a patient. The above pharmaceuticals may be administered subcutaneously, intramuscularly, intravenously, or orally, depending on a purpose of treatment. A dose may be also based on the kind and condition of the disorder of a patient to be treated, being normally between 0.1 mg and 50 mg by injection and between 0.1 mg and 5 g in an oral administration for an adult

The polymeric substances included are also preferably water-soluble at room temperature. A non-limiting list of such polymers include poly(alkylene oxide) homopolymers such as poly(ethylene glycol) or poly(propylene glycols), poly(oxyethylenated polyols), copolymers thereof and block copolymers thereof, provided that the water solubility of the block copolymers is maintained.

As an alternative to PEG-based polymers, effectively non-antigenic materials such as dextran, poly(vinyl pyrrolidones), poly(acrylamides), poly(vinyl alcohols), carbohydrate-based polymers, and the like can be used. Indeed, the activation of  $\alpha$ - and  $\omega$ -terminal groups of these polymeric substances can be effected in fashions similar to that used to convert poly(alkylene oxides) and thus will be apparent to those of ordinary skill. Those of ordinary skill in the art will realize that the foregoing list is merely illustrative and that all polymer materials having the qualities described herein are contemplated. For purposes of the present invention, "effectively non-antigenic" means all materials understood in the art as

being nontoxic and not eliciting an appreciable immunogenic response in mammals.

### ***Definitions***

5

The following is a list of abbreviations and the corresponding meanings as used interchangeably herein:

|    |                 |                        |
|----|-----------------|------------------------|
|    | <b>g</b>        | gram(s)                |
|    | <b>mg</b>       | milligram(s)           |
| 10 | <b>ml or mL</b> | milliliter(s)          |
|    | <b>RT</b>       | room temperature       |
|    | <b>PEG</b>      | poly (ethylene glycol) |

15 The complete content of all publications, patents, and patent applications cited in this disclosure are herein incorporated by reference as if each individual publication, patent, or patent application were specifically and individually indicated to be incorporated by reference.

20 Although the foregoing invention has been described in some detail by way of illustration and example for the purposes of clarity of understanding, it will be readily apparent to one skilled in the art in light of the teachings of this invention that  
25 changes and modifications can be made without departing from the spirit and scope of the present invention. The following examples are provided for exemplification purposes only and are not intended to limit the scope of the invention, which has been described in broad  
30 terms above.

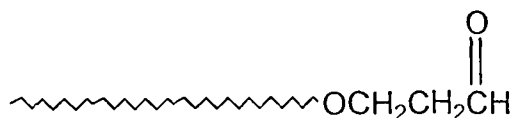
In the following examples, the ProGP polypeptide is that of ProGP-4, the amino acid sequence for which is shown in Fig 12. It is understood that other members of the ProGP family of polypeptides could also be

pegylated in a similar manner as exemplified in the subsequent examples.

## EXAMPLES

### EXAMPLE 1

Straight Chain 30,000 MW PEG-ProGP



PEG-Aldehyde 5, 20 and 30,000 MW

10

This example demonstrates a method for generation of substantially homogeneous preparations of N-terminally monopegylated ProGP by reductive alkylation. Methoxy-linear PEG-propionaldehyde reagent of approximately 30,000 MW (Shearwater Polymers Inc.) was selectively coupled via reductive amination to the N-terminus of ProGP by taking advantage of the difference in the relative  $pK_a$  value of the primary amine at the N-terminus versus  $pK_a$  values of primary amines at the  $\epsilon$ -amino position of lysine residues. ProGP protein dissolved at 1-5 mg/mL in 10mM sodium Succinate, pH 5.0, or in 10 mM sodium succinate (J. T. Baker, Phillipsburg, NJ), 8% acetonitrile (Burdick and Jackson, Muskegon, MI), pH 5.0, was reacted with Methoxy-PEG-propionaldehyde, M-PEG-ALD, (Shearwater Polymers Inc., Huntsville, AL) by addition of solid M-PEG-ALD to yield a relative PEG:ProGP (dimer) molar ratio of 2-12:1. Reactions were catalyzed by addition of stock 1M  $NaCNBH_4$  (Sigma Chemical, St. Louis, MO) dissolved in  $H_2O$  to a final concentration of 10 mM.

Reactions were carried out in the dark at 4°C for 18-24 hours. Reactions were stopped by addition of 1 M Tris base (Sigma Chemical, St. Louis, MO) to a final Tris concentration of 50 mM and a final pH of 8.5.

5

## EXAMPLE 2

Straight Chain 20,000 MW PEG-ProGP

- 10 Methoxy-linear 20,000 MW PEG-propionaldehyde reagent (Shearwater Polymers Inc.) was coupled to the N-terminus of ProGP using the procedure described for Example 1.

15

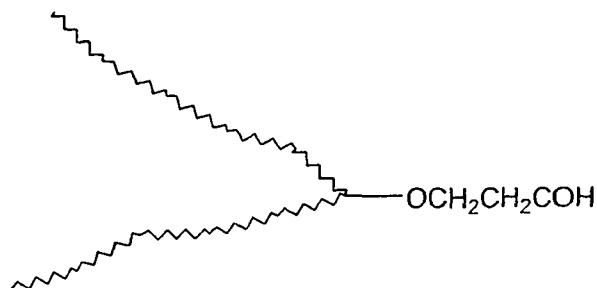
## EXAMPLE 3

Straight chain 5,000 MW PEG-ProGP

- 20 Methoxy-linear 5,000 MW PEG-propionaldehyde reagent (Fluka) was coupled to the N-terminus of ProGP using the procedure described for Example 1.

## - EXAMPLE 4

- 25 Branched chain 40,000 MW PEG-ProGP



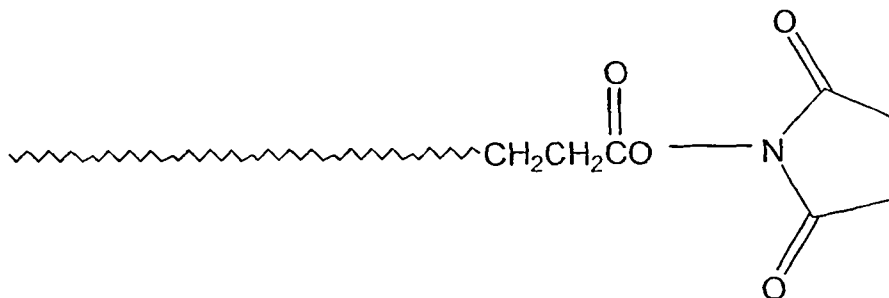
PEG2-ALD 40,000 MW

Methoxy-branched 40,000 MW PEG-propionaldehyde (PEG2-ALD) reagent (Shearwater Polymers Inc.) was coupled to the N-terminus of ProGP using the procedure described for Example 1.

5

EXAMPLE 5

Straight chain 20,000 MW PEG-ProGP

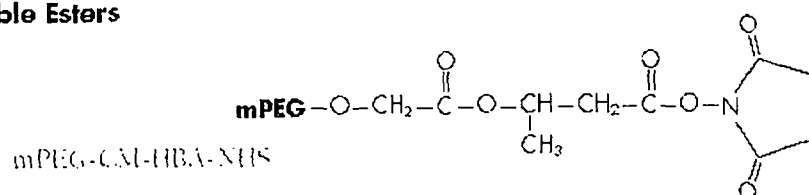


SPA-PEG 5 and 20,000 MW

10

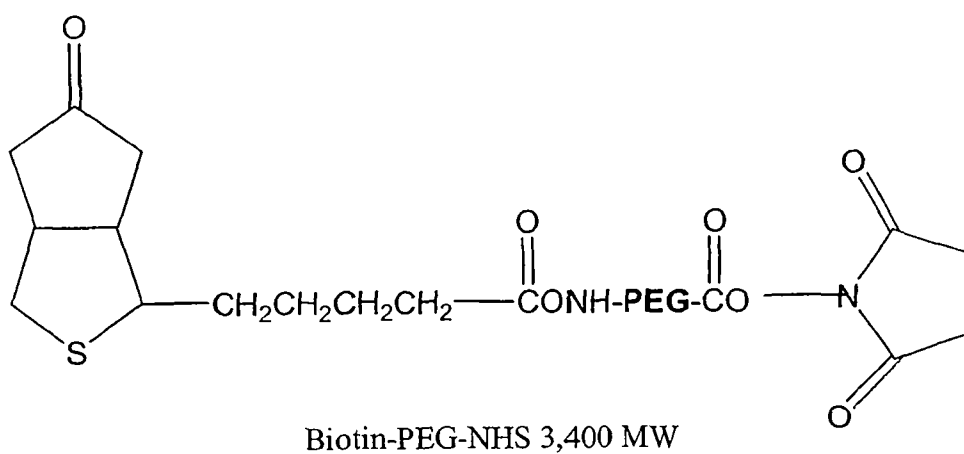
This example demonstrates a method for generation of substantially homogeneous preparations of monopegylated Progenipoietin (ProGP) using N-hydroxysuccinimidyl (NHS) active esters. ProGP protein stock solution is dissolved at 1-5 mg/mL in 10mM sodium Succinate, pH 5.0, is titrated to pH 7.2 by addition of 0.25 M HEPES buffer. The solution is then reacted with Methoxy-PEG-succinimidyl propionate (SPA-PEG) by addition of solid SPA-PEG to yield a relative PEG:Progenipoietin molar ratio of 6.5:1. Reactions are carried out at 4°C for 1 hour. Reactions are stopped by lowering the pH to 4.0 with 0.1 N acetic acid or by adding a 5X molar excess of Tris HCl. In a like manner CM-HBA-NHS 5 to 20,000 MW PEG could be used.

### mPEG-Double Esters



### EXAMPLE 6

5    Straight chain 3,400 MW Biotin-PEG-ProGP

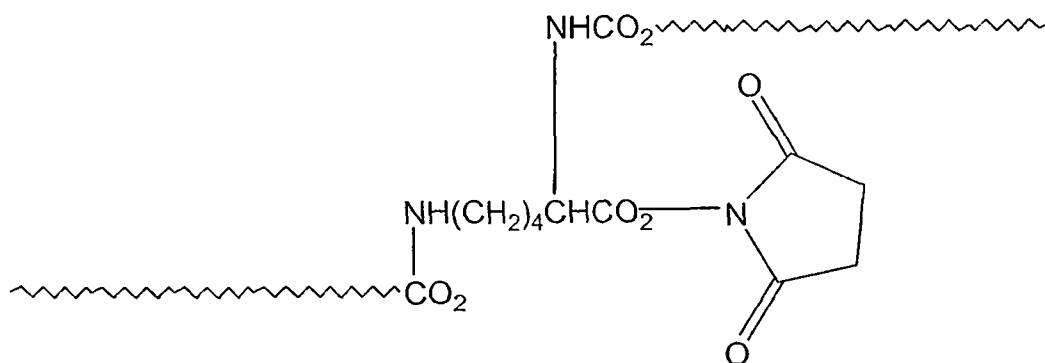


3,400 MW Biotin-PEG-CO<sub>2</sub>-NHS reagent (Shearwater Polymers  
10 Inc.) is coupled to ProGP using the procedure described  
for Example 5.

### EXAMPLE 7

15

Branched 10,000 MW PEG-ProGP



## PEG2-NHS 10, 20 and 40,000 MW

10,000 MW branched PEG2-NHS (Shearwater Polymers Inc.)  
 is coupled to ProGP using the procedure described for  
 5 Example 5.

## EXAMPLE 8

Branched 20,000 MW PEG-ProGP  
 10

20,000 MW branched PEG2-SPA (Shearwater Polymers Inc.)  
 is coupled to ProGP using the procedure described for  
 Example 5.

15 EXAMPLE 9

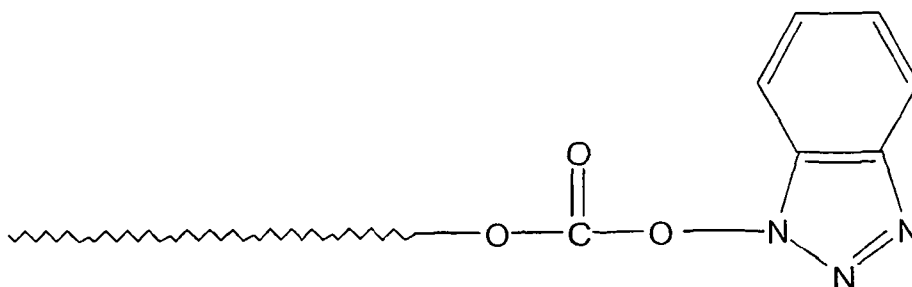
Branched 40,000 MW PEG-ProGP

40,000 MW branched PEG2-SPA (Shearwater Polymers Inc.)  
 20 is coupled to ProGP using the procedure described for  
 Example 5.

## EXAMPLE 10

25

Straight chain 20,000 MW PEG-ProGP



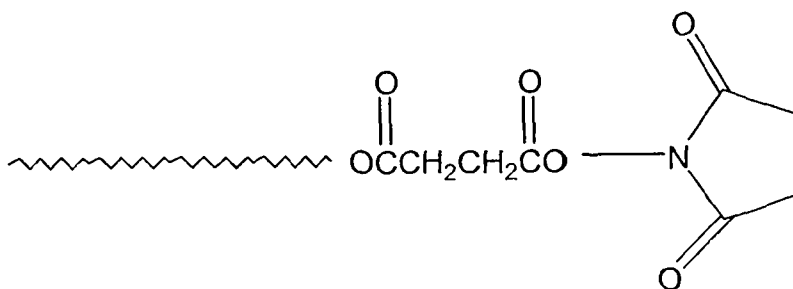
BTC-PEG 20,000 MW

20,000 MW PEG-BTC (Shearwater Polymers Inc.) is coupled  
5 to ProGP using the procedure described for Example 4.  
This example demonstrates a method for generation of  
substantially homogeneous preparations of pegylated  
Progenipoietin (ProGP) using benzotriazole carbonate  
derivatives of PEG.

10

EXAMPLE 11

Straight chain 5,000 MW PEG-ProGP



15

PEG-SS 5,000 MW

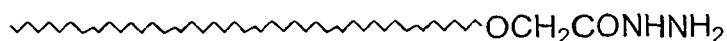
5,000 MW succinimidyl succinate-PEG (SS-PEG) (Shearwater Polymers Inc.) is coupled to ProGP using the procedure described for Example 5. This example demonstrates a method for generation of substantially homogeneous

preparations of pegylated Progenipoietin (ProGP) using a hydrolyzable linkage.

## EXAMPLE 12

5

Straight chain 20,000 MW PEG-ProGP



## PEG-Hydrazide 20,000 MW

- 10 This example demonstrates a method for generation of substantially homogeneous preparations of pegylated Progenipoietin (ProGP) using 20,000 MW methoxy-PEG-hydrazide, HZ-PEG (Shearwater Polymers Inc.). ProGP protein stock solution is dissolved at 1-5 mg/mL in
- 15 10mM sodium Succinate, pH 5.0. The solution is then reacted with HZ-PEG by addition of solid to yield a relative PEG:Progenipoietin molar ratio of 6.5 - 26:1 reactions are catalyzed with carbodiimide (EDC, EOAC) at a final concentration of 2mM. Reactions are carried
- 20 out at 4°C for 2 hours. Reactions are stopped by lowering the pH to 4 with 0.1 N acetic acid.

## EXAMPLES 13

## 25 Multi-pegylated species

- Modified ProGPs having two or more PEGs (multi-pegylated) attached were also obtained from Example 1-4 and were separated from the mono-pegylated species
- 30 using anion exchange chromatography. Modified ProGPs having two or more PEGs (multi-pegylated) attached are

also separated from mono-PEGylated species using cation exchange chromatography.

Modified ProGPs having two or more PEGs (multi-pegylated) attached can also be obtained from examples 5-13 and can be purified in similar fashion to examples 1-4.

#### EXAMPLE 14

##### 10 Purification of Pegylated ProGP

Pegylated ProGP species were purified from the reaction mixture to >95% (SEC analysis) using a single ion exchange chromatography step

15

##### *Anion exchange chromatography*

Mono-Pegylated 30K 20K and 5K PEG aldehyde ProGP species were purified from the reaction mixture to >95% (SEC analysis) using a single anion exchange chromatography step. Mono-Pegylated ProGP was purified from unmodified ProGP and multi-PEGylated ProGP species using anion exchange chromatography (figure 1). A typical 30K aldehyde ProGP reaction mixture (50-350 mg protein), as described above, was purified on a Q-Sepharose High Performance column (XK 26/20, 70 ml bed volume, Amersham Pharmacia Biotech, Piscataway, NJ) equilibrated in 50 mM Tris, pH 8.5 (Buffer A). The reaction mixture was diluted 5X with 50 mM Tris, 8% Acetonitrile, pH 8.5 and loaded onto the column at a flow rate of 10 mL/min. The column was washed with 5 column volumes of buffer A, followed by 5 column volumes of buffer A containing 30 mM NaCl. Subsequently, the various ProGP species were eluted

from the column in 20 column volumes of Buffer A and a linear NaCl gradient of 30-130 mM. The eluant was monitored by absorbance at 280 nm ( $A_{280}$ ) and 12 mL fractions were collected. Fractions were pooled as to  
5 extent of pegylation, e.g., mono, di, tri etc. (as assessed in example 15). The pH of the pool was lowered to 7.5 using 1M HCl, and the pool was then concentrated to 1-5 mg/mL in an 10 K Omegacell stirred cell concentrator (Filtron Technology Corporation,  
10 Northborough, MA). Protein concentration of pool was determined by  $A_{280}$  using an extinction coefficient of 0.97%. Total yield of purified mono 30 K PEG-aldehyde ProGP from this process was 25-30 %.

#### 15 *Cation Exchange Chromatography*

Cation exchange chromatography is carried out on an SP Sepharose high performance column (Pharmacia XK 26/20, 70 ml bed volume) equilibrated in 10 mM sodium acetate  
20 pH 4.5 (Buffer C). The reaction mixture is diluted 10X with buffer C and loaded onto the column at a flow rate of 5 mL/min. Next the column is washed with 5 column volumes of buffer C, followed by 5 column volumes of 12% buffer D (10 mM acetate pH 4.5, 1 M NaCl).  
25 Subsequently, the PEG-ProGP species are eluted from the column with a linear gradient of 12 to 27% buffer D in 20 column volumes. The eluant is monitored at 280 nm and 10 mL fractions are collected. Fractions are pooled according to extent of pegylation (mono, di, tri  
30 etc.), exchanged into 10 mM acetate pH 4.5 buffer and concentrated to 1-5 mg/mL in a stirred cell fitted with an Amicon YM10 membrane. Protein concentration of pool was determined by  $A_{280}$  nm using an extinction

coefficient of 0.71. Total yield of monopegylated ProGP from this process is 10 to 50%.

#### EXAMPLE 15

5

#### Biochemical Characterization

The purified pegylated ProGP pools were characterized by SDS-PAGE (FIG 3), Non denaturing and denaturing Size  
10 Exclusion Chromatography (FIG 2,4), RP HPLC (FIG 5), Tryptic mapping (FIG 7), and MALDI-TOF 6).

#### *Size Exclusion High Performance Liquid Chromatography (SEC-HPLC)*

15

#### *Non-denaturing SEC-HPLC*

The reaction of 30K Methoxy-PEG propionaldehyde with ProGP, anion exchange purification, and final purified products were assessed using non-denaturing SEC-HPLC  
20 (Figure 2a, 2b). Analytical non-denaturing SEC-HPLC was carried out using a Superdex 200 HR 10/30 column (Amersham Pharmacia Biotech, Piscataway, NJ) in 50 mM Tris pH 7.5, 150 mM NaCl at a flow rate of 0.4 mL/minute.

25 PEGylation greatly increases the hydrodynamic volume of the protein resulting in a shift to an earlier retention time. Two PEGylated species were observed in the 30K PEG aldehyde ProGP reaction mixture along with unmodified ProGP. These PEGylated and non-PEGylated  
30 species were separated on Q-Sepharose chromatography (Fig 1), and the resultant purified mono 30K PEG-Aldehyde ProGP) was subsequently shown to elute as a single peak on non-denaturing SEC (> 95% purity, Figure 2c). The Q-Sepharose chromatography step

effectively removed free PEG, non-PEGylated ProGP dimer and multi PEGylated species from the mono-Pegylated ProGP.

#### 5 *Denaturing SDS SEC-HPLC*

Denaturing SDS SEC, which disassociates the non-covalent ProGP dimer, was used to demonstrate that mono 30K PEG aldehyde ProGP is only PEGylated on one subunit  
10 (monomer) of the ProGP dimer (Fig 4). Denaturing SEC-HPLC was carried out in the same fashion as described for non-denaturing SEC-HPLC with the exception that 0.1% SDS was included in the running buffer. Protein elution was followed by monitoring the absorbance at  
15 220 nm. Purified mono 30K PEG aldehyde ProGP, which elutes as a single peak on non-denaturing SEC, is separated into a PEGylated subunit and a non-PEGylated subunit (as identified below) under denaturing conditions.

20

#### *SDS PAGE*

SDS-PAGE which disassociates the non-covalent ProGP dimer, was used to demonstrate purity and that mono 30K  
25 PEG aldehyde ProGP is only PEGylated on one subunit (monomer) of the ProGP dimer (Figure 3). SDS-PAGE was carried out on 1 mm thick 12% Tris glycine gels (Invitrogen, Carlsbad, CA) under reducing and non-reducing conditions and stained using a Novex Colloidal  
30 Coomassie <sup>TM</sup> G-250 staining kit gels (Invitrogen, Carlsbad, CA). Purified mono-30K PEG aldehyde ProGP, which elutes as a single peak on non-denaturing SEC, is separated into a PEGylated subunit and a non-PEGylated subunit.

*Reversed Phase HPLC (RP HPLC)*

RP HPLC was carried out on a Phenomenex Jupiter C<sub>18</sub>  
5 column (4.6 X 250 mm, 5µm particle size) at a  
temperature of 50°C samples were loaded onto the column  
equilibrated in 40% acetonitrile, 0.1% TFA at 1 mL/min.  
The column was washed with 3 mL 58% acetonitrile.  
Subsequently, the protein was eluted with a gradient  
10 from 58 to 63% acetonitrile over 27 minutes.  
Preparative and analytical RP-HPLC was carried out on a  
Jupiter C<sub>18</sub> column, 4.6 X 250 mm, 5mm particle size,  
(Phenomenex, Torrance, CA) at a temperature of 50 °C.  
Samples were loaded onto the column equilibrated in 40%  
15 acetonitrile, 0.1% TFA at 1 mL/min. The column was  
washed with 3 mL 58% acetonitrile. Subsequently, the  
protein was eluted with a gradient from 58 to 63%  
acetonitrile over 27 minutes. The eluent was monitored  
for absorbance at 214 nm. Purified PEG-ProGP, which  
20 elutes as a single peak on non-denaturing SEC, is  
separated (Fig 5) into a PEGylated subunit and a non-  
PEGylated subunit (as identified below) under  
denaturing conditions. In order to confirm the  
identity of each species, peaks from RP-HPLC elution  
25 (Fig 5) were collected for MALDI-TOF MS and N-terminal  
sequencing experiments.

*N-terminal Sequence and Peptide Mapping*

30 Automated Edman degradation chemistry was used to  
determine the NH<sub>2</sub>-terminal protein sequence (SOP  
400.324). An Applied Biosystems Model 494 Procise  
sequencer (Perkin Elmer, Wellesley, MA) was employed  
for the degradation. The respective PTH-AA derivatives

were identified by RP-HPLC analysis in an on-line fashion employing an Applied Biosystems Model 140C PTH analyzer fitted with a Perkin Elmer/Brownlee 2.1 mm i.d. PTH-C18 column. N-terminal sequencing of the RP-HPLC peak (figure 5) corresponding to the correct mass for PEG-ProGP resulted in two signals. A major signal (approximately 75% yield) had the expected sequence for PEG-ProGP except for the absence of the N-terminal amino acid. This result is as expected for a N-terminally PEGylated protein. The residue of the first cycle is unrecoverable due to the attached PEG moiety. A minor signal (approximately 25% yield) had the correct N-terminal amino acid sequence. Considering that the peak collected off the RP-HPLC is 100% PEGylated, these data suggest that 75% of the PEG modification is at the N-terminus with remainder apparently linked to one of several possible lysine residues.

#### 20 Tryptic digest

PEGylated ProGP was digested at 1 mg/mL with trypsin (Promega) Dulbecco's modified PBS (Pierce), 10 mM Tris, pH 7.5 (Sigma) Trypsin at 50:1, reconstituted in 40% ACN (B&J), 0.1% TFA (Pierce). Following digestion overnight at 37°, a second aliquot of trypsin was added and the solution again digested overnight at 37°. Digestion was terminated with 5% 1.0 N HCl (Fisher), and, when necessary, the digest was stored at 4° until use. 175 µg was injected onto a TosohHaas 3000PW column equilibrated in 35% ACN, 0.1% TFA at 0.5 mL/min, and eluted over 50 minutes (FIG 7). Fractions were collected manually from 0 to 25 minutes. The fraction containing PEGylated fragments were sequenced by Edman chemistry. The results indicated that about 77% of the

PEG conjugation occurred at the alpha amino group on the N-terminal alanine, with the remaining 23% distributed as 14% at K284, 5% at K201, and 4% at K252. Matrix Assisted Laser Desorption Ionization Time of Flight Mass Spectrometry (MALDI-TOF MS)

RP-HPLC purified PEGylated, non-PEGylated monomers of ProGP were concentrated, and approximately 1  $\mu$ L of the concentrate was spotted onto a MALDI target with 3, 5-dimethoxy-4-hydroxy-cinnamic acid as the matrix. Spectra were obtained using a Perseptive Biosystems Voyager MALDI-TOF (Perseptive Biosystems,) by monitoring positive ions in the linear mode. One hundred twenty three scans were collected and averaged. Masses were calculated using BSA as a standard. MALDI-TOF MS confirmed the correct masses for each subunit as mono-30K PEGylated-ProGP-4 (PEG-ProGP) monomer (Fig 6) and non-PEGylated ProGP-4 monomer (data not shown). The early eluting peak had a molecular mass of 71,000 kDa corresponding to 32,000 kDa PEG plus 39,000 kDa ProGP-4. The late eluting peak had correct the molecular mass (39,000 kDa ) for ProGP-4.

#### EXAMPLE 16

25

#### BAF3/G-CSFR Cell Proliferation Assay

Mouse BaF3 cell lines transfected with genes encoding the human G-CSF receptor (mBaF3/hG-CSFR) were used to examine hG-CSF agonist activity. mBaF3/hG-CSFR cells were seeded at  $2.5 \times 10^4$  cells/well in 96 well microtiter plates containing serial dilution of ProGP and PEGylated ProGP. Cells were pulsed at  $T_{56}$  hours with [methyl- $^3$ H]-thymidine at 0.5 mCi per well for 18

hours. Plates were harvested onto glass fiber filter mats, and the incorporated radioactivity was measured by scintillation spectroscopy. The assay medium for the cell lines consisted of IMDM supplemented with  
5 bovine serum albumin (BSA) (Boehringer Mannheim, Indianapolis, IN), 500  $\mu$ g/ml, human transferrin (Sigma, St. Louis, MO), 100  $\mu$ g/ml, a lipid substitute consisting of 2.5 mg of phosphatidyl choline/ml of BSA and 50 mM 2-mercaptoethanol. The G-CSF receptor agonist  
10 activity of PEG-ProGP was enhanced when compared to ProGP-4 (Table 1).  $EC_{50}$  value for PEG-ProGP (.005 nM) was approximately 4 fold lower ( $p < 0.05$ ) than that determined for ProGP-4 (.021 nM).

15

## EXAMPLE 17

## BAF3/Flt3 Cell Proliferation Assay

A chimeric Flt3/G-CSF receptor molecule was constructed  
20 using the extracellular and transmembrane domains of human Flt3, a human IL-3 leader sequence, and the cytoplasmic domain of human G-CSF receptor. The resulting construct was used to transfect the mouse lymphoid cell line Baf/3. The protocol described  
25 produced stable clones of Baf/3 that proliferated in response to human FL but not to other human cytokines tested. This clonal line was used to analyze the Flt3 agonist activity of ProGP and pegylated ProGP. Cells were seeded at  $2.5 \times 10^4$  cells/well in 96 well  
30 microtiter plates containing serial dilutions of each growth factor in serum free IMDM, human transferrin (100  $\mu$ g/ml), lipid substitute of 2.5 mg phosphatidyl choline/ml bovine serum albumin (500  $\mu$ g/ml), and 2-mercaptoethanol (50  $\mu$ m). After 56hr, cells were pulsed

with methyl  $^3\text{H}$  thymidine at 0.5  $\mu\text{Ci}$  per well for 14-18hr, harvested and incorporated radioactivity was measured by scintillation spectroscopy. The PEGylated forms of ProGP maintained the biological activity of ProGP-4 (Table 1).

Table 1 Comparison of ProGP-4 and 30 K PEG ALD ProGP-4 (Example 1) Induced Cell Proliferation

|                | BAF3/Flt                              |                            | BAF3/G-CSF                           |                            |
|----------------|---------------------------------------|----------------------------|--------------------------------------|----------------------------|
|                | Average<br>EC <sub>50</sub><br>(n=12) | Average<br>Rel.<br>Potency | Average<br>EC <sub>50</sub><br>(n=9) | Average<br>Rel.<br>Potency |
| r-hG-CSF       | >200                                  | n/a                        | 0.025 $\pm$<br>0.010                 | 1.00                       |
| r-hFlt3        | 0.03 $\pm$<br>0.03                    | 1.00                       | >2.0                                 | n/a                        |
| ProGP          | 0.25 $\pm$<br>0.17†                   | 0.16 $\pm$<br>0.17         | 0.021 $\pm$<br>0.013†                | 1.16 $\pm$<br>0.98         |
| Peg<br>ProGP-4 | 0.63 $\pm$<br>0.48†                   | 0.05 $\pm$<br>0.03         | 0.005 $\pm$<br>0.003†                | 8.37 $\pm$<br>5.78         |

10

## EXAMPLE 18

*CFU-GM clonogenic assays*

Expansion of hematopoietic progenitors was demonstrated using human bone marrow -derived CD34+ cells in a colony forming unit granulocyte/macrophage (CFU-GM) assay, where clonogenic progenitors divide and differentiate in a semi-solid media in response to growth factors. Fresh bone marrow (BM) aspirates were obtained through a collaboration with the St. Louis University Medical School. Mononuclear cell fractions were recovered following density gradient centrifugation with Ficoll-Hypaque. CD34<sup>+</sup> (stem and

progenitor) cells were subsequently isolated by positive selection using the Isolex 50 stem cell reagent kit (Baxter Healthcare Corporation, Deerfield, IL). This procedure yields an enriched cellular  
5 product where >90% of the cells express the CD34+ cell surface antigen. These CD34<sup>+</sup> cells were seeded in 35 mm tissue culture plates (10,000 cells/dish) in MethoCult H4230 (StemCell Technologies, Vancouver, BC) containing 0.9% Methylcellulose in Iscove's modified Dulbecco's  
10 medium (IMDM), 30% FBS, 1% BSA, 1 mM 2-mercaptoethanol and 2mM L-glutamine.

Cultures were incubated with growth factors for 10-12 days at 37°C in humidified air containing 5% CO<sub>2</sub>. The  
15 concentrations of the respective receptor agonists in co-addition experiments are equimolar each at the indicated concentration value. Hematopoietic colonies (>50 cells) were counted using an inverted microscope. The Peg ProGP induced differentiation and expansion of  
20 hematopoietic progenitor cells into colony forming unit granulocyte/macrophage cells (CFU-GM) was equal to the response elicited from ProGP-4 or co-administration of human flt3 ligand and hG-CSF (Fig 8).

25

## Example 19

## Growth Factor Administration For Pharmacokinetics (PK)

Female C57BL/6 (8-12 wk old, Charles River, Raleigh,  
30 NC) mice were housed in the Pharmacia animal facility. ProGP and Pegylated ProGP were diluted in PBS (Life Technologies, Grand Island, NY) and administered to mice at a dose of 100 µg/injection. Mice were injected a single subcutaneous (SC) dose.

## ProGP ELISA

ProGP and pegylated ProGP protein concentration levels  
5 in mouse plasma were determined using a sandwich ELISA.  
96-well microtiter plates were coated with 150  $\mu$ l/well  
affinity purified goat-anti-Flt3 ligand polyclonal  
diluted to 1  $\mu$ g/ml in 100mM NaHCO<sub>3</sub>, pH 8.2. Plates were  
incubated overnight at room temperature in a humidified  
10 chamber and blocked for one hour at 37 °C with  
phosphate buffered saline, containing 3 BSA and 0.05%  
Polyoxyethylene-Sorbitan Monolaurate (Tween 20), pH  
7.4. Plates were washed four times with 150 mM NaCl  
containing 0.05% Tween 20 (wash buffer). Plasma PK  
15 samples were diluted in assay buffer (PBS, 0.1% BSA,  
0.01% Tween 20), pH 7.4 and titered 1:2 in an assay  
matrix of mouse pooled plasma. The plasma  
concentration of the matrix and the samples were  
matched by percentage. Plates were incubated for 2.5  
20 hours at 37°C in a humidified chamber, then washed 4  
times with wash buffer. Affinity purified goat-anti-  
human G-CSF receptor agonist polyclonal antibody  
conjugated to horse radish peroxidase was diluted  
1:10000 (0.25-.05  $\mu$ g/mL) in assay buffer and 150  $\mu$ l  
25 were added to each well. Plates were incubated for 1.5  
hours at 37°C in a humidified chamber. Wells were  
emptied and each well was again washed four times with  
wash buffer. Each well then received 150  $\mu$ l of TMB  
peroxidase substrate solution. Plates were incubated  
30 at room temperature for about 10 minutes and read at a  
test wavelength of 650 nm on a microtiter plate reader  
(Molecular Devices Corporation). Concentrations of  
immuno-reactive ProGP in unknown PK samples were  
calculated from a standard curve of either ProGP-4 or

PEG-ProGP using a four parameter curve fitting program supplied by Molecular Devices.

#### Pharmacokinetic Data Analysis

5

PK parameters reported in Table 2 were determined by noncompartmental analysis using WinNonlin (version 3.0, Pharsight, Chapel Hill, NC). Plasma concentration data (n=3) were averaged and a single PK analysis was performed on the mean. The apparent terminal half life ( $t_{1/2}$ ) was manually selected during non-compartmental analysis by visual inspection of log-linear plot of plasma concentration vs. time. A comparison of the pharmacokinetics of ProGP-4 and PEG-ProGP are shown in Figure 9 and Table 2. The data show that a single 100  $\mu$ g dose of PEG-ProGP in mice, administered subcutaneously, has a protracted plasma residency time versus that of ProGP-4. At 48 hours the concentration of PEG-ProGP in the plasma was approximately 70 fold higher than ProGP-4. Detectable levels of PEG-ProGP were observed 96 hours after dosing while ProGP-4 was not detectable at 72 hours. PK values such as terminal half life ( $t_{1/2}$ ), clearance (Cl), time to maximum concentration (Tmax) and maximum concentration (Cmax) were not significantly different for PEG-ProGP and ProGP-4. In summary, PEGylation extends the time at which the protein circulates in the blood in mice.

10  
15  
20  
25

Table 2 Comparison of ProGP-4 and PEG ProGP-4  
(Example 1) Pharmacokinetics in mice

|                | Mice<br>(n) | Dose<br>( $\mu$ g/<br>mouse) | T*max                  | C*max  | AUC<br>(I) | CL/F   | Vd/F  | t <sub>1/2</sub> | C <sub>48 hr</sub> |
|----------------|-------------|------------------------------|------------------------|--------|------------|--------|-------|------------------|--------------------|
| ProGP          | 3           | 100                          | 8                      | 28,000 | 529        | 0.189  | 0.944 | 3.46             | 72                 |
| PEG<br>ProGP-4 | 3           | 100                          | (8)<br>24 <sup>a</sup> | 19,500 | 720        | 0.139  | 0.977 | 4.87             | 4744               |
| PEG<br>ProGP-4 | 3           | 100                          | 8                      | 40,500 | 1080       | 0.0926 | 0.657 | 4.92             | 4181               |

5

#### Growth Factor Administration for Pharmacodynamics (PD)

Female C57BL/6 (8-12 wk old, Charles River, Raleigh, NC) mice were housed in the Pharmacia animal facility.

10 ProGP-4 and PEG-ProGP were diluted in PBS (Life Technologies, Grand Island, NY) and administered to mice at doses ranging between 100 to 500  $\mu$ g/injection. Mice were injected subcutaneous (SC) as follows:  
ProGP-4 dosed daily either on days 0 - 6 or days 0 - 9  
15 (0.1 mg/injection); PEG-ProGP dosed either on days 0, 3 and 6 or 0, 3, 6 and 9 (0.3 mg /injection); PEG-ProGP dosed on days 0 or days 0 and 5 (0.5 mg/injection). Vehicle controls dosed daily on days 0 - 9 with PBS (0.1 ml/injection).

20

#### Peripheral Blood and Spleen Processing

Peripheral blood was collected from CO<sub>2</sub>-anesthetized mice into heparin-coated tubes by cardiac puncture.

25 Spleens were harvested from euthanized animals immediately following blood collection. A total white blood cell (WBC) count was done on whole blood using a cell counter (Coulter ZM, Miami Lakes, FL).

Erythrocytes were lysed using a 0.15 M hypotonic  
30 ammonium chloride solution (Stem Cell Technology,

Vancouver, BC). Cells were collected by centrifugation (300xg for 10 min) and washed with cold IMDM (Life Technologies, Grand Island, NY) containing 2% FBS (IMDM-FBS, Bioproducts for Science, Indianapolis, IN).  
5 Splens were collected and processed in cold IMDM-FBS, homogenized into a cell suspension and filtered through a 70 um nylon mesh. Erythrocytes were lysed using hypotonic ammonium chloride solution, spleen cells were washed with cold IMDM-FBS and filtered through a 70 um  
10 mesh. Spleen cells were resuspended in 25 ml of IMDM buffer containing 2% BSA and counted to determine total number of splenocytes/spleen.

#### Flow Cytometry Reagents

15 Fluorochrome- or biotin-conjugated monoclonal antibodies were purchased from Pharmingen (San Diego, CA). CD16/CD32 (Fc II/III receptor antibody, Fc Block), FITC-conjugated antibodies CD11c/HL3 and PE-conjugated  
20 antibodies MHC Class II (I-A<sup>b</sup>/AF6-120.1) were used at 1-5 µg/ml. Isotype matched controls were used for the different antibody combinations.

The total white blood cell (WBC) and dendritic cell (DC)  
25 responses in the spleen were similar for PEG-ProGP dosed every third day compared to ProGP-4 dosed daily (Fig 10) . The relative DC response in the peripheral blood at day 10 was greater for PEG-ProGP dosed every third day compared to ProGP-4 dosed every day. DC mobilization kinetics (Fig 11)  
30 are similar for ProGP-4 and PEG-ProGP-4 (Example 1) in the spleen; whereas, in the peripheral blood the DC mobilization kinetics are modified for PEG-ProGP-4 (Example 1) dosed every third day when compared to ProGP-4 dosed every day.

35

## WHAT IS CLAIMED IS:

1. A Progenipoietin conjugate having at least one water-soluble polymer molecule covalently attached  
5 to at least one amino acid residue of a biologically active Progenipoietin polypeptide.

2. The Progenipoietin conjugate of claim 1 wherein said polymer is a poly(ethylene oxide)  
10 molecule.

3. The Progenipoietin conjugate of claim 2 wherein said poly(ethylene oxide) molecule is a poly(ethylene glycol) molecule.  
15

4. The Progenipoietin conjugate of claim 3 wherein the poly(ethylene glycol) is attached at an amino acid residue having a free amino, carboxyl or sulfhydryl group(s).  
20

5. The Progenipoietin conjugate of claim 4 wherein said poly(ethylene glycol) is conjugated through a activated poly(ethylene glycol).

25 6. The Progenipoietin conjugate of claim 5 wherein said activated poly(ethylene glycol) is selected from the group consisting of, para-nitrophenyl, succinimidyl, carbonyl imidazole, azlactones, cyclic imide thiones, isocyanates,  
30 isothiocyanates, aldehydes, primary amines, hydrazine, acyl hydrazides, carbazates, semicarbamates, thiocarbazates, thiols, maleimides, sulfones, and phenyl glyoxals.

7. The Progenipoietin conjugate of claim 6 wherein  
said activated poly(ethylene glycol) is selected from the  
group consisting of, succinimidyl, carbonyl imidazole,  
aldehydes, acyl hydrazides, carbazates, semicarbamates, and  
5 maleimides.

8. The Progenipoietin conjugate of claim 7 wherein  
said poly(ethylene glycol) has a molecular weight of between  
about 0.5 kDa and about 100 kDa.

10

9. The Progenipoietin conjugate of claim 8 wherein  
said poly(ethylene glycol) has a molecular weight of between  
about 3.4 kDa and about 40 kDa.

15

10. The Progenipoietin conjugate of claim 4 wherein  
said poly(ethylene glycol) is a branched polymer.

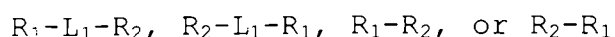
20

11. The Progenipoietin conjugate of claim 10 wherein  
branched poly(ethylene glycol) polymer has a molecular weight  
of between about 10 kDa and about 40 kDa.

12. The Progenipoietin conjugate of claim 4 wherein  
said poly(ethylene glycol) is a bifunctional polymer.

25

13. The Progenipoietin conjugate of any one of claims  
1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 wherein said  
Progenipoietin polypeptide is of the formula:



wherein  $R_1$  is a polypeptide comprising; a modified

flt-3 ligand amino acid sequence of the Formula:

```

    ThrGlnAspCysSerPheGlnHisSerProIleSerSerAspPheAlaValLysIleArg
                                10                                20
5   GluLeuSerAspTyrLeuLeuGlnAspTyrProValThrValAlaSerAsnLeuGlnAsp
                                30                                40
    GluGluLeuCysGlyGlyLeuTrpArgLeuValLeuAlaGlnArgTrpMetGluArgLeu
10  GluGluLeuCysGlyGlyLeuTrpArgLeuValLeuAlaGlnArgTrpMetGluArgLeu
                                50                                60
    LysThrValAlaGlySerLysMetGlnGlyLeuLeuGluArgValAsnThrGluIleHis
                                70                                80
15  PheValThrLysCysAlaPheGlnProProProSerCysLeuArgPheValGlnThrAsn
                                90                                100
    IleSerArgLeuLeuGlnGluThrSerGluGlnLeuValAlaLeuLysProTrpIleThr
                                110                               120
20  ArgGlnAsnPheSerArgCysLeuGluLeuGlnCysGlnProAsrSerSerThrLeu
                                130                               SEQ ID NO:1

```

wherein the N-terminus is joined to the C-terminus  
 25 directly or through a linker (L<sub>2</sub>) capable of joining the  
 N-terminus to the C-terminus and having new C- and N-  
 termini at amino acids;

|       |       |               |
|-------|-------|---------------|
| 28-29 | 42-43 | 93-94         |
| 29-30 | 64-65 | 94-95         |
| 30-31 | 65-66 | 95-96         |
| 31-32 | 66-67 | 96-97         |
| 32-33 | 86-87 | 97-98         |
| 34-35 | 87-88 | 98-99         |
| 36-37 | 88-89 | 99-100        |
| 37-38 | 89-90 | 100-101       |
| 38-39 | 90-91 | 101-102       |
| 39-40 | 91-92 | 102-103       |
| 40-41 | 92-93 | respectively; |
| 41-42 |       |               |

30

wherein R<sub>2</sub> is a factor selected from the group  
 consisting of: a colony stimulating factor, a cytokine,  
 a lymphokine, an interleukin, and a hematopoietic  
 growth factor;

35

wherein L<sub>1</sub> is a linker capable of linking R<sub>1</sub> to R<sub>2</sub>;

and

said Progenipoietin protein can optionally be immediately preceded by (methionine<sup>-1</sup>), (alanine<sup>-1</sup>) or (methionine<sup>-2</sup>, alanine<sup>-1</sup>).

5

14. A composition comprising the Progenipoietin protein of any one of claims 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 and at least one pharmaceutically acceptable carrier.

10 15. A use of the Progenipoietin conjugate of any one of claims 1 to 12 in the manufacture of a medicament for use in a method of treating a patient having a hematopoietic disorder comprising administering to said patient a therapeutically effective amount of the Progenipoietin  
15 conjugate.

16. The use of claim 15 wherein said hematopoietic disorder is neutropenia, leukopenia, thrombocytopenia, or anemia.

20

17. The use of claim 16 wherein said hematopoietic disorder is the result of chemotherapy, radiation therapy, or bone marrow suppressive drugs.

25 18. A use of the Progenipoietin conjugate of any one of claims 1 to 12 in the manufacture of a medicament for use in a method of treating a patient recovering and/or suffering from a bone marrow transplant, burn, wound, parasite, bacterial or viral infection comprising administering to said  
30 patient a therapeutically effective amount of the Progenipoietin conjugate.

19. A use of the Progenipoietin conjugate of any one of claims 1 to 12 in the manufacture of a medicament for use in a method of mobilizing hematopoietic progenitors and stem cells into peripheral blood comprising administering to a patient a therapeutically effective amount of the Progenipoietin conjugate.

20. A method for the production of dendritic cells comprising the steps of;

a) separating hematopoietic progenitor cells or CD34+ cells from other cells; and

b) culturing said hematopoietic progenitor cells or CD34+ cells in a growth medium, comprising the hematopoietic protein of any one of claims 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12.

21. The method of claim 20, further comprising the step of;

c) pulsing said culturing hematopoietic progenitor cells or CD34+ cells with an antigen.

22. The method of claim 20, wherein said growth medium, further comprises; one or more factor selected from the group consisting of; GM-CSF, IL-4, TNF- $\alpha$ , stem cell factor (SCF), flt-3 ligand, IL-3, an IL-3 variant, an IL-3 variant fusion protein, and a multi-functional receptor agonist.

23. The method of claim 21, wherein said growth medium, further comprises; one or more factor selected from the group consisting of; GM-CSF, IL-4, TNF- $\alpha$ , stem cell factor (SCF), flt-3 ligand, IL-3, an IL-3 variant, an IL-3 variant fusion protein, and a multi-functional receptor agonist.

24. A use of the hematopoietic protein of any one of claims 1 to 12 in the manufacture of a medicament for use in a method for treating a human having a tumor, infection or auto-immune disease, comprising the step of administering the  
5 hematopoietic protein to said human.

25. The use of claim 24, further comprising; administering one or more factor selected from the group consisting of; GM-CSF, IL-4, TNF- $\alpha$ , stem cell factor (SCF),  
10 flt-3 ligand, IL-3, an IL-3 variant, an IL-3 variant fusion protein, and a multi-functional receptor agonist.

26. A method of conjugating a poly(ethylene glycol) to a nucleophile wherein the conjugation is carried out in the  
15 presence of an inorganic solvent.

27. A Progenipoietin conjugate of claim 1, substantially as herein described with reference to any one of the illustrative examples.  
20

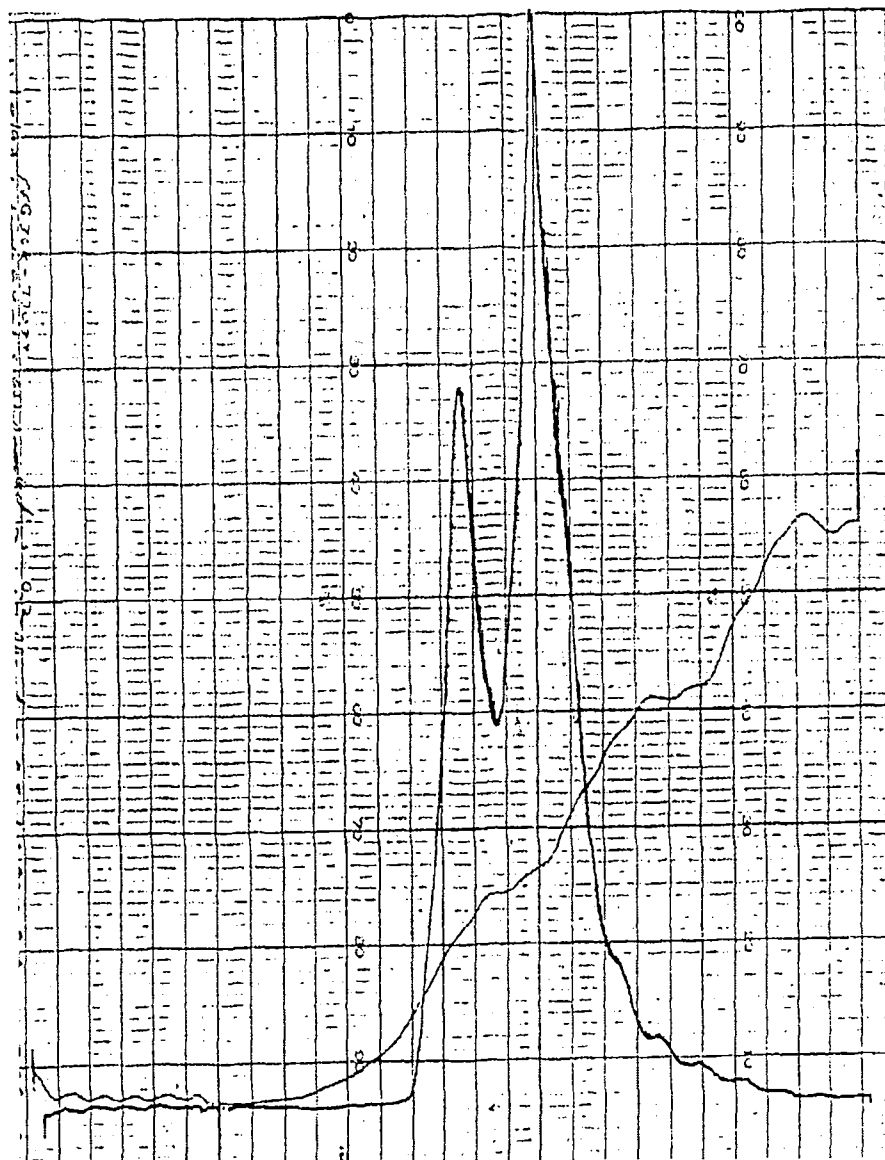
28. A composition of claim 14, substantially as herein described with reference to any one of the illustrative examples.

25 29. A method of claim 20, substantially as herein described with reference to any one of the illustrative examples.

30 30. A method of claim 26, substantially as herein described with reference to any one of the illustrative examples.

**FIG 1**

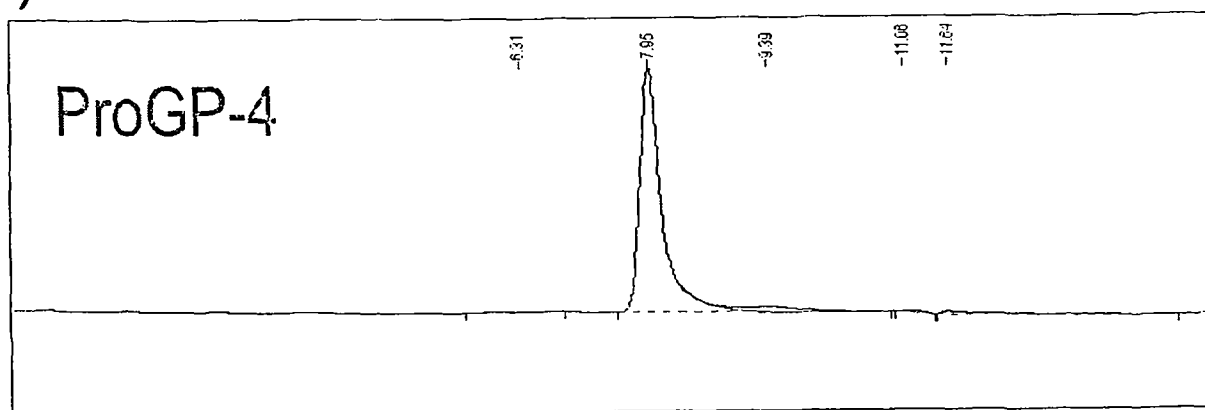
Absorbance 280 nm



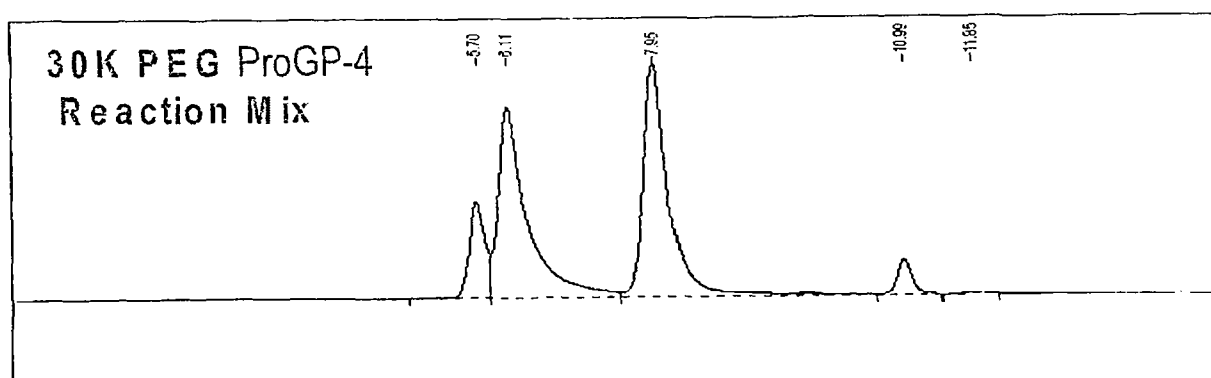
Conductivity

**FIG 2**

a)



b)



c)

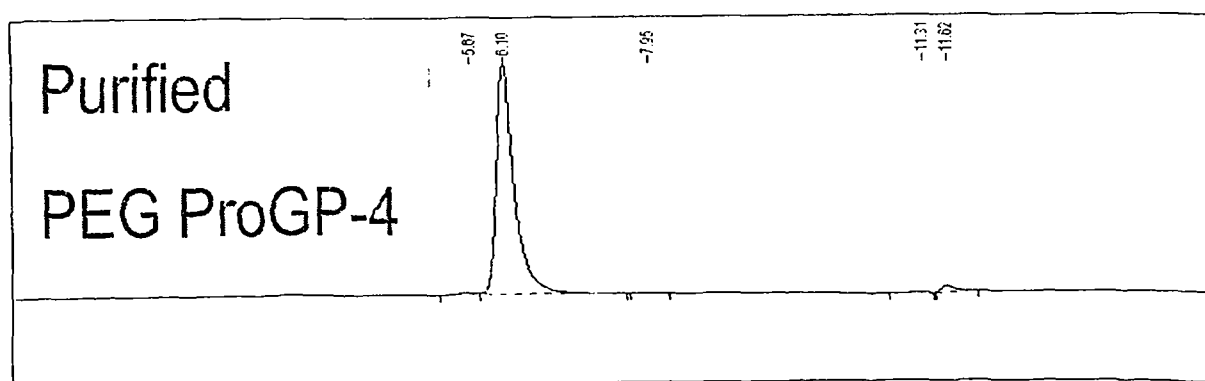


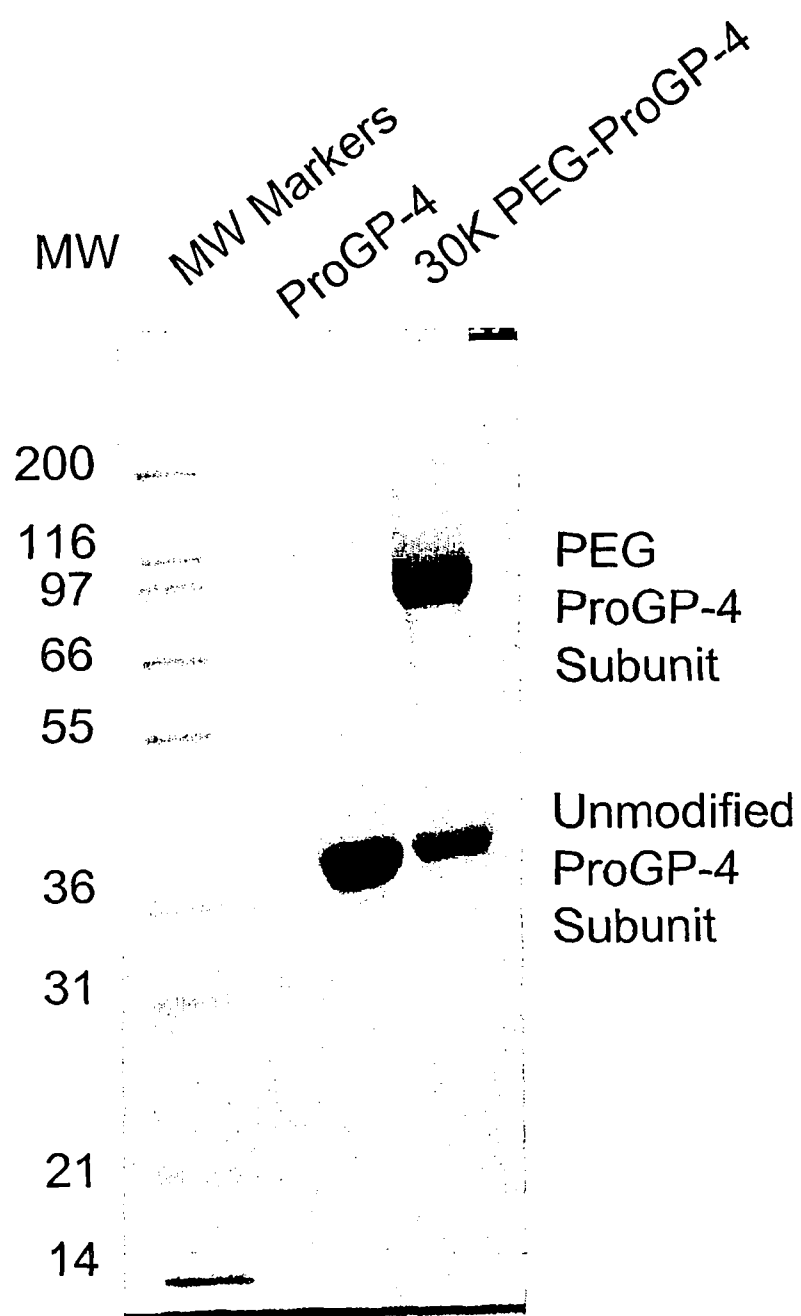
**FIG 3**

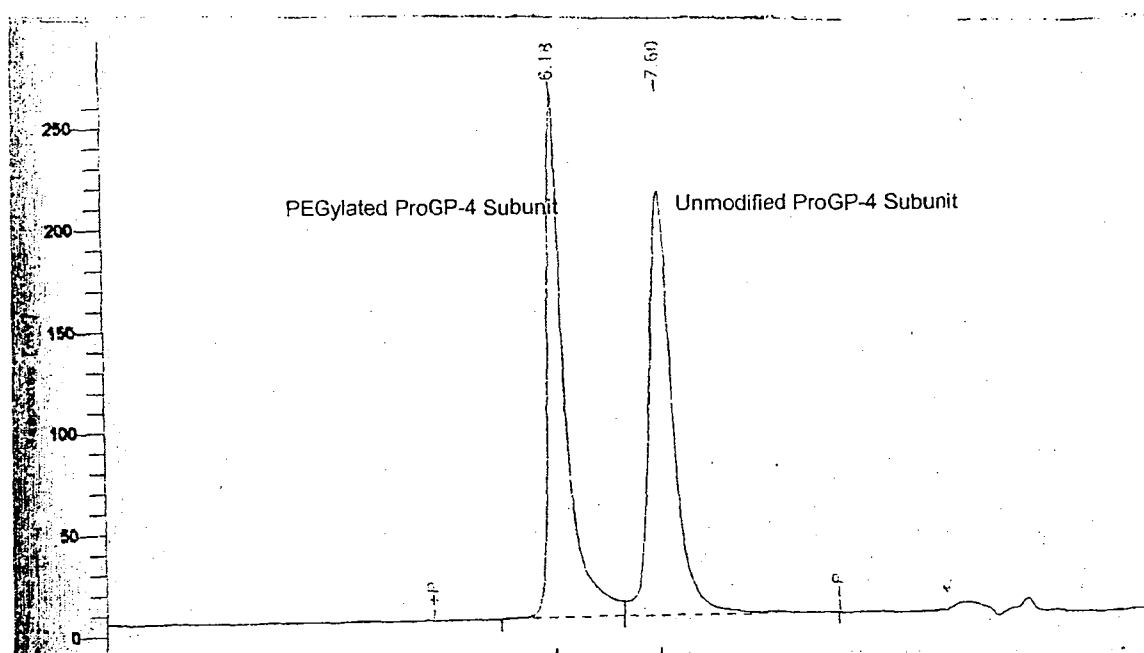
**FIG 4**

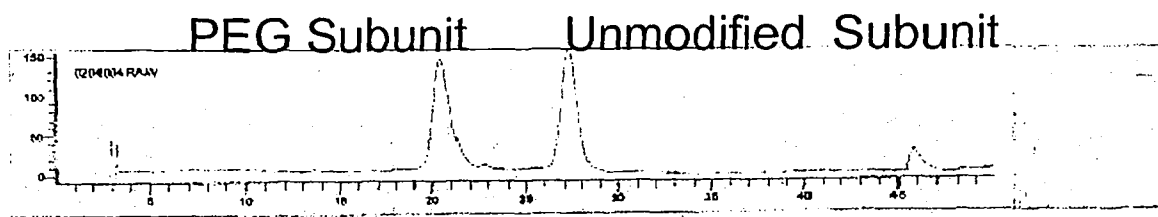
**FIG 5**

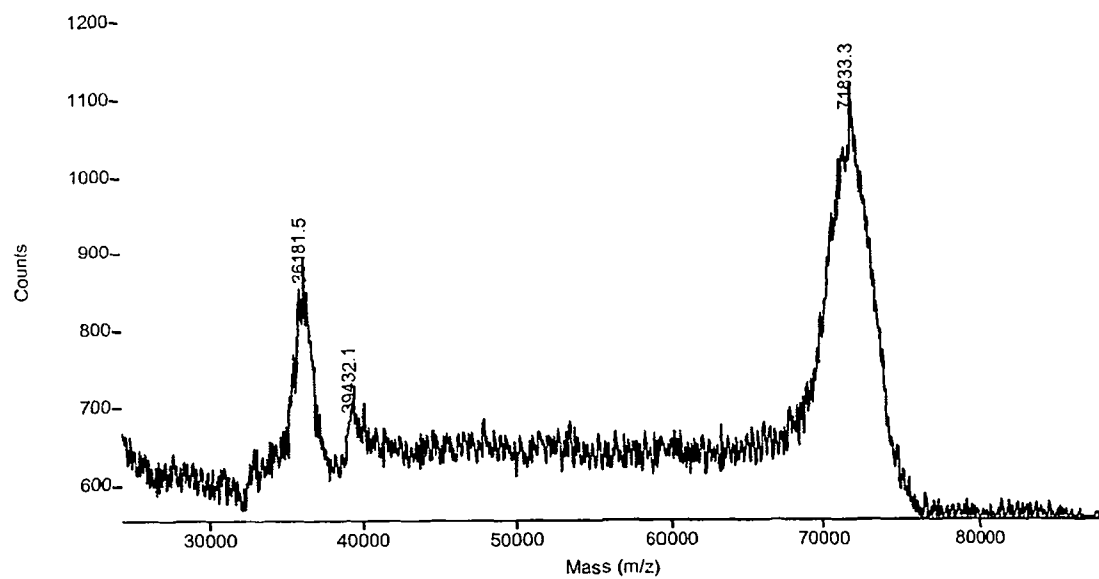
**FIG 6**

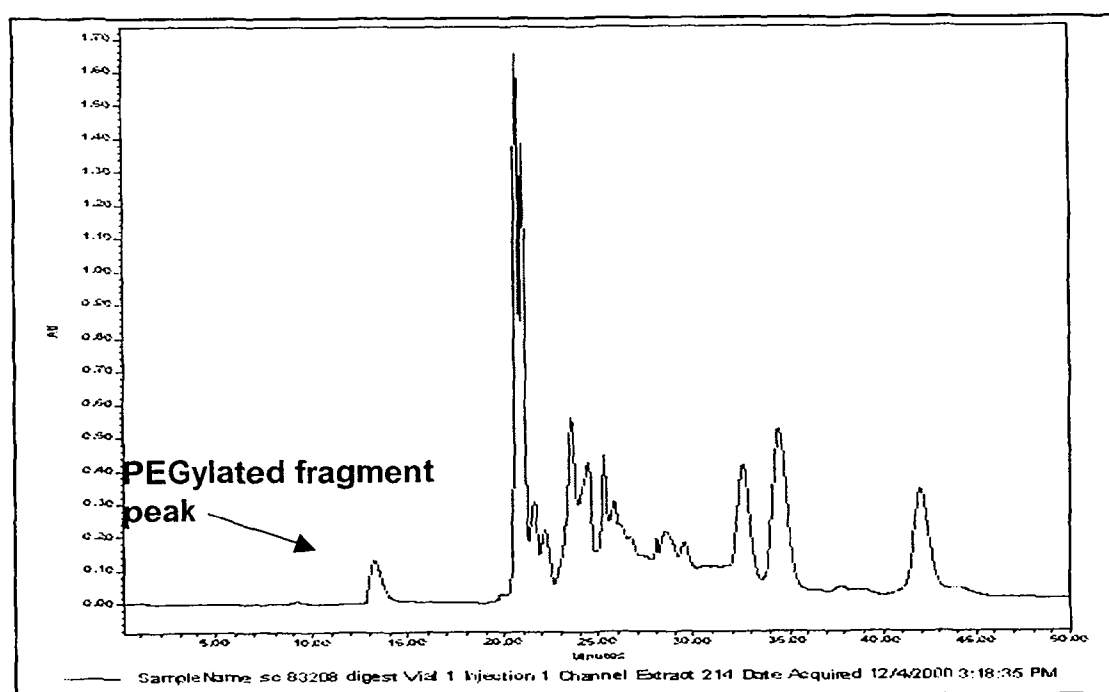
**FIG 7**

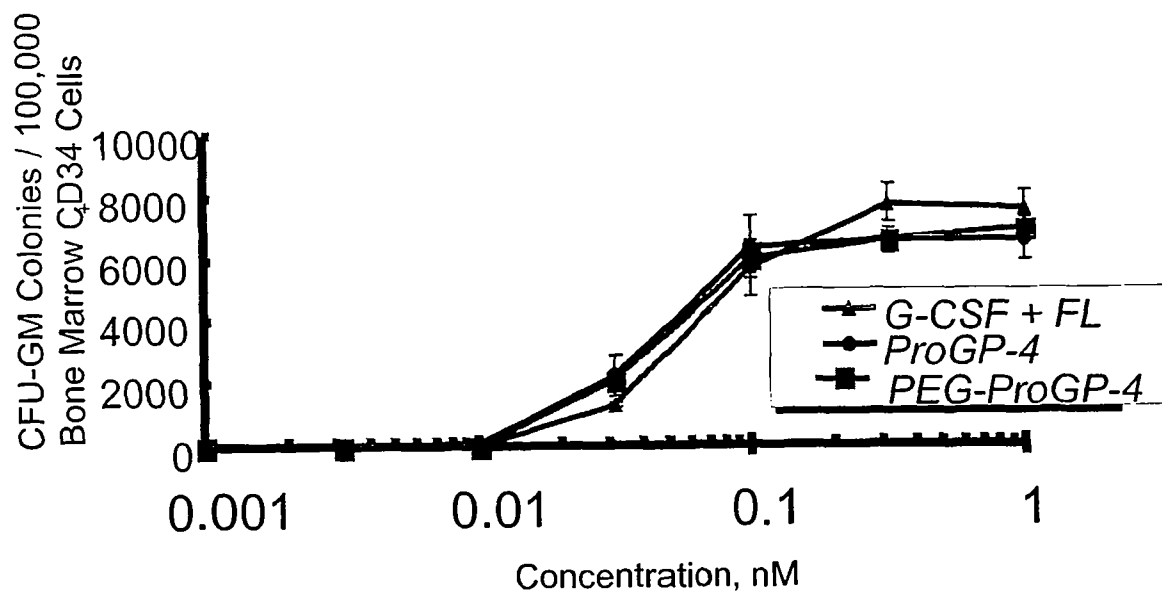
**FIG 8**

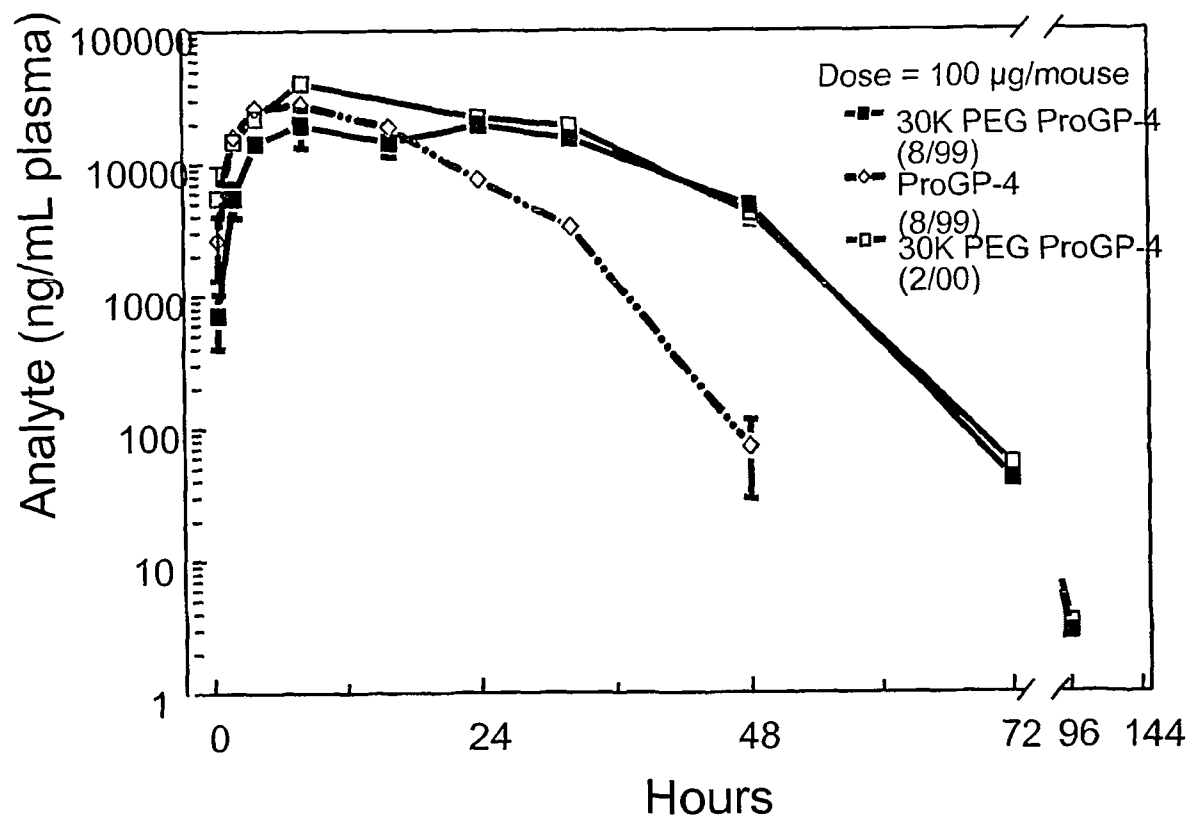
**FIG 9**

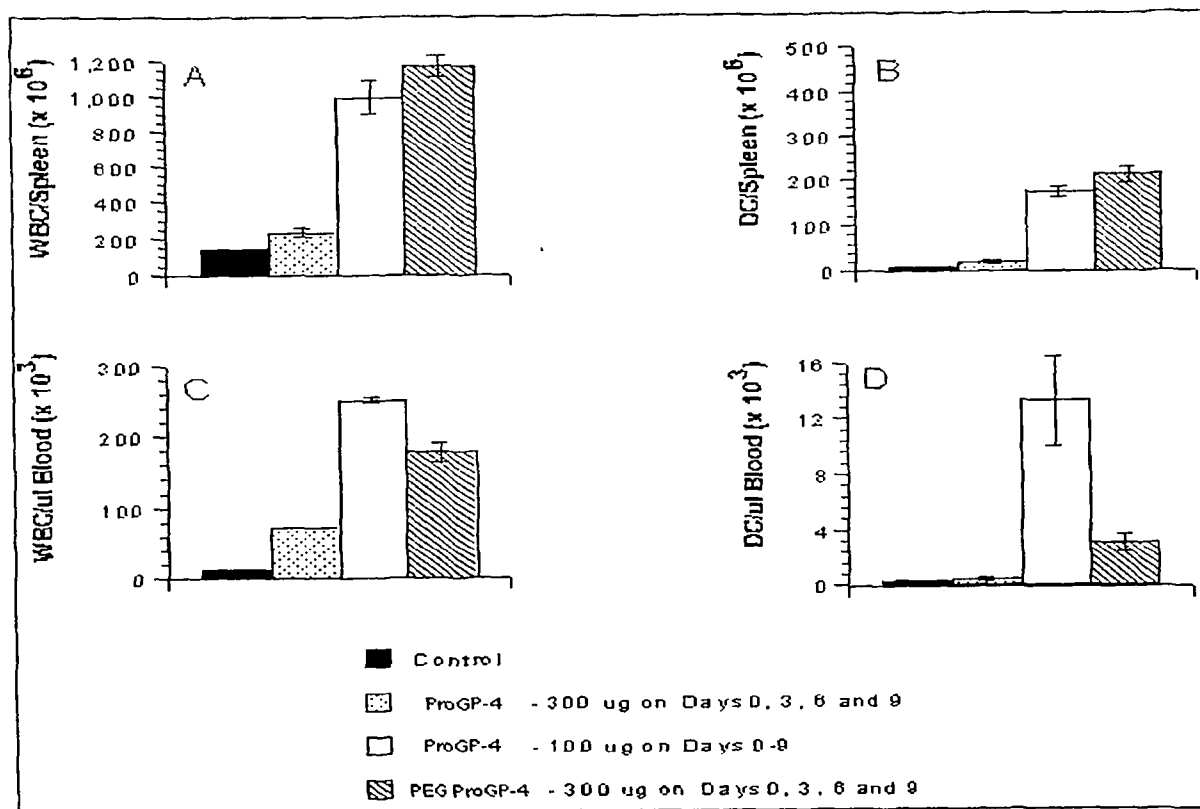
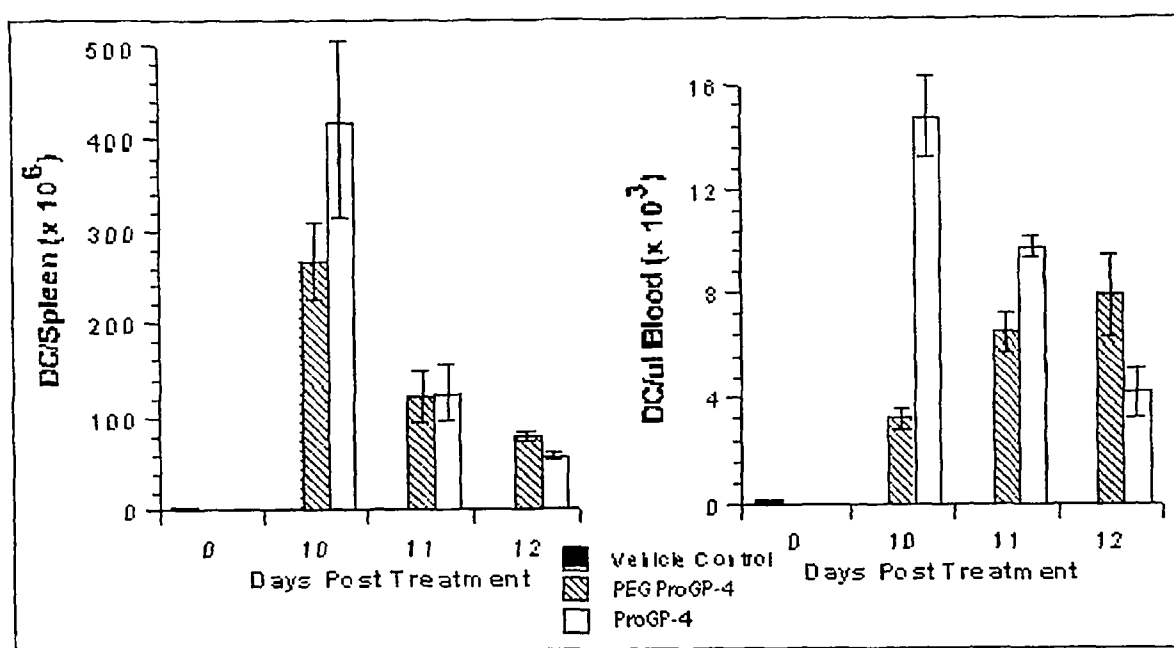
**FIG 10**

**FIG 11**

## FIG 12

AlaThrProLeuGlyProAlaSerSerLeuProGlnSerPheLeuLeuLysSerLeuGlu  
1 20

GlnValArgLysIleGlnGlyAspGlyAlaAlaLeuGlnGluLysLeuCysAlaThrTyr  
21 40

LysLeuCysHisProGluGluLeuValLeuLeuGlyHisSerLeuGlyIleProTrpAla  
41 60

ProLeuSerSerCysProSerGlnAlaLeuGlnLeuAlaGlyCysLeuSerGlnLeuHis  
61 80

SerGlyLeuPheLeuTyrGlnGlyLeuLeuGlnAlaLeuGluGlyIleSerProGluLeu  
81 100

GlyProThrLeuAspThrLeuGlnLeuAspValAlaAspPheAlaThrThrIleTrpGln  
101 120

GlnMetGluGluLeuGlyMetAlaProAlaLeuGlnProThrGlnGlyAlaMetProAla  
121 140

PheAlaSerAlaPheGlnArgArgAlaGlyGlyValLeuValAlaSerHisLeuGlnSer  
141 160

PheLeuGluValSerTyrArgValLeuArgHisLeuAlaGlnProTyrValGluGlyGly  
161 180

GlyGlySerProGlyGluProSerGlyProIleSerThrIleAsnProSerProProSer  
181 200

LysGluSerHisLysSerProAsnMetAlaLeuCysGlyGlyLeuTrpArgLeuValLeu  
201 220

AlaGlnArgTrpMetGluArgLeuLysThrValAlaGlySerLysMetGlnGlyLeuLeu  
221 240

GluArgValAsnThrGluIleHisPheValThrLysCysAlaPheGlnProProProSer  
241 260

CysLeuArgPheValGlnThrAsnIleSerArgLeuLeuGlnGluThrSerGluGlnLeu  
261 280

ValAlaLeuLysProTrpIleThrArgGlnAsnPheSerArgCysLeuGluLeuGlnCys  
281 300

GlnProAspSerSerThrLeuGlyGlyGlySerGlyGlyGlySerGlyGlyGlySerGly  
301 320

GlyGlySerGlyGlyGlySerGlyThrGlnAspCysSerPheGlnHisSerProIleSer  
321 340

SerAspPheAlaValLysIleArgGluLeuSerAspTyrLeuLeuGlnAspTyrProVal  
341 360

ThrValAlaSerAsnLeuGlnAspGluGlu SEQ ID NO:165  
361 370

## SEQUENCE LISTING

<110> Pharmacia  
 <120> TITLE OF THE INVENTION: Multi-functional Chimeric  
 Hematopoietic Receptor Agonists  
 <130> S0-3459/1/PCT  
 <140>  
 <141>  
 <150> US 60/300,362  
 <151> 2001-06-22  
 <160> 262  
 <210> 1  
 <211> 139  
 <212> PRT  
 <213> Unknown  
 <220>  
 <221> MUTAGEN  
 <222> 1-139  
 <223>  
 <400> 1

```

Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala
 1          5          10          15
Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val
          20          25          30
Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp
          35          40          45
Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala
          50          55          60
Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His
65          70          75          80
Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe
          85          90          95
Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu
          100          105          110
Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu
          115          120          125
Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu
          130          135

```

<210> 2  
 <211> 135  
 <212> PRT  
 <213> Unknown  
 <220>  
 <221> MUTAGEN  
 <222> 1-135

&lt;223&gt;

&lt;400&gt; 2

```

Ala Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe
 1          5          10          15
Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro
          20          25          30
Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Ala Leu
          35          40          45
Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val
 50          55          60
Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile
65          70          75          80
His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg
          85          90          95
Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln
          100          105          110
Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys
          115          120          125
Leu Glu Leu Gln Cys Gln Pro
130          135

```

&lt;210&gt; 3

&lt;211&gt; 140

&lt;212&gt; PRT

&lt;213&gt; Unknown

&lt;220&gt;

&lt;221&gt; MUTAGEN

&lt;222&gt; 1-140

&lt;223&gt;

&lt;400&gt; 3

```

Ala Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe
 1          5          10          15
Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro
          20          25          30
Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu
          35          40          45
Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val
 50          55          60
Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile
65          70          75          80
His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg
          85          90          95
Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln
          100          105          110
Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys
          115          120          125
Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu
130          135          140

```

&lt;210&gt; 4

&lt;211&gt; 122

&lt;212&gt; PRT

&lt;213&gt; Unknown

&lt;220&gt;

&lt;221&gt; MUTAGEN

&lt;222&gt; 1-122

&lt;223&gt;

&lt;400&gt; 4

```

Ala Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe
 1          5          10          15
Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro
          20          25          30
Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu
          35          40          45
Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val
          50          55          60
Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile
65          70          75          80
His Phe Val Thr Lys Cys Ala Phe Gln Glu Thr Ser Glu Gln Leu Val
          85          90          95
Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu
          100          105          110
Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu
          115          120

```

&lt;210&gt; 5

&lt;211&gt; 135

&lt;212&gt; PRT

&lt;213&gt; Unknown

&lt;220&gt;

&lt;221&gt; MUTAGEN

&lt;222&gt; 1-135

&lt;223&gt;

&lt;400&gt; 5

```

Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe
 1          5          10          15
Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro
          20          25          30
Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu
          35          40          45
Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val
          50          55          60
Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile
65          70          75          80
His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg
          85          90          95
Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln
          100          105          110
Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys
          115          120          125
Leu Glu Leu Gln Cys Gln Pro
          130          135

```

&lt;210&gt; 6

&lt;211&gt; 140

&lt;212&gt; PRT

&lt;213&gt; Unknown

&lt;220&gt;

&lt;221&gt; MUTAGEN

&lt;222&gt; 1-140

&lt;223&gt;

&lt;400&gt; 6

```

Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe
 1          5          10          15
Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro
          20          25          30
Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu
          35          40          45
Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val
          50          55          60
Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile
65          70          75          80
His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg
          85          90          95
Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln
          100          105          110
Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys
          115          120          125
Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu
          130          135          140

```

&lt;210&gt; 7

&lt;211&gt; 135

&lt;212&gt; PRT

&lt;213&gt; Unknown

&lt;220&gt;

&lt;221&gt; MUTAGEN

&lt;222&gt; 1-135

&lt;223&gt;

&lt;400&gt; 7

```

Ala Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe
 1          5          10          15
Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro
          20          25          30
Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu
          35          40          45
Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val
          50          55          60
Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile
65          70          75          80
His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg
          85          90          95
Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln
          100          105          110
Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys
          115          120          125
Leu Glu Leu Gln Cys Gln Pro
          130          135

```

&lt;210&gt; 8

&lt;211&gt; 140

&lt;212&gt; PRT

&lt;213&gt; Unknown

&lt;220&gt;

&lt;221&gt; MUTAGEN

&lt;222&gt; 1-140

&lt;223&gt;

&lt;400&gt; 8

```

Ala Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe
 1          5          10          15
Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro
          20          25          30
Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu
          35          40          45
Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val
          50          55          60
Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile
65          70          75          80
His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg
          85          90          95
Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln
          100          105          110
Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys
          115          120          125
Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu
          130          135          140

```

&lt;210&gt; 9

&lt;211&gt; 155

&lt;212&gt; PRT

&lt;213&gt; Unknown

&lt;220&gt;

&lt;221&gt; MUTAGEN

&lt;222&gt; 1-155

&lt;223&gt;

&lt;400&gt; 9

```

Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln
 1          5          10          15
Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly
          20          25          30
Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala
          35          40          45
Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser
          50          55          60
Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp
65          70          75          80
Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro
          85          90          95
Asp Ser Ser Thr Leu Ser Gly Gly Asn Gly Ser Gly Gly Asn Gly Ser
          100          105          110
Gly Gly Asn Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser
          115          120          125
Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln
          130          135          140
Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln
          145          150          155

```

&lt;210&gt; 10

&lt;211&gt; 150

&lt;212&gt; PRT

&lt;213&gt; Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-150  
 <223>

<400> 10

```

Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln
 1          5          10          15
Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly
      20          25          30
Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala
      35          40          45
Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser
      50          55          60
Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp
65          70          75          80
Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro
      85          90          95
Asp Ser Ser Thr Leu Ser Gly Gly Asn Gly Ser Gly Gly Asn Gly Thr
      100          105          110
Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val
      115          120          125
Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr
      130          135          140
Val Ala Ser Asn Leu Gln
145          150

```

<210> 11  
 <211> 145  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-145  
 <223>

<400> 11

```

Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln
 1          5          10          15
Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly
      20          25          30
Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala
      35          40          45
Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser
      50          55          60
Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp
65          70          75          80
Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro
      85          90          95
Asp Ser Ser Thr Leu Ser Gly Gly Asn Gly Thr Gln Asp Cys Ser Phe
      100          105          110
Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu
      115          120          125
Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu
      130          135          140
Gln
145

```

<210> 12  
 <211> 155  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-155  
 <223>

<400> 12

```

Ala Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His
 1              5              10              15
Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe
      20              25              30
Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu
      35              40              45
Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu
      50              55              60
Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Ser Gly Gly Asn Gly
65              70              75              80
Ser Gly Gly Asn Gly Ser Gly Gly Asn Gly Thr Gln Asp Cys Ser Phe
      85              90              95
Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu
      100             105             110
Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu
      115             120             125
Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln
      130             135             140
Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly
145              150              155

```

<210> 13  
 <211> 150  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-150  
 <223>

<400> 13

```

Ala Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His
 1              5              10              15
Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe
      20              25              30
Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu
      35              40              45
Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu
      50              55              60
Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Ser Gly Gly Asn Gly
65              70              75              80
Ser Gly Gly Asn Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile
      85              90              95
Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu
      100             105             110
Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu

```

115 120 125  
 Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg  
 130 135 140  
 Leu Lys Thr Val Ala Gly  
 145 150

<210> 14  
 <211> 145  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-145  
 <223>

<400> 14

Ala Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His  
 1 5 10 15  
 Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe  
 20 25 30  
 Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu  
 35 40 45  
 Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu  
 50 55 60  
 Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Ser Gly Gly Asn Gly  
 65 70 75 80  
 Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala  
 85 90 95  
 Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val  
 100 105 110  
 Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp  
 115 120 125  
 Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala  
 130 135 140  
 Gly  
 145

<210> 15  
 <211> 155  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-155  
 <223>

<400> 15

Ala Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser Arg Leu  
 1 5 10 15  
 Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp Ile Thr  
 20 25 30  
 Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser  
 35 40 45  
 Ser Thr Leu Ser Gly Gly Asn Gly Ser Gly Gly Asn Gly Ser Gly Gly  
 50 55 60  
 Asn Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp  
 65 70 75 80

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|
| Phe | Ala | Val | Lys | Ile | Arg | Glu | Leu | Ser | Asp | Tyr | Leu | Leu | Gln | Asp | Tyr |  |
|     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |  |
| Pro | Val | Thr | Val | Ala | Ser | Asn | Leu | Gln | Asp | Glu | Glu | Leu | Cys | Gly | Gly |  |
|     |     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |  |
| Leu | Trp | Arg | Leu | Val | Leu | Ala | Gln | Arg | Trp | Met | Glu | Arg | Leu | Lys | Thr |  |
|     |     |     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |  |
| Val | Ala | Gly | Ser | Lys | Met | Gln | Gly | Leu | Leu | Glu | Arg | Val | Asn | Thr | Glu |  |
|     |     |     |     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |  |
| Ile | His | Phe | Val | Thr | Lys | Cys | Ala | Phe | Gln | Pro |     |     |     |     |     |  |
|     |     |     |     | 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |  |

|       |         |
|-------|---------|
| <210> | 16      |
| <211> | 150     |
| <212> | PRT     |
| <213> | Unknown |

<220>  
<221> MUTAGEN  
<222> 1-150  
<223>

<400> 16

[illegible]

|       |         |
|-------|---------|
| <210> | 17      |
| <211> | 145     |
| <212> | PRT     |
| <213> | Unknown |

<220>  
<221> MUTAGEN  
<222> 1-145  
<223>

<400> 17

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ala | Pro | Pro | Ser | Cys | Leu | Arg | Phe | Val | Gln | Thr | Asn | Ile | Ser | Arg | Leu |
| 1   |     |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |
| Leu | Gln | Glu | Thr | Ser | Glu | Gln | Leu | Val | Ala | Leu | Lys | Pro | Trp | Ile | Thr |
|     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |
| Arg | Gln | Asn | Phe | Ser | Arg | Cys | Leu | Glu | Leu | Gln | Cys | Gln | Pro | Asp | Ser |

```

      35              40              45
Ser Thr Leu Ser Gly Gly Asn Gly Thr Gln Asp Cys Ser Phe Gln His
  50              55              60
Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp
  65              70              75              80
Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln Asp
      85              90              95
Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln Arg Trp
      100              105              110
Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly Leu Leu
      115              120              125
Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala Phe Gln
      130              135              140
Pro
145

```

```

<210>    18
<211>    155
<212>    PRT
<213>    Unknown

```

```

<220>
<221>    MUTAGEN
<222>    1-155
<223>

```

```

<400>    18

```

```

Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln
  1              5              10              15
Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly
      20              25              30
Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala
      35              40              45
Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser
      50              55              60
Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp
      65              70              75              80
Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro
      85              90              95
Asp Ser Ser Thr Leu Ser Gly Gly Ser Gly Ser Gly Gly Ser Gly Ser
      100              105              110
Gly Gly Ser Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser
      115              120              125
Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln
      130              135              140
Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln
145              150              155

```

```

<210>    19
<211>    150
<212>    PRT
<213>    Unknown

```

```

<220>
<221>    MUTAGEN
<222>    1-150
<223>

```

```

<400>    19

```

Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln  
 1 5 10 15  
 Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly  
 20 25 30  
 Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala  
 35 40 45  
 Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser  
 50 55 60  
 Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp  
 65 70 75 80  
 Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro  
 85 90 95  
 Asp Ser Ser Thr Leu Ser Gly Gly Ser Gly Ser Gly Gly Ser Gly Thr  
 100 105 110  
 Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val  
 115 120 125  
 Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr  
 130 135 140  
 Val Ala Ser Asn Leu Gln  
 145 150

<210> 20  
 <211> 145  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-145  
 <223>

<400> 20

Met Ala Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp  
 1 5 10 15  
 Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr  
 20 25 30  
 Pro Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly  
 35 40 45  
 Leu Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr  
 50 55 60  
 Val Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu  
 65 70 75 80  
 Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu  
 85 90 95  
 Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu  
 100 105 110  
 Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg  
 115 120 125  
 Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly  
 130 135 140  
 Ser  
 145

<210> 21  
 <211> 143  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN

&lt;222&gt; 1-143

&lt;223&gt;

&lt;400&gt; 21

```

Gly Ser Gly Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser
 1      5      10      15
Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln
      20      25      30
Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys
      35      40      45
Gly Gly Leu Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu
      50      55      60
Lys Thr Val Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn
65      70      75      80
Thr Glu Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser
      85      90      95
Cys Leu Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr
      100     105     110
Ser Glu Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe
      115     120     125
Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu
      130     135     140

```

&lt;210&gt; 22

&lt;211&gt; 149

&lt;212&gt; PRT

&lt;213&gt; Unknown

&lt;220&gt;

&lt;221&gt; MUTAGEN

&lt;222&gt; 1-149

&lt;223&gt;

&lt;400&gt; 22

```

Met Ala Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp
 1      5      10      15
Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr
      20      25      30
Pro Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly
      35      40      45
Leu Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr
      50      55      60
Val Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu
65      70      75      80
Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu
      85      90      95
Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu
      100     105     110
Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg
      115     120     125
Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly
      130     135     140
Ser Gly Gly Gly Ser
145

```

&lt;210&gt; 23

&lt;211&gt; 144

&lt;212&gt; PRT

&lt;213&gt; Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-144  
 <223>

<400> 23

```

Gly Ser Gly Gly Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile
 1           5           10           15
Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu
          20           25           30
Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu
          35           40           45
Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg
          50           55           60
Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val
65           70           75           80
Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro
          85           90           95
Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu
          100          105          110
Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn
          115          120          125
Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu
          130          135          140

```

<210> 24  
 <211> 153  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-153  
 <223>

<400> 24

```

Met Ala Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp
 1           5           10           15
Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr
          20           25           30
Pro Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly
          35           40           45
Leu Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr
          50           55           60
Val Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu
65           70           75           80
Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu
          85           90           95
Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu
          100          105          110
Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg
          115          120          125
Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly
          130          135          140
Ser Gly Gly Gly Ser Gly Gly Ser
          145          150

```

<210> 25

<211> 150  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-150  
 <223>

<400> 25

```

Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp Cys Ser
 1          5          10          15
Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu
          20          25          30
Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn
          35          40          45
Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala
          50          55          60
Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln
65          70          75          80
Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys
          85          90          95
Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile
          100          105          110
Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro
          115          120          125
Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln
          130          135          140
Pro Asp Ser Ser Thr Leu
145          150

```

<210> 26  
 <211> 146  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-146  
 <223>

<400> 26

```

Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln
 1          5          10          15
Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly
          20          25          30
Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala
          35          40          45
Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser
          50          55          60
Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp
65          70          75          80
Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro
          85          90          95
Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Thr Gln Asp Cys Ser
          100          105          110
Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu
          115          120          125
Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn

```

130 135 140  
 Leu Gln  
 145

<210> 27  
 <211> 147  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-147  
 <223>

<400> 27

Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln  
 1 5 10 15  
 Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly  
 20 25 30  
 Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala  
 35 40 45  
 Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser  
 50 55 60  
 Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp  
 65 70 75 80  
 Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro  
 85 90 95  
 Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Thr Gln Asp Cys  
 100 105 110  
 Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg  
 115 120 125  
 Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser  
 130 135 140  
 Asn Leu Gln  
 145

<210> 28  
 <211> 150  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-150  
 <223>

<400> 28

Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln  
 1 5 10 15  
 Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly  
 20 25 30  
 Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala  
 35 40 45  
 Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser  
 50 55 60  
 Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp  
 65 70 75 80  
 Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro  
 85 90 95

Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Thr  
 100 105 110  
 Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val  
 115 120 125  
 Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr  
 130 135 140  
 Val Ala Ser Asn Leu Gln  
 145 150

<210> 29  
 <211> 153  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-153  
 <223>

<400> 29

Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln  
 1 5 10 15  
 Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly  
 20 25 30  
 Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala  
 35 40 45  
 Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser  
 50 55 60  
 Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp  
 65 70 75 80  
 Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro  
 85 90 95  
 Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly  
 100 105 110  
 Ser Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp  
 115 120 125  
 Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr  
 130 135 140  
 Pro Val Thr Val Ala Ser Asn Leu Gln  
 145 150

<210> 30  
 <211> 155  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-155  
 <223>

<400> 30

Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln  
 1 5 10 15  
 Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly  
 20 25 30  
 Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala  
 35 40 45  
 Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser

```

      50              55              60
Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp
65              70              75              80
Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro
      85              90              95
Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly
      100              105              110
Ser Gly Gly Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser
      115              120              125
Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln
      130              135              140
Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln
145              150              155

```

```

<210>      31
<211>      161
<212>      PRT
<213>      Unknown

```

```

<220>
<221>      MUTAGEN
<222>      1-161
<223>

```

```

<400>      31

```

```

Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln
1              5              10              15
Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly
      20              25              30
Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala
      35              40              45
Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser
      50              55              60
Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp
65              70              75              80
Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro
      85              90              95
Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
      100              105              110
Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp Cys Ser Phe
      115              120              125
Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu
      130              135              140
Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu
145              150              155              160
Gln

```

```

<210>      32
<211>      281
<212>      PRT
<213>      Unknown

```

```

<220>
<221>      MUTAGEN
<222>      1-281
<223>

```

```

<400>      32

```

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1 5 10 15  
 Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp Val  
 20 25 30  
 Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser Phe  
 35 40 45  
 Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
 50 55 60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
 65 70 75 80  
 Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
 85 90 95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
 100 105 110  
 Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile  
 115 120 125  
 Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro  
 130 135 140  
 Asn Met Ala Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser  
 145 150 155 160  
 Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp  
 165 170 175  
 Tyr Pro Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly  
 180 185 190  
 Ala Leu Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys  
 195 200 205  
 Thr Val Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr  
 210 215 220  
 Glu Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys  
 225 230 235 240  
 Leu Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser  
 245 250 255  
 Glu Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser  
 260 265 270  
 Arg Cys Leu Glu Leu Gln Cys Gln Pro  
 275 280

<210> 33  
 <211> 286  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-286  
 <223>

<400> 33

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1 5 10 15  
 Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp Val  
 20 25 30  
 Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser Phe  
 35 40 45  
 Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
 50 55 60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
 65 70 75 80  
 Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
 85 90 95

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

<210> 34  
 <211> 296  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-296  
 <223>

<400> 34

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1                  5                  10                  15  
 Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp Val  
                   20                  25                  30  
 Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser Phe  
                   35                  40                  45  
 Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
                   50                  55                  60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
 65                  70                  75                  80  
 Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
                   85                  90                  95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
                   100                  105                  110  
 Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile  
                   115                  120                  125  
 Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro  
                   130                  135                  140  
 Asn Met Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu  
 145                  150                  155                  160  
 Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met  
                   165                  170                  175  
 Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys  
                   180                  185                  190

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Cys | Ala | Phe | Gln | Pro | Pro | Pro | Ser | Cys | Leu | Arg | Phe | Val | Gln | Thr | Asn |
|     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |
| Ile | Ser | Arg | Leu | Leu | Gln | Glu | Thr | Ser | Glu | Gln | Leu | Val | Ala | Leu | Lys |
|     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |
| Pro | Trp | Ile | Thr | Arg | Gln | Asn | Phe | Ser | Arg | Cys | Leu | Glu | Leu | Gln | Cys |
| 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |
| Gln | Pro | Asp | Ser | Ser | Thr | Leu | Ser | Gly | Gly | Asn | Gly | Ser | Gly | Gly | Asn |
|     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |
| Gly | Thr | Gln | Asp | Cys | Ser | Phe | Gln | His | Ser | Pro | Ile | Ser | Ser | Asp | Phe |
|     |     |     | 260 |     |     |     |     | 265 |     |     |     | 270 |     |     |     |
| Ala | Val | Lys | Ile | Arg | Glu | Leu | Ser | Asp | Tyr | Leu | Leu | Gln | Asp | Tyr | Pro |
|     |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |     |     |     |
| Val | Thr | Val | Ala | Ser | Asn | Leu | Gln |     |     |     |     |     |     |     |     |
|     | 290 |     |     |     |     | 295 |     |     |     |     |     |     |     |     |     |

|       |         |
|-------|---------|
| <210> | 35      |
| <211> | 296     |
| <212> | PRT     |
| <213> | Unknown |

|       |         |
|-------|---------|
| <220> |         |
| <221> | MUTAGEN |
| <222> | 1-296   |
| <223> |         |

<400> 35

|            |     |     |            |            |     |            |           |            |            |     |           |            |           |           |     |
|------------|-----|-----|------------|------------|-----|------------|-----------|------------|------------|-----|-----------|------------|-----------|-----------|-----|
| Ala<br>1   | Asn | Cys | Ser        | Ile<br>5   | Met | Ile        | Asp       | Glu        | Ile<br>10  | Ile | His       | His        | Leu       | Lys<br>15 | Arg |
| Pro        | Pro | Ala | Pro        | Leu<br>20  | Leu | Asp        | Pro       | Asn<br>25  | Asn        | Leu | Asn       | Asp        | Glu<br>30 | Asp       | Val |
| Ser        | Ile | Leu | Met        | Asp        | Arg | Asn        | Leu<br>40 | Arg        | Leu        | Pro | Asn       | Leu<br>45  | Glu       | Ser       | Phe |
| Val        | Arg | Ala | Val        | Lys        | Asn | Leu<br>55  | Glu       | Asn        | Ala        | Ser | Gly<br>60 | Ile        | Glu       | Ala       | Ile |
| Leu<br>65  | Arg | Asn | Leu        | Gln        | Pro | Cys<br>70  | Leu       | Pro        | Ser        | Ala | Thr<br>75 | Ala        | Ala       | Pro       | Ser |
| Arg        | His | Pro | Ile        | Ile<br>85  | Ile | Lys        | Ala       | Gly        | Asp<br>90  | Trp | Gln       | Glu        | Phe       | Arg       | Glu |
| Lys        | Leu | Thr | Phe<br>100 | Tyr        | Leu | Val        | Thr       | Leu<br>105 | Glu        | Gln | Ala       | Gln        | Glu       | Gln       | Gln |
| Tyr        | Val | Glu | Gly<br>115 | Gly        | Gly | Gly        | Ser       | Pro<br>120 | Gly        | Glu | Pro       | Ser        | Gly       | Pro       | Ile |
| Ser        | Thr | Ile | Asn        | Pro        | Ser | Pro<br>135 | Pro       | Ser        | Lys        | Glu | Ser       | His<br>140 | Lys       | Ser       | Pro |
| Asn<br>145 | Met | Ala | Asp        | Glu        | Glu | Leu<br>150 | Cys       | Gly        | Gly        | Leu | Trp       | Arg        | Leu       | Val       | Leu |
| Ala        | Gln | Arg | Trp        | Met<br>165 | Glu | Arg        | Leu       | Lys        | Thr<br>170 | Val | Ala       | Gly        | Ser       | Lys       | Met |
| Gln        | Gly | Leu | Leu<br>180 | Glu        | Arg | Val        | Asn       | Thr<br>185 | Glu        | Ile | His       | Phe        | Val       | Thr       | Lys |
| Cys        | Ala | Phe | Gln        | Pro        | Pro | Pro        | Ser       | Cys        | Leu        | Arg | Phe       | Val<br>205 | Gln       | Thr       | Asn |
| Ile        | Ser | Arg | Leu<br>210 | Leu        | Gln | Glu        | Thr       | Ser        | Glu        | Gln | Leu       | Val<br>220 | Ala       | Leu       | Lys |
| Pro<br>225 | Trp | Ile | Thr        | Arg        | Gln | Asn        | Phe       | Ser        | Arg        | Cys | Leu       | Glu        | Leu       | Gln       | Cys |
| Gln        | Pro | Asp | Ser        | Ser<br>245 | Thr | Leu        | Ser       | Gly        | Gly<br>250 | Asn | Gly       | Ser        | Gly       | Gly       | Asn |
| Gly        | Thr | Gln | Asp<br>260 | Cys        | Ser | Phe        | Gln       | His<br>265 | Ser        | Pro | Ile       | Ser        | Ser       | Asp       | Phe |

Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro  
           275                                  280                  285  
 Val Thr Val Ala Ser Asn Leu Gln  
       290                                  295

<210>      36  
 <211>      291  
 <212>      PRT  
 <213>      Unknown

<220>  
 <221>      MUTAGEN  
 <222>      1-291  
 <223>

<400>      36

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
   1                                  5                  10                  15  
 Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp Val  
                                   20                  25                  30  
 Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser Phe  
                                   35                  40                  45  
 Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
   50                                  55                  60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
 65                                  70                  75                  80  
 Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
                                   85                  90                  95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
                                   100                  105                  110  
 Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile  
                                   115                  120                  125  
 Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro  
   130                                  135                  140  
 Asn Met Ala Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu  
 145                                  150                  155                  160  
 Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu  
                                   165                  170                  175  
 Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu  
                                   180                  185                  190  
 Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg  
                                   195                  200                  205  
 Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Ser Gly Gly  
   210                                  215                  220  
 Asn Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp  
 225                                  230                  235                  240  
 Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr  
                                   245                  250                  255  
 Pro Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly  
                                   260                  265                  270  
 Leu Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr  
   275                                  280                  285  
 Val Ala Gly  
   290

<210>      37  
 <211>      296  
 <212>      PRT  
 <213>      Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-296  
 <223>

<400> 37

```

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg
 1          5          10          15
Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp Val
          20          25          30
Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser Phe
          35          40          45
Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile
          50          55          60
Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser
65          70          75          80
Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu
          85          90          95
Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
          100          105          110
Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile
          115          120          125
Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro
          130          135          140
Asn Met Ala Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu
145          150          155          160
Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu
          165          170          175
Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu
          180          185          190
Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg
          195          200          205
Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Ser Gly Gly
          210          215          220
Asn Gly Ser Gly Gly Asn Gly Thr Gln Asp Cys Ser Phe Gln His Ser
225          230          235          240
Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr
          245          250          255
Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln Asp Glu
          260          265          270
Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln Arg Trp Met
          275          280          285
Glu Arg Leu Lys Thr Val Ala Gly
          290          295

```

<210> 38  
 <211> 301  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-301  
 <223>

<400> 38

```

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg
 1          5          10          15
Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp Val

```

```

                20                25                30
Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser Phe
      35                40                45
Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile
      50                55                60
Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser
65      70                75                80
Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu
      85                90                95
Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
      100                105                110
Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile
      115                120                125
Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro
      130                135                140
Asn Met Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu
145      150                155                160
Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met
      165                170                175
Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys
      180                185                190
Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn
195      200                205
Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys
210      215                220
Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys
225      230                235                240
Gln Pro Asp Ser Ser Thr Leu Ser Gly Gly Asn Gly Ser Gly Gly Asn
      245                250                255
Gly Ser Gly Gly Asn Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro
      260                265                270
Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu
      275                280                285
Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln
290      295                300

```

```

<210>    39
<211>    291
<212>    PRT
<213>    Unknown

```

```

<220>
<221>    MUTAGEN
<222>    1-291
<223>

```

```

<400>    39

```

```

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg
  1                5                10                15
Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp Val
      20                25                30
Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser Phe
      35                40                45
Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile
      50                55                60
Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser
65      70                75                80
Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu
      85                90                95
Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln

```

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

<210> 40  
 <211> 296  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-296  
 <223>

<400> 40

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1 5 10 15  
 Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp Val  
 20 25 30  
 Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser Phe  
 35 40 45  
 Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
 50 55 60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
 65 70 75 80  
 Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
 85 90 95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
 100 105 110  
 Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile  
 115 120 125  
 Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro  
 130 135 140  
 Asn Met Ala Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser  
 145 150 155 160  
 Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp  
 165 170 175  
 Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro

```

      180      185      190
Asp Ser Ser Thr Leu Ser Gly Gly Asn Gly Ser Gly Gly Asn Gly Thr
      195      200      205
Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val
      210      215      220
Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr
225      230      235      240
Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg
      245      250      255
Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly
      260      265      270
Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe
      275      280      285
Val Thr Lys Cys Ala Phe Gln Pro
      290      295

```

```

<210>    41
<211>    301
<212>    PRT
<213>    Unknown

```

```

<220>
<221>    MUTAGEN
<222>    1-301
<223>

```

```

<400>    41

```

```

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg
 1      5      10      15
Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp Val
      20      25      30
Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser Phe
      35      40      45
Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile
      50      55      60
Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser
65      70      75      80
Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu
      85      90      95
Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
      100      105      110
Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile
      115      120      125
Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro
      130      135      140
Asn Met Ala Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser
145      150      155      160
Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp
      165      170      175
Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro
      180      185      190
Asp Ser Ser Thr Leu Ser Gly Gly Asn Gly Ser Gly Gly Asn Gly Ser
      195      200      205
Gly Gly Asn Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser
      210      215      220
Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln
225      230      235      240
Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys
      245      250      255
Gly Gly Leu Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu

```

260 265 270  
 Lys Thr Val Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn  
 275 280 285  
 Thr Glu Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro  
 290 295 300

<210> 42  
 <211> 281  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-281  
 <223>

<400> 42

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1 5 10 15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met  
 20 25 30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
 35 40 45  
 Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
 50 55 60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
 65 70 75 80  
 Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
 85 90 95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
 100 105 110  
 Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile  
 115 120 125  
 Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro  
 130 135 140  
 Asn Met Ala Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser  
 145 150 155 160  
 Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp  
 165 170 175  
 Tyr Pro Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly  
 180 185 190  
 Gly Leu Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys  
 195 200 205  
 Thr Val Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr  
 210 215 220  
 Glu Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys  
 225 230 235 240  
 Leu Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser  
 245 250 255  
 Glu Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser  
 260 265 270  
 Arg Cys Leu Glu Leu Gln Cys Gln Pro  
 275 280

<210> 43  
 <211> 286  
 <212> PRT  
 <213> Unknown

<220>

<221> MUTAGEN  
 <222> 1-286  
 <223>

<400> 43

```

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg
 1           5           10           15
Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met
           20           25           30
Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe
           35           40           45
Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile
           50           55           60
Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser
65           70           75           80
Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu
           85           90           95
Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
           100          105          110
Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile
           115          120          125
Ser Thr Ile Asn Pro Ser Pro Ser Lys Glu Ser His Lys Ser Pro
           130          135          140
Asn Met Ala Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser
145          150          155          160
Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp
           165          170          175
Tyr Pro Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly
           180          185          190
Gly Leu Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys
           195          200          205
Thr Val Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr
           210          215          220
Glu Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys
225          230          235          240
Leu Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser
           245          250          255
Glu Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser
           260          265          270
Arg Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu
           275          280          285

```

<210> 44  
 <211> 296  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-296  
 <223>

<400> 44

```

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg
 1           5           10           15
Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met
           20           25           30
Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe
           35           40           45

```

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

<210> 45  
 <211> 301  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-301  
 <223>

<400> 45

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1 5 10 15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met  
 20 25 30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
 35 40 45  
 Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
 50 55 60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
 65 70 75 80  
 Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
 85 90 95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln  
 100 105 110  
 Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile  
 115 120 125

Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro  
 130 135 140  
 Asn Met Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu  
 145 150 155 160  
 Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met  
 165 170 175  
 Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys  
 180 185 190  
 Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn  
 195 200 205  
 Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys  
 210 215 220  
 Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys  
 225 230 235 240  
 Gln Pro Asp Ser Ser Thr Leu Ser Gly Gly Asn Gly Ser Gly Gly Asn  
 245 250 255  
 Gly Ser Gly Gly Asn Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro  
 260 265 270  
 Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu  
 275 280 285  
 Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln  
 290 295 300

<210> 46  
 <211> 291  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-291  
 <223>

<400> 46

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1 5 10 15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met  
 20 25 30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
 35 40 45  
 Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
 50 55 60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
 65 70 75 80  
 Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
 85 90 95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
 100 105 110  
 Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile  
 115 120 125  
 Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro  
 130 135 140  
 Asn Met Ala Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu  
 145 150 155 160  
 Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu  
 165 170 175  
 Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu  
 180 185 190  
 Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg  
 195 200 205

Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Ser Gly Gly  
 210 215 220  
 Asn Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp  
 225 230 235 240  
 Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr  
 245 250 255  
 Pro Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly  
 260 265 270  
 Leu Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr  
 275 280 285  
 Val Ala Gly  
 290

<210> 47  
 <211> 296  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-296  
 <223>

<400> 47

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1 5 10 15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met  
 20 25 30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
 35 40 45  
 Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
 50 55 60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
 65 70 75 80  
 Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
 85 90 95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
 100 105 110  
 Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile  
 115 120 125  
 Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro  
 130 135 140  
 Asn Met Ala Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu  
 145 150 155 160  
 Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu  
 165 170 175  
 Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu  
 180 185 190  
 Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg  
 195 200 205  
 Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Ser Gly Gly  
 210 215 220  
 Asn Gly Ser Gly Gly Asn Gly Thr Gln Asp Cys Ser Phe Gln His Ser  
 225 230 235 240  
 Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr  
 245 250 255  
 Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln Asp Glu  
 260 265 270  
 Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln Arg Trp Met  
 275 280 285

Glu Arg Leu Lys Thr Val Ala Gly  
 290 295

<210> 48  
 <211> 301  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-301  
 <223>

<400> 48

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1 5 10 15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met  
 20 25 30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
 35 40 45  
 Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
 50 55 60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
 65 70 75 80  
 Arg His Pro Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
 85 90 95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
 100 105 110  
 Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile  
 115 120 125  
 Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro  
 130 135 140  
 Asn Met Ala Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu  
 145 150 155 160  
 Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu  
 165 170 175  
 Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu  
 180 185 190  
 Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg  
 195 200 205  
 Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Ser Gly Gly  
 210 215 220  
 Asn Gly Ser Gly Gly Asn Gly Ser Gly Gly Asn Gly Thr Gln Asp Cys  
 225 230 235 240  
 Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg  
 245 250 255  
 Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser  
 260 265 270  
 Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu  
 275 280 285  
 Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly  
 290 295 300

<210> 49  
 <211> 291  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN

&lt;222&gt; 1-291

&lt;223&gt;

&lt;400&gt; 49

```

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg
 1          5          10          15
Pro Pro Asn Pro Leu Leu Asp Pro Asn Leu Asn Ser Glu Asp Met
          20          25          30
Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe
          35          40          45
Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile
          50          55          60
Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser
65          70          75          80
Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu
          85          90          95
Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
          100          105          110
Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile
          115          120          125
Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro
          130          135          140
Asn Met Ala Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser
145          150          155          160
Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp
          165          170          175
Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro
          180          185          190
Asp Ser Ser Thr Leu Ser Gly Gly Asn Gly Thr Gln Asp Cys Ser Phe
          195          200          205
Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu
          210          215          220
Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu
225          230          235          240
Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln
          245          250          255
Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly
          260          265          270
Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala
          275          280          285
Phe Gln Pro
          290

```

&lt;210&gt; 50

&lt;211&gt; 296

&lt;212&gt; PRT

&lt;213&gt; Unknown

&lt;220&gt;

&lt;221&gt; MUTAGEN

&lt;222&gt; 1-296

&lt;223&gt;

&lt;400&gt; 50

```

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg
 1          5          10          15
Pro Pro Asn Pro Leu Leu Asp Pro Asn Leu Asn Ser Glu Asp Met
          20          25          30
Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe

```

```

      35              40              45
Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile
      50              55              60
Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser
      65              70              75              80
Arg His Pro Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu
      85              90              95
Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
      100             105             110
Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile
      115             120             125
Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro
      130             135             140
Asn Met Ala Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser
      145             150             155             160
Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp
      165             170             175
Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro
      180             185             190
Asp Ser Ser Thr Leu Ser Gly Gly Asn Gly Ser Gly Gly Asn Gly Thr
      195             200             205
Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val
      210             215             220
Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr
      225             230             235             240
Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg
      245             250             255
Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly
      260             265             270
Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe
      275             280             285
Val Thr Lys Cys Ala Phe Gln Pro
      290             295

```

```

<210>    51
<211>    301
<212>    PRT
<213>    Unknown

```

```

<220>
<221>    MUTAGEN
<222>    1-301
<223>

```

```

<400>    51

```

```

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg
  1              5              10              15
Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met
      20              25              30
Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe
      35              40              45
Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile
      50              55              60
Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser
      65              70              75              80
Arg His Pro Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu
      85              90              95
Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
      100             105             110
Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile

```

|                                                                 |     |     |
|-----------------------------------------------------------------|-----|-----|
| 115                                                             | 120 | 125 |
| Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro |     |     |
| 130                                                             | 135 | 140 |
| Asn Met Ala Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser |     |     |
| 145                                                             | 150 | 155 |
| Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp |     |     |
| 165                                                             | 170 | 175 |
| Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro |     |     |
| 180                                                             | 185 | 190 |
| Asp Ser Ser Thr Leu Ser Gly Gly Asn Gly Ser Gly Gly Asn Gly Ser |     |     |
| 195                                                             | 200 | 205 |
| Gly Gly Asn Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser |     |     |
| 210                                                             | 215 | 220 |
| Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln |     |     |
| 225                                                             | 230 | 235 |
| Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys |     |     |
| 245                                                             | 250 | 255 |
| Gly Gly Leu Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu |     |     |
| 260                                                             | 265 | 270 |
| Lys Thr Val Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn |     |     |
| 275                                                             | 280 | 285 |
| Thr Glu Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro             |     |     |
| 290                                                             | 295 | 300 |

<210> 52  
 <211> 296  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-296  
 <223>

<400> 52

|                                                                 |     |
|-----------------------------------------------------------------|-----|
| Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg |     |
| 1                                                               | 5   |
| Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met |     |
| 20                                                              | 25  |
| Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe |     |
| 35                                                              | 40  |
| Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile |     |
| 50                                                              | 55  |
| Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser |     |
| 65                                                              | 70  |
| Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu |     |
| 85                                                              | 90  |
| Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln |     |
| 100                                                             | 105 |
| Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile |     |
| 115                                                             | 120 |
| Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro |     |
| 130                                                             | 135 |
| Asn Met Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu |     |
| 145                                                             | 150 |
| Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met |     |
| 165                                                             | 170 |
| Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys |     |
| 180                                                             | 185 |
| Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn |     |

```

      195              200              205
Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys
  210              215              220
Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys
  225              230              235              240
Gln Pro Asp Ser Ser Thr Leu Ser Gly Gly Ser Gly Ser Gly Gly Ser
      245              250              255
Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe
      260              265              270
Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro
      275              280              285
Val Thr Val Ala Ser Asn Leu Gln
  290              295

```

```

<210>    53
<211>    301
<212>    PRT
<213>    Unknown

```

```

<220>
<221>    MUTAGEN
<222>    1-301
<223>

```

```

<400>    53

```

```

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg
  1              5              10              15
Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met
      20              25              30
Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe
      35              40              45
Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile
      50              55              60
Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser
  65              70              75              80
Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu
      85              90              95
Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
      100              105              110
Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile
      115              120              125
Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro
      130              135              140
Asn Met Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu
  145              150              155              160
Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met
      165              170              175
Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys
      180              185              190
Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn
      195              200              205
Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys
      210              215              220
Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys
  225              230              235              240
Gln Pro Asp Ser Ser Thr Leu Ser Gly Gly Ser Gly Ser Gly Gly Ser
      245              250              255
Gly Ser Gly Gly Ser Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro
      260              265              270
Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu

```

Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln

|       |         |
|-------|---------|
| <210> | 54      |
| <211> | 281     |
| <212> | PRT     |
| <213> | Unknown |

|       |         |
|-------|---------|
| <220> |         |
| <221> | MUTAGEN |
| <222> | 1-281   |
| <223> |         |

<400> 54

|         |     |     |     |         |     |     |     |         |        |     |     |        |        |        |         |
|---------|-----|-----|-----|---------|-----|-----|-----|---------|--------|-----|-----|--------|--------|--------|---------|
| Ala 1   | Thr | Gln | Asp | Cys 5   | Ser | Phe | Gln | His     | Ser 10 | Pro | Ile | Ser    | Ser    | Asp 15 | Phe     |
| Ala     | Val | Lys | Ile | Arg 20  | Glu | Leu | Ser | Asp 25  | Tyr    | Leu | Leu | Gln    | Asp 30 | Tyr    | Pro     |
| Val     | Thr | Val | Ala | Ser 35  | Asn | Leu | Gln | Asp 40  | Glu    | Glu | Leu | Cys 45 | Gly    | Gly    | Leu     |
| Trp     | Arg | Leu | Val | Leu 50  | Ala | Gln | Arg | Trp 55  | Met    | Glu | Arg | Leu 60 | Lys    | Thr    | Val     |
| Ala 65  | Gly | Ser | Lys | Met 70  | Gln | Gly | Leu | Leu 75  | Glu    | Arg | Val | Asn    | Thr    | Glu    | Ile 80  |
| His     | Phe | Val | Thr | Lys 85  | Cys | Ala | Phe | Gln 90  | Pro    | Pro | Pro | Ser    | Cys    | Leu    | Arg     |
| Phe     | Val | Gln | Thr | Asn 100 | Ile | Ser | Arg | Leu 105 | Leu    | Gln | Glu | Thr    | Ser    | Glu    | Gln     |
| Leu     | Val | Ala | Leu | Lys 115 | Pro | Trp | Ile | Thr 120 | Arg    | Gln | Asn | Phe    | Ser    | Arg    | Cys     |
| Leu     | Glu | Leu | Gln | Cys 130 | Gln | Pro | Tyr | Val 135 | Glu    | Gly | Gly | Gly    | Gly    | Ser    | Pro     |
| Gly 145 | Glu | Pro | Ser | Gly 150 | Pro | Ile | Ser | Thr     | Ile    | Asn | Pro | Ser    | Pro    | Pro    | Ser 160 |
| Lys     | Glu | Ser | His | Lys 165 | Ser | Pro | Asn | Met     | Ala    | Asn | Cys | Ser    | Ile    | Met    | Ile     |
| Asp     | Glu | Ile | Ile | His 180 | His | Leu | Lys | Arg     | Pro    | Pro | Asn | Pro    | Leu    | Leu    | Asp     |
| Pro     | Asn | Asn | Leu | Asn 195 | Ser | Glu | Asp | Met     | Asp    | Ile | Leu | Met    | Glu    | Arg    | Asn     |
| Leu     | Arg | Thr | Pro | Asn 210 | Leu | Leu | Ala | Phe     | Val    | Arg | Ala | Val    | Lys    | His    | Leu     |
| Glu 225 | Asn | Ala | Ser | Gly 230 | Ile | Glu | Ala | Ile     | Leu    | Arg | Asn | Leu    | Gln    | Pro    | Cys     |
| Leu     | Pro | Ser | Ala | Thr 245 | Ala | Ala | Pro | Ser     | Arg    | His | Pro | Ile    | Ile    | Ile    | Lys     |
| Ala     | Gly | Asp | Trp | Gln 260 | Glu | Phe | Arg | Glu     | Lys    | Leu | Thr | Phe    | Tyr    | Leu    | Val     |
| Thr     | Leu | Glu | Gln | Ala 275 | Gln | Glu | Gln | Gln     |        |     |     |        |        |        |         |

|       |         |
|-------|---------|
| <210> | 55      |
| <211> | 286     |
| <212> | PRT     |
| <213> | Unknown |

<220>  
<221> MUTAGEN  
<222> 1-286

&lt;223&gt;

&lt;400&gt; 55

```

Ala Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe
 1      5      10      15
Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro
 20      25      30
Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu
 35      40      45
Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val
 50      55      60
Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile
 65      70      75      80
His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg
 85      90      95
Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln
 100     105     110
Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys
 115     120     125
Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Tyr Val Glu Gly
 130     135     140
Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn
 145     150     155     160
Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala Asn
 165     170     175
Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro Pro
 180     185     190
Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met Asp Ile
 195     200     205
Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe Val Arg
 210     215     220
Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg
 225     230     235     240
Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His
 245     250     255
Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu
 260     265     270
Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
 275     280     285

```

&lt;210&gt; 56

&lt;211&gt; 268

&lt;212&gt; PRT

&lt;213&gt; Unknown

&lt;220&gt;

&lt;221&gt; MUTAGEN

&lt;222&gt; 1-368

&lt;223&gt;

&lt;400&gt; 56

```

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg
 1      5      10      15
Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met
 20      25      30
Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe
 35      40      45
Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile
 50      55      60

```

```

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

```

```

<210>    57
<211>    292
<212>    PRT
<213>    Unknown

```

```

<220>
<221>    MUTAGEN
<222>    1-292
<223>

```

```

<400>    57

```

```

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg
1          5          10         15
Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met
          20         25         30
Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe
          35         40         45
Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile
          50         55         60
Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser
65          70          75          80
Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu
          85          90          95
Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
          100         105         110
Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile
          115         120         125
Ser Thr Ile Asn Pro Ser Pro Ser Lys Glu Ser His Lys Ser Pro
          130         135         140
Asn Met Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu
145          150         155         160
Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met
          165         170         175

```

Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys  
 180 185 190  
 Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn  
 195 200 205  
 Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys  
 210 215 220  
 Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys  
 225 230 235 240  
 Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Thr Gln Asp  
 245 250 255  
 Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile  
 260 265 270  
 Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala  
 275 280 285  
 Ser Asn Leu Gln  
 290

<210> 58  
 <211> 293  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-293  
 <223>

<400> 58

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1 5 10 15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met  
 20 25 30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
 35 40 45  
 Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
 50 55 60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
 65 70 75 80  
 Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
 85 90 95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln  
 100 105 110  
 Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile  
 115 120 125  
 Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro  
 130 135 140  
 Asn Met Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu  
 145 150 155 160  
 Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met  
 165 170 175  
 Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys  
 180 185 190  
 Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn  
 195 200 205  
 Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys  
 210 215 220  
 Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys  
 225 230 235 240  
 Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Thr Gln  
 245 250 255

Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys  
                   260                  265                  270  
 Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val  
                   275                  280                  285  
 Ala Ser Asn Leu Gln  
                   290

<210> 59  
 <211> 296  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-296  
 <223>

<400> 59

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
   1                  5                  10                  15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met  
                   20                  25                  30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
                   35                  40                  45  
 Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
                   50                  55                  60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
   65                  70                  75                  80  
 Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
                   85                  90                  95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
                   100                  105                  110  
 Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile  
                   115                  120                  125  
 Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro  
                   130                  135                  140  
 Asn Met Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu  
   145                  150                  155                  160  
 Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met  
                   165                  170                  175  
 Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys  
                   180                  185                  190  
 Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn  
                   195                  200                  205  
 Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys  
                   210                  215                  220  
 Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys  
   225                  230                  235                  240  
 Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly  
                   245                  250                  255  
 Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe  
                   260                  265                  270  
 Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro  
                   275                  280                  285  
 Val Thr Val Ala Ser Asn Leu Gln  
                   290                  295

<210> 60  
 <211> 299  
 <212> PRT

<213> Unknown

<220>

<221> MUTAGEN

<222> 1-299

<223>

<400> 60

```

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg
 1           5           10           15
Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met
           20           25           30
Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe
           35           40           45
Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile
           50           55           60
Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser
65           70           75           80
Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu
           85           90           95
Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
           100          105          110
Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile
           115          120          125
Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro
           130          135          140
Asn Met Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu
145           150          155          160
Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met
           165          170          175
Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys
           180          185          190
Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn
           195          200          205
Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys
           210          215          220
Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys
225           230          235          240
Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly
           245          250          255
Gly Gly Ser Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser
           260          265          270
Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln
           275          280          285
Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln
290           295

```

<210> 61

<211> 301

<212> PRT

<213> Unknown

<220>

<221> MUTAGEN

<222> 1-301

<223>

<400> 61

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg

```

1           5           10           15
Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met
                20                25                30
Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Ala Phe
                35                40                45
Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile
                50                55                60
Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser
65                70                75                80
Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu
                85                90                95
Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
                100                105                110
Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile
                115                120                125
Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro
130                135                140
Asn Met Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu
145                150                155                160
Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met
                165                170                175
Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys
                180                185                190
Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn
195                200                205
Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys
210                215                220
Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys
225                230                235                240
Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly
                245                250                255
Gly Gly Ser Gly Gly Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro
                260                265                270
Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu
275                280                285
Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln
290                295                300

```

<210> 62  
 <211> 307  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-307  
 <223>

<400> 62

```

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg
1           5           10           15
Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met
                20                25                30
Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Ala Phe
                35                40                45
Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile
                50                55                60
Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser
65                70                75                80
Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu

```

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

<210> 63  
 <211> 292  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-292  
 <223>

<400> 63

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1 5 10 15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met  
 20 25 30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
 35 40 45  
 Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
 50 55 60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
 65 70 75 80  
 Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
 85 90 95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
 100 105 110  
 Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile  
 115 120 125  
 Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro  
 130 135 140  
 Asn Met Ala Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu

145                      150                      155                      160  
 Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu  
                                  165                      170                      175  
 Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu  
                                  180                      185                      190  
 Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg  
                                  195                      200                      205  
 Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly  
                                  210                      215                      220  
 Ser Gly Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser  
 225                      230                      235                      240  
 Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp  
                                  245                      250                      255  
 Tyr Pro Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly  
                                  260                      265                      270  
 Gly Leu Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys  
                                  275                      280                      285  
 Thr Val Ala Gly  
 290

<210>      64  
 <211>      293  
 <212>      PRT  
 <213>      Unknown

<220>  
 <221>      MUTAGEN  
 <222>      1-293  
 <223>

<400>      64

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1                      5                      10                      15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met  
                                  20                      25                      30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
                                  35                      40                      45  
 Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
                                  50                      55                      60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
 65                      70                      75                      80  
 Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
                                  85                      90                      95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
                                  100                      105                      110  
 Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile  
                                  115                      120                      125  
 Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro  
                                  130                      135                      140  
 Asn Met Ala Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu  
 145                      150                      155                      160  
 Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu  
                                  165                      170                      175  
 Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu  
                                  180                      185                      190  
 Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg  
                                  195                      200                      205  
 Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly  
                                  210                      215                      220  
 Ser Gly Gly Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser

|       |         |
|-------|---------|
| <210> | 65      |
| <211> | 296     |
| <212> | PRT     |
| <213> | Unknown |

|       |         |
|-------|---------|
| <220> |         |
| <221> | MUTAGEN |
| <222> | 1-296   |
| <223> |         |

<400> 65

45

<210> 66  
 <211> 299  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-299  
 <223>

<400> 66

```

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg
 1           5           10           15
Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met
          20           25           30
Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe
          35           40           45
Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile
          50           55           60
Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser
65           70           75           80
Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu
          85           90           95
Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
          100          105          110
Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile
          115          120          125
Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro
          130          135          140
Asn Met Ala Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu
145          150          155          160
Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu
          165          170          175
Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu
          180          185          190
Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg
          195          200          205
Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly
          210          215          220
Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp Cys Ser Phe
225          230          235          240
Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu
          245          250          255
Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu
          260          265          270
Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln
          275          280          285
Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly
          290          295

```

<210> 67  
 <211> 301  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-301  
 <223>

&lt;400&gt; 67

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1 5 10 15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met  
 20 25 30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
 35 40 45  
 Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
 50 55 60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
 65 70 75 80  
 Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
 85 90 95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
 100 105 110  
 Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile  
 115 120 125  
 Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro  
 130 135 140  
 Asn Met Ala Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu  
 145 150 155 160  
 Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu  
 165 170 175  
 Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu  
 180 185 190  
 Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg  
 195 200 205  
 Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly  
 210 215 220  
 Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Thr Gln Asp Cys  
 225 230 235 240  
 Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg  
 245 250 255  
 Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser  
 260 265 270  
 Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu  
 275 280 285  
 Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly  
 290 295 300

<210> 68  
 <211> 307  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-307  
 <223>

&lt;400&gt; 68

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1 5 10 15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met  
 20 25 30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
 35 40 45  
 Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
 50 55 60

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

<210> 69  
 <211> 292  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-292  
 <223>

<400> 69

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1 5 10 15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met  
 20 25 30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
 35 40 45  
 Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
 50 55 60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
 65 70 75 80  
 Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
 85 90 95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
 100 105 110  
 Tyr Val Glu Gly Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile  
 115 120 125

Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro  
 130 135 140  
 Asn Met Ala Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser  
 145 150 155 160  
 Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp  
 165 170 175  
 Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro  
 180 185 190  
 Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Thr Gln Asp Cys Ser  
 195 200 205  
 Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu  
 210 215 220  
 Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn  
 225 230 235 240  
 Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala  
 245 250 255  
 Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln  
 260 265 270  
 Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys  
 275 280 285  
 Ala Phe Gln Pro  
 290

<210> 70  
 <211> 293  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-293  
 <223>

<400> 70

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1 5 10 15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met  
 20 25 30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
 35 40 45  
 Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
 50 55 60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
 65 70 75 80  
 Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
 85 90 95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
 100 105 110  
 Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile  
 115 120 125  
 Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro  
 130 135 140  
 Asn Met Ala Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser  
 145 150 155 160  
 Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp  
 165 170 175  
 Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro  
 180 185 190  
 Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Thr Gln Asp Cys  
 195 200 205

Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg  
 210 215 220  
 Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser  
 225 230 235 240  
 Asn Leu Gln Asp Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu  
 245 250 255  
 Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met  
 260 265 270  
 Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys  
 275 280 285  
 Cys Ala Phe Gln Pro  
 290

<210> 71  
 <211> 296  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-296  
 <223>

<400> 71

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1 5 10 15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met  
 20 25 30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
 35 40 45  
 Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
 50 55 60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
 65 70 75 80  
 Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
 85 90 95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln  
 100 105 110  
 Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile  
 115 120 125  
 Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro  
 130 135 140  
 Asn Met Ala Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser  
 145 150 155 160  
 Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp  
 165 170 175  
 Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro  
 180 185 190  
 Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Thr  
 195 200 205  
 Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val  
 210 215 220  
 Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr  
 225 230 235 240  
 Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg  
 245 250 255  
 Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly  
 260 265 270  
 Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe  
 275 280 285

Val Thr Lys Cys Ala Phe Gln Pro  
290 295

<210> 72  
<211> 299  
<212> PRT  
<213> Unknown

<220>  
<221> MUTAGEN  
<222> 1-299  
<223>

<400> 72

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
1 5 10 15  
Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met  
20 25 30  
Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
35 40 45  
Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
50 55 60  
Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
65 70 75 80  
Arg His Pro Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
85 90 95  
Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
100 105 110  
Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile  
115 120 125  
Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro  
130 135 140  
Asn Met Ala Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser  
145 150 155 160  
Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp  
165 170 175  
Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro  
180 185 190  
Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly  
195 200 205  
Ser Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp  
210 215 220  
Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr  
225 230 235 240  
Pro Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly  
245 250 255  
Leu Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr  
260 265 270  
Val Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu  
275 280 285  
Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro  
290 295

<210> 73  
<211> 301  
<212> PRT  
<213> Unknown

<220>  
<221> MUTAGEN

&lt;222&gt; 1-301

&lt;223&gt;

&lt;400&gt; 73

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1 5 10 15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met  
 20 25 30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
 35 40 45  
 Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
 50 55 60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
 65 70 75 80  
 Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
 85 90 95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
 100 105 110  
 Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile  
 115 120 125  
 Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro  
 130 135 140  
 Asn Met Ala Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser  
 145 150 155 160  
 Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp  
 165 170 175  
 Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro  
 180 185 190  
 Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly  
 195 200 205  
 Ser Gly Gly Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser  
 210 215 220  
 Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln  
 225 230 235 240  
 Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys  
 245 250 255  
 Gly Gly Leu Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu  
 260 265 270  
 Lys Thr Val Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn  
 275 280 285  
 Thr Glu Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro  
 290 295 300

&lt;210&gt; 74

&lt;211&gt; 307

&lt;212&gt; PRT

&lt;213&gt; Unknown

&lt;220&gt;

&lt;221&gt; MUTAGEN

&lt;222&gt; 1-307

&lt;223&gt;

&lt;400&gt; 74

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1 5 10 15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met  
 20 25 30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe

```

      35              40              45
Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile
      50              55              60
Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser
65              70              75              80
Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu
      85              90              95
Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
      100             105             110
Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile
      115             120             125
Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro
      130             135             140
Asn Met Ala Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser
145             150             155             160
Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp
      165             170             175
Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro
      180             185             190
Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
      195             200             205
Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp Cys Ser Phe
      210             215             220
Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu
225             230             235             240
Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu
      245             250             255
Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln
      260             265             270
Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly
      275             280             285
Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala
      290             295             300
Phe Gln Pro
305

```

```

<210>      75
<211>      296
<212>      PRT
<213>      Unknown

```

```

<220>
<221>      MUTAGEN
<222>      1-296
<223>

```

```

<400>      75

```

```

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg
 1              5              10              15
Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met
      20              25              30
Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe
      35              40              45
Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile
      50              55              60
Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser
65              70              75              80
Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu
      85              90              95
Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln

```

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

<210> 76  
 <211> 301  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-301  
 <223>

<400> 76

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1 5 10 15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met  
 20 25 30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
 35 40 45  
 Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
 50 55 60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
 65 70 75 80  
 Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
 85 90 95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
 100 105 110  
 Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile  
 115 120 125  
 Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro  
 130 135 140  
 Asn Met Ala Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln Asp Glu  
 145 150 155 160  
 Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln Arg Trp Met  
 165 170 175  
 Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly Leu Leu Glu

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|
|     |     |     |     | 180 |     |     |     | 185 |     |     |     |     | 190 |     |     |  |
| Arg | Val | Asn | Thr | Glu | Ile | His | Phe | Val | Thr | Lys | Cys | Ala | Phe | Gln | Pro |  |
|     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |  |
| Pro | Pro | Ser | Cys | Leu | Arg | Phe | Val | Gln | Thr | Asn | Ile | Ser | Arg | Leu | Leu |  |
|     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |  |
| Gln | Glu | Thr | Ser | Glu | Gln | Leu | Val | Ala | Leu | Lys | Pro | Trp | Ile | Thr | Arg |  |
| 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |  |
| Gln | Asn | Phe | Ser | Arg | Cys | Leu | Glu | Leu | Gln | Cys | Gln | Pro | Asp | Ser | Ser |  |
|     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |  |
| Thr | Leu | Gly | Gly | Gly | Ser | Gly | Gly | Gly | Ser | Gly | Gly | Gly | Ser | Gly | Gly |  |
|     |     |     | 260 |     |     |     | 265 |     |     |     |     |     | 270 |     |     |  |
| Gly | Thr | Gln | Asp | Cys | Ser | Phe | Gln | His | Ser | Pro | Ile | Ser | Ser | Asp | Phe |  |
|     | 275 |     |     |     |     |     | 280 |     |     |     |     | 285 |     |     |     |  |
| Ala | Val | Lys | Ile | Arg | Glu | Leu | Ser | Asp | Tyr | Leu | Leu | Gln |     |     |     |  |
|     | 290 |     |     |     |     | 295 |     |     |     |     | 300 |     |     |     |     |  |

|       |         |
|-------|---------|
| <210> | 77      |
| <211> | 296     |
| <212> | PRT     |
| <213> | Unknown |

<220>  
<221> MUTAGEN  
<222> 1-296  
<223>

<400> 77

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ala | Asn | Cys | Ser | Ile | Met | Ile | Asp | Glu | Ile | Ile | His | His | Leu | Lys | Arg |
| 1   |     |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |
| Pro | Pro | Asn | Pro | Leu | Leu | Asp | Pro | Asn | Asn | Leu | Asn | Ser | Glu | Asp | Met |
|     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |
| Asp | Ile | Leu | Met | Glu | Arg | Asn | Leu | Arg | Thr | Pro | Asn | Leu | Leu | Ala | Phe |
|     |     | 35  |     |     |     |     | 40  |     |     |     |     | 45  |     |     |     |
| Val | Arg | Ala | Val | Lys | His | Leu | Glu | Asn | Ala | Ser | Gly | Ile | Glu | Ala | Ile |
|     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |
| Leu | Arg | Asn | Leu | Gln | Pro | Cys | Leu | Pro | Ser | Ala | Thr | Ala | Ala | Pro | Ser |
| 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     | 80  |     |
| Arg | His | Pro | Ile | Ile | Ile | Lys | Ala | Gly | Asp | Trp | Gln | Glu | Phe | Arg | Glu |
|     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |
| Lys | Leu | Thr | Phe | Tyr | Leu | Val | Thr | Leu | Glu | Gln | Ala | Gln | Glu | Gln | Gln |
|     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
| Tyr | Val | Glu | Gly | Gly | Gly | Gly | Ser | Pro | Gly | Glu | Pro | Ser | Gly | Pro | Ile |
|     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |
| Ser | Thr | Ile | Asn | Pro | Ser | Pro | Pro | Ser | Lys | Glu | Ser | His | Lys | Ser | Pro |
|     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
| Asn | Met | Ala | Ala | Ser | Asn | Leu | Gln | Asp | Glu | Glu | Leu | Cys | Gly | Gly | Leu |
| 145 |     |     |     | 150 |     |     |     |     |     | 155 |     |     |     |     | 160 |
| Trp | Arg | Leu | Val | Leu | Ala | Gln | Arg | Trp | Met | Glu | Arg | Leu | Lys | Thr | Val |
|     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |
| Ala | Gly | Ser | Lys | Met | Gln | Gly | Leu | Leu | Glu | Arg | Val | Asn | Thr | Glu | Ile |
|     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |
| His | Phe | Val | Thr | Lys | Cys | Ala | Phe | Gln | Pro | Pro | Pro | Ser | Cys | Leu | Arg |
|     | 195 |     |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |
| Phe | Val | Gln | Thr | Asn | Ile | Ser | Arg | Leu | Leu | Gln | Glu | Thr | Ser | Glu | Gln |
|     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |
| Leu | Val | Ala | Leu | Lys | Pro | Trp | Ile | Thr | Arg | Gln | Asn | Phe | Ser | Arg | Cys |
| 225 |     |     |     | 230 |     |     |     |     |     | 235 |     |     |     | 240 |     |
| Leu | Glu | Leu | Gln | Cys | Gln | Pro | Asp | Ser | Ser | Thr | Leu | Gly | Gly | Gly | Ser |
|     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |
| Gly | Gly | Gly | Ser | Gly | Gly | Thr | Gln | Asp | Cys | Ser | Phe | Gln | His | Ser | Pro |

```

      260      265      270
Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu
      275      280      285
Leu Gln Asp Tyr Pro Val Thr Val
      290      295

```

|       |         |
|-------|---------|
| <210> | 78      |
| <211> | 301     |
| <212> | PRT     |
| <213> | Unknown |

<220>  
<221> MUTAGEN  
<222> 1-301  
<223>

<400> 78

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ala | Asn | Cys | Ser | Ile | Met | Ile | Asp | Glu | Ile | Ile | His | His | Leu | Lys | Arg |
| 1   |     |     |     | 5   |     |     |     | 10  |     |     |     |     |     | 15  |     |
| Pro | Pro | Asn | Pro | Leu | Leu | Asp | Pro | Asn | Asn | Leu | Asn | Ser | Glu | Asp | Met |
|     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |
| Asp | Ile | Leu | Met | Glu | Arg | Asn | Leu | Arg | Thr | Pro | Asn | Leu | Leu | Ala | Phe |
|     |     | 35  |     |     |     | 40  |     |     |     |     | 45  |     |     |     |     |
| Val | Arg | Ala | Val | Lys | His | Leu | Glu | Asn | Ala | Ser | Gly | Ile | Glu | Ala | Ile |
|     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |
| Leu | Arg | Asn | Leu | Gln | Pro | Cys | Leu | Pro | Ser | Ala | Thr | Ala | Ala | Pro | Ser |
| 65  |     |     |     | 70  |     |     |     |     |     | 75  |     |     |     | 80  |     |
| Arg | His | Pro | Ile | Ile | Ile | Lys | Ala | Gly | Asp | Trp | Gln | Glu | Phe | Arg | Glu |
|     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |
| Lys | Leu | Thr | Phe | Tyr | Leu | Val | Thr | Leu | Glu | Gln | Ala | Gln | Glu | Gln | Gln |
|     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
| Tyr | Val | Glu | Gly | Gly | Gly | Gly | Ser | Pro | Gly | Glu | Pro | Ser | Gly | Pro | Ile |
|     |     | 115 |     |     |     | 120 |     |     |     |     | 125 |     |     |     |     |
| Ser | Thr | Ile | Asn | Pro | Ser | Pro | Pro | Ser | Lys | Glu | Ser | His | Lys | Ser | Pro |
|     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
| Asn | Met | Ala | Ala | Ser | Asn | Leu | Gln | Asp | Glu | Glu | Leu | Cys | Gly | Gly | Leu |
| 145 |     |     |     | 150 |     |     |     |     |     | 155 |     |     |     | 160 |     |
| Trp | Arg | Leu | Val | Leu | Ala | Gln | Arg | Trp | Met | Glu | Arg | Leu | Lys | Thr | Val |
|     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |
| Ala | Gly | Ser | Lys | Met | Gln | Gly | Leu | Leu | Glu | Arg | Val | Asn | Thr | Glu | Ile |
|     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |
| His | Phe | Val | Thr | Lys | Cys | Ala | Phe | Gln | Pro | Pro | Pro | Ser | Cys | Leu | Arg |
|     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |     |
| Phe | Val | Gln | Thr | Asn | Ile | Ser | Arg | Leu | Leu | Gln | Glu | Thr | Ser | Glu | Gln |
|     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |
| Leu | Val | Ala | Leu | Lys | Pro | Trp | Ile | Thr | Arg | Gln | Asn | Phe | Ser | Arg | Cys |
| 225 |     |     |     | 230 |     |     |     |     |     | 235 |     |     |     | 240 |     |
| Leu | Glu | Leu | Gln | Cys | Gln | Pro | Asp | Ser | Ser | Thr | Leu | Gly | Gly | Gly | Ser |
|     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |
| Gly | Gly | Gly | Ser | Gly | Gly | Gly | Ser | Gly | Gly | Gly | Thr | Gln | Asp | Cys | Ser |
|     |     |     | 260 |     |     |     | 265 |     |     |     |     |     | 270 |     |     |
| Phe | Gln | His | Ser | Pro | Ile | Ser | Ser | Asp | Phe | Ala | Val | Lys | Ile | Arg | Glu |
|     | 275 |     |     |     |     | 280 |     |     |     |     |     | 285 |     |     |     |
| Leu | Ser | Asp | Tyr | Leu | Leu | Gln | Asp | Tyr | Pro | Val | Thr | Val |     |     |     |
|     | 290 |     |     |     |     | 295 |     |     |     |     | 300 |     |     |     |     |

|       |         |
|-------|---------|
| <210> | 79      |
| <211> | 296     |
| <212> | PRT     |
| <213> | Unknown |

<220>  
 <221> MUTAGEN  
 <222> 1-296  
 <223>

<400> 79

```

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg
 1      5      10      15
Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met
      20      25      30
Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe
      35      40      45
Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile
      50      55      60
Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser
65      70      75      80
Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu
      85      90      95
Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
      100     105     110
Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile
      115     120     125
Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro
      130     135     140
Asn Met Ala Val Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val
145     150     155     160
Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro
      165     170     175
Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu
      180     185     190
Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn
      195     200     205
Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu
      210     215     220
Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Thr Gln Asp Cys Ser Phe
225     230     235     240
Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu
      245     250     255
Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu
      260     265     270
Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln
      275     280     285
Arg Trp Met Glu Arg Leu Lys Thr
      290     295

```

<210> 80  
 <211> 301  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-301  
 <223>

<400> 80

```

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg
 1      5      10      15

```

Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met  
                   20                  25                  30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
                   35                  40                  45  
 Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
                   50                  55                  60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
                   65                  70                  75                  80  
 Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
                   85                  90                  95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
                   100                  105                  110  
 Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile  
                   115                  120                  125  
 Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro  
                   130                  135                  140  
 Asn Met Ala Val Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val  
                   145                  150                  155                  160  
 Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro  
                   165                  170                  175  
 Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu  
                   180                  185                  190  
 Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn  
                   195                  200                  205  
 Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu  
                   210                  215                  220  
 Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Thr  
                   225                  230                  235                  240  
 Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val  
                   245                  250                  255  
 Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr  
                   260                  265                  270  
 Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg  
                   275                  280                  285  
 Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr  
                   290                  295                  300

<210> 81  
 <211> 296  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-296  
 <223>

<400> 81

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
   1                  5                  10                  15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met  
                   20                  25                  30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
                   35                  40                  45  
 Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
                   50                  55                  60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
                   65                  70                  75                  80  
 Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
                   85                  90                  95

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

<210> 82  
 <211> 301  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-301  
 <223>

<400> 82

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1 5 10 15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met  
 20 25 30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
 35 40 45  
 Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
 50 55 60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
 65 70 75 80  
 Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
 85 90 95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
 100 105 110  
 Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile  
 115 120 125  
 Ser Thr Ile Asn Pro Ser Pro Ser Lys Glu Ser His Lys Ser Pro  
 130 135 140  
 Asn Met Ala Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu  
 145 150 155 160  
 Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn  
 165 170 175

Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu  
 180 185 190  
 Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Thr  
 195 200 205  
 Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val  
 210 215 220  
 Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr  
 225 230 235 240  
 Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg  
 245 250 255  
 Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly  
 260 265 270  
 Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe  
 275 280 285  
 Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu  
 290 295 300

<210> 83  
 <211> 296  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-296  
 <223>

<400> 83

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1 5 10 15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met  
 20 25 30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
 35 40 45  
 Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
 50 55 60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
 65 70 75 80  
 Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
 85 90 95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
 100 105 110  
 Tyr Val Glu Gly Gly Gly Ser Ser Pro Gly Glu Pro Ser Gly Pro Ile  
 115 120 125  
 Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro  
 130 135 140  
 Asn Met Ala Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln  
 145 150 155 160  
 Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys  
 165 170 175  
 Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser  
 180 185 190  
 Gly Gly Gly Ser Gly Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro  
 195 200 205  
 Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu  
 210 215 220  
 Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu  
 225 230 235 240  
 Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu  
 245 250 255

Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg  
                   260                  265                  270  
 Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro  
                   275                  280                  285  
 Pro Ser Cys Leu Arg Phe Val Gln  
                   290                  295

<210> 84  
 <211> 301  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-301  
 <223>

<400> 84

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1                  5                  10                  15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met  
                   20                  25                  30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
                   35                  40                  45  
 Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
                   50                  55                  60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
 65                  70                  75                  80  
 Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
                   85                  90                  95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
                   100                  105                  110  
 Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile  
                   115                  120                  125  
 Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro  
                   130                  135                  140  
 Asn Met Ala Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln  
 145                  150                  155                  160  
 Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys  
                   165                  170                  175  
 Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser  
                   180                  185                  190  
 Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Thr Gln Asp Cys Ser  
                   195                  200                  205  
 Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu  
                   210                  215                  220  
 Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn  
 225                  230                  235                  240  
 Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala  
                   245                  250                  255  
 Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln  
                   260                  265                  270  
 Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys  
                   275                  280                  285  
 Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln  
                   290                  295                  300

<210> 85  
 <211> 292  
 <212> PRT

&lt;213&gt; Unknown

&lt;220&gt;

&lt;221&gt; MUTAGEN

&lt;222&gt; 1-292

&lt;223&gt;

&lt;400&gt; 85

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1 5 10 15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met  
 20 25 30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
 35 40 45  
 Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
 50 55 60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
 65 70 75 80  
 Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
 85 90 95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
 100 105 110  
 Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile  
 115 120 125  
 Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro  
 130 135 140  
 Asn Met Ala Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln Asp Glu  
 145 150 155 160  
 Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln Arg Trp Met  
 165 170 175  
 Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly Leu Leu Glu  
 180 185 190  
 Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro  
 195 200 205  
 Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu  
 210 215 220  
 Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg  
 225 230 235 240  
 Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser  
 245 250 255  
 Thr Leu Gly Gly Gly Ser Gly Gly Thr Gln Asp Cys Ser Phe Gln His  
 260 265 270  
 Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp  
 275 280 285  
 Tyr Leu Leu Gln  
 290

&lt;210&gt; 86

&lt;211&gt; 293

&lt;212&gt; PRT

&lt;213&gt; Unknown

&lt;220&gt;

&lt;221&gt; MUTAGEN

&lt;222&gt; 1-293

&lt;223&gt;

&lt;400&gt; 86

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg

```

1           5           10           15
Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met
                20                25                30
Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Ala Phe
                35                40                45
Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile
                50                55                60
Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser
65                70                75                80
Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu
                85                90                95
Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
                100                105                110
Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile
                115                120                125
Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro
130                135                140
Asn Met Ala Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln Asp Glu
145                150                155                160
Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln Arg Trp Met
                165                170                175
Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly Leu Leu Glu
                180                185                190
Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro
195                200                205
Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu
210                215                220
Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg
225                230                235                240
Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser
                245                250                255
Thr Leu Gly Gly Gly Ser Gly Gly Gly Thr Gln Asp Cys Ser Phe Gln
                260                265                270
His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser
275                280                285
Asp Tyr Leu Leu Gln
290

```

```

<210>      87
<211>      299
<212>      PRT
<213>      Unknown

```

```

<220>
<221>      MUTAGEN
<222>      1-299
<223>

```

```

<400>      87

```

```

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg
1           5           10           15
Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met
                20                25                30
Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Ala Phe
                35                40                45
Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile
                50                55                60
Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser
65                70                75                80
Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu

```

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

<210> 88  
 <211> 307  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-307  
 <223>

<400> 88

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1 5 10 15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met  
 20 25 30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
 35 40 45  
 Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
 50 55 60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
 65 70 75 80  
 Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
 85 90 95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
 100 105 110  
 Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile  
 115 120 125  
 Ser Thr Ile Asn Pro Ser Pro Ser Lys Glu Ser His Lys Ser Pro  
 130 135 140  
 Asn Met Ala Val Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val  
 145 150 155 160  
 Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro

165 170 175  
 Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu  
 180 185 190  
 Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn  
 195 200 205  
 Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu  
 210 215 220  
 Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Ser Gly Gly Gly Ser  
 225 230 235 240  
 Gly Gly Gly Ser Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile  
 245 250 255  
 Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu  
 260 265 270  
 Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu  
 275 280 285  
 Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg  
 290 295 300  
 Leu Lys Thr  
 305

<210> 89  
 <211> 292  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-292  
 <223>

<400> 89

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1 5 10 15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met  
 20 25 30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
 35 40 45  
 Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
 50 55 60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
 65 70 75 80  
 Arg His Pro Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
 85 90 95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
 100 105 110  
 Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile  
 115 120 125  
 Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro  
 130 135 140  
 Asn Met Ala Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu  
 145 150 155 160  
 Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val  
 165 170 175  
 Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile  
 180 185 190  
 His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg  
 195 200 205  
 Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln  
 210 215 220  
 Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys

[illegible]

|       |         |
|-------|---------|
| <210> | 90      |
| <211> | 293     |
| <212> | PRT     |
| <213> | Unknown |

|       |         |
|-------|---------|
| <220> |         |
| <221> | MUTAGEN |
| <222> | 1-293   |
| <223> |         |

<400> 90

[illegible]

<210> 91  
 <211> 299  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-299  
 <223>

<400> 91

```

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg
 1           5           10           15
Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met
          20           25           30
Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe
          35           40           45
Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile
          50           55           60
Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser
65          70           75           80
Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu
          85           90           95
Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
          100          105          110
Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile
          115          120          125
Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro
          130          135          140
Asn Met Ala Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu
145          150          155          160
Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val
          165          170          175
Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile
          180          185          190
His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg
          195          200          205
Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln
          210          215          220
Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys
225          230          235          240
Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser
          245          250          255
Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp Cys Ser Phe Gln
          260          265          270
His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser
          275          280          285
Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val
          290          295

```

<210> 92  
 <211> 307  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-307  
 <223>

&lt;400&gt; 92

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1 5 10 15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met  
 20 25 30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
 35 40 45  
 Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
 50 55 60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
 65 70 75 80  
 Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
 85 90 95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
 100 105 110  
 Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile  
 115 120 125  
 Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro  
 130 135 140  
 Asn Met Ala Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu  
 145 150 155 160  
 Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val  
 165 170 175  
 Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile  
 180 185 190  
 His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg  
 195 200 205  
 Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln  
 210 215 220  
 Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys  
 225 230 235 240  
 Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser  
 245 250 255  
 Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser  
 260 265 270  
 Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe  
 275 280 285  
 Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro  
 290 295 300  
 Val Thr Val  
 305

<210> 93  
 <211> 292  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-292  
 <223>

&lt;400&gt; 93

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1 5 10 15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met  
 20 25 30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
 35 40 45

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

<210> 94  
 <211> 293  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-293  
 <223>

<400> 94

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1 5 10 15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met  
 20 25 30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
 35 40 45  
 Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
 50 55 60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
 65 70 75 80  
 Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
 85 90 95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
 100 105 110  
 Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile  
 115 120 125

Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro  
 130 135 140  
 Asn Met Ala Val Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val  
 145 150 155 160  
 Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro  
 165 170 175  
 Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu  
 180 185 190  
 Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn  
 195 200 205  
 Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu  
 210 215 220  
 Gly Gly Gly Ser Gly Gly Gly Thr Gln Asp Cys Ser Phe Gln His Ser  
 225 230 235 240  
 Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr  
 245 250 255  
 Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln Asp Glu  
 260 265 270  
 Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln Arg Trp Met  
 275 280 285  
 Glu Arg Leu Lys Thr  
 290

<210> 95  
 <211> 299  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-299  
 <223>

<400> 95

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1 5 10 15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met  
 20 25 30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
 35 40 45  
 Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
 50 55 60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
 65 70 75 80  
 Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
 85 90 95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
 100 105 110  
 Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile  
 115 120 125  
 Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro  
 130 135 140  
 Asn Met Ala Val Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val  
 145 150 155 160  
 Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro  
 165 170 175  
 Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu  
 180 185 190  
 Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn  
 195 200 205

Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu  
 210 215 220  
 Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp  
 225 230 235 240  
 Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile  
 245 250 255  
 Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala  
 260 265 270  
 Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val  
 275 280 285  
 Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr  
 290 295

<210> 96  
 <211> 307  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-307  
 <223>

<400> 96

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1 5 10 15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Leu Asn Ser Glu Asp Met  
 20 25 30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
 35 40 45  
 Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
 50 55 60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
 65 70 75 80  
 Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
 85 90 95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
 100 105 110  
 Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile  
 115 120 125  
 Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro  
 130 135 140  
 Asn Met Ala Val Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val  
 145 150 155 160  
 Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro  
 165 170 175  
 Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu  
 180 185 190  
 Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn  
 195 200 205  
 Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu  
 210 215 220  
 Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser  
 225 230 235 240  
 Gly Gly Gly Ser Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile  
 245 250 255  
 Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu  
 260 265 270  
 Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu  
 275 280 285

Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg  
 290 295 300  
 Leu Lys Thr  
 305

<210> 97  
 <211> 292  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-292  
 <223>

<400> 97

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1 5 10 15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met  
 20 25 30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
 35 40 45  
 Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
 50 55 60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
 65 70 75 80  
 Arg His Pro Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
 85 90 95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
 100 105 110  
 Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile  
 115 120 125  
 Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro  
 130 135 140  
 Asn Met Ala Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu  
 145 150 155 160  
 Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn  
 165 170 175  
 Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu  
 180 185 190  
 Gly Gly Gly Ser Gly Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro  
 195 200 205  
 Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu  
 210 215 220  
 Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu  
 225 230 235 240  
 Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu  
 245 250 255  
 Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg  
 260 265 270  
 Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro  
 275 280 285  
 Pro Ser Cys Leu  
 290

<210> 98  
 <211> 293  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-293  
 <223>

<400> 98

```

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg
 1          5          10          15
Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met
          20          25          30
Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe
          35          40          45
Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile
          50          55          60
Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser
65          70          75          80
Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu
          85          90          95
Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
          100          105          110
Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile
          115          120          125
Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro
          130          135          140
Asn Met Ala Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu
145          150          155          160
Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn
          165          170          175
Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu
          180          185          190
Gly Gly Gly Ser Gly Gly Gly Thr Gln Asp Cys Ser Phe Gln His Ser
          195          200          205
Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr
          210          215          220
Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln Asp Glu
225          230          235          240
Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln Arg Trp Met
          245          250          255
Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly Leu Leu Glu
          260          265          270
Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro
          275          280          285
Pro Pro Ser Cys Leu
          290

```

<210> 99  
 <211> 299  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-299  
 <223>

<400> 99

```

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg
 1          5          10          15
Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met

```

20 25 30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
 35 40 45  
 Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
 50 55 60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
 65 70 75 80  
 Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
 85 90 95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln  
 100 105 110  
 Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile  
 115 120 125  
 Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro  
 130 135 140  
 Asn Met Ala Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu  
 145 150 155 160  
 Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn  
 165 170 175  
 Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu  
 180 185 190  
 Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp  
 195 200 205  
 Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile  
 210 215 220  
 Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala  
 225 230 235 240  
 Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val  
 245 250 255  
 Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys  
 260 265 270  
 Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr  
 275 280 285  
 Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu  
 290 295

<210> 100  
 <211> 307  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-307  
 <223>

<400> 100

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1 5 10 15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met  
 20 25 30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
 35 40 45  
 Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
 50 55 60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
 65 70 75 80  
 Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
 85 90 95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln

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

<210> 101  
 <211> 292  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-292  
 <223>

<400> 101

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1 5 10 15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Leu Asn Ser Glu Asp Met  
 20 25 30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
 35 40 45  
 Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
 50 55 60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
 65 70 75 80  
 Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
 85 90 95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
 100 105 110  
 Tyr Val Glu Gly Gly Gly Ser Ser Pro Gly Glu Pro Ser Gly Pro Ile  
 115 120 125  
 Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro  
 130 135 140  
 Asn Met Ala Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln  
 145 150 155 160  
 Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys

```

                165                170                175
Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser
                180                185                190
Gly Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp
                195                200                205
Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr
                210                215                220
Pro Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly
225                230                235                240
Leu Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr
                245                250                255
Val Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu
                260                265                270
Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu
                275                280                285
Arg Phe Val Gln
290

```

```

<210>    102
<211>    293
<212>    PRT
<213>    Unknown

```

```

<220>
<221>    MUTAGEN
<222>    1-293
<223>

```

```

<400>    102

```

```

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg
 1          5          10          15
Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met
                20          25          30
Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe
                35          40          45
Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile
 50          55          60
Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser
65          70          75          80
Arg His Pro Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu
                85          90          95
Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
                100          105          110
Tyr Val Glu Gly Gly Gly Ser Ser Pro Gly Glu Pro Ser Gly Pro Ile
                115          120          125
Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro
                130          135          140
Asn Met Ala Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln
145          150          155          160
Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys
                165          170          175
Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser
                180          185          190
Gly Gly Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser
                195          200          205
Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp
                210          215          220
Tyr Pro Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly
225          230          235          240
Gly Leu Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys

```

245 250 255  
 Thr Val Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr  
 260 265 270  
 Glu Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys  
 275 280 285  
 Leu Arg Phe Val Gln  
 290

<210> 103  
 <211> 299  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-299  
 <223>

<400> 103

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1 5 10 15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met  
 20 25 30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
 35 40 45  
 Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
 50 55 60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
 65 70 75 80  
 Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
 85 90 95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
 100 105 110  
 Tyr Val Glu Gly Gly Gly Ser Ser Pro Gly Glu Pro Ser Gly Pro Ile  
 115 120 125  
 Ser Thr Ile Asn Pro Ser Pro Ser Lys Glu Ser His Lys Ser Pro  
 130 135 140  
 Asn Met Ala Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln  
 145 150 155 160  
 Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys  
 165 170 175  
 Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser  
 180 185 190  
 Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp Cys Ser Phe Gln  
 195 200 205  
 His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser  
 210 215 220  
 Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln  
 225 230 235 240  
 Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln Arg  
 245 250 255  
 Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly Leu  
 260 265 270  
 Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala Phe  
 275 280 285  
 Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln  
 290 295

<210> 104  
 <211> 307

<212> PRT  
<213> Unknown

<220>  
<221> MUTAGEN  
<222> 1-307  
<223>

<400> 104

```

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg
1          5          10          15
Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met
          20          25          30
Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe
          35          40          45
Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile
          50          55          60
Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser
65          70          75          80
Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu
          85          90          95
Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
          100          105          110
Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile
          115          120          125
Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro
          130          135          140
Asn Met Ala Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln
145          150          155          160
Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys
          165          170          175
Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser
          180          185          190
Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser
          195          200          205
Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe
          210          215          220
Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro
225          230          235          240
Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu
          245          250          255
Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val
          260          265          270
Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile
          275          280          285
His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg
          290          295          300
Phe Val Gln
305

```

<210> 105  
<211> 749  
<212> PRT  
<213> Unknown

<220>  
<221> MUTAGEN  
<222> 1-749  
<223>

&lt;400&gt; 105

Gly Ser Thr Met Ser Arg Leu Pro Val Leu Leu Leu Leu Gln Leu Leu  
 1 5 10 15  
 Val Arg Pro Ala Met Ser Thr Asn Gln Asp Leu Pro Val Ile Lys Cys  
 20 25 30  
 Val Leu Ile Asn His Lys Asn Asn Asp Ser Ser Val Gly Lys Ser Ser  
 35 40 45  
 Ser Tyr Pro Met Val Ser Glu Ser Pro Glu Asp Leu Gly Cys Ala Leu  
 50 55 60  
 Arg Pro Gln Ser Ser Gly Thr Val Tyr Glu Ala Ala Val Glu Val  
 65 70 75 80  
 Asp Val Ser Ala Ser Ile Thr Leu Gln Val Leu Val Asp Ala Pro Gly  
 85 90 95  
 Asn Ile Ser Cys Leu Trp Val Phe Lys His Ser Ser Leu Asn Cys Gln  
 100 105 110  
 Pro His Phe Asp Leu Gln Asn Arg Gly Val Val Ser Met Val Ile Leu  
 115 120 125  
 Lys Met Thr Glu Thr Gln Ala Gly Glu Tyr Leu Leu Phe Ile Gln Ser  
 130 135 140  
 Glu Ala Thr Asn Tyr Thr Ile Leu Phe Thr Val Ser Ile Arg Asn Thr  
 145 150 155 160  
 Leu Leu Tyr Thr Leu Arg Arg Pro Tyr Phe Arg Lys Met Glu Asn Gln  
 165 170 175  
 Asp Ala Leu Val Cys Ile Ser Glu Ser Val Pro Glu Pro Ile Val Glu  
 180 185 190  
 Trp Val Leu Cys Asp Ser Gln Gly Glu Ser Cys Lys Glu Glu Ser Pro  
 195 200 205  
 Ala Val Val Lys Lys Glu Glu Lys Val Leu His Glu Leu Phe Gly Met  
 210 215 220  
 Asp Ile Arg Cys Cys Ala Arg Asn Glu Leu Gly Arg Glu Cys Thr Arg  
 225 230 235 240  
 Leu Phe Thr Ile Asp Leu Asn Gln Thr Pro Gln Thr Thr Leu Pro Gln  
 245 250 255  
 Leu Phe Leu Lys Val Gly Glu Pro Leu Trp Ile Arg Cys Lys Ala Val  
 260 265 270  
 His Val Asn His Gly Phe Gly Leu Thr Trp Glu Leu Glu Asn Lys Ala  
 275 280 285  
 Leu Glu Glu Gly Asn Tyr Phe Glu Met Ser Thr Tyr Ser Thr Asn Arg  
 290 295 300  
 Thr Met Ile Arg Ile Leu Phe Ala Phe Val Ser Ser Val Ala Arg Asn  
 305 310 315 320  
 Asp Thr Gly Tyr Tyr Thr Cys Ser Ser Ser Lys His Pro Ser Gln Ser  
 325 330 335  
 Ala Leu Val Thr Ile Val Glu Lys Gly Phe Ile Asn Ala Thr Asn Ser  
 340 345 350  
 Ser Glu Asp Tyr Glu Ile Asp Gln Tyr Glu Glu Phe Cys Phe Ser Val  
 355 360 365  
 Arg Phe Lys Ala Tyr Pro Gln Ile Arg Cys Thr Trp Thr Phe Ser Arg  
 370 375 380  
 Lys Ser Phe Pro Cys Glu Gln Lys Gly Leu Asp Asn Gly Tyr Ser Ile  
 385 390 395 400  
 Ser Lys Phe Cys Asn His Lys His Gln Pro Gly Glu Tyr Ile Phe His  
 405 410 415  
 Ala Glu Asn Asp Asp Ala Gln Phe Thr Lys Met Phe Thr Leu Asn Ile  
 420 425 430  
 Arg Arg Lys Pro Gln Val Leu Ala Glu Ala Ser Ala Ser Gln Ala Ser  
 435 440 445  
 Cys Phe Ser Asp Gly Tyr Pro Leu Pro Ser Trp Thr Trp Lys Lys Cys  
 450 455 460  
 Ser Asp Lys Ser Pro Asn Cys Thr Glu Glu Ile Thr Glu Gly Val Trp

465                      470                      475                      480  
 Asn Arg Lys Ala Asn Arg Lys Val Phe Gly Gln Trp Val Ser Ser Ser  
                                  485                      490                      495  
 Thr Leu Asn Met Ser Glu Ala Ile Lys Gly Phe Leu Val Lys Cys Cys  
                                  500                      505                      510  
 Ala Tyr Asn Ser Leu Gly Thr Ser Cys Glu Thr Ile Leu Leu Asn Ser  
                                  515                      520                      525  
 Pro Gly Pro Phe Pro Phe Ile Gln Asp Asn Glu Phe Ile Ile Leu Gly  
                                  530                      535                      540  
 Leu Phe Gly Leu Leu Leu Leu Thr Cys Leu Cys Gly Thr Ala Trp  
 545                      550                      555                      560  
 Leu Cys Cys Ser Pro Asn Arg Lys Asn Pro Leu Trp Pro Ser Val Pro  
                                  565                      570                      575  
 Asp Pro Ala His Ser Ser Leu Gly Ser Trp Val Pro Thr Ile Met Glu  
                                  580                      585                      590  
 Glu Asp Ala Phe Gln Leu Pro Gly Leu Gly Thr Pro Pro Ile Thr Lys  
                                  595                      600                      605  
 Leu Thr Val Leu Glu Glu Asp Glu Lys Lys Pro Val Pro Trp Glu Ser  
                                  610                      615                      620  
 His Asn Ser Ser Glu Thr Cys Gly Leu Pro Thr Leu Val Gln Thr Tyr  
 625                      630                      635                      640  
 Val Leu Gln Gly Asp Pro Arg Ala Val Ser Thr Gln Pro Gln Ser Gln  
                                  645                      650                      655  
 Ser Gly Thr Ser Asp Gln Val Leu Tyr Gly Gln Leu Leu Gly Ser Pro  
                                  660                      665                      670  
 Thr Ser Pro Gly Pro Gly His Tyr Leu Arg Cys Asp Ser Thr Gln Pro  
                                  675                      680                      685  
 Leu Leu Ala Gly Leu Thr Pro Ser Pro Lys Ser Tyr Glu Asn Leu Trp  
                                  690                      695                      700  
 Phe Gln Ala Ser Pro Leu Gly Thr Leu Val Thr Pro Ala Pro Ser Gln  
 705                      710                      715                      720  
 Glu Asp Asp Cys Val Phe Gly Pro Leu Leu Asn Phe Pro Leu Leu Gln  
                                  725                      730                      735  
 Gly Ile Arg Val His Gly Met Glu Ala Leu Gly Ser Phe  
                                  740                      745

<210>      106  
 <211>      349  
 <212>      PRT  
 <213>      Unknown

<220>  
 <221>      MUTAGEN  
 <222>      1-349  
 <223>

<400>      106

Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu  
 1                      5                      10                      15  
 Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu  
                                  20                      25                      30  
 Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu  
                                  35                      40                      45  
 Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser  
                                  50                      55                      60  
 Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His  
 65                      70                      75                      80  
 Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile  
                                  85                      90                      95  
 Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala

```

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

```

```

<210>    107
<211>    314
<212>    PRT
<213>    Unknown

```

```

<220>
<221>    MUTAGEN
<222>    1-314
<223>

```

```

<400>    107

```

```

Ala Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe
 1      5      10      15
Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro
      20      25      30
Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu
      35      40      45
Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val
      50      55      60
Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile
65      70      75      80
His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg
      85      90      95
Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln
      100      105      110
Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys
      115      120      125
Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Tyr Val Glu Gly

```

130 135 140  
 Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn  
 145 150 155 160  
 Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala Thr  
 165 170 175  
 Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val  
 180 185 190  
 Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr  
 195 200 205  
 Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg  
 210 215 220  
 Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly  
 225 230 235 240  
 Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe  
 245 250 255  
 Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val  
 260 265 270  
 Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val  
 275 280 285  
 Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu  
 290 295 300  
 Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu  
 305 310

<210> 108  
 <211> 349  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-349  
 <223>

<400> 108

Ala Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe  
 1 5 10 15  
 Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro  
 20 25 30  
 Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu  
 35 40 45  
 Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val  
 50 55 60  
 Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile  
 65 70 75 80  
 His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg  
 85 90 95  
 Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln  
 100 105 110  
 Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys  
 115 120 125  
 Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Tyr Val Glu Gly  
 130 135 140  
 Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn  
 145 150 155 160  
 Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala Thr  
 165 170 175  
 Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys Cys  
 180 185 190  
 Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu

195                      200                      205  
 Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu  
 210                      215                      220  
 Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro  
 225                      230                      235                      240  
 Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly  
 245                      250                      255  
 Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser Pro  
 260                      265                      270  
 Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp Phe  
 275                      280                      285  
 Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala  
 290                      295                      300  
 Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln  
 305                      310                      315                      320  
 Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu  
 325                      330                      335  
 Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro  
 340                      345

<210> 109  
 <211> 523  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-523  
 <223>

<400> 109

Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu  
 1                      5                      10                      15  
 Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu  
 20                      25                      30  
 Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu  
 35                      40                      45  
 Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser  
 50                      55                      60  
 Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His  
 65                      70                      75                      80  
 Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile  
 85                      90                      95  
 Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala  
 100                      105                      110  
 Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala  
 115                      120                      125  
 Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala  
 130                      135                      140  
 Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser  
 145                      150                      155                      160  
 Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro Tyr  
 165                      170                      175  
 Val Glu Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser  
 180                      185                      190  
 Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn  
 195                      200                      205  
 Met Ala Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp  
 210                      215                      220  
 Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|
| 225 |     |     |     |     | 230 |     |     |     | 235 |     |     |     | 240 |     |     |  |
| Pro | Val | Thr | Val | Ala | Ser | Asn | Leu | Gln | Asp | Glu | Glu | Leu | Cys | Gly | Gly |  |
|     |     |     |     | 245 |     |     |     | 250 |     |     |     | 255 |     |     |     |  |
| Leu | Trp | Arg | Leu | Val | Leu | Ala | Gln | Arg | Trp | Met | Glu | Arg | Leu | Lys | Thr |  |
|     |     |     |     | 260 |     |     |     | 265 |     |     |     | 270 |     |     |     |  |
| Val | Ala | Gly | Ser | Lys | Met | Gln | Gly | Leu | Leu | Glu | Arg | Val | Asn | Thr | Glu |  |
|     |     |     |     | 275 |     |     |     | 280 |     |     |     | 285 |     |     |     |  |
| Ile | His | Phe | Val | Thr | Lys | Cys | Ala | Phe | Gln | Pro | Pro | Pro | Ser | Cys | Leu |  |
|     |     |     |     | 290 |     |     |     | 295 |     |     |     | 300 |     |     |     |  |
| Arg | Phe | Val | Gln | Thr | Asn | Ile | Ser | Arg | Leu | Leu | Gln | Glu | Thr | Ser | Glu |  |
| 305 |     |     |     |     | 310 |     |     |     | 315 |     |     |     | 320 |     |     |  |
| Gln | Leu | Val | Ala | Leu | Lys | Pro | Trp | Ile | Thr | Arg | Gln | Asn | Phe | Ser | Arg |  |
|     |     |     |     | 325 |     |     |     | 330 |     |     |     | 335 |     |     |     |  |
| Cys | Leu | Glu | Leu | Gln | Cys | Gln | Pro | Asp | Ser | Ser | Thr | Leu | Tyr | Val | Glu |  |
|     |     |     |     | 340 |     |     |     | 345 |     |     |     | 350 |     |     |     |  |
| Gly | Gly | Gly | Gly | Ser | Pro | Gly | Glu | Pro | Ser | Gly | Pro | Ile | Ser | Thr | Ile |  |
|     |     |     |     | 355 |     |     |     | 360 |     |     |     | 365 |     |     |     |  |
| Asn | Pro | Ser | Pro | Pro | Ser | Lys | Glu | Ser | His | Lys | Ser | Pro | Asn | Met | Ala |  |
|     |     |     |     | 370 |     |     |     | 375 |     |     |     | 380 |     |     |     |  |
| Thr | Gln | Asp | Cys | Ser | Phe | Gln | His | Ser | Pro | Ile | Ser | Ser | Asp | Phe | Ala |  |
| 385 |     |     |     |     | 390 |     |     |     | 395 |     |     |     | 400 |     |     |  |
| Val | Lys | Ile | Arg | Glu | Leu | Ser | Asp | Tyr | Leu | Leu | Gln | Asp | Tyr | Pro | Val |  |
|     |     |     |     | 405 |     |     |     | 410 |     |     |     | 415 |     |     |     |  |
| Thr | Val | Ala | Ser | Asn | Leu | Gln | Asp | Glu | Glu | Leu | Cys | Gly | Gly | Leu | Trp |  |
|     |     |     |     | 420 |     |     |     | 425 |     |     |     | 430 |     |     |     |  |
| Arg | Leu | Val | Leu | Ala | Gln | Arg | Trp | Met | Glu | Arg | Leu | Lys | Thr | Val | Ala |  |
|     |     |     |     | 435 |     |     |     | 440 |     |     |     | 445 |     |     |     |  |
| Gly | Ser | Lys | Met | Gln | Gly | Leu | Leu | Glu | Arg | Val | Asn | Thr | Glu | Ile | His |  |
|     |     |     |     | 450 |     |     |     | 455 |     |     |     | 460 |     |     |     |  |
| Phe | Val | Thr | Lys | Cys | Ala | Phe | Gln | Pro | Pro | Pro | Ser | Cys | Leu | Arg | Phe |  |
| 465 |     |     |     |     | 470 |     |     |     | 475 |     |     |     | 480 |     |     |  |
| Val | Gln | Thr | Asn | Ile | Ser | Arg | Leu | Leu | Gln | Glu | Thr | Ser | Glu | Gln | Leu |  |
|     |     |     |     | 485 |     |     |     | 490 |     |     |     | 495 |     |     |     |  |
| Val | Ala | Leu | Lys | Pro | Trp | Ile | Thr | Arg | Gln | Asn | Phe | Ser | Arg | Cys | Leu |  |
|     |     |     |     | 500 |     |     |     | 505 |     |     |     | 510 |     |     |     |  |
| Glu | Leu | Gln | Cys | Gln | Pro | Asp | Ser | Ser | Thr | Leu |     |     |     |     |     |  |
|     |     |     |     | 515 |     |     |     | 520 |     |     |     |     |     |     |     |  |

|       |         |
|-------|---------|
| <210> | 110     |
| <211> | 460     |
| <212> | PRT     |
| <213> | Unknown |

<220>  
<221> MUTAGEN  
<222> 1-460  
<223>

<400>      110

|          |     |     |     |          |     |     |     |     |           |     |     |     |     |           |     |
|----------|-----|-----|-----|----------|-----|-----|-----|-----|-----------|-----|-----|-----|-----|-----------|-----|
| Ala<br>1 | Asn | Cys | Ser | Ile<br>5 | Met | Ile | Asp | Glu | Ile<br>10 | Ile | His | His | Leu | Lys<br>15 | Arg |
| Pro      | Pro | Ala | Pro | Leu      | Leu | Asp | Pro | Asn | Asn       | Leu | Asn | Asp | Glu | Asp       | Val |
|          |     |     | 20  |          |     |     |     | 25  |           |     |     |     | 30  |           |     |
| Ser      | Ile | Leu | Met | Asp      | Arg | Asn | Leu | Arg | Leu       | Pro | Asn | Leu | Glu | Ser       | Phe |
|          |     | 35  |     |          |     | 40  |     |     |           |     | 45  |     |     |           |     |
| Val      | Arg | Ala | Val | Lys      | Asn | Leu | Glu | Asn | Ala       | Ser | Gly | Ile | Glu | Ala       | Ile |
|          | 50  |     |     |          | 55  |     |     |     |           |     | 60  |     |     |           |     |
| Leu      | Arg | Asn | Leu | Gln      | Pro | Cys | Leu | Pro | Ser       | Ala | Thr | Ala | Ala | Pro       | Ser |
| 65       |     |     |     | 70       |     |     |     |     |           | 75  |     |     |     | 80        |     |
| Arg      | His | Pro | Ile | Ile      | Ile | Lys | Ala | Gly | Asp       | Trp | Gln | Glu | Phe | Arg       | Glu |

85 90 95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
 100 105 110  
 Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile  
 115 120 125  
 Ser Thr Ile Asn Pro Ser Pro Ser Lys Glu Ser His Lys Ser Pro  
 130 135 140  
 Asn Met Ala Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser  
 145 150 155 160  
 Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp  
 165 170 175  
 Tyr Pro Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly  
 180 185 190  
 Gly Leu Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys  
 195 200 205  
 Thr Val Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr  
 210 215 220  
 Glu Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys  
 225 230 235 240  
 Leu Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser  
 245 250 255  
 Glu Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser  
 260 265 270  
 Arg Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Tyr Val  
 275 280 285  
 Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr  
 290 295 300  
 Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met  
 305 310 315 320  
 Ala Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe  
 325 330 335  
 Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro  
 340 345 350  
 Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu  
 355 360 365  
 Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val  
 370 375 380  
 Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile  
 385 390 395 400  
 His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Ser Cys Leu Arg  
 405 410 415  
 Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln  
 420 425 430  
 Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys  
 435 440 445  
 Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu  
 450 455 460

<210> 111  
 <211> 523  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-523  
 <223>

<400> 111

Ala Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe

|                                                                 |     |     |     |
|-----------------------------------------------------------------|-----|-----|-----|
| 1                                                               | 5   | 10  | 15  |
| Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro |     |     |     |
| 20                                                              | 25  | 30  |     |
| Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu |     |     |     |
| 35                                                              | 40  | 45  |     |
| Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val |     |     |     |
| 50                                                              | 55  | 60  |     |
| Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile |     |     |     |
| 65                                                              | 70  | 75  | 80  |
| His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg |     |     |     |
| 85                                                              | 90  | 95  |     |
| Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln |     |     |     |
| 100                                                             | 105 | 110 |     |
| Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys |     |     |     |
| 115                                                             | 120 | 125 |     |
| Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Tyr Val Glu Gly |     |     |     |
| 130                                                             | 135 | 140 |     |
| Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn |     |     |     |
| 145                                                             | 150 | 155 | 160 |
| Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala Thr |     |     |     |
| 165                                                             | 170 | 175 |     |
| Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys Ser |     |     |     |
| 180                                                             | 185 | 190 |     |
| Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu |     |     |     |
| 195                                                             | 200 | 205 |     |
| Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu |     |     |     |
| 210                                                             | 215 | 220 |     |
| Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro |     |     |     |
| 225                                                             | 230 | 235 | 240 |
| Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly |     |     |     |
| 245                                                             | 250 | 255 |     |
| Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser Pro |     |     |     |
| 260                                                             | 265 | 270 |     |
| Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp Phe |     |     |     |
| 275                                                             | 280 | 285 |     |
| Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala |     |     |     |
| 290                                                             | 295 | 300 |     |
| Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln |     |     |     |
| 305                                                             | 310 | 315 | 320 |
| Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu |     |     |     |
| 325                                                             | 330 | 335 |     |
| Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro Tyr Val Glu |     |     |     |
| 340                                                             | 345 | 350 |     |
| Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile |     |     |     |
| 355                                                             | 360 | 365 |     |
| Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala |     |     |     |
| 370                                                             | 375 | 380 |     |
| Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala |     |     |     |
| 385                                                             | 390 | 395 | 400 |
| Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val |     |     |     |
| 405                                                             | 410 | 415 |     |
| Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp |     |     |     |
| 420                                                             | 425 | 430 |     |
| Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala |     |     |     |
| 435                                                             | 440 | 445 |     |
| Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His |     |     |     |
| 450                                                             | 455 | 460 |     |
| Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe |     |     |     |
| 465                                                             | 470 | 475 | 480 |
| Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu |     |     |     |
| 485                                                             | 490 | 495 |     |

Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu  
                   500                  505                  510  
 Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu  
                   515                  520

<210> 112  
 <211> 334  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-334  
 <223>

<400> 112

Ala Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe  
 1                  5                  10                  15  
 Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro  
                   20                  25                  30  
 Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu  
                   35                  40                  45  
 Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val  
                   50                  55                  60  
 Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile  
 65                  70                  75                  80  
 His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Ser Cys Leu Arg  
                   85                  90                  95  
 Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln  
                   100                  105                  110  
 Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys  
                   115                  120                  125  
 Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Tyr Val Glu Gly  
                   130                  135                  140  
 Gly Gly Gly Ser Pro Gly Gly Gly Ser Gly Gly Gly Ser Asn Met Ala  
 145                  150                  155                  160  
 Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys  
                   165                  170                  175  
 Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln  
                   180                  185                  190  
 Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val  
                   195                  200                  205  
 Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys  
                   210                  215                  220  
 Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser  
 225                  230                  235                  240  
 Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser  
                   245                  250                  255  
 Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp  
                   260                  265                  270  
 Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro  
                   275                  280                  285  
 Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe  
                   290                  295                  300  
 Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe  
 305                  310                  315                  320  
 Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro  
                   325                  330

<210> 113

<211> 296  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-296  
 <223>

<400> 113

```

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg
 1           5           10           15
Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met
           20           25           30
Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe
           35           40           45
Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile
           50           55           60
Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser
65           70           75           80
Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu
           85           90           95
Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
           100          105          110
Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile
           115          120          125
Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro
           130          135          140
Asn Met Ala Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln Asp Glu
145           150           155           160
Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln Arg Trp Met
           165           170           175
Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly Leu Leu Glu
           180          185          190
Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro
           195          200          205
Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu
           210          215          220
Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg
225           230           235           240
Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser
           245           250           255
Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Thr Gln Asp Cys
           260           265           270
Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg
           275           280           285
Glu Leu Ser Asp Tyr Leu Leu Gln
           290           295

```

<210> 114  
 <211> 301  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-301  
 <223>

<400> 114

```

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg
 1           5           10           15
Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met
           20           25           30
Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe
           35           40           45
Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile
           50           55           60
Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser
65           70           75           80
Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu
           85           90           95
Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
           100          105          110
Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile
           115          120          125
Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro
           130          135          140
Asn Met Ala Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln Asp Glu
145           150          155          160
Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln Arg Trp Met
           165          170          175
Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly Leu Leu Glu
           180          185          190
Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro
           195          200          205
Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu
           210          215          220
Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg
225           230          235          240
Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser
           245          250          255
Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly
           260          265          270
Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe
           275          280          285
Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln
290           295          300

```

```

<210>      115
<211>      296
<212>      PRT
<213>      Unknown

```

```

<220>
<221>      MUTAGEN
<222>      1-296
<223>

```

```

<400>      115

```

```

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg
 1           5           10           15
Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met
           20           25           30
Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe
           35           40           45
Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile
           50           55           60
Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser

```

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

|       |         |
|-------|---------|
| <210> | 116     |
| <211> | 301     |
| <212> | PRT     |
| <213> | Unknown |

<220>  
<221> MUTAGEN  
<222> 1-301  
<223>

<400> 116

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ala | Asn | Cys | Ser | Ile | Met | Ile | Asp | Glu | Ile | Ile | His | His | Leu | Lys | Arg |
| 1   |     |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |
| Pro | Pro | Asn | Pro | Leu | Leu | Asp | Pro | Asn | Asn | Leu | Asn | Ser | Glu | Asp | Met |
|     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |
| Asp | Ile | Leu | Met | Glu | Arg | Asn | Leu | Arg | Thr | Pro | Asn | Leu | Leu | Ala | Phe |
|     |     | 35  |     |     |     |     | 40  |     |     |     |     | 45  |     |     |     |
| Val | Arg | Ala | Val | Lys | His | Leu | Glu | Asn | Ala | Ser | Gly | Ile | Glu | Ala | Ile |
|     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |
| Leu | Arg | Asn | Leu | Gln | Pro | Cys | Leu | Pro | Ser | Ala | Thr | Ala | Ala | Pro | Ser |
| 65  |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |     |
| Arg | His | Pro | Ile | Ile | Ile | Lys | Ala | Gly | Asp | Trp | Gln | Glu | Phe | Arg | Glu |
|     |     |     | 85  |     |     |     |     |     | 90  |     |     |     |     | 95  |     |
| Lys | Leu | Thr | Phe | Tyr | Leu | Val | Thr | Leu | Glu | Gln | Ala | Gln | Glu | Gln | Gln |
|     |     | 100 |     |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
| Tyr | Val | Glu | Gly | Gly | Gly | Gly | Ser | Pro | Gly | Glu | Pro | Ser | Gly | Pro | Ile |
|     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |
| Ser | Thr | Ile | Asn | Pro | Ser | Pro | Pro | Ser | Lys | Glu | Ser | His | Lys | Ser | Pro |
|     | 130 |     |     |     |     | 135 |     |     |     |     |     | 140 |     |     |     |
| Asn | Met | Ala | Ala | Ser | Asn | Leu | Gln | Asp | Glu | Glu | Leu | Cys | Gly | Gly | Leu |

145                                      150                                      155                                      160  
 Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val  
                                          165                                      170                                      175  
 Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile  
                                          180                                      185                                      190  
 His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg  
                                          195                                      200                                      205  
 Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln  
                                          210                                      215                                      220  
 Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys  
 225                                      230                                      235                                      240  
 Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser  
                                          245                                      250                                      255  
 Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Thr Gln Asp Cys Ser  
                                          260                                      265                                      270  
 Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu  
                                          275                                      280                                      285  
 Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val  
                                          290                                      295                                      300

<210>      117  
 <211>      296  
 <212>      PRT  
 <213>      Unknown

<220>  
 <221>      MUTAGEN  
 <222>      1-296  
 <223>

<400>      117

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1                                      5                                      10                                      15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met  
                                          20                                      25                                      30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
                                          35                                      40                                      45  
 Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
                                          50                                      55                                      60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
 65                                      70                                      75                                      80  
 Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
                                          85                                      90                                      95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
                                          100                                      105                                      110  
 Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile  
                                          115                                      120                                      125  
 Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro  
                                          130                                      135                                      140  
 Asn Met Ala Val Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val  
 145                                      150                                      155                                      160  
 Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro  
                                          165                                      170                                      175  
 Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu  
                                          180                                      185                                      190  
 Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn  
                                          195                                      200                                      205  
 Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu  
                                          210                                      215                                      220  
 Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Thr Gln Asp Cys Ser Phe

|                                                                 |                                             |     |     |     |     |     |
|-----------------------------------------------------------------|---------------------------------------------|-----|-----|-----|-----|-----|
| 225                                                             |                                             | 230 |     | 235 |     | 240 |
| Gln His Ser Pro Ile                                             | Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu |     |     |     |     |     |
|                                                                 | 245                                         |     | 250 |     | 255 |     |
| Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu |                                             |     |     |     |     |     |
|                                                                 | 260                                         |     | 265 |     | 270 |     |
| Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln |                                             |     |     |     |     |     |
|                                                                 | 275                                         |     | 280 |     | 285 |     |
| Arg Trp Met Glu Arg Leu Lys Thr                                 |                                             |     |     |     |     |     |
|                                                                 | 290                                         |     | 295 |     |     |     |

<210> 118  
 <211> 301  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-301  
 <223>

<400> 118

|                                                                 |             |
|-----------------------------------------------------------------|-------------|
| Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg |             |
| 1 5 10 15                                                       |             |
| Pro Pro Asn Pro Leu Leu Asp Pro Asn Leu Asn Ser Glu Asp Met     |             |
| 20 25 30                                                        |             |
| Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe |             |
| 35 40 45                                                        |             |
| Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile |             |
| 50 55 60                                                        |             |
| Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser |             |
| 65 70 75 80                                                     |             |
| Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu |             |
| 85 90 95                                                        |             |
| Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln |             |
| 100 105 110                                                     |             |
| Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile |             |
| 115 120 125                                                     |             |
| Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro |             |
| 130 135 140                                                     |             |
| Asn Met Ala Val Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val |             |
| 145 150 155 160                                                 |             |
| Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro |             |
| 165 170 175                                                     |             |
| Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu |             |
| 180 185 190                                                     |             |
| Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn |             |
| 195 200 205                                                     |             |
| Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu |             |
| 210 215 220                                                     |             |
| Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Thr |             |
| 225 230 235 240                                                 |             |
| Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val |             |
|                                                                 | 245 250 255 |
| Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr |             |
|                                                                 | 260 265 270 |
| Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg |             |
|                                                                 | 275 280 285 |
| Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr             |             |
|                                                                 | 290 295 300 |

<210> 119  
 <211> 296  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-296  
 <223>

<400> 119

```

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg
 1          5          10          15
Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met
          20          25          30
Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe
          35          40          45
Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile
          50          55          60
Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser
65          70          75          80
Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu
          85          90          95
Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
          100          105          110
Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile
          115          120          125
Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro
          130          135          140
Asn Met Ala Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu
145          150          155          160
Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn
          165          170          175
Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu
          180          185          190
Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Thr Gln Asp Cys Ser Phe
          195          200          205
Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu
          210          215          220
Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu
225          230          235          240
Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln
          245          250          255
Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly
          260          265          270
Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala
          275          280          285
Phe Gln Pro Pro Pro Ser Cys Leu
          290          295

```

<210> 120  
 <211> 301  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-301  
 <223>

&lt;400&gt; 120

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1 5 10 15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met  
 20 25 30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
 35 40 45  
 Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
 50 55 60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
 65 70 75 80  
 Arg His Pro Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
 85 90 95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
 100 105 110  
 Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile  
 115 120 125  
 Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro  
 130 135 140  
 Asn Met Ala Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu  
 145 150 155 160  
 Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn  
 165 170 175  
 Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu  
 180 185 190  
 Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Thr  
 195 200 205  
 Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val  
 210 215 220  
 Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr  
 225 230 235 240  
 Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg  
 245 250 255  
 Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly  
 260 265 270  
 Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe  
 275 280 285  
 Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu  
 290 295 300

<210> 121  
 <211> 296  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-296  
 <223>

&lt;400&gt; 121

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1 5 10 15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met  
 20 25 30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
 35 40 45  
 Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
 50 55 60

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

<210> 122  
 <211> 301  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-301  
 <223>

<400> 122

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1 5 10 15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met  
 20 25 30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
 35 40 45  
 Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
 50 55 60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
 65 70 75 80  
 Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
 85 90 95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
 100 105 110  
 Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile  
 115 120 125  
 Ser Thr Ile Asn Pro Ser Pro Ser Lys Glu Ser His Lys Ser Pro  
 130 135 140

Asn Met Ala Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln  
 145 150 155 160  
 Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys  
 165 170 175  
 Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser  
 180 185 190  
 Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Thr Gln Asp Cys Ser  
 195 200 205  
 Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu  
 210 215 220  
 Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn  
 225 230 235 240  
 Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala  
 245 250 255  
 Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln  
 260 265 270  
 Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys  
 275 280 285  
 Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln  
 290 295 300

<210> 123  
 <211> 307  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-307  
 <223>

<400> 123

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1 5 10 15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met  
 20 25 30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
 35 40 45  
 Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
 50 55 60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
 65 70 75 80  
 Arg His Pro Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
 85 90 95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
 100 105 110  
 Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile  
 115 120 125  
 Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro  
 130 135 140  
 Asn Met Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp  
 145 150 155 160  
 Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala  
 165 170 175  
 Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His  
 180 185 190  
 Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe  
 195 200 205  
 Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu  
 210 215 220

Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu  
 225 230 235 240  
 Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly  
 245 250 255  
 Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly  
 260 265 270  
 Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala  
 275 280 285  
 Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val  
 290 295 300  
 Thr Val Ala  
 305

<210> 124  
 <211> 307  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-307  
 <223>

<400> 124

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1 5 10 15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met  
 20 25 30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
 35 40 45  
 Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
 50 55 60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
 65 70 75 80  
 Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
 85 90 95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
 100 105 110  
 Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile  
 115 120 125  
 Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro  
 130 135 140  
 Asn Met Ala Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg  
 145 150 155 160  
 Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly  
 165 170 175  
 Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe  
 180 185 190  
 Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val  
 195 200 205  
 Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val  
 210 215 220  
 Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu  
 225 230 235 240  
 Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly  
 245 250 255  
 Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Ser Gly Thr  
 260 265 270  
 Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val  
 275 280 285

Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr  
 290 295 300  
 Val Ala Ser  
 305

<210> 125  
 <211> 307  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-307  
 <223>

<400> 125

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1 5 10 15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met  
 20 25 30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
 35 40 45  
 Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
 50 55 60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
 65 70 75 80  
 Arg His Pro Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
 85 90 95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln  
 100 105 110  
 Tyr Val Glu Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile  
 115 120 125  
 Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro  
 130 135 140  
 Asn Met Ala Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu  
 145 150 155 160  
 Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser  
 165 170 175  
 Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val  
 180 185 190  
 Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln  
 195 200 205  
 Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala  
 210 215 220  
 Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu  
 225 230 235 240  
 Gln Cys Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly  
 245 250 255  
 Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln  
 260 265 270  
 Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys  
 275 280 285  
 Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val  
 290 295 300  
 Ala Ser Asn  
 305

<210> 126  
 <211> 307  
 <212> PRT

&lt;213&gt; Unknown

&lt;220&gt;

&lt;221&gt; MUTAGEN

&lt;222&gt; 1-307

&lt;223&gt;

&lt;400&gt; 126

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1 5 10 15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Leu Asn Ser Glu Asp Met  
 20 25 30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
 35 40 45  
 Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
 50 55 60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
 65 70 75 80  
 Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
 85 90 95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
 100 105 110  
 Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile  
 115 120 125  
 Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro  
 130 135 140  
 Asn Met Ala Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val  
 145 150 155 160  
 Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys  
 165 170 175  
 Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr  
 180 185 190  
 Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr  
 195 200 205  
 Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu  
 210 215 220  
 Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln  
 225 230 235 240  
 Cys Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser  
 245 250 255  
 Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp  
 260 265 270  
 Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile  
 275 280 285  
 Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala  
 290 295 300  
 Ser Asn Leu  
 305

&lt;210&gt; 127

&lt;211&gt; 305

&lt;212&gt; PRT

&lt;213&gt; Unknown

&lt;220&gt;

&lt;221&gt; MUTAGEN

&lt;222&gt; 1-305

&lt;223&gt;

&lt;400&gt; 127

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1 5 10 15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met  
 20 25 30  
 Asp Ile Leu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe Val Arg  
 35 40 45  
 Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg  
 50 55 60  
 Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His  
 65 70 75 80  
 Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu  
 85 90 95  
 Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln Tyr Val  
 100 105 110  
 Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr  
 115 120 125  
 Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met  
 130 135 140  
 Ala Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln Arg  
 145 150 155 160  
 Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly Leu  
 165 170 175  
 Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala Phe  
 180 185 190  
 Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser Arg  
 195 200 205  
 Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp Ile  
 210 215 220  
 Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro Asp  
 225 230 235 240  
 Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser  
 245 250 255  
 Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp Cys Ser Phe Gln  
 260 265 270  
 His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser  
 275 280 285  
 Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln  
 290 295 300  
 Asp  
 305

<210> 128  
 <211> 307  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-307  
 <223>

<400> 128

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1 5 10 15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met  
 20 25 30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
 35 40 45  
 Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile

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

<210>      129  
 <211>      307  
 <212>      PRT  
 <213>      Unknown

<220>  
 <221>      MUTAGEN  
 <222>      1-307  
 <223>

<400>      129

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1                                      5                                      10                                      15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met  
                                     20                                      25                                      30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
                                     35                                      40                                      45  
 Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
                                     50                                      55                                      60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
 65                                      70                                      75                                      80  
 Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
                                     85                                      90                                      95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln  
                                     100                                      105                                      110  
 Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile

```

      115              120              125
Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro
      130              135              140
Asn Met Ala Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln Arg
      145              150              155              160
Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly Leu
      165              170              175
Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala Phe
      180              185              190
Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser Arg
      195              200              205
Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp Ile
      210              215              220
Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro Asp
      225              230              235              240
Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser
      245              250              255
Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp Cys Ser Phe Gln
      260              265              270
His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser
      275              280              285
Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln
      290              295              300
Asp Glu Glu
      305

```

```

<210>      130
<211>      307
<212>      PRT
<213>      Unknown

```

```

<220>
<221>      MUTAGEN
<222>      1-307
<223>

```

```

<400>      130

```

```

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg
  1              5              10              15
Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met
      20              25              30
Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe
      35              40              45
Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile
      50              55              60
Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser
      65              70              75              80
Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu
      85              90              95
Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
      100              105              110
Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile
      115              120              125
Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro
      130              135              140
Asn Met Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp
      145              150              155              160
Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala
      165              170              175
Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His

```

180 185 190  
 Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe  
 195 200 205  
 Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu  
 210 215 220  
 Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu  
 225 230 235 240  
 Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly  
 245 250 255  
 Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Ser Gly  
 260 265 270  
 Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Ser Ala  
 275 280 285  
 Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val  
 290 295 300  
 Thr Val Ala  
 305

<210> 131  
 <211> 307  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-307  
 <223>

<400> 131

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1 5 10 15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met  
 20 25 30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
 35 40 45  
 Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
 50 55 60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
 65 70 75 80  
 Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
 85 90 95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
 100 105 110  
 Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile  
 115 120 125  
 Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro  
 130 135 140  
 Asn Met Ala Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val  
 145 150 155 160  
 Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys  
 165 170 175  
 Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr  
 180 185 190  
 Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr  
 195 200 205  
 Asn Ile Ser Arg Leu Leu Arg Glu Thr Ser Glu Gln Pro Val Ala Leu  
 210 215 220  
 Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln  
 225 230 235 240  
 Cys Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser

245 250 255  
 Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp  
 260 265 270  
 Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile  
 275 280 285  
 Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala  
 290 295 300  
 Ser Asn Leu  
 305

<210> 132  
 <211> 307  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-307  
 <223>

<400> 132

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1 5 10 15  
 Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met  
 20 25 30  
 Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe  
 35 40 45  
 Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile  
 50 55 60  
 Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser  
 65 70 75 80  
 Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu  
 85 90 95  
 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
 100 105 110  
 Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile  
 115 120 125  
 Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro  
 130 135 140  
 Asn Met Ala Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln Arg  
 145 150 155 160  
 Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly Leu  
 165 170 175  
 Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala Phe  
 180 185 190  
 Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser Arg  
 195 200 205  
 Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp Ile  
 210 215 220  
 Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Arg Pro Asp  
 225 230 235 240  
 Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser  
 245 250 255  
 Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp Cys Ser Phe Gln  
 260 265 270  
 His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser  
 275 280 285  
 Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln  
 290 295 300  
 Asp Glu Glu

305

<210> 133  
 <211> 302  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-302  
 <223>

<400> 133

Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln  
 1 5 10 15  
 Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly  
 20 25 30  
 Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala  
 35 40 45  
 Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser  
 50 55 60  
 Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp  
 65 70 75 80  
 Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro  
 85 90 95  
 Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly  
 100 105 110  
 Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp Cys Ser Phe  
 115 120 125  
 Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu  
 130 135 140  
 Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Tyr Val Glu Gly  
 145 150 155 160  
 Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn  
 165 170 175  
 Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala Asn  
 180 185 190  
 Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro Pro  
 195 200 205  
 Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met Asp Ile  
 210 215 220  
 Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe Val Arg  
 225 230 235 240  
 Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg  
 245 250 255  
 Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His  
 260 265 270  
 Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu  
 275 280 285  
 Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
 290 295 300

<210> 134  
 <211> 296  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-296

&lt;223&gt;

&lt;400&gt; 134

Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln  
 1 5 10 15  
 Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly  
 20 25 30  
 Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala  
 35 40 45  
 Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser  
 50 55 60  
 Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Arg Pro Trp  
 65 70 75 80  
 Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro  
 85 90 95  
 Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Thr  
 100 105 110  
 Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val  
 115 120 125  
 Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr  
 130 135 140  
 Val Ala Ser Asn Leu Gln Tyr Val Glu Gly Gly Gly Ser Pro Gly  
 145 150 155 160  
 Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys  
 165 170 175  
 Glu Ser His Lys Ser Pro Asn Met Ala Asn Cys Ser Ile Met Ile Asp  
 180 185 190  
 Glu Ile Ile His His Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro  
 195 200 205  
 Asn Asn Leu Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu  
 210 215 220  
 Arg Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu  
 225 230 235 240  
 Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu  
 245 250 255  
 Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala  
 260 265 270  
 Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr  
 275 280 285  
 Leu Glu Gln Ala Gln Glu Gln Gln  
 290 295

&lt;210&gt; 135

&lt;211&gt; 301

&lt;212&gt; PRT

&lt;213&gt; Unknown

&lt;220&gt;

&lt;221&gt; MUTAGEN

&lt;222&gt; 1-301

&lt;223&gt;

&lt;400&gt; 135

Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln  
 1 5 10 15  
 Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly  
 20 25 30  
 Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala  
 35 40 45

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

<210> 136  
 <211> 307  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-307  
 <223>

<400> 136

Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln  
 1 5 10 15  
 Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly  
 20 25 30  
 Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala  
 35 40 45  
 Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser  
 50 55 60  
 Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp  
 65 70 75 80  
 Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro  
 85 90 95  
 Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly  
 100 105 110  
 Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp Cys Ser Phe  
 115 120 125

Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu  
 130 135 140  
 Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu  
 145 150 155 160  
 Gln Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro  
 165 170 175  
 Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser  
 180 185 190  
 Pro Asn Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His  
 195 200 205  
 Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser  
 210 215 220  
 Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu  
 225 230 235 240  
 Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile  
 245 250 255  
 Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala  
 260 265 270  
 Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu  
 275 280 285  
 Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln  
 290 295 300  
 Glu Gln Gln  
 305

<210> 137  
 <211> 301  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-301  
 <223>

<400> 137

Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln  
 1 5 10 15  
 Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly  
 20 25 30  
 Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala  
 35 40 45  
 Phe Gln Pro Pro Pro Ser Cys Leu Arg Leu Val Gln Thr Asn Ile Ser  
 50 55 60  
 Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp  
 65 70 75 80  
 Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro  
 85 90 95  
 Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly  
 100 105 110  
 Ser Gly Gly Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser  
 115 120 125  
 Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln  
 130 135 140  
 Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln Tyr Val Glu Gly Gly  
 145 150 155 160  
 Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro  
 165 170 175  
 Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala Asn Cys  
 180 185 190

```

Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Asn
    195                      200                      205
Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met Asp Ile Leu
    210                      215                      220
Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe Val Arg Ala
    225                      230                      235                      240
Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn
    245                      250                      255
Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
    260                      265                      270
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr
    275                      280                      285
Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
    290                      295                      300

```

```

<210>    138
<211>    307
<212>    PRT
<213>    Unknown

```

```

<220>
<221>    MUTAGEN
<222>    1-307
<223>

```

```

<400>    138

```

```

Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln
  1          5          10          15
Arg Trp Met Gly Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly
    20          25          30
Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala
    35          40          45
Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser
    50          55          60
Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp
    65          70          75          80
Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro
    85          90          95
Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
    100         105         110
Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp Cys Ser Phe
    115         120         125
Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu
    130         135         140
Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu
    145         150         155         160
Gln Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro
    165         170         175
Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser
    180         185         190
Pro Asn Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
    195         200         205
Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser
    210         215         220
Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu
    225         230         235         240
Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile
    245         250         255
Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala
    260         265         270

```

Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu  
 275 280 285  
 Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln  
 290 295 300  
 Glu Gln Gln  
 305

<210> 139  
 <211> 302  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-302  
 <223>

<400> 139

Met Ala Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu  
 1 5 10 15  
 Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu  
 20 25 30  
 Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg  
 35 40 45  
 Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro  
 50 55 60  
 Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln  
 65 70 75 80  
 Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln  
 85 90 95  
 Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr  
 100 105 110  
 Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly  
 115 120 125  
 Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala  
 130 135 140  
 Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Tyr Val Glu Gly  
 145 150 155 160  
 Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn  
 165 170 175  
 Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala Asn  
 180 185 190  
 Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro Pro  
 195 200 205  
 Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met Asp Ile  
 210 215 220  
 Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe Val Arg  
 225 230 235 240  
 Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg  
 245 250 255  
 Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His  
 260 265 270  
 Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu  
 275 280 285  
 Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
 290 295 300

<210> 140  
 <211> 301  
 <212> PRT

&lt;213&gt; Unknown

&lt;220&gt;

&lt;221&gt; MUTAGEN

&lt;222&gt; 1-301

&lt;223&gt;

&lt;400&gt; 140

Ala Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg  
 1 5 10 15  
 Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly  
 20 25 30  
 Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe  
 35 40 45  
 Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val  
 50 55 60  
 Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val  
 65 70 75 80  
 Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu  
 85 90 95  
 Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly  
 100 105 110  
 Gly Ser Gly Gly Gly Ser Gly Gly Gly Thr Gln Asp Cys Ser Phe Gln  
 115 120 125  
 His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser  
 130 135 140  
 Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Tyr Val Glu Gly Gly  
 145 150 155 160  
 Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro  
 165 170 175  
 Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala Asn Cys  
 180 185 190  
 Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Asn  
 195 200 205  
 Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met Asp Ile Leu  
 210 215 220  
 Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe Val Arg Ala  
 225 230 235 240  
 Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn  
 245 250 255  
 Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro  
 260 265 270  
 Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr  
 275 280 285  
 Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
 290 295 300

&lt;210&gt; 141

&lt;211&gt; 301

&lt;212&gt; PRT

&lt;213&gt; Unknown

&lt;220&gt;

&lt;221&gt; MUTAGEN

&lt;222&gt; 1-301

&lt;223&gt;

&lt;400&gt; 141

Ala Val Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr

```

1           5           10           15
Glu Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys
20           25           30
Leu Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser
35           40           45
Glu Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser
50           55           60
Arg Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Gly Gly
65           70           75           80
Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Thr Gln Asp
85           90           95
Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile
100          105          110
Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala
115          120          125
Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val
130          135          140
Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Tyr Val Glu Gly Gly
145          150          155          160
Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro
165          170          175
Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala Asn Cys
180          185          190
Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Asn
195          200          205
Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met Asp Ile Leu
210          215          220
Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe Val Arg Ala
225          230          235          240
Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn
245          250          255
Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
260          265          270
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr
275          280          285
Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
290          295          300

```

```

<210>      142
<211>      301
<212>      PRT
<213>      Unknown

```

```

<220>
<221>      MUTAGEN
<222>      1-301
<223>

```

```

<400>      142

```

```

Ala Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His
1           5           10           15
Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe
20           25           30
Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu
35           40           45
Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu
50           55           60
Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly
65           70           75           80
Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Thr Gln Asp Cys Ser Phe

```

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

|       |         |
|-------|---------|
| <210> | 143     |
| <211> | 301     |
| <212> | PRT     |
| <213> | Unknown |

<220>  
<221> MUTAGEN  
<222> 1-301  
<223>

<400> 143

|            |     |     |     |          |     |     |     |           |     |     |     |     |     |           |     |
|------------|-----|-----|-----|----------|-----|-----|-----|-----------|-----|-----|-----|-----|-----|-----------|-----|
| Ala<br>1   | Pro | Pro | Ser | Cys<br>5 | Leu | Arg | Phe | Val<br>10 | Gln | Thr | Asn | Ile | Ser | Arg<br>15 | Leu |
| Leu        | Gln | Glu | Thr | Ser      | Glu | Gln | Leu | Val<br>25 | Ala | Leu | Lys | Pro | Trp | Ile       | Thr |
| Arg        | Gln | Asn | Phe | Ser      | Arg | Cys | Leu | Glu       | Leu | Gln | Cys | Gln | Pro | Asp       | Ser |
| Ser        | Thr | Leu | Gly | Gly      | Gly | Ser | Gly | Gly       | Gly | Ser | Gly | Gly | Gly | Ser       | Gly |
| Gly<br>65  | Gly | Thr | Gln | Asp      | Cys | Ser | Phe | Gln       | His | Ser | Pro | Ile | Ser | Ser       | Asp |
| Phe        | Ala | Val | Lys | Ile      | Arg | Glu | Leu | Ser       | Asp | Tyr | Leu | Leu | Gln | Asp       | Tyr |
| Pro        | Val | Thr | Val | Ala      | Ser | Asn | Leu | Gln       | Asp | Glu | Glu | Leu | Cys | Gly       | Gly |
| Leu        | Trp | Arg | Leu | Val      | Leu | Ala | Gln | Arg       | Trp | Met | Glu | Arg | Leu | Lys       | Thr |
| Val        | Ala | Gly | Ser | Lys      | Met | Gln | Gly | Leu       | Leu | Glu | Arg | Val | Asn | Thr       | Glu |
| Ile<br>145 | His | Phe | Val | Thr      | Lys | Cys | Ala | Phe       | Gln | Pro | Tyr | Val | Glu | Gly       | Gly |
| Gly        | Gly | Ser | Pro | Gly      | Glu | Pro | Ser | Gly       | Pro | Ile | Ser | Thr | Ile | Asn       | Pro |

```

                165                170                175
Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala Asn Cys
                180                185                190
Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Asn
                195                200                205
Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met Asp Ile Leu
                210                215                220
Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe Val Arg Ala
225                230                235                240
Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn
                245                250                255
Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
                260                265                270
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr
                275                280                285
Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
                290                295                300

```

```

<210>    144
<211>    301
<212>    PRT
<213>    Unknown

```

```

<220>
<221>    MUTAGEN
<222>    1-301
<223>

```

```

<400>    144

```

```

Ala Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val
 1                5                10                15
Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu
                20                25                30
Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly
                35                40                45
Gly Ser Gly Gly Gly Ser Gly Gly Gly Thr Gln Asp Cys Ser Phe Gln
                50                55                60
His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser
65                70                75                80
Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln
                85                90                95
Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln Arg
                100                105                110
Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly Leu
                115                120                125
Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala Phe
                130                135                140
Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Tyr Val Glu Gly Gly
145                150                155                160
Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro
                165                170                175
Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala Asn Cys
                180                185                190
Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Asn
                195                200                205
Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met Asp Ile Leu
                210                215                220
Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe Val Arg Ala
225                230                235                240
Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn

```

245 250 255  
 Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro  
 260 265 270  
 Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr  
 275 280 285  
 Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
 290 295 300

<210> 145  
 <211> 301  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-301  
 <223>

<400> 145

Ala Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser  
 1 5 10 15  
 Glu Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser  
 20 25 30  
 Arg Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Gly Gly  
 35 40 45  
 Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Thr Gln Asp  
 50 55 60  
 Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile  
 65 70 75 80  
 Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala  
 85 90 95  
 Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val  
 100 105 110  
 Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys  
 115 120 125  
 Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr  
 130 135 140  
 Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Phe Tyr Val Glu Gly Gly  
 145 150 155 160  
 Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro  
 165 170 175  
 Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala Asn Cys  
 180 185 190  
 Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Asn  
 195 200 205  
 Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met Asp Ile Leu  
 210 215 220  
 Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe Val Arg Ala  
 225 230 235 240  
 Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn  
 245 250 255  
 Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro  
 260 265 270  
 Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr  
 275 280 285  
 Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
 290 295 300

<210> 146  
 <211> 307

<212> PRT  
<213> Unknown

<220>  
<221> MUTAGEN  
<222> 1-307  
<223>

<400> 146

```

Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu
 1          5          10          15
Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser
      20          25          30
Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val
      35          40          45
Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln
      50          55          60
Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala
65          70          75          80
Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu
      85          90          95
Gln Cys Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly
      100          105          110
Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln
      115          120          125
Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys
      130          135          140
Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val
145          150          155          160
Ala Tyr Val Glu Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro
      165          170          175
Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser
      180          185          190
Pro Asn Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
      195          200          205
Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser
      210          215          220
Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu
225          230          235          240
Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile
      245          250          255
Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala
      260          265          270
Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu
      275          280          285
Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln
      290          295          300
Glu Gln Gln
305

```

<210> 147  
<211> 307  
<212> PRT  
<213> Unknown

<220>  
<221> MUTAGEN  
<222> 1-307  
<223>

&lt;400&gt; 147

Ala Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val  
 1 5 10 15  
 Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys  
 20 25 30  
 Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr  
 35 40 45  
 Lys Cys Ala Phe Gln Pro Pro Ser Cys Leu Arg Phe Val Gln Thr  
 50 55 60  
 Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu  
 65 70 75 80  
 Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln  
 85 90 95  
 Cys Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser  
 100 105 110  
 Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp  
 115 120 125  
 Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile  
 130 135 140  
 Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala  
 145 150 155 160  
 Ser Tyr Val Glu Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro  
 165 170 175  
 Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser  
 180 185 190  
 Pro Asn Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His  
 195 200 205  
 Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser  
 210 215 220  
 Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu  
 225 230 235 240  
 Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile  
 245 250 255  
 Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala  
 260 265 270  
 Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu  
 275 280 285  
 Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln  
 290 295 300  
 Glu Gln Gln  
 305

<210> 148  
 <211> 307  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-307  
 <223>

&lt;400&gt; 148

Ala Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu  
 1 5 10 15  
 Ala Gln Arg Leu Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met  
 20 25 30  
 Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys  
 35 40 45

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

<210> 149  
 <211> 307  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-307  
 <223>

<400> 149

Ala Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala  
 1 5 10 15  
 Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln  
 20 25 30  
 Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys  
 35 40 45  
 Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile  
 50 55 60  
 Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro  
 65 70 75 80  
 Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln  
 85 90 95  
 Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly  
 100 105 110

Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp Cys Ser  
 115 120 125  
 Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu  
 130 135 140  
 Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn  
 145 150 155 160  
 Leu Tyr Val Glu Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro  
 165 170 175  
 Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser  
 180 185 190  
 Pro Asn Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His  
 195 200 205  
 Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser  
 210 215 220  
 Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu  
 225 230 235 240  
 Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile  
 245 250 255  
 Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala  
 260 265 270  
 Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu  
 275 280 285  
 Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln  
 290 295 300  
 Glu Gln Gln  
 305

<210> 150  
 <211> 307  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-307  
 <223>

<400> 150

Ala Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln Arg  
 1 5 10 15  
 Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly Leu  
 20 25 30  
 Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala Phe  
 35 40 45  
 Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser Arg  
 50 55 60  
 Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp Ile  
 65 70 75 80  
 Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro Asp  
 85 90 95  
 Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Ser Gly Gly Gly Ser  
 100 105 110  
 Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp Cys Ser Phe Gln  
 115 120 125  
 His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser  
 130 135 140  
 Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln  
 145 150 155 160  
 Asp Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro  
 165 170 175

Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser  
 180 185 190  
 Pro Asn Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His  
 195 200 205  
 Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser  
 210 215 220  
 Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu  
 225 230 235 240  
 Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile  
 245 250 255  
 Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala  
 260 265 270  
 Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu  
 275 280 285  
 Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln  
 290 295 300  
 Glu Gln Gln  
 305

<210> 151  
 <211> 307  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-307  
 <223>

<400> 151

Ala Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln Arg Trp Met  
 1 5 10 15  
 Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly Leu Leu Glu  
 20 25 30  
 Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro  
 35 40 45  
 Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu  
 50 55 60  
 Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg  
 65 70 75 80  
 Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser  
 85 90 95  
 Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly  
 100 105 110  
 Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp Cys Ser Phe Gln His Ser  
 115 120 125  
 Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr  
 130 135 140  
 Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln Asp Glu  
 145 150 155 160  
 Glu Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro  
 165 170 175  
 Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser  
 180 185 190  
 Pro Asn Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His  
 195 200 205  
 Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser  
 210 215 220  
 Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu  
 225 230 235 240

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|
| Leu | Ala | Phe | Val | Arg | Ala | Val | Lys | His | Leu | Glu | Asn | Ala | Ser | Gly | Ile |  |
|     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |  |
| Glu | Ala | Ile | Leu | Arg | Asn | Leu | Gln | Pro | Cys | Leu | Pro | Ser | Ala | Thr | Ala |  |
|     |     |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |     |  |
| Ala | Pro | Ser | Arg | His | Pro | Ile | Ile | Ile | Lys | Ala | Gly | Asp | Trp | Gln | Glu |  |
|     |     |     |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |     |  |
| Phe | Arg | Glu | Lys | Leu | Thr | Phe | Tyr | Leu | Val | Thr | Leu | Glu | Gln | Ala | Gln |  |
|     |     |     |     | 290 |     |     |     |     | 295 |     |     |     |     | 300 |     |  |
| Glu | Gln | Gln |     |     |     |     |     |     |     |     |     |     |     |     |     |  |
| 305 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |

|       |         |
|-------|---------|
| <210> | 152     |
| <211> | 307     |
| <212> | PRT     |
| <213> | Unknown |

|       |         |
|-------|---------|
| <220> |         |
| <221> | MUTAGEN |
| <222> | 1-307   |
| <223> |         |

<400> 152

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ala | Leu | Cys | Gly | Gly | Leu | Trp | Arg | Leu | Val | Leu | Ala | Gln | Arg | Trp | Met |
| 1   |     |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |
| Glu | Arg | Leu | Lys | Thr | Val | Ala | Gly | Ser | Lys | Met | Gln | Gly | Leu | Leu | Glu |
|     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |
| Arg | Val | Asn | Thr | Glu | Ile | His | Phe | Val | Thr | Lys | Cys | Ala | Phe | Gln | Pro |
|     |     | 35  |     |     |     |     | 40  |     |     |     |     | 45  |     |     |     |
| Pro | Pro | Ser | Cys | Leu | Arg | Phe | Val | Gln | Thr | Asn | Ile | Ser | Arg | Leu | Leu |
|     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |
| Gln | Glu | Thr | Ser | Glu | Gln | Leu | Val | Ala | Leu | Lys | Pro | Trp | Ile | Thr | Arg |
| 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |
| Gln | Asn | Phe | Ser | Arg | Cys | Leu | Glu | Leu | Gln | Cys | Gln | Pro | Asp | Ser | Ser |
|     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |
| Thr | Leu | Gly | Gly | Gly | Ser | Gly | Gly | Gly | Ser | Gly | Gly | Gly | Ser | Gly | Gly |
|     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
| Gly | Ser | Gly | Gly | Gly | Ser | Gly | Thr | Gln | Asp | Cys | Ser | Phe | Gln | His | Ser |
|     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |
| Pro | Ile | Ser | Ser | Asp | Phe | Ala | Val | Lys | Ile | Arg | Glu | Leu | Ser | Asp | Tyr |
|     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
| Leu | Leu | Gln | Asp | Tyr | Pro | Val | Thr | Val | Ala | Ser | Asn | Leu | Gln | Asp | Glu |
| 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |
| Glu | Tyr | Val | Glu | Gly | Gly | Gly | Gly | Ser | Pro | Gly | Glu | Pro | Ser | Gly | Pro |
|     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |
| Ile | Ser | Thr | Ile | Asn | Pro | Ser | Pro | Pro | Ser | Lys | Glu | Ser | His | Lys | Ser |
|     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |
| Pro | Asn | Met | Ala | Asn | Cys | Ser | Ile | Met | Ile | Asp | Glu | Ile | Ile | His | His |
|     | 195 |     |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |
| Leu | Lys | Arg | Pro | Pro | Asn | Pro | Leu | Leu | Asp | Pro | Asn | Asn | Leu | Asn | Ser |
|     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |
| Glu | Asp | Met | Asp | Ile | Leu | Met | Glu | Arg | Asn | Leu | Arg | Thr | Pro | Asn | Leu |
| 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |
| Leu | Ala | Phe | Val | Arg | Ala | Val | Lys | His | Leu | Glu | Asn | Ala | Ser | Gly | Ile |
|     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |
| Glu | Ala | Ile | Leu | Arg | Asn | Leu | Gln | Pro | Cys | Leu | Pro | Ser | Ala | Thr | Ala |
|     |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |     |     |
| Ala | Pro | Ser | Arg | His | Pro | Ile | Ile | Lys | Ala | Gly | Asp | Trp | Gln | Glu |     |
|     |     | 275 |     |     |     |     | 280 |     |     |     | 285 |     |     |     |     |
| Phe | Arg | Glu | Lys | Leu | Thr | Phe | Tyr | Leu | Val | Thr | Leu | Glu | Gln | Ala | Gln |
|     | 290 |     |     |     |     | 295 |     |     |     |     | 300 |     |     |     |     |

Glu Gln Gln

305

<210> 153  
 <211> 307  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-307  
 <223>

<400> 153

Ala Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln Arg Trp Met  
 1 5 10 15  
 Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly Leu Leu Glu  
 20 25 30  
 Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro  
 35 40 45  
 Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu  
 50 55 60  
 Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg  
 65 70 75 80  
 Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Arg Pro Asp Ser Ser  
 85 90 95  
 Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly  
 100 105 110  
 Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp Cys Ser Phe Gln His Ser  
 115 120 125  
 Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr  
 130 135 140  
 Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln Asp Glu  
 145 150 155 160  
 Glu Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro  
 165 170 175  
 Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser  
 180 185 190  
 Pro Asn Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His  
 195 200 205  
 Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser  
 210 215 220  
 Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu  
 225 230 235 240  
 Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile  
 245 250 255  
 Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala  
 260 265 270  
 Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu  
 275 280 285  
 Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln  
 290 295 300  
 Glu Gln Gln  
 305

<210> 154  
 <211> 301  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-301  
 <223>

<400> 154

```

Ala Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His
 1          5          10          15
Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe
          20          25          30
Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu
          35          40          45
Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu
          50          55          60
Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly
65          70          75          80
Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Thr Gln Asp Cys Ser Phe
          85          90          95
Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu
          100          105          110
Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu
          115          120          125
Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln
          130          135          140
Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Tyr Val Glu Gly Gly
145          150          155          160
Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro
          165          170          175
Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala Asn Cys
          180          185          190
Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Asn
          195          200          205
Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met Asp Ile Leu
          210          215          220
Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe Val Arg Ala
225          230          235          240
Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn
          245          250          255
Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
          260          265          270
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr
          275          280          285
Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
          290          295          300

```

<210> 155  
 <211> 315  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-315  
 <223>

<400> 155

```

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

```

20 25 30  
 Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys  
 35 40 45  
 Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile  
 50 55 60  
 Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro  
 65 70 75 80  
 Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln  
 85 90 95  
 Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly  
 100 105 110  
 Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly  
 115 120 125  
 Gly Ser Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser  
 130 135 140  
 Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp  
 145 150 155 160  
 Tyr Pro Val Thr Val Ala Ser Asn Leu Tyr Val Glu Gly Gly Gly Gly  
 165 170 175  
 Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro  
 180 185 190  
 Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala Asn Cys Ser Ile  
 195 200 205  
 Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Asn Pro Leu  
 210 215 220  
 Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met Asp Ile Leu Met Glu  
 225 230 235 240  
 Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys  
 245 250 255  
 His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln  
 260 265 270  
 Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile  
 275 280 285  
 Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr  
 290 295 300  
 Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln  
 305 310 315

<210> 156  
 <211> 301  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-301  
 <223>

<400> 156

Ala Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala  
 1 5 10 15  
 Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln  
 20 25 30  
 Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys  
 35 40 45  
 Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile  
 50 55 60  
 Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro  
 65 70 75 80  
 Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln

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

|       |         |
|-------|---------|
| <210> | 157     |
| <211> | 307     |
| <212> | PRT     |
| <213> | Unknown |

<220>  
<221> MUTAGEN  
<222> 1-307  
<223>

<400> 157

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ala | Gln | Asp | Glu | Glu | Leu | Cys | Gly | Gly | Leu | Trp | Arg | Leu | Val | Leu | Ala |
| 1   |     |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |
| Gln | Arg | Trp | Met | Glu | Arg | Leu | Lys | Thr | Val | Ala | Gly | Ser | Lys | Met | Gln |
|     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |
| Gly | Leu | Leu | Glu | Arg | Val | Asn | Thr | Glu | Ile | His | Phe | Val | Thr | Lys | Cys |
|     |     | 35  |     |     |     |     | 40  |     |     |     |     | 45  |     |     |     |
| Ala | Phe | Gln | Pro | Pro | Pro | Ser | Cys | Leu | Arg | Phe | Val | Gln | Thr | Asn | Ile |
| 50  |     |     |     |     |     | 55  |     |     |     | 60  |     |     |     |     |     |
| Ser | Arg | Leu | Leu | Gln | Glu | Thr | Ser | Glu | Gln | Leu | Val | Ala | Leu | Lys | Pro |
| 65  |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |     |
| Trp | Ile | Thr | Arg | Gln | Asn | Phe | Ser | Arg | Cys | Leu | Glu | Leu | Gln | Cys | Gln |
|     |     |     |     | 85  |     |     |     | 90  |     |     |     |     | 95  |     |     |
| Pro | Asp | Ser | Ser | Thr | Leu | Pro | Pro | Pro | Trp | Ser | Pro | Arg | Pro | Leu | Gly |
|     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |     |
| Ala | Thr | Ala | Pro | Thr | Ala | Gly | Gln | Pro | Pro | Leu | Thr | Gln | Asp | Cys | Ser |
|     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |
| Phe | Gln | His | Ser | Pro | Ile | Ser | Ser | Asp | Phe | Ala | Val | Lys | Ile | Arg | Glu |
| 130 |     |     |     |     |     | 135 |     |     |     | 140 |     |     |     |     |     |
| Leu | Ser | Asp | Tyr | Leu | Leu | Gln | Asp | Tyr | Pro | Val | Thr | Val | Ala | Ser | Asn |
| 145 |     |     |     | 150 |     |     |     |     |     | 155 |     |     |     | 160 |     |
| Leu | Tyr | Val | Glu | Gly | Gly | Gly | Gly | Ser | Pro | Gly | Glu | Pro | Ser | Gly | Pro |

```

                165                170                175
Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser
                180                185                190
Pro Asn Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
                195                200                205
Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser
                210                215                220
Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu
225                230                235                240
Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile
                245                250                255
Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala
                260                265                270
Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu
                275                280                285
Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln
                290                295                300
Glu Gln Gln
305

```

```

<210>    158
<211>    370
<212>    PRT
<213>    Unknown

```

```

<220>
<221>    MUTAGEN
<222>    1-370
<223>

```

```

<400>    158

```

```

Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1          5          10          15
Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
          20          25          30
Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
          35          40          45
Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
          50          55          60
Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65          70          75          80
Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
          85          90          95
Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
          100          105          110
Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
          115          120          125
Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
          130          135          140
Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145          150          155          160
Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro Tyr
          165          170          175
Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser
          180          185          190
Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn
          195          200          205
Met Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala
210          215          220
Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln

```

225                      230                      235                      240  
 Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys  
                                  245                      250                      255  
 Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile  
                                  260                      265                      270  
 Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro  
                                  275                      280                      285  
 Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln  
                                  290                      295                      300  
 Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly  
 305                                   310                      315                      320  
 Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp Cys Ser  
                                  325                      330                      335  
 Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu  
                                  340                      345                      350  
 Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn  
                                  355                      360                      365  
 Leu Gln  
 370

<210>      159  
 <211>      370  
 <212>      PRT  
 <213>      Unknown

<220>  
 <221>      MUTAGEN  
 <222>      1-370  
 <223>

<400>      159

Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu  
 1                      5                      10                      15  
 Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu  
                                  20                      25                      30  
 Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu  
                                  35                      40                      45  
 Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser  
                                  50                      55                      60  
 Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His  
 65                                   70                      75                      80  
 Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile  
                                  85                      90                      95  
 Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala  
                                  100                      105                      110  
 Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala  
                                  115                      120                      125  
 Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala  
                                  130                      135                      140  
 Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser  
 145                                   150                      155                      160  
 Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro Tyr  
                                  165                      170                      175  
 Val Glu Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser  
                                  180                      185                      190  
 Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn  
                                  195                      200                      205  
 Met Ala Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu  
                                  210                      215                      220  
 Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser

225                      230                      235                      240  
 Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val  
                                  245                      250                      255  
 Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln  
                                  260                      265                      270  
 Ile Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala  
                                  275                      280                      285  
 Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu  
                                  290                      295                      300  
 Gln Cys Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly  
 305                      310                      315                      320  
 Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln  
                                  325                      330                      335  
 Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys  
                                  340                      345                      350  
 Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val  
                                  355                      360                      365  
 Ala Ser  
 370

<210>      160  
 <211>      370  
 <212>      PRT  
 <213>      Unknown

<220>  
 <221>      MUTAGEN  
 <222>      1-370  
 <223>

<400>      160

Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu  
 1                      5                      10                      15  
 Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu  
                                  20                      25                      30  
 Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu  
                                  35                      40                      45  
 Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser  
                                  50                      55                      60  
 Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His  
 65                      70                      75                      80  
 Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile  
                                  85                      90                      95  
 Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala  
                                  100                      105                      110  
 Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala  
                                  115                      120                      125  
 Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala  
                                  130                      135                      140  
 Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser  
 145                      150                      155                      160  
 Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro Tyr  
                                  165                      170                      175  
 Val Glu Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser  
                                  180                      185                      190  
 Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn  
                                  195                      200                      205  
 Met Ala Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser Arg  
                                  210                      215                      220  
 Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp Ile

[illegible]

|       |         |
|-------|---------|
| <210> | 161     |
| <211> | 370     |
| <212> | PRT     |
| <213> | Unknown |

|       |         |
|-------|---------|
| <220> |         |
| <221> | MUTAGEN |
| <222> | 1-370   |
| <223> |         |

<400> 161

|         |     |     |         |         |     |     |     |         |        |     |     |     |         |        |     |
|---------|-----|-----|---------|---------|-----|-----|-----|---------|--------|-----|-----|-----|---------|--------|-----|
| Ala 1   | Thr | Pro | Leu     | Gly 5   | Pro | Ala | Ser | Ser     | Leu 10 | Pro | Gln | Ser | Phe     | Leu 15 | Leu |
| Lys     | Ser | Leu | Glu     | Gln 20  | Val | Arg | Lys | Ile 25  | Gln    | Gly | Asp | Gly | Ala 30  | Ala    | Leu |
| Gln     | Glu | Lys | Leu     | Cys 35  | Ala | Thr | Tyr | Lys 40  | Leu    | Cys | His | Pro | Glu 45  | Glu    | Leu |
| Val     | Leu | Leu | Gly     | His 50  | Ser | Leu | Gly | Ile 55  | Pro    | Trp | Ala | Pro | Leu 60  | Ser    | Ser |
| Cys 65  | Pro | Ser | Gln     | Ala 70  | Leu | Gln | Leu | Ala 75  | Gly    | Cys | Leu | Ser | Gln 80  | Leu    | His |
| Ser     | Gly | Leu | Phe     | Leu 85  | Tyr | Gln | Gly | Leu 90  | Leu    | Gln | Ala | Leu | Glu 95  | Gly    | Ile |
| Ser     | Pro | Glu | Leu     | Gly 100 | Pro | Thr | Leu | Asp 105 | Thr    | Leu | Gln | Leu | Asp 110 | Val    | Ala |
| Asp     | Phe | Ala | Thr     | Thr 115 | Ile | Trp | Gln | Gln 120 | Met    | Glu | Glu | Leu | Gly 125 | Met    | Ala |
| Pro     | Ala | Leu | Gln     | Pro 130 | Thr | Gln | Gly | Ala 135 | Met    | Pro | Ala | Phe | Ala 140 | Ser    | Ala |
| Phe 145 | Gln | Arg | Arg     | Ala 150 | Gly | Val | Leu | Val 155 | Ala    | Ser | His | Leu | Gln 160 | Ser    |     |
| Phe     | Leu | Glu | Val     | Ser 165 | Tyr | Arg | Val | Leu 170 | Arg    | His | Leu | Ala | Gln 175 | Pro    | Tyr |
| Val     | Glu | Gly | Gly 180 | Gly     | Gly | Ser | Pro | Gly 185 | Glu    | Pro | Ser | Gly | Pro 190 | Ile    | Ser |
| Thr     | Ile | Asn | Pro 195 | Ser     | Pro | Pro | Ser | Lys 200 | Glu    | Ser | His | Lys | Ser 205 | Pro    | Asn |
| Met     | Ala | Leu | Gln     | Asp 210 | Glu | Glu | Leu | Cys 215 | Gly    | Gly | Leu | Trp | Arg 220 | Leu    | Val |
| Leu     | Ala | Gln | Arg     | Trp     | Met | Glu | Arg | Leu     | Lys    | Thr | Val | Ala | Gly     | Ser    | Lys |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |
| Met | Gln | Gly | Leu | Leu | Glu | Arg | Val | Asn | Thr | Glu | Ile | His | Phe | Val | Thr |
|     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |
| Lys | Cys | Ala | Phe | Gln | Pro | Pro | Pro | Ser | Cys | Leu | Arg | Phe | Val | Gln | Thr |
|     |     |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |     |
| Asn | Ile | Ser | Arg | Leu | Leu | Gln | Glu | Thr | Ser | Glu | Gln | Leu | Val | Ala | Leu |
|     |     |     |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |     |
| Lys | Pro | Trp | Ile | Thr | Arg | Gln | Asn | Phe | Ser | Arg | Cys | Leu | Glu | Leu | Gln |
|     |     |     |     | 290 |     |     |     |     | 295 |     |     |     |     | 300 |     |
| Cys | Gln | Pro | Asp | Ser | Ser | Thr | Leu | Gly | Gly | Gly | Ser | Gly | Gly | Gly | Ser |
| 305 |     |     |     |     | 310 |     |     |     |     | 315 |     |     |     |     | 320 |
| Gly | Gly | Gly | Ser | Gly | Gly | Gly | Ser | Gly | Gly | Gly | Ser | Gly | Thr | Gln | Asp |
|     |     |     |     | 325 |     |     |     |     | 330 |     |     |     |     | 335 |     |
| Cys | Ser | Phe | Gln | His | Ser | Pro | Ile | Ser | Ser | Asp | Phe | Ala | Val | Lys | Ile |
|     |     |     |     | 340 |     |     |     |     | 345 |     |     |     |     | 350 |     |
| Arg | Glu | Leu | Ser | Asp | Tyr | Leu | Leu | Gln | Asp | Tyr | Pro | Val | Thr | Val | Ala |
|     |     |     |     | 355 |     |     |     |     | 360 |     |     |     |     | 365 |     |
| Ser | Asn |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|     |     | 370 |     |     |     |     |     |     |     |     |     |     |     |     |     |

|       |         |
|-------|---------|
| <210> | 162     |
| <211> | 370     |
| <212> | PRT     |
| <213> | Unknown |

|       |         |
|-------|---------|
| <220> |         |
| <221> | MUTAGEN |
| <222> | 1-370   |
| <223> |         |

<400> 162

|          |     |     |     |          |     |     |     |     |           |     |     |     |     |           |     |
|----------|-----|-----|-----|----------|-----|-----|-----|-----|-----------|-----|-----|-----|-----|-----------|-----|
| Ala<br>1 | Thr | Pro | Leu | Gly<br>5 | Pro | Ala | Ser | Ser | Leu<br>10 | Pro | Gln | Ser | Phe | Leu<br>15 | Leu |
| Lys      | Ser | Leu | Glu | Gln      | Val | Arg | Lys | Ile | Gln       | Gly | Asp | Gly | Ala | Ala       | Leu |
|          |     |     | 20  |          |     |     |     | 25  |           |     |     |     | 30  |           |     |
| Gln      | Glu | Lys | Leu | Cys      | Ala | Thr | Tyr | Lys | Leu       | Cys | His | Pro | Glu | Glu       | Leu |
|          |     | 35  |     |          |     |     | 40  |     |           |     | 45  |     |     |           |     |
| Val      | Leu | Leu | Gly | His      | Ser | Leu | Gly | Ile | Pro       | Trp | Ala | Pro | Leu | Ser       | Ser |
|          | 50  |     |     |          |     | 55  |     |     |           | 60  |     |     |     |           |     |
| Cys      | Pro | Ser | Gln | Ala      | Leu | Gln | Leu | Ala | Gly       | Cys | Leu | Ser | Gln | Leu       | His |
| 65       |     |     |     | 70       |     |     |     |     | 75        |     |     |     |     |           | 80  |
| Ser      | Gly | Leu | Phe | Leu      | Tyr | Gln | Gly | Leu | Leu       | Gln | Ala | Leu | Glu | Gly       | Ile |
|          |     |     | 85  |          |     |     |     | 90  |           |     |     |     | 95  |           |     |
| Ser      | Pro | Glu | Leu | Gly      | Pro | Thr | Leu | Asp | Thr       | Leu | Gln | Leu | Asp | Val       | Ala |
|          |     |     | 100 |          |     |     | 105 |     |           |     | 110 |     |     |           |     |
| Asp      | Phe | Ala | Thr | Thr      | Ile | Trp | Gln | Gln | Met       | Glu | Glu | Leu | Gly | Met       | Ala |
|          | 115 |     |     |          |     | 120 |     |     |           | 125 |     |     |     |           |     |
| Pro      | Ala | Leu | Gln | Pro      | Thr | Gln | Gly | Ala | Met       | Pro | Ala | Phe | Ala | Ser       | Ala |
|          | 130 |     |     |          |     | 135 |     |     |           | 140 |     |     |     |           |     |
| Phe      | Gln | Arg | Arg | Ala      | Gly | Gly | Val | Leu | Val       | Ala | Ser | His | Leu | Gln       | Ser |
| 145      |     |     |     | 150      |     |     |     |     | 155       |     |     |     |     |           | 160 |
| Phe      | Leu | Glu | Val | Ser      | Tyr | Arg | Val | Leu | Arg       | His | Leu | Ala | Gln | Pro       | Tyr |
|          |     |     | 165 |          |     |     | 170 |     |           |     | 175 |     |     |           |     |
| Val      | Glu | Gly | Gly | Gly      | Gly | Ser | Pro | Gly | Glu       | Pro | Ser | Gly | Pro | Ile       | Ser |
|          |     | 180 |     |          |     |     | 185 |     |           |     | 190 |     |     |           |     |
| Thr      | Ile | Asn | Pro | Ser      | Pro | Pro | Ser | Lys | Glu       | Ser | His | Lys | Ser | Pro       | Asn |
|          | 195 |     |     |          |     |     | 200 |     |           |     | 205 |     |     |           |     |
| Met      | Ala | Gln | Asp | Glu      | Glu | Leu | Cys | Gly | Gly       | Leu | Trp | Arg | Leu | Val       | Leu |
|          | 210 |     |     |          |     | 215 |     |     |           | 220 |     |     |     |           |     |
| Ala      | Gln | Arg | Trp | Met      | Glu | Arg | Leu | Lys | Thr       | Val | Ala | Gly | Ser | Lys       | Met |

```

225          230          235          240
Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys
          245          250          255
Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn
          260          265          270
Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys
          275          280          285
Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys
          290          295          300
Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly
305          310          315          320
Gly Gly Ser Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp Cys
          325          330          335
Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg
          340          345          350
Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser
          355          360          365
Asn Leu
370

```

```

<210>      163
<211>      370
<212>      PRT
<213>      Unknown

```

```

<220>
<221>      MUTAGEN
<222>      1-370
<223>

```

```

<400>      163

```

```

Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1          5          10          15
Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
          20          25          30
Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
          35          40          45
Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
          50          55          60
Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65          70          75          80
Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
          85          90          95
Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
          100          105          110
Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
          115          120          125
Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
          130          135          140
Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145          150          155          160
Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro Tyr
          165          170          175
Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser
          180          185          190
Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn
          195          200          205
Met Ala Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln
          210          215          220
Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly

```

225                      230                      235                      240  
 Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala  
                                  245                      250                      255  
 Phe Gln Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser  
                                  260                      265                      270  
 Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp  
                                  275                      280                      285  
 Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro  
                                  290                      295                      300  
 Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly  
 305                                   310                                   315                                   320  
 Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp Cys Ser Phe  
                                  325                                   330                                   335  
 Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu  
                                  340                                   345                                   350  
 Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu  
                                  355                                   360                                   365  
 Gln Asp  
 370

<210>      164  
 <211>      370  
 <212>      PRT  
 <213>      Unknown

<220>  
 <221>      MUTAGEN  
 <222>      1-370  
 <223>

<400>      164

Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu  
 1                      5                      10                      15  
 Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu  
                                  20                      25                      30  
 Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu  
                                  35                      40                      45  
 Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser  
                                  50                      55                      60  
 Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His  
 65                                   70                                   75                                   80  
 Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile  
                                  85                                   90                                   95  
 Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala  
                                  100                      105                      110  
 Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala  
                                  115                      120                      125  
 Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala  
                                  130                      135                      140  
 Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser  
 145                                   150                                   155                                   160  
 Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro Tyr  
                                  165                      170                      175  
 Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser  
                                  180                      185                      190  
 Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn  
                                  195                      200                      205  
 Met Ala Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln Arg  
                                  210                      215                      220  
 Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly Leu

225                      230                      235                      240  
 Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala Phe  
                                  245                      250                      255  
 Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser Arg  
                                  260                      265                      270  
 Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp Ile  
                                  275                      280                      285  
 Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro Asp  
                                  290                      295                      300  
 Ser Ser Thr Leu Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser  
 305                                   310                                   315                                   320  
 Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp Cys Ser Phe Gln  
                                  325                                   330                                   335  
 His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser  
                                  340                                   345                                   350  
 Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln  
                                  355                                   360                                   365  
 Asp Glu  
 370

<210>      165  
 <211>      370  
 <212>      PRT  
 <213>      Unknown

<220>  
 <221>      MUTAGEN  
 <222>      1-370  
 <223>

<400>      165

Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu  
 1                      5                      10                      15  
 Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu  
                                  20                      25                      30  
 Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu  
                                  35                      40                      45  
 Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser  
 50                      55                      60  
 Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His  
 65                      70                      75                      80  
 Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile  
                                  85                      90                      95  
 Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala  
                                  100                      105                      110  
 Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala  
                                  115                      120                      125  
 Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala  
                                  130                      135                      140  
 Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser  
 145                      150                      155                      160  
 Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro Tyr  
                                  165                      170                      175  
 Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser  
                                  180                      185                      190  
 Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn  
                                  195                      200                      205  
 Met Ala Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln Arg Trp  
 210                      215                      220  
 Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly Leu Leu

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |
| Glu | Arg | Val | Asn | Thr | Glu | Ile | His | Phe | Val | Thr | Lys | Cys | Ala | Phe | Gln |
|     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |
| Pro | Pro | Pro | Ser | Cys | Leu | Arg | Phe | Val | Gln | Thr | Asn | Ile | Ser | Arg | Leu |
|     |     |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |     |
| Leu | Gln | Glu | Thr | Ser | Glu | Gln | Leu | Val | Ala | Leu | Lys | Pro | Trp | Ile | Thr |
|     |     |     |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |     |
| Arg | Gln | Asn | Phe | Ser | Arg | Cys | Leu | Glu | Leu | Gln | Cys | Gln | Pro | Asp | Ser |
|     |     |     |     | 290 |     |     |     |     | 295 |     |     |     |     | 300 |     |
| Ser | Thr | Leu | Gly | Gly | Gly | Ser | Gly | Gly | Gly | Ser | Gly | Gly | Gly | Ser | Gly |
| 305 |     |     |     |     | 310 |     |     |     |     | 315 |     |     |     |     | 320 |
| Gly | Gly | Ser | Gly | Gly | Gly | Ser | Gly | Thr | Gln | Asp | Cys | Ser | Phe | Gln | His |
|     |     |     |     | 325 |     |     |     |     | 330 |     |     |     |     | 335 |     |
| Ser | Pro | Ile | Ser | Ser | Asp | Phe | Ala | Val | Lys | Ile | Arg | Glu | Leu | Ser | Asp |
|     |     |     |     | 340 |     |     |     |     | 345 |     |     |     |     | 350 |     |
| Tyr | Leu | Leu | Gln | Asp | Tyr | Pro | Val | Thr | Val | Ala | Ser | Asn | Leu | Gln | Asp |
|     |     |     |     | 355 |     |     |     |     | 360 |     |     |     |     | 365 |     |
| Glu | Glu |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|     |     | 370 |     |     |     |     |     |     |     |     |     |     |     |     |     |

|       |         |
|-------|---------|
| <210> | 166     |
| <211> | 364     |
| <212> | PRT     |
| <213> | Unknown |

|       |         |
|-------|---------|
| <220> |         |
| <221> | MUTAGEN |
| <222> | 1-364   |
| <223> |         |

<400> 166

|         |         |         |         |         |     |        |         |         |        |        |        |         |         |         |         |
|---------|---------|---------|---------|---------|-----|--------|---------|---------|--------|--------|--------|---------|---------|---------|---------|
| Ala 1   | Thr     | Pro     | Leu     | Gly 5   | Pro | Ala    | Ser     | Ser     | Leu 10 | Pro    | Gln    | Ser     | Phe     | Leu 15  | Leu     |
| Lys     | Ser     | Leu     | Glu     | Gln 20  | Val | Arg    | Lys     | Ile 25  | Gln    | Gly    | Asp    | Gly     | Ala 30  | Ala     | Leu     |
| Gln     | Glu     | Lys 35  | Leu     | Cys     | Ala | Thr    | Tyr 40  | Lys     | Leu    | Cys    | His 45 | Pro     | Glu     | Glu     | Leu     |
| Val     | Leu 50  | Leu     | Gly     | His     | Ser | Leu 55 | Gly     | Ile     | Pro    | Trp    | Ala 60 | Pro     | Leu     | Ser     | Ser     |
| Cys 65  | Pro     | Ser     | Gln     | Ala 70  | Leu | Gln    | Leu     | Ala     | Gly    | Cys 75 | Leu    | Ser     | Gln     | Leu     | His 80  |
| Ser     | Gly     | Leu     | Phe     | Leu 85  | Tyr | Gln    | Gly     | Leu 90  | Leu    | Gln    | Ala    | Leu     | Glu     | Gly 95  | Ile     |
| Ser     | Pro     | Glu     | Leu 100 | Gly     | Pro | Thr    | Leu     | Asp 105 | Thr    | Leu    | Gln    | Leu     | Asp 110 | Val     | Ala     |
| Asp     | Phe     | Ala 115 | Thr     | Thr     | Ile | Trp    | Gln 120 | Gln     | Met    | Glu    | Glu    | Leu 125 | Gly     | Met     | Ala     |
| Pro     | Ala 130 | Leu     | Gln     | Pro     | Thr | Gln    | Gly 135 | Ala     | Met    | Pro    | Ala    | Phe 140 | Ala     | Ser     | Ala     |
| Phe 145 | Gln     | Arg     | Arg     | Ala 150 | Gly | Gly    | Val     | Leu     | Val    | Ala    | Ser    | His 155 | Leu     | Gln     | Ser 160 |
| Phe     | Leu     | Glu     | Val     | Ser 165 | Tyr | Arg    | Val     | Leu 170 | Arg    | His    | Leu    | Ala     | Gln     | Pro 175 | Tyr     |
| Val     | Glu     | Gly     | Gly 180 | Gly     | Gly | Ser    | Pro     | Gly 185 | Glu    | Pro    | Ser    | Gly     | Pro 190 | Ile     | Ser     |
| Thr     | Ile     | Asn 195 | Pro     | Ser     | Pro | Pro    | Ser 200 | Lys     | Glu    | Ser    | His    | Lys 205 | Ser     | Pro     | Asn     |
| Met     | Ala 210 | Asp     | Glu     | Glu     | Leu | Cys    | Gly 215 | Gly     | Leu    | Trp    | Arg    | Leu     | Val     | Leu     | Ala     |
| Gln     | Arg     | Trp     | Met     | Glu     | Arg | Leu    | Lys     | Thr     | Val    | Ala    | Gly    | Ser     | Lys     | Met     | Gln     |

```

225          230          235          240
Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys
          245          250          255
Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile
          260          265          270
Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro
          275          280          285
Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln
          290          295          300
Pro Asp Ser Ser Thr Leu Pro Pro Pro Trp Ser Pro Arg Pro Leu Gly
305          310          315          320
Ala Thr Ala Pro Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile
          325          330          335
Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu
          340          345          350
Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln
          355          360

```

```

<210>      167
<211>      378
<212>      PRT
<213>      Unknown

```

```

<220>
<221>      MUTAGEN
<222>      1-378
<223>

```

```

<400>      167

```

```

Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1          5          10          15
Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
          20          25          30
Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
          35          40          45
Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
          50          55          60
Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65          70          75          80
Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
          85          90          95
Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
          100          105          110
Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
          115          120          125
Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
          130          135          140
Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145          150          155          160
Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro Tyr
          165          170          175
Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser
          180          185          190
Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn
          195          200          205
Met Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala
          210          215          220
Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln
225          230          235          240
Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys

```

```

                245                250                255
Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile
                260                265                270
Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro
                275                280                285
Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln
                290                295                300
Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly
305                310                315                320
Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly
                325                330                335
Gly Ser Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser
                340                345                350
Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp
                355                360                365
Tyr Pro Val Thr Val Ala Ser Asn Leu Gln
                370                375

```

```

<210>    168
<211>    370
<212>    PRT
<213>    Unknown

```

```

<220>
<221>    MUTAGEN
<222>    1-370
<223>

```

```

<400>    168

```

```

Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1          5          10          15
Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
          20          25          30
Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
          35          40          45
Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
          50          55          60
Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65          70          75          80
Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
          85          90          95
Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
          100          105          110
Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
          115          120          125
Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
          130          135          140
Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145          150          155          160
Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro Tyr
          165          170          175
Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Scr
          180          185          190
Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn
          195          200          205
Met Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala
          210          215          220
Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln
225          230          235          240
Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys

```

245 250 255  
 Ala Phe Gln Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile  
 260 265 270  
 Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro  
 275 280 285  
 Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln  
 290 295 300  
 Pro Asp Ser Ser Thr Leu Pro Pro Pro Trp Ser Pro Arg Pro Leu Gly  
 305 310 315 320  
 Ala Thr Ala Pro Thr Ala Gly Gln Pro Pro Leu Thr Gln Asp Cys Ser  
 325 330 335  
 Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu  
 340 345 350  
 Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn  
 355 360 365  
 Leu Gln  
 370

<210> 169  
 <211> 155  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-155  
 <223>

<400> 169

Ala Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu  
 1 5 10 15  
 Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg  
 20 25 30  
 Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val  
 35 40 45  
 Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro  
 50 55 60  
 Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu  
 65 70 75 80  
 Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn  
 85 90 95  
 Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu  
 100 105 110  
 Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Thr  
 115 120 125  
 Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val  
 130 135 140  
 Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln  
 145 150 155

<210> 170  
 <211> 155  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-155  
 <223>

&lt;400&gt; 170

Ala Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg  
 1 5 10 15  
 Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly  
 20 25 30  
 Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe  
 35 40 45  
 Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val  
 50 55 60  
 Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val  
 65 70 75 80  
 Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu  
 85 90 95  
 Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly  
 100 105 110  
 Gly Ser Gly Gly Gly Ser Gly Gly Gly Thr Gln Asp Cys Ser Phe Gln  
 115 120 125  
 His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser  
 130 135 140  
 Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val  
 145 150 155

<210> 171  
 <211> 155  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-155  
 <223>

&lt;400&gt; 171

Ala Val Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr  
 1 5 10 15  
 Glu Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys  
 20 25 30  
 Leu Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser  
 35 40 45  
 Glu Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser  
 50 55 60  
 Arg Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Gly Gly  
 65 70 75 80  
 Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Thr Gln Asp  
 85 90 95  
 Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile  
 100 105 110  
 Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala  
 115 120 125  
 Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val  
 130 135 140  
 Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr  
 145 150 155

<210> 172  
 <211> 155  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-155  
 <223>

<400> 172

```

Ala Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His
 1          5          10          15
Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe
          20          25          30
Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu
          35          40          45
Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu
          50          55          60
Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly
65          70          75          80
Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Thr Gln Asp Cys Ser Phe
          85          90          95
Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu
          100          105          110
Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu
          115          120          125
Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln
          130          135          140
Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly
          145          150          155

```

<210> 173  
 <211> 155  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-155  
 <223>

<400> 173

```

Ala Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser Arg Leu
 1          5          10          15
Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp Ile Thr
          20          25          30
Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser
          35          40          45
Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly
          50          55          60
Gly Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp
65          70          75          80
Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr
          85          90          95
Pro Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly
          100          105          110
Leu Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr
          115          120          125
Val Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu
          130          135          140
Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro
          145          150          155

```

<210> 174  
 <211> 155  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-155  
 <223>

<400> 174

```

Ala Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser
 1              5              10              15
Glu Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser
              20              25              30
Arg Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Gly Gly
              35              40              45
Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Thr Gln Asp
              50              55              60
Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile
65              70              75              80
Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala
              85              90              95
Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val
              100             105             110
Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys
              115             120             125
Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr
              130             135             140
Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu
145              150              155

```

<210> 175  
 <211> 155  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-155  
 <223>

<400> 175

```

Ala Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val
 1              5              10              15
Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu
              20              25              30
Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly
              35              40              45
Gly Ser Gly Gly Gly Ser Gly Gly Gly Gly Thr Gln Asp Cys Ser Phe Gln
              50              55              60
His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser
65              70              75              80
Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln
              85              90              95
Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln Arg
              100             105             110
Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly Leu
              115             120             125

```

Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala Phe  
 130 135 140  
 Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln  
 145 150 155

<210> 176  
 <211> 370  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-370  
 <223>

<400> 176

Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln  
 1 5 10 15  
 Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly  
 20 25 30  
 Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala  
 35 40 45  
 Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser  
 50 55 60  
 Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp  
 65 70 75 80  
 Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro  
 85 90 95  
 Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly  
 100 105 110  
 Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp Cys Ser Phe  
 115 120 125  
 Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu  
 130 135 140  
 Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu  
 145 150 155 160  
 Gln Tyr Val Glu Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro  
 165 170 175  
 Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser  
 180 185 190  
 Pro Asn Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser  
 195 200 205  
 Phe Leu Leu Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly  
 210 215 220  
 Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro  
 225 230 235 240  
 Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro  
 245 250 255  
 Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser  
 260 265 270  
 Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu  
 275 280 285  
 Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu  
 290 295 300  
 Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu  
 305 310 315 320  
 Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe  
 325 330 335  
 Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His  
 340 345 350

Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala  
 355 360 365  
 Gln Pro  
 370

<210> 177  
 <211> 370  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-370  
 <223>

<400> 177

Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln  
 1 5 10 15  
 Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly  
 20 25 30  
 Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala  
 35 40 45  
 Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser  
 50 55 60  
 Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp  
 65 70 75 80  
 Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro  
 85 90 95  
 Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly  
 100 105 110  
 Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp Cys Ser Phe  
 115 120 125  
 Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu  
 130 135 140  
 Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu  
 145 150 155 160  
 Gln Tyr Val Glu Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro  
 165 170 175  
 Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser  
 180 185 190  
 Pro Asn Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser  
 195 200 205  
 Phe Leu Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly  
 210 215 220  
 Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro  
 225 230 235 240  
 Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro  
 245 250 255  
 Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser  
 260 265 270  
 Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu  
 275 280 285  
 Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu  
 290 295 300  
 Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu  
 305 310 315 320  
 Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe  
 325 330 335  
 Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His  
 340 345 350

Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala  
                   355                                  360                                  365  
 Gln Pro  
       370

<210>      178  
 <211>      354  
 <212>      PRT  
 <213>      Unknown

<220>  
 <221>      MUTAGEN  
 <222>      1-354  
 <223>

<400>      178

Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln  
   1                                  5                                  10                                  15  
 Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly  
                   20                                  25                                  30  
 Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala  
                   35                                  40                                  45  
 Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser  
   50                                  55                                  60  
 Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp  
 65                                  70                                  75                                  80  
 Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro  
                                   85                                  90                                  95  
 Asp Ser Ser Thr Leu Pro Pro Pro Trp Ser Pro Arg Pro Leu Gly Ala  
                   100                                  105                                  110  
 Thr Ala Pro Thr Ala Gly Gln Pro Pro Leu Thr Gln Asp Cys Ser Phe  
                   115                                  120                                  125  
 Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu  
   130                                  135                                  140  
 Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu  
 145                                  150                                  155                                  160  
 Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Gly Gly Ser Gly Gly Gly  
                                   165                                  170                                  175  
 Ser Asn Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser  
                   180                                  185                                  190  
 Phe Leu Leu Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly  
                   195                                  200                                  205  
 Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro  
                   210                                  215                                  220  
 Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro  
 225                                  230                                  235                                  240  
 Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser  
                   245                                  250                                  255  
 Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu  
                   260                                  265                                  270  
 Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu  
                   275                                  280                                  285  
 Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu  
   290                                  295                                  300  
 Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe  
 305                                  310                                  315                                  320  
 Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His  
                   325                                  330                                  335  
 Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala  
                   340                                  345                                  350

Gln Pro

<210> 179  
 <211> 363  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-363  
 <223>

<400> 179

Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln  
 1 5 10 15  
 Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly  
 20 25 30  
 Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala  
 35 40 45  
 Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser  
 50 55 60  
 Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp  
 65 70 75 80  
 Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro  
 85 90 95  
 Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly  
 100 105 110  
 Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly  
 115 120 125  
 Ser Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp  
 130 135 140  
 Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr  
 145 150 155 160  
 Pro Val Thr Val Ala Ser Asn Leu Gln Tyr Val Glu Gly Gly Gly Gly  
 165 170 175  
 Ser Pro Gly Gly Gly Ser Gly Gly Gly Ser Asn Met Ala Thr Pro Leu  
 180 185 190  
 Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys Ser Leu Glu  
 195 200 205  
 Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu  
 210 215 220  
 Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly  
 225 230 235 240  
 His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln  
 245 250 255  
 Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly Leu Phe  
 260 265 270  
 Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu Leu  
 275 280 285  
 Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp Phe Ala Thr  
 290 295 300  
 Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln  
 305 310 315 320  
 Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg  
 325 330 335  
 Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu Glu Val  
 340 345 350  
 Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro  
 355 360

<210> 180  
 <211> 348  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-348  
 <223>

<400> 180

```

Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln
 1          5          10          15
Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly
          20          25          30
Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala
          35          40          45
Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser
          50          55          60
Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp
65          70          75          80
Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro
          85          90          95
Asp Ser Ser Thr Leu Pro Pro Pro Trp Ser Pro Arg Pro Leu Gly Ala
          100          105          110
Thr Ala Pro Thr Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser
          115          120          125
Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln
          130          135          140
Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Tyr Val Glu Gly Gly Gly
145          150          155          160
Gly Ser Pro Gly Gly Gly Ser Gly Gly Gly Ser Asn Met Ala Thr Pro
          165          170          175
Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys Ser Leu
          180          185          190
Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys
          195          200          205
Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu Leu
          210          215          220
Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser
225          230          235          240
Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly Leu
          245          250          255
Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu
          260          265          270
Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp Phe Ala
          275          280          285
Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu
          290          295          300
Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg
305          310          315          320
Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu Glu
          325          330          335
Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
          340          345

```

<210> 181  
 <211> 359  
 <212> PRT

&lt;213&gt; Unknown

&lt;220&gt;

&lt;221&gt; MUTAGEN

&lt;222&gt; 1-359

&lt;223&gt;

&lt;400&gt; 181

Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln  
 1 5 10 15  
 Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly  
 20 25 30  
 Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala  
 35 40 45  
 Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser  
 50 55 60  
 Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Arg Pro Trp  
 65 70 75 80  
 Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro  
 85 90 95  
 Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Thr  
 100 105 110  
 Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val  
 115 120 125  
 Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr  
 130 135 140  
 Val Ala Ser Asn Leu Gln Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly  
 145 150 155 160  
 Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys  
 165 170 175  
 Glu Ser His Lys Ser Pro Asn Met Ala Thr Pro Leu Gly Pro Ala Ser  
 180 185 190  
 Ser Leu Pro Gln Ser Phe Leu Leu Lys Cys Leu Glu Gln Val Arg Lys  
 195 200 205  
 Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr  
 210 215 220  
 Lys Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly  
 225 230 235 240  
 Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu  
 245 250 255  
 Ala Gly Cys Leu Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly  
 260 265 270  
 Leu Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu  
 275 280 285  
 Asp Thr Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln  
 290 295 300  
 Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly  
 305 310 315 320  
 Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val  
 325 330 335  
 Leu Val Ala Ser His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val  
 340 345 350  
 Leu Arg His Leu Ala Gln Pro  
 355

&lt;210&gt; 182

&lt;211&gt; 364

&lt;212&gt; PRT

&lt;213&gt; Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-364  
 <223>

<400> 182

```

Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln
 1          5          10          15
Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly
 20          25          30
Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala
 35          40          45
Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser
 50          55          60
Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp
 65          70          75          80
Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro
 85          90          95
Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
 100          105          110
Ser Gly Gly Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser
 115          120          125
Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln
 130          135          140
Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln Tyr Val Glu Gly Gly
 145          150          155          160
Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro
 165          170          175
Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala Thr Pro
 180          185          190
Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys Cys Leu
 195          200          205
Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys
 210          215          220
Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu Leu
 225          230          235          240
Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser
 245          250          255
Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly Leu
 260          265          270
Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu
 275          280          285
Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp Phe Ala
 290          295          300
Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu
 305          310          315          320
Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg
 325          330          335
Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu Glu
 340          345          350
Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 355          360

```

<210> 183  
 <211> 370  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN

&lt;222&gt; 1-370

&lt;223&gt;

&lt;400&gt; 183

Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln  
 1 5 10 15  
 Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly  
 20 25 30  
 Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala  
 35 40 45  
 Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser  
 50 55 60  
 Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp  
 65 70 75 80  
 Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro  
 85 90 95  
 Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly  
 100 105 110  
 Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp Cys Ser Phe  
 115 120 125  
 Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu  
 130 135 140  
 Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu  
 145 150 155 160  
 Gln Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro  
 165 170 175  
 Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser  
 180 185 190  
 Pro Asn Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser  
 195 200 205  
 Phe Leu Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly  
 210 215 220  
 Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro  
 225 230 235 240  
 Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro  
 245 250 255  
 Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser  
 260 265 270  
 Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu  
 275 280 285  
 Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu  
 290 295 300  
 Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu  
 305 310 315 320  
 Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe  
 325 330 335  
 Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His  
 340 345 350  
 Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Val Arg His Leu Ala  
 355 360 365  
 Gln Pro  
 370

&lt;210&gt; 184

&lt;211&gt; 364

&lt;212&gt; PRT

&lt;213&gt; Unknown

&lt;220&gt;

&lt;221&gt; MUTAGEN

&lt;222&gt; 1-364

&lt;223&gt;

&lt;400&gt; 184

Ala Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser Arg Leu  
 1 5 10 15  
 Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp Ile Thr  
 20 25 30  
 Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser  
 35 40 45  
 Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly  
 50 55 60  
 Gly Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp  
 65 70 75 80  
 Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr  
 85 90 95  
 Pro Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly  
 100 105 110  
 Leu Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr  
 115 120 125  
 Val Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu  
 130 135 140  
 Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro Tyr Val Glu Gly Gly  
 145 150 155 160  
 Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro  
 165 170 175  
 Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala Thr Pro  
 180 185 190  
 Leu Gly Pro Ala Ser Ser Val Pro Gln Ser Phe Leu Leu Lys Cys Leu  
 195 200 205  
 Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys  
 210 215 220  
 Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu Leu  
 225 230 235 240  
 Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser  
 245 250 255  
 Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly Leu  
 260 265 270  
 Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu  
 275 280 285  
 Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp Phe Ala  
 290 295 300  
 Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu  
 305 310 315 320  
 Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg  
 325 330 335  
 Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu Glu  
 340 345 350  
 Val Ser Tyr Arg Val Ile Arg His Leu Ala Gln Pro  
 355 360

&lt;210&gt; 185

&lt;211&gt; 370

&lt;212&gt; PRT

&lt;213&gt; Unknown

&lt;220&gt;

&lt;221&gt; MUTAGEN

&lt;222&gt; 1-370

&lt;223&gt;

&lt;400&gt; 185

Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu  
 1 5 10 15  
 Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser  
 20 25 30  
 Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val  
 35 40 45  
 Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln  
 50 55 60  
 Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala  
 65 70 75 80  
 Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu  
 85 90 95  
 Gln Cys Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly  
 100 105 110  
 Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln  
 115 120 125  
 Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys  
 130 135 140  
 Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val  
 145 150 155 160  
 Ala Tyr Val Glu Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro  
 165 170 175  
 Ile Ser Thr Ile Asn Pro Ser His Pro Ser Lys Glu Ser His Lys Ser  
 180 185 190  
 Pro Asn Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser  
 195 200 205  
 Phe Leu Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly  
 210 215 220  
 Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro  
 225 230 235 240  
 Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro  
 245 250 255  
 Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser  
 260 265 270  
 Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu  
 275 280 285  
 Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu  
 290 295 300  
 Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu  
 305 310 315 320  
 Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe  
 325 330 335  
 Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His  
 340 345 350  
 Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala  
 355 360 365  
 Gln Pro  
 370

<210> 186  
 <211> 370  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-370  
 <223>

&lt;400&gt; 186

Ala Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val  
 1 5 10 15  
 Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys  
 20 25 30  
 Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr  
 35 40 45  
 Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr  
 50 55 60  
 Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu  
 65 70 75 80  
 Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln  
 85 90 95  
 Cys Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser  
 100 105 110  
 Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp  
 115 120 125  
 Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile  
 130 135 140  
 Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala  
 145 150 155 160  
 Ser Tyr Val Glu Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro  
 165 170 175  
 Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser  
 180 185 190  
 Pro Asn Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser  
 195 200 205  
 Phe Leu Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly  
 210 215 220  
 Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro  
 225 230 235 240  
 Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro  
 245 250 255  
 Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser  
 260 265 270  
 Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu  
 275 280 285  
 Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu  
 290 295 300  
 Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu  
 305 310 315 320  
 Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe  
 325 330 335  
 Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His  
 340 345 350  
 Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Ile Arg His Leu Ala  
 355 360 365  
 Gln Pro  
 370

<210> 187  
 <211> 370  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-370  
 <223>

&lt;400&gt; 187

Ala Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu  
 1 5 10 15  
 Ala Gln Arg Leu Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met  
 20 25 30  
 Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys  
 35 40 45  
 Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn  
 50 55 60  
 Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys  
 65 70 75 80  
 Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys  
 85 90 95  
 Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly  
 100 105 110  
 Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp Cys  
 115 120 125  
 Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg  
 130 135 140  
 Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser  
 145 150 155 160  
 Asn Tyr Val Glu Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro  
 165 170 175  
 Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser  
 180 185 190  
 Pro Asn Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser  
 195 200 205  
 Phe Leu Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly  
 210 215 220  
 Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro  
 225 230 235 240  
 Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro  
 245 250 255  
 Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser  
 260 265 270  
 Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu  
 275 280 285  
 Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu  
 290 295 300  
 Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu  
 305 310 315 320  
 Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe  
 325 330 335  
 Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His  
 340 345 350  
 Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala  
 355 360 365  
 Gln Pro  
 370

<210> 188  
 <211> 370  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-370  
 <223>

&lt;400&gt; 188

Ala Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln Arg Trp Met  
 1 5 10 15  
 Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly Leu Glu  
 20 25 30  
 Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro  
 35 40 45  
 Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu  
 50 55 60  
 Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg  
 65 70 75 80  
 Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser  
 85 90 95  
 Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly  
 100 105 110  
 Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp Cys Ser Phe Gln His Ser  
 115 120 125  
 Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr  
 130 135 140  
 Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln Asp Glu  
 145 150 155 160  
 Glu Tyr Val Glu Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro  
 165 170 175  
 Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser  
 180 185 190  
 Pro Asn Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser  
 195 200 205  
 Phe Leu Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly  
 210 215 220  
 Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro  
 225 230 235 240  
 Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro  
 245 250 255  
 Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser  
 260 265 270  
 Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu  
 275 280 285  
 Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu  
 290 295 300  
 Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu  
 305 310 315 320  
 Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe  
 325 330 335  
 Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His  
 340 345 350  
 Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala  
 355 360 365  
 Gln Pro  
 370

<210> 189  
 <211> 364  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-364  
 <223>

&lt;400&gt; 189

Ala Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His  
 1 5 10 15  
 Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Ser Cys Leu Arg Phe  
 20 25 30  
 Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu  
 35 40 45  
 Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu  
 50 55 60  
 Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly  
 65 70 75 80  
 Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Thr Gln Asp Cys Ser Phe  
 85 90 95  
 Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu  
 100 105 110  
 Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu  
 115 120 125  
 Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln  
 130 135 140  
 Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Tyr Val Glu Gly Gly  
 145 150 155 160  
 Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro  
 165 170 175  
 Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala Thr Pro  
 180 185 190  
 Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys Cys Leu  
 195 200 205  
 Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys  
 210 215 220  
 Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu Leu  
 225 230 235 240  
 Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser  
 245 250 255  
 Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly Leu  
 260 265 270  
 Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu  
 275 280 285  
 Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp Phe Ala  
 290 295 300  
 Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu  
 305 310 315 320  
 Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg  
 325 330 335  
 Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu Glu  
 340 345 350  
 Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro  
 355 360

<210> 190  
 <211> 364  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-364  
 <223>

&lt;400&gt; 190

Ala Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His  
 1 5 10 15  
 Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe  
 20 25 30  
 Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu  
 35 40 45  
 Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu  
 50 55 60  
 Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly  
 65 70 75 80  
 Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Thr Gln Asp Cys Ser Phe  
 85 90 95  
 Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu  
 100 105 110  
 Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu  
 115 120 125  
 Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln  
 130 135 140  
 Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Tyr Val Glu Gly Gly  
 145 150 155 160  
 Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro  
 165 170 175  
 Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala Thr Pro  
 180 185 190  
 Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys Cys Leu  
 195 200 205  
 Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys  
 210 215 220  
 Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu Leu  
 225 230 235 240  
 Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser  
 245 250 255  
 Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly Leu  
 260 265 270  
 Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu  
 275 280 285  
 Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp Phe Ala  
 290 295 300  
 Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu  
 305 310 315 320  
 Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg  
 325 330 335  
 Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu Glu  
 340 345 350  
 Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro  
 355 360

<210> 191  
 <211> 370  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-370  
 <223>

<400> 191

Ala Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln Arg Trp Met

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|
| 1   |     |     |     | 5   |     |     |     |     | 10  |     |     |     | 15  |     |     |  |
| Glu | Arg | Leu | Lys | Thr | Val | Ala | Gly | Ser | Lys | Met | Gln | Gly | Leu | Leu | Glu |  |
|     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |  |
| Arg | Val | Asn | Thr | Glu | Ile | His | Phe | Val | Thr | Lys | Cys | Ala | Phe | Gln | Pro |  |
|     |     | 35  |     |     |     |     | 40  |     |     |     |     | 45  |     |     |     |  |
| Pro | Pro | Ser | Cys | Leu | Arg | Phe | Val | Gln | Thr | Asn | Ile | Ser | Arg | Leu | Leu |  |
|     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |  |
| Gln | Glu | Thr | Ser | Glu | Gln | Leu | Val | Ala | Leu | Lys | Pro | Trp | Ile | Thr | Arg |  |
| 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |  |
| Gln | Asn | Phe | Ser | Arg | Cys | Leu | Glu | Leu | Gln | Cys | Arg | Pro | Asp | Ser | Ser |  |
|     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |  |
| Thr | Leu | Gly | Gly | Gly | Ser | Gly | Gly | Gly | Ser | Gly | Gly | Gly | Ser | Gly | Gly |  |
|     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |  |
| Gly | Ser | Gly | Gly | Gly | Ser | Gly | Thr | Gln | Asp | Cys | Ser | Phe | Gln | His | Ser |  |
|     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |  |
| Pro | Ile | Ser | Ser | Asn | Phe | Ala | Val | Lys | Ile | Arg | Glu | Leu | Ser | Asp | Tyr |  |
|     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |  |
| Leu | Leu | Gln | Asp | Tyr | Pro | Val | Thr | Val | Ala | Ser | Asn | Leu | Gln | Asp | Glu |  |
| 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |  |
| Glu | Tyr | Val | Glu | Gly | Gly | Gly | Gly | Ser | Pro | Gly | Glu | Pro | Ser | Gly | Pro |  |
|     |     |     | 165 |     |     |     |     |     | 170 |     |     |     |     | 175 |     |  |
| Ile | Phe | Thr | Ile | Asn | Pro | Ser | Pro | Pro | Ser | Lys | Glu | Ser | His | Lys | Ser |  |
|     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |  |
| Pro | Asn | Met | Ala | Thr | Pro | Leu | Gly | Pro | Ala | Ser | Ser | Leu | Pro | Gln | Ser |  |
|     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |  |
| Phe | Leu | Leu | Lys | Cys | Leu | Glu | Gln | Val | Arg | Lys | Ile | Gln | Gly | Asp | Gly |  |
|     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |  |
| Ala | Ala | Leu | Gln | Glu | Lys | Leu | Cys | Ala | Thr | Tyr | Lys | Leu | Cys | His | Pro |  |
| 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |  |
| Glu | Glu | Leu | Val | Leu | Leu | Gly | His | Ser | Leu | Gly | Ile | Pro | Trp | Ala | Pro |  |
|     |     |     | 245 |     |     |     |     |     | 250 |     |     |     |     | 255 |     |  |
| Leu | Ser | Ser | Cys | Pro | Ser | Gln | Ala | Leu | Gln | Leu | Ala | Gly | Cys | Leu | Ser |  |
|     |     |     | 260 |     |     |     | 265 |     |     |     |     | 270 |     |     |     |  |
| Gln | Leu | His | Ser | Gly | Leu | Phe | Leu | Tyr | Gln | Gly | Leu | Leu | Gln | Ala | Leu |  |
|     |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |     |     |     |  |
| Glu | Gly | Ile | Ser | Pro | Glu | Leu | Gly | Pro | Thr | Leu | Asp | Thr | Leu | Gln | Leu |  |
|     | 290 |     |     |     |     | 295 |     |     |     |     | 300 |     |     |     |     |  |
| Asp | Val | Ala | Asp | Phe | Ala | Thr | Thr | Ile | Trp | Gln | Gln | Met | Glu | Glu | Leu |  |
| 305 |     |     |     |     | 310 |     |     |     | 315 |     |     |     |     |     | 320 |  |
| Gly | Met | Ala | Pro | Ala | Leu | Gln | Pro | Thr | Gln | Gly | Ala | Met | Pro | Ala | Phe |  |
|     |     |     | 325 |     |     |     |     |     | 330 |     |     |     |     | 335 |     |  |
| Ala | Ser | Ala | Phe | Gln | Arg | Arg | Ala | Gly | Gly | Val | Leu | Val | Ala | Ser | His |  |
|     |     |     | 340 |     |     |     |     | 345 |     |     |     |     |     |     |     |  |

|       |         |
|-------|---------|
| <210> | 192     |
| <211> | 370     |
| <212> | PRT     |
| <213> | Unknown |

<220>  
<221> MUTAGEN  
<222> 1-370  
<223>

<400> 192

Ala Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln Arg Trp

```

1           5           10           15
Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly Leu Leu
20           25           30
Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala Phe Gln
35           40           45
Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser Arg Leu
50           55           60
Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp Ile Thr
65           70           75           80
Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser
85           90           95
Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly
100          105          110
Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp Cys Ser Phe Gln His
115          120          125
Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp
130          135          140
Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln Asp
145          150          155          160
Glu Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro
165          170          175
Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser
180          185          190
Pro Asn Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser
195          200          205
Phe Leu Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly
210          215          220
Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro
225          230          235          240
Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro
245          250          255
Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser
260          265          270
Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu
275          280          285
Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu
290          295          300
Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu
305          310          315          320
Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe
325          330          335
Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His
340          345          350
Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala
355          360          365
Gln Pro
370

```

```

<210> 193
<211> 370
<212> PRT
<213> Unknown

```

```

<220>
<221> MUTAGEN
<222> 1-370
<223>

```

```

<400> 193

```

Ala Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln Arg

1 5 10 15  
 Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly Leu  
 20 25 30  
 Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala Phe  
 35 40 45  
 Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser Arg  
 50 55 60  
 Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp Ile  
 65 70 75 80  
 Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro Asp  
 85 90 95  
 Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser  
 100 105 110  
 Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp Cys Ser Phe Gln  
 115 120 125  
 His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser  
 130 135 140  
 Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln  
 145 150 155 160  
 Asp Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro  
 165 170 175  
 Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser  
 180 185 190  
 Pro Asn Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser  
 195 200 205  
 Phe Leu Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly  
 210 215 220  
 Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro  
 225 230 235 240  
 Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro  
 245 250 255  
 Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser  
 260 265 270  
 Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu  
 275 280 285  
 Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu  
 290 295 300  
 Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu  
 305 310 315 320  
 Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe  
 325 330 335  
 Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His  
 340 345 350  
 Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala  
 355 360 365  
 Gln Pro  
 370

<210> 194  
 <211> 370  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-370  
 <223>

<400> 194

Ala Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala

```

1           5           10           15
Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln
20           25           30
Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys
35           40           45
Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile
50           55           60
Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro
65           70           75           80
Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln
85           90           95
Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly
100          105          110
Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp Cys Ser
115          120          125
Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu
130          135          140
Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn
145          150          155          160
Leu Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro
165          170          175
Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser
180          185          190
Pro Asn Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser
195          200          205
Phe Leu Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly
210          215          220
Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro
225          230          235          240
Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro
245          250          255
Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser
260          265          270
Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu
275          280          285
Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu
290          295          300
Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu
305          310          315          320
Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe
325          330          335
Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His
340          345          350
Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala
355          360          365
Gln Pro
370

```

```

<210> 195
<211> 364
<212> PRT
<213> Unknown

```

```

<220>
<221> MUTAGEN
<222> 1-364
<223>

```

```

<400> 195

```

Ala Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val

```

1           5           10           15
Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu
20           25           30
Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly
35           40           45
Gly Ser Gly Gly Gly Ser Gly Gly Thr Gln Asp Cys Ser Phe Gln
50           55           60
His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser
65           70           75           80
Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln
85           90           95
Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln Arg
100          105          110
Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly Leu
115          120          125
Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala Phe
130          135          140
Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Tyr Val Glu Gly Gly
145          150          155          160
Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro
165          170          175
Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala Thr Pro
180          185          190
Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys Cys Leu
195          200          205
Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys
210          215          220
Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu Leu
225          230          235          240
Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser
245          250          255
Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly Leu
260          265          270
Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu
275          280          285
Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp Phe Ala
290          295          300
Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu
305          310          315          320
Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg
325          330          335
Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu Glu
340          345          350
Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
355          360

```

```

<210>    196
<211>    355
<212>    PRT
<213>    Unknown

```

```

<220>
<221>    MUTAGEN
<222>    1-355
<223>

```

```

<400>    196

```

```

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

```

20 25 30  
 Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala  
 35 40 45  
 Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser  
 50 55 60  
 Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp  
 65 70 75 80  
 Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro  
 85 90 95  
 Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly  
 100 105 110  
 Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp Cys Ser Phe  
 115 120 125  
 Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu  
 130 135 140  
 Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu  
 145 150 155 160  
 Gln Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Gly Gly Ser Gly Gly  
 165 170 175  
 Gly Ser Asn Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln  
 180 185 190  
 Ser Phe Leu Leu Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp  
 195 200 205  
 Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His  
 210 215 220  
 Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala  
 225 230 235 240  
 Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu  
 245 250 255  
 Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala  
 260 265 270  
 Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln  
 275 280 285  
 Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu  
 290 295 300  
 Leu Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala  
 305 310 315 320  
 Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser  
 325 330 335  
 His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu  
 340 345 350  
 Ala Gln Pro  
 355

<210> 197  
 <211> 370  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-370  
 <223>

<400> 197

Ala Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala  
 1 5 10 15  
 Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln  
 20 25 30  
 Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys

35 40 45  
 Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile  
 50 55 60  
 Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro  
 65 70 75 80  
 Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln  
 85 90 95  
 Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly  
 100 105 110  
 Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp Cys Ser  
 115 120 125  
 Phe Gln His Ser Pro Ile Ser Ser Asp Ser Ala Val Lys Ile Arg Glu  
 130 135 140  
 Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn  
 145 150 155 160  
 Leu Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro  
 165 170 175  
 Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser  
 180 185 190  
 Pro Asn Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser  
 195 200 205  
 Phe Leu Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly  
 210 215 220  
 Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro  
 225 230 235 240  
 Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro  
 245 250 255  
 Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser  
 260 265 270  
 Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu  
 275 280 285  
 Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu  
 290 295 300  
 Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu  
 305 310 315 320  
 Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe  
 325 330 335  
 Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His  
 340 345 350  
 Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala  
 355 360 365  
 Gln Pro  
 370

<210> 198  
 <211> 366  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-366  
 <223>

<400> 198

Ala Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln Arg Trp Met  
 1 5 10 15  
 Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly Leu Leu Glu  
 20 25 30  
 Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Tyr Ala Phe Gln Pro

35 40 45  
 Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu  
 50 55 60  
 Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg  
 65 70 75 80  
 Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Arg Pro Asp Ser Ser  
 85 90 95  
 Thr Leu Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly  
 100 105 110  
 Gly Ser Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser  
 115 120 125  
 Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp  
 130 135 140  
 Tyr Pro Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Tyr Val Glu  
 145 150 155 160  
 Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile  
 165 170 175  
 Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala  
 180 185 190  
 Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys  
 195 200 205  
 Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln  
 210 215 220  
 Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val  
 225 230 235 240  
 Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys  
 245 250 255  
 Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser  
 260 265 270  
 Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser  
 275 280 285  
 Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp  
 290 295 300  
 Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro  
 305 310 315 320  
 Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe  
 325 330 335  
 Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe  
 340 345 350  
 Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro  
 355 360 365

<210> 199  
 <211> 364  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-364  
 <223>

<400> 199

Ala Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His  
 1 5 10 15  
 Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Ser Cys Leu Arg Phe  
 20 25 30  
 Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu  
 35 40 45  
 Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Phe Arg Cys Leu

|                     |                     |                             |
|---------------------|---------------------|-----------------------------|
| 50                  | 55                  | 60                          |
| Glu Leu Gln Cys Gln | Pro Asp Ser Ser Thr | Leu Gly Gly Gly Ser Gly     |
| 65                  | 70                  | 75                          |
| Gly Gly Ser Gly Gly | Gly Ser Gly Gly Thr | Gln Asp Cys Ser Phe         |
| 85                  | 90                  | 95                          |
| Gln His Ser Pro Ile | Ser Ser Asp Phe Ala | Val Lys Ile Arg Glu Leu     |
| 100                 | 105                 | 110                         |
| Ser Asp Tyr Leu Leu | Gln Asp Tyr Pro     | Val Thr Val Ala Ser Asn Leu |
| 115                 | 120                 | 125                         |
| Gln Asp Glu Glu Leu | Cys Gly Gly Leu Trp | Arg Leu Val Leu Ala Gln     |
| 130                 | 135                 | 140                         |
| Arg Trp Met Glu Arg | Leu Lys Thr Val Ala | Gly Tyr Val Glu Gly Gly     |
| 145                 | 150                 | 155                         |
| Gly Gly Ser Pro Gly | Glu Pro Ser Gly Pro | Ile Ser Thr Ile Asn Pro     |
| 165                 | 170                 | 175                         |
| Ser Pro Pro Ser Lys | Glu Ser His Lys Ser | Pro Asn Met Ala Thr Pro     |
| 180                 | 185                 | 190                         |
| Leu Gly Pro Ala Ser | Ser Ser Leu Pro Gln | Ser Phe Leu Leu Lys Cys Leu |
| 195                 | 200                 | 205                         |
| Glu Gln Val Arg Lys | Ile Gln Gly Asp Gly | Ala Ala Leu Gln Glu Lys     |
| 210                 | 215                 | 220                         |
| Leu Cys Ala Thr Tyr | Lys Leu Cys His Pro | Glu Glu Leu Val Leu Leu     |
| 225                 | 230                 | 235                         |
| Gly His Ser Leu Gly | Ile Pro Trp Ala Pro | Leu Ser Ser Cys Pro Ser     |
| 245                 | 250                 | 255                         |
| Gln Ala Leu Gln Leu | Ala Gly Cys Leu Ser | Gln Leu His Ser Gly Leu     |
| 260                 | 265                 | 270                         |
| Phe Leu Tyr Gln Gly | Leu Leu Gln Ala Leu | Glu Gly Ile Ser Pro Glu     |
| 275                 | 280                 | 285                         |
| Leu Gly Pro Thr Leu | Asp Thr Leu Gln Leu | Asp Val Ala Asp Phe Ala     |
| 290                 | 295                 | 300                         |
| Thr Thr Ile Trp Gln | Gln Met Glu Glu Leu | Gly Met Ala Pro Ala Leu     |
| 305                 | 310                 | 315                         |
| Gln Pro Thr Gln Gly | Ala Met Pro Ala Phe | Ala Ser Ala Phe Gln Arg     |
| 325                 | 330                 | 335                         |
| Arg Ala Gly Gly Val | Leu Val Ala Ser His | Leu Gln Ser Phe Leu Glu     |
| 340                 | 345                 | 350                         |
| Val Ser Tyr Arg Val | Leu Arg His Leu Ala | Gln Pro                     |
| 355                 | 360                 |                             |

<210> 200  
 <211> 378  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-378  
 <223>

<400> 200

|                     |                 |                 |                 |
|---------------------|-----------------|-----------------|-----------------|
| Ala Gln Asp Glu Glu | Leu Cys Gly Gly | Leu Trp Arg Leu | Val Leu Ala     |
| 1                   | 5               | 10              | 15              |
| Gln Arg Trp Met Glu | Arg Leu Lys Thr | Val Ala Gly Ser | Lys Met Gln     |
| 20                  | 25              | 30              |                 |
| Gly Leu Leu Glu Arg | Val Asn Thr Glu | Ile His Phe Val | Thr Lys Cys     |
| 35                  | 40              | 45              |                 |
| Ala Phe Gln Pro Pro | Pro Ser Cys Leu | Arg Phe Val     | Gln Thr Asn Ile |
| 50                  | 55              | 60              |                 |
| Ser Arg Leu Leu Gln | Glu Thr Ser Glu | Gln Leu Val     | Ala Leu Lys Pro |

[illegible]

|       |         |
|-------|---------|
| <210> | 201     |
| <211> | 364     |
| <212> | PRT     |
| <213> | Unknown |

<220>  
<221> MUTAGEN  
<222> 1-364  
<223>

<400>      201

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ala | Gln | Asp | Glu | Glu | Leu | Cys | Gly | Gly | Leu | Trp | Arg | Leu | Val | Leu | Ala |
| 1   |     |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |
| Gln | Arg | Trp | Met | Glu | Arg | Leu | Lys | Thr | Val | Ala | Gly | Ser | Lys | Met | Gln |
|     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |
| Gly | Leu | Leu | Glu | Arg | Val | Asn | Thr | Glu | Ile | His | Phe | Val | Thr | Lys | Cys |
|     |     | 35  |     |     |     |     | 40  |     |     |     |     | 45  |     |     |     |
| Ala | Phe | Gln | Pro | Pro | Pro | Ser | Cys | Leu | Arg | Phe | Val | Gln | Thr | Asn | Ile |
|     | 50  |     |     |     |     | 55  |     |     |     | 60  |     |     |     |     |     |
| Ser | Arg | Leu | Leu | Gln | Glu | Thr | Ser | Glu | Gln | Leu | Val | Ala | Leu | Lys | Pro |

```

65          70          75          80
Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln
          85          90          95
Pro Asp Ser Ser Thr Leu Pro Pro Pro Trp Ser Pro Arg Pro Leu Gly
          100          105          110
Ala Thr Ala Pro Thr Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile
          115          120          125
Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu
          130          135          140
Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Tyr Val Glu Gly Gly
145          150          155          160
Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro
          165          170          175
Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala Thr Pro
          180          185          190
Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys Cys Leu
          195          200          205
Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys
          210          215          220
Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu Leu
225          230          235          240
Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser
          245          250          255
Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly Leu
          260          265          270
Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu
          275          280          285
Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp Phe Ala
290          295          300
Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu
305          310          315          320
Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg
          325          330          335
Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu Glu
          340          345          350
Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
          355          360

```

```

<210>      202
<211>      370
<212>      PRT
<213>      Unknown

```

```

<220>
<221>      MUTAGEN
<222>      1-370
<223>

```

```

<400>      202

```

```

Ala Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala
 1          5          10          15
Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln
          20          25          30
Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys
          35          40          45
Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile
          50          55          60
Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro
65          70          75          80
Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln

```

```

      85              90              95
Pro Asp Ser Ser Thr Leu Pro Pro Pro Trp Ser Pro Arg Pro Leu Gly
      100              105              110
Ala Thr Ala Pro Thr Ala Gly Gln Pro Pro Leu Thr Gln Asp Cys Ser
      115              120              125
Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu
      130              135              140
Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn
      145              150              155              160
Leu Tyr Val Glu Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro
      165              170              175
Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser
      180              185              190
Pro Asn Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser
      195              200              205
Phe Leu Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly
      210              215              220
Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro
      225              230              235              240
Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro
      245              250              255
Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser
      260              265              270
Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu
      275              280              285
Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu
      290              295              300
Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu
      305              310              315              320
Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe
      325              330              335
Ala Ser Ala Phe Gln Arg Arg Ala Gly Val Leu Val Ala Ser His
      340              345              350
Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala
      355              360              365
Gln Pro
      370

```

```

<210>      203
<211>      378
<212>      PRT
<213>      Unknown

```

```

<220>
<221>      MUTAGEN
<222>      1-378
<223>

```

```

<400>      203

```

```

Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln
  1              5              10              15
Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly
      20              25              30
Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala
      35              40              45
Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser
      50              55              60
Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp
      65              70              75              80
Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro

```

<400> 204

168

```

      85              90              95
Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
      100              105              110
Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
      115              120              125
Ser Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp
      130              135              140
Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr
145              150              155              160
Pro Val Thr Val Ala Ser Asn Leu Gln Tyr Val Glu Gly Gly Gly Gly
      165              170              175
Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro
      180              185              190
Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala Thr Pro Leu Gly
      195              200              205
Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys Cys Leu Glu Gln
210              215              220
Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys
225              230              235              240
Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly His
      245              250              255
Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala
      260              265              270
Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly Leu Phe Leu
      275              280              285
Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly
290              295              300
Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr
305              310              315              320
Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro
      325              330              335
Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg Ala
      340              345              350
Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu Glu Val Ser
      355              360              365
Tyr Arg Val Leu Arg His Leu Ala Gln Pro
370              375

```

```

<210>      205
<211>      370
<212>      PRT
<213>      Unknown

```

```

<220>
<221>      MUTAGEN
<222>      1-370
<223>

```

```

<400>      205

```

```

Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln
 1              5              10              15
Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly
      20              25              30
Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala
      35              40              45
Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser
      50              55              60
Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp
65              70              75              80
Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro

```

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|     |     |     |     | 85  |     |     |     | 90  |     |     |     | 95  |     |     |     |
| Asp | Ser | Ser | Thr | Leu | Pro | Pro | Pro | Trp | Ser | Pro | Arg | Pro | Leu | Gly | Ala |
| 100 |     |     |     |     |     |     |     | 105 |     |     |     | 110 |     |     |     |
| Thr | Ala | Pro | Thr | Ala | Gly | Gln | Pro | Pro | Leu | Thr | Gln | Asp | Cys | Ser | Phe |
| 115 |     |     |     |     |     |     |     | 120 |     |     |     | 125 |     |     |     |
| Gln | His | Ser | Pro | Ile | Ser | Ser | Asp | Phe | Ala | Val | Lys | Ile | Arg | Glu | Leu |
| 130 |     |     |     | 135 |     |     |     |     |     |     |     | 140 |     |     |     |
| Ser | Asp | Tyr | Leu | Leu | Gln | Asp | Tyr | Pro | Val | Thr | Val | Ala | Ser | Asn | Leu |
| 145 |     |     |     | 150 |     |     |     |     |     |     |     | 155 |     |     |     |
| Gln | Tyr | Val | Glu | Gly | Gly | Gly | Gly | Thr | Pro | Gly | Glu | Pro | Ser | Gly | Pro |
| 165 |     |     |     |     |     |     |     | 170 |     |     |     | 175 |     |     |     |
| Ile | Ser | Thr | Ile | Asn | Pro | Ser | Pro | Pro | Ser | Lys | Glu | Ser | His | Lys | Ser |
| 180 |     |     |     |     |     |     |     | 185 |     |     |     | 190 |     |     |     |
| Pro | Asn | Met | Ala | Thr | Pro | Leu | Gly | Pro | Ala | Ser | Ser | Leu | Pro | Gln | Ser |
| 195 |     |     |     | 200 |     |     |     |     |     |     |     | 205 |     |     |     |
| Phe | Leu | Leu | Lys | Cys | Leu | Glu | Gln | Val | Arg | Lys | Ile | Gln | Gly | Asp | Gly |
| 210 |     |     |     | 215 |     |     |     |     |     |     |     | 220 |     |     |     |
| Ala | Ala | Leu | Gln | Glu | Lys | Leu | Cys | Ala | Thr | Tyr | Lys | Leu | Cys | His | Pro |
| 225 |     |     |     | 230 |     |     |     |     |     |     |     | 235 |     |     |     |
| Glu | Glu | Leu | Val | Leu | Leu | Gly | His | Ser | Leu | Gly | Ile | Pro | Trp | Ala | Pro |
| 245 |     |     |     |     |     |     |     | 250 |     |     |     | 255 |     |     |     |
| Leu | Ser | Ser | Cys | Pro | Ser | Gln | Ala | Leu | Gln | Leu | Ala | Gly | Cys | Leu | Ser |
| 260 |     |     |     |     |     |     |     | 265 |     |     |     | 270 |     |     |     |
| Gln | Leu | His | Ser | Gly | Leu | Phe | Leu | Tyr | Gln | Gly | Leu | Leu | Gln | Ala | Leu |
| 275 |     |     |     | 280 |     |     |     |     |     |     |     | 285 |     |     |     |
| Glu | Gly | Ile | Ser | Pro | Glu | Leu | Gly | Pro | Thr | Leu | Asp | Thr | Leu | Gln | Leu |
| 290 |     |     |     | 295 |     |     |     |     |     |     |     | 300 |     |     |     |
| Asp | Val | Ala | Asp | Phe | Ala | Thr | Thr | Ile | Trp | Gln | Gln | Met | Glu | Glu | Leu |
| 305 |     |     |     | 310 |     |     |     |     |     |     |     | 315 |     |     |     |
| Gly | Met | Ala | Pro | Ala | Leu | Gln | Pro | Thr | Gln | Gly | Ala | Met | Pro | Ala | Phe |
| 325 |     |     |     |     |     |     |     | 330 |     |     |     | 335 |     |     |     |
| Ala | Ser | Ala | Phe | Gln | Arg | Arg | Ala | Gly | Gly | Val | Leu | Val | Ala | Ser | His |
| 340 |     |     |     |     |     |     |     | 345 |     |     |     | 350 |     |     |     |
| Leu | Gln | Ser | Phe | Leu | Glu | Val | Ser | Tyr | Arg | Val | Leu | Arg | His | Leu | Ala |
| 355 |     |     |     | 360 |     |     |     |     |     |     |     | 365 |     |     |     |
| Gln | Pro |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
| 370 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |

|       |         |
|-------|---------|
| <210> | 206     |
| <211> | 347     |
| <212> | PRT     |
| <213> | Unknown |

<220>  
<221> MUTAGEN  
<222> 1-347  
<223>

<400> 206

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ala | Asp | Glu | Glu | Leu | Cys | Gly | Gly | Leu | Trp | Arg | Leu | Val | Leu | Ala | Gln |
| 1   |     |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |
| Arg | Trp | Met | Glu | Arg | Leu | Lys | Thr | Val | Ala | Gly | Ser | Lys | Met | Gln | Gly |
|     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |
| Leu | Leu | Glu | Arg | Val | Asn | Thr | Glu | Ile | His | Phe | Val | Thr | Lys | Cys | Ala |
|     |     | 35  |     |     |     | 40  |     |     |     |     | 45  |     |     |     |     |
| Phe | Gln | Pro | Pro | Pro | Ser | Cys | Leu | Arg | Phe | Val | Gln | Thr | Asn | Ile | Ser |
|     | 50  |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |     |
| Arg | Leu | Leu | Gln | Glu | Thr | Ser | Glu | Gln | Leu | Val | Ala | Leu | Lys | Pro | Trp |
| 65  |     |     |     | 70  |     |     |     |     |     | 75  |     |     |     | 80  |     |
| Ile | Thr | Arg | Gln | Asn | Phe | Ser | Arg | Cys | Leu | Glu | Leu | Gln | Cys | Gln | Pro |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |    |  |  |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|----|--|--|
|     |     |     |     |     |     |     |     |     |     | 85  |     |     | 90  |     |     | 95 |  |  |
| Val | Glu | Thr | Val | Phe | His | Arg | Val | Ser | Gln | Asp | Gly | Leu | Asp | Leu | Leu |    |  |  |
|     |     |     | 100 |     |     |     | 105 |     |     | 110 |     |     |     |     |     |    |  |  |
| Thr | Ser | Thr | Gln | Asp | Cys | Ser | Phe | Gln | His | Ser | Pro | Ile | Ser | Ser | Asp |    |  |  |
|     |     |     | 115 |     |     |     | 120 |     |     | 125 |     |     |     |     |     |    |  |  |
| Phe | Ala | Val | Lys | Ile | Arg | Glu | Leu | Ser | Asp | Tyr | Leu | Leu | Gln | Asp | Tyr |    |  |  |
|     |     |     | 130 | 135 |     |     | 140 |     |     |     |     |     |     |     |     |    |  |  |
| Pro | Val | Thr | Val | Ala | Ser | Asn | Leu | Gln | Tyr | Val | Glu | Gly | Gly | Gly | Gly |    |  |  |
| 145 |     |     |     | 150 |     |     | 155 |     |     | 160 |     |     |     |     |     |    |  |  |
| Ser | Pro | Gly | Gly | Gly | Ser | Gly | Gly | Gly | Ser | Asn | Met | Ala | Thr | Pro | Leu |    |  |  |
|     |     |     | 165 |     |     | 170 |     |     | 175 |     |     |     |     |     |     |    |  |  |
| Gly | Pro | Ala | Ser | Ser | Leu | Pro | Gln | Ser | Phe | Leu | Leu | Lys | Ser | Leu | Glu |    |  |  |
|     |     |     | 180 |     |     | 185 |     |     | 190 |     |     |     |     |     |     |    |  |  |
| Gln | Val | Arg | Lys | Ile | Gln | Gly | Asp | Gly | Ala | Ala | Leu | Gln | Glu | Lys | Leu |    |  |  |
|     |     |     | 195 |     |     | 200 |     |     | 205 |     |     |     |     |     |     |    |  |  |
| Cys | Ala | Thr | Asn | Lys | Leu | Cys | His | Pro | Glu | Glu | Leu | Val | Leu | Leu | Gly |    |  |  |
|     |     |     | 210 |     |     | 215 |     |     | 220 |     |     |     |     |     |     |    |  |  |
| His | Ser | Leu | Gly | Ile | Pro | Trp | Ala | Pro | Leu | Ser | Ser | Cys | Pro | Ser | Gln |    |  |  |
| 225 |     |     |     | 230 |     |     | 235 |     |     | 240 |     |     |     |     |     |    |  |  |
| Ala | Leu | Gln | Leu | Ala | Gly | Cys | Leu | Ser | Gln | Leu | His | Ser | Gly | Leu | Phe |    |  |  |
|     |     |     | 245 |     |     | 250 |     |     | 255 |     |     |     |     |     |     |    |  |  |
| Leu | Tyr | Gln | Gly | Leu | Leu | Gln | Ala | Leu | Glu | Gly | Ile | Ser | Pro | Glu | Leu |    |  |  |
|     |     |     | 260 |     |     | 265 |     |     | 270 |     |     |     |     |     |     |    |  |  |
| Gly | Pro | Thr | Leu | Asp | Thr | Leu | Gln | Leu | Asp | Val | Ala | Asp | Phe | Ala | Thr |    |  |  |
|     |     |     | 275 |     |     | 280 |     |     | 285 |     |     |     |     |     |     |    |  |  |
| Thr | Ile | Trp | Gln | Gln | Met | Glu | Glu | Leu | Gly | Met | Ala | Pro | Ala | Leu | Gln |    |  |  |
|     |     |     | 290 |     |     | 295 |     |     | 300 |     |     |     |     |     |     |    |  |  |
| Pro | Thr | Gln | Gly | Ala | Met | Pro | Ala | Phe | Ala | Ser | Ala | Phe | Gln | Arg | Arg |    |  |  |
| 305 |     |     |     | 310 |     |     | 315 |     |     | 320 |     |     |     |     |     |    |  |  |
| Ala | Gly | Gly | Val | Leu | Val | Ala | Ser | His | Leu | Gln | Ser | Phe | Leu | Glu | Val |    |  |  |
|     |     |     | 325 |     |     | 330 |     |     | 335 |     |     |     |     |     |     |    |  |  |
| Ser | Tyr | Arg | Val | Leu | Arg | His | Leu | Ala | Gln | Pro |     |     |     |     |     |    |  |  |
|     |     |     | 340 |     |     | 345 |     |     |     |     |     |     |     |     |     |    |  |  |

|       |         |
|-------|---------|
| <210> | 207     |
| <211> | 384     |
| <212> | PRT     |
| <213> | Unknown |

|       |         |
|-------|---------|
| <220> |         |
| <221> | MUTAGEN |
| <222> | 1-384   |
| <223> |         |

<400> 207

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ala | Asp | Glu | Glu | Leu | Cys | Gly | Gly | Leu | Trp | Arg | Leu | Val | Leu | Ala | Gln |
| 1   |     |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |
| Arg | Trp | Met | Glu | Arg | Leu | Lys | Thr | Val | Ala | Gly | Ser | Lys | Met | Gln | Gly |
|     |     | 20  |     |     |     |     |     | 25  |     |     |     |     | 30  |     |     |
| Leu | Leu | Glu | Arg | Val | Asn | Thr | Glu | Ile | His | Phe | Val | Thr | Lys | Cys | Ala |
|     |     | 35  |     |     |     |     | 40  |     |     |     |     | 45  |     |     |     |
| Phe | Gln | Pro | Pro | Pro | Ser | Cys | Leu | Arg | Phe | Val | Gln | Thr | Asn | Ile | Ser |
|     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |
| Arg | Leu | Leu | Gln | Glu | Thr | Ser | Glu | Gln | Leu | Val | Ala | Leu | Lys | Pro | Trp |
| 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     | 80  |     |
| Ile | Thr | Arg | Gln | Asn | Phe | Ser | Arg | Cys | Leu | Glu | Leu | Gln | Cys | Gln | Pro |
|     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |
| Asp | Ser | Ser | Thr | Leu | Tyr | Val | Glu | Gly | Gly | Gly | Gly | Ser | Pro | Gly | Glu |
|     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
| Pro | Ser | Gly | Pro | Ile | Ser | Thr | Ile | Asn | Pro | Ser | Pro | Pro | Ser | Lys | Glu |

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

|       |         |
|-------|---------|
| <210> | 208     |
| <211> | 349     |
| <212> | PRT     |
| <213> | Unknown |

|       |         |
|-------|---------|
| <220> |         |
| <221> | MUTAGEN |
| <222> | 1-349   |
| <223> |         |

<400> 208

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ala | Thr | Gln | Asp | Cys | Ser | Phe | Gln | His | Ser | Pro | Ile | Ser | Ser | Asp | Phe |
| 1   |     |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |
| Ala | Val | Lys | Ile | Arg | Glu | Leu | Ser | Asp | Tyr | Leu | Leu | Gln | Asp | Tyr | Pro |
|     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |
| Val | Thr | Val | Ala | Ser | Asn | Leu | Gln | Glu | Pro | Lys | Ser | Pro | Asp | Thr | His |
|     |     | 35  |     |     |     |     | 40  |     |     |     |     | 45  |     |     |     |
| Thr | Ser | Pro | Pro | Ser | Pro | Thr | Pro | Leu | Gly | Pro | Ala | Ser | Ser | Leu | Pro |
|     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |
| Gln | Ser | Phe | Leu | Leu | Lys | Ser | Leu | Glu | Gln | Val | Arg | Lys | Ile | Gln | Gly |
| 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     | 80  |     |
| Asp | Gly | Ala | Ala | Leu | Gln | Glu | Lys | Leu | Cys | Ala | Thr | Tyr | Lys | Leu | Cys |
|     |     |     | 85  |     |     |     |     |     | 90  |     |     |     |     | 95  |     |
| His | Pro | Glu | Glu | Leu | Val | Leu | Leu | Gly | His | Ser | Leu | Gly | Ile | Pro | Trp |
|     |     | 100 |     |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
| Ala | Pro | Leu | Ser | Ser | Cys | Pro | Ser | Gln | Ala | Leu | Gln | Leu | Ala | Gly | Cys |

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

<210> 209  
 <211> 347  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-347  
 <223>

<400> 209

Ala Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe  
 1 5 10 15  
 Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro  
 20 25 30  
 Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu  
 35 40 45  
 Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val  
 50 55 60  
 Ala Gly Ser Lys Met Gln Gly Trp Gln Gly Arg Val Asn Thr Glu Ile  
 65 70 75 80  
 His Phe Val Thr Lys Cys Ala Phe Pro Lys Ser Pro Asp Thr His Thr  
 85 90 95  
 Ser Pro Pro Ser Pro Gly Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro  
 100 105 110  
 Gln Ser Phe Leu Leu Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly  
 115 120 125  
 Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Tyr Lys Leu Cys His  
 130 135 140  
 Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala

145                      150                      155                      160  
 Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu  
                                  165                      170                      175  
 Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala  
                                  180                      185                      190  
 Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln  
                                  195                      200                      205  
 Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu  
                                  210                      215                      220  
 Leu Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala  
 225                      230                      235                      240  
 Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser  
                                  245                      250                      255  
 His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu  
                                  260                      265                      270  
 Ala Gln Pro Ser Ala Glu Pro Lys Ser Pro Asp Thr His Thr Ser Pro  
                                  275                      280                      285  
 Pro Ser Pro Gly Lys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe  
                                  290                      295                      300  
 Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu  
 305                      310                      315                      320  
 Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu  
                                  325                      330                      335  
 Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu  
                                  340                      345

<210>      210  
 <211>      355  
 <212>      PRT  
 <213>      Unknown

<220>  
 <221>      MUTAGEN  
 <222>      1-355  
 <223>

<400>      210

Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln  
 1                      5                      10                      15  
 Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly  
                                  20                      25                      30  
 Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Ser Ala  
                                  35                      40                      45  
 Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser  
                                  50                      55                      60  
 Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp  
 65                      70                      75                      80  
 Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro  
                                  85                      90                      95  
 Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly  
                                  100                      105                      110  
 Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp Ser Ser Phe  
                                  115                      120                      125  
 Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu  
                                  130                      135                      140  
 Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu  
 145                      150                      155                      160  
 Gln Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Gly Gly Ser Gly Gly  
                                  165                      170                      175  
 Gly Ser Asn Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln

180 185 190  
 Ser Phe Leu Leu Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp  
 195 200 205  
 Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Asn Lys Leu Cys His  
 210 215 220  
 Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala  
 225 230 235 240  
 Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu  
 245 250 255  
 Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala  
 260 265 270  
 Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln  
 275 280 285  
 Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu  
 290 295 300  
 Leu Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala  
 305 310 315 320  
 Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser  
 325 330 335  
 His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu  
 340 345 350  
 Ala Gln Pro  
 355

<210> 211  
 <211> 370  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-370  
 <223>

<400> 211

Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu  
 1 5 10 15  
 Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu  
 20 25 30  
 Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu  
 35 40 45  
 Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser  
 50 55 60  
 Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His  
 65 70 75 80  
 Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile  
 85 90 95  
 Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala  
 100 105 110  
 Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala  
 115 120 125  
 Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala  
 130 135 140  
 Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser  
 145 150 155 160  
 Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro Tyr  
 165 170 175  
 Val Glu Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser  
 180 185 190  
 Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn

195                      200                      205  
 Met Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala  
       210                      215                      220  
 Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln  
 225                      230                      235                      240  
 Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Ser  
                          245                      250                      255  
 Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile  
                          260                      265                      270  
 Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro  
                          275                      280                      285  
 Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln  
                          290                      295                      300  
 Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly  
 305                      310                      315                      320  
 Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp Ser Ser  
                          325                      330                      335  
 Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu  
                          340                      345                      350  
 Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn  
                          355                      360                      365  
 Leu Gln  
 370

<210>      212  
 <211>      355  
 <212>      PRT  
 <213>      Unknown

<220>  
 <221>      MUTAGEN  
 <222>      1-355  
 <223>

<400>      212

Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln  
   1                      5                      10                      15  
 Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly  
                          20                      25                      30  
 Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala  
                          35                      40                      45  
 Phe Gln Pro Pro Pro Ser Ser Leu Arg Phe Val Gln Thr Asn Ile Ser  
                          50                      55                      60  
 Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp  
 65                      70                      75                      80  
 Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Ser Gln Pro  
                          85                      90                      95  
 Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly  
                          100                      105                      110  
 Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp Cys Ser Phe  
                          115                      120                      125  
 Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu  
                          130                      135                      140  
 Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu  
 145                      150                      155                      160  
 Gln Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Gly Gly Ser Gly Gly  
                          165                      170                      175  
 Gly Ser Asn Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln  
                          180                      185                      190  
 Ser Phe Leu Leu Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp

[illegible]

|       |         |
|-------|---------|
| <210> | 213     |
| <211> | 370     |
| <212> | PRT     |
| <213> | Unknown |

|       |         |
|-------|---------|
| <220> |         |
| <221> | MUTAGEN |
| <222> | 1-370   |
| <223> |         |

<400> 213

|         |     |     |     |         |     |     |     |         |        |     |     |     |        |        |         |
|---------|-----|-----|-----|---------|-----|-----|-----|---------|--------|-----|-----|-----|--------|--------|---------|
| Ala 1   | Thr | Pro | Leu | Gly 5   | Pro | Ala | Ser | Ser     | Leu 10 | Pro | Gln | Ser | Phe    | Leu 15 | Leu     |
| Lys     | Ser | Leu | Glu | Gln 20  | Val | Arg | Lys | Ile 25  | Gln    | Gly | Asp | Gly | Ala 30 | Ala    | Leu     |
| Gln     | Glu | Lys | Leu | Cys 35  | Ala | Thr | Tyr | Lys 40  | Leu    | Cys | His | Pro | Glu    | Glu    | Leu     |
| Val     | Leu | Leu | Gly | His 50  | Ser | Leu | Gly | Ile 55  | Pro    | Trp | Ala | Pro | Leu    | Ser    | Ser     |
| Cys 65  | Pro | Ser | Gln | Ala 70  | Leu | Gln | Leu | Ala 75  | Gly    | Cys | Leu | Ser | Gln    | Leu    | His 80  |
| Ser     | Gly | Leu | Phe | Leu 85  | Tyr | Gln | Gly | Leu 90  | Leu    | Gln | Ala | Leu | Glu    | Gly    | Ile 95  |
| Ser     | Pro | Glu | Leu | Gly 100 | Pro | Thr | Leu | Asp 105 | Thr    | Leu | Gln | Leu | Asp    | Val    | Ala     |
| Asp     | Phe | Ala | Thr | Thr 115 | Ile | Trp | Gln | Gln 120 | Met    | Glu | Glu | Leu | Gly    | Met    | Ala     |
| Pro     | Ala | Leu | Gln | Pro 130 | Thr | Gln | Gly | Ala 135 | Met    | Pro | Ala | Phe | Ala    | Ser    | Ala     |
| Phe 145 | Gln | Arg | Arg | Ala 150 | Gly | Gly | Val | Leu 155 | Val    | Ala | Ser | His | Leu    | Gln    | Ser 160 |
| Phe     | Leu | Glu | Val | Ser 165 | Tyr | Arg | Val | Leu 170 | Arg    | His | Leu | Ala | Gln    | Pro    | Tyr 175 |
| Val     | Glu | Gly | Gly | Gly 180 | Gly | Ser | Pro | Gly 185 | Glu    | Pro | Ser | Gly | Pro    | Ile    | Ser     |
| Thr     | Ile | Asn | Pro | Ser 195 | Pro | Pro | Ser | Lys 200 | Glu    | Ser | His | Lys | Ser    | Pro    | Asn     |
| Met     | Ala | Asp | Glu | Glu     | Leu | Cys | Gly | Gly     | Leu    | Trp | Arg | Leu | Val    | Leu    | Ala     |

210                      215                      220  
 Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln  
 225                      230                      235                      240  
 Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys  
                     245                      250                      255  
 Ala Phe Gln Pro Pro Pro Ser Ser Leu Arg Phe Val Gln Thr Asn Ile  
                     260                      265                      270  
 Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro  
                     275                      280                      285  
 Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Ser Gln  
 290                      295                      300  
 Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly  
 305                      310                      315                      320  
 Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp Cys Ser  
                     325                      330                      335  
 Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu  
                     340                      345                      350  
 Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn  
                     355                      360                      365  
 Leu Gln  
 370

<210>      214  
 <211>      334  
 <212>      PRT  
 <213>      Unknown

<220>  
 <221>      MUTAGEN  
 <222>      1-334  
 <223>

<400>      214

Ala Thr Gln Asp Ser Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe  
 1                      5                      10                      15  
 Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro  
                     20                      25                      30  
 Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu  
                     35                      40                      45  
 Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val  
 50                      55                      60  
 Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile  
 65                      70                      75                      80  
 His Phe Val Thr Lys Ser Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg  
                     85                      90                      95  
 Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln  
                     100                      105                      110  
 Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys  
                     115                      120                      125  
 Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Tyr Val Glu Gly  
 130                      135                      140  
 Gly Gly Gly Ser Pro Gly Gly Gly Ser Gly Gly Gly Ser Asn Met Ala  
 145                      150                      155                      160  
 Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys  
                     165                      170                      175  
 Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln  
                     180                      185                      190  
 Glu Lys Leu Cys Ala Thr Asn Lys Leu Cys His Pro Glu Glu Leu Val  
 195                      200                      205  
 Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys

```

      210              215              220
Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser
225              230              235              240
Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser
      245              250              255
Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp
      260              265              270
Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro
      275              280              285
Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe
      290              295              300
Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe
305              310              315              320
Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
      325              330

```

```

<210>      215
<211>      334
<212>      PRT
<213>      Unknown

```

```

<220>
<221>      MUTAGEN
<222>      1-334
<223>

```

```

<400>      215

```

```

Ala Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe
 1              5              10              15
Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro
      20              25              30
Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu
      35              40              45
Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val
      50              55              60
Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile
      65              70              75              80
His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Ser Leu Arg
      85              90              95
Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln
      100              105              110
Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys
      115              120              125
Leu Glu Leu Gln Ser Gln Pro Asp Ser Ser Thr Leu Tyr Val Glu Gly
      130              135              140
Gly Gly Gly Ser Pro Gly Gly Gly Ser Gly Gly Ser Asn Met Ala
      145              150              155              160
Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys
      165              170              175
Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln
      180              185              190
Glu Lys Leu Cys Ala Thr Asn Lys Leu Cys His Pro Glu Glu Leu Val
      195              200              205
Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys
      210              215              220
Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser
      225              230              235              240
Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser
      245              250              255
Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp

```

|     |                                                             |     |     |     |     |
|-----|-------------------------------------------------------------|-----|-----|-----|-----|
|     | 260                                                         |     | 265 |     | 270 |
| Phe | Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro |     |     |     |     |
|     | 275                                                         |     | 280 |     | 285 |
| Ala | Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe |     |     |     |     |
|     | 290                                                         |     | 295 |     | 300 |
| Gln | Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe |     |     |     |     |
| 305 |                                                             | 310 |     | 315 | 320 |
| Leu | Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro         |     |     |     |     |
|     | 325                                                         |     | 330 |     |     |

<210> 216  
 <211> 326  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-326  
 <223>

<400> 216

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ala | Thr | Gln | Asp | Cys | Ser | Phe | Gln | His | Ser | Pro | Ile | Ser | Ser | Asp | Phe |
| 1   |     |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |
| Ala | Val | Lys | Ile | Arg | Glu | Leu | Ser | Asp | Tyr | Leu | Leu | Gln | Asp | Tyr | Pro |
|     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |
| Val | Thr | Val | Ala | Ser | Asn | Leu | Gln | Asp | Glu | Glu | Leu | Cys | Gly | Gly | Leu |
|     | 35  |     |     |     |     |     | 40  |     |     |     |     | 45  |     |     |     |
| Trp | Arg | Leu | Val | Leu | Ala | Gln | Arg | Trp | Met | Glu | Arg | Leu | Lys | Thr | Val |
|     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |
| Ala | Gly | Ser | Lys | Met | Gln | Gly | Leu | Leu | Glu | Arg | Val | Asn | Thr | Glu | Ile |
| 65  |     |     |     |     | 70  |     |     |     | 75  |     |     |     |     | 80  |     |
| His | Phe | Val | Thr | Lys | Cys | Ala | Phe | Gln | Pro | Pro | Pro | Ser | Cys | Leu | Arg |
|     |     |     |     | 85  |     |     |     | 90  |     |     |     |     |     | 95  |     |
| Phe | Val | Gln | Thr | Asn | Ile | Ser | Arg | Leu | Leu | Gln | Glu | Thr | Ser | Glu | Gln |
|     |     |     | 100 |     |     |     | 105 |     |     |     |     | 110 |     |     |     |
| Leu | Val | Ala | Leu | Lys | Pro | Trp | Ile | Thr | Arg | Gln | Asn | Phe | Ser | Arg | Cys |
|     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |     |
| Leu | Glu | Leu | Gln | Tyr | Val | Glu | Gly | Gly | Gly | Gly | Ser | Pro | Gly | Gly | Gly |
|     | 130 |     |     |     |     | 135 |     |     |     | 140 |     |     |     |     |     |
| Ser | Gly | Gly | Gly | Ser | Asn | Met | Ala | Thr | Pro | Leu | Gly | Pro | Ala | Ser | Ser |
| 145 |     |     |     |     | 150 |     |     |     | 155 |     |     |     |     | 160 |     |
| Leu | Pro | Gln | Ser | Phe | Leu | Leu | Lys | Ser | Leu | Glu | Gln | Val | Arg | Lys | Ile |
|     |     |     |     | 165 |     |     |     | 170 |     |     |     |     |     | 175 |     |
| Gln | Gly | Asp | Gly | Ala | Ala | Leu | Gln | Glu | Lys | Leu | Cys | Ala | Thr | Asn | Lys |
|     |     | 180 |     |     |     |     | 185 |     |     |     |     |     | 190 |     |     |
| Leu | Cys | His | Pro | Glu | Glu | Leu | Val | Leu | Leu | Gly | His | Ser | Leu | Gly | Ile |
|     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |     |
| Pro | Trp | Ala | Pro | Leu | Ser | Ser | Cys | Pro | Ser | Gln | Ala | Leu | Gln | Leu | Ala |
|     | 210 |     |     |     |     | 215 |     |     |     | 220 |     |     |     |     |     |
| Gly | Cys | Leu | Ser | Gln | Leu | His | Ser | Gly | Leu | Phe | Leu | Tyr | Gln | Gly | Leu |
| 225 |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |     |
| Leu | Gln | Ala | Leu | Glu | Gly | Ile | Ser | Pro | Glu | Leu | Gly | Pro | Thr | Leu | Asp |
|     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |     |
| Thr | Leu | Gln | Leu | Asp | Val | Ala | Asp | Phe | Ala | Thr | Thr | Ile | Trp | Gln | Gln |
|     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |     |     |     |
| Met | Glu | Glu | Leu | Gly | Met | Ala | Pro | Ala | Leu | Gln | Pro | Thr | Gln | Gly | Ala |
|     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |     |     |     |     |
| Met | Pro | Ala | Phe | Ala | Ser | Ala | Phe | Gln | Arg | Arg | Ala | Gly | Gly | Val | Leu |
|     | 290 |     |     |     | 295 |     |     |     |     | 300 |     |     |     |     |     |
| Val | Ala | Ser | His | Leu | Gln | Ser | Phe | Leu | Glu | Val | Ser | Tyr | Arg | Val | Leu |

305                      310  
Arg His Leu Ala Gln Pro  
                         325

315

320

<210>      217  
<211>      334  
<212>      PRT  
<213>      Unknown

<220>  
<221>      MUTAGEN  
<222>      1-334  
<223>

<400>      217

Ala Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe  
1                      5                      10                      15  
Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro  
                         20                      25                      30  
Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu  
                         35                      40                      45  
Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val  
                         50                      55                      60  
Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile  
65                      70                      75                      80  
His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg  
                         85                      90                      95  
Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln  
                         100                      105                      110  
Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys  
                         115                      120                      125  
Leu Glu Leu Gln Ser Gln Pro Asp Ser Ser Thr Leu Tyr Val Glu Gly  
                         130                      135                      140  
Gly Gly Gly Ser Pro Gly Gly Gly Ser Gly Gly Gly Ser Asn Met Ala  
145                      150                      155                      160  
Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys  
                         165                      170                      175  
Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln  
                         180                      185                      190  
Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val  
                         195                      200                      205  
Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys  
                         210                      215                      220  
Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser  
225                      230                      235                      240  
Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser  
                         245                      250                      255  
Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp  
                         260                      265                      270  
Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro  
                         275                      280                      285  
Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe  
                         290                      295                      300  
Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe  
305                      310                      315                      320  
Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro  
                         325                      330

<210>      218  
<211>      334

<212> PRT  
<213> Unknown

<220>  
<221> MUTAGEN  
<222> 1-334  
<223>

<400> 218

```

Ala Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe
 1      5      10      15
Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro
 20      25      30
Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu
 35      40      45
Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val
 50      55      60
Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile
 65      70      75      80
His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg
 85      90      95
Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln
 100     105     110
Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Arg
 115     120     125
Leu Glu Leu Gln Ser Gln Pro Asp Ser Ser Thr Leu Tyr Val Glu Gly
 130     135     140
Gly Gly Gly Ser Pro Gly Gly Gly Ser Gly Gly Ser Asn Met Ala
 145     150     155     160
Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys
 165     170     175
Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln
 180     185     190
Glu Lys Leu Cys Ala Thr Asn Lys Leu Cys His Pro Glu Glu Leu Val
 195     200     205
Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys
 210     215     220
Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser
 225     230     235     240
Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser
 245     250     255
Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp
 260     265     270
Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro
 275     280     285
Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe
 290     295     300
Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe
 305     310     315     320
Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 325     330

```

<210> 219  
<211> 352  
<212> PRT  
<213> Unknown

<220>  
<221> MUTAGEN  
<222> 1-352

&lt;223&gt;

&lt;400&gt; 219

Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln  
 1 5 10 15  
 Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly  
 20 25 30  
 Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala  
 35 40 45  
 Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser  
 50 55 60  
 Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp  
 65 70 75 80  
 Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro  
 85 90 95  
 Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly  
 100 105 110  
 Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp Cys Ser Phe  
 115 120 125  
 Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu  
 130 135 140  
 Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu  
 145 150 155 160  
 Gln Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Gly Gly Ser Gly Gly  
 165 170 175  
 Gly Ser Asn Met Ala Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala  
 180 185 190  
 Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser  
 195 200 205  
 Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro Ser  
 210 215 220  
 Gly Gly Ser Gly Gly Ser Gln Ser Phe Leu Leu Lys Ser Leu Glu Gln  
 225 230 235 240  
 Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys  
 245 250 255  
 Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly His  
 260 265 270  
 Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala  
 275 280 285  
 Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly Leu Phe Leu  
 290 295 300  
 Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly  
 305 310 315 320  
 Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr  
 325 330 335  
 Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro  
 340 345 350

&lt;210&gt; 220

&lt;211&gt; 367

&lt;212&gt; PRT

&lt;213&gt; Unknown

&lt;220&gt;

&lt;221&gt; MUTAGEN

&lt;222&gt; 1-367

&lt;223&gt;

&lt;400&gt; 220

Ala Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg  
 1 5 10 15  
 Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu Glu Val  
 20 25 30  
 Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro Ser Gly Gly Ser Gly  
 35 40 45  
 Gly Ser Gln Ser Phe Leu Leu Lys Ser Leu Glu Gln Val Arg Lys Ile  
 50 55 60  
 Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys  
 65 70 75 80  
 Leu Cys His Pro Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile  
 85 90 95  
 Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala  
 100 105 110  
 Gly Cys Leu Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu  
 115 120 125  
 Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp  
 130 135 140  
 Thr Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln  
 145 150 155 160  
 Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro Tyr Val Glu Gly  
 165 170 175  
 Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn  
 180 185 190  
 Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala Asp  
 195 200 205  
 Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln Arg Trp  
 210 215 220  
 Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly Leu Leu  
 225 230 235 240  
 Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala Phe Gln  
 245 250 255  
 Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser Arg Leu  
 260 265 270  
 Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp Ile Thr  
 275 280 285  
 Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser  
 290 295 300  
 Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly  
 305 310 315 320  
 Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp Cys Ser Phe Gln His  
 325 330 335  
 Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp  
 340 345 350  
 Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln  
 355 360 365

<210> 221  
 <211> 344  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-344  
 <223>

<400> 221

Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln  
 1 5 10 15

Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly  
 20 25 30  
 Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala  
 35 40 45  
 Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser  
 50 55 60  
 Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp  
 65 70 75 80  
 Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro  
 85 90 95  
 Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly  
 100 105 110  
 Ser Gly Gly Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser  
 115 120 125  
 Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln  
 130 135 140  
 Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln Tyr Val Glu Gly Gly  
 145 150 155 160  
 Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro  
 165 170 175  
 Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala Asp Glu  
 180 185 190  
 Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln Arg Trp Met  
 195 200 205  
 Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly Leu Leu Glu  
 210 215 220  
 Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro  
 225 230 235 240  
 Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu  
 245 250 255  
 Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg  
 260 265 270  
 Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser  
 275 280 285  
 Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly  
 290 295 300  
 Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe  
 305 310 315 320  
 Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro  
 325 330 335  
 Val Thr Val Ala Ser Asn Leu Gln  
 340

<210> 222  
 <211> 335  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-335  
 <223>

<400> 222

Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln  
 1 5 10 15  
 Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly  
 20 25 30  
 Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala  
 35 40 45

Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser  
 50 55 60  
 Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp  
 65 70 75 80  
 Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro  
 85 90 95  
 Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly  
 100 105 110  
 Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp Cys Ser Phe  
 115 120 125  
 Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu  
 130 135 140  
 Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu  
 145 150 155 160  
 Gln Tyr Val Glu Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro  
 165 170 175  
 Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser  
 180 185 190  
 Pro Asn Met Ala Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser  
 195 200 205  
 Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln  
 210 215 220  
 Asn Tyr Pro Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys  
 225 230 235 240  
 Gly Gly Leu Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu  
 245 250 255  
 Lys Thr Val Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn  
 260 265 270  
 Thr Glu Ile His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Ser  
 275 280 285  
 Cys Leu Arg Phe Val Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr  
 290 295 300  
 Ser Glu Gln Leu Val Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe  
 305 310 315 320  
 Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu  
 325 330 335

<210> 223  
 <211> 550  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-550  
 <223>

<400> 223

Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln  
 1 5 10 15  
 Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly  
 20 25 30  
 Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala  
 35 40 45  
 Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser  
 50 55 60  
 Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp  
 65 70 75 80  
 Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro  
 85 90 95

Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly  
 100 105 110  
 Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp Cys Ser Phe  
 115 120 125  
 Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu  
 130 135 140  
 Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu  
 145 150 155 160  
 Gln Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Gly Gly Ser Gly Gly  
 165 170 175  
 Gly Ser Asn Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln  
 180 185 190  
 Ser Phe Leu Leu Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp  
 195 200 205  
 Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His  
 210 215 220  
 Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala  
 225 230 235 240  
 Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu  
 245 250 255  
 Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala  
 260 265 270  
 Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln  
 275 280 285  
 Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu  
 290 295 300  
 Leu Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala  
 305 310 315 320  
 Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser  
 325 330 335  
 His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu  
 340 345 350  
 Ala Gln Pro Tyr Val Glu Gly Gly Gly Ser Pro Gly Glu Pro Ser  
 355 360 365  
 Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His  
 370 375 380  
 Lys Ser Pro Asn Met Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg  
 385 390 395 400  
 Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly  
 405 410 415  
 Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe  
 420 425 430  
 Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val  
 435 440 445  
 Gln Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val  
 450 455 460  
 Ala Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu  
 465 470 475 480  
 Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly  
 485 490 495  
 Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Ser Gly Thr  
 500 505 510  
 Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val  
 515 520 525  
 Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr  
 530 535 540  
 Val Ala Ser Asn Leu Gln  
 545 550

&lt;210&gt; 224

&lt;211&gt; 544

<212> PRT  
<213> Unknown

<220>  
<221> MUTAGEN  
<222> 1-544  
<223>

<400> 224

```

'Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
  1      5      10      15
Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
  20      25      30
Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
  35      40      45
Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
  50      55      60
Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
  65      70      75      80
Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
  85      90      95
Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
  100      105      110
Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
  115      120      125
Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
  130      135      140
Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
  145      150      155      160
Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro Tyr
  165      170      175
Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser
  180      185      190
Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn
  195      200      205
Met Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala
  210      215      220
Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln
  225      230      235      240
Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys
  245      250      255
Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile
  260      265      270
Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro
  275      280      285
Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln
  290      295      300
Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly
  305      310      315      320
Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp Cys Ser
  325      330      335
Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu
  340      345      350
Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn
  355      360      365
Leu Gln Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly
  370      375      380
Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys
  385      390      395      400
Ser Pro Asn Met Ala Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile

```

<400> 225

189

245 250 255  
 Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile  
 260 265 270  
 Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro  
 275 280 285  
 Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln  
 290 295 300  
 Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly  
 305 310 315 320  
 Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp Cys Ser  
 325 330 335  
 Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu  
 340 345 350  
 Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn  
 355 360 365  
 Leu Gln Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly  
 370 375 380  
 Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys  
 385 390 395 400  
 Ser Pro Asn Met Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu  
 405 410 415  
 Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser  
 420 425 430  
 Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val  
 435 440 445  
 Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln  
 450 455 460  
 Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala  
 465 470 475 480  
 Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu  
 485 490 495  
 Gln Cys Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly  
 500 505 510  
 Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln  
 515 520 525  
 Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys  
 530 535 540  
 Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val  
 545 550 555 560  
 Ala Ser Asn Leu Gln  
 565

<210> 226  
 <211> 502  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-502  
 <223>

<400> 226

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg  
 1 5 10 15  
 Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp Val  
 20 25 30  
 Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser Phe  
 35 40 45  
 Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile

|           |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |
|-----------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|--|
|           | 50  |     |     |     |     |     | 55  |     |     |     | 60  |     |     |     |     |  |  |
| Leu<br>65 | Arg | Asn | Leu | Gln | Pro | Cys | Leu | Pro | Ser | Ala | Thr | Ala | Ala | Pro | Ser |  |  |
|           |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |  |  |
| Arg       | His | Pro | Ile | Ile | Ile | Lys | Ala | Gly | Asp | Trp | Gln | Glu | Phe | Arg | Glu |  |  |
|           |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |  |  |
| Lys       | Leu | Thr | Phe | Tyr | Leu | Val | Thr | Leu | Glu | Gln | Ala | Gln | Glu | Gln | Gln |  |  |
|           |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |  |  |
| Tyr       | Val | Glu | Gly | Gly | Gly | Gly | Ser | Pro | Gly | Glu | Pro | Ser | Gly | Pro | Ile |  |  |
|           |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |  |  |
| Ser       | Thr | Ile | Asn | Pro | Ser | Pro | Pro | Ser | Lys | Glu | Ser | His | Lys | Ser | Pro |  |  |
|           | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |  |  |
| Asn       | Met | Ala | Asp | Glu | Glu | Leu | Cys | Gly | Gly | Leu | Trp | Arg | Leu | Val | Leu |  |  |
| 145       |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |  |  |
| Ala       | Gln | Arg | Trp | Met | Glu | Arg | Leu | Lys | Thr | Val | Ala | Gly | Ser | Lys | Met |  |  |
|           |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |  |  |
| Gln       | Gly | Leu | Leu | Glu | Arg | Val | Asn | Thr | Glu | Ile | His | Phe | Val | Thr | Lys |  |  |
|           |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |  |  |
| Cys       | Ala | Phe | Gln | Pro | Pro | Pro | Ser | Cys | Leu | Arg | Phe | Val | Gln | Thr | Asn |  |  |
|           |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |  |  |
| Ile       | Ser | Arg | Leu | Leu | Gln | Glu | Thr | Ser | Glu | Gln | Leu | Val | Ala | Leu | Lys |  |  |
|           | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |  |  |
| Pro       | Trp | Ile | Thr | Arg | Gln | Asn | Phe | Ser | Arg | Cys | Leu | Glu | Leu | Gln | Cys |  |  |
| 225       |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |  |  |
| Gln       | Pro | Asp | Ser | Ser | Thr | Leu | Gly | Gly | Gly | Ser | Gly | Gly | Gly | Ser | Gly |  |  |
|           |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |  |  |
| Gly       | Gly | Ser | Gly | Gly | Gly | Ser | Gly | Gly | Gly | Ser | Gly | Thr | Gln | Asp | Cys |  |  |
|           |     |     | 260 |     |     |     | 265 |     |     |     |     |     | 270 |     |     |  |  |
| Ser       | Phe | Gln | His | Ser | Pro | Ile | Ser | Ser | Asp | Phe | Ala | Val | Lys | Ile | Arg |  |  |
|           | 275 |     |     |     |     |     | 280 |     |     |     |     | 285 |     |     |     |  |  |
| Glu       | Leu | Ser | Asp | Tyr | Leu | Leu | Gln | Asp | Tyr | Pro | Val | Thr | Val | Ala | Ser |  |  |
|           | 290 |     |     |     |     | 295 |     |     |     |     | 300 |     |     |     |     |  |  |
| Asn       | Leu | Gln | Tyr | Val | Glu | Gly | Gly | Gly | Gly | Ser | Pro | Gly | Glu | Pro | Ser |  |  |
| 305       |     |     |     |     | 310 |     |     |     |     | 315 |     |     |     |     | 320 |  |  |
| Gly       | Pro | Ile | Ser | Thr | Ile | Asn | Pro | Ser | Pro | Pro | Ser | Lys | Glu | Ser | His |  |  |
|           |     |     |     | 325 |     |     |     |     | 330 |     |     |     |     | 335 |     |  |  |
| Lys       | Ser | Pro | Asn | Met | Ala | Asp | Glu | Glu | Leu | Cys | Gly | Gly | Leu | Trp | Arg |  |  |
|           |     |     | 340 |     |     |     | 345 |     |     |     |     |     | 350 |     |     |  |  |
| Leu       | Val | Leu | Ala | Gln | Arg | Trp | Met | Glu | Arg | Leu | Lys | Thr | Val | Ala | Gly |  |  |
|           | 355 |     |     |     |     | 360 |     |     |     |     |     | 365 |     |     |     |  |  |
| Ser       | Lys | Met | Gln | Gly | Leu | Leu | Glu | Arg | Val | Asn | Thr | Glu | Ile | His | Phe |  |  |
|           | 370 |     |     |     |     | 375 |     |     |     |     | 380 |     |     |     |     |  |  |
| Val       | Thr | Lys | Cys | Ala | Phe | Gln | Pro | Pro | Pro | Ser | Cys | Leu | Arg | Phe | Val |  |  |
| 385       |     |     |     |     | 390 |     |     |     |     | 395 |     |     |     |     | 400 |  |  |
| Gln       | Thr | Asn | Ile | Ser | Arg | Leu | Leu | Gln | Glu | Thr | Ser | Glu | Gln | Leu | Val |  |  |
|           |     |     | 405 |     |     |     |     |     | 410 |     |     |     |     | 415 |     |  |  |
| Al        |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |

|       |     |
|-------|-----|
| <210> | 227 |
| <211> | 562 |
| <212> | PRT |

&lt;213&gt; Unknown

&lt;220&gt;

&lt;221&gt; MUTAGEN

&lt;222&gt; 1-562

&lt;223&gt;

&lt;400&gt; 227

Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln  
 1 5 10 15  
 Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly  
 20 25 30  
 Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala  
 35 40 45  
 Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser  
 50 55 60  
 Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp  
 65 70 75 80  
 Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro  
 85 90 95  
 Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly  
 100 105 110  
 Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln Asp Cys Ser Phe  
 115 120 125  
 Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu  
 130 135 140  
 Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu  
 145 150 155 160  
 Gln Tyr Val Glu Gly Gly Gly Ser Pro Gly Gly Gly Ser Gly Gly  
 165 170 175  
 Gly Ser Asn Met Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu  
 180 185 190  
 Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser  
 195 200 205  
 Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val  
 210 215 220  
 Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln  
 225 230 235 240  
 Thr Asn Ile Ser Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala  
 245 250 255  
 Leu Lys Pro Trp Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu  
 260 265 270  
 Gln Cys Gln Pro Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly  
 275 280 285  
 Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Thr Gln  
 290 295 300  
 Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys  
 305 310 315 320  
 Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val  
 325 330 335  
 Ala Ser Asn Leu Gln Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu  
 340 345 350  
 Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu  
 355 360 365  
 Ser His Lys Ser Pro Asn Met Ala Thr Pro Leu Gly Pro Ala Ser Ser  
 370 375 380  
 Leu Pro Gln Ser Phe Leu Leu Lys Cys Leu Glu Gln Val Arg Lys Ile  
 385 390 395 400  
 Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys  
 405 410 415

Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile  
                   420                  425                  430  
 Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala  
                   435                  440                  445  
 Gly Cys Leu Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu  
                   450                  455                  460  
 Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp  
 465                  470                  475                  480  
 Thr Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln  
                   485                  490                  495  
 Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala  
                   500                  505                  510  
 Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu  
                   515                  520                  525  
 Val Ala Ser His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu  
                   530                  535                  540  
 Arg His Leu Ala Gln Pro Ser Thr Pro Ser Thr Pro Gly Ser Glu Phe  
 545                  550                  555                  560  
 Gly Ser

<210> 228  
 <211> 490  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-490  
 <223>

<400> 228

Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln  
 1                  5                  10                  15  
 Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly  
                   20                  25                  30  
 Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala  
                   35                  40                  45  
 Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser  
                   50                  55                  60  
 Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp  
 65                  70                  75                  80  
 Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro  
                   85                  90                  95  
 Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly  
                   100                  105                  110  
 Ser Gly Gly Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser  
                   115                  120                  125  
 Ser Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln  
                   130                  135                  140  
 Asp Tyr Pro Val Thr Val Ala Ser Asn Leu Gln Tyr Val Glu Gly Gly  
 145                  150                  155                  160  
 Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro  
                   165                  170                  175  
 Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala Asn Cys  
                   180                  185                  190  
 Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Asn  
                   195                  200                  205  
 Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met Asp Ile Leu  
 210                  215                  220

Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe Val Arg Ala  
 225 230 235 240  
 Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn  
 245 250 255  
 Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro  
 260 265 270  
 Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr  
 275 280 285  
 Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln Tyr Val Glu  
 290 295 300  
 Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile  
 305 310 315 320  
 Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala  
 325 330 335  
 Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln Arg  
 340 345 350  
 Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly Leu  
 355 360 365  
 Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala Phe  
 370 375 380  
 Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser Arg  
 385 390 395 400  
 Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp Ile  
 405 410 415  
 Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro Asp  
 420 425 430  
 Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser  
 435 440 445  
 Gly Gly Gly Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser  
 450 455 460  
 Asp Phe Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp  
 465 470 475 480  
 Tyr Pro Val Thr Val Ala Ser Asn Leu Gln  
 485 490

<210> 229  
 <211> 398  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-398  
 <223>

<400> 229

Ala Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln  
 1 5 10 15  
 Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly  
 20 25 30  
 Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala  
 35 40 45  
 Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser  
 50 55 60  
 Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp  
 65 70 75 80  
 Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro  
 85 90 95  
 Asp Ser Ser Thr Leu Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly  
 100 105 110

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

<210> 230  
 <211> 377  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-377  
 <223>

<400> 230

Ala Thr Gln Asp Cys Ser Phe Gln His Ser Pro Ile Ser Ser Asp Phe  
 1 5 10 15  
 Ala Val Lys Ile Arg Glu Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro  
 20 25 30  
 Val Thr Val Ala Ser Asn Leu Gln Asp Glu Glu Leu Cys Gly Gly Leu  
 35 40 45  
 Trp Arg Leu Val Leu Ala Gln Arg Trp Met Glu Arg Leu Lys Thr Val  
 50 55 60  
 Ala Gly Ser Lys Met Gln Gly Leu Leu Glu Arg Val Asn Thr Glu Ile  
 65 70 75 80  
 His Phe Val Thr Lys Cys Ala Phe Gln Pro Pro Pro Ser Cys Leu Arg  
 85 90 95

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

<210> 231  
 <211> 4  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-4  
 <223>

<400> 231

Gly Gly Gly Ser  
 1

<210> 232  
 <211> 8  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-8  
 <223>

<400> 232

Gly Gly Gly Ser Gly Gly Gly Ser  
1 5

<210> 233  
<211> 12  
<212> PRT  
<213> Unknown

<220>  
<221> MUTAGEN  
<222> 1-12  
<223>

<400> 233

Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser  
1 5 10

<210> 234  
<211> 7  
<212> PRT  
<213> Unknown

<220>  
<221> MUTAGEN  
<222> 1-7  
<223>

<400> 234

Ser Gly Gly Ser Gly Gly Ser  
1 5

<210> 235  
<211> 5  
<212> PRT  
<213> Unknown

<220>  
<221> MUTAGEN  
<222> 1-5  
<223>

<400> 235

Glu Phe Gly Asn Met  
1 5

<210> 236  
<211> 6  
<212> PRT  
<213> Unknown

<220>  
<221> MUTAGEN  
<222> 1-6  
<223>

<400> 236

Glu Phe Gly Gly Asn Met  
1 5

<210> 237  
<211> 9  
<212> PRT  
<213> Unknown

<220>  
<221> MUTAGEN  
<222> 1-9  
<223>

<400> 237

Glu Phe Gly Gly Asn Gly Gly Asn Met  
1 5

<210> 238  
<211> 7  
<212> PRT  
<213> Unknown

<220>  
<221> MUTAGEN  
<222> 1-7  
<223>

<400> 238

Gly Gly Ser Asp Met Ala Gly  
1 5

<210> 239  
<211> 5  
<212> PRT  
<213> Unknown

<220>  
<221> MUTAGEN  
<222> 1-5  
<223>

<400> 239

Ser Gly Gly Asn Gly  
1 5

<210> 240  
<211> 10  
<212> PRT  
<213> Unknown

<220>  
<221> MUTAGEN  
<222> 1-10  
<223>

<400> 240

Ser Gly Gly Asn Gly Ser Gly Gly Asn Gly  
 1 5 10

<210> 241  
 <211> 15  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-15  
 <223>

<400> 241

Ser Gly Gly Asn Gly Ser Gly Gly Asn Gly Ser Gly Gly Asn Gly  
 1 5 10 15

<210> 242  
 <211> 10  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-10  
 <223>

<400> 242

Ser Gly Gly Ser Gly Ser Gly Gly Ser Gly  
 1 5 10

<210> 243  
 <211> 15  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-15  
 <223>

<400> 243

Ser Gly Gly Ser Gly Ser Gly Gly Ser Gly Ser Gly Gly Ser Gly  
 1 5 10 15

<210> 244  
 <211> 6  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 1-6  
 <223>

<400> 244

Gly Gly Gly Ser Gly Gly  
1 5

<210> 245  
<211> 7  
<212> PRT  
<213> Unknown

<220>  
<221> MUTAGEN  
<222> 1-7  
<223>

<400> 245

Gly Gly Gly Ser Gly Gly Gly  
1 5

<210> 246  
<211> 10  
<212> PRT  
<213> Unknown

<220>  
<221> MUTAGEN  
<222> 1-10  
<223>

<400> 246

Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly  
1 5 10

<210> 247  
<211> 13  
<212> PRT  
<213> Unknown

<220>  
<221> MUTAGEN  
<222> 1-13  
<223>

<400> 247

Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly  
1 5 10

<210> 248  
<211> 15  
<212> PRT  
<213> Unknown

<220>  
<221> MUTAGEN  
<222> 1-15  
<223>

<400> 248

Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly

|   |   |    |    |
|---|---|----|----|
| 1 | 5 | 10 | 15 |
|---|---|----|----|

<210> 249  
 <211> 21  
 <212> PRT  
 <213> Unknown  
  
 <220>  
 <221> MUTAGEN  
 <222> 1-21  
 <223>  
  
 <400> 249

Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser  
 1 5 10 15  
 Gly Gly Gly Ser Gly  
 20

<210> 250  
 <211> 21  
 <212> PRT  
 <213> Unknown  
  
 <220>  
 <221> MUTAGEN  
 <222> 1-21  
 <223>  
  
 <400> 250

Pro Pro Pro Trp Ser Pro Arg Pro Leu Gly Ala Thr Ala Pro Thr Ala  
 1 5 10 15  
 Gly Gln Pro Pro Leu  
 20

<210> 251  
 <211> 15  
 <212> PRT  
 <213> Unknown  
  
 <220>  
 <221> MUTAGEN  
 <222> 1-15  
 <223>  
  
 <400> 251

Pro Pro Pro Trp Ser Pro Arg Pro Leu Gly Ala Thr Ala Pro Thr  
 1 5 10 15

<210> 252  
 <211> 16  
 <212> PRT  
 <213> Unknown  
  
 <220>  
 <221> MUTAGEN  
 <222> 1-16  
 <223>

&lt;400&gt; 252

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Val | Glu | Thr | Val | Phe | His | Arg | Val | Ser | Gln | Asp | Gly | Leu | Leu | Thr | Ser |
| 1   |     |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |

&lt;210&gt; 253

&lt;211&gt; 36

&lt;212&gt; PRT

&lt;213&gt; Unknown

&lt;220&gt;

&lt;221&gt; MUTAGEN

&lt;222&gt; 1-36

&lt;223&gt;

&lt;400&gt; 253

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Gly | Gly | Gly | Ser | Gly | Gly | Gly | Ser | Gly | Gly | Gly | Ser | Glu | Gly | Gly | Gly |
| 1   |     |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |
| Ser | Glu | Gly | Gly | Gly | Ser | Glu | Gly | Gly | Gly | Ser | Glu | Gly | Gly | Gly | Ser |
|     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |
| Gly | Gly | Gly | Ser |     |     |     |     |     |     |     |     |     |     |     |     |
|     |     |     | 35  |     |     |     |     |     |     |     |     |     |     |     |     |

&lt;210&gt; 254

&lt;211&gt; 24

&lt;212&gt; PRT

&lt;213&gt; Unknown

&lt;220&gt;

&lt;221&gt; MUTAGEN

&lt;222&gt; 1-24

&lt;223&gt;

&lt;400&gt; 254

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ile | Ser | Glu | Pro | Ser | Gly | Pro | Ile | Ser | Thr | Ile | Asn | Pro | Ser | Pro | Pro |
| 1   |     |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |
| Ser | Lys | Glu | Ser | His | Lys | Ser | Pro |     |     |     |     |     |     |     |     |
|     |     |     | 20  |     |     |     |     |     |     |     |     |     |     |     |     |

&lt;210&gt; 255

&lt;211&gt; 28

&lt;212&gt; PRT

&lt;213&gt; Unknown

&lt;220&gt;

&lt;221&gt; MUTAGEN

&lt;222&gt; 1-28

&lt;223&gt;

&lt;400&gt; 255

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ile | Glu | Gly | Arg | Ile | Ser | Glu | Pro | Ser | Gly | Pro | Ile | Ser | Thr | Ile | Asn |
| 1   |     |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |
| Pro | Ser | Pro | Pro | Ser | Lys | Glu | Ser | His | Lys | Ser | Pro |     |     |     |     |
|     |     |     | 20  |     |     |     |     | 25  |     |     |     |     |     |     |     |

&lt;210&gt; 256

&lt;211&gt; 112

&lt;212&gt; PRT

&lt;213&gt; Unknown

&lt;220&gt;

&lt;221&gt; MUTAGEN

&lt;222&gt; 1-112

&lt;223&gt;

&lt;400&gt; 256

```

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg
 1           5           10           15
Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala Glu Asp Val
          20           25           30
Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser Phe
          35           40           45
Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile
          50           55           60
Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser
65           70           75           80
Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu
          85           90           95
Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
          100          105          110

```

&lt;210&gt; 257

&lt;211&gt; 112

&lt;212&gt; PRT

&lt;213&gt; Unknown

&lt;220&gt;

&lt;221&gt; MUTAGEN

&lt;222&gt; 1-112

&lt;223&gt;

&lt;400&gt; 257

```

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg
 1           5           10           15
Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met
          20           25           30
Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe
          35           40           45
Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile
          50           55           60
Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser
65           70           75           80
Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu
          85           90           95
Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
          100          105          110

```

&lt;210&gt; 258

&lt;211&gt; 112

&lt;212&gt; PRT

&lt;213&gt; Unknown

&lt;220&gt;

&lt;221&gt; MUTAGEN

&lt;222&gt; 1-112

&lt;223&gt;

&lt;400&gt; 258

```

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Val
 1           5           10           15
Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn Ser Glu Asp Met
          20           25           30
Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn Leu Leu Ala Phe
          35           40           45
Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile
          50           55           60
Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser
65           70           75           80
Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu
          85           90           95
Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
          100           105           110

```

```

<210> 259
<211> 111
<212> PRT
<213> Unknown

```

```

<220>
<221> MUTAGEN
<222> 1-111
<223>

```

&lt;400&gt; 259

```

Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro
 1           5           10           15
Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp Val Ser
          20           25           30
Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser Phe Val
          35           40           45
Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu
          50           55           60
Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg
65           70           75           80
His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
          85           90           95
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
          100           105           110

```

```

<210> 260
<211> 174
<212> PRT
<213> Unknown

```

```

<220>
<221> MUTAGEN
<222> 1
<223> Xaa at position 1 is Thr, Ser, Arg, Tyr or Gly;

```

```

<220>
<221> MUTAGEN
<222> 2
<223> Xaa at position 2 is Pro or Leu;

```

```

<220>
<221> MUTAGEN

```

<222> 3  
<223> Xaa at position 3 is Leu, Arg, Tyr or Ser;

<220>  
<221> MUTAGEN  
<222> 13  
<223> Xaa at position 13 is Phe, Ser, His, Thr or Pro;

<220>  
<221> MUTAGEN  
<222> 16  
<223> Xaa at position 16 is Lys, Pro, Ser, thr or His;

<220>  
<221> MUTAGEN  
<222> 17  
<223> Xaa at position 17 is Cys, Ser, Gly, Ala, Ile, Tyr or Arg;

<220>  
<221> MUTAGEN  
<222> 18  
<223> Xaa at position 18 is Leu, Thr, Pro, His, Ile or Cys;

<220>  
<221> MUTAGEN  
<222> 22  
<223> Xaa at position 22 is Arg, Tyr, Ser, Thr or Ala;

<220>  
<221> MUTAGEN  
<222> 24  
<223> Xaa at position 24 is Ile, Pro, Tyr or Leu;

<220>  
<221> MUTAGEN  
<222> 27  
<223> Xaa at position 27 is Asp or Gly;

<220>  
<221> MUTAGEN  
<222> 30  
<223> Xaa at position 30 is Ala, Ile, Leu or Gly;

<220>  
<221> MUTAGEN  
<222> 34  
<223> Xaa at position 34 is Lys or Ser;

<220>  
<221> MUTAGEN  
<222> 36  
<223> Xaa at position 36 is Cys or Ser;

<220>  
<221> MUTAGEN  
<222> 42  
<223> Xaa at position 42 is Cys or Ser;

<220>  
<221> MUTAGEN  
<222> 43

<223> Xaa at position 43 is His, Thr, Gly, Val, Lys, Trp, Ala, Arg,  
Cys, or Leu;

<220>

<221> MUTAGEN

<222> 44

<223> Xaa at position 44 is Pro, Gly, Arg, Asp, Val, Ala, His, Trp,  
Gln, or Thr;

<220>

<221> MUTAGEN

<222> 46

<223> Xaa at position 46 is Glu, Arg, Phe, Arg, Ile or Ala;

<220>

<221> MUTAGEN

<222> 47

<223> Xaa at position 47 is Leu or Thr;

<220>

<221> MUTAGEN

<222> 49

<223> Xaa at position 49 is Leu, Phe, Arg or Ser;

<220>

<221> MUTAGEN

<222> 50

<223> Xaa at position 50 is Leu, Ile, His, Pro or Tyr;

<220>

<221> MUTAGEN

<222> 54

<223> Xaa at position 54 is Leu or His;

<220>

<221> MUTAGEN

<222> 64

<223> Xaa at position 64 is Cys or Ser;

<220>

<221> MUTAGEN

<222> 67

<223> Xaa at position 67 is Gln, Lys, Leu or Cys;

<220>

<221> MUTAGEN

<222> 70

<223> Xaa at position 70 is Gln, Pro, Leu, Arg or Ser;

<220>

<221> MUTAGEN

<222> 74

<223> Xaa at position 74 is Cys or Ser;

<220>

<221> MUTAGEN

<222> 104

<223> Xaa at position 104 is Asp, Gly or Val;

<220>

<221> MUTAGEN

<222> 108  
<223> Xaa at position 108 is Leu, Ala, Val, Arg, Trp, Gln or Gly;

<220>  
<221> MUTAGEN  
<222> 115  
<223> Xaa at position 115 is Thr, His, Leu or Ala;

<220>  
<221> MUTAGEN  
<222> 120  
<223> Xaa at position 120 is Gln, Gly, Arg, Lys or His

<220>  
<221> MUTAGEN  
<222> 123  
<223> Xaa at position 123 is Glu, Arg, Phe or Thr

<220>  
<221> MUTAGEN  
<222> 144  
<223> Xaa at position 144 is Phe, His, Arg, Pro, Leu, Gln or Glu;

<220>  
<221> MUTAGEN  
<222> 146  
<223> Xaa at position 146 is Arg or Gln;

<220>  
<221> MUTAGEN  
<222> 147  
<223> Xaa at position 147 is Arg or Gln;

<220>  
<221> MUTAGEN  
<222> 156  
<223> Xaa at position 156 is His, Gly or Ser;

<220>  
<221> MUTAGEN  
<222> 159  
<223> Xaa at position 159 is Ser, Arg, Thr, Tyr, Val or Gly;

<220>  
<221> MUTAGEN  
<222> 162  
<223> Xaa at position 162 is Glu, Leu, Gly or Trp;

<220>  
<221> MUTAGEN  
<222> 163  
<223> Xaa at position 163 is Val, Gly, Arg or Ala;

<220>  
<221> MUTAGEN  
<222> 169  
<223> Xaa at position 169 is Arg, Ser, Leu, Arg or Cys;

<220>  
<221> MUTAGEN  
<222> 170

<223> Xaa at position 170 is His, Arg or Ser;

<400> 260

Xaa Xaa Xaa Gly Pro Ala Ser Ser Leu Pro Gln Ser Xaa Leu Leu Xaa  
1 5 10 15

Xaa Xaa Glu Gln Val Xaa Lys Xaa Gln Gly Xaa Gly Ala Xaa Leu Gln  
20 25 30

Glu Xaa Leu Xaa Ala Thr Tyr Lys Leu Xaa Xaa Xaa Glu Xaa Xaa Val  
35 40 45

Xaa Xaa Gly His Ser Xaa Gly Ile Pro Trp Ala Pro Leu Ser Ser Xaa  
50 55 60

Pro Ser Xaa Ala Leu Xaa Leu Ala Gly Xaa Leu Ser Gln Leu His Ser  
65 70 75 80

Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser  
85 90 95

Pro Glu Leu Gly Pro Thr Leu Xaa Thr Leu Gln Xaa Asp Val Ala Asp  
100 105 110

Phe Ala Xaa Thr Ile Trp Gln Gln Met Glu Xaa Xaa Gly Met Ala Pro  
115 120 125

Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Xaa  
130 135 140

Gln Xaa Xaa Ala Gly Gly Val Leu Val Ala Ser Xaa Leu Gln Xaa Phe  
145 150 155 160

Leu Xaa Xaa Ser Tyr Arg Val Leu Xaa Xaa Leu Ala Gln Pro  
165 170

<210> 261

<211> 133

<212> PRT

<213> Unknown

<220>

<221> MUTAGEN

<222> 17

<223> Xaa at position 17 is Ser, Lys, Gly, Asp, Met, Gln, or Arg;

<220>

<221> MUTAGEN

<222> 18

<223> Xaa at position 18 is Asn, His, Leu, Ile, Phe, Arg, or Gln;

<220>

<221> MUTAGEN

<222> 19

<223> Xaa at position 19 is Met, Phe, Ile, Arg, Gly, Ala, or Cys;

<220>

<221> MUTAGEN

<222> 20

<223> Xaa at position 20 is Ile, Cys, Gln, Glu, Arg, Pro, or Ala;

<220>  
<221> MUTAGEN  
<222> 21  
<223> Xaa at position 21 is Asp, Phe, Lys, Arg, Ala, Gly, Glu, Gln, Asn, Thr, Ser or Val;

<220>  
<221> MUTAGEN  
<222> 22  
<223> Xaa at position 22 is Glu, Trp, Pro, Ser, Ala, His, Asp, Asn, Gln, Leu, Val or Gly;

<220>  
<221> MUTAGEN  
<222> 23  
<223> Xaa at position 23 is Ile, Val, Ala, Gly, Trp, Lys, Phe, Leu, Ser, or Arg;

<220>  
<221> MUTAGEN  
<222> 24  
<223> Xaa at position 24 is Ile, Gly, Val, Arg, Ser, Phe, Leu;

<220>  
<221> MUTAGEN  
<222> 25  
<223> Xaa at position 25 is Thr, His, Gly, Gln, Arg, Pro, or Ala;

<220>  
<221> MUTAGEN  
<222> 26  
<223> Xaa at position 26 is His, Thr, Phe, Gly, Arg, Ala, Trp;

<220>  
<221> MUTAGEN  
<222> 27  
<223> Xaa at position 27 is Leu, Gly, Arg, Thr, Ser, or Ala;

<220>  
<221> MUTAGEN  
<222> 28  
<223> Xaa at position 28 is Lys, Arg, Leu, Gln, Gly, Pro, Val or Trp;

<220>  
<221> MUTAGEN  
<222> 29  
<223> Xaa at position 29 is Gln, Asn, Leu, Pro, Arg, or Val;

<220>  
<221> MUTAGEN  
<222> 30  
<223> Xaa at position 30 is Pro, His, Thr, Gly, Asp, Gln, Ser, Leu, or Leu

<220>  
<221> MUTAGEN  
<222> 31  
<223> Xaa at position 31 is Pro, Asp, Gly, Ala, Arg, Leu, or Gln;

<220>  
<221> MUTAGEN  
<222> 32  
<223> Xaa at position 32 is Leu, Val, Arg, Gln, Asn, Gly, Ala, or  
Glu;

<220>  
<221> MUTAGEN  
<222> 33  
<223> Xaa at position 33 is Pro, Leu, Gln, Ala, Thr, or Glu;

<220>  
<221> MUTAGEN  
<222> 34  
<223> Xaa at position 34 is Leu, Val, Gly, Ser, Lys, Glu, Gln, Thr,  
Arg, Ala, Phe, Ile or Met;

<220>  
<221> MUTAGEN  
<222> 35  
<223> Xaa at position 35 is Leu, Ala, Gly, Asn, Pro, Gln, or Val;

<220>  
<221> MUTAGEN  
<222> 36  
<223> Xaa at position 36 is Asp, Leu, or Val;

<220>  
<221> MUTAGEN  
<222> 37  
<223> Xaa at position 37 is Phe, Ser, Pro, Trp, or Ile;

<220>  
<221> MUTAGEN  
<222> 38  
<223> Xaa at position 38 is Asn, or Ala;

<220>  
<221> MUTAGEN  
<222> 40  
<223> Xaa at position 40 is Leu, Trp, or Arg;

<220>  
<221> MUTAGEN  
<222> 41  
<223> Xaa at position 41 is Asn, Cys, Arg, Leu, His, Met, or pro;

<220>  
<221> MUTAGEN  
<222> 42  
<223> Xaa at position 42 is Gly, Asp, Ser, Cys, Asn, Lys, Thr, Leu,  
Val, Glu, Phe, Tyr, Ile, Met or Ala;

<220>  
<221> MUTAGEN  
<222> 43  
<223> Xaa at position 43 is Glu, Asn, Tyr, Leu, Phe, Asp, Ala, Cys,  
Gln, Arg, Thr, Gly, or Ser;

<220>  
<221> MUTAGEN

<222> 44  
<223> Xaa at position 44 is Asp, Ser, Leu, Arg, Lys, Thr, Met, Trp, Glu, Asn, Gln, Ala or Pro;

<220>  
<221> MUTAGEN  
<222> 45  
<223> Xaa at position 45 is Gln, Pro, Phe, Val, Met, Leu, Thr, Lys, Trp, Asp, Asn, Arg, Ser, Ala, Ile, Glu or His;

<220>  
<221> MUTAGEN  
<222> 46  
<223> Xaa at position 46 is Asp, Phe, Ser, Thr, Cys, Glu, Asn, Gln, Lys, His, Ala, Tyr, Ile, Val or Gly;

<220>  
<221> MUTAGEN  
<222> 47  
<223> Xaa at position 47 is Ile, Gly, Val, Ser, Arg, Pro, or His;

<220>  
<221> MUTAGEN  
<222> 48  
<223> Xaa at position 48 is Leu, Ser, Cys, Arg, Ile, His, Phe, Glu, Lys, Thr, Ala, Met, Val or Asn;

<220>  
<221> MUTAGEN  
<222> 49  
<223> Xaa at position 49 is Met, Arg, Ala, Gly, Pro, Asn, His, or Asp;

<220>  
<221> MUTAGEN  
<222> 50  
<223> Xaa at position 50 is Glu, Leu, Thr, Asp, Tyr, Lys, Asn, Ser, Ala, Ile, Val, His, Phe, Met or Gln;

<220>  
<221> MUTAGEN  
<222> 51  
<223> Xaa at position 51 is Asn, Arg, Met, Pro, Ser, Thr, or his;

<220>  
<221> MUTAGEN  
<222> 52  
<223> Xaa at position 52 is Asn, His, Arg, Leu, Gly, Ser, or Thr;

<220>  
<221> MUTAGEN  
<222> 53  
<223> Xaa at position 53 is Leu, Thr, Ala, Gly, Glu, Pro, Lys, Ser, or M...

<220>  
<221> MUTAGEN  
<222> 54  
<223> Xaa at position 54 is Arg, Asp, Ile, Ser, Val, Thr, Gln, Asn, Lys, His, Ala or Leu;

<220>  
<221> MUTAGEN  
<222> 55  
<223> Xaa at position 55 is Arg, Thr, Val, Ser, Leu, or Gly;

<220>  
<221> MUTAGEN  
<222> 56  
<223> Xaa at position 56 is Pro, Gly, Cys, Ser, Gln, Glu, Arg, His, Thr, Ala, Tyr, Phe, Leu, Val or Lys;

<220>  
<221> MUTAGEN  
<222> 57  
<223> Xaa at position 57 is Asn or Gly;

<220>  
<221> MUTAGEN  
<222> 58  
<223> Xaa at position 58 is Leu, Ser, Asp, Arg, Gln, Val, or Cys;

<220>  
<221> MUTAGEN  
<222> 59  
<223> Xaa at position 59 is Glu, Tyr, His, Leu, Pro, or Arg;

<220>  
<221> MUTAGEN  
<222> 60  
<223> Xaa at position 60 is Ala, Ser, Pro, Tyr, Asn, or Thr;

<220>  
<221> MUTAGEN  
<222> 61  
<223> Xaa at position 61 is Phe, Asn, Glu, Pro, Lys, Arg, or Ser;

<220>  
<221> MUTAGEN  
<222> 62  
<223> Xaa at position 62 is Asn, His, Val, Arg, Pro, Thr, Asp, or Ile;

<220>  
<221> MUTAGEN  
<222> 63  
<223> Xaa at position 63 is Arg, Tyr, Trp, Lys, Ser, His, Pro, or Val;

<220>  
<221> MUTAGEN  
<222> 64  
<223> Xaa at position 64 is Ala, Asn, Pro, Ser, or Lys;

<220>  
<221> MUTAGEN  
<222> 65  
<223> Xaa at position 65 is Val, Thr, Pro, His, Leu, Phe, or Ser;

<220>  
<221> MUTAGEN  
<222> 66

<223> Xaa at position 66 is Lys, Ile, Arg, Val, Asn, Glu, or Ser;

<220>  
<221> MUTAGEN  
<222> 67  
<223> Xaa at position 67 is Ser, Ala, Phe, Val, Gly, Asn, Ile, Pro,  
or His;

<220>  
<221> MUTAGEN  
<222> 68  
<223> Xaa at position 68 is Leu, Val, Trp, Ser, Ile, Phe, Thr, or  
His;

<220>  
<221> MUTAGEN  
<222> 69  
<223> Xaa at position 69 is Gln, Ala, Pro, Thr, Glu, Arg, Trp, Gly,  
or Leu

<220>  
<221> MUTAGEN  
<222> 70  
<223> Xaa at position 70 is Asn, Leu, Val, Trp, pro, or Ala;

<220>  
<221> MUTAGEN  
<222> 71  
<223> Xaa at position 71 is Ala, Met, Leu, Pro, Arg, Glu, Thr, Gln,  
Trp, or Asn;

<220>  
<221> MUTAGEN  
<222> 72  
<223> Xaa at position 72 is Ser, Glu, Met, Ala, His, Asn, Arg, or  
Asp;

<220>  
<221> MUTAGEN  
<222> 73  
<223> Xaa at position 73 is Ala, Glu, Asp, Leu, Ser, Gly, Thr, or  
Arg;

<220>  
<221> MUTAGEN  
<222> 74  
<223> Xaa at position 74 is Ile, Met, Thr, Pro, Arg, Gly, Ala;

<220>  
<221> MUTAGEN  
<222> 75  
<223> Xaa at position 75 is Glu, Lys, Gly, Asp, Pro, Trp, Arg, Ser,  
Gln, or Leu;

<220>  
<221> MUTAGEN  
<222> 76  
<223> Xaa at position 76 is Ser, Val, Ala, Asn, Trp, Glu, Pro, Gly,  
or Ala

<220>

<221> MUTAGEN  
<222> 77  
<223> Xaa at position 77 is Ile, Ser, Arg, Thr, or Leu;

<220>  
<221> MUTAGEN  
<222> 78  
<223> Xaa at position 78 is Leu, Ala, Ser, Glu, Phe, Gly, or Arg;

<220>  
<221> MUTAGEN  
<222> 79  
<223> Xaa at position 79 is Lys, Thr, Asn, Met, Arg, Ile, Gly, or  
Asp;

<220>  
<221> MUTAGEN  
<222> 80  
<223> Xaa position at 80 is Asn, Trp, Val, Gly, Thr, Leu, Glu, or  
Arg;

<220>  
<221> MUTAGEN  
<222> 81  
<223> Xaa at position 81 is Leu, Gln, Gly, Ala, Trp, Arg, Val, or  
Lys;

<220>  
<221> MUTAGEN  
<222> 82  
<223> Xaa at position 82 is Leu, Gln, Lys, Trp, Arg, Asp, Glu, Asn,  
His, Thr, Ser, Ala, Tyr, Phe, Ile, Met or Val;

<220>  
<221> MUTAGEN  
<222> 83  
<223> Xaa at position 83 is Pro, Ala, Thr, Trp, Arg, or Met;

<220>  
<221> MUTAGEN  
<222> 84  
<223> Xaa at position 84 is Cys, Glu, Gly, Arg, Met, or Val;

<220>  
<221> MUTAGEN  
<222> 85  
<223> Xaa at position 85 is Leu, Asn, Val, or Gln;

<220>  
<221> MUTAGEN  
<222> 86  
<223> Xaa at position 86 is Pro, Cys, Arg, Ala, or Lys;

<220>  
<221> MUTAGEN  
<222> 87  
<223> Xaa at position 87 is Leu, Ser, Trp, or Gly;

<220>  
<221> MUTAGEN  
<222> 88

<223> Xaa at position 88 is Ala, Lys, Arg, Val, or Trp;

<220>  
<221> MUTAGEN  
<222> 89  
<223> Xaa at position 89 is Thr, Asp, Cys, Leu, Val, Glu, His, Asn,  
or Ser

<220>  
<221> MUTAGEN  
<222> 90  
<223> Xaa at position 90 is Ala, Pro, Ser, Thr, Gly, Asp, Ile, or  
,Met;

<220>  
<221> MUTAGEN  
<222> 91  
<223> Xaa at position 91 is Ala, Pro, Ser, Thr, Phe, Leu, Asp, or  
His;

<220>  
<221> MUTAGEN  
<222> 92  
<223> Xaa at position 92 is Pro, Phe, Arg, Ser, Lys, His, Ala, Gly,  
Ile or Leu;

<220>  
<221> MUTAGEN  
<222> 93  
<223> Xaa at position 93 is Thr, Asp, Ser, Asn, Pro, Ala, Leu, or  
Arg;

<220>  
<221> MUTAGEN  
<222> 94  
<223> Xaa at position 94 is Arg, Ile, Ser, Glu, Leu, Val, Gln, Lys,  
His, Ala, or Pro;

<220>  
<221> MUTAGEN  
<222> 95  
<223> Xaa at position 95 is His, Gln, Pro, Arg, Val, Leu, Gly, Thr,  
Asn, Lys, Ser, Ala, Trp, Phe, Ile, or Tyr;

<220>  
<221> MUTAGEN  
<222> 96  
<223> Xaa at position 96 is Pro, Lys, Tyr, Gly, Ile, or Thr;

<220>  
<221> MUTAGEN  
<222> 97  
<223> Xaa at position 97 is Ile, Val, Lys, Ala, or Asn;

<220>  
<221> MUTAGEN  
<222> 98  
<223> Xaa at position 98 is His, Ile, Asn, Leu, Asp, Ala, Thr, Glu,  
Gln, Ser, Phe, Met, Val, Lys, Arg, Tyr, or Pro;

<220>

<221> MUTAGEN  
<222> 99  
<223> Xaa at position 99 is Ile, Leu, Arg, Asp, Val, Pro, Gln, Gly,  
Ser, Phe, or His;

<220>  
<221> MUTAGEN  
<222> 100  
<223> Xaa at position 100 is Lys, Tyr, Leu, His, Arg, Ile, Ser, Gln,  
or ...

<220>  
<221> MUTAGEN  
<222> 101  
<223> Xaa at position is Asp, Pro, Met, Lys, His, Thr, Val, Tyr, Glu,  
Asn, Ser, Ala, Gly, Ile, Leu, or Gln;

<220>  
<221> MUTAGEN  
<222> 102  
<223> Xaa at position 102 is Gly, Leu, Glu, Lys, Ser, Tyr, or Pro;

<220>  
<221> MUTAGEN  
<222> 103  
<223> Xaa at position 103 is Asp, or Ser;

<220>  
<221> MUTAGEN  
<222> 104  
<223> Xaa at position 104 is Trp, Val, Cys, Tyr, Thr, Met, Pro, Leu,  
Gln, Lys, Ala, Phe, or Gly;

<220>  
<221> MUTAGEN  
<222> 105  
<223> Xaa at position 105 is Asn, Pro, Ala, Phe, Ser, Trp, Gln, Tyr,  
Leu, Lys, Ile, Asp, or His;

<220>  
<221> MUTAGEN  
<222> 106  
<223> Xaa at position 106 is Glu, Ser, Ala, Lys, Thr, Ile, Gly, or  
Pro;

<220>  
<221> MUTAGEN  
<222> 108  
<223> Xaa at position 108 is Arg, Lys, Asp, Leu, Thr, Ile, Gln, His,  
Ser, Ala or Pro;

<220>  
<221> MUTAGEN  
<222> 109  
<223> Xaa at position 109 is Arg, Thr, Pro, Glu, Tyr, Leu, Ser, or  
Gly;

<220>  
<221> MUTAGEN  
<222> 110

<223> Xaa at position 110 is Lys, Ala, Asn, Thr, Leu, Arg, Gln, His, Glu, Ser, or Trp;

<220>

<221> MUTAGEN

<222> 111

<223> Xaa at position 111 is Leu, Ile, Arg, Asp, or Met;

<220>

<221> MUTAGEN

<222> 112

<223> Xaa at position 112 is Thr, Val, Gln, Tyr, Glu, His, Ser, or Phe;

<220>

<221> MUTAGEN

<222> 113

<223> Xaa at position 113 is Phe, Ser, Cys, His, Gly, Trp, Tyr, Asp, Lys, Leu, Ile, Val or Asn;

<220>

<221> MUTAGEN

<222> 114

<223> Xaa at position 114 is Tyr, Cys, His, Ser, Trp, Arg, or Leu;

<220>

<221> MUTAGEN

<222> 115

<223> Xaa at position 115 is Leu, Asn, Val, Pro, Arg, Ala, His, Thr, Trp, or Met;

<220>

<221> MUTAGEN

<222> 116

<223> Xaa at position 116 is Lys, Leu, Pro, Thr, Met, Asp, Val, Glu, Arg, Trp, Ser, Asn, His, Ala, Tyr, Phe, Gln, or Ile;

<220>

<221> MUTAGEN

<222> 117

<223> Xaa at position 117 is Thr, Ser, Asn, Ile, Trp, Lys, or Pro;

<220>

<221> MUTAGEN

<222> 118

<223> Xaa at position 118 is Leu, Ser, Pro, Ala, Glu, Cys, Asp, or Tyr;

<220>

<221> MUTAGEN

<222> 119

<223> Xaa at position 119 is Glu, Ser, Lys, Pro, leu, Thr, Tyr, or Arg;

<220>

<221> MUTAGEN

<222> 120

<223> Xaa at position 120 is Asn, Ala, Pro, Leu, His, Val, or Gln;

<220>

<221> MUTAGEN

<222> 121  
 <223> Xaa at position 121 is Ala, Ser, Ile, Asn, Pro, Lys, Asp, or  
 Gly;

<220>  
 <221> MUTAGEN  
 <222> 122  
 <223> Xaa at position 122 is Gln, Ser, Met, Trp, Arg, Phe, Pro, His,  
 Ile, Tyr, or Cys;

<220>  
 <221> MUTAGEN  
 <222> 123  
 <223> Xaa at position 123 is Ala, Met, Glu, His, Ser, Pro, Tyr, or  
 Leu;

<400> 261

Ala Pro Met Thr Gln Thr Thr Ser Leu Lys Thr Ser Trp Val Asn Cys  
 1 5 10 15

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa  
 20 25 30

Xaa Xaa Xaa Xaa Xaa Xaa Asn Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa  
 35 40 45

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

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa  
 65 70 75 80

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa  
 85 90 95

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Phe Xaa Xaa Xaa Xaa Xaa  
 100 105 110

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Gln Gln Thr Thr Leu  
 115 120 125

Ser Leu Ala Ile Phe  
 130

<210> 262  
 <211> 153  
 <212> PRT  
 <213> Unknown

<220>  
 <221> MUTAGEN  
 <222> 112  
 <223> position 112 is deleted or Leu, Ala, Val, Ile, Pro, Phe, Trp or  
 Met

<220>  
 <221> MUTAGEN  
 <222> 113  
 <223> position 113 is deleted or Pro, Phe, Ala, Val, Leu, Ile, Trp or  
 Met

&lt;220&gt;

&lt;221&gt; MUTAGEN

&lt;222&gt; 114

&lt;223&gt; position 114 is deleted or Pro, Phe, Ala, Val, Leu, Ile, Trp or

Met

&lt;220&gt;

&lt;221&gt; MUTAGEN

&lt;222&gt; 115

&lt;223&gt; position 115 is deleted or Gln, Gly, Ser, Thr, Tyr, or Asn

&lt;400&gt; 262

Ser Pro Ala Pro Pro Ala Cys Asp Leu Arg Val Leu Ser Lys Leu Leu  
 1 5 10 15

Arg Asp Ser His Val Leu His Ser Arg Leu Ser Gln Cys Pro Glu Val  
 20 25 30

His Pro Leu Pro Thr Pro Val Leu Leu Pro Ala Val Asp Phe Ser Leu  
 35 40 45

Gly Glu Trp Lys Thr Gln Met Glu Glu Thr Lys Ala Gln Asp Ile Leu  
 50 55 60

Gly Ala Val Thr Leu Leu Leu Glu Gly Val Met Ala Ala Arg Gly Gln  
 65 70 75 80

Leu Gly Pro Thr Cys Leu Ser Ser Leu Leu Gly Gln Leu Ser Gly Gln  
 85 90 95

Val Arg Leu Leu Leu Gly Ala Leu Gln Ser Leu Leu Gly Thr Gln Xaa  
 100 105 110

Xaa Xaa Xaa Gly Arg Thr Thr Ala His Lys Asp Pro Asn Ala Ile Phe  
 115 120 125

Leu Ser Phe Gln His Leu Leu Arg Gly Lys Val Arg Phe Leu Met Leu  
 130 135 140

Val Gly Gly Ser Thr Leu Cys Val Arg  
 145 150