(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
9 February 2017 (09.02.2017)

WIPO | PCT

(10) International Publication Number
WO 2017/024060 A1

(51) International Patent Classification:
A61P 7/04 (2006.01) *A61K 47/42* (2006.01)
A61K 38/36 (2006.01) *A61L 15/32* (2006.01)
A61K 38/16 (2006.01)

(21) International Application Number:
PCT/US2016/045401

(22) International Filing Date:
3 August 2016 (03.08.2016)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
62/200,590 3 August 2015 (03.08.2015) US
62/281,993 22 January 2016 (22.01.2016) US

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report (Art. 21(3))*

— *with sequence listing part of description (Rule 5.2(a))*

WO 2017/024060 A1

(54) Title: FACTOR IX FUSION PROTEINS AND METHODS OF MAKING AND USING SAME

(57) Abstract: The present invention provides Factor IX (FIX) fusion proteins comprising at least one heterologous moiety, such as an XTEN. The present invention further discloses methods of making and using the FIX fusion proteins.

FACTOR IX FUSION PROTEINS AND METHODS OF MAKING AND USING SAME

REFERENCE TO SEQUENCE LISTING SUBMITTED ELECTRONICALLY

[0001] The content of the electronically submitted sequence listing in ASCII text file (Name: 2159_466PC03_SeqListing_ST25.txt; Size: 688,154 bytes; and Date of Creation: August 2, 2016) filed with the application is incorporated herein by reference in its entirety.

BACKGROUND

[0002] Hemophilia B (also known as Christmas disease) is one of the most common inherited bleeding disorders in the world. It results in decreased *in vivo* and *in vitro* blood clotting activity and requires extensive medical monitoring throughout the life of the affected individual. In the absence of intervention, the afflicted individual will suffer from spontaneous bleeding in the joints, which produces severe pain and debilitating immobility; bleeding into muscles results in the accumulation of blood in those tissues; spontaneous bleeding in the throat and neck can cause asphyxiation if not immediately treated; renal bleeding; and severe bleeding following surgery, minor accidental injuries, or dental extractions also are prevalent.

[0003] Normal *in vivo* blood coagulation at minimum requires the serine proteases Factors II (prothrombin), VII, IX, X and XI (soluble plasma proteins); cofactors including the transmembrane protein tissue factor and the plasma proteins Factors V and VIII; fibrinogen, the transglutaminase Factor XIII, phospholipid (including activated platelets), and calcium. Additional proteins including kallikrein, high molecular weight kininogen, and Factor XII are required for some *in vitro* clotting tests, and can play a role *in vivo* under pathologic conditions.

[0004] In hemophilia, blood clotting is disturbed by a lack of certain plasma blood clotting factors. Hemophilia B is caused by a deficiency in Factor IX (FIX) that can result from either the decreased synthesis or absence of the FIX protein or a defective molecule with reduced activity. The treatment of hemophilia occurs by replacement of the missing clotting factor by exogenous factor concentrates highly enriched in FIX.

However, generating such a concentrate from blood is fraught with technical difficulties, as is described below.

[0005] Purification of FIX from plasma (plasma derived FIX; pdFIX) almost exclusively yields fully-γ-carboxylated FIX. However, such purification of FIX from plasma is very difficult because FIX is only present in low concentration in plasma (5 µg/mL). Andersson, Thrombosis Research 7: 451 459 (1975). Further, purification from blood requires the removal or inactivation of infectious agents such as HIV and HCV. In addition, pdFIX has a short half-life and therefore requires frequent dosing. Recombinant Factor IX (rFIX) is also available, but suffers from the same short half-life and need for frequent dosing (*e.g.*, 2-3 times per week for prophylaxis) as pdFIX.

[0006] Reduced mortality, prevention of joint damage and improved quality of life have been important achievements due to the development of plasma-derived and recombinant FIX. Prolonged protection from bleeding would represent another key advancement in the treatment of hemophilia B subjects. Therefore, there remains a need for improved recombinant FIX, which has a longer half-life, while maintaining an effective activity.

BRIEF SUMMARY OF THE INVENTION

[0007] Disclosed are specific Factor IX fusion proteins that include at least one XTEN. In one aspect, the invention provides a Factor IX (FIX) fusion protein comprising a FIX polypeptide and at least one XTEN which is inserted within the FIX polypeptide at an insertion site corresponding to an amino acid selected from the group consisting of amino acid 103 of SEQ ID NO: 2, amino acid 105 of SEQ ID NO: 2, amino acid 142 of SEQ ID NO: 2, amino acid 149 of SEQ ID NO: 2, amino acid 162 of SEQ ID NO: 2, amino acid 166 of SEQ ID NO: 2, amino acid 174 of SEQ ID NO: 2, amino acid 224 of SEQ ID NO: 2, amino acid 226 of SEQ ID NO: 2, amino acid 228 of SEQ ID NO: 2, amino acid 413 of SEQ ID NO: 2, and any combination thereof, and wherein the FIX fusion protein exhibits procoagulant activity.

[0008] The invention also provides for an FIX fusion protein comprising a FIX polypeptide and a heterologous moiety comprising an XTEN, wherein the XTEN is fused to the C-terminus of the FIX polypeptide and comprises an amino acid sequence of longer than 42 amino acids and shorter than 144 amino acids in length.

[0009] The FIX fusion proteins of the invention have several uses including providing a method of preventing, treating, ameliorating, or managing a clotting disease or condition in a patient in need thereof. In one embodiment, the method includes the step of administering an effective amount of the FIX fusion protein described herein (e.g., by subcutaneous administration).

[0010] The invention also provides for a method of extending a half-life of a FIX polypeptide comprising inserting an XTEN within the FIX polypeptide at an insertion site corresponding to an amino acid selected from the group consisting of amino acid 103 of SEQ ID NO: 2, amino acid 105 of SEQ ID NO: 2, amino acid 142 of SEQ ID NO: 2, amino acid 149 of SEQ ID NO: 2, amino acid 162 of SEQ ID NO: 2, amino acid 166 of SEQ ID NO: 2, amino acid 174 of SEQ ID NO: 2, amino acid 224 of SEQ ID NO: 2, amino acid 226 of SEQ ID NO: 2, amino acid 228 of SEQ ID NO: 2, amino acid 413 of SEQ ID NO: 2, and any combination thereof, thereby constructing a FIX fusion protein, wherein the FIX protein exhibits procoagulant activity.

[0011] Additional invention embodiments will be apparent from the description and figures that follow.

INCORPORATION BY REFERENCE

[0012] All publications, patents, and patent applications disclosed herein are incorporated by reference to the same extent as if each individual publication, patent or patent application was specifically and individually indicated to be incorporated by reference.

BRIEF DESCRIPTION OF THE DRAWINGS

[0013] Figure 1 is a graph depicting the activity of FIX fusion proteins comprising an XTEN of 42 amino acids (*e.g.*, AE42) inserted at various insertions sites (*e.g.*, at amino acid 52, amino acid 59, amino acid 66, amino acid 80, amino acid 85, amino acid 89, amino acid 103, amino acid 105, amino acid 113, amino acid 129, amino acid 142, amino acid 149, amino acid 162, amino acid 166, amino acid 174, amino acid 188, amino acid 202, amino acid 224, amino acid 226, amino acid 228, amino acid 230, amino acid 240, amino acid 257, amino acid 265, amino acid 277, amino acid 283, amino acid 292, amino acid 316, amino acid 341, amino acid 354, amino acid 392, amino acid 403, and amino acid 413, corresponding to amino acids of SEQ ID

NO: 2) or fused to the C-terminus (C-term) of the FIX polypeptide. C-terminus fused XTEN sequences contain an thrombin-cleavable site between FIX and the C-terminal fusion. The Y-axis shows the FIX activity as a percent of the activity of the base construct (FIX-R338L) in conditioned media by chromogenic assay. The X-axis shows the specific insertion sites as the amino acid number (corresponding to SEQ ID NO: 2) and the single-letter amino acid abbreviation. The corresponding domains (*e.g.*, GLA, EGF1, EGF2, linker, AP, and the catalytic domain), linker regions, and C-terminus ("C-term") of FIX are indicated below the X-axis.

[0014] Figure 2 is a graph depicting the activity of FIX fusion proteins comprising an XTEN of 42 amino acids (AE42), 72 amino acids (AE72), 144 amino acids (AE144), 288 amino acids (AE288), and 864 amino acids (AE864) inserted at various insertions sites (*e.g.*, at amino acid 103, amino acid 105, amino acid 142, amino acid 149, amino acid 162, amino acid 166, amino acid 174, amino acid 224, and amino acid 413, corresponding to amino acids of SEQ ID NO:2) or fused to the C-terminus (C-term, amino acid 415) of the FIX polypeptide. The Y-axis shows the FIX activity as a percent of the activity of the base construct (FIX-R338L) in conditioned media by chromogenic assay. The X-axis shows the domain (*e.g.*, EGF2, AP, and catalytic domains) or region (*e.g.*, linker and C-terminus) of each insertion site and the specific insertion sites as the amino acid number (corresponding to SEQ ID NO: 2). Arrows indicate the insertion sites selected for further experimentation (*see* FIGs. 3A-3B).

[0015] FIG. 3A is a schematic representation of the regions and domains of the R338L FIX variant. Specific amino acid residues (*e.g.*, N105, D166, and E224) and the C-terminus are highlighted as potential heterologous moiety, *e.g.*, XTEN, insertion sites. FIG. 3B shows illustrations of the three-dimensional structure of the porcine FIX (PDB:1PFX) from three different angles. The insertion sites N105, D166, and E224, the C-terminus, and the location of the R338L mutation (*e.g.*, in the R338L FIX variant) are labeled.

[0016] Figure 4 summarizes the relative activities of FIX fusion proteins comprising one or two XTENs (*e.g.*, XTEN of 42, 72, 144, and 288 amino acids), or comprising one XTEN and one Fc domain, or FIXFc. The Y-axis shows the FIX activity as a percent of the activity of the base construct (FIX-R338L) in conditioned media by chromogenic assay. The X-axis shows the construct number, and the table below the X-axis shows the composition of XTEN and Fc for each construct tested. EGF2 (105), AP (166), 60 loop (224), and C-term XTEN or Fc indicate the position where the

XTEN or Fc is inserted or fused. The numbers (*e.g.*, 42, 72, 144, and 288, indicating the size of the XTEN) and "Fc" in each box in the table below the X-axis indicate which moiety is inserted within or fused to the C-terminus of the FIX polypeptide.

[0017] FIG. 5A provides a graph depicting the plasma percentile of dosed FIX clotting activities against time of various FIX fusion proteins with thrombin-cleavable C-terminal XTEN fusions of various length (*e.g.*, FIX-CT.288 (XTEN of 288 amino acids, *e.g.*, AE288) and FIX-CT.864 (XTEN of 864 amino acids, e.g., AE864)), compared to rFIX and rFIXFc as measured after single bolus intravenous dosing in hemophilia-B mice. FIG. 5B provides a graph depicting the plasma percentile of dosed FIX clotting activities against time of various FIX fusion proteins with XTEN fusions of various length inserted into the activation peptide (AP) domain (*e.g.*, FIX-AP.144, FIX-AP.72, and FIX-AP.42) compared to rFIX and rFIXFc, as measured after single bolus intravenous dosing in hemophilia-B mice. FIG. 5C provides a graphical compilation of the calculated pharmacokinetic parameters of a single intravenous bolus dosed FIX fusion protein shown in FIGs. 5A and 5B. Indicated on the Y-axis is percentile of plasma activity recovery for each of the indicated molecules. The X-axis shows the calculated mean residence time (MRT, in hours), and the area of the dots represent the relative calculated area under the curve per dose (AUC/D, in h/kg/mL).

[0018] FIG. 6A provides a graph depicting the plasma percentile of dosed FIX clotting activities against time of various FIX fusion proteins with XTEN fusions of various length inserted into the activation peptide (AP) domain (*e.g.*, FIXFc-AP.72 and FIXFc-AP.42) or EGF2 domain (*e.g.*, FIXFc-EGF.42) compared to rFIX and rFIXFc, as measured after single bolus intravenous dosing in hemophilia-B mice. FIG. 6B provides a graphical compilation of the calculated pharmacokinetic parameters of a single intravenous bolus dosed FIX fusion proteins shown in FIG. 6A. Indicated on the Y-axis is percentile of plasma activity recovery for each of the indicated molecules. The X-axis shows the calculated mean residence time (MRT, in hours). The area of the dots represents the relative calculated area under the curve per dose (AUC/D, in h/kg/mL).

[0019] FIG. 7A provides a graph depicting the plasma percentile of dosed FIX clotting activities against time of a FIX fusion protein comprising an thrombin-cleavable XTEN of 288 amino acids fused to the C terminus of a FIX polypeptide (rFIX-CT.288), a FIX fusion protein comprising an XTEN of 72 amino acids inserted

within the AP domain of a FIX polypeptide (rFIXFc-AP.72), and a FIX fusion protein comprising an XTEN of 42 amino acids inserted within the EGF2 domain of a FIX polypeptide (rFIXFc-EGF2.42) compared to rFIX and rFIXFc, as measured after single bolus subcutaneous dosing in hemophilia-B mice. FIG. 7B provides a graphical compilation of the calculated pharmacokinetic parameters of a single subcutaneous bolus dosed FIX fusion proteins shown in FIG. 7A. Indicated on the Y-axis is percentile of bioavailability for each of the indicated molecules. The X-axis shows the calculated mean residence time (MRT, in hours). The area of the dots represents the relative calculated area under the curve per dose (AUC/D, in h/kg/mL).

[0020] FIG. 8A provides a graphical depiction of clotting time in seconds measured by rotational thromboelastometry (ROTEM) of rFIXFc and a FIX fusion protein comprising an XTEN of 72 amino acids inserted within the AP domain of FIX (e.g., rFIXFc-AP-XTEN.72) in human hemophilia B blood. FIG. 8B provides a graphical depiction of alpha angle in degrees of rFIXFc and a FIX fusion protein (e.g., rFIXFc-AP-XTEN.72) in human hemophilia B blood. FIG. 8C provides a graphical depiction of maximum clot firmness (MCF) in mm of rFIXFc and a FIX fusion protein (e.g., rFIXFc-AP-XTEN.72) in human hemophilia B blood.

[0021] FIG. 9 is a graph showing the acute efficacy of rFIXFc-AP.72 compared to rFIXFc in the tail clip bleeding model. Results presented are individual and median blood loss (µl) at 5 minutes post dosing, over a 30 minutes period for treatments and dosing as indicated. Asterisks indicate significant p values for vehicle versus all other treatments. Data indicate similar or improved efficacy in mice dosed with rFIXFc-AP.72 compared to rFIXFc.

[0022] FIG. 10 is a graph showing the percentage of HemB mice surviving (Y-axis) plotted against the time in hours post tail vein transection (X-axis). All mice were pre-dosed 72 hours prior to the tail vein transection intravenously with FIXFc (dotted lines) or subcutaneously with FIXFc-AP.72 at the indicated IU/kg (FIXFc-AP.72: 100 IU/kg (solid black circle), 50 IU/kg (solid grey triangle), and 15 IU/kg (solid inverted grey triangle); rFIXFc: 100 IU/kg (open circle), 50 IU/kg (open triangle), and 15 IU/kg (open inverted triangle); and vehicle (closed grey circle). Survival plots for mice dosed with either rFIXFc or FIXFc-AP.72 are all significantly different when compared to vehicle treated mice ($p < 0.0001$, Log-rank (Mantel-Cox) test.

[0023] FIG. 11A is a graph showing the plasma levels of FX activity as measured by a one-stage plasma assay plotted versus time for Hemophilia B mice which were

dosed by either intravenous (dashed lines) or subcutaneous injection (solid lines) with a single bolus (200 IU/kg) of rFIX (grey) or the rFIXFc-AP.72 fusion protein (black). FIG. 11B shows pharmacokinetic parameters as determined using non-compartmental analysis (NCA) using Phoenix WinNonLin 6.2.1 software (Pharsight, Certara).

[0024] FIG. 12A is a schematic drawing illustrating the domain structure of rFIXFc-AP.72 single chain Fc. FIG. 12B is a schematic drawing showing the domain structure of rFIXFc-AP.72 dual chain Fc. "FIX HC" refers to the heavy chain of FIX; "FIX LC" refers to the light chain of FIX, which includes the EGF and GLA domains of FIX; and AP refers to the activation peptide of FIX.

[0025] FIG. 13 is a table summarizing the FIX-XTEN constructs as used in the examples with matching sequence identification number, description and plasmid code.

DETAILED DESCRIPTION

[0026] This disclosure provides a FIX fusion protein comprising a FIX polypeptide and at least one heterologous moiety and methods of making and using the same. In certain aspects, the FIX fusion protein comprises at least one heterologous moiety inserted within the FIX polypeptide, fused to the C-terminus of the FIX polypeptide, or both, wherein the FIX fusion protein exhibits procoagulant activity. In a particular aspect, the heterologous moiety is XTEN.

I. DEFINITIONS

[0027] Throughout this disclosure, the term "a" or "an" entity refers to one or more of that entity; for example, "a polynucleotide," is understood to represent one or more polynucleotides. As such, the terms "a" (or "an"), "one or more," and "at least one" can be used interchangeably herein.

[0028] Furthermore, "and/or" where used herein is to be taken as specific disclosure of each of the two specified features or components with or without the other. Thus, the term "and/or" as used in a phrase such as "A and/or B" herein is intended to include "A and B," "A or B," "A" (alone), and "B" (alone). Likewise, the term "and/or" as used in a phrase such as "A, B, and/or C" is intended to encompass each of the following aspects: A, B, and C; A, B, or C; A or C; A or B; B or C; A and C; A and B; B and C; A (alone); B (alone); and C (alone).

[0029] It is understood that wherever aspects are described herein with the language "comprising," otherwise analogous aspects described in terms of "consisting of" and/or "consisting essentially of" are also provided.

[0030] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this disclosure is related. For example, the Concise Dictionary of Biomedicine and Molecular Biology, Juo, Pei-Show, 2nd ed., 2002, CRC Press; The Dictionary of Cell and Molecular Biology, 3rd ed., 1999, Academic Press; and the Oxford Dictionary Of Biochemistry And Molecular Biology, Revised, 2000, Oxford University Press, provide one of skill with a general dictionary of many of the terms used in this disclosure.

[0031] Units, prefixes, and symbols are denoted in their Système International de Unites (SI) accepted form. Numeric ranges are inclusive of the numbers defining the range. Unless otherwise indicated, amino acid sequences are written left to right in amino to carboxy orientation. The headings provided herein are not limitations of the various aspects of the disclosure, which can be had by reference to the specification as a whole. Accordingly, the terms defined immediately below are more fully defined by reference to the specification in its entirety.

[0032] The term "about" is used herein to mean approximately, roughly, around, or in the regions of. When the term "about" is used in conjunction with a numerical range, it modifies that range by extending the boundaries above and below the numerical values set forth. In general, the term "about" can modify a numerical value above and below the stated value by a variance of, *e.g.*, 10 percent, up or down (higher or lower).

[0033] The term "polynucleotide" or "nucleotide" is intended to encompass a singular nucleic acid as well as plural nucleic acids, and refers to an isolated nucleic acid molecule or construct, *e.g.*, messenger RNA (mRNA) or plasmid DNA (pDNA). In certain embodiments, a polynucleotide comprises a conventional phosphodiester bond or a non-conventional bond (*e.g.*, an amide bond, such as found in peptide nucleic acids (PNA)). The term "nucleic acid" refers to any one or more nucleic acid segments, *e.g.*, DNA or RNA fragments, present in a polynucleotide. By "isolated" nucleic acid or polynucleotide is intended a nucleic acid molecule, DNA or RNA, which has been removed from its native environment. For example, a recombinant polynucleotide encoding a FIX polypeptide contained in a vector is considered isolated for the purposes of the present invention. Further examples of an isolated

polynucleotide include recombinant polynucleotides maintained in heterologous host cells or purified (partially or substantially) from other polynucleotides in a solution. Isolated RNA molecules include *in vivo* or *in vitro* RNA transcripts of polynucleotides of the present invention. Isolated polynucleotides or nucleic acids according to the present invention further include such molecules produced synthetically. In addition, a polynucleotide or a nucleic acid can include regulatory elements such as promoters, enhancers, ribosome binding sites, or transcription termination signals.

[0034] As used herein, a "coding region" or "coding sequence" is a portion of polynucleotide, which consists of codons translatable into amino acids. Although a "stop codon" (TAG, TGA, or TAA) is typically not translated into an amino acid, it may be considered to be part of a coding region, but any flanking sequences, for example promoters, ribosome binding sites, transcriptional terminators, introns, and the like, are not part of a coding region. The boundaries of a coding region are typically determined by a start codon at the 5' terminus, encoding the amino terminus of the resultant polypeptide, and a translation stop codon at the 3' terminus, encoding the carboxyl terminus of the resulting polypeptide. Two or more coding regions of the present invention can be present in a single polynucleotide construct, *e.g.*, on a single vector, or in separate polynucleotide constructs, *e.g.*, on separate (different) vectors. It follows, then, that a single vector can contain just a single coding region, or comprise two or more coding regions, *e.g.*, a single vector can separately encode a binding domain-A and a binding domain-B as described below. In addition, a vector, polynucleotide, or nucleic acid of the invention can encode heterologous coding regions, either fused or unfused to a nucleic acid encoding a binding domain of the invention. Heterologous coding regions include without limitation specialized elements or motifs, such as a secretory signal peptide or a heterologous functional domain.

[0035] Certain proteins secreted by mammalian cells are associated with a secretory signal peptide, which is cleaved from the mature protein once export of the growing protein chain across the rough endoplasmic reticulum has been initiated. Those of ordinary skill in the art are aware that signal peptides are generally fused to the N-terminus of the polypeptide, and are cleaved from the complete or "full-length" polypeptide to produce a secreted or "mature" form of the polypeptide. In certain embodiments, a native signal peptide or a functional derivative of that sequence that

retains the ability to direct the secretion of the polypeptide that is operably associated with it. Alternatively, a heterologous mammalian signal peptide, *e.g.*, a human tissue plasminogen activator (TPA) or mouse ß-glucuronidase signal peptide, or a functional derivative thereof, can be used.

[0036] The term "downstream" refers to a nucleotide sequence that is located 3' to a reference nucleotide sequence. In certain embodiments, downstream nucleotide sequences relate to sequences that follow the starting point of transcription. For example, the translation initiation codon of a gene is located downstream of the start site of transcription. "Downstream" can also refer to a peptide sequence that is located C-terminal to a reference peptide sequence.

[0037] The term "upstream" refers to a nucleotide sequence that is located 5' to a reference nucleotide sequence. In certain embodiments, upstream nucleotide sequences relate to sequences that are located on the 5' side of a coding region or starting point of transcription. For example, most promoters are located upstream of the start site of transcription. "Upstream" can also refer to a peptide sequence that is located N-terminal to a reference peptide sequence.

[0038] As used herein, the term "regulatory region" refers to nucleotide sequences located upstream (5' non-coding sequences), within, or downstream (3' non-coding sequences) of a coding region, and which influence the transcription, RNA processing, stability, or translation of the associated coding region. Regulatory regions may include promoters, translation leader sequences, introns, polyadenylation recognition sequences, RNA processing sites, effector binding sites and stem-loop structures. If a coding region is intended for expression in a eukaryotic cell, a polyadenylation signal and transcription termination sequence will usually be located 3' to the coding sequence.

[0039] A polynucleotide, which encodes a gene product, *e.g.*, a polypeptide, can include a promoter and/or other transcription or translation control elements operably associated with one or more coding regions. In an operable association a coding region for a gene product, *e.g.*, a polypeptide, is associated with one or more regulatory regions in such a way as to place expression of the gene product under the influence or control of the regulatory region(s). For example, a coding region and a promoter are "operably associated" if induction of promoter function results in the transcription of mRNA encoding the gene product encoded by the coding region, and if the nature of the linkage between the promoter and the coding region does not

interfere with the ability of the promoter to direct the expression of the gene product or interfere with the ability of the DNA template to be transcribed. Other transcription control elements, besides a promoter, for example enhancers, operators, repressors, and transcription termination signals, can also be operably associated with a coding region to direct gene product expression.

[0040] A variety of transcription control regions are known to those skilled in the art. These include, without limitation, transcription control regions, which function in vertebrate cells, such as, but not limited to, promoter and enhancer segments from cytomegaloviruses (the immediate early promoter, in conjunction with intron-A), simian virus 40 (the early promoter), and retroviruses (such as Rous sarcoma virus). Other transcription control regions include those derived from vertebrate genes such as actin, heat shock protein, bovine growth hormone and rabbit ß-globin, as well as other sequences capable of controlling gene expression in eukaryotic cells. Additional suitable transcription control regions include tissue-specific promoters and enhancers as well as lymphokine-inducible promoters (*e.g.*, promoters inducible by interferons or interleukins).

[0041] Similarly, a variety of translation control elements are known to those of ordinary skill in the art. These include, but are not limited to ribosome binding sites, translation initiation and termination codons, and elements derived from picornaviruses (particularly an internal ribosome entry site, or IRES, also referred to as a CITE sequence).

[0042] The term "expression" as used herein refers to a process by which a polynucleotide produces a gene product, for example, an RNA or a polypeptide. It includes without limitation transcription of the polynucleotide into messenger RNA (mRNA), transfer RNA (tRNA), small hairpin RNA (shRNA), small interfering RNA (siRNA) or any other RNA product, and the translation of an mRNA into a polypeptide. Expression produces a "gene product." As used herein, a gene product can be either a nucleic acid, *e.g.*, a messenger RNA produced by transcription of a gene, or a polypeptide which is translated from a transcript. Gene products described herein further include nucleic acids with post transcriptional modifications, *e.g.*, polyadenylation or splicing, or polypeptides with post translational modifications, *e.g.*, methylation, glycosylation, the addition of lipids, association with other protein subunits, or proteolytic cleavage.

[0043] A "vector" refers to any vehicle for the cloning of and/or transfer of a nucleic acid into a host cell. A vector may be a replicon to which another nucleic acid segment may be attached so as to bring about the replication of the attached segment. A "replicon" refers to any genetic element (*e.g.*, plasmid, phage, cosmid, chromosome, virus) that functions as an autonomous unit of replication *in vivo*, *i.e.*, capable of replication under its own control. The term "vector" includes both viral and nonviral vehicles for introducing the nucleic acid into a cell *in vitro*, *ex vivo* or *in vivo*. A large number of vectors are known and used in the art including, for example, plasmids, modified eukaryotic viruses, or modified bacterial viruses. Insertion of a polynucleotide into a suitable vector can be accomplished by ligating the appropriate polynucleotide fragments into a chosen vector that has complementary cohesive termini.

[0044] Vectors may be engineered to encode selectable markers or reporters that provide for the selection or identification of cells that have incorporated the vector. Expression of selectable markers or reporters allows identification and/or selection of host cells that incorporate and express other coding regions contained on the vector. Examples of selectable marker genes known and used in the art include: genes providing resistance to ampicillin, streptomycin, gentamycin, kanamycin, hygromycin, neomycin, puromycin, bialaphos herbicide, sulfonamide, and the like; and genes that are used as phenotypic markers, *i.e.*, anthocyanin regulatory genes, isopentanyl transferase gene, and the like. Examples of reporters known and used in the art include: luciferase (Luc), green fluorescent protein (GFP), chloramphenicol acetyltransferase (CAT), -galactosidase (LacZ), -glucuronidase (Gus), and the like. Selectable markers may also be considered to be reporters.

[0045] The term "plasmid" refers to an extra-chromosomal element often carrying a gene that is not part of the central metabolism of the cell, and usually in the form of circular double-stranded DNA molecules. Such elements may be autonomously replicating sequences, genome integrating sequences, phage or nucleotide sequences, linear, circular, or supercoiled, of a single- or double-stranded DNA or RNA, derived from any source, in which a number of nucleotide sequences have been joined or recombined into a unique construction which is capable of introducing a promoter fragment and DNA sequence for a selected gene product along with appropriate 3' untranslated sequence into a cell.

[0046] Eukaryotic viral vectors that can be used include, but are not limited to, adenovirus vectors, retrovirus vectors, adeno-associated virus vectors, and poxvirus, *e.g.*, vaccinia virus vectors, baculovirus vectors, or herpesvirus vectors. Non-viral vectors include plasmids, liposomes, electrically charged lipids (cytofectins), DNA-protein complexes, and biopolymers.

[0047] A "cloning vector" refers to a "replicon," which is a unit length of a nucleic acid that replicates sequentially and which comprises an origin of replication, such as a plasmid, phage or cosmid, to which another nucleic acid segment may be attached so as to bring about the replication of the attached segment. Certain cloning vectors are capable of replication in one cell type, *e.g.*, bacteria and expression in another, *e.g.*, eukaryotic cells. Cloning vectors typically comprise one or more sequences that can be used for selection of cells comprising the vector and/or one or more multiple cloning sites for insertion of nucleic acid sequences of interest.

[0048] The term "expression vector" refers to a vehicle designed to enable the expression of an inserted nucleic acid sequence following insertion into a host cell. The inserted nucleic acid sequence is placed in operable association with regulatory regions as described above.

[0049] Vectors are introduced into host cells by methods well known in the art, *e.g.*, transfection, electroporation, microinjection, transduction, cell fusion, DEAE dextran, calcium phosphate precipitation, lipofection (lysosome fusion), use of a gene gun, or a DNA vector transporter.

[0050] "Culture," "to culture" and "culturing," as used herein, means to incubate cells under *in vitro* conditions that allow for cell growth or division or to maintain cells in a living state. "Cultured cells," as used herein, means cells that are propagated *in vitro*.

[0051] As used herein, the term "polypeptide" is intended to encompass a singular "polypeptide" as well as plural "polypeptides," and refers to a molecule composed of monomers (amino acids) linearly linked by amide bonds (also known as peptide bonds). The term "polypeptide" refers to any chain or chains of two or more amino acids, and does not refer to a specific length of the product. Thus, peptides, dipeptides, tripeptides, oligopeptides, "protein," "amino acid chain," or any other term used to refer to a chain or chains of two or more amino acids, are included within the definition of "polypeptide," and the term "polypeptide" can be used instead of, or interchangeably with any of these terms. The term "polypeptide" is also intended to refer to the products of post-expression modifications of the polypeptide, including

without limitation glycosylation, acetylation, phosphorylation, amidation, derivatization by known protecting/blocking groups, proteolytic cleavage, or modification by non-naturally occurring amino acids. A polypeptide can be derived from a natural biological source or produced recombinant technology, but is not necessarily translated from a designated nucleic acid sequence. It can be generated in any manner, including by chemical synthesis.

[0052] An "isolated" polypeptide or a fragment, variant, or derivative thereof refers to a polypeptide that is not in its natural milieu. No particular level of purification is required. For example, an isolated polypeptide can simply be removed from its native or natural environment. Recombinantly produced polypeptides and proteins expressed in host cells are considered isolated for the purpose of the invention, as are native or recombinant polypeptides which have been separated, fractionated, or partially or substantially purified by any suitable technique.

[0053] As used herein, the term "host cell" refers to a cell or a population of cells harboring or capable of harboring a recombinant nucleic acid. Host cells can be a prokaryotic cells (*e.g.*, *E. coli*), or alternatively, the host cells can be eukaryotic, for example, fungal cells (*e.g.*, yeast cells such as *Saccharomyces cerevisiae*, *Pichia pastoris*, or *Schizosaccharomyces pombe*), and various animal cells, such as insect cells (*e.g.*, Sf-9) or mammalian cells (*e.g.*, HEK293F, CHO, COS- 7, NIH-3T3).

[0054] Also included in the present invention are fragments or variants of polypeptides, and any combination thereof. The term "fragment" or "variant" when referring to polypeptide binding domains or binding molecules of the present invention include any polypeptides which retain at least some of the properties (*e.g.*, FcRn binding affinity for an FcRn binding domain or Fc variant, or coagulation activity for a FIX variant) of the reference polypeptide. Fragments of polypeptides include proteolytic fragments, as well as deletion fragments, in addition to specific antibody fragments discussed elsewhere herein, but do not include the naturally occurring full-length polypeptide (or mature polypeptide). Variants of polypeptide binding domains or binding molecules of the present invention include fragments as described above, and also polypeptides with altered amino acid sequences due to amino acid substitutions, deletions, or insertions. Variants can be naturally or non-naturally occurring. Non-naturally occurring variants can be produced using art-known mutagenesis techniques. Variant polypeptides can comprise conservative or non-conservative amino acid substitutions, deletions or additions. One particular FIX

variant disclosed herein is the R338L FIX (Padua) variant (SEQ ID NO: 2). *See, e.g.*, Simioni, P., *et al.*, "X-Linked Thrombophilia with a Mutant Factor IX (Factor IX Padua)," *NEJM 361*:1671-75 (October 2009), which is incorporated by reference herein in its entirety.

[0055] A "conservative amino acid substitution" is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined in the art, including basic side chains (*e.g.*, lysine, arginine, histidine), acidic side chains (*e.g.*, aspartic acid, glutamic acid), uncharged polar side chains (*e.g.*, glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine), nonpolar side chains (*e.g.*, alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (*e.g.*, threonine, valine, isoleucine) and aromatic side chains (*e.g.*, tyrosine, phenylalanine, tryptophan, histidine). Thus, if an amino acid in a polypeptide is replaced with another amino acid from the same side chain family, the substitution is considered to be conservative. In another embodiment, a string of amino acids can be conservatively replaced with a structurally similar string that differs in order and/or composition of side chain family members.

[0056] The term "percent sequence identity" between two polynucleotide or polypeptide sequences refers to the number of identical matched positions shared by the sequences over a comparison window, taking into account additions or deletions (*i.e.*, gaps) that must be introduced for optimal alignment of the two sequences. A matched position is any position where an identical nucleotide or amino acid is presented in both the target and reference sequence. Gaps presented in the target sequence are not counted since gaps are not nucleotides or amino acids. Likewise, gaps presented in the reference sequence are not counted since target sequence nucleotides or amino acids are counted, not nucleotides or amino acids from the reference sequence.

[0057] The percentage of sequence identity is calculated by determining the number of positions at which the identical amino-acid residue or nucleic acid base occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the window of comparison and multiplying the result by 100 to yield the percentage of sequence identity. The comparison of sequences and determination of percent sequence identity between two sequences may be accomplished using readily available software both for online use

and for download. Suitable software programs are available from various sources, and for alignment of both protein and nucleotide sequences. One suitable program to determine percent sequence identity is bl2seq, part of the BLAST suite of programs available from the U.S. government's National Center for Biotechnology Information BLAST web site (blast.ncbi.nlm.nih.gov). Bl2seq performs a comparison between two sequences using either the BLASTN or BLASTP algorithm. BLASTN is used to compare nucleic acid sequences, while BLASTP is used to compare amino acid sequences. Other suitable programs are, *e.g.*, Needle, Stretcher, Water, or Matcher, part of the EMBOSS suite of bioinformatics programs and also available from the European Bioinformatics Institute (EBI) at www.ebi.ac.uk/Tools/psa.

[0058] Different regions within a single polynucleotide or polypeptide target sequence that aligns with a polynucleotide or polypeptide reference sequence can each have their own percent sequence identity. It is noted that the percent sequence identity value is rounded to the nearest tenth. For example, 80.11, 80.12, 80.13, and 80.14 are rounded down to 80.1, while 80.15, 80.16, 80.17, 80.18, and 80.19 are rounded up to 80.2. It also is noted that the length value will always be an integer.

[0059] One skilled in the art will appreciate that the generation of a sequence alignment for the calculation of a percent sequence identity is not limited to binary sequence-sequence comparisons exclusively driven by primary sequence data. Sequence alignments can be derived from multiple sequence alignments. One suitable program to generate multiple sequence alignments is ClustalW2, available from www.clustal.org. Another suitable program is MUSCLE, available from www.drive5.com/muscle/. ClustalW2 and MUSCLE are alternatively available, *e.g.*, from the EBI.

[0060] It will also be appreciated that sequence alignments can be generated by integrating sequence data with data from heterogeneous sources such as structural data (*e.g.*, crystallographic protein structures), functional data (*e.g.*, location of mutations), or phylogenetic data. A suitable program that integrates heterogeneous data to generate a multiple sequence alignment is T-Coffee, available at www.tcoffee.org, and alternatively available, *e.g.*, from the EBI. It will also be appreciated that the final alignment used to calculate percent sequence identity may be curated either automatically or manually.

[0061] As used herein, an "amino acid corresponding to," "site corresponding to," or "equivalent amino acid" in a Factor IX protein sequence is identified by alignment to

maximize the identity or similarity between a first FIX sequence and a second FIX sequence. The number used to identify an equivalent amino acid in a second FIX sequence is based on the number used to identify the corresponding amino acid in the first FIX sequence.

[0062] As used herein, the term "insertion site" refers to an amino acid residue number in aFIX polypeptide (typically a mature FIX polypeptide), or fragment, variant, or derivative thereof, which is immediately upstream of the position at which a heterologous moiety can be inserted. An "insertion site" is specified as a number, the number being the number of the amino acid in the R338L FIX (Padua) variant (SEQ ID NO: 2) to which the insertion site corresponds, which is immediately N-terminal to the position of the insertion. For example, the phrase "the EGF2 domain comprises an XTEN at an insertion site which corresponds to amino acid 105 of SEQ ID NO: 2" indicates that the heterologous moiety is located between two amino acids corresponding to amino acid 105 and amino acid 106 of SEQ ID NO: 2. However, one of skill in the art would readily be able to identify a corresponding position in any FIX variant, and the present disclosure is not limited to insertions made solely in the R338L FIX (Padua) variant. Rather, the insertions disclosed herein can be made in any FIX variant or fragment thereof having procoagulant activity at a position corresponding to a position of the R338L FIX variant.

[0063] The phrase "immediately downstream of an amino acid" as used herein refers to position right next to the terminal carboxyl group of the amino acid. Similarly, the phrase "immediately upstream of an amino acid" refers to the position right next to the terminal amine group of the amino acid. Therefore, the phrase "between two amino acids of an insertion site" as used herein refers to a position in which an XTEN or any other polypeptide is inserted between two adjacent amino acids.

[0064] The terms "inserted," "is inserted," "inserted into" or grammatically related terms, as used herein refers to the position of an XTEN in a fusion polypeptide relative to the analogous position in the R338L FIX (Padua) variant (SEQ ID NO: 2). Those of skill in the field will understand how to identify corresponding insertion positions with respect to other FIX polypeptide sequences such as that shown as SEQ ID NO:1. As used herein the terms refer to the characteristics of the recombinant FIX polypeptide relative to the R338L FIX (Padua) variant, and do not indicate, imply or infer any methods or process by which the fusion polypeptide was made. For example, in reference to a fusion polypeptide provided herein, the phrase "an XTEN

is inserted into the EGF2 domain immediately downstream of residue 105 of the FIX polypeptide" means that the fusion polypeptide comprises an XTEN immediately downstream of an amino acid which corresponds to amino acid 105 in the R338L FIX variant (SEQ ID NO: 2), *e.g.*, bounded by amino acids corresponding to amino acids 105 and 106 of the R338L FIX variant.

[0065] A "fusion" or "chimeric" protein comprises a first amino acid sequence linked to a second amino acid sequence with which it is not naturally linked in nature. The amino acid sequences which normally exist in separate proteins can be brought together in the fusion polypeptide, or the amino acid sequences which normally exist in the same protein can be placed in a new arrangement in the fusion polypeptide, *e.g.*, fusion of a FIX domain of the invention with an Ig Fc domain. A fusion protein is created, for example, by chemical synthesis, or by creating and translating a polynucleotide in which the peptide regions are encoded in the desired relationship. A fusion protein can further comprise a second amino acid sequence associated with the first amino acid sequence by a covalent, non-peptide bond or a non-covalent bond.

[0066] The terms "heterologous" and "heterologous moiety" mean that a polynucleotide, polypeptide, or other moiety is derived from a distinct entity from that of the entity to which it is being compared. For instance, a heterologous polypeptide can be synthetic, or derived from a different species, different cell type of an individual, or the same or different type of cell of distinct individuals. In one aspect, a heterologous moiety is a polypeptide fused to another polypeptide to produce a fusion polypeptide or protein. In another aspect, a heterologous moiety is a non-polypeptide such as PEG conjugated to a polypeptide or protein.

[0067] As used herein, the term "half-life" refers to a biological half-life of a particular polypeptide *in vivo*. Half-life may be represented by the time required for half the quantity administered to a subject to be cleared from the circulation and/or other tissues in the animal. When a clearance curve of a given polypeptide is constructed as a function of time, the curve is usually biphasic with a rapid α-phase and longer β-phase. The α-phase typically represents an equilibration of the administered polypeptide between the intra- and extra-vascular space and is, in part, determined by the size of the polypeptide. The β-phase typically represents the catabolism of the polypeptide in the intravascular space. In some embodiments, FIX and fusion proteins comprising FIX are monophasic, and thus do not have an alpha phase, but just the single beta phase. Therefore, in certain embodiments, the term half-

life as used herein refers to the half-life of the polypeptide in the β-phase. The typical β-phase half-life of a human antibody in humans is 21 days.

[0068] The terms "linked" and "fused" as used herein refers to a first amino acid sequence or nucleotide sequence covalently or non-covalently joined to a second amino acid sequence or nucleotide sequence, respectively. The first amino acid or nucleotide sequence can be directly joined or juxtaposed to the second amino acid or nucleotide sequence or alternatively an intervening sequence can covalently join the first sequence to the second sequence. The term "linked" means not only a fusion of a first amino acid sequence to a second amino acid sequence at the C-terminus or the N-terminus, but also includes insertion of the whole first amino acid sequence (or the second amino acid sequence) into any two amino acids in the second amino acid sequence (or the first amino acid sequence, respectively). In one embodiment, the first amino acid sequence is linked to a second amino acid sequence by a peptide bond or a linker. The first nucleotide sequence can be linked to a second nucleotide sequence by a phosphodiester bond or a linker. The linker can be a peptide or a polypeptide (for polypeptide chains) or a nucleotide or a nucleotide chain (for nucleotide chains) or any chemical moiety (for both polypeptide and polynucleotide chains). The term "linked" is also indicated by a hyphen (-).

[0069] As used herein the term "associated with" refers to a covalent or non-covalent bond formed between a first amino acid chain and a second amino acid chain. In one embodiment, the term "associated with" means a covalent, non-peptide bond or a non-covalent bond. This association can be indicated by a colon, *i.e.,* (:). In another embodiment, it means a covalent bond except a peptide bond. For example, the amino acid cysteine comprises a thiol group that can form a disulfide bond or bridge with a thiol group on a second cysteine residue. In most naturally occurring IgG molecules, the CH1 and CL regions are associated by a disulfide bond and the two heavy chains are associated by two disulfide bonds at positions corresponding to 239 and 242 using the Kabat numbering system (position 226 or 229, EU numbering system). Examples of covalent bonds include, but are not limited to, a peptide bond, a metal bond, a hydrogen bond, a disulfide bond, a sigma bond, a pi bond, a delta bond, a glycosidic bond, an agnostic bond, a bent bond, a dipolar bond, a Pi backbond, a double bond, a triple bond, a quadruple bond, a quintuple bond, a sextuple bond, conjugation, hyperconjugation, aromaticity, hapticity, or antibonding. Non-limiting examples of

non-covalent bond include an ionic bond (*e.g.,* cation-pi bond or salt bond), a metal bond, an hydrogen bond (*e.g.,* dihydrogen bond, dihydrogen complex, low-barrier hydrogen bond, or symmetric hydrogen bond), van der Walls force, London dispersion force, a mechanical bond, a halogen bond, aurophilicity, intercalation, stacking, entropic force, or chemical polarity.

[0070] As used herein, the term "cleavage site" or "enzymatic cleavage site" refers to a site recognized by an enzyme. Certain enzymatic cleavage sites comprise an intracellular processing site. In one embodiment, a polypeptide has an enzymatic cleavage site cleaved by an enzyme that is activated during the clotting cascade, such that cleavage of such sites occurs at the site of clot formation. Exemplary such sites include, *e.g.,* those recognized by thrombin, Factor XIa or Factor Xa. Exemplary FXIa cleavage sites include, *e.g.,* TQSFNDFTR (SEQ ID NO: 166) and SVSQTSKLTR (SEQ ID NO: 167). Exemplary thrombin cleavage sites include, *e.g.,* DFLAEGGGVR (SEQ ID NO: 168), TTKIKPR (SEQ ID NO: 169), LVPRG (SEQ ID NO: 170) and ALRPR (SEQ ID NO: 171). Other enzymatic cleavage sites are known in the art.

[0071] As used herein, the term "processing site" or "intracellular processing site" refers to a type of enzymatic cleavage site in a polypeptide which is a target for enzymes that function after translation of the polypeptide. In one embodiment, such enzymes function during transport from the Golgi lumen to the trans-Golgi compartment. Intracellular processing enzymes cleave polypeptides prior to secretion of the protein from the cell. Examples of such processing sites include, *e.g.,* those targeted by the PACE/furin (where PACE is an acronym for Paired basic Amino acid Cleaving Enzyme) family of endopeptidases. These enzymes are localized to the Golgi membrane and cleave proteins on the carboxyterminal side of the sequence motif Arg-[any residue]-(Lys or Arg)-Arg. As used herein the "furin" family of enzymes includes, *e.g.,* PCSK1 (also known as PC1/Pc3), PCSK2 (also known as PC2), PCSK3 (also known as furin or PACE), PCSK4 (also known as PC4), PCSK5 (also known as PC5 or PC6), PCSK6 (also known as PACE4), or PCSK7 (also known as PC7/LPC, PC8, or SPC7). Other processing sites are known in the art. The term "processable linker" referred to herein means a linker comprising an intracellular processing site.

[0072] In constructs that include more than one processing or cleavage site, it will be understood that such sites may be the same or different.

[0073] A "processable linker" as used herein refers to a linker comprising at least one intracellular processing site, which is described elsewhere herein.

[0074] "Baseline," as used herein, is the lowest measured plasma FIX level in a subject prior to administering a dose. The FIX plasma levels can be measured at two time points prior to dosing: at a screening visit and immediately prior to dosing. Alternatively, (a) the baseline in subjects whose pretreatment FIX activity is <1%, who have no detectable FIX antigen, and have nonsense genotypes can be defined as 0%, (b) the baseline for subjects with pretreatment FIX activity <1% and who have detectable FIX antigen can be set at 0.5%, (c) the baseline for subjects whose pretreatment FIX activity is between 1 – 2% is Cmin (the lowest activity throughout the PK study), and (d) the baseline for subjects whose pretreatment FIX activity is ≥2% can be set at 2%.

[0075] "Subject," as used herein means a human. Subject as used herein includes an individual who is known to have at least one incidence of uncontrolled bleeding episodes, who has been diagnosed with a disease or disorder associated with uncontrolled bleeding episodes, *e.g.*, a bleeding disease or disorder, *e.g.*, hemophilia B, who are susceptible to uncontrolled bleeding episodes, *e.g.*, hemophilia, or any combinations thereof. Subjects can also include an individual who is in danger of one or more uncontrollable bleeding episodes prior to a certain activity, *e.g.*, a surgery, a sport activity, or any strenuous activities. The subject can have a baseline FIX activity less than 1%, less than 0.5%, less than 2%, less than 2.5%, less than 3%, or less than 4%. Subjects also include pediatric humans. Pediatric human subjects are birth to 20 years, preferably birth to 18 years, birth to 16 years, birth to 15 years, birth to 12 years, birth to 11 years, birth to 6 years, birth to 5 years, birth to 2 years, and 2 to 11 years of age.

[0076] Treat, treatment, treating, as used herein refers to, *e.g.*, the reduction in severity of a disease or condition; the reduction in the duration of a disease course; the amelioration of one or more symptoms associated with a disease or condition; the provision of beneficial effects to a subject with a disease or condition, without necessarily curing the disease or condition, or the prophylaxis of one or more symptoms associated with a disease or condition. In one embodiment, the term "treating" or "treatment" means maintaining a FIX trough level at least about 1 IU/dL, 2 IU/dL, 3 IU/dL, 4 IU/dL, 5 IU/dL, 6 IU/dL, 7 IU/dL, 8 IU/dL, 9 IU/dL, 10 IU/dL, 11 IU/dL, 12 IU/dL, 13 IU/dL, 14 IU/dL, 15 IU/dL, 16 IU/dL, 17 IU/dL, 18 IU/dL, 19 IU/dL, or 20 IU/dL in a subject by administering a fusion protein of the invention. In another embodiment, treating or treatment means maintaining a FIX trough level

between about 1 and about 20 IU/dL, about 2 and about 20 IU/dL, about 3 and about 20 IU/dL, about 4 and about 20 IU/dL, about 5 and about 20 IU/dL, about 6 and about 20 IU/dL, about 7 and about 20 IU/dL, about 8 and about 20 IU/dL, about 9 and about 20 IU/dL, or about 10 and about 20 IU/dL. Treatment or treating of a disease or condition can also include maintaining FIX activity in a subject at a level comparable to at least about 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 11%, 12%, 13%, 14%, 15%, 16%, 17%, 18%, 19%, or 20% of the FIX activity in a non-hemophiliac subject. The minimum trough level required for treatment can be measured by one or more known methods and can be adjusted (increased or decreased) for each person.

[0077] Hemostatic disorder, as used herein, means a genetically inherited or acquired condition characterized by a tendency to hemorrhage, either spontaneously or as a result of trauma, due to an impaired ability or inability to form a fibrin clot. Examples of such disorders include the hemophilias. The three main forms are hemophilia A (Factor VIII deficiency), hemophilia B (Factor IX deficiency or "Christmas disease") and hemophilia C (Factor XI deficiency, mild bleeding tendency). Other hemostatic disorders include, *e.g.,* Von Willebrand disease, Factor XI deficiency (PTA deficiency), Factor XII deficiency, deficiencies or structural abnormalities in fibrinogen, prothrombin, Factor V, Factor VII, Factor X or Factor XIII, Bernard-Soulier syndrome, which is a defect or deficiency in GPIb. GPIb, the receptor for VWF, can be defective and lead to lack of primary clot formation (primary hemostasis) and increased bleeding tendency), and thrombasthenia of Glanzman and Naegeli (Glanzmann thrombasthenia). In liver failure (acute and chronic forms), there is insufficient production of coagulation factors by the liver; this may increase bleeding risk.

[0078] As used herein the term "acute bleeding" refers to a bleeding episode regardless of the underlying cause. For example, a subject may have trauma, uremia, a hereditary bleeding disorder (*e.g.,* Factor VII deficiency) a platelet disorder, or resistance owing to the development of antibodies to clotting factors.

II. FIX FUSION PROTEINS

[0079] The present invention is directed to a FIX fusion protein comprising a FIX polypeptide and at least one heterologous moiety inserted within the FIX polypeptide, fused to the C-terminus of the FIX polypeptide, or both. The FIX fusion protein, after the insertion of or the fusion to the heterologous moiety, can retain one or more FIX

activities. In one embodiment, the FIX activity is a procoagulant activity. The term "procoagulant activity" is meant the ability of the FIX protein of the invention to participate in the clotting cascade in blood, substituting for native FIX. For example, a recombinant FIX protein of the invention has procoagulant activity when it can convert Factor X (FX) to activated Factor X (FXa) in the presence of Factor VIII (FVIII), as tested, *e.g.*, in a chromogenic assay. In another embodiment, the FIX activity is an ability to generate a tenase complex. In other embodiments, the FIX activity is an ability to generate thrombin (or a clot).

[0080] A recombinant FIX protein of the invention need not exhibit 100% of the procoagulant activity of native mature human FIX. In fact, in certain aspects a heterologous moiety inserted into a FIX polypeptide of the invention can increase the half-life or stability of the protein significantly, such that lower activity is perfectly acceptable. Thus, in certain aspects, a FIX fusion protein of the invention has at least about 10%, about 20%, about 30%, about 40%, about 50%, about 60%, about 70%, about 80%, about 90% or about 100% of the procoagulant activity of native FIX. However in some invention embodiments, the , recombinant FIX protein of the invention could have greater than 100% of native FIX activity for proteins containing the FIX Padua R338L high activity variant, for example, at least about 105%, 110%, 120%, 130%, 140%, 150%, 160%, 170%, 180%, 190% or 200% or more of that activity.

[0081] Procoagulant activity can be measured by any suitable *in vitro* or *in vivo* assay. The activity of FIX can be measured either downstream of the coagulation cascade by monitoring the generation of a clot (clotting assays), or upstream by measuring directly the enzymatic activity of FX following activation by the FVIII-FIX complex (chromogenic assays) (see, *e.g.*, Barrowcliffe *et al.*, *Semin. Thromb. Haemost.* 28: 247-56 (2002); Lee *et al.*, *Thromb. Haemost.* 82: 1644-47 (1999); Lippi *et al.*, *Clin. Chem. Lab. Med.* 45: 2-12 (2007); Matsumoto *et al.*, *J. Thromb. Haemost.* 4: 377-84 (2006)). Thus, procoagulant activity can be measured using a chromogenic substrate assay, a clotting assay (*e.g.*, a one stage or a two stage clotting assay), or both. The chromogenic assay mechanism is based on the principles of the blood coagulation cascade, where activated FIX converts FX into FX_a in the presence of FVIII, phospholipids and calcium ions. The FX_a activity is assessed by hydrolysis of a p-nitroanilide (pNA) substrate specific to FX_a. The initial rate of release of p-nitroaniline measured at 405 nM is directly proportional to the FX_a activity and thus

to the FIX activity in the sample. The chromogenic assay is recommended by the Factor VIII and Factor IX Subcommittee of the Scientific and Standardization Committee (SSC) of the International Society on Thrombosis and Hemostasis (ISTH).

[0082] Other suitable assays useful to determine pro-coagulant activity include those disclosed, *e.g.*, in U.S. Application Publication No. 2010/0022445 to Scheiflinger and Dockal, which is incorporated herein by reference in its entirety.

[0083] In certain aspects the procoagulant activity of a recombinant FIX protein of the invention is compared to native mature FIX, in certain aspects it is compared to an international standard.

[0084] The at least one heterologous moiety, as described in more detail below, can comprise any heterologous moiety or can be a moiety that can provide an improved property to the FIX protein. For example, in one aspect, a heterologous moiety useful for the invention can be a moiety that is capable of extending a half-life of the FIX protein or a moiety that is capable of improving stability of the FIX protein. The FIX fusion protein of the invention can have more than one heterologous moieties inserted in or fused to the FIX polypeptide. In one embodiment, the more than one heterologous moieties are identical. In another embodiments, the more than one heterologous moieties are different. In other embodiments, the heterologous moiety is selected from the group consisting of an XTEN, an albumin, an albumin binding peptide, an albumin small binding molecule, an Fc domain, an FcRn binding partner, a PAS, a CTP, a PEG, an HES, a PSA, or any combination thereof.

[0085] In some embodiments, at least one heterologous moiety is inserted within a domain of the FIX polypeptide, but not between the domains. A FIX polypeptide comprises multiple domains, *e.g.*, a γ-carboxyglutamic acid (GLA) domain, an epidermal growth factor-like 1 (EGF1) domain, an epidermal growth factor-like 2 (EGF2) domain, an activation peptide (AP) domain, a linker between the EGF2 domain and the AP domain, and a catalytic domain (*e.g.*, a serine protease domain). A FIX zymogen comprises 461 amino acids: amino acids 1-28 (corresponding to SEQ ID NO: 3) is a signal peptide; amino acids 29-46 (corresponding to SEQ ID NO: 3) is a propeptide; followed by the 415 amino acid FIX protein sequence. This 415 processed FIX comprises amino acids 1-145 (corresponding to SEQ ID NO: 1 or SEQ ID NO: 2) is a FIX light chain; amino acids 146-180 is an activation peptide; and amino acids 181 to 415 (corresponding to SEQ ID NO: 1 or SEQ ID NO: 2) is the catalytic FIX heavy chain. Within the light and heavy chains, the GLA domain

corresponds to amino acids 1 to 46 of SEQ ID NO: 1 or SEQ ID NO: 2; the EGF1 domain corresponds to amino acids 47 to 84 of SEQ ID NO: 1 or SEQ ID NO: 2; the EGF2 domain corresponds to amino acids 85 to 127 of SEQ ID NO: 1 or SEQ ID NO: 2; the linker between the EGF2 domain and the AP domain corresponds to amino acids 128 to 145 of SEQ ID NO: 1 or SEQ ID NO: 2; the AP domain corresponds to amino acids 146 to 180 of SEQ ID NO: 1 or SEQ ID NO: 2; and the catalytic domain corresponds to amino acids 181 to 415 of SEQ ID NO: 1 or SEQ ID NO: 2

[0086] In certain embodiments, at least one heterologous moiety is inserted within one or more domains of a FIX polypeptide. For example, at least one heterologous moiety, *e.g.*, XTEN, can be inserted within a domain selected from the group consisting of the GLA domain, the EGF1 domain, the EGF2 domain, the AP domain, the linker between the EGF2 domain and the AP domain, the catalytic domain, and any combination thereof. In one particular embodiment, the at least one heterologous moiety, *e.g.*, XTEN, is inserted within the GLA domain, *e.g.*, amino acids 1 to 46 of SEQ ID NO: 1 or SEQ ID NO: 2. In one particular embodiment, the at least one heterologous moiety, *e.g.*, XTEN, is inserted within the EGF1 domain, *e.g.*, amino acids 47 to 83 of SEQ ID NO: 1 or SEQ ID NO: 2. In one particular embodiment, the at least one heterologous moiety, *e.g.*, XTEN, is inserted within the EGF2 domain, *e.g.*, amino acids 84 to 125 of SEQ ID NO: 1 or SEQ ID NO: 2. In some embodiments, the at least one heterologous moiety, *e.g.*, XTEN, is inserted within the linker between the EGF2 domain and the AP domain, *e.g.*, amino acids 132 to 145 of SEQ ID NO: 1 or SEQ ID NO: 2. In one particular embodiment, the at least one heterologous moiety, *e.g.*, XTEN, is inserted within the AP domain, *e.g.*, amino acids 146 to 180 of SEQ ID NO: 1 or SEQ ID NO: 2. In some embodiments, the at least one heterologous moiety, *e.g.*, XTEN, is inserted within the catalytic domain, *e.g.*, amino acids 181 to 415 of SEQ ID NO: 1 or SEQ ID NO: 2.

[0087] In some embodiments, one or more heterologous moieties can be inserted within various insertion sites. In certain embodiments, the insertions of at least one heterologous moiety, *e.g.*, an XTEN, at one or more of these sites do not result in a loss of FIX activity and/or induce an improved property of the FIX protein. For example, at least one heterologous moiety can be inserted within the FIX polypeptide at an insertion site corresponding to an amino acid selected from the group consisting of amino acid 103 of SEQ ID NO: 2 (*i.e.*, immediately downstream of an amino acid corresponding to amino acid 103 of SEQ ID NO: 2), amino acid 105 of SEQ ID NO:

2 (*i.e.*, immediately downstream of an amino acid corresponding to amino acid 105 of SEQ ID NO: 2), amino acid 142 of SEQ ID NO: 2 (*i.e.*, immediately downstream of an amino acid corresponding to amino acid 142 of SEQ ID NO: 2), amino acid 149 of SEQ ID NO: 2 (*i.e.*, immediately downstream of an amino acid corresponding to amino acid 149 of SEQ ID NO: 2), amino acid 162 of SEQ ID NO: 2 (*i.e.*, immediately downstream of an amino acid corresponding to amino acid 162 of SEQ ID NO: 2), amino acid 166 of SEQ ID NO: 2 (*i.e.*, immediately downstream of an amino acid corresponding to amino acid 166 of SEQ ID NO: 2), amino acid 174 of SEQ ID NO: 2 (*i.e.*, immediately downstream of an amino acid corresponding to amino acid 174 of SEQ ID NO: 2), amino acid 224 of SEQ ID NO: 2 (*i.e.*, immediately downstream of an amino acid corresponding to amino acid 224 of SEQ ID NO: 2), amino acid 226 of SEQ ID NO: 2 (*i.e.*, immediately downstream of an amino acid corresponding to amino acid 226 of SEQ ID NO: 2), amino acid 228 of SEQ ID NO: 2 (*i.e.*, immediately downstream of an amino acid corresponding to amino acid 228 of SEQ ID NO: 2), amino acid 413 of SEQ ID NO: 2 (*i.e.*, immediately downstream of an amino acid corresponding to amino acid 413 of SEQ ID NO: 2) and any combination thereof, wherein the FIX fusion protein exhibits procoagulant activity.

[0088] In one embodiment, the heterologous moiety, *e.g.*, XTEN, is inserted within the FIX polypeptide at an insertion site corresponding to an amino acid selected from the group consisting of amino acid 149 of SEQ ID NO: 1 or SEQ ID NO: 2, amino acid 162 of SEQ ID NO: 1 or SEQ ID NO: 2, amino acid 166 of SEQ ID NO: 1 or SEQ ID NO: 2, amino acid 174 of SEQ ID NO: 1 or SEQ ID NO: 2 and any combination thereof. In another embodiment, the heterologous moiety, *e.g.*, XTEN, is inserted within the FIX polypeptide at an insertion site corresponding to an amino acid selected from the group consisting of amino acid 224 of SEQ ID NO: 1 or SEQ ID NO: 2, amino acid 226 of SEQ ID NO: 1 or SEQ ID NO: 2, amino acid 228 of SEQ ID NO: 1 or SEQ ID NO: 2, amino acid 413 of SEQ ID NO: 1 or SEQ ID NO: 2, and any combination thereof. In other embodiments, the heterologous moiety, *e.g.*, XTEN, is inserted within the FIX polypeptide at an insertion site corresponding to an amino acid selected from the group consisting of amino acid 103 of SEQ ID NO: 1 or SEQ ID NO: 2, amino acid 105 of SEQ ID NO: 1 or SEQ ID NO: 2, and both. In another embodiment, the heterologous moiety, *e.g.*, XTEN, is inserted within the FIX

polypeptide at an insertion site corresponding to amino acid 142 of SEQ ID NO: 1 or SEQ ID NO: 2.

[0089] As discussed in more detail below, the heterologous moiety can be an XTEN, which can be of varying lengths. For example, the XTEN can comprise at least about 42 amino acids, at least about 72 amino acids, at least about 144 amino acids, at least about 288 amino acids, or at least about 864 amino acids. In some embodiments, the XTEN is selected from the group consisting of AE42, AG42, AE72, AG72, AE144, AG144, AE288, AG288, AE864, and AG864. Non-limiting examples of the XTENs that can be inserted in or fused to a FIX polypeptide are included elsewhere herein.

[0090] In some embodiments, an XTEN comprising 42 amino acids, *e.g.*, AE42 or AG42, is inserted within the FIX polypeptide at an insertion site corresponding to an amino acid selected from the group consisting of amino acid 103 of SEQ ID NO: 1 or 2, amino acid 105 of SEQ ID NO: 1 or 2, amino acid 142 of SEQ ID NO: 1 or 2, amino acid 149 of SEQ ID NO: 1 or 2, amino acid 162 of SEQ ID NO: 1 or 2, amino acid 166 of SEQ ID NO: 1 or 2, amino acid 174 of SEQ ID NO: 1 or 2, amino acid 224 of SEQ ID NO: 1 or 2, amino acid 226 of SEQ ID NO: 1 or 2, amino acid 228 of SEQ ID NO: 1 or 2, amino acid 413 of SEQ ID NO: 1 or 2 and any combination thereof, wherein the FIX fusion protein exhibits procoagulant activity.

[0091] In some embodiments, an XTEN comprising 72 amino acids, *e.g.*, AE72 or AG72, is inserted within the FIX polypeptide at an insertion site corresponding to an amino acid selected from the group consisting of amino acid 149 of SEQ ID NO: 1 or 2, amino acid 162 of SEQ ID NO: 1 or 2, amino acid 166 of SEQ ID NO: 1 or 2, amino acid 174 of SEQ ID NO: 1 or 2, amino acid 224 of SEQ ID NO: 1 or 2, amino acid 226 of SEQ ID NO: 1 or 2, amino acid 228 of SEQ ID NO: 1 or 2, amino acid 413 of SEQ ID NO: 1 or 2 and any combination thereof, or the XTEN is fused to the C-terminus, wherein the FIX fusion protein exhibits procoagulant activity.

[0092] In some embodiments, an XTEN comprising 144 amino acids, *e.g.*, AE144 or AG144, is inserted within the FIX polypeptide at an insertion site corresponding to an amino acid selected from the group consisting of amino acid 149 of SEQ ID NO: 1 or 2, amino acid 162 of SEQ ID NO: 1 or 2, amino acid 166 of SEQ ID NO: 1 or 2, amino acid 174 of SEQ ID NO: 1 or 2, amino acid 224 of SEQ ID NO: 1 or 2, amino acid 226 of SEQ ID NO: 1 or 2, amino acid 228 of SEQ ID NO: 1 or 2,amino acid 413 of SEQ ID NO: 1 or 2 and any combination thereof, wherein the FIX fusion protein exhibits procoagulant activity.

[0093] In some embodiments, an XTEN comprising 288 amino acids, *e.g.*, AE288 or AG288, is inserted within the FIX polypeptide at an insertion site corresponding to an amino acid selected from the group consisting of amino acid 149 of SEQ ID NO: 1 or 2, amino acid 162 of SEQ ID NO: 1 or 2, amino acid 166 of SEQ ID NO: 1 or 2, amino acid 174 of SEQ ID NO: 1 or 2, amino acid 224 of SEQ ID NO: 1 or 2, amino acid 226 of SEQ ID NO: 1 or 2, amino acid 228 of SEQ ID NO: 1 or 2, amino acid 413 of SEQ ID NO: 1 or 2 and any combination thereof, wherein the FIX fusion protein exhibits procoagulant activity.

[0094] In still other embodiments, an XTEN comprising 864 amino acids, *e.g.*, AE864 or AG8648, is inserted within the FIX polypeptide at an insertion site corresponding to an amino acid selected from the group consisting of amino acid 149 of SEQ ID NO: 1 or 2, amino acid 162 of SEQ ID NO: 1 or 2, amino acid 166 of SEQ ID NO: 1 or 2, amino acid 174 of SEQ ID NO: 1 or 2, amino acid 224 of SEQ ID NO: 1 or 2, amino acid 224 of SEQ ID NO: 1 or 2, amino acid 226 of SEQ ID NO: 1 or 2, amino acid 228 of SEQ ID NO: 1 or 2, amino acid 413 of SEQ ID NO: 1 or 2 and any combination thereof, wherein the FIX fusion protein exhibits procoagulant activity.

[0095] The FIX fusion protein of the present invention can further comprise a second heterologous moiety, *e.g.*, a second XTEN, inserted within the FIX, fused to the C-terminus of the FIX, or both. The second heterologous moiety can be inserted within the FIX polypeptide at an insertion site corresponding to an amino acid selected from the group consisting of amino acid 103 of SEQ ID NO: 1 or 2, amino acid 105 of SEQ ID NO: 1 or 2, amino acid 142 of SEQ ID NO: 1 or 2, amino acid 149 of SEQ ID NO: 1 or 2, amino acid 162 of SEQ ID NO: 1 or 2, amino acid 166 of SEQ ID NO: 1 or 2, amino acid 174 of SEQ ID NO: 1 or 2, amino acid 224 of SEQ ID NO: 1 or 2, amino acid 226 of SEQ ID NO: 1 or 2, amino acid 228 of SEQ ID NO: 1 or 2, amino acid 413 of SEQ ID NO: 1 or 2, and any combination thereof or wherein the second XTEN is fused to the C-terminus of the FIX polypeptide. In some embodiments, the first XTEN and the second XTEN are inserted within the FIX polypeptide at insertion sites corresponding to an amino acid of SEQ ID NO: 1 or 2 and/or fused to the C-terminus of the FIX polypeptide selected from the group consisting of amino acid 105 of SEQ ID NO: 1 or 2 and amino acid 166 of SEQ ID NO: 1 or 2; amino acid 105 of SEQ ID NO: 1 or 2 and amino acid 224 of SEQ ID NO: 1 or 2; amino acid 105 of SEQ ID NO: 1 or 2 and fused to the C-terminus; amino acid 166 of SEQ ID NO: 1 or 2 and amino acid 224 of SEQ ID NO: 1 or 2; amino acid 166 of SEQ ID NO: 1 or 2 and

fused to the C-terminus; and amino acid 224 of SEQ ID NO: 1 or 2 and fused to the C-terminus, respectively. In one embodiment, the first XTEN is inserted within the FIX polypeptide at an insertion site corresponding to amino acid 166 of SEQ ID NO: 1 or 2, and the second XTEN is fused to the C-terminus of the FIX polypeptide.

[0096] The second XTEN can comprise at least about 6 amino acids, at least about 12 amino acids, at least about 36 amino acids, at least about 42 amino acids, at least about 72 amino acids, at least about 144 amino acids, or at least about 288 amino acids. In some embodiments, the second XTEN comprises 6 amino acids, 12 amino acids, 36 amino acids, 42 amino acids, 72 amino acids, 144 amino acids, or 288 amino acids. The second XTEN can be selected from the group consisting of AE42, AE72, AE864, AE576, AE288, AE144, AG864, AG576, AG288, AG144, and any combination thereof. In one particular embodiment, the second XTEN is AE72 or AE144.

[0097] In one particular embodiment, the second XTEN comprises an amino acid sequence at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, at least about 99%, or about 100% identical to an amino acid sequence selected from the group consisting of SEQ ID NOs: 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, and any combination thereof.

[0098] In some embodiments, the FIX fusion protein further comprises a third, a fourth, a fifth, and/or a sixth XTEN.

[0099] In some embodiments, the FIX fusion protein comprises an amino acid sequence at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, at least about 99%, or about 100% identical to a sequence selected from the group consisting of SEQ ID NO: 54 to SEQ ID NO: 153 without the signal peptide and the propeptide sequence. In certain embodiments, the FIX fusion protein comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 54 to SEQ ID NO: 153 without the signal peptide and the propeptide sequence. In one embodiment, the FIX fusion protein comprises an amino acid sequence at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, at least about 99%, or about 100% identical to a sequence selected from the group consisting of SEQ ID NOs: 119, 120, 121, and 123 without the signal peptide and the propeptide sequence. In another embodiment, the FIX fusion protein

comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 119, 120, 123, 121 and 226 or 122 without the signal peptide and the propeptide sequence. In some embodiments, the FIX fusion protein is selected from group consisting of FIX-AP.72, FIX-AP.144, FIX-CT.72, FIX-CT.144, FIX-AP.288, and FIX-CT.288 without the signal peptide and the propeptide sequence.

[0100] In some embodiments, the FIX fusion protein comprises two different types of heterologous moieties. In some embodiments, the FIX fusion protein comprises a FIX polypeptide, an XTEN, and an Fc domain (or an FcRn binding partner) or a fragment thereof. In some embodiments, the XTEN is inserted within the FIX, and the Fc domain (or an FcRn binding partner) or a fragment thereof is fused to the C-terminus of the FIX. In some embodiments, the XTEN is inserted within the FIX polypeptide at one or more insertion sites selected from the insertion sites listed in table 3. In one embodiment, the XTEN is inserted within the FIX polypeptide at an insertion site corresponding to an amino acid selected from the group consisting of amino acid 103 of SEQ ID NO: 1 or 2, amino acid 105 of SEQ ID NO: 1 or 2, amino acid 142 of SEQ ID NO: 1 or 2, amino acid 149 of SEQ ID NO: 1 or 2, amino acid 162 of SEQ ID NO: 1 or 2, amino acid 166 of SEQ ID NO: 1 or 2, amino acid 174 of SEQ ID NO: 1 or 2, amino acid 224 of SEQ ID NO: 1 or 2, amino acid 226 of SEQ ID NO: 1 or 2, amino acid 228 of SEQ ID NO: 1 or 2, and amino acid 413 of SEQ ID NO: 1 or 2; and the Fc domain (or an FcRn binding partner) or a fragment thereof is fused to the C-terminus of the FIX. In certain embodiments, the XTEN is inserted within the FIX polypeptide at an insertion site corresponding to an amino acid selected from the group consisting of amino acid 105 of SEQ ID NO: 1 or 2, amino acid 166 of SEQ ID NO: 1 or 2, and amino acid 224 of SEQ ID NO: 1 or 2; and the Fc domain (or an FcRn binding partner) or a fragment thereof is fused to the C-terminus of the FIX. In some embodiments, the XTEN is selected from AE42, AE72, and AE144.

[0101] In certain aspects of the invention, the FIX fusion protein comprises one or two polypeptide chains. In one embodiment, the FIX fusion protein comprises two polypeptide chains, wherein the first polypeptide chain comprises the FIX polypeptide fused to an Fc domain (or an FcRn binding partner), and the second polypeptide chain comprises a second Fc domain, wherein the first Fc domain (or an FcRn binding partner) and the second Fc domain (or an FcRn binding partner) are associated by a covalent bond.

[0102] In another embodiment, the FIX fusion protein comprises a single polypeptide chain comprising a FIX polypeptide and an Fc domain (or an FcRn binding partner). In one particular embodiment, the FIX fusion protein further comprises a linker, which links the FIX polypeptide and the Fc domain (or an FcRn binding partner). In another embodiment, the FIX fusion protein comprises a FIX polypeptide, an Fc domain, and a second Fc domain (or an FcRn binding partner). In one particular embodiment, the FIX fusion protein further comprises a linker, which links the Fc domain (or an FcRn binding partner) and the second Fc domain (or an FcRn binding partner). In another embodiment, the FIX fusion protein comprises a FIX polypeptide, an Fc domain (or an FcRn binding partner), and a second Fc domain (or an FcRn binding partner), wherein the FIX polypeptide is linked to the Fc domain (or an FcRn binding partner) by a linker. In another embodiment, the FIX fusion protein comprises a FIX polypeptide, an Fc domain (or an FcRn binding partner), and a second Fc domain (or an FcRn binding partner), wherein the FIX polypeptide is linked to the Fc domain (or an FcRn binding partner) by a first linker, and wherein the Fc domain (or an FcRn binding partner) is linked to the second Fc domain (or an FcRn binding partner) by a linker. In certain embodiments, the FIX fusion protein comprises a formula selected from the group consisting of:

(i) FIX(X)-F1;
(ii) FIX(X)-L1-F1;
(iii) FIX(X)-F1-F2;
(iv) FIX(X)-L1-F1-F2;
(v) FIX(X)-L1-F1-L2-F2;
(vi) FIX(X)-F1-L1-F2;
(vii) FIX(X)-F1:F2;
(viii) FIX(X)-L1-F1:F2; and
(ix) any combination thereof,

wherein FIX(X) is a FIX polypeptide having an XTEN inserted one or more insertion sites described herein; each of L1 and L2 is a linker; F1 is an Fc domain or an FcRn binding partner; F2 is a second Fc domain or a second FcRn binding partner, (-) is a peptide bond or one or more amino acids; and (:) is a covalent bond, *e.g.*, a disulfide bond.

[0103] The linkers (L1 and L2) can be the same or different. The linker can be cleavable or non-cleavable, and the linker can comprise one or more intracellular

processing sites. Non-limiting examples of the linkers are described elsewhere herein. Any of the linkers can be used to combine FIX with a heterologous moiety (*e.g.*, XTEN or Fc) or a first heterologous moiety (*e.g.*, first Fc) with a second heterologous moiety (*e.g.*, second Fc)

[0104] In certain embodiments, the linker comprises a thrombin cleavage site. In one particular embodiment, the thrombin cleavage site comprises XVPR, wherein X is any aliphatic amino acid (*e.g.*, glycine, alanine, valine, leucine, or isoleucine). In one particular embodiment, the thrombin cleave site comprises LVPR. In some embodiments, the linker comprises a PAR1 exosite interaction motif, which comprises SFLLRN (SEQ ID NO: 190). In some embodiments, the PAR1 exosite interaction motif further comprises an amino acid sequence selected from P, PN, PND, PNDK (SEQ ID NO: 191), PNDKY (SEQ ID NO: 192), PNDKYE (SEQ ID NO: 193), PNDKYEP (SEQ ID NO: 194), PNDKYEPF (SEQ ID NO: 195), PNDKYEPFW (SEQ ID NO: 196), PNDKYEPFWE (SEQ ID NO: 197), PNDKYEPFWED (SEQ ID NO: 198), PNDKYEPFWEDE (SEQ ID NO: 199), PNDKYEPFWEDEE (SEQ ID NO: 200), PNDKYEPFWEDEES (SEQ ID NO: 201), or any combination thereof. In other embodiments the linker comprises the FXIa cleavage site LDPR.

[0105] In one particular embodiment, the FIX fusion protein comprises a FIX polypeptide and a heterologous moiety, which comprises an XTEN, wherein the XTEN is fused with or without a linker, which linker may or may not be cleavable, to the C-terminus of the FIX polypeptide and comprises an amino acid sequence of longer than 42 amino acids and shorter than 864 amino acids in length, preferably shorter than 144 amino acids in length. The XTEN can comprise an amino acid sequence of longer than 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, or 71 amino acids and shorter than 140, 139, 138, 137, 136, 135, 134, 133, 132, 131, 130, 129, 128, 127, 126, 125, 124, 123, 122, 121, 120, 119, 118, 117, 116, 115, 114, 113, 112, 111, 110, 109, 108, 107, 106, 105, 104, 103, 102, 101, 100, 99, 98, 97, 96, 95, 94, 93, 92, 91, 90, 89, 88, 87, 86, 85, 84, 83, 82, 81, 80, 79, 78, 76, 75, 74, or 73 etc, amino acids or any combination thereof. In some embodiments, the XTEN is 72 amino acids in length. In one particular embodiment, the XTEN is AE72. In another embodiment, the XTEN comprises an amino acid sequence at least about 80%, at least about 85%, at least

about 90%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, at least about 99%, or 100% identical to SEQ ID NO: 35.

[0106] In some embodiments, the FIX fusion protein comprises a FIX polypeptide that contains at least one inserted XTEN sequence and a heterologous moiety comprising an XTEN, wherein the XTEN is fused with or without a linker, which linker may or may not be cleavable, to the C-terminus of the FIX polypeptide. In some embodiments, the XTEN is shorter than 864 amino acids in length, preferably shorter than 144 amino acids in length. In other embodiments, the XTEN comprises an amino acid sequence of shorter than 244, 140, 130, 120, 110, 100, 90, 80, or 75 amino acids in length.

[0107] In other embodiments, the FIX fusion protein comprises a formula selected from the group consisting of:

(i) FIX-X

(ii) FIX-L1-X

(iii) FIX(X)-X

(iv) FIX(X)-L1-X

(v) FIX(X)-L1:X

(vi) any combination thereof,

wherein FIX is a FIX polypeptide; FIX(X) is a FIX polypeptide having at least one XTEN inserted into one or more insertion sites described herein; (X) is an XTEN which is longer than 42 amino acids and shorter than 144 amino acids; X is an XTEN which is longer than 42 amino acids and shorter than 864 amino acids such as 288 amino acids, preferably shorter than 144 amino acids (e.g., an XTEN with 72 amino acids); L1 is a linker; (-) is a peptide bond or one or more amino acids; and (:) is a covalent bond, *e.g.,* a disulfide bond.

[0108] The linker (L1) can be the same or different. The linker can be cleavable or non-cleavable as needed, and the linker can comprise one or more intracellular processing sites. Non-limiting examples of the linkers are described elsewhere herein. Any of the linkers can be used to combine FIX with a heterologous moiety (*e.g.,* XTEN or Fc).The following are non-limiting examples of linkers that are suitable for many invention embodiments:

a) GPEGPS**KLTRAET**GAGSPGAETAEQKLISEEDLSPATGHHHHHHHH (SEQ ID NO: 219, Thrombin);

b) GAGSPGAE**TALVPR**GAGSPGAETAG (SEQ ID NO: 220, Thrombin-PAR1);

c) GAGSPGAETA**LVPRSFLLRNPNDKYEPFWEDEE**SGAGSPGAETA (SEQ ID NO: 221);

d) GPEGPS**KLTRAET**GAGSPGAETA (SEQ ID NO: 222)

e) GGGGA**LRPRV**VGGAGSPGAETA (SEQ ID NO: 223)

f) GGGGT**LDPRSFLLRNPNDKYEPFWEDEE**KGGAGSPGAETA (SEQ ID NO: 224)

g) GGAGSPGAETA (SEQ ID NO: 225)

[0109] In certain other embodiments, the linker comprises a thrombin cleavage site. In one particular embodiment, the thrombin cleavage site comprises XVPR, wherein X is any aliphatic amino acid (*e.g.*, glycine, alanine, valine, leucine, or isoleucine). In one particular embodiment, the thrombin cleave site comprises LVPR.. In some embodiments, the linker comprises a PAR1 exosite interaction motif, which comprises SFLLRN (SEQ ID NO: 190). In some embodiments, the PAR1 exosite interaction motif further comprises an amino acid sequence selected from P, PN, PND, PNDK (SEQ ID NO: 191), PNDKY (SEQ ID NO: 192), PNDKYE (SEQ ID NO: 193), PNDKYEP (SEQ ID NO: 194), PNDKYEPF (SEQ ID NO: 195), PNDKYEPFW (SEQ ID NO: 196), PNDKYEPFWE (SEQ ID NO: 197), PNDKYEPFWED (SEQ ID NO: 198), PNDKYEPFWEDE (SEQ ID NO: 199), PNDKYEPFWEDEE (SEQ ID NO: 200), PNDKYEPFWEDEES (SEQ ID NO: 201), or any combination thereof. In certain other embodiment the linker comprises a FXIa cleavage site comprising LDPR, which can be combined with the PAR1 exosite interaction motif.

[0110] In certain embodiments, the FIX polypeptide fused to an XTEN at the C-terminus can further comprise a second XTEN. The second XTEN can be fused to or inserted in any part of the FIX fusion protein, including but not limited to the insertion sites disclosed herein. The FIX fusion protein can further comprise a third XTEN, a fourth XTEN, a fifth XTEN, or a sixth XTEN.

[0111] The FIX fusion protein of the present invention maintains a level of activity compared to native FIX. In some embodiments, the FIX fusion protein has at least about 10%, at least about 20%, at least about 30%, at least about 40%, at least about 50%, at least about 60%, at least about 70%, at least about 80%, at least about 90% or 100% of the procoagulant activity of native FIX. Procoagulant activity can be

measured by any method known in the art, including but not limited to a chromogenic substrate assay, a one stage clotting assay, or both.

II.A. Factor IX

[0112] Human Factor IX (FIX) is a serine protease that is an important component of the intrinsic pathway of the blood coagulation cascade. "Factor IX" or "FIX," as used herein, refers to a coagulation factor protein and species and sequence variants thereof, and includes, but is not limited to, the 461 single-chain amino acid sequence of human FIX precursor polypeptide ("prepro"), the 415 single-chain amino acid sequence of mature human FIX (SEQ ID NO: 1), and the R338L FIX (Padua) variant (SEQ ID NO: 2). FIX includes any form of FIX molecule with the typical characteristics of blood coagulation FIX. As used herein "Factor IX" and "FIX" are intended to encompass polypeptides that comprise the domains Gla (region containing γ-carboxyglutamic acid residues), EGF1 and EGF2 (regions containing sequences homologous to human epidermal growth factor), activation peptide ("AP," formed by residues R136-R180 of the mature FIX), and the C-terminal protease domain ("Pro"), or synonyms of these domains known in the art, or can be a truncated fragment or a sequence variant that retains at least a portion of the biological activity of the native protein. FIX or sequence variants have been cloned, as described in U.S. Patent Nos. 4,770,999 and 7,700,734, and cDNA coding for human Factor IX has been isolated, characterized, and cloned into expression vectors (see, for example, Choo et al., Nature 299:178-180 (1982); Fair et al., Blood 64:194-204 (1984); and Kurachi et al., Proc. Natl. Acad. Sci., U.S.A. 79:6461-6464 (1982)). One particular variant of FIX, the R338L FIX (Padua) variant (SEQ ID NO: 2), characterized by Simioni et al, 2009, comprises a gain-of-function mutation, which correlates with a nearly 8-fold increase in the activity of the Padua variant relative to native FIX (Table 1). FIX variants can also include any FIX polypeptide having one or more conservative amino acid substitutions, which do not affect the FIX activity of the FIX polypeptide.

Table 1: Example FIX Sequences

SEQ ID NO: 1 (mature FIX polypeptide)
1:YNSGKLEEFV QGNLERECME EKCSFEEARE VFENTERTTE FWKQYVDGDQ CESNPCLNGG
61:SCKDDINSYE CWCPFGFEGK NCELDVTCNI KNGRCEQFCK NSADNKVVCS CTEGYRLAEN
121:QKSCEPAVPF PCGRVSVSQT SKLTRAETVF PDVDYVNSTE AETILDNITQ STQSFNDFTR
181:VVGGEDAKPG QFPWQVVLNG KVDAFCGGSI VNEKWIVTAA HCVETGVKIT VVAGEHNIEE
241:TEHTEQKRNV IRIIPHHNYN AAINKYNHDI ALLELDEPLV LNSYVTPICI ADKEYTNIFL

301:KFGSGYVSGW GRVFHKGRSA LVLQYLRVPL VDRATCLRST KFTIYNNMFC AGFHEGGRDS
361:CQGDSGGPHV TEVEGTSFLT GIISWGEECA MKGKYGIYTK VSRYVNWIKE KTKLT
SEQ ID NO: 2 (mature Padua(R338**L**)FIX Polypeptide)
1:YNSGKLEEFV QGNLERECME EKCSFEEARE VFENTERTTE FWKQYVDGDQ CESNPCLNGG
61:SCKDDINSYE CWCPFGFEGK NCELDVTCNI KNGRCEQFCK NSADNKVVCS CTEGYRLAEN
121:QKSCEPAVPF PCGRVSVSQT SKLTRAETVF PDVDYVNSTE AETILDNITQ STQSFNDFTR
181:VVGGEDAKPG QFPWQVVLNG KVDAFCGGSI VNEKWIVTAA HCVETGVKIT VVAGEHNIEE
241:TEHTEQKRNV IRIIPHHNYN AAINKYNHDI ALLELDEPLV LNSYVTPICI ADKEYTNIFL
301:KFGSGYVSGW GRVFHKGRSA LVLQYLRVPL VDRATCL**L**ST KFTIYNNMFC AGFHEGGRDS
361:CQGDSGGPHV TEVEGTSFLT GIISWGEECA MKGKYGIYTK VSRYVNWIKE KTKLT
SEQ ID NO: 3 (FIX Signal Polypeptide and *Propeptide*)
1: MQRVNMIMAE SPGLITICLL GYLLSAEC*TV FLDHENANKI LNRPKR*

[0113] The FIX polypeptide is 55 kDa, synthesized as a prepropolypetide chain (SEQ ID NO: 1) composed of three regions: a signal peptide of 28 amino acids (amino acids 1 to 28 of SEQ ID NO: 3), a propeptide of 18 amino acids (amino acids 29 to 46), which is required for gamma-carboxylation of glutamic acid residues, and a mature Factor IX of 415 amino acids (SEQ ID NO: 1 or 2). The propeptide is an 18-amino acid residue sequence N-terminal to the gamma-carboxyglutamate domain. The propeptide binds vitamin K-dependent gamma carboxylase and then is cleaved from the precursor polypeptide of FIX by an endogenous protease, most likely PACE (paired basic amino acid cleaving enzyme), also known as furin or PCSK3. Without the gamma carboxylation, the Gla domain is unable to bind calcium to assume the correct conformation necessary to anchor the protein to negatively charged phospholipid surfaces, thereby rendering Factor IX nonfunctional. Even if it is carboxylated, the Gla domain also depends on cleavage of the propeptide for proper function, since retained propeptide interferes with conformational changes of the Gla domain necessary for optimal binding to calcium and phospholipid. In humans, the resulting mature Factor IX is secreted by liver cells into the blood stream as an inactive zymogen, a single chain protein of 415 amino acid residues that contains approximately 17% carbohydrate by weight (Schmidt, A. E., et al. (2003) Trends Cardiovasc Med, 13: 39).

[0114] The mature FIX is composed of several domains that in an N- to C-terminus configuration are: a GLA domain, an EGF1 domain, an EGF2 domain, an activation peptide (AP) domain, and a protease (or catalytic) domain. A short linker connects the EGF2 domain with the AP domain. FIX contains two activation peptides formed by R145-A146 and R180-V181, respectively. Following activation, the single-chain FIX becomes a 2-chain molecule, in which the two chains are linked by a disulfide bond. Clotting factors can be engineered by replacing their activation peptides resulting in

altered activation specificity. In mammals, mature FIX must be activated by activated Factor XI to yield Factor IXa. The protease domain provides, upon activation of FIX to FIXa, the catalytic activity of FIX. Activated Factor VIII (FVIIIa) is the specific cofactor for the full expression of FIXa activity.

[0115] In other embodiments, a FIX polypeptide comprises an Thr148 allelic form of plasma derived Factor IX and has structural and functional characteristics similar to endogenous Factor IX.

[0116] A great many functional FIX variants are known. International publication number WO 02/040544 A3 discloses mutants that exhibit increased resistance to inhibition by heparin at page 4, lines 9-30 and page 15, lines 6-31. International publication number WO 03/020764 A2 discloses FIX mutants with reduced T cell immunogenicity in Tables 2 and 3 (on pages 14-24), and at page 12, lines 1-27. International publication number WO 2007/149406 A2 discloses functional mutant FIX molecules that exhibit increased protein stability, increased *in vivo* and *in vitro* half-life, and increased resistance to proteases at page 4, line 1 to page 19, line 11. WO 2007/149406 A2 also discloses chimeric and other variant FIX molecules at page 19, line 12 to page 20, line 9. International publication number WO 08/118507 A2 discloses FIX mutants that exhibit increased clotting activity at page 5, line 14 to page 6, line 5. International publication number WO 09/051717 A2 discloses FIX mutants having an increased number of N-linked and/or O-linked glycosylation sites, which results in an increased half-life and/or recovery at page 9, line 11 to page 20, line 2. International publication number WO 09/137254 A2 also discloses Factor IX mutants with increased numbers of glycosylation sites at page 2, paragraph [006] to page 5, paragraph [011] and page 16, paragraph [044] to page 24, paragraph [057]. International publication number WO 09/130198 A2 discloses functional mutant FIX molecules that have an increased number of glycosylation sites, which result in an increased half-life, at page 4, line 26 to page 12, line 6. International publication number WO 09/140015 A2 discloses functional FIX mutants that an increased number of Cys residues, which can be used for polymer (*e.g.,* PEG) conjugation, at page 11, paragraph [0043] to page 13, paragraph [0053]. The FIX polypeptides described in International Application No. PCT/US2011/043569 filed July 11, 2011 and published as WO 2012/006624 on January 12, 2012 are also incorporated herein by reference in its entirety.

[0117] In addition, hundreds of non-functional mutations in FIX have been identified in hemophilia subjects, many of which are disclosed in Table 5, at pages 11-14 of International publication number WO 09/137254 A2. Such non-functional mutations are not included in the invention, but provide additional guidance for which mutations are more or less likely to result in a functional FIX polypeptide.

[0118] In one embodiment, the FIX polypeptide (or Factor IX portion of a fusion polypeptide) comprises an amino acid sequence at least 70%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the sequence set forth in SEQ ID NO: 1 or 2 (amino acids 1 to 415 of SEQ ID NO: 1 or 2), or alternatively, with a propeptide sequence, or with a propeptide and signal sequence (full length FIX). In another embodiment, the FIX polypeptide comprises an amino acid sequence at least 70%, at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the sequence set forth in SEQ ID NO: 2.

[0119] Factor IX coagulant activity is expressed as International Unit(s) (IU). One IU of FIX activity corresponds approximately to the quantity of FIX in one milliliter of normal human plasma. Several assays are available for measuring Factor IX activity, including the one stage clotting assay (activated partial thromboplastin time; aPTT), thrombin generation time (TGA) and rotational thromboelastometry (ROTEM®). The invention contemplates sequences that have homology to FIX sequences, sequence fragments that are natural, such as from humans, non-human primates, mammals (including domestic animals), and non-natural sequence variants which retain at least a portion of the biologic activity or biological function of FIX and/or that are useful for preventing, treating, mediating, or ameliorating a coagulation factor-related disease, deficiency, disorder or condition (*e.g.*, bleeding episodes related to trauma, surgery, of deficiency of a coagulation factor). Sequences with homology to human FIX can be found by standard homology searching techniques, such as NCBI BLAST.

II.B. Heterologous Moieties

[0120] An FIX fusion protein of the invention can comprise at least one heterologous moiety inserted into one or more sites within the FIX polypeptide, fused to the C-terminus, or both, wherein the FIX fusion protein has procoagulant activity and can be expressed *in vivo* or *in vitro* in a host cell. A "heterologous moiety" can comprise a heterologous polypeptide, or a non-polypeptide moiety, or both. In certain aspects, the

heterologous moiety is an XTEN. In some aspects, a FIX fusion protein of the invention comprises at least one XTEN inserted into one or more sites within the FIX polypeptide. In other aspects, a FIX fusion protein comprises at least one heterologous moiety inserted into one or more sites within the FIX polypeptide, wherein the heterologous moiety is a half-life extending moiety (*e.g.*, an *in vivo* half-life extending moiety).

[0121] It is believed that the discovery of the insertions sites wherein the FIX retains at least some of its procoagulant activity would also permit the insertion of other peptides and polypeptides with either unstructured or structured characteristics that are associated with the prolongation of half-life when fused to a FIX protein in one or more of those same sites. Non-limiting examples of heterologous moieties (*e.g.*, a half-life extending moiety) include albumin, albumin fragments, Fc fragments of immunoglobulins, FcRn binding partners, the C-terminal peptide (CTP) of the β subunit of human chorionic gonadotropin, a HAP sequence, a transferrin, the PAS polypeptides of U.S. Pat Application No. 20100292130, polyglycine linkers, polyserine linkers, peptides and short polypeptides of 6-40 amino acids of two types of amino acids selected from glycine (G), alanine (A), serine (S), threonine (T), glutamate (E) and proline (P) with varying degrees of secondary structure from less than 50% to greater than 50%, amongst others, would be suitable for insertion in the identified active insertions sites of FIX.

[0122] In certain aspects a heterologous moiety increases the *in vivo* or *in vitro* half-life of the FIX fusion protein. In other aspects a heterologous moiety facilitates visualization or localization of the FIX fusion protein. Visualization and/or location of the FIX fusion protein can be *in vivo*, *in vitro*, *ex vivo*, or combinations thereof. In other aspects a heterologous moiety increases stability of the FIX fusion protein. As used herein, the term "stability" refers to an art-recognized measure of the maintenance of one or more physical properties of the FIX fusion protein in response to an environmental condition (*e.g.*, an elevated or lowered temperature). In certain aspects, the physical property is the maintenance of the covalent structure of the FIX fusion protein (*e.g.*, the absence of proteolytic cleavage, unwanted oxidation or deamidation). In other aspects, the physical property can also be the presence of the FIX fusion protein in a properly folded state (*e.g.*, the absence of soluble or insoluble aggregates or precipitates). In one aspect, the stability of the FIX fusion protein is measured by assaying a biophysical property of the FIX fusion protein, for example

thermal stability, pH unfolding profile, stable removal of glycans, solubility, biochemical function (*e.g.*, ability to bind to another protein), etc., and/or combinations thereof. In another aspect, biochemical function is demonstrated by the binding affinity of the interaction. In one aspect, a measure of protein stability is thermal stability, *i.e.*, resistance to thermal challenge. Stability can be measured using methods known in the art, such as, HPLC (high performance liquid chromatography), SEC (size exclusion chromatography), DLS (dynamic light scattering), *etc.* Methods to measure thermal stability include, but are not limited to differential scanning calorimetry (DSC), differential scanning fluorometry (DSF), circular dichroism (CD), and thermal challenge assay.

[0123] In a specific aspect, a heterologous moiety inserted in one or more insertion cites in a FIX fusion protein retains the biochemical activity of the FIX fusion protein. In certain embodiments, the heterologous moiety is an XTEN. In one embodiment, the biochemical activity is FIX activity, which can be measured by chromogenic assay.

[0124] In some embodiments, at least one heterologous moiety is inserted indirectly in an insertion site via linkers located at the N-terminus, the C-terminus, or both the N-terminus and C-terminus of the heterologous moiety. The linkers at the N-terminus and C-terminus of the heterologous moiety can be the same or different. In some embodiments, several linkers can flank one or both termini of the heterologous moiety in tandem. In some embodiments, the linker is "Gly-Ser peptide linker." The term "Gly-Ser peptide linker" refers to a peptide that comprises glycine and serine residues.

[0125] An exemplary Gly/Ser peptide linker includes, but is not limited to, the amino acid sequence $(Gly_4Ser)_n$ (SEQ ID NO:161), wherein n is an integer that is the same or higher than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 46, 50, 55, 60, 70, 80, 90, or 100. In one embodiment, n=1, *i.e.*, the linker is (Gly_4Ser) (SEQ ID NO: 161). In one embodiment, n=2, *i.e.*, the linker is $(Gly_4Ser)_2$ (SEQ ID NO: 162). In another embodiment, n=3, *i.e.*, the linker is $(Gly_4Ser)_3$ (SEQ ID NO: 172). In another embodiment, n=4, *i.e.*, the linker is $(Gly_4Ser)_4$ (SEQ ID NO: 173). In another embodiment, n=5, *i.e.*, the linker is $(Gly_4Ser)_5$ (SEQ ID NO: 174). In yet another embodiment, n=6, *i.e.*, the linker is $(Gly_4Ser)_6$ (SEQ ID NO: 175). In another embodiment, n=7, *i.e.*, the linker is $(Gly_4Ser)_7$ (SEQ ID NO: 176). In yet another embodiment, n=8, *i.e.*, the linker is $(Gly_4Ser)_8$ (SEQ ID NO: 177). In another

embodiment, n=9, *i.e.*, the linker is $(Gly_4Ser)_9$ (SEQ ID NO: 178). In yet another embodiment, n=10, *i.e.*, the linker is $(Gly_4Ser)_{10}$ (SEQ ID NO: 179).

[0126] Another exemplary Gly/Ser peptide linker comprises the amino acid sequence $Ser(Gly_4Ser)_n$ (SEQ ID NO: 180), wherein n is an integer that is the same or higher than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 46, 50, 55, 60, 70, 80, 90, or 100. In one embodiment, n=1, *i.e.*, the linker is $Ser(Gly_4Ser)$ (SEQ ID NO: 180). In one embodiment, n=2, *i.e.*, the linker is $Ser(Gly_4Ser)_2$ (SEQ ID NO: 181). In another embodiment, n=3, *i.e.*, the linker is $Ser(Gly_4Ser)_3$ (SEQ ID NO: 182). In another embodiment, n=4, *i.e.*, the linker is $Ser(Gly_4Ser)_4$ (SEQ ID NO: 183). In another embodiment, n=5, *i.e.*, the linker is $Ser(Gly_4Ser)_5$ (SEQ ID NO: 184). In yet another embodiment, n=6, *i.e.*, the linker is $Ser(Gly_4Ser)_6$ (SEQ ID NO: 185). In yet another embodiment, n=7, *i.e.*, the linker is $Ser(Gly_4Ser)_7$ (SEQ ID NO: 186). In yet another embodiment, n=8, *i.e.*, the linker is $Ser(Gly_4Ser)_8$ (SEQ ID NO: 187). In yet another embodiment, n=9, *i.e.*, the linker is $Ser(Gly_4Ser)_9$ (SEQ ID NO: 188). In yet another embodiment, n=10, *i.e.*, the linker is $Ser(Gly_4Ser)_{10}$ (SEQ ID NO: 189).

[0127] In certain aspects, a FIX fusion protein comprises one heterologous moiety inserted at an insertion site listed in TABLE 7. In other aspects, a FIX fusion protein comprises two heterologous moieties inserted in two insertion sites listed in TABLE 7. In a particular embodiment, the two heterologous moieties are inserted in two insertion sites listed in TABLE 8. In certain aspects, a FIX fusion protein comprises three heterologous moieties inserted in three insertion sites listed in TABLE 7. In certain aspects, a FIX fusion protein comprises four heterologous moieties inserted in four insertion sites listed in TABLE 7. In certain aspects, a FIX fusion protein comprises five heterologous moieties inserted in five insertion sites listed in TABLE 7. In certain aspects, a FIX fusion protein comprises six heterologous moieties inserted in six insertion sites listed in TABLE 7. In some aspects, all the inserted heterologous moieties are identical. In other aspects, at least one of the inserted heterologous moieties is different from the rest of inserted heterologous moieties.

[0128] Fusion of the FIX polypeptide to the at least one heterologous moiety, *e.g.*, XTEN, can affect the physical or chemical properties, *e.g.*, pharmacokinetics, of the fusion protein of the present invention. In a specific embodiment, the heterologous moiety linked to a FIX protein increases at least one pharmacokinetic property, *e.g.*, increased terminal half-life or increased area under the curve (AUC), so that the fusion protein described herein stays *in vivo* for an increased period of time compared

to wild type FIX or a corresponding FIX lacking the heterologous moiety. In further embodiments, the XTEN sequence used in this invention increases at least one pharmacokinetic property, *e.g.*, increased terminal half-life, increased recovery and/or increased bioavailability for subcutaneous dosing, increased area under the curve (AUC), so that FIX protein stays *in vivo* for an increased period of time compared to wild type FIX or a corresponding FIX lacking the heterologous moiety.

[0129] In certain aspects, a heterologous moiety which increases half-life of the FIX fusion protein of the invention comprises, without limitation, a heterologous polypeptide such as albumin, an immunoglobulin Fc region, an XTEN sequence, the C-terminal peptide (CTP) of the β subunit of human chorionic gonadotropin, a PAS sequence, a HAP sequence, a transferrin, albumin-binding moieties, or any fragments, derivatives, variants, or combinations of these polypeptides. In certain aspects the FIX fusion protein of the invention comprises a heterologous polypeptide which increases half-life, wherein the heterologous polypeptide is an XTEN sequence. In other related aspects a heterologous moiety can include an attachment site for a non-polypeptide moiety such as polyethylene glycol (PEG), hydroxyethyl starch (HES), polysialic acid, or any derivatives, variants, or combinations of these moieties.

[0130] In other embodiments, a FIX fusion protein of the invention is conjugated to one or more polymers. The polymer can be water-soluble or non-water-soluble. The polymer can be covalently or non-covalently attached to FIX or to other moieties conjugated to FIX. Non-limiting examples of the polymer can be poly(alkylene oxide), poly(vinyl pyrrolidone), poly(vinyl alcohol), polyoxazoline, or poly(acryloylmorpholine).

[0131] In certain aspects, a FIX fusion protein of the invention comprises one, two, three or more heterologous moieties, which can each be the same or different molecules. In some embodiments, the FIX fusion protein comprises one or more XTENs. In other embodiments, the FIX fusion protein comprises one or more XTENs and one or more Fc domains. In one particular embodiment, the FIX fusion protein can comprise an XTEN inserted within the FIX and an Fc fused to the C-terminus of the FIX.

[0132] The FIX fusion proteins of the present invention can have an increased *in vivo* half-life as compared to native FIX, rFIXFc, or FIX R338L. In some embodiments, the FIX fusion protein can have at least about 1.5 fold, at least about 2-fold, at least about 3-fold, or at least about 4-fold greater *in vivo* half-life as compared to native

FIX lacking the heterologous moiety or as compared to FIX R338L lacking the heterologous moiety. In one particular embodiment, the FIX fusion protein has an *in vivo* half-life more than 2-fold greater than the FIX polypeptide without the heterologous moiety.

[0133] In other embodiments, the FIX fusion protein can have an *in vivo* half-life that is at least about 5 hours, at least about 6 hours, at least about 7 hours, at east about 8 hours, at least about 9 hours, at least about 10 hours, at east about 11 hours, at least about 12 hours, at least about 13 hours, at east about 14 hours, at least about 15 hours, at least about 16 hours, at east about 17 hours, at least about 18 hours, at least about 19 hours, at east about 20 hours, at least about 21 hours, at least about 22 hours, at east about 23 hours, at least about 24 hours, at least about 25 hours, at east about 26 hours, at least about 27 hours, at least about 28 hours, at east about 29 hours, at least about 30 hours, at least about 31 hours, at east about 32 hours, at least about 33 hours, or at least about 34 hours longer than the *in vivo* half-life of a FIX polypeptide lacking a heterologous moiety.

II.B.1. XTENs

[0134] In some embodiments, the at least one heterologous moiety is an XTEN. As used here "XTEN sequence" refers to extended length polypeptides with non-naturally occurring, substantially non-repetitive sequences that are composed mainly of small hydrophilic amino acids, with the sequence having a low degree or no secondary or tertiary structure under physiologic conditions. As a fusion protein partner, XTENs can serve as a carrier, conferring certain desirable pharmacokinetic, physicochemical and pharmaceutical properties when linked to a FIX sequence of the invention to create a fusion protein. Such desirable properties include but are not limited to enhanced pharmacokinetic parameters and solubility characteristics. As used herein, "XTEN" specifically excludes antibodies or antibody fragments such as single-chain antibodies or Fc fragments of a light chain or a heavy chain.

[0135] In certain aspects, a FIX fusion protein of the invention comprises at least one XTEN or fragment, variant, or derivative thereof inserted into the FIX, wherein the FIX fusion protein has procoagulant activity and can be expressed *in vivo* or *in vitro* in a host cell. In certain aspects, two of the heterologous moieties are XTEN sequences. In some aspects, three of the heterologous moieties are XTEN sequences. In some aspects, four of the heterologous moieties are XTEN sequences. In some

aspects, five of the heterologous moieties are XTEN sequences. In some aspects, six or more of the heterologous moieties are XTEN sequences.

[0136] In some embodiments, the XTEN sequence useful for the invention is a peptide or a polypeptide having greater than about 20, 30, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950, 1000, 1200, 1400, 1600, 1800, or 2000 amino acid residues. In certain embodiments, XTEN is a peptide or a polypeptide having greater than about 20 to about 3000 amino acid residues, greater than 30 to about 2500 residues, greater than 40 to about 2000 residues, greater than 50 to about 1500 residues, greater than 60 to about 1000 residues, greater than 70 to about 900 residues, greater than 80 to about 800 residues, greater than 90 to about 700 residues, greater than 100 to about 600 residues, greater than 110 to about 500 residues, or greater than 120 to about 400 residues. In one particular embodiment, the XTEN comprises an amino acid sequence of longer than 42 amino acids and shorter than 144 amino acids in length.

[0137] The XTEN sequence of the invention can comprise one or more sequence motif of 5 to 14 (e.g., 9 to 14) amino acid residues or an amino acid sequence at least 80%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the sequence motif, wherein the motif comprises, consists essentially of, or consists of 4 to 6 types of amino acids (e.g., 5 amino acids) selected from the group consisting of glycine (G), alanine (A), serine (S), threonine (T), glutamate (E) and proline (P). *See* US 2010-0239554 A1.

[0138] In some embodiments, the XTEN comprises non-overlapping sequence motifs in which about 80%, or at least about 85%, or at least about 90%, or about 91%, or about 92%, or about 93%, or about 94%, or about 95%, or about 96%, or about 97%, or about 98%, or about 99% or about 100% of the sequence consists of multiple units of non-overlapping sequences selected from a single motif family selected from Table 2A, resulting in a family sequence. As used herein, "family" means that the XTEN has motifs selected only from a single motif category from Table 2A; *i.e.,* AD, AE, AF, AG, AM, AQ, BC, or BD XTEN, and that any other amino acids in the XTEN not from a family motif are selected to achieve a needed property, such as to permit incorporation of a restriction site by the encoding nucleotides, incorporation of a cleavage sequence, or to achieve a better linkage to FIX. In some embodiments of XTEN families, an XTEN sequence comprises multiple units of non-overlapping sequence motifs of the AD motif family, or of the AE motif family, or of the AF motif

family, or of the AG motif family, or of the AM motif family, or of the AQ motif family, or of the BC family, or of the BD family, with the resulting XTEN exhibiting the range of homology described above. In other embodiments, the XTEN comprises multiple units of motif sequences from two or more of the motif families of Table 2A. These sequences can be selected to achieve desired physical/chemical characteristics, including such properties as net charge, hydrophilicity, lack of secondary structure, or lack of repetitiveness that are conferred by the amino acid composition of the motifs, described more fully below. In the embodiments hereinabove described in this paragraph, the motifs incorporated into the XTEN can be selected and assembled using the methods described herein to achieve an XTEN of about 36 to about 3000 amino acid residues.

Table 2A. XTEN Sequence Motifs of 12 Amino Acids and Motif Families

Motif Family*	MOTIF SEQUENCE	SEQ ID NO:
AD	GESPGGSSGSES	4
AD	GSEGSSGPGESS	5
AD	GSSESGSSEGGP	6
AD	GSGGEPSESGSS	7
AE, AM	GSPAGSPTSTEE	8
AE, AM, AQ	GSEPATSGSETP	9
AE, AM, AQ	GTSESATPESGP	10
AE, AM, AQ	GTSTEPSEGSAP	11
AF, AM	GSTSESPSGTAP	12
AF, AM	GTSTPESGSASP	13
AF, AM	GTSPSGESSTAP	14
AF, AM	GSTSSTAESPGP	15
AG, AM	GTPGSGTASSSP	16
AG, AM	GSSTPSGATGSP	17
AG, AM	GSSPSASTGTGP	18
AG, AM	GASPGTSSTGSP	19
AQ	GEPAGSPTSTSE	20
AQ	GTGEPSSTPASE	21
AQ	GSGPSTESAPTE	22
AQ	GSETPSGPSETA	23
AQ	GPSETSTSEPGA	24
AQ	GSPSEPTEGTSA	25
BC	GSGASEPTSTEP	26
BC	GSEPATSGTEPS	27
BC	GTSEPSTSEPGA	28
BC	GTSTEPSEPGSA	29
BD	GSTAGSETSTEA	30
BD	GSETATSGSETA	31

Motif Family*	MOTIF SEQUENCE	SEQ ID NO:
BD	GTSESATSESGA	32
BD	GTSTEASEGSAS	33

* Denotes individual motif sequences that, when used together in various permutations, results in a "family sequence"

[0139] XTEN can have varying lengths for insertion into or linkage to FIX. In one embodiment, the length of the XTEN sequence(s) is chosen based on the property or function to be achieved in the fusion protein. Depending on the intended property or function, XTEN can be short or intermediate length sequence or longer sequence that can serve as carriers. In certain embodiments, the XTEN includes short segments of about 6 to about 99 amino acid residues, intermediate lengths of about 100 to about 399 amino acid residues, and longer lengths of about 400 to about 1000 and up to about 3000 amino acid residues. Thus, the XTEN inserted into or linked to FIX can have lengths of about 6, about 12, about 36, about 40, about 42, about 72, about 96, about 144, about 288, about 400, about 500, about 576, about 600, about 700, about 800, about 864, about 900, about 1000, about 1500, about 2000, about 2500, or up to about 3000 amino acid residues in length. In other embodiments, the XTEN sequences is about 6 to about 50, about 50 to about 100, about 100 to 150, about 150 to 250, about 250 to 400, about 400 to about 500, about 500 to about 900, about 900 to 1500, about 1500 to 2000, or about 2000 to about 3000 amino acid residues in length. The precise length of an XTEN inserted into or linked to FIX can vary without adversely affecting the activity of the FIX. In one embodiment, one or more of the XTENs used herein have 42 amino acids, 72 amino acids, 144 amino acids, 288 amino acids, 576 amino acids, or 864 amino acids in length and can be selected from one or more of the XTEN family sequences; *i.e.,* AD, AE, AF, AG, AM, AQ, BC or BD.

[0140] In some embodiments, the XTEN sequence used in the invention is at least 60%, 70%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to a sequence selected from the group consisting of AE42, AG42, AE48, AM48, AE72, AG72, AE108, AG108, AE144, AF144, AG144, AE180, AG180, AE216, AG216, AE252, AG252, AE288, AG288, AE324, AG324, AE360, AG360, AE396, AG396, AE432, AG432, AE468, AG468, AE504, AG504, AF504, AE540, AG540, AF540, AD576, AE576, AF576, AG576, AE612, AG612, AE624, AE648, AG648, AG684, AE720, AG720, AE756, AG756, AE792, AG792, AE828,

AG828, AD836, AE864, AF864, AG864, AM875, AE912, AM923, AM1318, BC864, BD864, AE948, AE1044, AE1140, AE1236, AE1332, AE1428, AE1524, AE1620, AE1716, AE1812, AE1908, AE2004A, AG948, AG1044, AG1140, AG1236, AG1332, AG1428, AG1524, AG1620, AG1716, AG1812, AG1908, AG2004, and any combination thereof. *See* US 2010-0239554 A1. In one particular embodiment, the XTEN comprises AE42, AE72, AE144, AE288, AE576, AE864, AG 42, AG72, AG144, AG288, AG576, AG864, or any combination thereof.

[0141] In one embodiment, the XTEN sequence is at least 60%, 70%, 80%, 90%, 95%, 96%, 97%, 98%, 99% or 100% identical to an amino acid sequence selected from the group consisting of AE36 (SEQ ID NO: 217), AE42 (SEQ ID NO: 34), AE72 (SEQ ID NO: 35), AE78 (SEQ ID NO: 218), AE144 (SEQ ID NO: 36), AE144_2A (SEQ ID NO: 37), AE144_3B (SEQ ID NO: 38), AE144_4A (SEQ ID NO: 39), AE144_5A (SEQ ID NO: 40), AE144_6B (SEQ ID NO: 41), AG144 (SEQ ID NO: 42), AG144_A (SEQ ID NO: 43), AG144_B (SEQ ID NO: 44), AG144_C (SEQ ID NO: 45), AG144_F (SEQ ID NO: 46), AE288 (SEQ ID NO: 47), AE288_2 (SEQ ID NO: 48), AG288 (SEQ ID NO: 49), AE576 (SEQ ID NO: 50), AG576 (SEQ ID NO: 51), AE864 (SEQ ID NO: 52), AG864 (SEQ ID NO: 53), XTEN_AE72_2A_1 (SEQ ID NO:202), XTEN_AE72_2A_2 (SEQ ID NO:203), XTEN_AE72_3B_1 (SEQ ID NO:204), XTEN_AE72_3B_2 (SEQ ID NO:205), XTEN_AE72_4A_2 (SEQ ID NO: 206), XTEN_AE72_5A_2 (SEQ ID NO:207), XTEN_AE72_6B_1 (SEQ ID NO: 208), XTEN_AE72_6B_2 (SEQ ID NO:209), XTEN_AE72_1A_1 (SEQ ID NO: 210), XTEN_AE72_1A_2 (SEQ ID NO:211), XTEN_AE144_1A (SEQ ID NO:212), AE150 (SEQ ID NO:213), AG150 (SEQ ID NO:214), AE294 (SEQ ID NO:215), AG294 (SEQ ID NO:216), and any combination thereof.

[0142] In some embodiments, less than 100% of amino acids of an XTEN are selected from glycine (G), alanine (A), serine (S), threonine (T), glutamate (E) and proline (P), or less than 100% of the sequence consists of the sequence motifs from Table 2A or the XTEN sequences of Table 2B. In such embodiments, the remaining amino acid residues of the XTEN are selected from any of the other 14 natural L-amino acids, but can be preferentially selected from hydrophilic amino acids such that the XTEN sequence contains at least about 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or at least about 99% hydrophilic amino acids. The content of hydrophobic amino acids in the XTEN utilized in the conjugation constructs can be

less than 5%, or less than 2%, or less than 1% hydrophobic amino acid content. Hydrophobic residues that are less favored in construction of XTEN include tryptophan, phenylalanine, tyrosine, leucine, isoleucine, valine, and methionine. Additionally, XTEN sequences can contain less than 5% or less than 4% or less than 3% or less than 2% or less than 1% or none of the following amino acids: methionine (for example, to avoid oxidation), or asparagine and glutamine (to avoid desamidation).

[0143] In another embodiment, the XTEN sequence is selected from the group consisting of AE36 (SEQ ID NO: 217), AE42 (SEQ ID NO: 34), AE72 (SEQ ID NO: 35), AE78 (SEQ ID NO: 218), AE144 (SEQ ID NO: 36), AE144_2A (SEQ ID NO: 37), AE144_3B (SEQ ID NO: 38), AE144_4A (SEQ ID NO: 39), AE144_5A (SEQ ID NO: 40), AE144_6B (SEQ ID NO: 41), AG144 (SEQ ID NO: 42), AG144_A (SEQ ID NO: 43), AG144_B (SEQ ID NO: 44), AG144_C (SEQ ID NO: 45), AG144_F (SEQ ID NO: 46), AE288 (SEQ ID NO: 47), AE288_2 (SEQ ID NO: 48), AG288 (SEQ ID NO: 49), AE576 (SEQ ID NO: 50), AG576 (SEQ ID NO: 51), AE864 (SEQ ID NO: 52), AG864 (SEQ ID NO: 53), XTEN_AE72_2A_1 (SEQ ID NO:202), XTEN_AE72_2A_2 (SEQ ID NO:203), XTEN_AE72_3B_1 (SEQ ID NO:204), XTEN_AE72_3B_2 (SEQ ID NO:205), XTEN_AE72_4A_2 (SEQ ID NO:206), XTEN_AE72_5A_2 (SEQ ID NO:207), XTEN_AE72_6B_1 (SEQ ID NO: 208), XTEN_AE72_6B_2 (SEQ ID NO: 209), XTEN_AE72_1A_1 (SEQ ID NO: 210), XTEN_AE72_1A_2 (SEQ ID NO: 211), XTEN_AE144_1A (SEQ ID NO: 212), AE150 (SEQ ID NO: 213), AG150 (SEQ ID NO: 214), AE294 (SEQ ID NO: 215), AG294 (SEQ ID NO:216), and any combinations thereof. In a specific embodiment, the XTEN sequence is selected from the group consisting of AE72, AE144, and AE288. The amino acid sequences for certain XTEN sequences of the invention are shown in Table 2B.

TABLE 2B. XTEN Sequences

XTEN	Amino Acid Sequence
AE36 SEQ ID NO: 217	GSPAGSPTSTEEGTSESATPESGPGSEPATSGSETP
AE42 SEQ ID NO: 34	GAPGSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPASS
AE72 SEQ ID NO: 35	GAPTSESATPESGPGSEPATSGSETPGTSESATPESGPGSEPATSGSETPGTSESATPESGPGTSTEPSEGSAPGASS
AE78	GAPTSESATPESGPGSEPATSGSETPGTSESATPESGPGSEPATSGSETPGTSESATPESGPGTSTEPSEGSAPGASS

SEQ ID NO: 218	
AE144 SEQ ID NO: 36	GSEPATSGSETPGTSESATPESGPGSEPATSGSETPGSPAGSPTSTEEGTSTEP SEGSAPGSEPATSGSETPGSEPATSGSETPGSEPATSGSETPGTSTEPSEGSAP GTSESAPESGPGSEPATSGSETPGTSTEPSEGSAP
AE144_2A SEQ ID NO: 37	TSTEPSEGSAPGSPAGSPTSTEEGTSTEPSEGSAPGTSTEPSEGSAPGTSESAT PESGPGTSTEPSEGSAPGTSESATPESGPGSEPATSGSETPGTSTEPSEGSAPG TSTEPSEGSAPGTSESATPESGPGTSESATPESGPG
AE144_3B SEQ ID NO: 38	SPAGSPTSTEEGTSESATPESGPGSEPATSGSETPGTSESATPESGPGTSTEPS EGSAPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPG TSTEPSEGSAPGSPAGSPTSTEEGTSTEPSEGSAPG
AE144_4A SEQ ID NO: 39	TSESATPESGPGSEPATSGSETPGTSESATPESGPGSEPATSGSETPGTSESAT PESGPGTSTEPSEGSAPGTSESATPESGPGSPAGSPTSTEEGSPAGSPTSTEEG SPAGSPTSTEEGTSESATPESGPGTSTEPSEGSAPG
AE144_5A SEQ ID NO: 40	TSESATPESGPGSEPATSGSETPGTSESATPESGPGSEPATSGSETPGTSESAT PESGPGTSTEPSEGSAPGSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPG TSESATPESGPGSPAGSPTSTEEGSPAGSPTSTEEG
AE144_6B SEQ ID NO: 41	TSTEPSEGSAPGTSESATPESGPGTSESATPESGPGTSESATPESGPGSEPATS GSETPGSEPATSGSETPGSPAGSPTSTEEGTSTEPSEGSAPGTSTEPSEGSAPG SEPATSGSETPGTSESATPESGPGTSTEPSEGSAPG
AG144 SEQ ID NO:42	GTPGSGTASSSPGSSTPSGATGSPGSSPSASTGTGPGSSPSASTGTGPGASPGT SSTGSPGASPGTSSTGSPGSSTPSGATGSPGSSPSASTGTGPGASPGTSSTGSP GSSPSASTGTGPGTPGSGTASSSPGSSTPSGATGSP
AG144_A SEQ ID NO: 43	GASPGTSSTGSPGSSPSASTGTGPGSSPSASTGTGPGTPGSGTASSSPGSSTPS GATGSPGSSPSASTGTGPGASPGTSSTGSPGTPGSGTASSSPGSSTPSGATGSP GTPGSGTASSSPGASPGTSSTGSPGASPGTSSTGSP
AG144_B SEQ ID NO: 44	GTPGSGTASSSPGSSTPSGATGSPGASPGTSSTGSPGTPGSGTASSSPGSSTPS GATGSPGSSPSASTGTGPGSSPSASTGTGPGSSTPSGATGSPGSSTPSGATGSP GASPGTSSTGSPGASPGTSSTGSPGASPGTSSTGSP
AG144_C SEQ ID NO: 45	GTPGSGTASSSPGASPGTSSTGSPGASPGTSSTGSPGASPGTSSTGSPGSSPSA STGTGPGTPGSGTASSSPGASPGTSSTGSPGASPGTSSTGSPGASPGTSSTGSP GSSTPSGATGSPGSSTPSGATGSPGASPGTSSTGSP
AG144_F SEQ ID NO: 46	GSSPSASTGTGPGSSPSASTGTGPGASPGTSSTGSPGASPGTSSTGSPGSSTPS GATGSPGSSPSASTGTGPGASPGTSSTGSPGSSPSASTGTGPGTPGSGTASSSP GSSTPSGATGSPGSSTPSGATGSPGASPGTSSTGSP
AE288 SEQ ID NO: 47	GTSESATPESGPGSEPATSGSETPGTSESATPESGPGSEPATSGSETPGTSESA TPESGPGTSTEPSEGSAPGSPAGSPTSTEEGTSESATPESGPGSEPATSGSETP GTSESATPESGPGSPAGSPTSTEEGSPAGSPTSTEEGTSTEPSEGSAPGTSESA TPESGPGTSESATPESGPGTSESATPESGPGSEPATSGSETPGSEPATSGSETP GSPAGSPTSTEEGTSTEPSEGSAPGTSTEPSEGSAPGSEPATSGSETPGTSESA TPESGPGTSTEPSEGSAP
AE288_2 SEQ ID NO: 48	GSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPGTSESATPESGPGTSTEP SEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAP GTSTEPSEGSAPGSPAGSPTSTEEGTSTEPSEGSAPGTSESATPESGPGSEPAT SGSETPGTSESATPESGPGSEPATSGSETPGTSESATPESGPGTSTEPSEGSAP GTSESATPESGPGSPAGSPTSTEEGSPAGSPTSTEEGSPAGSPTSTEEGTSESA TPESGPGTSTEPSEGSAP
AG288 SEQ ID NO: 49	PGASPGTSSTGSPGASPGTSSTGSPGTPGSGTASSSPGSSTPSGATGSPGTPGS GTASSSPGSSTPSGATGSPGTPGSGTASSSPGSSTPSGATGSPGSSTPSGATGS PGSSPSASTGTGPGSSPSASTGTGPGASPGTSSTGSPGTPGSGTASSSPGSSTP SGATGSPGSSPSASTGTGPGSSPSASTGTGPGASPGTSSTGSPGASPGTSSTGS PGSSTPSGATGSPGSSPSASTGTGPGASPGTSSTGSPGSSPSASTGTGPGTPGS GTASSSPGSSTPSGATGS
AE576 SEQ ID NO: 50	GSPAGSPTSTEEGTSESATPESGPGTSTEPSEGSAPGSPAGSPTSTEEGTSTEP SEGSAPGTSTEPSEGSAPGTSESATPESGPGSEPATSGSETPGSEPATSGSETP

	GSPAGSPTSTEEGTSESATPESGPGTSTEPSEGSAPGTSTEPSEGSAPGSPAGS PTSTEEGTSTEPSEGSAPGTSTEPSEGSAPGTSESATPESGPGTSTEPSEGSAP GTSESATPESGPGSEPATSGSETPGTSTEPSEGSAPGTSTEPSEGSAPGTSESA TPESGPGTSESATPESGPGSPAGSPTSTEEGTSESATPESGPGSEPATSGSETP GTSESATPESGPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEP SEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGSPAGSPTSTEEGTSTEPSEGSAP GTSESATPESGPGSEPATSGSETPGTSESATPESGPGSEPATSGSETPGTSESA TPESGPGTSTEPSEGSAPGTSESATPESGPGSPAGSPTSTEEGSPAGSPTSTEE GSPAGSPTSTEEGTSESATPESGPGTSTEPSEGSAP
AG576 SEQ ID NO: 51	PGTPGSGTASSSPGSSTPSGATGSPGSSPSASTGTGPGSSPSASTGTGPGSSTP SGATGSPGSSTPSGATGSPGASPGTSSTGSPGASPGTSSTGSPGASPGTSSTGS PGTPGSGTASSSPGASPGTSSTGSPGASPGTSSTGSPGASPGTSSTGSPGSSPS ASTGTGPGTPGSGTASSSPGASPGTSSTGSPGASPGTSSTGSPGASPGTSSTGS PGSSTPSGATGSPGSSTPSGATGSPGASPGTSSTGSPGTPGSGTASSSPGSSTP SGATGSPGSSTPSGATGSPGSSTPSGATGSPGSSPSASTGTGPGASPGTSSTGS PGASPGTSSTGSPGTPGSGTASSSPGASPGTSSTGSPGASPGTSSTGSPGASPG TSSTGSPGASPGTSSTGSPGTPGSGTASSSPGSSTPSGATGSPGTPGSGTASSS PGSSTPSGATGSPGTPGSGTASSSPGSSTPSGATGSPGSSTPSGATGSPGSSPS ASTGTGPGSSPSASTGTGPGASPGTSSTGSPGTPGSGTASSSPGSSTPSGATGS PGSSPSASTGTGPGSSPSASTGTGPGASPGTSSTGS
AE864 SEQ ID NO: 52	GSPAGSPTSTEEGTSESATPESGPGTSTEPSEGSAPGSPAGSPTSTEEGTSTEP SEGSAPGTSTEPSEGSAPGTSESATPESGPGSEPATSGSETPGSEPATSGSETP GSPAGSPTSTEEGTSESATPESGPGTSTEPSEGSAPGTSTEPSEGSAPGSPAGS PTSTEEGTSTEPSEGSAPGTSTEPSEGSAPGTSESATPESGPGTSTEPSEGSAP GTSESATPESGPGSEPATSGSETPGTSTEPSEGSAPGTSTEPSEGSAPGTSESA TPESGPGTSESATPESGPGSPAGSPTSTEEGTSESATPESGPGSEPATSGSETP GTSESATPESGPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEP SEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGSPAGSPTSTEEGTSTEPSEGSAP GTSESATPESGPGSEPATSGSETPGTSESATPESGPGSEPATSGSETPGTSESA TPESGPGTSTEPSEGSAPGTSESATPESGPGSPAGSPTSTEEGSPAGSPTSTEE GSPAGSPTSTEEGTSESATPESGPGTSTEPSEGSAPGTSESATPESGPGSEPAT SGSETPGTSESATPESGPGSEPATSGSETPGTSESATPESGPGTSTEPSEGSAP GSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPGTSESATPESGPGSPAGS PTSTEEGSPAGSPTSTEEGTSTEPSEGSAPGTSESATPESGPGTSESATPESGP GTSESATPESGPGSEPATSGSETPGSEPATSGSETPGSPAGSPTSTEEGTSTEP SEGSAPGTSTEPSEGSAPGSEPATSGSETPGTSESATPESGPGTSTEPSEGSAP
AG864 SEQ ID NO: 53	GASPGTSSTGSPGSSPSASTGTGPGSSPSASTGTGPGTPGSGTASSSPGSSTPS GATGSPGSSPSASTGTGPGASPGTSSTGSPGTPGSGTASSSPGSSTPSGATGSP GTPGSGTASSSPGASPGTSSTGSPGASPGTSSTGSPGTPGSGTASSSPGSSTPS GATGSPGASPGTSSTGSPGTPGSGTASSSPGSSTPSGATGSPGSSPSASTGTGP GSSPSASTGTGPGSSTPSGATGSPGSSTPSGATGSPGASPGTSSTGSPGASPGT SSTGSPGASPGTSSTGSPGTPGSGTASSSPGASPGTSSTGSPGASPGTSSTGSP GASPGTSSTGSPGSSPSASTGTGPGTPGSGTASSSPGASPGTSSTGSPGASPGT SSTGSPGASPGTSSTGSPGSSTPSGATGSPGSSTPSGATGSPGASPGTSSTGSP GTPGSGTASSSPGSSTPSGATGSPGSSTPSGATGSPGSSTPSGATGSPGSSPSA STGTGPGASPGTSSTGSPGASPGTSSTGSPGTPGSGTASSSPGASPGTSSTGSP GASPGTSSTGSPGASPGTSSTGSPGASPGTSSTGSPGTPGSGTASSSPGSSTPS GATGSPGTPGSGTASSSPGSSTPSGATGSPGTPGSGTASSSPGSSTPSGATGSP GSSTPSGATGSPGSSPSASTGTGPGSSPSASTGTGPGASPGTSSTGSPGTPGSG TASSSPGSSTPSGATGSPGSSPSASTGTGPGSSPSASTGTGPGASPGTSSTGSP GASPGTSSTGSPGSSTPSGATGSPGSSPSASTGTGPGASPGTSSTGSPGSSPSA STGTGPGTPGSGTASSSPGSSTPSGATGSPGSSTPSGATGSPGASPGTSSTGSP
XTEN_AE72_2 A_1	TSTEPSEGSAPGSPAGSPTSTEEGTSTEPSEGSAPGTSTEPSEGSAPGTSESAT PESGPGTSTEPSEGSAPG

SEQ ID NO: 202	
XTEN_AE72_2A_2 SEQ ID NO: 203	TSESATPESGPGSEPATSGSETPGTSTEPSEGSAPGTSTEPSEGSAPGTSESATPESGPGTSESATPESGPG
XTEN_AE72_3B_1 SEQ ID NO:204	SPAGSPTSTEEGTSESATPESGPGSEPATSGSETPGTSESATPESGPGTSTEPSEGSAPGTSTEPSEGSAPG
XTEN_AE72_3B_2 SEQ ID NO: 205	TSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGSPAGSPTSTEEGTSTEPSEGSAPG
XTEN_AE72_4A_2 SEQ ID NO: 206	TSESATPESGPGSPAGSPTSTEEGSPAGSPTSTEEGSPAGSPTSTEEGTSESATPESGPGTSTEPSEGSAPG
XTEN_AE72_5A_2 SEQ ID NO: 207	SPAGSPTSTEEGTSESATPESGPGSEPATSGSETPGTSESATPESGPGSPAGSPTSTEEGSPAGSPTSTEEG
XTEN_AE72_6B_1 (SEQ ID NO: 208)	TSTEPSEGSAPGTSESATPESGPGTSESATPESGPGTSESATPESGPGSEPATSGSETPGSEPATSGSETPG
XTEN_AE72_6B_2 SEQ ID NO: 209	SPAGSPTSTEEGTSTEPSEGSAPGTSTEPSEGSAPGSEPATSGSETPGTSESATPESGPGTSTEPSEGSAPG
XTEN_AE72_1A_1 SEQ ID NO: 210	SPAGSPTSTEEGTSESATPESGPGTSTEPSEGSAPGSPAGSPTSTEEGTSTEPSEGSAPGTSTEPSEGSAPG
XTEN_AE72_1A_2 SEQ ID NO: 211	TSESATPESGPGSEPATSGSETPGSEPATSGSETPGSPAGSPTSTEEGTSESATPESGPGTSTEPSEGSAPG
XTEN_AE144_1A SEQ ID NO: 212	SPAGSPTSTEEGTSESATPESGPGTSTEPSEGSAPGSPAGSPTSTEEGTSTEPSEGSAPGTSTEPSEGSAPGTSESATPESGPGSEPATSGSETPGSEPATSGSETPGSPAGSPTSTEEGTSESATPESGPGTSTEPSEGSAPG
AE150 SEQ ID NO: 213	GAPGSEPATSGSETPGTSESATPESGPGSEPATSGSETPGSPAGSPTSTEEGTSTEPSEGSAPGSEPATSGSETPGSEPATSGSETPGSEPATSGSETPGTSTEPSEGSAPGTSESATPESGPGSEPATSGSETPGTSTEPSEGSAPASS
G150 SEQ ID NO: 214	GAPGTPGSGTASSSPGSSTPSGATGSPGSSPSASTGTGPGSSPSASTGTGPGASPGTSSTGSPGASPGTSSTGSPGSSTPSGATGSPGSSPSASTGTGPGASPGTSSTGSPGSSPSASTGTGPGTPGSGTASSSPGSSTPSGATGSPASS
AE294 SEQ ID NO: 215	GAPGTSESATPESGPGSEPATSGSETPGTSESATPESGPGSEPATSGSETPGTSESATPESGPGTSTEPSEGSAPGSPAGSPTSTEEGTSESATPESGPGSEPATSGS

	ETPGTSESATPESGPGSPAGSPTSTEEGSPAGSPTSTEEGTSTEPSEGSAPGTS ESATPESGPGTSESATPESGPGTSESATPESGPGSEPATSGSETPGSEPATSGS ETPGSPAGSPTSTEEGTSTEPSEGSAPGTSTEPSEGSAPGSEPATSGSETPGTS ESATPESGPGTSTEPSEGSAPASS
AG294 SEQ ID NO: 216	GAPPGASPGTSSTGSPGASPGTSSTGSPGTPGSGTASSSPGSSTPSGATGSPGT PGSGTASSSPGSSTPSGATGSPGTPGSGTASSSPGSSTPSGATGSPGSSTPSGA TGSPGSSPSASTGTGPGSSPSASTGTGPGASPGTSSTGSPGTPGSGTASSSPGS STPSGATGSPGSSPSASTGTGPGSSPSASTGTGPGASPGTSSTGSPGASPGTSS TGSPGSSTPSGATGSPGSSPSASTGTGPGASPGTSSTGSPGSSPSASTGTGPGT PGSGTASSSPGSSTPSGATGSASS

[0144] In further embodiments, the XTEN sequence used in the invention affects the physical or chemical property, *e.g.*, pharmacokinetics, of the fusion protein of the present invention. The XTEN sequence used in the present invention can exhibit one or more of the following advantageous properties: conformational flexibility, enhanced aqueous solubility, high degree of protease resistance, low immunogenicity, low binding to mammalian receptors, or increased hydrodynamic (or Stokes) radii. In a specific embodiment, the XTEN sequence linked to a FIX protein in this invention increases pharmacokinetic properties such as longer terminal half-life, increased bioavailability or increased area under the curve (AUC), so that the protein described herein stays *in vivo* for an increased period of time compared to wild type FIX. In further embodiments, the XTEN sequence used in this invention increases pharmacokinetic properties such as longer terminal half-life or increased area under the curve (AUC), so that FIX protein stays *in vivo* for an increased period of time compared to wild type FIX.

[0145] In some embodiments, the FIX protein exhibits an *in vivo* half-life at least about 1.5 fold, at least about 2-fold, at least about 3-fold, or at least about 4-fold greater than native FIX, rFIXFc, FIX R338L, or a corresponding FIX protein lacking the XTEN. In one particular embodiment, the FIX fusion protein can have an *in vivo* half-life more than 2-fold greater than a FIX polypeptide without the heterologous moiety.

[0146] In other embodiments, the FIX fusion protein exhibits an *in vivo* half-life which is at least about 5 hours, at least about 6 hours, at least about 7 hours, at least about 8 hours, at least about 9 hours, at least about 10 hours, at least about 11 hours, at least about 12 hours, at least about 13 hours, at least about 14 hours, at least about 15 hours, at least about 16 hours, at least about 17 hours, at least about 18 hours, at least about 19 hours, at least about 20 hours, at least about 21 hours, at least about 22

hours, at least about 23 hours, at least about 24 hours, at least about 25 hours, at least about 26 hours, at least about 27 hours, at least about 28 hours, at least about 29 hours, at least about 30 hours, at least about 31 hours, at east about 32 hours, at least about 33 hours, or at least about 34 hours longer than the *in vivo* half-life of a FIX polypeptide lacking the heterologous moiety.

[0147] A variety of methods and assays can be employed to determine the physical/chemical properties of proteins comprising the XTEN sequence. Such methods include, but are not limited to analytical centrifugation, EPR, HPLC-ion exchange, HPLC-size exclusion, HPLC-reverse phase, light scattering, capillary electrophoresis, circular dichroism, differential scanning calorimetry, fluorescence, HPLC-ion exchange, HPLC-size exclusion, IR, NMR, Raman spectroscopy, refractometry, and UV/Visible spectroscopy. Additional methods are disclosed in Amau *et al., Prot Expr and Purif* 48, 1-13 (2006).

[0148] Additional examples of XTEN sequences that can be used according to the present invention and are disclosed in US Patent Publication Nos. 2010/0239554 A1, 2010/0323956 A1, 2011/0046060 A1, 2011/0046061 A1, 2011/0077199 A1, or 2011/0172146 A1, or International Patent Publication Nos. WO 2010091122 A1, WO 2010144502 A2, WO 2010144508 A1, WO 2011028228 A1, WO 2011028229 A1, WO 2011028344 A2, WO 2014/011819 A2, or WO 2015/023891.

[0149] In some aspects, a FIX fusion protein comprises one or more XTEN sequences inserted within FIX, fused to the C-terminus of FIX, or both. In one embodiment, the one or more XTEN sequences are inserted within the GLA domain. In another embodiment, the one or more XTEN sequences are inserted within EGF1 domain. In other embodiments, the one or more XTEN sequences are inserted within EGF2. In still other embodiments, the one or more XTEN sequences are inserted within AP. In yet other embodiments, the one or more XTEN sequences are inserted within the catalytic domain. In some embodiments, the one or more XTEN sequences are fused to the C-terminus of the FIX.

[0150] In certain aspects, a FIX fusion protein comprises one XTEN sequence inserted at an insertion site listed in Table 7. In other aspects, a FIX fusion protein comprises two XTEN sequences inserted in two insertion sites listed in Table 7. In a particular embodiment, the two XTEN sequences are inserted in two insertion sites listed in Table 8. In certain aspects, a FIX fusion protein comprises three XTEN sequences inserted in three insertion sites listed in Table 7. In certain aspects, a FIX

fusion protein comprises four XTEN sequences inserted in four insertion sites listed in Table 7. In certain aspects, a FIX fusion protein comprises five XTEN sequences inserted in five insertion sites listed in Table 7. In certain aspects, a FIX fusion protein comprises six XTEN sequences inserted in six insertion sites listed in Table 7. In some aspects, all the inserted XTEN sequences are identical. In other aspects, at least one of the inserted XTEN sequences is different from the rest of inserted XTEN sequences.

[0151] In some aspects, a FIX fusion protein comprises one XTEN sequence inserted within the FIX polypeptide at an insertion site corresponding to an amino acid selected from the group consisting of amino acid 103 of SEQ ID NO: 2, amino acid 105 of SEQ ID NO: 2, amino acid 142 of SEQ ID NO: 2, amino acid 149 of SEQ ID NO: 2, amino acid 162 of SEQ ID NO: 2, amino acid 166 of SEQ ID NO: 2, amino acid 174 of SEQ ID NO: 2, amino acid 224 of SEQ ID NO: 2, amino acid 226 of SEQ ID NO: 2, amino acid 228 of SEQ ID NO: 2, amino acid 413 of SEQ ID NO: 2, and any combination thereof, wherein the FIX fusion protein exhibits procoagulant activity. In some aspects, a FIX fusion protein comprises a second XTEN sequence within the FIX polypeptide at an insertion site corresponding to an amino acid selected from the group consisting of amino acid 103 of SEQ ID NO: 2, amino acid 105 of SEQ ID NO: 2, amino acid 142 of SEQ ID NO: 2, amino acid 149 of SEQ ID NO: 2, amino acid 162 of SEQ ID NO: 2, amino acid 166 of SEQ ID NO: 2, amino acid 174 of SEQ ID NO: 2, amino acid 224 of SEQ ID NO: 2, amino acid 226 of SEQ ID NO: 2, amino acid 228 of SEQ ID NO: 2, amino acid 413 of SEQ ID NO: 2, and any combination thereof or wherein the second XTEN is fused to the C-terminus of the FIX polypeptide, wherein the FIX fusion protein exhibits procoagulant activity. In one particular aspect, a FIX fusion protein comprises one XTEN sequence fused to the C-terminus of the FIX, wherein the XTEN comprises an amino acid sequence of longer than 42 amino acids and shorter than 144 amino acids in length.

II.B.2. Fc regions or FcRn binding partners

[0152] In some embodiments, the at least one heterologous moiety is an Fc region (*e.g.,* an FcRn binding partner) or a fragment thereof. In certain aspects, a FIX fusion protein of the invention comprises at least one Fc region (*e.g.,* an FcRn binding partner) inserted within the FIX, fused to the C-terminus of the FIX, or both, wherein the FIX fusion protein has procoagulant activity and can be expressed *in vivo* or *in*

vitro in a host cell. "Fc" or "Fc region" as used herein, can be a functional neonatal Fc receptor (FcRn) binding partner comprising an Fc domain, variant, or fragment thereof, unless otherwise specified. An FcRn binding partner is any molecule that can be specifically bound by the FcRn receptor with consequent active transport by the FcRn receptor of the FcRn binding partner, including, but not limited to, albumin. Thus, the term Fc includes any variants of IgG Fc that are functional. The region of the Fc portion of IgG that binds to the FcRn receptor has been described based on X-ray crystallography (Burmeister *et al.*, *Nature 372*:379 (1994), incorporated herein by reference in its entirety). The major contact area of the Fc with the FcRn is near the junction of the CH2 and CH3 domains. Fc-FcRn contacts are all within a single Ig heavy chain. FcRn binding partners include, but are not limited to, whole IgG, the Fc fragment of IgG, and other fragments of IgG that include the complete binding region of FcRn. An Fc can comprise the CH2 and CH3 domains of an immunoglobulin with or without the hinge region of the immunoglobulin. Also included are Fc fragments, variants, or derivatives which maintain the desirable properties of an Fc region in a fusion protein, *e.g.*, an increase in half-life, *e.g., in vivo* half-life. Myriad mutants, fragments, variants, and derivatives are described, *e.g.*, in PCT Publication Nos. WO 2011/069164 A2, WO 2012/006623 A2, WO 2012/006635 A2 , or WO 2012/006633 A2, all of which are incorporated herein by reference in their entireties.

[0153] The one or more Fc domains can be inserted within the FIX polypeptide, fused to the C-terminus of the polypeptide, or both. In some embodiments, the Fc domain is fused to the FIX polypeptide. In some embodiments, the Fc domain is fused to another heterologous moiety, such as an XTEN, which is inserted within the FIX or fused to the C-terminus of the XTEN. In some embodiments, the FIX fusion protein comprises a second Fc domain. The second Fc domain can be associated with the first Fc domain, *e.g.*, through one or more covalent bonds.

II.B.3. Albumins

[0154] In some embodiments, the at least one heterologous moiety is an albumin, an albumin binding domain, or an albumin binding small molecule, or a variant, derivative, or fragment thereof. In certain aspects, a FIX fusion protein of the invention comprises at least one albumin polypeptide or fragment, variant, or derivative thereof inserted the FIX, fused to the C-terminus of the FIX, or both, wherein the FIX fusion protein has procoagulant activity and can be expressed *in vivo*

or *in vitro* in a host cell. Human serum albumin (HSA, or HA), a protein of 609 amino acids in its full-length form, is responsible for a significant proportion of the osmotic pressure of serum and also functions as a carrier of endogenous and exogenous ligands. The term "albumin" as used herein includes full-length albumin or a functional fragment, variant, derivative, or analog thereof. Examples of albumin or the fragments or variants thereof are disclosed in US Pat. Publ. Nos. 2008/0194481A1, 2008/0004206 A1, 2008/0161243 A1, 2008/0261877 A1, or 2008/0153751 A1 or PCT Appl. Publ. Nos. 2008/033413 A2, 2009/058322 A1, or 2007/021494 A2, which are incorporated herein by reference in their entireties.

[0155] The albumin-binding polypeptides (ABPs) can compromise, without limitation, bacterial albumin-binding domains, albumin-binding peptides, or albumin-binding antibody fragments that can bind to albumin. Domain 3 from streptococcal protein G, as disclosed by Kraulis *et al.*, FEBS Lett. 378:190-194 (1996) and Linhult *et al.*, Protein Sci. 11:206-213 (2002) is an example of a bacterial albumin-binding domain. Examples of albumin-binding peptides include a series of peptides having the core sequence DICLPRWGCLW (SEQ ID NO: 163). See, *e.g.*, Dennis *et al.*, J. Biol. Chem. 2002, 277: 35035-35043 (2002). Examples of albumin-binding antibody fragments are disclosed in Muller and Kontermann, *Curr. Opin. Mol. Ther.* 9:319-326 (2007); Roovers *et al.*, *Cancer Immunol. Immunother.* 56:303-317 (2007), and Holt *et al.*, Prot. Eng. Design Sci., 21:283-288 (2008), which are incorporated herein by reference in their entireties.

[0156] In certain aspects, a FIX fusion protein of the invention comprises at least one attachment site for a non-polypeptide small molecule, variant, or derivative thereof that can bind to albumin (*e.g.*, an albumin binding small molecule) inserted into the FIX, fused to the C-terminus of the FIX, or both, wherein the FIX fusion protein has procoagulant activity and can be expressed *in vivo* or *in vitro* in a host cell. For example, a FIX fusion protein of the invention can include one or more organic albumin-binding moieties attached in one or more insertion sites within the FIX, or fused to the C-terminus of the FIX, or both, wherein the FIX fusion protein has procoagulant activity and can be expressed *in vivo* or *in vitro* in a host cell. An example of such albumin-binding moieties is 2-(3-maleimidopropanamido)-6-(4-(4-iodophenyl)butanamido)hexanoate ("Albu" tag) as disclosed by Trussel *et al.*, Bioconjugate Chem. 20:2286-2292 (2009).

[0157] In some embodiments, the albumin-binding polypeptide sequence is flanked at the C-terminus, the N-terminus, or both termini, by a Gly-Ser peptide linker sequence. In some embodiments, the Gly-Ser peptide linker is Gly_4Ser (SEQ ID NO: 161). In other embodiments, the Gly-Ser peptide linker is $(Gly_4Ser)_2$ (SEQ ID NO: 162).

II.B.4. CTP

[0158] In some embodiments, the at least one heterologous moiety is a C-terminal peptide (CTP) of the β subunit of human chorionic gonadotropin or fragment, variant, or derivative thereof. In certain aspects, a FIX fusion protein of the invention comprises at least one CTP or fragment, variant, or derivative thereof inserted into the FIX, fused to the C-terminus of the FIX, or both, wherein the FIX fusion protein has procoagulant activity and can be expressed in vivo or in vitro in a host cell. One or more CTP peptides inserted into a recombinant protein is known to increase the half-life of that protein. *See, e.g.*, U.S. Patent No. 5,712,122, incorporated by reference herein in its entirety. Exemplary CTP peptides include DPRFQDSSSSKAPPPSLPSPSRLPGPSDTPIL (SEQ ID NO: 164) or SSSSKAPPPSLPSPSRLPGPSDTPILPQ (SEQ ID NO: 165). See, *e.g.*, U.S. Patent Application Publication No. US 2009/0087411 A1, incorporated by reference. In some embodiments, the CTP sequence is flanked at the C-terminus, the N-terminus, or both termini, by a Gly-Ser peptide linker sequence. In some embodiments, the Gly-Ser peptide linker is Gly_4Ser (SEQ ID NO: 161). In other embodiments, the Gly-Ser peptide linker is $(Gly_4Ser)_2$ (SEQ ID NO: 162).

II.B.5. PAS

[0159] In some embodiments, the at least one heterologous moiety is a PAS peptide. In certain aspects, a FIX fusion protein of the invention comprises at least one PAS peptide or fragment, variant, or derivative thereof inserted into the FIX, fused to the C-terminus of the FIX, or both, wherein the FIX fusion protein has procoagulant activity and can be expressed *in vivo* or *in vitro* in a host cell. A "PAS peptide" or "PAS sequence," as used herein, means an amino acid sequence comprising mainly alanine and serine residues or comprising mainly alanine, serine, and proline residues, the amino acid sequence forming random coil conformation under physiological conditions. Accordingly, the PAS sequence is a building block, an amino acid polymer, or a sequence cassette comprising, consisting essentially of, or consisting of

alanine, serine, and proline which can be used as a part of the heterologous moiety in the fusion protein. An amino acid polymer also can form random coil conformation when residues other than alanine, serine, and proline are added as a minor constituent in the PAS sequence. By "minor constituent" is meant that that amino acids other than alanine, serine, and proline can be added in the PAS sequence to a certain degree, *e.g.*, up to about 12%, *i.e.*, about 12 of 100 amino acids of the PAS sequence, up to about 10%, up to about 9%, up to about 8%, about 6%, about 5%, about 4%, about 3%, *i.e.* about 2%, or about 1%, of the amino acids. The amino acids different from alanine, serine and proline can be selected from the group consisting of Arg, Asn, Asp, Cys, Gln, Glu, Gly, His, Ile, Leu, Lys, Met, Phe, Thr, Trp, Tyr, and Val. Under physiological conditions, a PAS peptide forms a random coil conformation and thereby can mediate an increased *in vivo* and/or *in vitro* stability to a recombinant protein of the invention, and has procoagulant activity.

[0160] Non-limiting examples of the PAS peptides include ASPAAPAPASPAAPAPSAPA (SEQ ID NO: 154), AAPASPAPAAPSAPAPAAPS (SEQ ID NO: 155), APSSPSPSAPSSPSPASPSS (SEQ ID NO: 156), APSSPSPSAPSSPSPASPS (SEQ ID NO: 157), SSPSAPSPSSPASPSPSSPA (SEQ ID NO: 158), AASPAAPSAPPAAASPAAPSAPPA (SEQ ID NO: 159), ASAAAPAAASAAASAPSAAA (SEQ ID NO: 160) or any variants, derivatives, fragments, or combinations thereof. Additional examples of PAS sequences are known from, *e.g.*, US Pat. Publ. No. 2010/0292130 A1 and PCT Appl. Publ. No. WO 2008/155134 A1. European issued patent EP2173890.

[0161] In some embodiments, the PAS sequence is flanked at the C-terminus, the N-terminus, or both termini, by a Gly-Ser peptide linker sequence. In some embodiments, the Gly-Ser peptide linker is Gly_4Ser (SEQ ID NO: 161). In other embodiments, the Gly/Ser peptide linker is $(Gly_4Ser)_2$ (SEQ ID NO: 162).

II.B.6. HAP

[0162] In some embodiments, the at least one heterologous moiety is a homo-amino acid polymer (HAP) peptide or fragment, variant, or derivative thereof. In certain aspects, a FIX fusion protein of the invention comprises at least one homo-amino acid polymer (HAP) peptide or fragment, variant, or derivative thereof inserted within the FIX, fused to the C-terminus of the FIX, or both, wherein the FIX fusion protein has procoagulant activity and can be expressed *in vivo* or *in vitro* in a host cell. A HAP

peptide can comprise a repetitive sequence of glycine, which has at least 50 amino acids, at least 100 amino acids, 120 amino acids, 140 amino acids, 160 amino acids, 180 amino acids, 200 amino acids, 250 amino acids, 300 amino acids, 350 amino acids, 400 amino acids, 450 amino acids, or 500 amino acids in length. A HAP sequence is capable of extending half-life of a moiety fused to or linked to the HAP sequence. Non-limiting examples of the HAP sequence include, but are not limited to $(Gly)_n$, $(Gly_4Ser)_n$ or $S(Gly_4Ser)_n$, wherein n is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20. In one embodiment, n is 20, 21, 22, 23, 24, 25, 26, 26, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, or 40. In another embodiment, n is 50, 60, 70, 80, 90, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, or 200. See, *e.g.*, Schlapschy M *et al.*, Protein Eng. Design Selection, 20: 273-284 (2007).

II.B.7. Organic Polymers

[0163] In some embodiments, the at least one heterologous moiety is an organic polymer, *e.g.*, a polyethylene glycol, a polysialic acid, or hydroxyethyl starch. In certain aspects, a FIX fusion protein of the invention comprises at least one attachment site for a non-polypeptide heterologous moiety or fragment, variant, or derivative thereof inserted into the FIX, fused to the C-terminus of the FIX, or both, wherein the FIX fusion protein has procoagulant activity and can be expressed *in vivo* or *in vitro* in a host cell. For example, a FIX fusion protein of the invention can include one or more polyethylene glycol (PEG) moieties attached within the FIX sequence, attached to the C-terminus of the FIX, or both, wherein the FIX fusion protein has procoagulant activity and can be expressed *in vivo* or *in vitro* in a host cell.

[0164] PEGylated FIX can refer to a conjugate formed between FIX and at least one polyethylene glycol (PEG) molecule. PEG is commercially available in a large variety of molecular weights and average molecular weight ranges. Typical examples of PEG average molecular weight ranges include, but are not limited to, about 200, about 300, about 400, about 600, about 1000, about 1300-1600, about 1450, about 2000, about 3000, about 3000-3750, about 3350, about 3000-7000, about 3500-4500, about 5000-7000, about 7000-9000, about 8000, about 10000, about 8500-11500, about 16000-24000, about 35000, about 40000, about 60000, and about 80000 daltons. These average molecular weights are provided merely as examples and are not meant to be limiting in any way.

[0165] A FIX fusion protein of the invention can be PEGylated to include mono- or poly-(*e.g.*, 2-4) PEG moieties. PEGylation can be carried out by any of the PEGylation reactions known in the art. Methods for preparing a PEGylated protein product will generally include (i) reacting a polypeptide with polyethylene glycol (such as a reactive ester or aldehyde derivative of PEG) under conditions whereby the peptide of the invention becomes attached to one or more PEG groups; and (ii) obtaining the reaction product(s). In general, the optimal reaction conditions for the reactions will be determined case by case based on known parameters and the desired result.

[0166] There are a number of PEG attachment methods available to those skilled in the art, for example Malik F *et al.*, *Exp. Hematol.* 20:1028-35 (1992); Francis, *Focus on Growth Factors* 3(2):4-10 (1992); European Pat. Pub. Nos. EP0401384, EP0154316, and EP0401384; and International Pat. Appl. Pub. Nos. WO92/16221 and WO95/34326. As a non-limiting example, FIX variants can contain cysteine substitutions at or near one or more insertion sites as described herein, and the cysteines can be further conjugated to PEG polymer. See Mei *et al., Blood* 116:270-279 (2010) and U.S. Patent No. 7,632,921, which are incorporated herein by reference in their entireties.

[0167] In other embodiments, the organic polymer is a polysialic acid (PSA). PSAs are naturally occurring unbranched polymers of sialic acid produced by certain bacterial strains and in mammals in certain cells. See, *e.g.*, Roth J. *et al.* (1993) in *Polysialic Acid: From Microbes to Man*, eds. Roth J., Rutishauser U., Troy F. A. (BirkhäuserVerlag, Basel, Switzerland), pp. 335–348. PSAs can be produced in various degrees of polymerization from n=about 80 or more sialic acid residues down to n=2 by limited acid hydrolysis or by digestion with neuraminidases, or by fractionation of the natural, bacterially derived forms of the polymer. There are a number of PSA attachment methods available to those skilled in the art, *e.g.*, the same PEG attachment methods described above. In certain aspects, an activated PSA can also be attached to a cysteine amino acid residue on FIX. See, *e.g.*, U.S. Patent No. 5846951.

[0168] In other embodiments, the organic polymer is a hydroxyethyl starch (HES) polymer. In certain aspects, a FIX fusion protein of the invention comprises at least one HES polymer conjugated at one or more cite within the FIX, fused to the C-

terminus of the FIX, or both, wherein the FIX fusion protein has procoagulant activity and can be expressed *in vivo* or *in vitro* in a host cell.

III. POLYNUCLEOTIDES, VECTORS, HOST CELLS, AND METHODS OF MAKING

[0169] The present invention further provides a polynucleotide encoding a FIX fusion protein described herein, an expression vector comprising the polynucleotide, a host cell comprising the polynucleotide or the vector, or methods of making the FIX fusion protein.

[0170] The polynucleotide encoding a FIX fusion protein can be a single nucleotide sequence, two nucleotide sequences, three nucleotide sequences, or more. In one embodiment, a single nucleotide sequence encodes a FIX fusion protein comprising a FIX polypeptide and a heterologous moiety (*e.g.,* XTEN), *e.g.,* a FIX fusion protein comprising a FIX polypeptide and an XTEN inserted within the FIX polypeptide, an Fc domain fused to the C terminus of the FIX polypeptide, and a second Fc domain fused to the FIX polypeptide by an optional linker. In another embodiment, the polynucleotide comprises two nucleotide sequences, the first nucleotide sequence encoding a FIX polypeptide and an XTEN inserted within the FIX polypeptide and the second nucleotide sequence encoding a heterologous moiety, *e.g.,* Fc. In other embodiments, the polynucleotide comprises two nucleotide sequences, the first nucleotide sequence encoding a FIX polypeptide, an XTEN inserted within the FIX polypeptide, and an Fc domain fused to the FIX polypeptide, and the second nucleotide sequence encoding a second Fc domain. The encoded Fc domains can form a covalent bond after expression.

[0171] In some embodiments, the polynucleotide encoding the FIX fusion protein is codon-optimized.

[0172] As used herein, an expression vector refers to any nucleic acid construct which contains the necessary elements for the transcription and translation of an inserted coding sequence, or in the case of an RNA viral vector, the necessary elements for replication and translation, when introduced into an appropriate host cell. Expression vectors can include plasmids, phagemids, viruses, and derivatives thereof.

[0173] A gene expression control sequence as used herein is any regulatory nucleotide sequence, such as a promoter sequence or promoter-enhancer combination, which facilitates the efficient transcription and translation of the coding nucleic acid to which it is operably linked. The gene expression control sequence may, for

example, be a mammalian or viral promoter, such as a constitutive or inducible promoter. Constitutive mammalian promoters include, but are not limited to, the promoters for the following genes: hypoxanthine phosphoribosyl transferase (HPRT), adenosine deaminase, pyruvate kinase, beta-actin promoter, and other constitutive promoters. Exemplary viral promoters which function constitutively in eukaryotic cells include, for example, promoters from the cytomegalovirus (CMV), simian virus (*e.g.*, SV40), papilloma virus, adenovirus, human immunodeficiency virus (HIV), Rous sarcoma virus, cytomegalovirus, the long terminal repeats (LTR) of Moloney leukemia virus, and other retroviruses, and the thymidine kinase promoter of herpes simplex virus. Other constitutive promoters are known to those of ordinary skill in the art. The promoters useful as gene expression sequences of the invention also include inducible promoters. Inducible promoters are expressed in the presence of an inducing agent. For example, the metallothionein promoter is induced to promote transcription and translation in the presence of certain metal ions. Other inducible promoters are known to those of ordinary skill in the art.

[0174] For the purposes of this invention, numerous expression vector systems can be employed. These expression vectors are typically replicable in the host organisms either as episomes or as an integral part of the host chromosomal DNA. Expression vectors can include expression control sequences including, but not limited to, promoters (*e.g.*, naturally-associated or heterologous promoters), enhancers, signal sequences, splice signals, enhancer elements, and transcription termination sequences. Preferably, the expression control sequences are eukaryotic promoter systems in vectors capable of transforming or transfecting eukaryotic host cells. Expression vectors can also utilize DNA elements which are derived from animal viruses such as bovine papilloma virus, polyoma virus, adenovirus, vaccinia virus, baculovirus, retroviruses (RSV, MMTV or MOMLV), cytomegalovirus (CMV), or SV40 virus. Others involve the use of polycistronic systems with internal ribosome binding sites.

[0175] Commonly, expression vectors contain selection markers (*e.g.*, ampicillin-resistance, hygromycin-resistance, tetracycline resistance or neomycin resistance) to permit detection of those cells transformed with the desired DNA sequences (*see*, *e.g.*, Itakura *et al.*, US Patent No. 4,704,362). Cells which have integrated the DNA into their chromosomes can be selected by introducing one or more markers which allow selection of transfected host cells. The marker can provide for prototrophy to an

auxotrophic host, biocide resistance (*e.g.*, antibiotics) or resistance to heavy metals such as copper. The selectable marker gene can either be directly linked to the DNA sequences to be expressed, or introduced into the same cell by cotransformation.

[0176] An example of a vector useful for expressing an optimized FIX sequence is NEOSPLA (U.S. Patent No. 6,159,730). This vector contains the cytomegalovirus promoter/enhancer, the mouse beta globin major promoter, the SV40 origin of replication, the bovine growth hormone polyadenylation sequence, neomycin phosphotransferase exon 1 and exon 2, the dihydrofolate reductase gene and leader sequence. This vector has been found to result in very high level expression of antibodies upon incorporation of variable and constant region genes, transfection in cells, followed by selection in G418 containing medium and methotrexate amplification. Vector systems are also taught in US Patent Nos. 5,736,137 and 5,658,570, each of which is incorporated by reference in its entirety herein. This system provides for high expression levels, *e.g.*, > 30 pg/cell/day. Other exemplary vector systems are disclosed *e.g.*, in US Patent No. 6,413,777.

[0177] In other embodiments the polypeptides of the instant invention are expressed using polycistronic constructs. In these expression systems, multiple gene products of interest such as multiple polypeptides of multimer binding protein can be produced from a single polycistronic construct. These systems advantageously use an internal ribosome entry site (IRES) to provide relatively high levels of polypeptides in eukaryotic host cells. Compatible IRES sequences are disclosed in US Patent No. 6,193,980 which is also incorporated herein.

[0178] More generally, once the vector or DNA sequence encoding a polypeptide has been prepared, the expression vector can be introduced into an appropriate host cell. That is, the host cells can be transformed. Introduction of the plasmid into the host cell can be accomplished by various techniques well known to those of skill in the art, as discussed above. The transformed cells are grown under conditions appropriate to the production of the FIX polypeptide, and assayed for FIX polypeptide synthesis. Exemplary assay techniques include enzyme-linked immunosorbent assay (ELISA), radioimmunoassay (RIA), or flourescence-activated cell sorter analysis (FACS), immunohistochemistry, and the like.

[0179] In descriptions of processes for isolation of polypeptides from recombinant hosts, the terms "cell" and "cell culture" are used interchangeably to denote the source of polypeptide unless it is clearly specified otherwise. In other words, recovery of

polypeptides from the "cells" can mean either from spun down whole cells, or from the cell culture containing both the medium and the suspended cells.

[0180] The host cell line used for protein expression is preferably of mammalian origin; most preferably of human or mouse origin. Exemplary host cell lines have been described above. In one embodiment of the method to produce a polypeptide with FIX activity, the host cell is a HEK293 cell. In another embodiment of the method to produce a polypeptide with FIX activity, the host cell is a CHO cell.

[0181] Genes encoding the polypeptides of the invention can also be expressed in non-mammalian cells such as bacteria or yeast or plant cells. In this regard it will be appreciated that various unicellular non-mammalian microorganisms such as bacteria can also be transformed; *i.e.,* those capable of being grown in cultures or fermentation. Bacteria, which are susceptible to transformation, include members of the enterobacteriaceae, such as strains of *Escherichia coli* or Salmonella; Bacillaceae, such as *Bacillus subtilis*; Pneumococcus; Streptococcus, and *Haemophilus influenzae*. It will further be appreciated that, when expressed in bacteria, the polypeptides typically become part of inclusion bodies. The polypeptides must be isolated, purified and then assembled into functional molecules.

[0182] Alternatively, polynucleotide sequences of the invention can be incorporated in transgenes for introduction into the genome of a transgenic animal and subsequent expression in the milk of the transgenic animal (*see*, *e.g.*, Deboer *et al.*, US 5,741,957, Rosen, US 5,304,489, and Meade *et al.*, US 5,849,992). Suitable transgenes include coding sequences for polypeptides in operable linkage with a promoter and enhancer from a mammary gland specific gene, such as casein or beta lactoglobulin.

[0183] *In vitro* production allows scale-up to give large amounts of the desired polypeptides. Techniques for mammalian cell cultivation under tissue culture conditions are known in the art and include homogeneous suspension culture, *e.g.*, in an airlift reactor or in a continuous stirrer reactor, or immobilized or entrapped cell culture, *e.g.*, in hollow fibers, microcapsules, on agarose microbeads or ceramic cartridges. If necessary and/or desired, the solutions of polypeptides can be purified by the customary chromatography methods, for example gel filtration, ion-exchange chromatography, chromatography over DEAE-cellulose or (immuno-)affinity chromatography, *e.g.*, after preferential biosynthesis of a synthetic hinge region polypeptide or prior to or subsequent to the HIC chromatography step described

herein. An affinity tag sequence (*e.g.*, a His(6) tag) can optionally be attached or included within the polypeptide sequence to facilitate downstream purification.

[0184] Once expressed, the FIX protein can be purified according to standard procedures of the art, including ammonium sulfate precipitation, affinity column chromatography, HPLC purification, gel electrophoresis and the like (*see generally* Scopes, Protein Purification (Springer-Verlag, N.Y., (1982)). Substantially pure proteins of at least about 90% to 95% homogeneity are preferred, and 98% to 99% or more homogeneity most preferred, for pharmaceutical uses.

[0185] In one embodiment, the host cell is a eukaryotic cell. As used herein, a eukaryotic cell refers to any animal or plant cell having a definitive nucleus. Eukaryotic cells of animals include cells of vertebrates, *e.g.*, mammals, and cells of invertebrates, *e.g.*, insects. Eukaryotic cells of plants specifically can include, without limitation, yeast cells. A eukaryotic cell is distinct from a prokaryotic cell, *e.g.*, bacteria.

[0186] In certain embodiments, the eukaryotic cell is a mammalian cell. A mammalian cell is any cell derived from a mammal. Mammalian cells specifically include, but are not limited to, mammalian cell lines. In one embodiment, the mammalian cell is a human cell. In another embodiment, the mammalian cell is a HEK 293 cell, which is a human embryonic kidney cell line. HEK 293 cells are available as CRL-1533 from American Type Culture Collection, Manassas, VA, and as 293-H cells, Catalog No. 11631-017 or 293-F cells, Catalog No. 11625-019 from Invitrogen (Carlsbad, Calif.). In some embodiments, the mammalian cell is a PER.C6® cell, which is a human cell line derived from retina. PER.C6® cells are available from Crucell (Leiden, The Netherlands). In other embodiments, the mammalian cell is a Chinese hamster ovary (CHO) cell. CHO cells are available from American Type Culture Collection, Manassas, VA. (*e.g.*, CHO-K1; CCL-61). In still other embodiments, the mammalian cell is a baby hamster kidney (BHK) cell. BHK cells are available from American Type Culture Collection, Manassas, Va. (*e.g.*, CRL-1632). In some embodiments, the mammalian cell is a HKB11 cell, which is a hybrid cell line of a HEK293 cell and a human B cell line. Mei *et al.*, Mol. Biotechnol. 34(2): 165-78 (2006).

[0187] In still other embodiments, transfected cells are stably transfected. These cells can be selected and maintained as a stable cell line, using conventional techniques known to those of skill in the art.

[0188] Host cells containing DNA constructs of the protein are grown in an appropriate growth medium. As used herein, the term "appropriate growth medium" means a medium containing nutrients required for the growth of cells. Nutrients required for cell growth may include a carbon source, a nitrogen source, essential amino acids, vitamins, minerals, and growth factors. Optionally, the media can contain one or more selection factors. Optionally the media can contain bovine calf serum or fetal calf serum (FCS). In one embodiment, the media contains substantially no IgG. The growth medium will generally select for cells containing the DNA construct by, for example, drug selection or deficiency in an essential nutrient which is complemented by the selectable marker on the DNA construct or co-transfected with the DNA construct. Cultured mammalian cells are generally grown in commercially available serum-containing or serum-free media (*e.g.*, MEM, DMEM, DMEM/F12). In one embodiment, the medium is CD293 (Invitrogen, Carlsbad, CA.). In another embodiment, the medium is CD17 (Invitrogen, Carlsbad, CA.). Selection of a medium appropriate for the particular cell line used is within the level of those ordinary skilled in the art.

[0189] In some embodiments, the nucleic acid, vector, or host cell further comprises an additional nucleotide which encodes a protein convertase. The protein convertase can be selected from the group consisting of proprotein convertase subtilisin/kexin type 5 (PCSK5 or PC5), proprotein convertase subtilisin/kexin type 7 (PCSK7 or PC5), a yeast Kex 2, proprotein convertase subtilisin/kexin type 3 (PACE or PCSK3), and two or more combinations thereof. In some embodiments, the protein convertase is PACE, PC5, or PC7. In a specific embodiment, the protein convertase is PC5 or PC7. See International Appl. Publ. No. WO 2012/006623, which is incorporated herein by reference. In another embodiment, the protein convertase is PACE/Furin.

[0190] In certain aspects, the present invention relates to the FIX fusion protein produced by the methods described herein.

[0191] In certain aspects, host cells of the invention can express the FIX fusion protein *in vivo* or *in vitro*. *In vitro* production allows scale-up to give large amounts of the desired altered polypeptides of the invention. a FIX fusion protein can be produced by culturing the host cells described herein under conditions in which the FIX fusion protein is expressed. Techniques for mammalian cell cultivation under tissue culture conditions are known in the art and include homogeneous suspension culture, *e.g.* in an airlift reactor or in a continuous stirrer reactor, or immobilized or

entrapped cell culture, *e.g.* in hollow fibers, microcapsules, on agarose microbeads or ceramic cartridges. If necessary and/or desired, the solutions of polypeptides can be purified by the customary chromatography methods, for example gel filtration, ion-exchange chromatography, hydrophobic interaction chromatography (HIC, chromatography over DEAE-cellulose or affinity chromatography. In other aspects, the host cells express the FIX fusion protein *in vivo*.

[0192] In one embodiment, the invention includes a method of making a FIX fusion protein comprising inserting a heterologous moiety in an insertion site, fusing a heterologous moiety to the C-terminus of the FIX, or both as described herein, wherein the FIX fusion protein exhibits procoagulant activity.

[0193] In another embodiment, the invention includes a method of increasing half-life of a FIX protein without eliminating or reducing procoagulant activity of the FIX protein, comprising inserting a heterologous moiety in an insertion site, fusing a heterologous moiety to the C-terminus of the FIX, or both as described herein, wherein the FIX fusion protein exhibits procoagulant activity and increased half-life compared to the FIX protein without the heterologous moiety.

[0194] In other embodiments, the invention provides a method of constructing a FIX fusion protein comprising designing a nucleotide sequence encoding the FIX fusion protein comprising at least one heterologous moiety in an insertion site, fused to the C-terminus of the FIX, or both as described herein.

[0195] In certain embodiments, the present invention includes a method of increasing expression of a FIX fusion protein comprising inserting a heterologous moiety in an insertion site, fused to the C-terminus of the FIX, or both as described herein, wherein the FIX fusion protein exhibits procoagulant activity

[0196] In still other embodiments, the invention provides a method of retaining procoagulant activity of a FIX fusion protein, comprising inserting a heterologous moiety in an insertion site, fusing a heterologous moiety to the C-terminus of the FIX, or both as described herein, wherein the FIX fusion protein exhibits procoagulant activity.

IV. PHARMACEUTICAL COMPOSITIONS AND METHODS OF TREATMENT

[0197] The present invention further provides a method for preventing, treating, ameliorating, or managing a clotting disease or condition or a bleeding condition in a human subject in need thereof using a pharmaceutical composition comprising a FIX

fusion protein of the invention. An exemplary method comprises administering to the subject in need thereof a therapeutically effective amount of a pharmaceutical composition/formulation comprising a FIX fusion protein of the invention. In other aspects, a composition comprising a DNA encoding the fusion protein of the invention can be administered to a subject in need thereof. In certain aspects of the invention, a cell expressing a FIX fusion protein of the invention can be administered to a subject in need thereof. In certain aspects of the invention, the pharmaceutical composition comprises (i) a FIX fusion protein, (ii) an isolated nucleic acid encoding a FIX fusion protein, (iii) a vector comprising a nucleic acid encoding a FIX fusion protein, (iv) a cell comprising an isolated nucleic acid encoding a FIX fusion protein and/or a vector comprising a nucleic encoding a FIX fusion protein, or (v) a combination thereof, and the pharmaceutical compositions further comprises an acceptable excipient or carrier.

[0198] The FIX fusion protein of the invention can be administered to a patient intravenously, subcutaneously, or orally. In certain embodiments, the FIX fusion protein is administered to a subject by intravenous injection. In other embodiments, the FIX fusion protein is administered to a subject by subcutaneous injection. The injections can comprise a single bolus. Subjects may receive more than one injection.

[0199] The fusion proteins of the invention can be used prophylactically. As used herein the term "prophylactic treatment" refers to the administration of a molecule prior to a bleeding episode. In one embodiment, the subject in need of a general hemostatic agent is undergoing, or is about to undergo, surgery. The fusion protein of the invention can be administered prior to or after surgery as a prophylactic. The fusion protein of the invention can be administered during or after surgery to control an acute bleeding episode. The surgery can include, but is not limited to, liver transplantation, liver resection, dental procedures, or stem cell transplantation.

[0200] The fusion protein of the invention is also used for on-demand treatment. The term "on-demand treatment" refers to the administration of a fusion protein in response to symptoms of a bleeding episode or before an activity that may cause bleeding. In one aspect, the on-demand treatment is given to a subject when bleeding starts, such as after an injury, or when bleeding is expected, such as before surgery. In another aspect, the on-demand treatment is given prior to activities that increase the risk of bleeding, such as contact sports.

[0201] In other embodiments, the fusion protein is used to control, ameliorate, or treat an acute bleeding episode. In other embodiments, the FIX fusion protein exhibits one or more pharmacokinetic parameters compared to a corresponding FIX protein without the heterologous moiety. PK parameters can be based on FIX antigen level (often denoted parenthetically herein as "antigen") or FIX activity level (often denoted parenthetically herein as "activity"). In the literature, PK parameters are often based on FIX activity level due to the presence in the plasma of some subjects of endogenous, inactive FIX, which interferes with the ability to measure administered (*i.e.*, exogenous) FIX using antibody against FIX. However, when FIX is administered as part of an Fc fusion protein as provided herein, administered (*i.e.*, exogenous) FIX antigen can be accurately measured using antibody to the heterologous polypeptide. In addition, certain PK parameters can be based on model predicted data (often denoted parenthetically herein as "model predicted") or on observed data (often denoted parenthetically herein as "observed"), and preferably are based on observed data.

[0202] The FIX fusion protein can be administered to a subject through any means known in the art. For example, the FIX fusion protein can be administered through topical (*e.g.*, transdermal or ocular), oral, buccal, nasal, vaginal, rectal, or parenteral (*e.g.*, subcutaneous, intradermal, intravascular/intravenous, intramuscular, spinal, intracranial, intrathecal, intraocular, periocular, intraorbital, intrasynovial, and intraperitoneal injection) administration. In one particular embodiment, the FIX fusion protein is administered via a subcutaneous injection. The subcutaneous injection can include one or more bolus, including, for example, a single bolus of a dose of the FIX fusion protein. Alternatively, the FIX fusion protein can be administered via intravenous injection.

[0203] The dose of the FIX fusion protein can vary depending on the nature of the particular fusion protein and the nature of the subject's condition. In some embodiments, the dose of the FIX fusion protein can comprise between 1 and 1000 IU/kg of the FIX fusion protein.

[0204] The bleeding condition can be caused by a blood coagulation disorder. A blood coagulation disorder can also be referred to as a coagulopathy. In one example, the blood coagulation disorder, which can be treated with a pharmaceutical composition of the current disclosure, is hemophilia. In another example, the blood

coagulation disorder, which can be treated with a pharmaceutical composition of the present disclosure is hemophilia B.

[0205] In some embodiments, the type of bleeding associated with the bleeding condition is selected from hemarthrosis, muscle bleed, oral bleed, hemorrhage, hemorrhage into muscles, oral hemorrhage, trauma, trauma capitis, gastrointestinal bleeding, intracranial hemorrhage, intra-abdominal hemorrhage, intrathoracic hemorrhage, bone fracture, central nervous system bleeding, bleeding in the retropharyngeal space, bleeding in the retroperitoneal space, and bleeding in the illiopsoas sheath.

[0206] In other embodiments, the subject suffering from bleeding condition is in need of treatment for surgery, including, *e.g.*, surgical prophylaxis or peri-operative management. In one example, the surgery is selected from minor surgery and major surgery. Exemplary surgical procedures include tooth extraction, tonsillectomy, inguinal herniotomy, synovectomy, craniotomy, osteosynthesis, trauma surgery, intracranial surgery, intra-abdominal surgery, intrathoracic surgery, joint replacement surgery (*e.g.*, total knee replacement, hip replacement, and the like), heart surgery, and caesarean section.

[0207] In another example, the subject is concomitantly treated with Factor VIII. Because the compounds of the invention are capable of activating FIXa, they could be used to pre-activate the FIXa polypeptide before administration of the FIXa to the subject.

[0208] The methods of the invention may be practiced on a subject in need of prophylactic treatment or on-demand treatment.

[0209] Pharmaceutical compositions comprising a FIX fusion protein of the invention may be formulated for any appropriate manner of administration, including, for example, topical (*e.g.*, transdermal or ocular), oral, buccal, nasal, vaginal, rectal or parenteral administration.

[0210] The term parenteral as used herein includes subcutaneous, intradermal, intravascular (*e.g.*, intravenous), intramuscular, spinal, intracranial, intrathecal, intraocular, periocular, intraorbital, intrasynovial and intraperitoneal injection, as well as any similar injection or infusion technique. In particular, the pharmaceutical compositions comprising a FIX fusion protein of the invention may be formulated for subcutaneous administration. The composition can be also for example a suspension, emulsion, sustained release formulation, cream, gel or powder. The composition can

be formulated as a suppository, with traditional binders and carriers such as triglycerides.

[0211] In one example, the pharmaceutical formulation is a liquid formulation, *e.g.*, a buffered, isotonic, aqueous solution. In another example, the pharmaceutical composition has a pH that is physiologic, or close to physiologic. In other examples, the aqueous formulation has a physiologic or close to physiologic osmolarity and salinity. It can contain sodium chloride and/or sodium acetate. In some examples, the composition of the present invention is lyophilized.

[0212] A fusion protein thereof of the invention can be produced *in vivo* in a mammal, *e.g.*, a human patient, using a gene therapy approach to treatment of a bleeding disease or disorder selected from the group consisting of a bleeding coagulation disorder, hemarthrosis, muscle bleed, oral bleed, hemorrhage, hemorrhage into muscles, oral hemorrhage, trauma, trauma capitis, gastrointestinal bleeding, intracranial hemorrhage, intra-abdominal hemorrhage, intrathoracic hemorrhage, bone fracture, central nervous system bleeding, bleeding in the retropharyngeal space, bleeding in the retroperitoneal space, and bleeding in the illiopsoas sheath would be therapeutically beneficial. In one embodiment, the bleeding disease or disorder is hemophilia. In another embodiment, the bleeding disease or disorder is hemophilia B. This involves administration of a suitable fusion protein-encoding nucleic acid operably linked to suitable expression control sequences. In certain embodiment, these sequences are incorporated into a viral vector. Suitable viral vectors for such gene therapy include adenoviral vectors, lentiviral vectors, baculoviral vectors, Epstein Barr viral vectors, papovaviral vectors, vaccinia viral vectors, herpes simplex viral vectors, and adeno associated virus (AAV) vectors. The viral vector can be a replication-defective viral vector. In other embodiments, an adenoviral vector has a deletion in its E1 gene or E3 gene. When an adenoviral vector is used, the mammal may not be exposed to a nucleic acid encoding a selectable marker gene. In other embodiments, the sequences are incorporated into a non-viral vector known to those skilled in the art.

[0213] The practice of the present invention will employ, unless otherwise indicated, conventional techniques of cell biology, cell culture, molecular biology, transgenic biology, microbiology, recombinant DNA, and immunology, which are within the skill of the art. Such techniques are explained fully in the literature. *See*, for example, Molecular Cloning A Laboratory Manual, 2nd Ed., Sambrook *et al.*, ed., Cold Spring

Harbor Laboratory Press: (1989); Molecular Cloning: A Laboratory Manual, Sambrook *et al.,* ed., Cold Springs Harbor Laboratory, New York (1992), DNA Cloning, D. N. Glover ed., Volumes I and II (1985); Oligonucleotide Synthesis, M. J. Gait ed., (1984); Mullis *et al.* U.S. Pat. No: 4,683,195; Nucleic Acid Hybridization, B. D. Hames & S. J. Higgins eds. (1984); Transcription And Translation, B. D. Hames & S. J. Higgins eds. (1984); Culture Of Animal Cells, R. I. Freshney, Alan R. Liss, Inc., (1987); Immobilized Cells And Enzymes, IRL Press, (1986); B. Perbal, A Practical Guide To Molecular Cloning (1984); the treatise, Methods In Enzymology, Academic Press, Inc., N.Y.; Gene Transfer Vectors For Mammalian Cells, J. H. Miller and M. P. Calos eds., Cold Spring Harbor Laboratory (1987); Methods In Enzymology, Vols. 154 and 155 (Wu *et al.* eds.); Immunochemical Methods In Cell And Molecular Biology, Mayer and Walker, eds., Academic Press, London (1987); Handbook Of Experimental Immunology, Volumes I-IV, D. M. Weir and C. C. Blackwell, eds., (1986); Manipulating the Mouse Embryo, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., (1986); and in Ausubel *et al.,* Current Protocols in Molecular Biology, John Wiley and Sons, Baltimore, Maryland (1989).

[0214] Standard reference works setting forth general principles of immunology include Current Protocols in Immunology, John Wiley & Sons, New York; Klein, J., Immunology: The Science of Self-Nonself Discrimination, John Wiley & Sons, New York (1982); Roitt, I., Brostoff, J. and Male D., Immunology, 6th ed. London: Mosby (2001); Abbas A., Abul, A. and Lichtman, A., Cellular and Molecular Immunology, Ed. 5, Elsevier Health Sciences Division (2005); and Harlow and Lane, Antibodies: A Laboratory Manual, Cold Spring Harbor Press (1988).

[0215] Having now described the present invention in detail, the same will be more clearly understood by reference to the following examples, which are included herewith for purposes of illustration only and are not intended to be limiting of the invention.

EXAMPLES

Example 1: Identification of Active FIX-XTEN Variants

[0216] FIX fusion proteins comprising a FIX polypeptide with one or more XTEN insertions to improve the properties of the FIX protein were constructed. However,

the location, length, composition and number of XTEN modifications can be readily varied, and impact of these modifications on the activity and clearance of FIX can be evaluated.

[0217] The present example aims to identify sites in FIX that can accommodate the introduction of XTENs without abrogating FIX activity and apply this approach to both otherwise non-modified FIX and a recombinant FIX-Fc fusion protein.

Methods

[0218] The FIX polypeptide coding sequence was ligated into expression vector pcDNA4/myc-His C (INVITROGEN™, Carlsbad, CA) between the BsiWI and PmeI sites following introduction of a Kozak translation initiation sequence (GCCGCCACC) immediately 5' to the ATG codon encoding the start Met residue.

[0219] HEK293F cells (INVITROGEN™, Carlsbad, CA) were transfected with plasmid using polyethyleneimine (PEI, Polysciences Inc., Warrington, PA). The transiently transfected cells were grown in FREESTYLE™ 293 medium or a mixture of FREESTYLE™ 293 and CD OPTICHO™ media (INVITROGEN™, Carlsbad, CA). The cell culture medium was harvested 5 days after transfection and analyzed for FIX activity by chromogenic or aPTT FIX activity assay.

[0220] The chromogenic FIX activity was measured using the BIOPHEN Factor IX kit from Aniara and all incubations were performed on a 37°C plate heater with shaking. Cell culture harvests from transient transfection media of FIX-XTEN variants from 6 well plates were diluted to the desired FIX activity range using Tris-BSA dilution buffer (R4). FIX standards were also prepared in Tris-BSA dilution buffer. The standards, diluted cell culture samples, and a pooled normal human plasma assay control (50 µL/well) were added to IMMULON® 2HB 96-well plates in duplicates. Human Factor X, FVIII:C and fibrin polymerization inhibitor (50 µL), 50 µL of mixture of Factor XIa, with thrombin, phospholipids and Calcium, and 50 µL of Factor Xa specific Chromogenic substrate (SXa-11) were added sequentially into each well, with 2 minutes incubation between each addition. After incubating with the substrate, 50 µL of 20% acetic acid was added to terminate the color reaction, and the absorbance at 405 nm was measured with a SPECTRAMAX® plus (MOLECULAR DEVICES®) instrument. Data analysis was performed using SOFTMAX® Pro Software (version 5.2).

[0221] A one stage activated partial thromboplastin time (aPTT) coagulation assay was employed to assess FIX activity. The FIX-XTEN aPTT activity was measured using the SYSMEX® CA-1500 instrument (Siemens Healthcare Diagnostics Inc., Tarrytown, NY). To create a standard curve for the assay, WHO Factor IX standard was diluted with mock transfection media with matching culture media concentration as the testing sample. Cell culture harvests from transient transfection media of FIX-XTEN variants from 6 well plates were diluted to the desired FIX activity range using mock transfection media. After dilution, the aPTT assay was performed using the Sysmex instrument as follow: 50 µl of diluted standards and samples were mixed with 50 µl Siemens human FIX depleted Plasma and then 50 µl of Siemens Actin FSL (ellagic acid) activator. The mixture was incubated for 1 min. Subsequently, 50 µl of Siemens $CaCl_2$ was added to the mixture and the mixture was incubated for 240 seconds. The clotting time was measured immediately following this incubation. To determine test samples FIX activity, the clotting times of the standards were plotted using log scales to extrapolate the equation between clotting time and FIX activity, and FIX-XTEN activity was then calculated against the standard curve.

Selection of Insertion Sites

[0222] FIX structures from Protein Data Bank, 1PFX, 1IXA, 1CFI, 1CFH,1EDM, 3LC3, 3LC5, 1RFN, 1X7A and 3KCG, were analyzed to select sites in FIX for XTEN insertion. XTEN insertion within the GLA domain was avoided due to the essential role of the GLA domain in anchoring FIX to phospholipid surfaces and subendothelial type IV collagen. XTEN insertion sites were selected by analysis of available FIX structures in the Protein Data Bank in conjunction with the following criteria: 1) calculated accessible surface area by algorithm software ASA View (http://www.abren.net/asaview/) and Get Area (http://curie.utmb.edu/getarea.html), 2) solvent accessibility assessed by hydrogen/deuterium exchange mass spectrometry (H/DX-MS), 3) exclusion of sites within defined secondary structural elements, 4) preference for positions with significant inter-species protein sequence variability, and 5) exclusion of sites proximal to known hemophilia B mutations.

[0223] Four sites in the EGF1 domain, 5 sites in the EGF2 domain, 2 sites in the linker region between the AP domain and the EGF2 domain, 4 sites in the AP (activation peptide) domain and 18 sites in the catalytic domain were selected for insertion of XTEN (Table 6).

Table 6: Potential sites for XTEN insertion into FIX (insertion at the c-terminus of the indicated residue)

FIX Domain	Selected Sites
EGF1	E52, G59, I66, K80
EGF2	D85, N89, A103, N105, E113
Linker	P129, K142
AP	V149, E162, D166, S174
Catalytic	K188, V202, E224, G226, K228, T230, E240, H257, K265, E277, S283, D292, K316, K341, H354, K392, R403, K413

Activity Screen of 42-Amino Acid XTEN Insertions and C-Terminal Fusion

[0224] The highly active FIX Padua variant (R338L) was used as a scaffold to counter potential FIX activity loss due to reduced activity caused by the introduction of XTENs. A 42-residue XTEN element (AE42) was inserted at sites selected by using the criteria above or fused at the C-terminus of FIX. FIX activities of these variants were evaluated in conditioned medium of transfected HEK293 cells as described above. FIX activities of FIX-AE42s are shown as percentage of the base construct without XTEN, FIX-R338L (Figure 1).

[0225] XTEN insertion was tolerated at limited sites as determined by FIX chromogenic assay (Figure 1 and Table 7). A total of 33 sites in FIX were selected and evaluated by insertion of AE-42. Of these, two in the EGF2 domain, one in the linker region between the EGF2 domain and the AP domain, four in the AP domain, and four in the catalytic domain, including the C terminus, were identified as permissive sites by FIX activity assay (Figure 1 and Table 7).

Table 7: Example FIX Insertion Sites

Insertion Site	Domain	Activity AE42	Activity AE72	Activity AE144	Activity AE288	Activity AE4864
52	EGF1	ND				
59	EGF1	ND				
66	EGF1	ND				
80	EGF1	ND				
85	EGF2	ND				
89	EGF2	ND				
103	EGF2	+	ND	ND	ND	ND
105	EGF2	+	ND	ND	ND	ND
113	EGF2	ND				
129	EGF2-AP Linker	ND				
142	EGF2-AP Linker	++	ND	ND	ND	ND
149	AP	+++	+	+	+	ND

162	AP	++	+	+	+	ND
166	AP	+++	+	+	+	ND
174	AP	+++	+	+	+	ND
188	Catalytic Domain	ND				
202	Catalytic Domain	+				
224	Catalytic Domain	+	+	ND	ND	ND
226	Catalytic Domain	+				
228	Catalytic Domain	+				
230	Catalytic Domain	ND				
240	Catalytic Domain	ND				
257	Catalytic Domain	+				
265	Catalytic Domain	ND				
277	Catalytic Domain	ND				
283	Catalytic Domain	ND				
292	Catalytic Domain	ND				
316	Catalytic Domain	ND				
341	Catalytic Domain	ND				
354	Catalytic Domain	ND				
392	Catalytic Domain	ND				
403	Catalytic Domain	ND				
413	Catalytic Domain	++	+	+	+	ND
415	C-Terminus	+++	+++	++	++	+

Note: ND = No activity detected; (+) = less than 30% activity detected; (++) = between 30% and 70% activity detected; and (+++) = greater than 70% activity detected as percent of base construct, by chromogenic assay (*see* Figures 5A-5C and 6A-6B).

Activity of Longer XTEN Insertions and C-Terminal Fusion

[0226] Longer XTENs (AE-72, -144 and -288) were then similarly tested at sites shown to be permissive for AE42 insertion. FIX activities were determined as previously described and are shown as percentage of the base construct without XTEN, FIX-R338L (Figure 2).

[0227] Only sites in AP and sites at or close to the C-terminus of FIX tolerated longer XTENs (AE144, AE288 or AE864) (Figure 2). FIX activity detected in conditioned medium inversely correlated with the length of XTEN introduced (Figure 2, table 7). Four insertion permissive sites in different domains of FIX were selected to generate a combinatorial library.

Multiple XTEN Insertions

[0228] Based on results obtained with single XTEN variants, FIX variants with multiple XTEN insertions of varying lengths and at four different locations (*see* Figure 4 and Table 8) were evaluated for FIX activity in conditioned medium of

transfected HEK293 cells, by aPTT assay (Tables 8-10). FIX activities are shown as percentage of the base construct without XTEN, FIX-R338L (Figure 4).

Table 8: Example FIX Double Insertions

Insertion Site 1	XTEN 1 (or Fc)	Insertion Site 2	XTEN 2 (or Fc)	Activity
105	AE42			++
166	AE42			++
166	AE72			+
166	AE144			+
224	AE42			+
C-Term	AE72			++
C-Term	AE144			+
C-Term	AE288			+
C-Term	Fc			++
166	AE42	C-Term	AE72	++
166	AE42	C-Term	AE144	+
166	AE42	C-Term	AE288	+
166	AE72	C-Term	AE72	+
166	AE72	C-Term	AE144	+
166	AE72	C-Term	AE288	+
166	AE144	C-Term	AE72	+
166	AE144	C-Term	AE144	+
166	AE144	C-Term	AE288	+
105	AE42	166	AE42	+
105	AE42	166	AE72	+
105	AE42	166	AE144	ND
105	AE42	C-Term	AE72	+
105	AE42	C-Term	AE144	+
105	AE42	C-Term	AE288	+
105	AE42	224	AE42	+
166	AE42	224	AE42	+
166	AE72	224	AE42	+
166	AE144	224	AE42	ND
224	AE42	C-Term	AE72	+
224	AE42	C-Term	AE144	+
224	AE42	C-Term	AE288	+
105	AE42	C-Term	Fc	+
224	AE42	C-Term	Fc	+
166	AE42	C-Term	Fc	+
166	AE72	C-Term	Fc	+
166	AE144	C-Term	Fc	+

Note: ND = No activity detected; (+) = less than 30% activity detected; (++) = between 30% and 70% activity detected; and (+++) = greater than 70% activity detected as percent of base construct, by chromogenic assay (*see* Figures 8A-8C).

Table 9: XTEN Elements Inserted into Each Domain

Location	Element
EGF2	AE42
AP	AE42, AE72, AE144
Catalytic 60-loop	AE42
C-term	AE72, AE144, AE288, Fc

Table 10: Total Number of Constructs Inserted as Single, Dual, Triple, and Quadruple Combinations

Combination	# Constructs
Single	9
Dual	27
Triple	31
Quadruple	12
	Total 79

[0229] Three groups, FIX with a single XTEN, FIX with dual XTEN insertions and FIX-Fc with a single XTEN insertion, showed detectable activity, while combination of insertion/fusion at three or more sites abolished FIX activity (Figure 4).

[0230] In conclusion, several permissive sites for XTEN insertion are present in FIX and select combinations of XTEN insertions variants retain FIX activity. Active FIX-XTEN variants identified here are candidates for pharmacokinetic characterization in hemophilia B mice.

Example 2: FIX Fusion Proteins and Its Plasma Recovery and AUC/D

[0231] Factor IX deficient (HemB, B6.129P2-F9tm1Dws/J, MGI:1932297) mice (Lin. et al., 1997) were originally acquired from Dr. Darrel Stafford (University of North Carolina, Chapel Hill). Male/female HemB mice were each injected intravenously with a single intravenous bolus injection of 50 or 200 IU/kg of FIX fusion proteins (*e.g.*, FIX-CT.288 (AE288 XTEN fused to the C-terminus of an FIX polypeptide), FIX-CT.864 (AE864 XTEN fused to the C-terminus of an FIX

polypeptide), FIX-AP.144 (AE144 XTEN inserted after D166 within the AP domain of a FIX polypeptide), FIX-AP.72 (AE72 XTEN inserted after D166 within the AP domain of a FIX polypeptide), FIX-AP.42 (AE42 XTEN inserted after D166 within the AP domain of a FIX polypeptide), FIXFc, and FIX) at a dosing volume of 10 mL/kg at t = 0 hour. Blood was collected at 5 minutes post dosing up to 168 hours (7 days) post dosing. For each indicated time point ~ 100 µl citrated blood was collected by retroorbital or terminal vena cava bleeding from 3-4 mice per time point. Up to 3 time points per mouse were generated. Plasma was isolated by centrifugation at 5000 rpm for 8 minutes and plasma samples were snap frozen in a dry-ice ethanol bath and stored at -80 °C until they were analyzed with one stage activated thromboplastin time (aPTT)-assay on a Sysmex-CA1500 coagulation analyzer, using Dade Behring reagents and actin FSL as activator and dosing material as activity standards. In Figures 5A-5B the plasma activities are plotted as % of injected dose. Mean Residence Time (MRT) and other pharmacokinetic (PK) parameters were calculated using non-compartmental modeling with Phoenix WinNonlin 6.2.1 (Pharsight, Certera by NCA analysis). Figure. 5C depicts the relative plasma recoveries (Y-axis) versus MRT (X-axis). The area of the dots represent the Area under the Curve per Dose (AUC/D, in h/kg/mL) and shows that FIX plasma activity recovery and AUC/D increase with increasing XTEN length (Figure 5C). The figures show that the FIX fusion proteins with increased XTEN length (288 and 864 at the C-terminus or 144, 72, and 42 in the AP domain) exhibit a size-dependent increase in plasma recovery up to 60% and increased AUC/D following intravenous bolus dosing.

Example 3: FIX Fusion Proteins and Their Half-Life

[0232] FIX deficient mice were intravenously dosed with 50 or 200 IU/kg of the FIX fusion proteins: FIX fused to an XTEN with 288 amino acids (e.g., AE288); FIX-Fc wherein an XTEN with 72 amino acids (e.g., AE72) is inserted at the AP domain after D166; FIX-Fc wherein an XTEN with 42 amino acids (e.g., AE42) is inserted at the AP domain after D166; and controls (e.g., FIXFc and FIX). Plasma was collected and FIX activity and PK analysis was performed identically to the methods described in Example 5. Figure 6A plots the plasma activities as % of injected dose. Pharmacokinetic (PK) parameters were calculated using WinNonlin 6.2.1 (Pharsight, Certera by NCA analysis and FIGURE 6B depicts the relative plasma recoveries (Y-

axis) versus MRT (X-axis). The area of the dots represents the Area under the Curve per Dose (AUC/D, in h/kg/mL) and shows that insertion of XTEN sequences into the activation peptide (AP) domain of FIXFc extends the mean residence time longer than that of rFIXFc alone compared to FIX (Figure 6B). In addition, plasma activity recovery and AUC/D are improved with increasing XTEN length (Figures 6A-6B). The AUC/D for rFIX-CT.288 (SEQ ID NO: 226) and rFIXFc-AP.72 (SEQ ID NO: 151) were 3.4 and 4.5-fold improved in comparison to rFIXFc, respectively (Figures 6A-6B). This is equivalent to a 8.5 and 14.5 fold improvement of AUC/D when compared to intravenously dosed rFIX, respectively (Figures 6A-6B). Therefore, combinations of XTEN insertions in the AP domain with Fc-mediated half-life extension in rFIXFc-R338L extend both the half-life and increase in the plasma recovery and AUC/Dose compared to that of rFIX and rFIXFc.

Example 4: Improved Pharmacokinetics of FIX Fusion Proteins by Subcutaneous Delivery.

[0233] FIX deficient mice were subcutaneously dosed at t=0 with 50 or 200 IU/kg of the FIX fusion proteins: FIX fused to an XTEN of 288 amino acids (e.g., AE288) at the C terminus (FIX-CT.288); FIXFc having an XTEN of 72 amino acids (e.g., AE72) in the AP domain (FIXFc-AP.72); FIXFc having an XTEN of 42 amino acids (e.g., AE42) in the EGF2 domain (e.g., FIXFc-EGF.42); and controls (FIXFc and FIX). Plasma was collected and FIX activity and PK analysis was performed identically to the methods described in Example 1. Figure 7A plots the plasma activities as % of injected dose. Pharmacokinetic (PK) parameters were calculated using WinNonlin 6.2.1 (Pharsight, Certera by NCA analysis, and Figure 7B depicts the relative bioavailability (Y-axis) versus MRT (X-axis). The area of the dots represents the Area under the Curve per Dose (AUC/D, in h/kg/mL) and shows that fusion of XTEN polypeptide sequences at the carboxy-terminus of rFIX or insertion of XTEN sequences into the activation peptide (AP) domain or EGF2 domain of FIXFc greatly improves the subcutaneous dosing profile of the FIX fusion proteins (Figure 7B). rFIXFc-AP.72 and rFIX-CT.288 have a 6 to 9-fold improved AUC/D, 1.5 to 2 fold improved bioavailability and 3 to 10 fold improved C_{max}/D for, compared to rFIXFc in HemB mice for subcutaneous dosing. When compared to rFIX the improvement in pharmacokinetic parameters is 28 to 40-fold improved AUC/D, 3-fold increased

bioavailability and 15 to 30-fold improved C_{max}/D compared to rFIX for FIXFc-AP.72 and rFIX-CT.288, respectively (Figures 7A-7B).

[0234] Taken together, the FIX fusion proteins (e.g., rFIX-CT.288 and rFIXFc-AP.72) showed a 2.6- and 1.9-fold improved AUC/D for subcutaneous dosing when compared to intravenous dosing of rFIXFc, the latter supporting once weekly or less frequent intravenous dosing in humans for prophylaxis.

Example 5: *In Vitro* Efficacy of FIX Fusion Proteins

[0235] Human hemophilia-B blood was spiked with the indicated doses of 3 10, and 30 IU/dL of rFIXFc (open circles, dotted line) or a FIX fusion protein (e.g., rFIXFc-AP.72) (solid dots, solid line) or vehicle (open triangle) (Figures 8A-8C). Whole blood clotting characteristics were determined using rotational thromboelastometry (ROTEM) and coagulation was initiated by recalcification of the blood (NATEM). rFIXFc-AP.72 showed similar activity compared to rFIXFc in hemophila-B blood, in respect to clotting time (CT in seconds), alpha angle (in degrees) and maximum clot firmness (MCF in mm) (Figures 8A-8C). The data each time point is the average +/- standard deviation of 4 to 5 replicate samples (Figures 8A-8C).

[0236] rFIXFc-AP.72 and rFIX-CT.288 show greatly improved subcutaneous pharmacokinetics in HemB mice compared to both rFIX and rFIXFc. Further studies are ongoing to address the efficacy and allometric scaling in preclinical animal models.

Example 6: *In Vivo* Efficacy of rFIXFc-AP.72 in an Acute Murine Tail Clip Bleeding Model

[0237] Acute efficacy was studied in a blinded murine tail-clip bleeding model, in which total blood loss in dosed mice is measured after tail tip amputation, as described previously (Dumont et al., Blood, 119(13):3024–3030, 2012). Briefly, 8-15 weeks old male Hemophilia B mice (Lin et al., Blood (1997) 90: 3962-3966) were anesthetized with a cocktail of 50 mg/kg ketamine and 0.5 mg/kg dexmedetomidine. The tails were immersed in 37°C saline for 10 minutes, to dilate the lateral vein followed by intravenous tail vein injection of either vehicle (3.88 g/L L-Histidine, 23.8 g/L Mannitol, 11.9 g/L Sucrose, 3.25 g/L Sodium Chloride, 0.01 % (w/v) Polysorbate 20 (pH 7.1), 3% human serum albumin), rFIXFc-AP.72, or rFIXFc at 50,

100, and 200 IU/kg. Five minutes post-dosing, the 5 mm distal tip of the tail was clipped and submerged into a pre-weighted tube containing 13 mL saline for the period of 30 minutes. Blood loss was quantified by weight. Statistical significance was calculated using unpaired two-tailed t-test in GraphPad Prism 6. Such two tailed t-tests showed that the 50, 100, and 200 IU /kg doses of rFIXFc-AP.72 were significantly different from vehicle (p-value < 0.0001). In addition, the data show that a low dose, e.g., 50 IU/kg, of rFIXFc-AP.72 results in significantly lower blood loss compared to the same low dose, i.e., 50 IU/kg, of rFIXFc. These results demonstrate equal or improved acute efficacy for rFIXFc-AP.72 compared to rFIXFc in this bleeding model.

Example 7: In vivo Efficacy of FIXFc-AP.72 in a Prophylactic Murine Tail Vein Transection Bleeding Model

[0238] Prolonged efficacy was studied in a blinded murine tail vein transection (TVT) bleeding model, in which survival time of dosed hemophilia-B mice is measured after transection of one lateral tail vein, as described previously (Toby et al., *PLOS One*, DOI:10.1371/journal.pone.0148255, 2016; Pan et al., *Blood 114*:2802-2822 (2009)). Briefly, 8-15 weeks old male hemophilia B mice (Lin et al., *Blood 90*: 3962-3966 (1997)) were pre-dosed intravenously with 15, 50, 100 IU/kg FIX activity of rFIXFc or matching subcutaneous doses of FIXFc-AP.72 and compared to mice receiving a bolus dose of vehicle. At 72 hours post dosing, all mice were anesthetized and one lateral tail vein was transected at a 2.7 mm tail diameter. During the 9 to 11 hours immediately following the TVT and then at an overnight time point at 24 hours, qualitative end points were monitored and recorded hourly, including rebleeding and time to death (as defined as the time to euthanization, as determined when the animal was moribund). All mice were euthanized at the end of 24 hour study, while animals not dead or moribund were determined to have survived at 24 hours.

[0239] Data were plotted as percent survival following TVT using GraphPad Prism 6. Mice dosed subcutaneously with vehicle (dotted line), subcutaneously with FIXFc-AP.72 (solid lines, closed symbols) or intravenously dosed with FIXFc (dashed lines, open symbols) (15 IU/ kg, 50 IU/kg, 100 IU/kg n = 20/dose except for vehicle dose; n = 30) (FIG. 10). The survival curves for mice treated with matching IU/kg doses of subcutaneously dosed FIXFc-AP.72 versus intravenously dosed rFIXFc showed

improved survival of HemB mice dosed subcutaneously with FIXFc-AP.72 compared to the equivalent intravenously dosed rFIXFc at all doses tested (FIG. 10).

Example 8: Improved intravenous and subcutaneous pharmacokinetic parameters for FIXFc-AP.72 (FIX-216, dual chain Fc) compared to rFIX in HemB mice.

[0240] Hemophilia-B mice were dosed with either 200 IU/kg FIXFc-AP.72 (FIX-216, dual chain Fc) or rFIX. Blood was collected by retro-orbital bleeding at the indicated times. Plasma levels of FIX were determined by one-stage clotting assay activity using dosing material as activity standards. In FIG. 11A plasma activity is plotted as % of injected dose. Fig. 11B shows a table of the pharmacokinetic parameters calculated using Phoenix WinNonLin 6.2.1 (Pharsight, Certara) by NCA (non-compartmental) analysis. Improved pharmacokinetic parameters shown for FIX-216 versus rFIX include the Mean Residence Time (MRT), the AUC/dose and other parameters.

[0241] Subcutaneous dosing of FIXFc-AP.72 shows a t_{max} around 20 hours post dosing in mice, and improved plasma activity levels compared to similar (IU/kg) intravenously dosed rFIX or rFIXFc. Using the TVT bleeding model in HemB mice we show that at 72 hours post dosing, subcutaneously dosed FIXFc-AP.72 has improved *in vivo* efficacy compared to intravenously dosed rFIXFc at all tested doses. Similarly, acute efficacy testing in the HemB mouse tail-clip bleeding model showed improved efficacy of intravenously dosed FIXFc-AP.72 compared to rFIXFc. These data support the potential of once weekly or less frequent subcutaneous prophylactic dosing of FIXFc-AP.72 in humans.

[0242] The foregoing description of the specific embodiments will so fully reveal the general nature of the invention that others can, by applying knowledge within the skill of the art, readily modify and/or adapt for various applications such specific embodiments, without undue experimentation, without departing from the general concept of the present invention. Therefore, such adaptations and modifications are intended to be within the meaning and range of equivalents of the disclosed embodiments, based on the teaching and guidance presented herein. It is to be understood that the phraseology or terminology herein is for the purpose of description and not of limitation, such that the terminology or phraseology of the

present specification is to be interpreted by the skilled artisan in light of the teachings and guidance.

[0243] Other embodiments of the invention will be apparent to those skilled in the art from consideration of the specification and practice of the invention disclosed herein. It is intended that the specification and examples be considered as exemplary only, with a true scope and spirit of the invention being indicated by the following claims.

[0244] The present application claims benefit to U.S. Provisional Application Nos. 62/200,590 filed August 3, 2015 and 62/281,993 filed January 22, 2016, which are incorporated herein by reference in their entirety.

EMBODIMENTS

[0245] E1. A Factor IX (FIX) fusion protein comprising a FIX polypeptide and at least one XTEN which is inserted within the FIX polypeptide at an insertion site corresponding to an amino acid selected from the group consisting of amino acid 103 of SEQ ID NO: 2, amino acid 105 of SEQ ID NO: 2, amino acid 142 of SEQ ID NO: 2, amino acid 149 of SEQ ID NO: 2, amino acid 162 of SEQ ID NO: 2, amino acid 166 of SEQ ID NO: 2, amino acid 174 of SEQ ID NO: 2, amino acid 224 of SEQ ID NO: 2, amino acid 226 of SEQ ID NO: 2, amino acid 228 of SEQ ID NO: 2, amino acid 413 of SEQ ID NO: 2, and any combination thereof, and wherein the FIX fusion protein exhibits procoagulant activity.

[0246] E2. The FIX fusion protein of E1, wherein the insertion site corresponds to an amino acid selected from the group consisting of amino acid 149 of SEQ ID NO: 2, amino acid 162 of SEQ ID NO: 2, amino acid 166 of SEQ ID NO: 2, amino acid 174 of SEQ ID NO: 2 and any combination thereof.

[0247] E3. The FIX fusion protein of E1 or E2, wherein the insertion site corresponds to an amino acid selected from the group consisting of amino acid 224 of SEQ ID NO: 2, amino acids 226 of SEQ ID NO: 2, amino acids 228 of SEQ ID NO: 2; amino acid 413 of SEQ ID NO: 2, and any combination thereof.

[0248] E4. The FIX fusion protein of any one of E1 to E3, wherein the insertion site corresponds to an amino acid selected from the group consisting of amino acid 103 of SEQ ID NO: 2, amino acid 105 of SEQ ID NO: 2, and both.

[0249] E5. The FIX fusion protein of any one of E1 to E4, wherein the insertion site corresponds to amino acid 142 of SEQ ID NO: 2.

[0250] E6. The FIX fusion protein of any one of E1 to E5, wherein the XTEN comprises at least about 6 amino acids, at least about 12 amino acids, at least about 36 amino acids, at least about 42 amino acids, at least about 72 amino acids, at least about 144 amino acids, or at least about 288 amino acids.

[0251] E7. The FIX fusion protein of any one of E1 to E6, wherein the XTEN comprises AE42, AE72, AE864, AE576, AE288, AE144, AG864, AG576, AG288, AG144, or any combination thereof.

[0252] E8. The FIX fusion protein of any one of E1 to E7, wherein the XTEN comprises an amino acid sequence at least about 80%, at least about 85%, at least

about 90%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, at least about 99%, or about 100% identical to an amino acid sequence selected from the group consisting of SEQ ID NOs: 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, and any combination thereof.

[0253] E9. The FIX fusion protein of E7 or E8, wherein the XTEN comprises AE72 or AE144.

[0254] E10. The FIX fusion protein of any one of E1 to E9, which further comprises a second XTEN.

[0255] E11. The FIX fusion protein of E10, wherein the second XTEN is inserted within the FIX polypeptide at an insertion site corresponding to an amino acid selected from the group consisting of amino acid 103 of SEQ ID NO: 2, amino acid 105 of SEQ ID NO: 2, amino acid 142 of SEQ ID NO: 2, amino acid 149 of SEQ ID NO: 2, amino acid 162 of SEQ ID NO: 2, amino acid 166 of SEQ ID NO: 2, amino acid 174 of SEQ ID NO: 2, amino acid 224 of SEQ ID NO: 2, amino acid 226 of SEQ ID NO: 2, amino acid 228 of SEQ ID NO: 2, amino acid 413 of SEQ ID NO: 2, and any combination thereof or wherein the second XTEN is fused to either the C-terminus of the FIX polypeptide or a linker fused to the C-terminus of the FIX polypeptide.

[0256] E12. The FIX fusion protein of E10 or E11, wherein the XTEN and the second XTEN are inserted within the FIX polypeptide at an insertion site corresponding to an amino acid and/or fused to the C-terminus of the FIX polypeptide selected from the group consisting of:

i. amino acid 105 of SEQ ID NO: 2 and amino acid 166 of SEQ ID NO: 2;

ii. amino acid 105 of SEQ ID NO: 2 and amino acid 224 of SEQ ID NO: 2;

iii. amino acid 105 of SEQ ID NO: 2 and fused to the C-terminus;

iv. amino acid 166 of SEQ ID NO: 2 and amino acid 224 of SEQ ID NO: 2;

v. amino acid 166 of SEQ ID NO: 2 and fused to the C-terminus; and

vi. amino acid 224 of SEQ ID NO: 2 and fused to the C-terminus, respectively.

[0257] E13. The FIX fusion protein of E10 or E11, wherein the XTEN is inserted within the FIX polypeptide at an insertion site corresponding to amino acid 166 of

SEQ ID NO: 2, and wherein the second XTEN is fused to the C-terminus of the FIX polypeptide.

[0258] E14. The FIX fusion protein of any one of E10 to E13, wherein the second XTEN comprises at least about 6 amino acids, at least about 12 amino acids, at least about 36 amino acids, at least about 42 amino acids, at least about 72 amino acids, at least about 144 amino acids, or at least about 288 amino acids.

[0259] E15. The FIX fusion protein of any one of E10 to E14, wherein the second XTEN is selected from the group consisting of AE42, AE72, AE864, AE576, AE288, AE144, AG864, AG576, AG288, AG144, and any combination thereof.

[0260] E16. The FIX fusion protein of E15, wherein the second XTEN is AE72 or AE144.

[0261] E17. The FIX fusion protein of any one of E10 to E16, wherein the second XTEN comprises an amino acid sequence at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, at least about 99%, or about 100% identical to an amino acid sequence selected from the group consisting of SEQ ID NOs: 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, and any combination thereof.

[0262] E18. The FIX fusion protein of any one of E10 to E17, which further comprises a third, a fourth, a fifth, or a sixth XTEN.

[0263] E19. A FIX fusion protein comprising a FIX polypeptide and a heterologous moiety comprising an XTEN, wherein the XTEN is fused to the C-terminus of the FIX polypeptide and comprises an amino acid sequence of longer than 42 amino acids and shorter than 144 amino acids in length.

[0264] E20. The FIX fusion protein of E19, wherein the XTEN comprises an amino acid sequence of longer than 50, 55, 60, 65, or 70 amino acids and shorter than 140, 130, 120, 110, 100, 90, or 80 amino acids or any combination thereof.

[0265] E21. The FIX fusion protein of E20, wherein the XTEN is 72 amino acids in length.

[0266] E22. The FIX fusion protein of E21, wherein the XTEN is AE72.

[0267] E23. The FIX fusion protein of E19, wherein the XTEN comprises an amino acid sequence at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, at least about 99%, or 100% identical to SEQ ID NO: 35.

[0268] E24. The FIX fusion protein of any one of E1 to E23, further comprising an Fc domain.

[0269] E25. The FIX fusion protein of E24, wherein the Fc domain is fused to the FIX polypeptide or the XTEN.

[0270] E26. The FIX fusion protein of E24 or E25, comprising a second Fc domain.

[0271] E27. The FIX fusion protein of E26, wherein the second Fc domain is associated with the first Fc domain.

[0272] E28. The FIX fusion protein of E26 or E27, which comprises two polypeptide chains, wherein the first polypeptide chain comprises the FIX polypeptide fused to the Fc domain, and the second polypeptide chain comprises the second Fc domain, wherein the first Fc domain and the second Fc domain are associated by a covalent bond.

[0273] E29. The FIX fusion protein of E26 or E27, which is a single polypeptide chain comprising the FIX polypeptide, the Fc domain, the second Fc domain, and a linker which links the Fc domain and the second Fc domain.

[0274] E30. The FIX fusion protein of E29, wherein the linker further comprises one or more intracellular processing sites.

[0275] E31. The FIX fusion protein of E29 or E30, wherein the linker comprises $(Gly_4Ser)_n$, wherein n is an integer selected from 1 to 100.

[0276] E32. The FIX fusion protein of E1 to E31, comprising an amino acid sequence at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, at least about 99%, or about 100% identical to a sequence selected from the group consisting of SEQ ID NO: 54 to SEQ ID NO: 153 without the signal peptide and the propeptide sequence.

[0277] E33. The FIX fusion protein of any one of E1 to E32, which has at least about 10%, at least about 20%, at least about 30%, at least about 40%, at least about 50%, at least about 60%, at least about 70%, at least about 80%, at least about 90% or 100% of the procoagulant activity of native FIX.

[0278] E34. The FIX fusion protein of E33, wherein the procoagulant activity is measured by a chromogenic substrate assay, a one stage clotting assay, or both.

[0279] E35. The FIX fusion protein of any one of E1 to E34, wherein the FIX polypeptide is a R338L FIX variant.

[0280] E36. The FIX fusion protein of E35, wherein the R338L FIX variant comprises an amino acid sequence at least about 80%, at least about 85%, at least

about 90%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, at least about 99%, or 100% identical to SEQ ID NO: 2.

[0281] E37. An isolated polynucleotide comprising a sequence encoding the FIX fusion protein of any one of E1 to E36.

[0282] E38. An expression vector comprising the polynucleotide of E37.

[0283] E39. A host cell comprising the polynucleotide of E37 or the vector of E38.

[0284] E40. The host cell of E39, wherein the FIX fusion protein is expressed *in vivo*.

[0285] E41. The host cell of E39, wherein the FIX fusion protein is expressed *in vitro*.

[0286] E42. A method of producing a FIX fusion protein comprising culturing the host cell of E39 under conditions in which the FIX fusion protein is expressed.

[0287] E43. A composition comprising the FIX fusion protein of any one of E1 to E36, the polynucleotide of E37, the expression vector of E38, or the host cell of any one of E39 to E41 and a pharmaceutically acceptable carrier.

[0288] E44. A method of preventing, treating, ameliorating, or managing a clotting disease or condition in a patient in need thereof comprising administering an effective amount of the FIX fusion protein of any one of E1 to E36, the polynucleotide of E37, the expression vector of E38, the host cell of any one of E39 to E41, or the composition of E43.

[0289] E45. The method of E44, wherein the administering comprises subcutaneous administration to the patient.

[0290] E46. A method for diagnosing or imaging a clotting disease or condition in a subject comprising contacting the FIX fusion protein of any one of E1 to E36, the polynucleotide of E37, the expression vector of E38, or the host cell of any one of E39 to E41 with a sample of the subject.

[0291] E47. A method of extending a half-life of a FIX polypeptide comprising inserting an XTEN within the FIX polypeptide at an insertion site corresponding to an amino acid selected from the group consisting of amino acid 103 of SEQ ID NO: 2, amino acid 105 of SEQ ID NO: 2, amino acid 142 of SEQ ID NO: 2, amino acid 149 of SEQ ID NO: 2, amino acid 162 of SEQ ID NO: 2, amino acid 166 of SEQ ID NO: 2, amino acid 174 of SEQ ID NO: 2, amino acid 224 of SEQ ID NO: 2, amino acid 226 of SEQ ID NO: 2, amino acid 228 of SEQ ID NO: 2, amino acid 413 of SEQ ID

NO: 2, and any combination thereof, thereby constructing a FIX fusion protein, wherein the FIX protein exhibits procoagulant activity.

[0292] E48. A Factor IX (FIX) fusion protein comprising a first chain and a second chain, wherein:

a. the first chain comprises:

i. a FIX polypeptide;

ii. at least one XTEN, wherein the at least one XTEN is inserted within the FIX polypeptide at an insertion site corresponding to amino acid 166 of SEQ ID NO: 2, and wherein the at least one XTEN comprises an amino acid sequence having at least about 72 amino acids; and

iii. a first Fc domain, wherein the first Fc domain is fused to the FIX polypeptide of the at least one XTEN; and

b. the second chain comprises a second Fc domain

wherein the first Fc domain and the second Fc domain are associated by a covalent bond; and wherein the FIX fusion protein exhibits procoagulant activity.

[0293] E49. The FIX fusion protein of E48, wherein the at least one XTEN comprises an amino acid sequence at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, at least about 99%, or about 100% identical to the amino acid sequence of SEQ ID NO: 35.

[0294] E50. The FIX fusion protein of E48 or E49, wherein the first chain of the FIX fusion protein comprises an amino acid sequence at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, or at least about 99% identical to the amino acid sequence of SEQ ID NO: 227; and wherein the second chain of the FIX fusion protein comprises an amino acid sequence at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, or at least about 99% identical to the amino acid sequence of SEQ ID NO: 228.

[0295] E51. The FIX fusion protein of any one of E48 to E50, wherein the first chain of the FIX fusion protein comprises an amino acid sequence of SEQ ID NO: 227; and wherein the second chain of the FIX fusion protein comprises an amino acid sequence of SEQ ID NO: 228.

[0296] The following vector sequences are referenced in the proceeding examples and elsewhere in the present application. The following key will aid in understanding the information:

Key:
Signal peptide (pre-peptide)
Pro-peptide
Linker with or without protein tag
Cleavage site
Insertion or fusion of XTEN and/or Fc

SEQ ID NO: 54 E0113 AE42; PNL118
MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTE**GAPGSPAGSPTSTEEGTSESATPESGP**
GSEPATSGSETPASSGYRLAENQKSCEPAVPFPCGRVSVSQTSKLTRAETVFPDVDYVNSTE
AETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHC
VETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSY
VTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYN
NMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWI
KEKTKLTGPEGPSKLTRAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 55 N0089 AE42 pNL116
MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCN**GAPGSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPASS**IKNGRCEQF
CKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQTSKLTRAETVFPDVDYVNSTE
AETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHC
VETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSY
VTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYN
NMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWI
KEKTKLTGPEGPSKLTRAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 56 **A**0103 AE42 pNL117
MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSA**GAPGSPAGSPTSTEEGTSESATPESGPGSEPATSGSE**
TPASSDNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQTSKLTRAETVFPDVDYVNSTE
AETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHC
VETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSY
VTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYN
NMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWI
KEKTKLTGPEGPSKLTRAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 57 P0129 AE42 pNL119
MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVP**GAPGSPAGSPT**
STEEGTSESATPESGPGSEPATSGSETPASSFPCGRVSVSQTSKLTRAETVFPDVDYVNSTE
AETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHC
VETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSY
VTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYN
NMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWI
KEKTKLTGPEGPSKLTRAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 58 K0142_AE42 pNL120

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SK**GAPGSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPASS**LTRAETVFPDVDYVNSTE
AETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHC
VETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSY
VTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYN
NMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWI
KEKTKLTGPEGPSKLTRAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 59 V0149_AE42 pNL121

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETV**GAPGSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPASS**FPDVDYVNSTE
AETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHC
VETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSY
VTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYN
NMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWI
KEKTKLTGPEGPSKLTRAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 60 E0162_AE42 pNL122

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAE**GAPGSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPA**
SSTILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHC
VETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSY
VTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYN
NMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWI
KEKTKLTGPEGPSKLTRAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 61 D0166_AE42 pNL123

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILD**GAPGSPAGSPTSTEEGTSESATPESGPGSEPATSGS**
ETPASSNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHC
VETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSY
VTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYN
NMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWI
KEKTKLTGPEGPSKLTRAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 62 S0174_AE42 pNL124

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILDNITQSTQS**GAPGSPAGSPTSTEEGTSESATPESGPG**
SEPATSGSETPASSFNDFTRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHC
VETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSY
VTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYN
NMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWI
KEKTKLTGPEGPSKLTRAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 63 K0188_AE42 pNL125

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE

GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILDNITQSTQSFNDFTRVVGGEDAK**GAPGSPAGSPTSTE**
EGTSESATPESGPGSEPATSGSETPASSPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHC
VETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSY
VTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYN
NMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWI
KEKTKLTGPEGPSKLTRAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 64 V0202_AE42 pNL126

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKV
GAPGSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPASSDAFCGGSIVNEKWIVTAAHC
VETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSY
VTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYN
NMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWI
KEKTKLTGPEGPSKLTRAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 65 E0224_AE42 pNL127

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKV
DAFCGGSIVNEKWIVTAAHCVE**GAPGSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPA**
SSTGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSY
VTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYN
NMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWI
KEKTKLTGPEGPSKLTRAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 66 E0240_AE42 pNL128

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKV
DAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNIEE**GAPGSPAGSPTSTEEGTSESATPE**
SGPGSEPATSGSETPASSTEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSY
VTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYN
NMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWI
KEKTKLTGPEGPSKLTRAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 67 H0257_AE42 pNL129

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKV
DAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHH**GAPGSPA**
GSPTSTEEGTSESATPESGPGSEPATSGSETPASSNYNAAINKYNHDIALLELDEPLVLNSY
VTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYN
NMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWI
KEKTKLTGPEGPSKLTRAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 68 K0265_AE42 pNL130

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKV
DAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAIN

K**GAPGSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPASS**YNHDIALLELDEPLVLNSY
VTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYN
NMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWI
KEKTKLTGPEGPSKLTRAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 69 E0277_AE42 pNL131

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKV
DAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAIN
KYNHDIALLELDE**GAPGSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPASS**PLVLNSY
VTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYN
NMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWI
KEKTKLTGPEGPSKLTRAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 70 D0292_AE42 pNL132

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKV
DAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAIN
KYNHDIALLELDEPLVLNSYVTPICIAD**GAPGSPAGSPTSTEEGTSESATPESGPGSEPATS**
GSETPASSKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYN
NMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWI
KEKTKLTGPEGPSKLTRAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 71 K0316_AE42 pNL133

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKV
DAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAIN
KYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFLKFGSGYVSGWGRVFHK**GAPGSPAGSP**
TSTEEGTSESATPESGPGSEPATSGSETPASSGRSALVLQYLRVPLVDRATCLLSTKFTIYN
NMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWI
KEKTKLTGPEGPSKLTRAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 72 K0341_AE42 pNL134

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKV
DAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAIN
KYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYL
RVPLVDRATCLLSTK**GAPGSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPASS**FTIYN
NMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWI
KEKTKLTGPEGPSKLTRAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 73 H0354_AE42 pNL135

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKV
DAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAIN
KYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYL
RVPLVDRATCLLSTKFTIYNNMFCAGFH**GAPGSPAGSPTSTEEGTSESATPESGPGSEPATS**

GSETPASSEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWI
KEKTKLTGPEGPSKLTRAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHHH

SEQ ID NO: 74 K0392_AE42 pNL136
MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKV
DAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAIN
KYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYL
RVPLVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEE
CAMK**GAPGSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPASS**GKYGIYTKVSRYVNWI
KEKTKLTGPEGPSKLTRAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHHH

SEQ ID NO: 75 R0403_AE42 pNL137
MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKV
DAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAIN
KYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYL
RVPLVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEE
CAMKGKYGIYTKVSR**GAPGSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPASS**YVNWI
KEKTKLTGPEGPSKLTRAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHHH

SEQ ID NO: 76 K0413_AE42 pNL138
MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKV
DAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAIN
KYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYL
RVPLVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEE
CAMKGKYGIYTKVSRYVNWIKEKTK**GAPGSPAGSPTSTEEGTSESATPESGPGSEPATSGSE
TPASS**LTGPEGPSKLTRAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHHH

SEQ ID NO: 77 CT_AE42 pNL140
MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKV
DAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAIN
KYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYL
RVPLVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEE
CAMKGKYGIYTKVSRYVNWIKEKTKLTGAGSPGAETA***LVPRSFLLRNPNDKYEPFWEDEES***G
AGSPGAETA**GAPGSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPASS**GAETAEQKLIS
EEDLSPATGHHHHHHHHH

SEQ ID NO: 78 E0052_AE42 pNL141
MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCE**GAPGSPAGSPTSTEEGTSESATPESG
PGSEPATSGSETPASS**SNPCLNGGSCKDDINSYECWCPFGFEGKNCELDVTCNIKNGRCEQF
CKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQTSKLTRAETVFPDVDYVNSTE
AETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHC
VETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSY
VTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYN
NMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWI
KEKTKLTGPEGPSKLTRAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHHH

SEQ ID NO: 79 G0059_AE42 pNL142

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNG**GAPGSPAGSPTSTEEGTSE**
SATPESGPGSEPATSGSETPASSGSCKDDINSYECWCPFGFEGKNCELDVTCNIKNGRCEQF
CKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQTSKLTRAETVFPDVDYVNSTE
AETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHC
VETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSY
VTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYN
NMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWI
KEKTKLTGPEGPSKLTRAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 80 I0066_AE42 pNL143

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDI**GAPGSPAGSPTS**
TEEGTSESATPESGPGSEPATSGSETPASSNSYECWCPFGFEGKNCELDVTCNIKNGRCEQF
CKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQTSKLTRAETVFPDVDYVNSTE
AETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHC
VETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSY
VTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYN
NMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWI
KEKTKLTGPEGPSKLTRAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 81 K0080_AE42 pNL144

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GK**GAPGSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPASS**NCELDVTCNIKNGRCEQF
CKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQTSKLTRAETVFPDVDYVNSTE
AETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHC
VETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSY
VTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYN
NMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWI
KEKTKLTGPEGPSKLTRAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 82 D0085_AE42 pNL145

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELD**GAPGSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPASS**VTCNIKNGRCEQF
CKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQTSKLTRAETVFPDVDYVNSTE
AETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHC
VETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSY
VTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYN
NMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWI
KEKTKLTGPEGPSKLTRAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 83 CT_AE144 pNL164

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKV
DAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAIN
KYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYL
RVPLVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEE
CAMKGKYGIYTKVSRYVNWIKEKTKLTGAGSPGAETA***LVPRSFLLRNPNDKYEPFWEDEES***G
AGSPGAETA**GAPTSTEPSEGSAPGTSESATPESGPGTSESATPESGPGTSESATPESGPGSE**
PATSGSETPGSEPATSGSETPGSPAGSPTSTEEGTSTEPSEGSAPGTSTEPSEGSAPGSEPA
TSGSETPGTSESATPESGPGTSTEPSEGSAPGASSGAETAEQKLISEEDLSPATGHHHHHHH
H

SEQ ID NO: 84 CT_AE288 pNL165

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKV
DAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAIN
KYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYL
RVPLVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEE
CAMKGKYGIYTKVSRYVNWIKEKTKLTGAGSPGAETA***LVPRSFLLRNPNDKYEPFWEDEES***G
AGSPGAETA**GAPGTSESATPESGPGSEPATSGSETPGTSESATPESGPGSEPATSGSETPGT**
SESATPESGPGTSTEPSEGSAPGSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPGTSE
SATPESGPGSPAGSPTSTEEGSPAGSPTSTEEGTSTEPSEGSAPGTSESATPESGPGTSESA
TPESGPGTSESATPESGPGSEPATSGSETPGSEPATSGSETPGSPAGSPTSTEEGTSTEPSE
GSAPGTSTEPSEGSAPGSEPATSGSETPGTSESATPESGPGTSTEPSEGSAPASSGAETAEQ
KLISEEDLSPATGHHHHHHHHH

SEQ ID NO: 85 CT_AE864 pNL166

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKV
DAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAIN
KYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYL
RVPLVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEE
CAMKGKYGIYTKVSRYVNWIKEKTKLTGAGSPGAETA***LVPRSFLLRNPNDKYEPFWEDEES***G
AGSPGAETA**GAPGSPAGSPTSTEEGTSESATPESGPGTSTEPSEGSAPGSPAGSPTSTEEGT**
STEPSEGSAPGTSTEPSEGSAPGTSESATPESGPGSEPATSGSETPGSEPATSGSETPGSPA
GSPTSTEEGTSESATPESGPGTSTEPSEGSAPGTSTEPSEGSAPGSPAGSPTSTEEGTSTEP
SEGSAPGTSTEPSEGSAPGTSESATPESGPGTSTEPSEGSAPGTSESATPESGPGSEPATSG
SETPGTSTEPSEGSAPGTSTEPSEGSAPGTSESATPESGPGTSESATPESGPGSPAGSPTST
EEGTSESATPESGPGSEPATSGSETPGTSESATPESGPGTSTEPSEGSAPGTSTEPSEGSAP
GTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGSPAGSPTSTEEGT
STEPSEGSAPGTSESATPESGPGSEPATSGSETPGTSESATPESGPGSEPATSGSETPGTSE
SATPESGPGTSTEPSEGSAPGTSESATPESGPGSPAGSPTSTEEGSPAGSPTSTEEGSPAGS
PTSTEEGTSESATPESGPGTSTEPSEGSAPGTSESATPESGPGSEPATSGSETPGTSESATP
ESGPGSEPATSGSETPGTSESATPESGPGTSTEPSEGSAPGSPAGSPTSTEEGTSESATPES
GPGSEPATSGSETPGTSESATPESGPGSPAGSPTSTEEGSPAGSPTSTEEGTSTEPSEGSAP
GTSESATPESGPGTSESATPESGPGTSESATPESGPGSEPATSGSETPGSEPATSGSETPGS
PAGSPTSTEEGTSTEPSEGSAPGTSTEPSEGSAPGSEPATSGSETPGTSESATPESGPGTST
EPSEGSAPASSGAETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 86 K0142_AE72 pNL167

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SK**GAPSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPGTSESATPESGPGTSTEPSEGS**
APGTSTEPSEGSAPGASSLTRAETVFPDVDYVNSTEAETILDNITQSTQSFNDFTRVVGGED
AKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNIEETEHTEQKR
NVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFLKFGSGYVSGW
GRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQGDSGGPHVTE
VEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWIKEKTKLTGPEGPSKLTRAETGAGSPG
AETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 87 K0142_AE144 pNL168

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT

SK**GAPSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPGTSESATPESGPGTSTEPSEGS**
APGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAP
GSPAGSPTSTEEGTSTEPSEGSAPGASSLTRAETVFPDVDYVNSTEAETILDNITQSTQSFN
DFTRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNI
EETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFL
KFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQ
GDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWIKEKTKLTGPEGPSKLT
RAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHHH

SEQ ID NO: 88 K0142_AE288 pNL169

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SK**GAPGTSESATPESGPGSEPATSGSETPGTSESATPESGPGSEPATSGSETPGTSESATPE**
SGPGTSTEPSEGSAPGSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPGTSESATPESG
PGSPAGSPTSTEEGSPAGSPTSTEEGTSTEPSEGSAPGTSESATPESGPGTSESATPESGPG
TSESATPESGPGSEPATSGSETPGSEPATSGSETPGSPAGSPTSTEEGTSTEPSEGSAPGTS
TEPSEGSAPGSEPATSGSETPGTSESATPESGPGTSTEPSEGSAPASSLTRAETVFPDVDYV
NSTEAETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVT
AAHCVETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLV
LNSYVTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKF
TIYNNMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRY
VNWIKEKTKLTGPEGPSKLTRAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHHH

SEQ ID NO: 89 V0149_AE72 pNL170

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETV**GAPSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPGTSESATPESGPGTS**
TEPSEGSAPGTSTEPSEGSAPGASSFPDVDYVNSTEAETILDNITQSTQSFNDFTRVVGGED
AKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNIEETEHTEQKR
NVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFLKFGSGYVSGW
GRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQGDSGGPHVTE
VEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWIKEKTKLTGPEGPSKLTRAETGAGSPG
AETAEQKLISEEDLSPATGHHHHHHHHH

SEQ ID NO: 90 V0149_AE144 pNL171

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETV**GAPSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPGTSESATPESGPGTS**
TEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGTSTE
PSEGSAPGSPAGSPTSTEEGTSTEPSEGSAPGASSFPDVDYVNSTEAETILDNITQSTQSFN
DFTRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNI
EETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFL
KFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQ
GDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWIKEKTKLTGPEGPSKLT
RAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHHH

SEQ ID NO: 91 V0149_AE288 pNL172

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETV**GAPGTSESATPESGPGSEPATSGSETPGTSESATPESGPGSEPATSGSETPGT**
SESATPESGPGTSTEPSEGSAPGSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPGTSE
SATPESGPGSPAGSPTSTEEGSPAGSPTSTEEGTSTEPSEGSAPGTSESATPESGPGTSESA
TPESGPGTSESATPESGPGSEPATSGSETPGSEPATSGSETPGSPAGSPTSTEEGTSTEPSE
GSAPGTSTEPSEGSAPGSEPATSGSETPGTSESATPESGPGTSTEPSEGSAPASSFPDVDYV

NSTEAETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVT
AAHCVETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLV
LNSYVTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKF
TIYNNMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRY
VNWIKEKTKLTGPEGPSKLTRAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 92 E0162_AE72 pNL173

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAE**GAPSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPGT**
SESATPESGPGTSTEPSEGSAPGTSTEPSEGSAPGASSTILDNITQSTQSFNDFTRVVGGED
AKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNIEETEHTEQKR
NVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFLKFGSGYVSGW
GRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQGDSGGPHVTE
VEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWIKEKTKLTGPEGPSKLTRAETGAGSPG
AETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 93 E0162_AE144 pNL174

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAE**GAPSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPGT**
SESATPESGPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGTST
EPSEGSAPGTSTEPSEGSAPGSPAGSPTSTEEGTSTEPSEGSAPGASSTILDNITQSTQSFN
DFTRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNI
EETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFL
KFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQ
GDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWIKEKTKLTGPEGPSKLT
RAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 94 E0162_AE288 pNL175

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAE**GAPGTSESATPESGPGSEPATSGSETPGTSESATPESGPG**
SEPATSGSETPGTSESATPESGPGTSTEPSEGSAPGSPAGSPTSTEEGTSESATPESGPGSE
PATSGSETPGTSESATPESGPGSPAGSPTSTEEGSPAGSPTSTEEGTSTEPSEGSAPGTSES
ATPESGPGTSESATPESGPGTSESATPESGPGSEPATSGSETPGSEPATSGSETPGSPAGSP
TSTEEGTSTEPSEGSAPGTSTEPSEGSAPGSEPATSGSETPGTSESATPESGPGTSTEPSEG
SAPASSTILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVT
AAHCVETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLV
LNSYVTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKF
TIYNNMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRY
VNWIKEKTKLTGPEGPSKLTRAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 95 D0166_AE72 pNL176

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILD**GAPSPAGSPTSTEEGTSESATPESGPGSEPATSGSE**
TPGTSESATPESGPGTSTEPSEGSAPGTSTEPSEGSAPGASSNITQSTQSFNDFTRVVGGED
AKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNIEETEHTEQKR
NVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFLKFGSGYVSGW
GRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQGDSGGPHVTE
VEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWIKEKTKLTGPEGPSKLTRAETGAGSPG
AETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 96 D0166_AE144 pNL177

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILD**GAPSPAGSPTSTEEGTSESATPESGPGSEPATSGSE**
TPGTSESATPESGPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAP
GTSTEPSEGSAPGTSTEPSEGSAPGSPAGSPTSTEEGTSTEPSEGSAPGASSNITQSTQSFN
DFTRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNI
EETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFL
KFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQ
GDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWIKEKTKLTGPEGPSKLT
RAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 97 D0166_AE288 pNL178

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILD**GAPGTSESATPESGPGSEPATSGSETPGTSESATPE**
SGPGSEPATSGSETPGTSESATPESGPGTSTEPSEGSAPGSPAGSPTSTEEGTSESATPESG
PGSEPATSGSETPGTSESATPESGPGSPAGSPTSTEEGSPAGSPTSTEEGTSTEPSEGSAPG
TSESATPESGPGTSESATPESGPGTSESATPESGPGSEPATSGSETPGSEPATSGSETPGSP
AGSPTSTEEGTSTEPSEGSAPGTSTEPSEGSAPGSEPATSGSETPGTSESATPESGPGTSTE
PSEGSAPASSNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVT
AAHCVETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLV
LNSYVTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKF
TIYNNMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRY
VNWIKEKTKLTGPEGPSKLTRAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 98 S0174_AE72 pNL179

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILDNITQSTQS**GAPSPAGSPTSTEEGTSESATPESGPGS**
EPATSGSETPGTSESATPESGPGTSTEPSEGSAPGTSTEPSEGSAPGASSFNDFTRVVGGED
AKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNIEETEHTEQKR
NVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFLKFGSGYVSGW
GRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQGDSGGPHVTE
VEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWIKEKTKLTGPEGPSKLTRAETGAGSPG
AETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 99 S0174_AE144 pNL180

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILDNITQSTQS**GAPSPAGSPTSTEEGTSESATPESGPGS**
EPATSGSETPGTSESATPESGPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGTST
EPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGSPAGSPTSTEEGTSTEPSEGSAPGASSFN
DFTRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNI
EETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFL
KFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQ
GDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWIKEKTKLTGPEGPSKLT
RAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 100 S0174_AE288 pNL181

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILDNITQSTQS**GAPGTSESATPESGPGSEPATSGSETPG**

TSESATPESGPGSEPATSGSETPGTSESATPESGPGTSTEPSEGSAPGSPAGSPTSTEEGTS
ESATPESGPGSEPATSGSETPGTSESATPESGPGSPAGSPTSTEEGSPAGSPTSTEEGTSTE
PSEGSAPGTSESATPESGPGTSESATPESGPGTSESATPESGPGSEPATSGSETPGSEPATS
GSETPGSPAGSPTSTEEGTSTEPSEGSAPGTSTEPSEGSAPGSEPATSGSETPGTSESATPE
SGPGTSTEPSEGSAPASSFNDFTRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVT
AAHCVETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLV
LNSYVTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKF
TIYNNMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRY
VNWIKEKTKLTGPEGPSKLTRAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHHH

SEQ ID NO: 101 E0224_AE72 pNL182
MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKV
DAFCGGSIVNEKWIVTAAHCVE**GAPSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPGT**
SESATPESGPGTSTEPSEGSAPGTSTEPSEGSAPGASSTGVKITVVAGEHNIEETEHTEQKR
NVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFLKFGSGYVSGW
GRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQGDSGGPHVTE
VEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWIKEKTKLTGPEGPSKLTRAETGAGSPG
AETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 102 E0224_AE144 pNL183
MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKV
DAFCGGSIVNEKWIVTAAHCVE**GAPSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPGT**
SESATPESGPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGTST
EPSEGSAPGTSTEPSEGSAPGSPAGSPTSTEEGTSTEPSEGSAPGASSTGVKITVVAGEHNI
EETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFL
KFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQ
GDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWIKEKTKLTGPEGPSKLT
RAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 103 E0224_AE288 pNL184
MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKV
DAFCGGSIVNEKWIVTAAHCVE**GAPGTSESATPESGPGSEPATSGSETPGTSESATPESGPG**
SEPATSGSETPGTSESATPESGPGTSTEPSEGSAPGSPAGSPTSTEEGTSESATPESGPGSE
PATSGSETPGTSESATPESGPGSPAGSPTSTEEGSPAGSPTSTEEGTSTEPSEGSAPGTSES
ATPESGPGTSESATPESGPGTSESATPESGPGSEPATSGSETPGSEPATSGSETPGSPAGSP
TSTEEGTSTEPSEGSAPGTSTEPSEGSAPGSEPATSGSETPGTSESATPESGPGTSTEPSEG
SAPASSTGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLV
LNSYVTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKF
TIYNNMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRY
VNWIKEKTKLTGPEGPSKLTRAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 104 K0413_AE72 pNL185
MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKV
DAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAIN
KYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYL
RVPLVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEE

CAMKGKYGIYTKVSRYVNWIKEKTK**GAPSPAGSPTSTEEGTSESATPESGPGSEPATSGSET**
PGTSESATPESGPGTSTEPSEGSAPGTSTEPSEGSAPGASSLTGPEGPSKLTRAETGAGSPG
AETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 105 K0413_AE144 pNL186

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKV
DAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAIN
KYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYL
RVPLVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEE
CAMKGKYGIYTKVSRYVNWIKEKTK**GAPSPAGSPTSTEEGTSESATPESGPGSEPATSGSET**
PGTSESATPESGPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPG
TSTEPSEGSAPGTSTEPSEGSAPGSPAGSPTSTEEGTSTEPSEGSAPGASSLTGPEGPSKLT
RAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 106 K0413_AE288 pNL187

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKV
DAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAIN
KYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYL
RVPLVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEE
CAMKGKYGIYTKVSRYVNWIKEKTK**GAPGTSESATPESGPGSEPATSGSETPGTSESATPES**
GPGSEPATSGSETPGTSESATPESGPGTSTEPSEGSAPGSPAGSPTSTEEGTSESATPESGP
GSEPATSGSETPGTSESATPESGPGSPAGSPTSTEEGSPAGSPTSTEEGTSTEPSEGSAPGT
SESATPESGPGTSESATPESGPGTSESATPESGPGSEPATSGSETPGSEPATSGSETPGSPA
GSPTSTEEGTSTEPSEGSAPGTSTEPSEGSAPGSEPATSGSETPGTSESATPESGPGTSTEP
SEGSAPASSLTGPEGPSKLTRAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 107 A0103_AE72 pNL188

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSA**GAPSPAGSPTSTEEGTSESATPESGPGSEPATSGSET**
PGTSESATPESGPGTSTEPSEGSAPGTSTEPSEGSAPGASSDNKVVCSCTEGYRLAENQKSC
EPAVPFPCGRVSVSQTSKLTRAETVFPDVDYVNSTEAETILDNITQSTQSFNDFTRVVGGED
AKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNIEETEHTEQKR
NVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFLKFGSGYVSGW
GRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQGDSGGPHVTE
VEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWIKEKTKLTGPEGPSKLTRAETGAGSPG
AETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 108 A0103_AE144 pNL189

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSA**GAPSPAGSPTSTEEGTSESATPESGPGSEPATSGSET**
PGTSESATPESGPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPG
TSTEPSEGSAPGTSTEPSEGSAPGSPAGSPTSTEEGTSTEPSEGSAPGASSDNKVVCSCTEG
YRLAENQKSCEPAVPFPCGRVSVSQTSKLTRAETVFPDVDYVNSTEAETILDNITQSTQSFN
DFTRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNI
EETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFL
KFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQ
GDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWIKEKTKLTGPEGPSKLT
RAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 109 A0103_AE288 pNL190

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSA**GAPGTSESATPESGPGSEPATSGSETPGTSESATPES**
GPGSEPATSGSETPGTSESATPESGPGTSTEPSEGSAPGSPAGSPTSTEEGTSESATPESGP
GSEPATSGSETPGTSESATPESGPGSPAGSPTSTEEGSPAGSPTSTEEGTSTEPSEGSAPGT
SESATPESGPGTSESATPESGPGTSESATPESGPGSEPATSGSETPGSEPATSGSETPGSPA
GSPTSTEEGTSTEPSEGSAPGTSTEPSEGSAPGSEPATSGSETPGTSESATPESGPGTSTEP
SEGSAPASSDNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQTSKLTRAETVFPDVDYV
NSTEAETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVT
AAHCVETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLV
LNSYVTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKF
TIYNNMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRY
VNWIKEKTKLTGPEGPSKLTRAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHHH

SEQ ID NO: 110 G0226_AE42 pNL195

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKV
DAFCGGSIVNEKWIVTAAHCVETG**GAPGSPAGSPTSTEEGTSESATPESGPGSEPATSGSET**
PASSVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSY
VTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYN
NMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWI
KEKTKLTGPEGPSKLTRAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 111 K0228_AE42 pNL196

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKV
DAFCGGSIVNEKWIVTAAHCVETGVK**GAPGSPAGSPTSTEEGTSESATPESGPGSEPATSGS**
ETPASSITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSY
VTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYN
NMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWI
KEKTKLTGPEGPSKLTRAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 112 T0230_AE42 pNL197

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKV
DAFCGGSIVNEKWIVTAAHCVETGVKIT**GAPGSPAGSPTSTEEGTSESATPESGPGSEPATS**
GSETPASSVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSY
VTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYN
NMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWI
KEKTKLTGPEGPSKLTRAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 113 N0105_AE42 pNL198

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADN**GAPGSPAGSPTSTEEGTSESATPESGPGSEPATSG**
SETPASSKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQTSKLTRAETVFPDVDYVNSTE
AETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHC
VETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSY
VTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYN
NMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWI
KEKTKLTGPEGPSKLTRAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 114 S0283_AE42 pNL199

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKV
DAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAIN
KYNHDIALLELDEPLVLNS**GAPGSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPASS**Y
VTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYN
NMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWI
KEKTKLTGPEGPSKLTRAETGAGSPGAETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 115 CT_AE72 pNL202

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKV
DAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAIN
KYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYL
RVPLVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEE
CAMKGKYGIYTKVSRYVNWIKEKTKLTGAGSPGAETA***LVPRSFLLRNPNDKYEPFWEDEES***G
AGSPGAETA**GAPSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPGTSESATPESGPGTS**
TEPSEGSAPGTSTEPSEGSAPGASSGAETAEQKLISEEDLSPATGHHHHHHHH

SEQ ID NO: 116 C-term-AE864 FIX-092

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKV
DAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAIN
KYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYL
RVPLVDRATCLRSTKFTIYNNMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEE
CAMKGKYGIYTKVSRYVNWIKEKTKLTGPEGPS***KLTRAET***GSP**GSPAGSPTSTEEGTSESAT**
PESGPGTSTEPSEGSAPGSPAGSPTSTEEGTSTEPSEGSAPGTSTEPSEGSAPGTSESATPE
SGPGSEPATSGSETPGSEPATSGSETPGSPAGSPTSTEEGTSESATPESGPGTSTEPSEGSA
PGTSTEPSEGSAPGSPAGSPTSTEEGTSTEPSEGSAPGTSTEPSEGSAPGTSESATPESGPG
TSTEPSEGSAPGTSESATPESGPGSEPATSGSETPGTSTEPSEGSAPGTSTEPSEGSAPGTS
ESATPESGPGTSESATPESGPGSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPGTSES
ATPESGPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPS
EGSAPGTSTEPSEGSAPGSPAGSPTSTEEGTSTEPSEGSAPGTSESATPESGPGSEPATSGS
ETPGTSESATPESGPGSEPATSGSETPGTSESATPESGPGTSTEPSEGSAPGTSESATPESG
PGSPAGSPTSTEEGSPAGSPTSTEEGSPAGSPTSTEEGTSESATPESGPGTSTEPSEGSAPG
TSESATPESGPGSEPATSGSETPGTSESATPESGPGSEPATSGSETPGTSESATPESGPGTS
TEPSEGSAPGSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPGTSESATPESGPGSPAG
SPTSTEEGSPAGSPTSTEEGTSTEPSEGSAPGTSESATPESGPGTSESATPESGPGTSESAT
PESGPGSEPATSGSETPGSEPATSGSETPGSPAGSPTSTEEGTSTEPSEGSAPGTSTEPSEG
SAPGSEPATSGSETPGTSESATPESGPGTSTEPSEGSAPGSSS

SEQ ID NO: 117 C-Term-AE144 pJH0131

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKV
DAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAIN
KYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYL
RVPLVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEE
CAMKGKYGIYTKVSRYVNWIKEKTKLTGAGSPGAETA***LVPRSFLLRNPNDKYEPFWEDEES***G
AGSPGAETA**GAPSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPGTSESATPESGPGTS**

TEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGTSTE PSEGSAPGSPAGSPTSTEEGTSTEPSEGSAPGASS

SEQ ID NO: 118 N105-AE42 pJH44

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE GKNCELDVTCNIKNGRCEQFCKNSADN**GAPGSPAGSPTSTEEGTSESATPESGPGSEPATSG SETPASS**KVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQTSKLTRAETVFPDVDYVNSTE AETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHC VETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSY VTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYN NMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWI KEKTKLT

SEQ ID NO: 119 D166-AE72 pJH46

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT SKLTRAETVFPDVDYVNSTEAETILD**GAPSPAGSPTSTEEGTSESATPESGPGSEPATSGSE TPGTSESATPESGPGTSTEPSEGSAPGTSTEPSEGSAPGASS**NITQSTQSFNDFTRVVGGED AKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNIEETEHTEQKR NVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFLKFGSGYVSGW GRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQGDSGGPHVTE VEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWIKEKTKLT

SEQ ID NO: 120 D166-AE144 pJH47

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT SKLTRAETVFPDVDYVNSTEAETILD**GAPSPAGSPTSTEEGTSESATPESGPGSEPATSGSE TPGTSESATPESGPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAP GTSTEPSEGSAPGTSTEPSEGSAPGSPAGSPTSTEEGTSTEPSEGSAPGASS**NITQSTQSFN DFTRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNI EETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFL KFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQ GDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWIKEKTKLT

SEQ ID NO: 121 C-Term-AE144 pJH50

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT SKLTRAETVFPDVDYVNSTEAETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKV DAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAIN KYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYL RVPLVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEE CAMKGKYGIYTKVSRYVNWIKEKTKLTGAGSPGAETA***LVPRSFLLRNPNDKYEPFWEDEES***G AGSPGAETA**GAPTSTEPSEGSAPGTSESATPESGPGTSESATPESGPGTSESATPESGPGSE PATSGSETPGSEPATSGSETPGSPAGSPTSTEEGTSTEPSEGSAPGTSTEPSEGSAPGSEPA TSGSETPGTSESATPESGPGTSTEPSEGSAPGASS**

SEQ ID NO: 122 C-Term-AE288 pJH51

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT SKLTRAETVFPDVDYVNSTEAETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKV DAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAIN KYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYL

RVPLVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEE
CAMKGKYGIYTKVSRYVNWIKEKTKLTGAGSPGAETA***LVPRSFLLRNPNDKYEPFWEDEES***G
AGSPGAETA**GAPGTSESATPESGPGSEPATSGSETPGTSESATPESGPGSEPATSGSETPGT**
SESATPESGPGTSTEPSEGSAPGSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPGTSE
SATPESGPGSPAGSPTSTEEGSPAGSPTSTEEGTSTEPSEGSAPGTSESATPESGPGTSESA
TPESGPGTSESATPESGPGSEPATSGSETPGSEPATSGSETPGSPAGSPTSTEEGTSTEPSE
GSAPGTSTEPSEGSAPGSEPATSGSETPGTSESATPESGPGTSTEPSEGSAPASS

SEQ ID NO: 123 C-Term-AE72 pJH52
MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKV
DAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAIN
KYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYL
RVPLVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEE
CAMKGKYGIYTKVSRYVNWIKEKTKLTGAGSPGAETA***LVPRSFLLRNPNDKYEPFWEDEES***G
AGSPGAETA**GAPTSESATPESGPGSEPATSGSETPGTSESATPESGPGSEPATSGSETPGTS**
ESATPESGPGTSTEPSEGSAPGASS

SEQ ID NO: 124 E224-AE42 pJH54
MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKV
DAFCGGSIVNEKWIVTAAHCVE**GAPGSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPA**
SSTGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSY
VTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYN
NMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWI
KEKTKLT

SEQ ID NO: 125 D166-AE42 pJH55
MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILD**GAPGSPAGSPTSTEEGTSESATPESGPGSEPATSGS**
ETPASSNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHC
VETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSY
VTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYN
NMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWI
KEKTKL

SEQ ID NO: 126 D166-AE42, C-Term-AE72 pJH59
MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILD**GAPGSPAGSPTSTEEGTSESATPESGPGSEPATSGS**
ETPASSNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHC
VETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSY
VTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYN
NMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWI
KEKTKLTGAGSPGAETA***LVPRSFLLRNPNDKYEPFWEDEES***GAGSPGAETA**GAPTSESATPE**
SGPGSEPATSGSETPGTSESATPESGPGSEPATSGSETPGTSESATPESGPGTSTEPSEGSA
PGAS

SEQ ID NO: 127 D166-AE42, C-Term-AE144 pJH60
MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE

GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILD**GAPGSPAGSPTSTEEGTSESATPESGPGSEPATSGS**
ETPASSNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHC
VETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSY
VTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYN
NMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWI
KEKTKLTGAGSPGAETA***LVPRSFLLRNPNDKYEPFWEDEES***GAGSPGAETA**GAPSPAGSPTS**
TEEGTSESATPESGPGSEPATSGSETPGTSESATPESGPGTSTEPSEGSAPGTSTEPSEGSA
PGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGSPAGSPTSTEEG
TSTEPSEGSAPGASS

SEQ ID NO: 128 D166-AE42, C-Term-AE288 pJH61

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILD**GAPGSPAGSPTSTEEGTSESATPESGPGSEPATSGS**
ETPASSNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHC
VETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSY
VTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYN
NMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWI
KEKTKLTGAGSPGAETA***LVPRSFLLRNPNDKYEPFWEDEES***GAGSPGAETAGAP**GTSESATP**
ESGPGSEPATSGSETPGTSESATPESGPGSEPATSGSETPGTSESATPESGPGTSTEPSEGS
APGSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPGTSESATPESGPGSPAGSPTSTEE
GSPAGSPTSTEEGTSTEPSEGSAPGTSESATPESGPGTSESATPESGPGTSESATPESGPGS
EPATSGSETPGSEPATSGSETPGSPAGSPTSTEEGTSTEPSEGSAPGTSTEPSEGSAPGSEP
ATSGSETPGTSESATPESGPGTSTEPSEGSAPASS

SEQ ID NO: 129 D166-AE72, C-Term-AE72 pJH62

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILD**GAPSPAGSPTSTEEGTSESATPESGPGSEPATSGSE**
TPGTSESATPESGPGTSTEPSEGSAPGTSTEPSEGSAPGASSNITQSTQSFNDFTRVVGGED
AKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNIEETEHTEQKR
NVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFLKFGSGYVSGW
GRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQGDSGGPHVTE
VEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWIKEKTKLTGAGSPGAETA***LVPRSFLLR***
NPNDKYEPFWEDEESGAGSPGAETA**GAPTSESATPESGPGSEPATSGSETPGTSESATPESG**
PGSEPATSGSETPGTSESATPESGPGTSTEPSEGSAPGASS

SEQ ID NO: 130 D166-AE72, C-Term-AE144 pJH63

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILD**GAPSPAGSPTSTEEGTSESATPESGPGSEPATSGSE**
TPGTSESATPESGPGTSTEPSEGSAPGTSTEPSEGSAPGASSNITQSTQSFNDFTRVVGGED
AKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNIEETEHTEQKR
NVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFLKFGSGYVSGW
GRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQGDSGGPHVTE
VEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWIKEKTKLTGAGSPGAETA***LVPRSFLLR***
NPNDKYEPFWEDEESGAGSPGAETA**GAPSPAGSPTSTEEGTSESATPESGPGSEPATSGSET**
PGTSESATPESGPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPG
TSTEPSEGSAPGTSTEPSEGSAPGSPAGSPTSTEEGTSTEPSEGSAPGASS

SEQ ID NO: 131 D166-AE72, C-Term-AE288 pJH64

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT

SKLTRAETVFPDVDYVNSTEAETILD**GAPSPAGSPTSTEEGTSESATPESGPGSEPATSGSE**
TPGTSESATPESGPGTSTEPSEGSAPGTSTEPSEGSAPGASSNITQSTQSFNDFTRVVGGED
AKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNIEETEHTEQKR
NVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFLKFGSGYVSGW
GRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQGDSGGPHVTE
VEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWIKEKTKLTGAGSPGAETA***LVPRSFLLR***
NPNDKYEPFWEDEESGAGSPGAETA**GAPGTSESATPESGPGSEPATSGSETPGTSESATPES**
GPGSEPATSGSETPGTSESATPESGPGTSTEPSEGSAPGSPAGSPTSTEEGTSESATPESGP
GSEPATSGSETPGTSESATPESGPGSPAGSPTSTEEGSPAGSPTSTEEGTSTEPSEGSAPGT
SESATPESGPGTSESATPESGPGTSESATPESGPGSEPATSGSETPGSEPATSGSETPGSPA
GSPTSTEEGTSTEPSEGSAPGTSTEPSEGSAPGSEPATSGSETPGTSESATPESGPGTSTEP
SEGSAPASS

SEQ ID NO: 132 D166-AE144, C-Term-AE72 pJH65

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILD**GAPSPAGSPTSTEEGTSESATPESGPGSEPATSGSE**
TPGTSESATPESGPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAP
GTSTEPSEGSAPGTSTEPSEGSAPGSPAGSPTSTEEGTSTEPSEGSAPGASSNITQSTQSFN
DFTRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNI
EETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFL
KFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQ
GDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWIKEKTKLTGAGSPGAET
A***LVPRSFLLRNPNDKYEPFWEDEES***GAGSPGAETA**GAPTSESATPESGPGSEPATSGSETPG**
TSESATPESGPGSEPATSGSETPGTSESATPESGPGTSTEPSEGSAPGASS

SEQ ID NO: 133 D166-AE144, C-Term-AE144 pJH66

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILD**GAPSPAGSPTSTEEGTSESATPESGPGSEPATSGSE**
TPGTSESATPESGPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAP
GTSTEPSEGSAPGTSTEPSEGSAPGSPAGSPTSTEEGTSTEPSEGSAPGASSNITQSTQSFN
DFTRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNI
EETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFL
KFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQ
GDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWIKEKTKLTGAGSPGAET
A***LVPRSFLLRNPNDKYEPFWEDEES***GAGSPGAETA**GAPSPAGSPTSTEEGTSESATPESGPG**
SEPATSGSETPGTSESATPESGPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGTS
TEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGSPAGSPTSTEEGTSTEPSEGSAPGASS

SEQ ID NO: 134 D166-AE144, C-Term-AE288 pJH67

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILD**GAPSPAGSPTSTEEGTSESATPESGPGSEPATSGSE**
TPGTSESATPESGPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAP
GTSTEPSEGSAPGTSTEPSEGSAPGSPAGSPTSTEEGTSTEPSEGSAPGASSNITQSTQSFN
DFTRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNI
EETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFL
KFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQ
GDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWIKEKTKLTGAGSPGAET
A***LVPRSFLLRNPNDKYEPFWEDEES***GAGSPGAETA**GAPGTSESATPESGPGSEPATSGSETP**
GTSESATPESGPGSEPATSGSETPGTSESATPESGPGTSTEPSEGSAPGSPAGSPTSTEEGT
SESATPESGPGSEPATSGSETPGTSESATPESGPGSPAGSPTSTEEGSPAGSPTSTEEGTST
EPSEGSAPGTSESATPESGPGTSESATPESGPGTSESATPESGPGSEPATSGSETPGSEPAT

SGSETPGSPAGSPTSTEEGTSTEPSEGSAPGTSTEPSEGSAPGSEPATSGSETPGTSESATP ESGPGTSTEPSEGSAPASS

SEQ ID NO: 135 N105-AE42, D166-AE42 pJH68

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE GKNCELDVTCNIKNGRCEQFCKNSADN**GAPGSPAGSPTSTEEGTSESATPESGPGSEPATSG SETPASS**KVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQTSKLTRAETVFPDVDYVNSTE AETILD**GAPGSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPASS**NITQSTQSFNDFTR VVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNIEETE HTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFLKFGS GYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQGDSG GPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWIKEKTKLT

SEQ ID NO: 136 N105-AE42, D166-AE72 pJH69

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE GKNCELDVTCNIKNGRCEQFCKNSADN**GAPGSPAGSPTSTEEGTSESATPESGPGSEPATSG SETPASS**KVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQTSKLTRAETVFPDVDYVNSTE AETILD**GAPSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPGTSESATPESGPGTSTEP SEGSAPGTSTEPSEGSAPGASS**NITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKVDAFC GGSIVNEKWIVTAAHCVETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNH DIALLELDEPLVLNSYVTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPL VDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMK GKYGIYTKVSRYVNWIKEKTKLT

SEQ ID NO: 137 N105-AE42, D166-AE144 pJH70

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE GKNCELDVTCNIKNGRCEQFCKNSADN**GAPGSPAGSPTSTEEGTSESATPESGPGSEPATSG SETPASS**KVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQTSKLTRAETVFPDVDYVNSTE AETILD**GAPSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPGTSESATPESGPGTSTEP SEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSE GSAPGSPAGSPTSTEEGTSTEPSEGSAPGASS**NITQSTQSFNDFTRVVGGEDAKPGQFPWQV VLNGKVDAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHN YNAAINKYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSA LVLQYLRVPLVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGI ISWGEECAMKGKYGIYTKVSRYVNWIKEKTKLT

SEQ ID NO: 138 N105-AE42, C-Term-AE72 pJH71

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQ GNLERECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWC PFGFEGKNCELDVTCNIKNGRCEQFCKNSADN**GAPGSPAGSPTSTEEGTSESATPESGPGSE PATSGSETPASS**KVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQTSKLTRAETVFPDVDY VNSTEAETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIV TAAHCVETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPL VLNSYVTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTK FTIYNNMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSR YVNWIKEKTKLTGAGSPGAETA***LVPRSFLLRNPNDKYEPFWEDEES***GAGSPGAETAGAP**TSE SATPESGPGSEPATSGSETPGTSESATPESGPGSEPATSGSETPGTSESATPESGPGTSTEP SEGSAPGASS**

SEQ ID NO: 139 N105-AE42, C-Term-AE144 pJH72

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE GKNCELDVTCNIKNGRCEQFCKNSADN**GAPGSPAGSPTSTEEGTSESATPESGPGSEPATSG SETPASS**KVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQTSKLTRAETVFPDVDYVNSTE AETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHC

VETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSY
VTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYN
NMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWI
KEKTKLTGAGSPGAETA***LVPRSFLLRNPNDKYEPFWEDEES***GAGSPGAETA**GAPSPAGSPTS**
TEEGTSESATPESGPGSEPATSGSETPGTSESATPESGPGTSTEPSEGSAPGTSTEPSEGSA
PGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGSPAGSPTSTEEG
TSTEPSEGSAPGASS

SEQ ID NO: 140 N105-AE42, C-Term-AE288 pJH73
MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADN**GAPGSPAGSPTSTEEGTSESATPESGPGSEPATSG**
SETPASSKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQTSKLTRAETVFPDVDYVNSTE
AETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHC
VETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSY
VTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYN
NMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWI
KEKTKLTGAGSPGAETA***LVPRSFLLRNPNDKYEPFWEDEES***GAGSPGAETA**GAPGTSESATP**
ESGPGSEPATSGSETPGTSESATPESGPGSEPATSGSETPGTSESATPESGPGTSTEPSEGS
APGSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPGTSESATPESGPGSPAGSPTSTEE
GSPAGSPTSTEEGTSTEPSEGSAPGTSESATPESGPGTSESATPESGPGTSESATPESGPGS
EPATSGSETPGSEPATSGSETPGSPAGSPTSTEEGTSTEPSEGSAPGTSTEPSEGSAPGSEP
ATSGSETPGTSESATPESGPGTSTEPSEGSAPASS

SEQ ID NO: 141 N105-AE42, E224-AE42 pJH74
MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADN**GAPGSPAGSPTSTEEGTSESATPESGPGSEPATSG**
SETPASSKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQTSKLTRAETVFPDVDYVNSTE
AETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHC
VE**GAPGSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPASS**TGVKITVVAGEHNIEETE
HTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFLKFGS
GYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQGDSG
GPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWIKEKTKLT

SEQ ID NO: 142 D166-AE42, E224-AE42 pJH75
MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILD**GAPGSPAGSPTSTEEGTSESATPESGPGSEPATSGS**
ETPASSNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHC
VE**GAPGSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPASS**TGVKITVVAGEHNIEETE
HTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFLKFGS
GYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQGDSG
GPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWIKEKTKLT

SEQ ID NO: 143 D166-AE72, E224-AE42 pJH76
MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILD**GAPSPAGSPTSTEEGTSESATPESGPGSEPATSGSE**
TPGTSESATPESGPGTSTEPSEGSAPGTSTEPSEGSAPGASSNITQSTQSFNDFTRVVGGED
AKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHCVE**GAPGSPAGSPTSTEEGTSESATPE**
SGPGSEPATSGSETPASSTGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNH
DIALLELDEPLVLNSYVTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPL
VDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMK
GKYGIYTKVSRYVNWIKEKTKLT

SEQ ID NO: 144 D166-AE144, E224-AE42 pJH77

MEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFEGK
NCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQTSK
LTRAETVFPDVDYVNSTEAETILD**GAPSPAGSPTSTEEGTSESATPESGPGSEPATSGSETP**
GTSESATPESGPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGT
STEPSEGSAPGTSTEPSEGSAPGSPAGSPTSTEEGTSTEPSEGSAPGASSNITQSTQSFNDF
TRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHCVE**GAPGSPAGSPTSTEEG**
TSESATPESGPGSEPATSGSETPASSTGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYN
AAINKYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALV
LQYLRVPLVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIIS
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SEQ ID NO: 145 E224-AE42, C-Term-AE72 pJH78

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKV
DAFCGGSIVNEKWIVTAAHCVE**GAPGSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPA**
SSTGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSY
VTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYN
NMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWI
KEKTKLTGAGSPGAETA***LVPRSFLLRNPNDKYEPFWEDEES***GAGSPGAETAGAP**TSESATPE**
SGPGSEPATSGSETPGTSESATPESGPGSEPATSGSETPGTSESATPESGPGTSTEPSEGSA
PGASS

SEQ ID NO: 146 E224-AE42, C-Term-AE144 pJH79

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKV
DAFCGGSIVNEKWIVTAAHCVE**GAPGSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPA**
SSTGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSY
VTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYN
NMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWI
KEKTKLTGAGSPGAETA***LVPRSFLLRNPNDKYEPFWEDEES***GAGSPGAETA**GAPSPAGSPTS**
TEEGTSESATPESGPGSEPATSGSETPGTSESATPESGPGTSTEPSEGSAPGTSTEPSEGSA
PGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGSPAGSPTSTEEG
TSTEPSEGSAPGASS

SEQ ID NO: 147 E224-AE42, C-Term-AE288 pJH80

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKV
DAFCGGSIVNEKWIVTAAHCVE**GAPGSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPA**
SSTGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSY
VTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYN
NMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWI
KEKTKLTGAGSPGAETA***LVPRSFLLRNPNDKYEPFWEDEES***GAGSPGAETA**GAPGTSESATP**
ESGPGSEPATSGSETPGTSESATPESGPGSEPATSGSETPGTSESATPESGPGTSTEPSEGS
APGSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPGTSESATPESGPGSPAGSPTSTEE
GSPAGSPTSTEEGTSTEPSEGSAPGTSESATPESGPGTSESATPESGPGTSESATPESGPGS
EPATSGSETPGSEPATSGSETPGSPAGSPTSTEEGTSTEPSEGSAPGTSTEPSEGSAPGSEP
ATSGSETPGTSESATPESGPGTSTEPSEGSAPASS

SEQ ID NO: 148 N105-AE42, C-Term-Fc pJH81

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE

GKNCELDVTCNIKNGRCEQFCKNSADN**GAPGSPAGSPTSTEEGTSESATPESGPGSEPATSG**
SETPASSKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQTSKLTRAETVFPDVDYVNSTE
AETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHC
VETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSY
VTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYN
NMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWI
KEKTKLT**DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF**
NWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTIS
KAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLD
SDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGGSGGGGSGGGG
SGGGGS**DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFN**
WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISK
AKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDS
DGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

SEQ ID NO: 149 E224-AE42, C-Term-Fc pJH82

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKV
DAFCGGSIVNEKWIVTAAHCVE**GAPGSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPA**
SSTGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSY
VTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYN
NMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWI
KEKTKLT**DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF**
NWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTIS
KAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLD
SDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGGSGGGGSGGGG
SGGGGS**DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFN**
WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISK
AKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDS
DGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

SEQ ID NO: 150 D166-AE42, C-Term-Fc pJH83

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILD**GAPGSPAGSPTSTEEGTSESATPESGPGSEPATSGS**
ETPASSNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHC
VETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSY
VTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYN
NMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWI
KEKTKLT**DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF**
NWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTIS
KAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLD
SDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGGSGGGGSGGGG
SGGGGS**DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFN**
WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISK
AKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDS
DGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

SEQ ID NO: 151 D166-AE72, C-Term-Fc pJH84

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILD**GAPSPAGSPTSTEEGTSESATPESGPGSEPATSGSE**
TPGTSESATPESGPGTSTEPSEGSAPGTSTEPSEGSAPGASSNITQSTQSFNDFTRVVGGED
AKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNIEETEHTEQKR

NVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFLKFGSGYVSGW
GRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQGDSGGPHVTE
VEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWIKEKTKLT**DKTHTCPPCPAPELLGGPS**
VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYR
VVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQV
SLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSC
SVMHEALHNHYTQKSLSLSPGKGGGGSGGGGSGGGGSGGGGS**DKTHTCPPCPAPELLGGPSV**
FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRV
VSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVS
LTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCS
VMHEALHNHYTQKSLSLSPGK

SEQ ID NO: 152 D166-AE144, C-Term-Fc pJH85

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQ
GNLERECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWC
PFGFEGKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRV
SVSQTSKLTRAETVFPDVDYVNSTEAETILD**GAPSPAGSPTSTEEGTSESATPESGPGSEPA**
TSGSETPGTSESATPESGPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPSEGSAPGTSTEPS
EGSAPGTSTEPSEGSAPGTSTEPSEGSAPGSPAGSPTSTEEGTSTEPSEGSAPGASSNITQS
TQSFNDFTRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHCVETGVKITVVA
GEHNIEETEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSYVTPICIADKEY
TNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLLSTKFTIYNNMFCAGFHEGG
RDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWIKEKTKLT**DKTH**
TCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHN
AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQV
YTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKL
TVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGGSGGGGSGGGGSGGGGS**DKTHT**
CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNA
KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVY
TLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQ

SEQ ID NO: 153 C-Term-Fc pJH56

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLER
ECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFE
GKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQT
SKLTRAETVFPDVDYVNSTEAETILDNITQSTQSFNDFTRVVGGEDAKPGQFPWQVVLNGKV
DAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNIEETEHTEQKRNVIRIIPHHNYNAAIN
KYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYL
RVPLVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEE
CAMKGKYGIYTKVSRYVNWIKEKTKLT**DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISR**
TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGK
EYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAV
EWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSL
SLSPGKGGGGSGGGGSGGGGSGGGGS**DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRT**
PEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVE
WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLS
LSPGK

SEQ ID NO: 226 C-Term-AE288 pSYN-FIX-102

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLERECMEEKCSFEEAR
EVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFEGKNCELDVTCNIKNGRCEQFCKNSAD
NKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQTSKLTRAETVFPDVDYVNSTEAETILDNITQSTQSFNDFT
RVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNIEETEHTEQKRNVIRII
PHHNYNAAINKYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRVP
LVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRY
VNWIKEKTKLTGPEGP***SKLTRAET***GAGSPGAETA**GTSESATPESGPGSEPATSGSETPGTSESATPESGPGSEPA**
TSGSETPGTSESATPESGPGTSTEPSEGSAPGSPAGSPTSTEEGTSESATPESGPGSEPATSGSETPGTSESATP
ESGPGSPAGSPTSTEEGSPAGSPTSTEEGTSTEPSEGSAPGTSESATPESGPGTSESATPESGPGTSESATPESG

PGSEPATSGSETPGSEPATSGSETPGSPAGSPTSTEEGTSTEPSEGSAPGTSTEPSEGSAPGSEPATSGSETPGT SESATPESGPGTSTEPSEGSAPGAETAEQKLISEEDLSPATGHHHHHH*

SEQ ID NO: 227 dual chain D166-AE72, C-Term-Fc pSYN-FIX-216

MQRVNMIMAESPGLITICLLGYLLSAECTVFLDHENANKILNRPKRYNSGKLEEFVQGNLERECMEEKCSFEEAR
EVFENTERTTEFWKQYVDGDQCESNPCLNGGSCKDDINSYECWCPFGFEGKNCELDVTCNIKNGRCEQFCKNSAD
NKVVCSCTEGYRLAENQKSCEPAVPFPCGRVSVSQTSKLTRAETVFPDVDYVNSTEAETILD**GPSPGSPTSTEEG
TSESATPESGPGSEPATSGSETPGTSESATPESGPGTSTEPSEGSAPGTSTEPSEGSAPGASS**NITQSTQSFNDF
TRVVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNIEETEHTEQKRNVIRI
IPHHNYNAAINKYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFLKFGSGYVSGWGRVFHKGRSALVLQYLRV
PLVDRATCLLSTKFTIYNNMFCAGFHEGGRDSCQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSR
YVNWIKEKTKLT**DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE
VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDEL
TKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALH
NHYTQKSLSLSPG**

SEQ ID NO: 228 dual chain D166-AE72, C-Term-Fc pSYN-FIX-216-Fc chain part

**DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQ
YNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVK
GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSP
G**

WHAT IS CLAIMED IS:

1. A Factor IX (FIX) fusion protein comprising a FIX polypeptide and at least one XTEN which is inserted within the FIX polypeptide at an insertion site corresponding to an amino acid selected from the group consisting of amino acid 103 of SEQ ID NO: 2, amino acid 105 of SEQ ID NO: 2, amino acid 142 of SEQ ID NO: 2, amino acid 149 of SEQ ID NO: 2, amino acid 162 of SEQ ID NO: 2, amino acid 166 of SEQ ID NO: 2, amino acid 174 of SEQ ID NO: 2, amino acid 224 of SEQ ID NO: 2, amino acid 226 of SEQ ID NO: 2, amino acid 228 of SEQ ID NO: 2, amino acid 413 of SEQ ID NO: 2, and any combination thereof, and wherein the FIX fusion protein exhibits procoagulant activity.

2. The FIX fusion protein of claim 1, wherein the insertion site corresponds to an amino acid selected from the group consisting of amino acid 149 of SEQ ID NO: 2, amino acid 162 of SEQ ID NO: 2, amino acid 166 of SEQ ID NO: 2, amino acid 174 of SEQ ID NO: 2 and any combination thereof.

3. The FIX fusion protein of claim 1 or 2, wherein the XTEN comprises at least about 5 amino acids, at least about 6 amino acids, at least about 12 amino acids, at least about 36 amino acids, at least about 42 amino acids, at least about 72 amino acids, at least about 144 amino acids, or at least about 288 amino acids.

4. The FIX fusion protein of any one of claims 1 to 3, which further comprises a second XTEN.

5. The FIX fusion protein of claim 4, wherein the XTEN is inserted within the FIX polypeptide at an insertion site corresponding to amino acid 166 of SEQ ID NO: 2, and wherein the second XTEN is fused to the C-terminus of the FIX polypeptide.

6. The FIX fusion protein of any one of claims 1 to 5, further comprising an Fc domain.

7. The FIX fusion protein of claim 6, comprising a second Fc domain.

8. The FIX fusion protein of claim 7, which comprises two polypeptide chains, wherein the first polypeptide chain comprises the FIX polypeptide fused to the Fc domain, and the second polypeptide chain comprises the second Fc domain, wherein the first Fc domain and the second Fc domain are associated by a covalent bond.

9. The FIX fusion protein of any one of claims 1 to 8, wherein the FIX polypeptide is a R338L FIX variant.

10. An isolated polynucleotide comprising a sequence encoding the FIX fusion protein of any one of claims 1 to 9.

11. An expression vector comprising the polynucleotide of claim 10.

12. A host cell comprising the polynucleotide of claim 10 or the vector of claim 11.

13. A composition comprising the FIX fusion protein of any one of claims 1 to 9, the polynucleotide of claim 10, the expression vector of claim 11, or the host cell of claim 12, and a pharmaceutically acceptable carrier.

14. A method of preventing, treating, ameliorating, or managing a clotting disease or condition in a patient in need thereof comprising administering an effective amount of the FIX fusion protein of any one of claims 1 to 9, the polynucleotide of claim 10, the expression vector of claim 11, the host cell of claim 12, or the composition of claim 13.

15. A Factor IX (FIX) fusion protein comprising a first chain and a second chain, wherein:

a. the first chain comprises:
   i. a FIX polypeptide;
   ii. at least one XTEN, wherein the at least one XTEN is inserted within the FIX polypeptide at an insertion site corresponding to amino acid 166 of SEQ ID NO: 2, and wherein the at least one XTEN comprises an amino acid sequence having at least about 72 amino acids; and

iii. a first Fc domain, wherein the first Fc domain is fused to the FIX polypeptide of the at least one XTEN; and

b. the second chain comprises a second Fc domain

wherein the first Fc domain and the second Fc domain are associated by a covalent bond; and wherein the FIX fusion protein exhibits procoagulant activity.

Figure 1 - Activity Screen of AE42 Insertions and C-Terminal Fusion

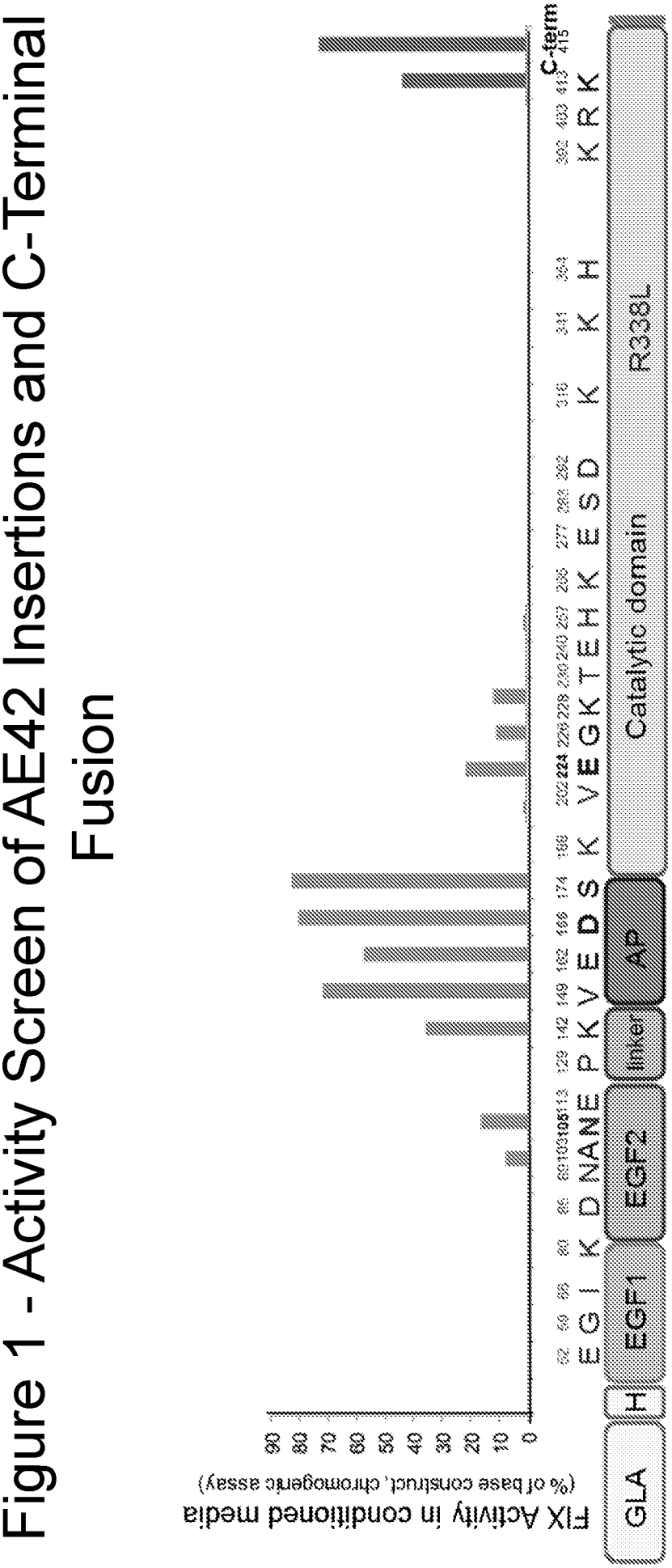


Figure 2 – Activity Screen of XTEN Insertion Sites and Lengths

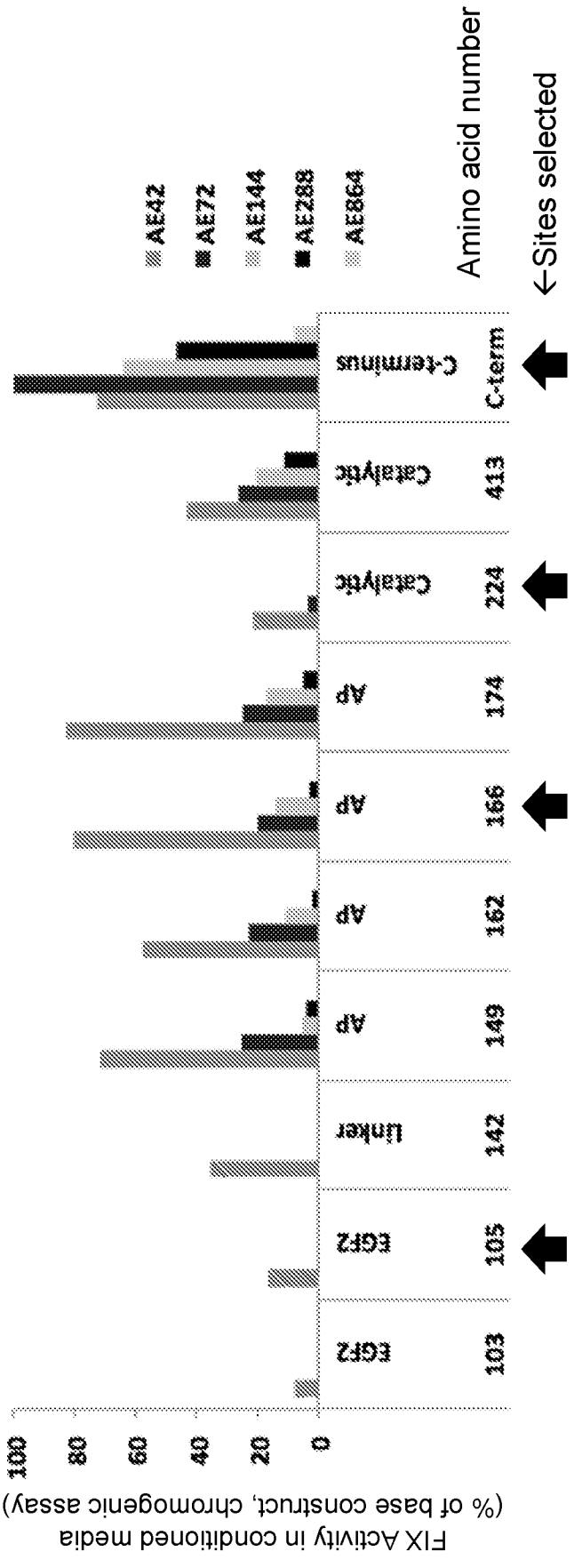


Figure 3 – Four Selected Sites for a Combination Library in FIX

FIG. 3A

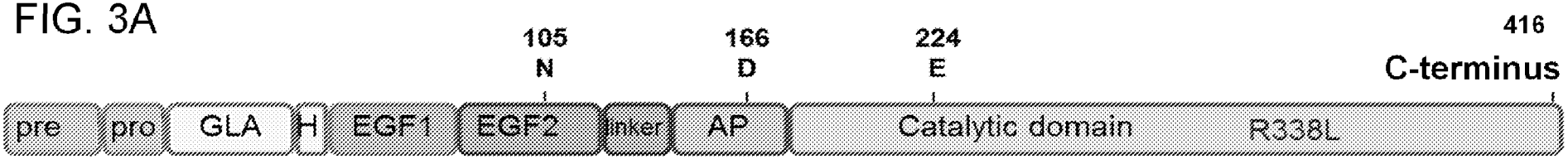


FIG. 3B

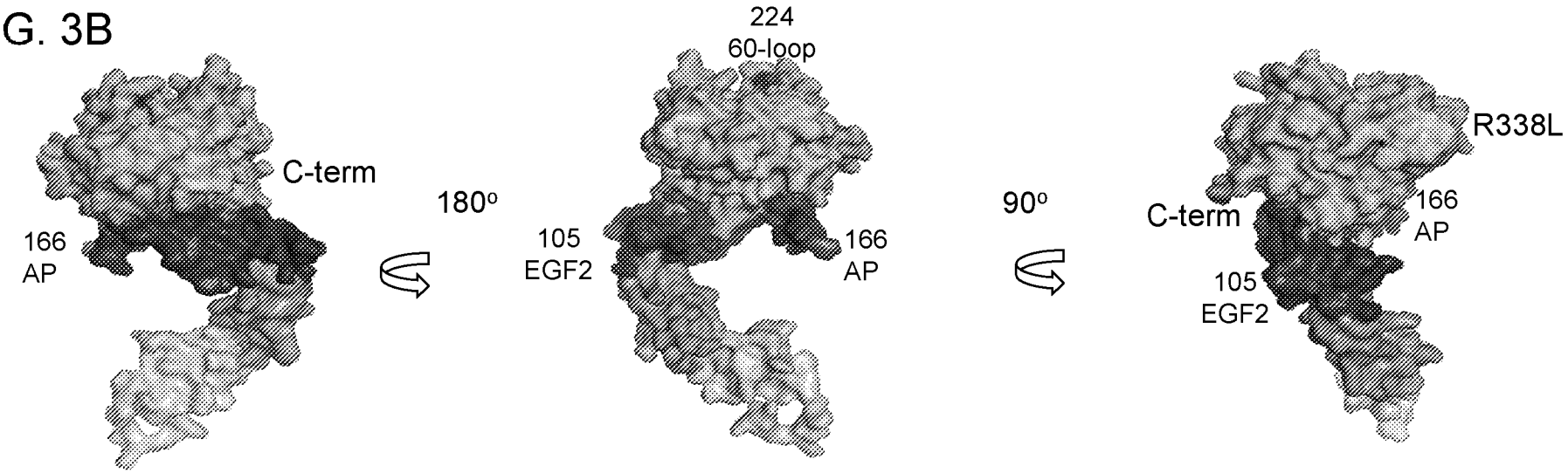


Figure 4 – Three Groups of FIX-XTEN Having Detectable Activity

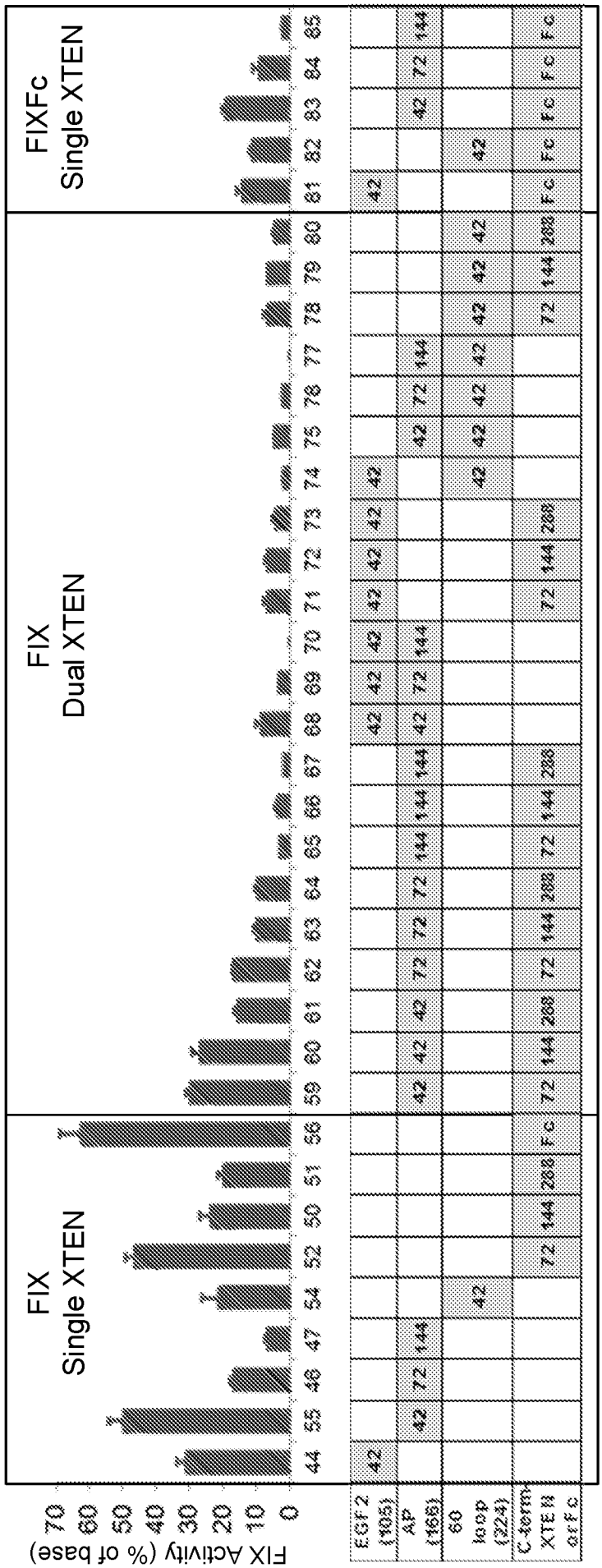
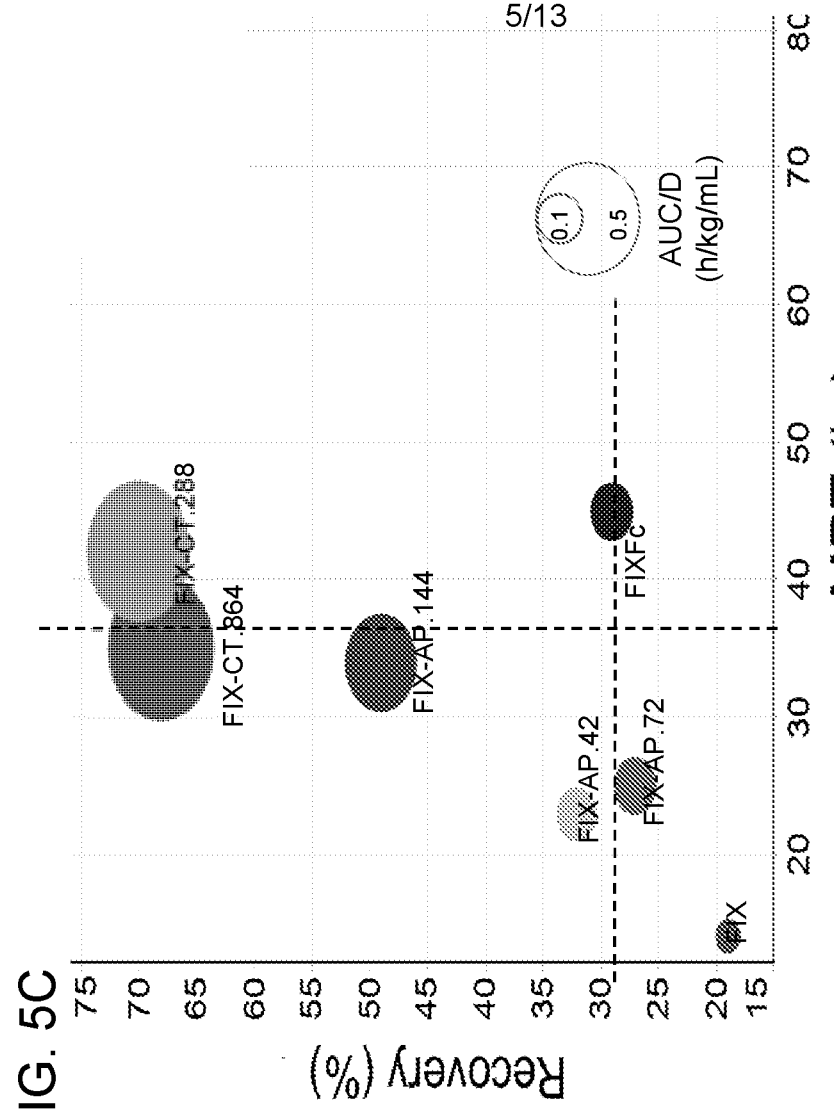


Figure 5


FIG. 5C
Recovery (%)
MRT (hr)
AUC/D (h/kg/mL)
0.1
0.5
FIX-CT.288
FIX-CT.864
FIX-AP.144
FIXFc
FIX-AP.42
FIX-AP.72
FIX

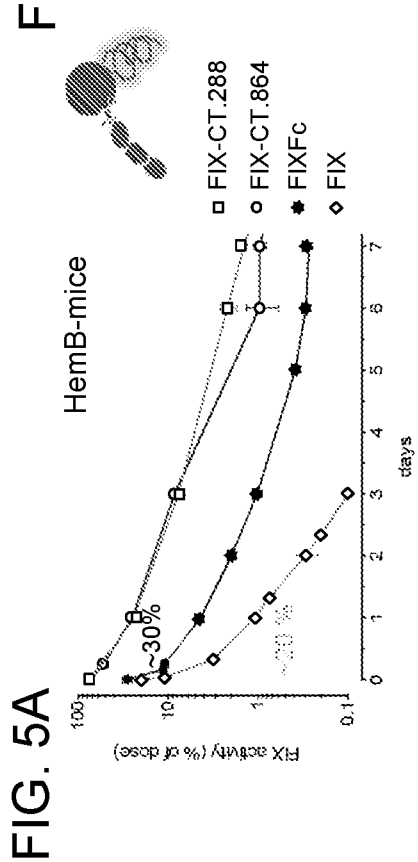
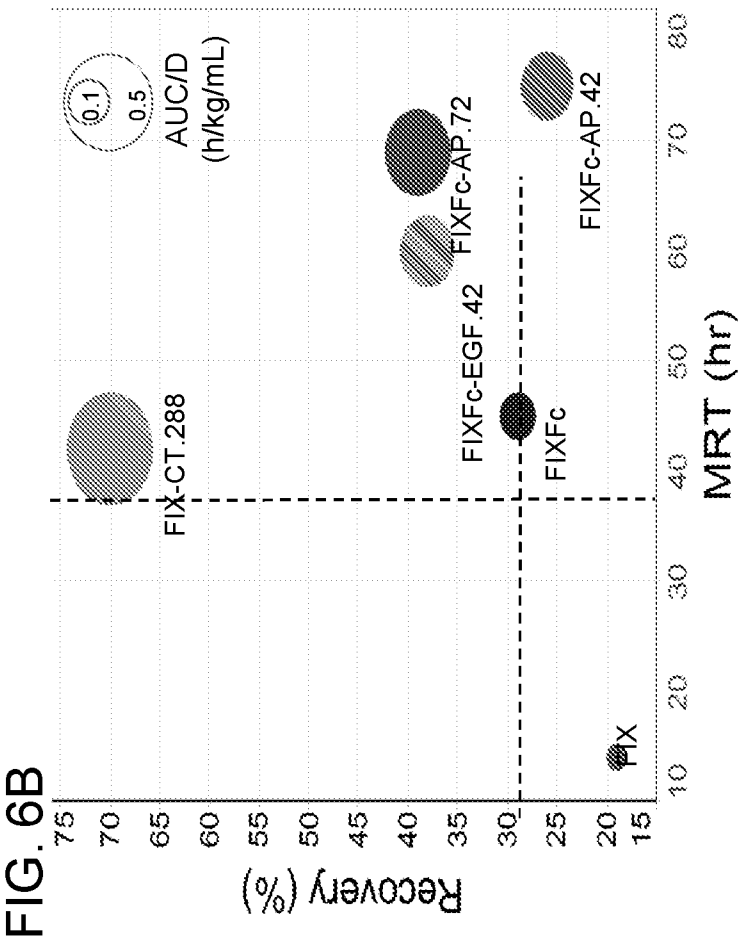

FIG. 5A
HemB-mice
FIX-CT.288
FIX-CT.864
FIXFc
FIX
~30%
FIX activity (% of dose)
days

FIG. 5B
FIX-AP.144
FIXFc
FIX-AP.72
FIX-AP.42
FIX
~50%
FIX activity (% of dose)
days

Figure 6


FIG. 6B
Recovery (%)
MRT (hr)
AUC/D (h/kg/mL)
0.1
0.5
FIX-CT.288
FIXFc-EGF.42
FIXFc-AP.72
FIXFc
FIXFc-AP.42
FIX

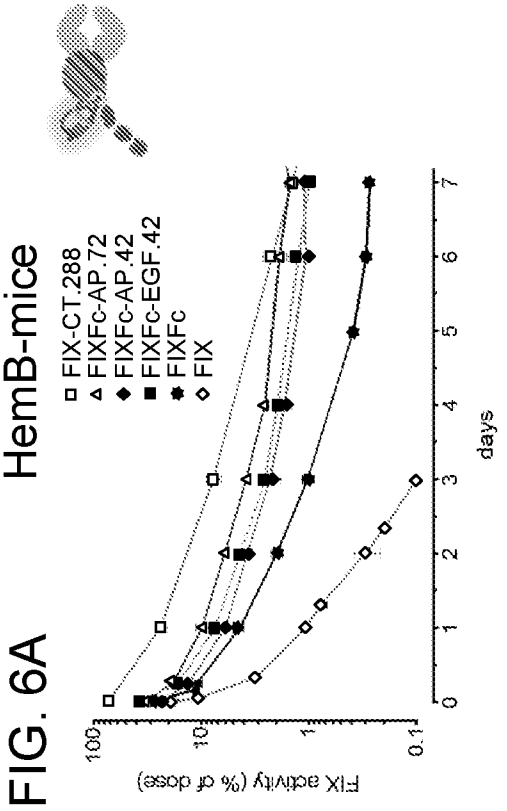

FIG. 6A
HemB-mice
FIX-CT.288
FIXFc-AP.72
FIXFc-AP.42
FIXFc-EGF.42
FIXFc
FIX
FIX activity (% of dose)
days

Figure 7

FIG. 7B

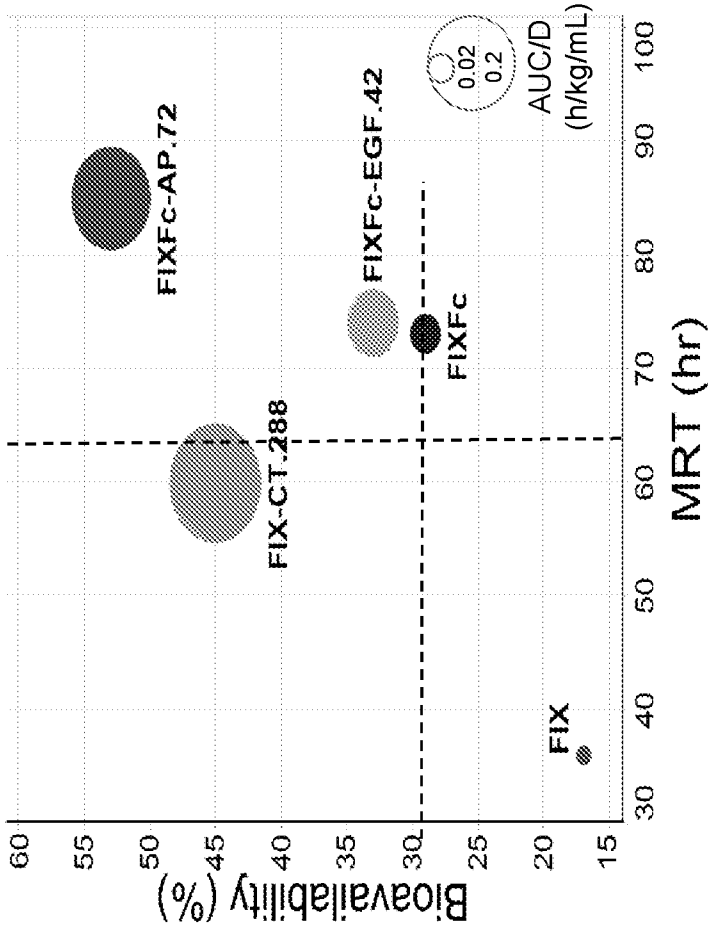


FIG. 7A

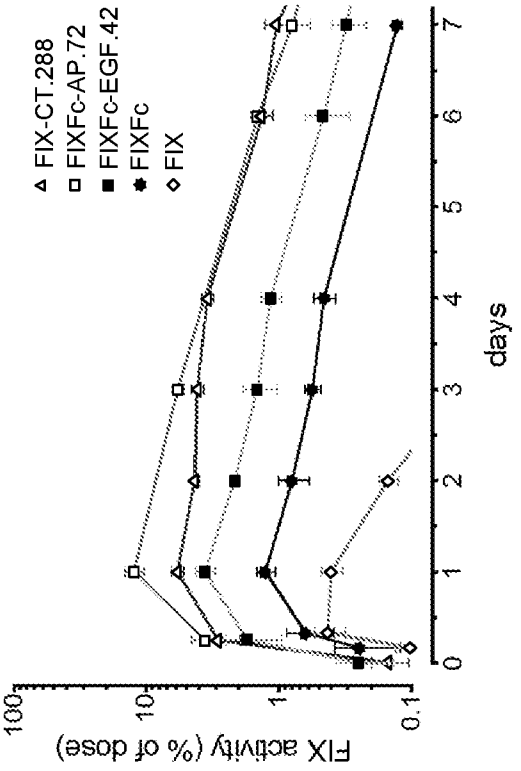


Figure 8

FIG. 8A

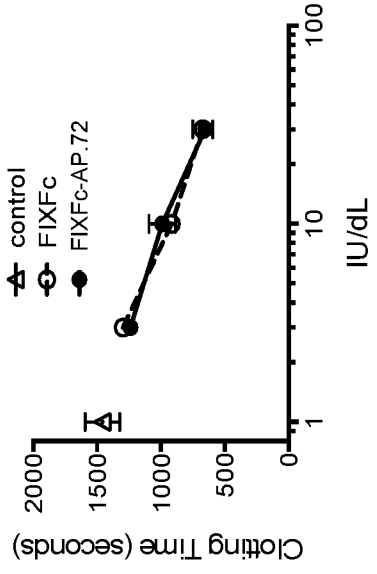


FIG. 8B

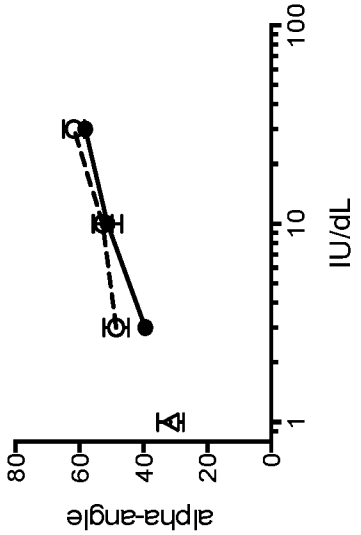


FIG. 8C

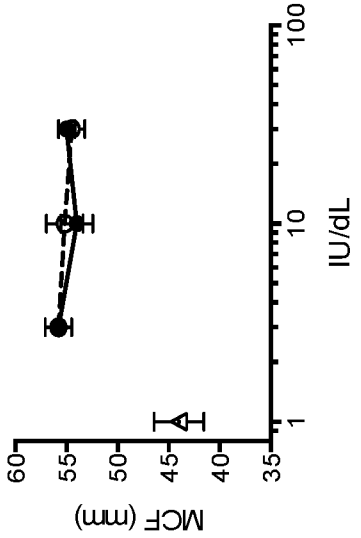
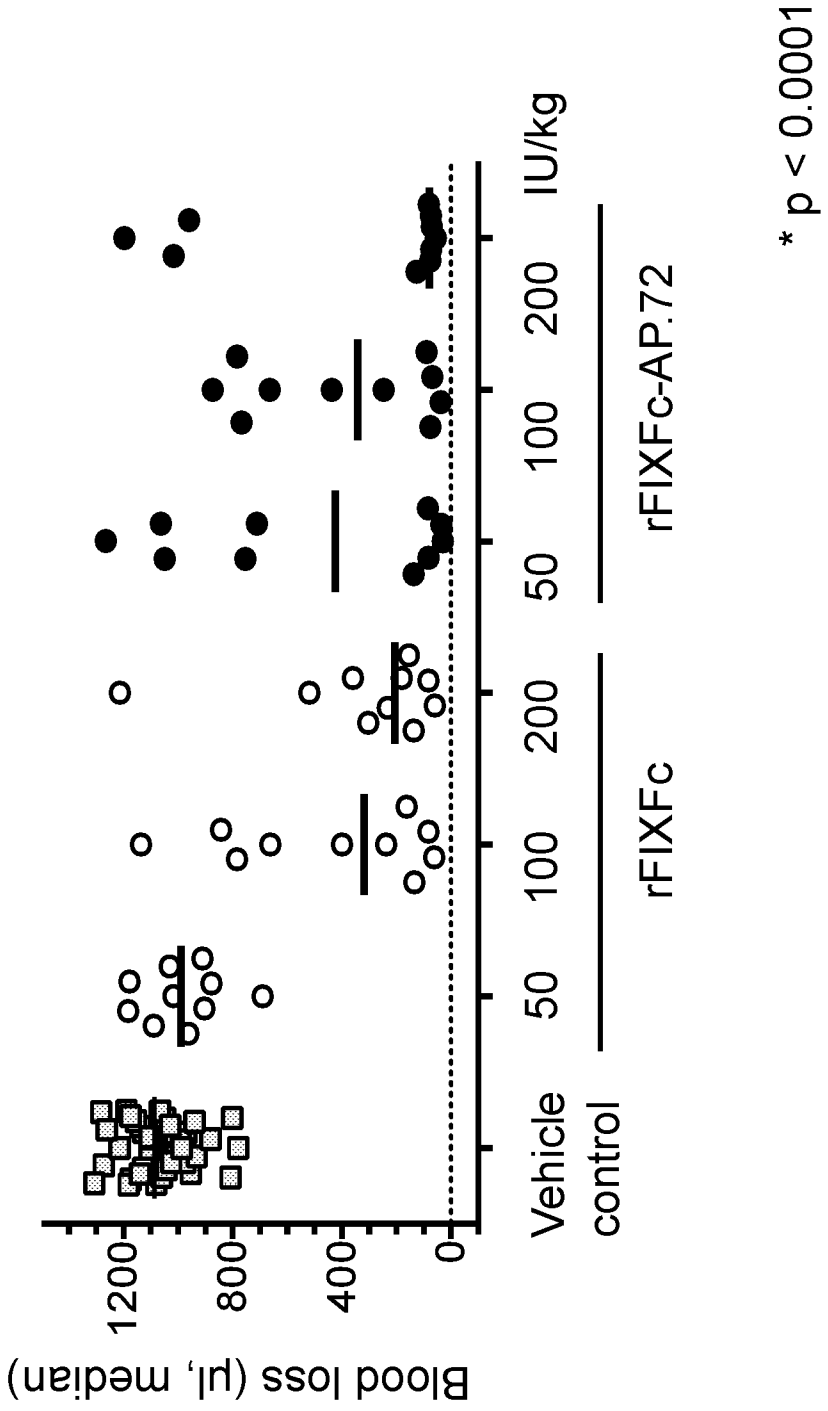


Figure 9


Blood loss (µl, median)
1200
800
400
0
Vehicle control
50
100
200
50
100
200
IU/kg
rFIXFc
rFIXFc-AP.72
* p < 0.0001

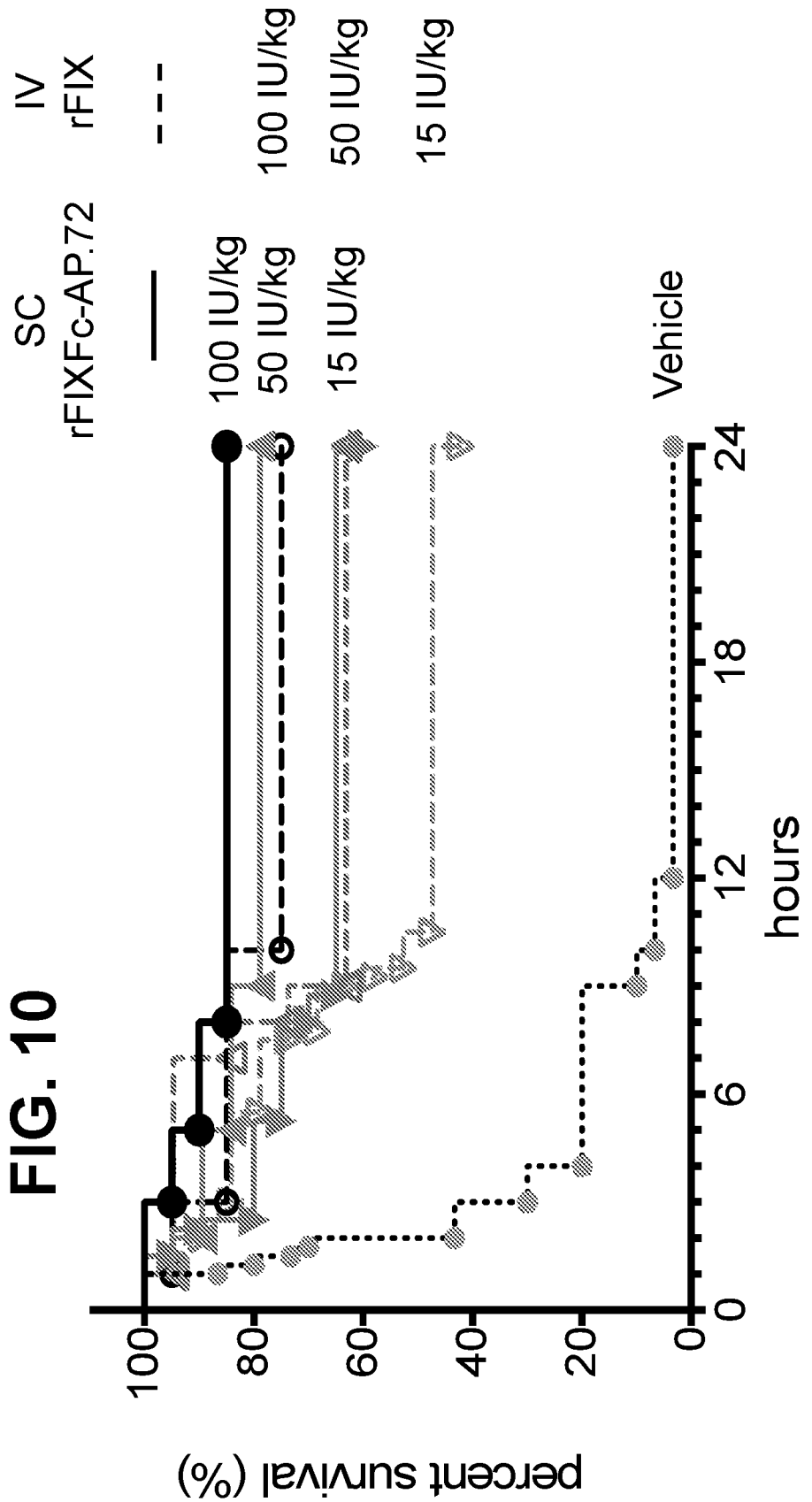

SC
rFIXFc-AP.72
IV
rFIX
100 IU/kg
50 IU/kg
15 IU/kg
100 IU/kg
50 IU/kg
15 IU/kg
Vehicle
percent survival (%)
100
80
60
40
20
0
0
6
12
18
24
hours

FIG. 10

FIG. 11A

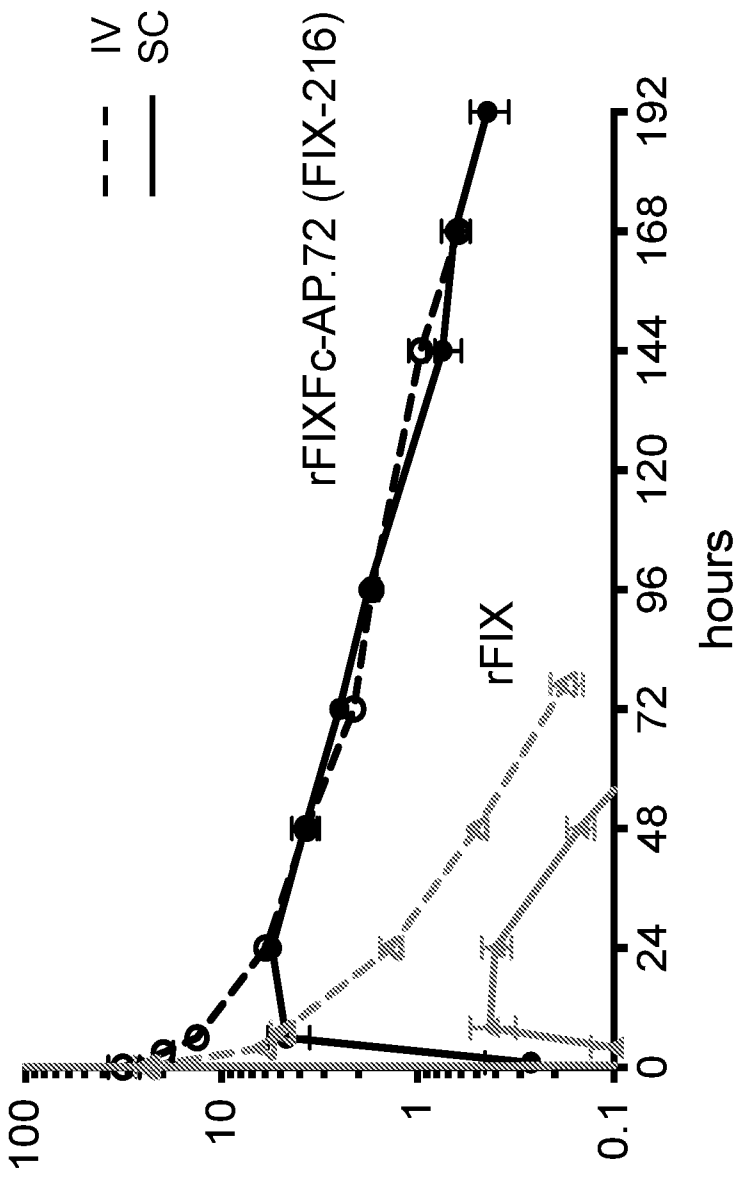
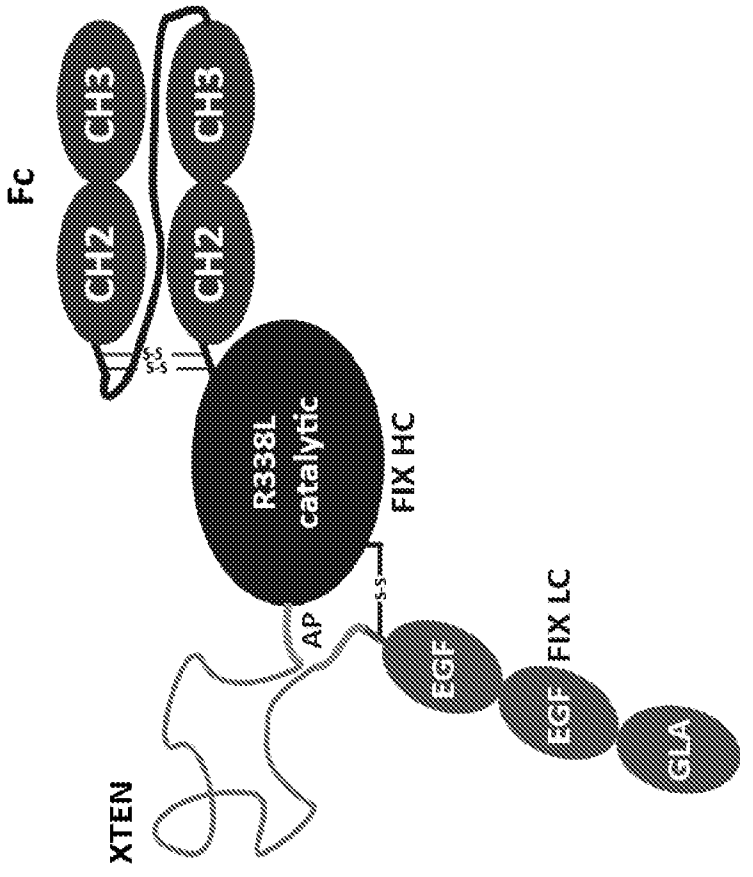


FIG. 11B

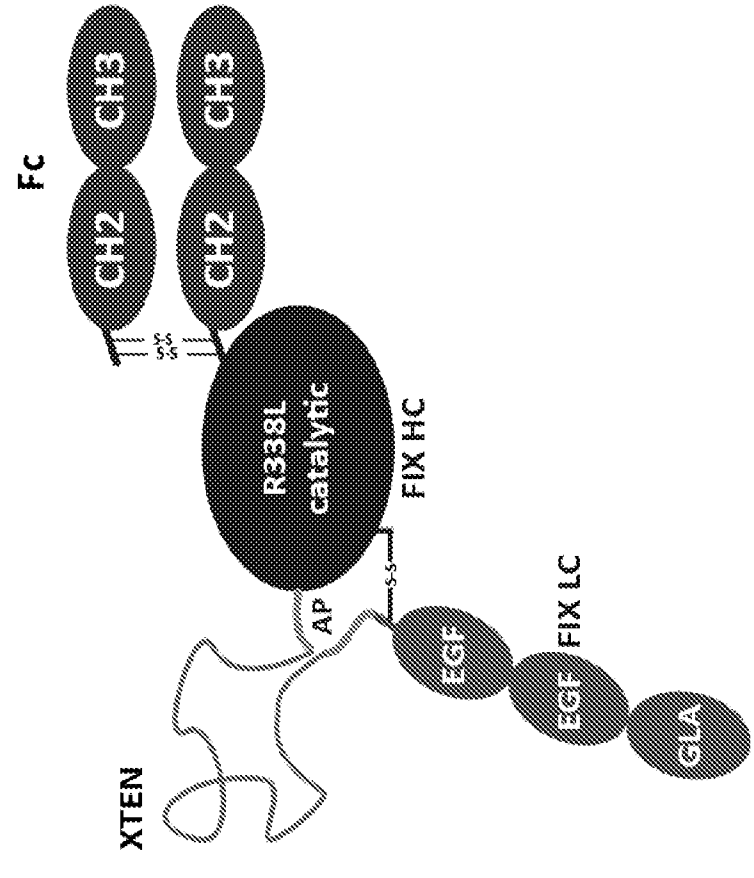
	Intravenous					Subcutaneous				
	I.R. (%)	$t_{1/2}$ (hr)	MRT (hr)	AUC/D (h*kg/mL)	Cl (mL/h/kg)	F (%)	$t_{1/2}$ (hr)	MRT (hr)	AUC/D (h*kg/mL)	Cl (mL/h/kg)
rFIX	21	17	17	0.043	23.2	14	21	38	0.006	175
rFIXFc-AP.72	32	51	53	0.165	6.0	70	48	72	0.116	8.6

FIG. 12A



rFIXFc-AP.72
(Single Fc chain)

FIG. 12B



rFIXFc-AP.72
(dual Fc chain)

FIG. 13

FIX construct name	SEQ ID NO	description	plasmid name
rFIX-CT.72	123	R338L, C-term AE72	pJH52
rFIX-CT.144	121	R338L, C-term AE144	pJH50
rFIX-CT-288	226	R338L, C-term AE288-tag	FIX-102
rFIX-CT.288	122	R338L, C-term AE288	pJH51
rFIX-CT.864	116	R338L, C-term AE864	FIX-92
rFIX-AP.72	119	R338L, D166-AE72	pJH46
rFIX-AP.144	120	R338L, D166-AE144	pJH47
rFIXFc-EGF.42	148	R338L, N105-AE42, C-term-Fc	pJH81
rFIXFc-AP.42	150	R338L, D166-AE42, C-term Fc	pJH83
rFIXFc-AP.72	151	R338L, D166-AE72, C-term Fc	pJH84
rFIXFc-AP.72 (dual chain Fc)	227 & 228	R338L, D166-AE72, C-term Fc (dual chain Fc)	FIX-216

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US16/45401

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61P 7/04; A61K 38/36, 38/16, 47/42; A61L 15/32 (2016.01)
CPC - A61K 38/36, 38/16, 38/1709, 47/42; A61L 15/32
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC(8):A61P 7/04; A61K 38/36, 38/16, 47/42, 38/00, 47/48, 38/48; A61L 15/32; C07K 14/745; C12N 9/64 (2016.01)
CPC:A61K 38/36, 38/16, 38/1709, 47/42; A61L 15/32; C12N 9/6437, 9/644, 9/96; C07K 2319/00, 2319/50

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PatSeer (US, EP, WO, JP, DE, GB, CN, FR, KR, ES, AU, IN, CA, INPADOC Data); Lens sequence search database; Google Scholar; Pubmed; EBSCO; NCBI database; Factor IX, FIX, fusion, polypeptide, XTEN, amino acid, insert*, coagulat*

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2011/0046060 A1 (SCHELLENBERGER, V et al.) 24 February, 2011; paragraphs [0010], [0046], [0134]; figures 1A-1B	1-2, 3/1-2, 15
A	US 2012/0178691 A1 (SCHELLENBERGER, V et al.) 12 July, 2012; paragraphs [0255], [0257], [0535]	1-2, 3/1-2, 15
A	(VENKATESWARLU, D) Structural Insights into the Interaction of Blood Coagulation Co-factor VIIIa with Factor IXa: A Computational Protein-Protein Docking and Molecular Dynamics Refinement Study. Biochemical and Biophysical Research Communications. 23 August, 2014; Vol. 452, No. 3; pages 1-16; whole document; Genbank Supplement pages 1-5.	1-2, 3/1-2, 15

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
07 October 2016 (07.10.2016)	28 OCT 2016
Name and mailing address of the ISA/ Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300	Authorized officer Shane Thomas PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US16/45401

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☒ Claims Nos.: 4-14
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

SEQUENCE LISTING

<110> LIU, Zhiqian
VAN DER FLIER, Arjan
LIGHT, David R.
CHHABRA, Ekta Seth
LIU, Tongyao
PETERS, Robert T.
KULMAN, John
ISMAIL, Ayman

<120> FACTOR IX FUSION PROTEINS AND METHODS OF MAKING AND USING SAME

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<151> 2016-01-22

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35 40 45

Asp Gln Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp
50 55 60

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65 70 75 80

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Arg Ala Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu
145 150 155 160

Ala Glu Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn
165 170 175

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180 185 190

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195 200 205

Ser Ile Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu
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Thr Gly Val Lys Ile Thr Val Val Ala Gly Glu His Asn Ile Glu Glu
225                 230                 235                 240

Thr Glu His Thr Glu Gln Lys Arg Asn Val Ile Arg Ile Ile Pro His
                245                 250                 255

His Asn Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu
            260                 265                 270

Leu Glu Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr Val Thr Pro Ile
        275                 280                 285

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

Gly Tyr Val Ser Gly Trp Gly Arg Val Phe His Lys Gly Arg Ser Ala
305                 310                 315                 320

Leu Val Leu Gln Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys
                325                 330                 335

Leu Arg Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly
            340                 345                 350

Phe His Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro
        355                 360                 365

His Val Thr Glu Val Glu Gly Thr Ser Phe Leu Thr Gly Ile Ile Ser
    370                 375                 380

Trp Gly Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly Ile Tyr Thr Lys
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20 25 30

Glu Asn Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly
35 40 45

Asp Gln Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp
50 55 60

Asp Ile Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys
65 70 75 80

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

Leu Glu Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr Val Thr Pro Ile
275 280 285

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

Gly Tyr Val Ser Gly Trp Gly Arg Val Phe His Lys Gly Arg Ser Ala
305 310 315 320

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325 330 335

Leu Leu Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly
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Phe His Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro
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<223> AE, AM, AQ

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<210> 23
<211> 12
<212> PRT
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<220>
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<400> 23

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1 5 10

<210> 24
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1 5 10

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<400> 28

Gly Thr Ser Glu Pro Ser Thr Ser Glu Pro Gly Ala

1 5 10

<210> 29
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> BC

<400> 29

Gly Thr Ser Thr Glu Pro Ser Glu Pro Gly Ser Ala
1 5 10

<210> 30
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> BD

<400> 30

Gly Ser Thr Ala Gly Ser Glu Thr Ser Thr Glu Ala
1 5 10

<210> 31
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> BD

<400> 31

Gly Ser Glu Thr Ala Thr Ser Gly Ser Glu Thr Ala
1 5 10

<210> 32
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> BD

<400> 32

Gly Thr Ser Glu Ser Ala Thr Ser Glu Ser Gly Ala
1 5 10

<210> 33
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> BD

<400> 33

Gly Thr Ser Thr Glu Ala Ser Glu Gly Ser Ala Ser
1 5 10

<210> 34
<211> 42
<212> PRT
<213> Artificial Sequence

<220>
<223> AE42

<400> 34

Gly Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly
1 5 10 15

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala

20 25 30

Thr Ser Gly Ser Glu Thr Pro Ala Ser Ser
35 40

<210> 35
<211> 78
<212> PRT
<213> Artificial Sequence

<220>
<223> AE72

<400> 35

Gly Ala Pro Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser
1 5 10 15

Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala
20 25 30

Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu
35 40 45

Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr
50 55 60

Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ala Ser Ser
65 70 75

<210> 36
<211> 144
<212> PRT
<213> Artificial Sequence

<220>
<223> AE144

<400> 36

Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu
1 5 10 15

Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly
20 25 30

Ser Glu Thr Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu
35 40 45

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Glu Pro
50 55 60

Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Glu Pro Ala Thr Ser Gly
65 70 75 80

Ser Glu Thr Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro
85 90 95

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu
100 105 110

Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly
115 120 125

Ser Glu Thr Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
130 135 140

<210> 37
<211> 144
<212> PRT
<213> Artificial Sequence

<220>
<223> AE144_2A

<400> 37

Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Pro Ala Gly
1 5 10 15

Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly
20 25 30

Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly
35 40 45

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu
50 55 60

Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
65 70 75 80

Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly
85 90 95

Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu
100 105 110

Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
115 120 125

Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
130 135 140

<210> 38
<211> 144
<212> PRT

<213> Artificial Sequence

<220>
<223> AE144_3B

<400> 38

Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser
1 5 10 15

Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser
20 25 30

Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
35 40 45

Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu
50 55 60

Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly
65 70 75 80

Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly
85 90 95

Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu
100 105 110

Pro Ser Glu Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser
115 120 125

Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly
130 135 140

<210> 39

<211> 144
<212> PRT
<213> Artificial Sequence

<220>
<223> AE144_4A

<400> 39

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala
1 5 10 15

Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
20 25 30

Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly
35 40 45

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu
50 55 60

Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
65 70 75 80

Ser Gly Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly
85 90 95

Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Ser Pro Ala Gly
100 105 110

Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu
115 120 125

Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly
130 135 140

<210> 40
<211> 144
<212> PRT
<213> Artificial Sequence

<220>
<223> AE144_5A

<400> 40

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala
1 5 10 15

Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
20 25 30

Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly
35 40 45

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu
50 55 60

Pro Ser Glu Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser
65 70 75 80

Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
85 90 95

Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser
100 105 110

Ala Thr Pro Glu Ser Gly Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser
115 120 125

Thr Glu Glu Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly

130 135 140

<210> 41
<211> 144
<212> PRT
<213> Artificial Sequence

<220>
<223> AE144_6B

<400> 41

Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser
1 5 10 15

Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
20 25 30

Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
35 40 45

Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Glu Pro Ala
50 55 60

Thr Ser Gly Ser Glu Thr Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser
65 70 75 80

Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly
85 90 95

Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Glu Pro Ala
100 105 110

Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
115 120 125

Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly
130 135 140

<210> 42
<211> 144
<212> PRT
<213> Artificial Sequence

<220>
<223> AG144

<400> 42

Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro Gly Ser Ser Thr
1 5 10 15

Pro Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser Pro Ser Ala Ser Thr
20 25 30

Gly Thr Gly Pro Gly Ser Ser Pro Ser Ala Ser Thr Gly Thr Gly Pro
35 40 45

Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Ala Ser Pro
50 55 60

Gly Thr Ser Ser Thr Gly Ser Pro Gly Ser Ser Thr Pro Ser Gly Ala
65 70 75 80

Thr Gly Ser Pro Gly Ser Ser Pro Ser Ala Ser Thr Gly Thr Gly Pro
85 90 95

Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Ser Ser Pro
100 105 110

Ser Ala Ser Thr Gly Thr Gly Pro Gly Thr Pro Gly Ser Gly Thr Ala

115 120 125

Ser Ser Ser Pro Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro
130 135 140

<210> 43
<211> 144
<212> PRT
<213> Artificial Sequence

<220>
<223> AG144_A

<400> 43

Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Ser Ser Pro
1 5 10 15

Ser Ala Ser Thr Gly Thr Gly Pro Gly Ser Ser Pro Ser Ala Ser Thr
20 25 30

Gly Thr Gly Pro Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro
35 40 45

Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser Pro
50 55 60

Ser Ala Ser Thr Gly Thr Gly Pro Gly Ala Ser Pro Gly Thr Ser Ser
65 70 75 80

Thr Gly Ser Pro Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro
85 90 95

Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro Gly Thr Pro Gly
100 105 110

Ser Gly Thr Ala Ser Ser Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser
115 120 125

Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro
130 135 140

<210> 44
<211> 144
<212> PRT
<213> Artificial Sequence

<220>
<223> AG144_B

<400> 44

Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro Gly Ser Ser Thr
1 5 10 15

Pro Ser Gly Ala Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser
20 25 30

Thr Gly Ser Pro Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro
35 40 45

Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser Pro
50 55 60

Ser Ala Ser Thr Gly Thr Gly Pro Gly Ser Ser Pro Ser Ala Ser Thr
65 70 75 80

Gly Thr Gly Pro Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro
85 90 95

Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro Gly Ala Ser Pro

100 105 110

Gly Thr Ser Ser Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser
115 120 125

Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro
130 135 140

<210> 45
<211> 144
<212> PRT
<213> Artificial Sequence

<220>
<223> AG144_C

<400> 45

Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro Gly Ala Ser Pro
1 5 10 15

Gly Thr Ser Ser Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser
20 25 30

Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro
35 40 45

Gly Ser Ser Pro Ser Ala Ser Thr Gly Thr Gly Pro Gly Thr Pro Gly
50 55 60

Ser Gly Thr Ala Ser Ser Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser
65 70 75 80

Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro
85 90 95

Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Ser Ser Thr
100 105 110

Pro Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser Thr Pro Ser Gly Ala
115 120 125

Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro
130 135 140

<210> 46
<211> 144
<212> PRT
<213> Artificial Sequence

<220>
<223> AG144_F

<400> 46

Gly Ser Ser Pro Ser Ala Ser Thr Gly Thr Gly Pro Gly Ser Ser Pro
1 5 10 15

Ser Ala Ser Thr Gly Thr Gly Pro Gly Ala Ser Pro Gly Thr Ser Ser
20 25 30

Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro
35 40 45

Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser Pro
50 55 60

Ser Ala Ser Thr Gly Thr Gly Pro Gly Ala Ser Pro Gly Thr Ser Ser
65 70 75 80

Thr Gly Ser Pro Gly Ser Ser Pro Ser Ala Ser Thr Gly Thr Gly Pro

85 90 95

Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro Gly Ser Ser Thr
100 105 110

Pro Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser Thr Pro Ser Gly Ala
115 120 125

Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro
130 135 140

<210> 47
<211> 288
<212> PRT
<213> Artificial Sequence

<220>
<223> AE288

<400> 47

Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro
1 5 10 15

Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro
20 25 30

Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro
35 40 45

Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr
50 55 60

Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr
65 70 75 80

Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
85 90 95

Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu
100 105 110

Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Pro Ala Gly Ser Pro Thr
115 120 125

Ser Thr Glu Glu Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu
130 135 140

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu
145 150 155 160

Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro
165 170 175

Glu Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
180 185 190

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

Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Pro Ala Gly Ser Pro Thr
210 215 220

Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
225 230 235 240

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Glu Pro
245 250 255

Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro
260 265 270

Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
275 280 285

<210> 48
<211> 288
<212> PRT
<213> Artificial Sequence

<220>
<223> AE288_2

<400> 48

Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu
1 5 10 15

Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly
20 25 30

Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
35 40 45

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr
50 55 60

Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu
65 70 75 80

Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
85 90 95

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr

100 105 110

Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr
115 120 125

Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
130 135 140

Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro
145 150 155 160

Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro
165 170 175

Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro
180 185 190

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

Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro
210 215 220

Glu Ser Gly Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu
225 230 235 240

Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Ser Pro Ala
245 250 255

Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro
260 265 270

Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro

275 280 285

<210> 49
<211> 288
<212> PRT
<213> Artificial Sequence

<220>
<223> AG288

<400> 49

Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Ala Ser
1 5 10 15

Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Thr Pro Gly Ser Gly Thr
20 25 30

Ala Ser Ser Ser Pro Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser
35 40 45

Pro Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro Gly Ser Ser
50 55 60

Thr Pro Ser Gly Ala Thr Gly Ser Pro Gly Thr Pro Gly Ser Gly Thr
65 70 75 80

Ala Ser Ser Ser Pro Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser
85 90 95

Pro Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser
100 105 110

Pro Ser Ala Ser Thr Gly Thr Gly Pro Gly Ser Ser Pro Ser Ala Ser
115 120 125

Thr Gly Thr Gly Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser
130 135 140

Pro Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro Gly Ser Ser
145 150 155 160

Thr Pro Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser Pro Ser Ala Ser
165 170 175

Thr Gly Thr Gly Pro Gly Ser Ser Pro Ser Ala Ser Thr Gly Thr Gly
180 185 190

Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Ala Ser
195 200 205

Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Ser Ser Thr Pro Ser Gly
210 215 220

Ala Thr Gly Ser Pro Gly Ser Ser Pro Ser Ala Ser Thr Gly Thr Gly
225 230 235 240

Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Ser Ser
245 250 255

Pro Ser Ala Ser Thr Gly Thr Gly Pro Gly Thr Pro Gly Ser Gly Thr
260 265 270

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

<210> 50
<211> 576
<212> PRT

<213> Artificial Sequence

<220>
<223> AE576

<400> 50

Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu
1 5 10 15

Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu
20 25 30

Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu
35 40 45

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr
50 55 60

Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro
65 70 75 80

Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro
85 90 95

Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Pro Ala
100 105 110

Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro
115 120 125

Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
130 135 140

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Pro Ala

145 150 155 160

Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu
165 170 175

Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
180 185 190

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

Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro
210 215 220

Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro
225 230 235 240

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr
245 250 255

Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro
260 265 270

Glu Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
275 280 285

Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu
290 295 300

Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly
305 310 315 320

Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro

325 330 335

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr
340 345 350

Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu
355 360 365

Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
370 375 380

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr
385 390 395 400

Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr
405 410 415

Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
420 425 430

Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro
435 440 445

Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro
450 455 460

Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro
465 470 475 480

Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr
485 490 495

Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro

500 505 510

Glu Ser Gly Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu
515 520 525

Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Ser Pro Ala
530 535 540

Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro
545 550 555 560

Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
565 570 575

<210> 51
<211> 576
<212> PRT
<213> Artificial Sequence

<220>
<223> AG576

<400> 51

Pro Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro Gly Ser Ser
1 5 10 15

Thr Pro Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser Pro Ser Ala Ser
20 25 30

Thr Gly Thr Gly Pro Gly Ser Ser Pro Ser Ala Ser Thr Gly Thr Gly
35 40 45

Pro Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser
50 55 60

```
Thr Pro Ser Gly Ala Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser
65                  70                  75                  80

Ser Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser
                85                  90                  95

Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Thr Pro
            100                 105                 110

Gly Ser Gly Thr Ala Ser Ser Ser Pro Gly Ala Ser Pro Gly Thr Ser
        115                 120                 125

Ser Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser
    130                 135                 140

Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Ser Ser
145                 150                 155                 160

Pro Ser Ala Ser Thr Gly Thr Gly Pro Gly Thr Pro Gly Ser Gly Thr
                165                 170                 175

Ala Ser Ser Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser
            180                 185                 190

Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Ala Ser
        195                 200                 205

Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Ser Ser Thr Pro Ser Gly
    210                 215                 220

Ala Thr Gly Ser Pro Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser
225                 230                 235                 240
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Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Thr Pro
245 250 255

Gly Ser Gly Thr Ala Ser Ser Ser Pro Gly Ser Ser Thr Pro Ser Gly
260 265 270

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

Pro Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser
290 295 300

Pro Ser Ala Ser Thr Gly Thr Gly Pro Gly Ala Ser Pro Gly Thr Ser
305 310 315 320

Ser Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser
325 330 335

Pro Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro Gly Ala Ser
340 345 350

Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser
355 360 365

Ser Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser
370 375 380

Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Thr Pro
385 390 395 400

Gly Ser Gly Thr Ala Ser Ser Ser Pro Gly Ser Ser Thr Pro Ser Gly
405 410 415

```
Ala Thr Gly Ser Pro Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser
            420                 425                 430

Pro Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro Gly Thr Pro
        435                 440                 445

Gly Ser Gly Thr Ala Ser Ser Ser Pro Gly Ser Ser Thr Pro Ser Gly
    450                 455                 460

Ala Thr Gly Ser Pro Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser
465                 470                 475                 480

Pro Gly Ser Ser Pro Ser Ala Ser Thr Gly Thr Gly Pro Gly Ser Ser
                485                 490                 495

Pro Ser Ala Ser Thr Gly Thr Gly Pro Gly Ala Ser Pro Gly Thr Ser
            500                 505                 510

Ser Thr Gly Ser Pro Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser
        515                 520                 525

Pro Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser
    530                 535                 540

Pro Ser Ala Ser Thr Gly Thr Gly Pro Gly Ser Ser Pro Ser Ala Ser
545                 550                 555                 560

Thr Gly Thr Gly Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser
                565                 570                 575
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<210> 52
<211> 864
<212> PRT

<213> Artificial Sequence

<220>
<223> AE864

<400> 52

Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu
1 5 10 15

Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu
20 25 30

Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu
35 40 45

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr
50 55 60

Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro
65 70 75 80

Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro
85 90 95

Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Pro Ala
100 105 110

Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro
115 120 125

Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
130 135 140

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Pro Ala

145 150 155 160

Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu
165 170 175

Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
180 185 190

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

Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro
210 215 220

Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro
225 230 235 240

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr
245 250 255

Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro
260 265 270

Glu Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
275 280 285

Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu
290 295 300

Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly
305 310 315 320

Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro

325 330 335

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr
340 345 350

Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu
355 360 365

Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
370 375 380

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr
385 390 395 400

Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr
405 410 415

Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
420 425 430

Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro
435 440 445

Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro
450 455 460

Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro
465 470 475 480

Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr
485 490 495

Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro

500 505 510

Glu Ser Gly Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu
515 520 525

Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Ser Pro Ala
530 535 540

Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro
545 550 555 560

Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
565 570 575

Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro
580 585 590

Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro
595 600 605

Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro
610 615 620

Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr
625 630 635 640

Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr
645 650 655

Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
660 665 670

Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu

675 680 685

Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Pro Ala Gly Ser Pro Thr
690 695 700

Ser Thr Glu Glu Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu
705 710 715 720

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu
725 730 735

Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro
740 745 750

Glu Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
755 760 765

Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Glu Pro
770 775 780

Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Pro Ala Gly Ser Pro Thr
785 790 795 800

Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
805 810 815

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Glu Pro
820 825 830

Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro
835 840 845

Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro

850 855 860

<210> 53
<211> 864
<212> PRT
<213> Artificial Sequence

<220>
<223> AG864

<400> 53

Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Ser Ser Pro
1 5 10 15

Ser Ala Ser Thr Gly Thr Gly Pro Gly Ser Ser Pro Ser Ala Ser Thr
20 25 30

Gly Thr Gly Pro Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro
35 40 45

Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser Pro
50 55 60

Ser Ala Ser Thr Gly Thr Gly Pro Gly Ala Ser Pro Gly Thr Ser Ser
65 70 75 80

Thr Gly Ser Pro Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro
85 90 95

Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro Gly Thr Pro Gly
100 105 110

Ser Gly Thr Ala Ser Ser Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser
115 120 125

Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro
130 135 140

Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro Gly Ser Ser Thr
145 150 155 160

Pro Ser Gly Ala Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser
165 170 175

Thr Gly Ser Pro Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro
180 185 190

Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser Pro
195 200 205

Ser Ala Ser Thr Gly Thr Gly Pro Gly Ser Ser Pro Ser Ala Ser Thr
210 215 220

Gly Thr Gly Pro Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro
225 230 235 240

Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro Gly Ala Ser Pro
245 250 255

Gly Thr Ser Ser Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser
260 265 270

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

Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro Gly Ala Ser Pro
290 295 300

Gly Thr Ser Ser Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser
305 310 315 320

Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro
325 330 335

Gly Ser Ser Pro Ser Ala Ser Thr Gly Thr Gly Pro Gly Thr Pro Gly
340 345 350

Ser Gly Thr Ala Ser Ser Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser
355 360 365

Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro
370 375 380

Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Ser Ser Thr
385 390 395 400

Pro Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser Thr Pro Ser Gly Ala
405 410 415

Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro
420 425 430

Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro Gly Ser Ser Thr
435 440 445

Pro Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser Thr Pro Ser Gly Ala
450 455 460

Thr Gly Ser Pro Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro
465 470 475 480

Gly Ser Ser Pro Ser Ala Ser Thr Gly Thr Gly Pro Gly Ala Ser Pro
485 490 495

Gly Thr Ser Ser Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser
500 505 510

Thr Gly Ser Pro Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro
515 520 525

Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Ala Ser Pro
530 535 540

Gly Thr Ser Ser Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser
545 550 555 560

Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro
565 570 575

Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro Gly Ser Ser Thr
580 585 590

Pro Ser Gly Ala Thr Gly Ser Pro Gly Thr Pro Gly Ser Gly Thr Ala
595 600 605

Ser Ser Ser Pro Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro
610 615 620

Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro Gly Ser Ser Thr
625 630 635 640

Pro Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser Thr Pro Ser Gly Ala
645 650 655

Thr Gly Ser Pro Gly Ser Ser Pro Ser Ala Ser Thr Gly Thr Gly Pro
660 665 670

Gly Ser Ser Pro Ser Ala Ser Thr Gly Thr Gly Pro Gly Ala Ser Pro
675 680 685

Gly Thr Ser Ser Thr Gly Ser Pro Gly Thr Pro Gly Ser Gly Thr Ala
690 695 700

Ser Ser Ser Pro Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro
705 710 715 720

Gly Ser Ser Pro Ser Ala Ser Thr Gly Thr Gly Pro Gly Ser Ser Pro
725 730 735

Ser Ala Ser Thr Gly Thr Gly Pro Gly Ala Ser Pro Gly Thr Ser Ser
740 745 750

Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro
755 760 765

Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser Pro
770 775 780

Ser Ala Ser Thr Gly Thr Gly Pro Gly Ala Ser Pro Gly Thr Ser Ser
785 790 795 800

Thr Gly Ser Pro Gly Ser Ser Pro Ser Ala Ser Thr Gly Thr Gly Pro
805 810 815

Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro Gly Ser Ser Thr
820 825 830

Pro Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser Thr Pro Ser Gly Ala
835 840 845

Thr Gly Ser Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro
850 855 860

<210> 54
<211> 549
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL118

<400> 54

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile

100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145 150 155 160

Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr
165 170 175

Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr
180 185 190

Ser Gly Ser Glu Thr Pro Ala Ser Ser Gly Tyr Arg Leu Ala Glu Asn
195 200 205

Gln Lys Ser Cys Glu Pro Ala Val Pro Phe Pro Cys Gly Arg Val Ser
210 215 220

Val Ser Gln Thr Ser Lys Leu Thr Arg Ala Glu Thr Val Phe Pro Asp
225 230 235 240

Val Asp Tyr Val Asn Ser Thr Glu Ala Glu Thr Ile Leu Asp Asn Ile
245 250 255

Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe Thr Arg Val Val Gly Gly
260 265 270

Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp Gln Val Val Leu Asn Gly

275 280 285

Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile
290 295 300

Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val
305 310 315 320

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

Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn
340 345 350

Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val
355 360 365

Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr
370 375 380

Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg
385 390 395 400

Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val
405 410 415

Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile
420 425 430

Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser
435 440 445

Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr

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    450                 455                 460

Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys
465                 470                 475                 480

Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile
                485                 490                 495

Lys Glu Lys Thr Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr
            500                 505                 510

Arg Ala Glu Thr Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln
        515                 520                 525

Lys Leu Ile Ser Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His
    530                 535                 540

His His His His His
545
```

<210> 55
<211> 549
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL116

<400> 55

```
Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1               5                   10                  15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
            20                  25                  30
```

```
Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
        35                  40                  45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
    50                  55                  60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65                  70                  75                  80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
                85                  90                  95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
            100                 105                 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
        115                 120                 125

Glu Leu Asp Val Thr Cys Asn Gly Ala Pro Gly Ser Pro Ala Gly Ser
    130                 135                 140

Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser
145                 150                 155                 160

Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Ala Ser
                165                 170                 175

Ser Ile Lys Asn Gly Arg Cys Glu Gln Phe Cys Lys Asn Ser Ala Asp
            180                 185                 190

Asn Lys Val Val Cys Ser Cys Thr Glu Gly Tyr Arg Leu Ala Glu Asn
        195                 200                 205
```

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Gln Lys Ser Cys Glu Pro Ala Val Pro Phe Pro Cys Gly Arg Val Ser
    210                 215                 220

Val Ser Gln Thr Ser Lys Leu Thr Arg Ala Glu Thr Val Phe Pro Asp
225                 230                 235                 240

Val Asp Tyr Val Asn Ser Thr Glu Ala Glu Thr Ile Leu Asp Asn Ile
                245                 250                 255

Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe Thr Arg Val Val Gly Gly
            260                 265                 270

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

Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile
    290                 295                 300

Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val
305                 310                 315                 320

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

Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn
            340                 345                 350

Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val
        355                 360                 365

Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr
    370                 375                 380
```

Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg
385 390 395 400

Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val
405 410 415

Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile
420 425 430

Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser
435 440 445

Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr
450 455 460

Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys
465 470 475 480

Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile
485 490 495

Lys Glu Lys Thr Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr
500 505 510

Arg Ala Glu Thr Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln
515 520 525

Lys Leu Ile Ser Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His
530 535 540

His His His His His
545

<210> 56
<211> 549
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL117

<400> 56

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe

130 135 140

Cys Lys Asn Ser Ala Gly Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr
145 150 155 160

Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
165 170 175

Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Ala Ser Ser Asp
180 185 190

Asn Lys Val Val Cys Ser Cys Thr Glu Gly Tyr Arg Leu Ala Glu Asn
195 200 205

Gln Lys Ser Cys Glu Pro Ala Val Pro Phe Pro Cys Gly Arg Val Ser
210 215 220

Val Ser Gln Thr Ser Lys Leu Thr Arg Ala Glu Thr Val Phe Pro Asp
225 230 235 240

Val Asp Tyr Val Asn Ser Thr Glu Ala Glu Thr Ile Leu Asp Asn Ile
245 250 255

Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe Thr Arg Val Val Gly Gly
260 265 270

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

Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile
290 295 300

Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val

305 310 315 320

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

Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn
340 345 350

Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val
355 360 365

Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr
370 375 380

Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg
385 390 395 400

Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val
405 410 415

Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile
420 425 430

Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser
435 440 445

Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr
450 455 460

Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys
465 470 475 480

Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile

485 490 495

Lys Glu Lys Thr Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr
500 505 510

Arg Ala Glu Thr Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln
515 520 525

Lys Leu Ile Ser Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His
530 535 540

His His His His His
545

<210> 57
<211> 549
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL119

<400> 57

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

```
Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65                  70                  75                  80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
                85                  90                  95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
            100                 105                 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
        115                 120                 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
    130                 135                 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145                 150                 155                 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Gly
                165                 170                 175

Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr
            180                 185                 190

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

Ser Gly Ser Glu Thr Pro Ala Ser Ser Phe Pro Cys Gly Arg Val Ser
    210                 215                 220

Val Ser Gln Thr Ser Lys Leu Thr Arg Ala Glu Thr Val Phe Pro Asp
225                 230                 235                 240
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Val Asp Tyr Val Asn Ser Thr Glu Ala Glu Thr Ile Leu Asp Asn Ile
                245                 250                 255

Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe Thr Arg Val Val Gly Gly
            260                 265                 270

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

Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile
    290                 295                 300

Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val
305                 310                 315                 320

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

Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn
            340                 345                 350

Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val
        355                 360                 365

Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr
    370                 375                 380

Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg
385                 390                 395                 400

Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val
                405                 410                 415
```

Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile
420 425 430

Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser
435 440 445

Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr
450 455 460

Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys
465 470 475 480

Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile
485 490 495

Lys Glu Lys Thr Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr
500 505 510

Arg Ala Glu Thr Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln
515 520 525

Lys Leu Ile Ser Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His
530 535 540

His His His His His
545

<210> 58
<211> 549
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL120

<400> 58

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe

165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Gly Ala Pro Gly
180 185 190

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

Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser
210 215 220

Glu Thr Pro Ala Ser Ser Leu Thr Arg Ala Glu Thr Val Phe Pro Asp
225 230 235 240

Val Asp Tyr Val Asn Ser Thr Glu Ala Glu Thr Ile Leu Asp Asn Ile
245 250 255

Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe Thr Arg Val Val Gly Gly
260 265 270

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

Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile
290 295 300

Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val
305 310 315 320

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

Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn

340 345 350

Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val
355 360 365

Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr
370 375 380

Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg
385 390 395 400

Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val
405 410 415

Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile
420 425 430

Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser
435 440 445

Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr
450 455 460

Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys
465 470 475 480

Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile
485 490 495

Lys Glu Lys Thr Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr
500 505 510

Arg Ala Glu Thr Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln

515 520 525

Lys Leu Ile Ser Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His
530 535 540

His His His His His
545

<210> 59
<211> 549
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL121

<400> 59

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
180 185 190

Glu Thr Val Gly Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr
195 200 205

Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser
210 215 220

Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Ala Ser Ser Phe Pro Asp
225 230 235 240

Val Asp Tyr Val Asn Ser Thr Glu Ala Glu Thr Ile Leu Asp Asn Ile
245 250 255

Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe Thr Arg Val Val Gly Gly
260 265 270

```
Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp Gln Val Val Leu Asn Gly
        275                 280                 285

Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile
    290                 295                 300

Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val
305                 310                 315                 320

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

Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn
            340                 345                 350

Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val
        355                 360                 365

Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr
    370                 375                 380

Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg
385                 390                 395                 400

Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val
                405                 410                 415

Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile
            420                 425                 430

Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser
        435                 440                 445
```

Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr
450 455 460

Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys
465 470 475 480

Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile
485 490 495

Lys Glu Lys Thr Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr
500 505 510

Arg Ala Glu Thr Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln
515 520 525

Lys Leu Ile Ser Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His
530 535 540

His His His His His
545

<210> 60
<211> 549
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL122

<400> 60

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu

20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
180 185 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu

195 200 205

Gly Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly
210 215 220

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala
225 230 235 240

Thr Ser Gly Ser Glu Thr Pro Ala Ser Ser Thr Ile Leu Asp Asn Ile
245 250 255

Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe Thr Arg Val Val Gly Gly
260 265 270

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

Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile
290 295 300

Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val
305 310 315 320

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

Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn
340 345 350

Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val
355 360 365

Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr

370 375 380

Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg
385 390 395 400

Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val
405 410 415

Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile
420 425 430

Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser
435 440 445

Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr
450 455 460

Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys
465 470 475 480

Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile
485 490 495

Lys Glu Lys Thr Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr
500 505 510

Arg Ala Glu Thr Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln
515 520 525

Lys Leu Ile Ser Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His
530 535 540

His His His His His

545

<210> 61
<211> 549
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL123

<400> 61

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

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Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
    130                 135                 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145                 150                 155                 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
                165                 170                 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
            180                 185                 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
        195                 200                 205

Thr Ile Leu Asp Gly Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser
    210                 215                 220

Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
225                 230                 235                 240

Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Ala Ser Ser Asn Ile
                245                 250                 255

Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe Thr Arg Val Val Gly Gly
            260                 265                 270

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

Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile
    290                 295                 300
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Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val
305                 310                 315                 320

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

Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn
            340                 345                 350

Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val
        355                 360                 365

Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr
    370                 375                 380

Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg
385                 390                 395                 400

Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val
                405                 410                 415

Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile
            420                 425                 430

Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser
        435                 440                 445

Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr
    450                 455                 460

Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys
465                 470                 475                 480
```

Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile
485 490 495

Lys Glu Lys Thr Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr
500 505 510

Arg Ala Glu Thr Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln
515 520 525

Lys Leu Ile Ser Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His
530 535 540

His His His His His
545

<210> 62
<211> 549
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL124

<400> 62

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys

50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
180 185 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
195 200 205

Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Gly Ala Pro Gly
210 215 220

Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser

225 230 235 240

Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser
245 250 255

Glu Thr Pro Ala Ser Ser Phe Asn Asp Phe Thr Arg Val Val Gly Gly
260 265 270

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

Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile
290 295 300

Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val
305 310 315 320

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

Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn
340 345 350

Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val
355 360 365

Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr
370 375 380

Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg
385 390 395 400

Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val

405 410 415

Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile
420 425 430

Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser
435 440 445

Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr
450 455 460

Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys
465 470 475 480

Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile
485 490 495

Lys Glu Lys Thr Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr
500 505 510

Arg Ala Glu Thr Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln
515 520 525

Lys Leu Ile Ser Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His
530 535 540

His His His His His
545

<210> 63
<211> 549
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL125

<400> 63

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
180 185 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
195 200 205

Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe
210 215 220

Thr Arg Val Val Gly Gly Glu Asp Ala Lys Gly Ala Pro Gly Ser Pro
225 230 235 240

Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr
245 250 255

Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr
260 265 270

Pro Ala Ser Ser Pro Gly Gln Phe Pro Trp Gln Val Val Leu Asn Gly
275 280 285

Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile
290 295 300

Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val
305 310 315 320

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

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Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn
            340                 345                 350

Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val
        355                 360                 365

Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr
    370                 375                 380

Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg
385                 390                 395                 400

Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val
                405                 410                 415

Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile
            420                 425                 430

Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser
        435                 440                 445

Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr
    450                 455                 460

Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys
465                 470                 475                 480

Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile
                485                 490                 495

Lys Glu Lys Thr Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr
            500                 505                 510
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Arg Ala Glu Thr Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln
515 520 525

Lys Leu Ile Ser Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His
530 535 540

His His His His His
545

<210> 64
<211> 549
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL126

<400> 64

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln

85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
180 185 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
195 200 205

Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe
210 215 220

Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp
225 230 235 240

Gln Val Val Leu Asn Gly Lys Val Gly Ala Pro Gly Ser Pro Ala Gly
245 250 255

Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu

260 265 270

Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Ala
275 280 285

Ser Ser Asp Ala Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile
290 295 300

Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val
305 310 315 320

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

Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn
340 345 350

Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val
355 360 365

Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr
370 375 380

Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg
385 390 395 400

Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val
405 410 415

Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile
420 425 430

Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser

435 440 445

Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr
450 455 460

Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys
465 470 475 480

Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile
485 490 495

Lys Glu Lys Thr Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr
500 505 510

Arg Ala Glu Thr Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln
515 520 525

Lys Leu Ile Ser Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His
530 535 540

His His His His His
545

<210> 65
<211> 549
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL127

<400> 65

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

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Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
            20                  25                  30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
        35                  40                  45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
    50                  55                  60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65                  70                  75                  80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
                85                  90                  95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
            100                 105                 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
        115                 120                 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
    130                 135                 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145                 150                 155                 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
                165                 170                 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
            180                 185                 190
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Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
        195                 200                 205

Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe
    210                 215                 220

Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp
225                 230                 235                 240

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

Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Gly Ala
            260                 265                 270

Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser
        275                 280                 285

Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser
    290                 295                 300

Gly Ser Glu Thr Pro Ala Ser Ser Thr Gly Val Lys Ile Thr Val Val
305                 310                 315                 320

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

Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn
            340                 345                 350

Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val
        355                 360                 365
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Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr
    370                 375                 380

Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg
385                 390                 395                 400

Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val
                405                 410                 415

Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile
            420                 425                 430

Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser
        435                 440                 445

Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr
    450                 455                 460

Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys
465                 470                 475                 480

Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile
                485                 490                 495

Lys Glu Lys Thr Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr
            500                 505                 510

Arg Ala Glu Thr Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln
        515                 520                 525

Lys Leu Ile Ser Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His
    530                 535                 540
```

His His His His His
545

<210> 66
<211> 549
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL128

<400> 66

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys

115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
180 185 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
195 200 205

Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe
210 215 220

Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp
225 230 235 240

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

Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly
260 265 270

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

Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser

290 295 300

Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser
305 310 315 320

Gly Ser Glu Thr Pro Ala Ser Ser Thr Glu His Thr Glu Gln Lys Arg
325 330 335

Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn
340 345 350

Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val
355 360 365

Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr
370 375 380

Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg
385 390 395 400

Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val
405 410 415

Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile
420 425 430

Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser
435 440 445

Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr
450 455 460

Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys

465 470 475 480

Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile
485 490 495

Lys Glu Lys Thr Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr
500 505 510

Arg Ala Glu Thr Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln
515 520 525

Lys Leu Ile Ser Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His
530 535 540

His His His His His
545

<210> 67
<211> 549
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL129

<400> 67

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
180 185 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
195 200 205

Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe
210 215 220

```
Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp
225                 230                 235                 240

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

Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly
            260                 265                 270

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

His Thr Glu Gln Lys Arg Asn Val Ile Arg Ile Ile Pro His His Gly
    290                 295                 300

Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr
305                 310                 315                 320

Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr
                325                 330                 335

Ser Gly Ser Glu Thr Pro Ala Ser Ser Asn Tyr Asn Ala Ala Ile Asn
            340                 345                 350

Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val
        355                 360                 365

Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr
    370                 375                 380

Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg
385                 390                 395                 400
```

Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val
405 410 415

Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile
420 425 430

Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser
435 440 445

Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr
450 455 460

Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys
465 470 475 480

Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile
485 490 495

Lys Glu Lys Thr Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr
500 505 510

Arg Ala Glu Thr Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln
515 520 525

Lys Leu Ile Ser Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His
530 535 540

His His His His His
545

<210> 68
<211> 549
<212> PRT

<213> Artificial Sequence

<220>
<223> pNL130

<400> 68

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly

145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
180 185 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
195 200 205

Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe
210 215 220

Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp
225 230 235 240

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

Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly
260 265 270

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

His Thr Glu Gln Lys Arg Asn Val Ile Arg Ile Ile Pro His His Asn
290 295 300

Tyr Asn Ala Ala Ile Asn Lys Gly Ala Pro Gly Ser Pro Ala Gly Ser
305 310 315 320

Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser

325 330 335

Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Ala Ser
340 345 350

Ser Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val
355 360 365

Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr
370 375 380

Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg
385 390 395 400

Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val
405 410 415

Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile
420 425 430

Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser
435 440 445

Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr
450 455 460

Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys
465 470 475 480

Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile
485 490 495

Lys Glu Lys Thr Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr

500 505 510

Arg Ala Glu Thr Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln
515 520 525

Lys Leu Ile Ser Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His
530 535 540

His His His His His
545

<210> 69
<211> 549
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL131

<400> 69

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

```
Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
                85                  90                  95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
            100                 105                 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
        115                 120                 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
    130                 135                 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145                 150                 155                 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
                165                 170                 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
            180                 185                 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
        195                 200                 205

Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe
    210                 215                 220

Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp
225                 230                 235                 240

Gln Val Val Leu Asn Gly Lys Val Asp Ala Phe Cys Gly Gly Ser Ile
                245                 250                 255
```

Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly
260 265 270

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

His Thr Glu Gln Lys Arg Asn Val Ile Arg Ile Ile Pro His His Asn
290 295 300

Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu Glu
305 310 315 320

Leu Asp Glu Gly Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr
325 330 335

Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser
340 345 350

Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Ala Ser Ser Pro Leu Val
355 360 365

Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr
370 375 380

Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg
385 390 395 400

Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val
405 410 415

Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile
420 425 430

Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser
435 440 445

Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr
450 455 460

Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys
465 470 475 480

Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile
485 490 495

Lys Glu Lys Thr Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr
500 505 510

Arg Ala Glu Thr Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln
515 520 525

Lys Leu Ile Ser Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His
530 535 540

His His His His His
545

<210> 70
<211> 549
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL132

<400> 70

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr

```
1               5                   10                  15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
            20                  25                  30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
        35                  40                  45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
    50                  55                  60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65                  70                  75                  80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
                85                  90                  95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
            100                 105                 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
        115                 120                 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
    130                 135                 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145                 150                 155                 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
                165                 170                 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
```

180 185 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
195 200 205

Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe
210 215 220

Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp
225 230 235 240

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

Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly
260 265 270

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

His Thr Glu Gln Lys Arg Asn Val Ile Arg Ile Ile Pro His His Asn
290 295 300

Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu Glu
305 310 315 320

Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile
325 330 335

Ala Asp Gly Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu
340 345 350

Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu

355 360 365

Pro Ala Thr Ser Gly Ser Glu Thr Pro Ala Ser Ser Lys Glu Tyr Thr
370 375 380

Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg
385 390 395 400

Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val
405 410 415

Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile
420 425 430

Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser
435 440 445

Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr
450 455 460

Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys
465 470 475 480

Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile
485 490 495

Lys Glu Lys Thr Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr
500 505 510

Arg Ala Glu Thr Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln
515 520 525

Lys Leu Ile Ser Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His

530 535 540

His His His His His
545

<210> 71
<211> 549
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL133

<400> 71

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
180 185 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
195 200 205

Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe
210 215 220

Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp
225 230 235 240

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

Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly
260 265 270

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

```
His Thr Glu Gln Lys Arg Asn Val Ile Arg Ile Ile Pro His His Asn
    290                 295                 300

Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu Glu
305                 310                 315                 320

Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile
                325                 330                 335

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

Val Ser Gly Trp Gly Arg Val Phe His Lys Gly Ala Pro Gly Ser Pro
        355                 360                 365

Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr
    370                 375                 380

Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr
385                 390                 395                 400

Pro Ala Ser Ser Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val
                405                 410                 415

Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile
            420                 425                 430

Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser
        435                 440                 445

Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr
    450                 455                 460
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```
Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys
465                 470                 475                 480

Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile
                485                 490                 495

Lys Glu Lys Thr Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr
            500                 505                 510

Arg Ala Glu Thr Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln
        515                 520                 525

Lys Leu Ile Ser Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His
    530                 535                 540

His His His His His
545
```

<210> 72
<211> 549
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL134

<400> 72

```
Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1               5                   10                  15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
            20                  25                  30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
```

35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
180 185 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
195 200 205

Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe

210 215 220

Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp
225 230 235 240

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

Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly
260 265 270

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

His Thr Glu Gln Lys Arg Asn Val Ile Arg Ile Ile Pro His His Asn
290 295 300

Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu Glu
305 310 315 320

Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile
325 330 335

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

Val Ser Gly Trp Gly Arg Val Phe His Lys Gly Arg Ser Ala Leu Val
355 360 365

Leu Gln Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu Leu
370 375 380

Ser Thr Lys Gly Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr

385 390 395 400

Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser
405 410 415

Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Ala Ser Ser Phe Thr Ile
420 425 430

Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser
435 440 445

Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr
450 455 460

Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys
465 470 475 480

Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile
485 490 495

Lys Glu Lys Thr Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr
500 505 510

Arg Ala Glu Thr Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln
515 520 525

Lys Leu Ile Ser Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His
530 535 540

His His His His His
545

<210> 73

<211> 549
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL135

<400> 73

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

```
Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145                 150                 155                 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
                165                 170                 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
            180                 185                 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
        195                 200                 205

Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe
    210                 215                 220

Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp
225                 230                 235                 240

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

Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly
            260                 265                 270

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

His Thr Glu Gln Lys Arg Asn Val Ile Arg Ile Ile Pro His His Asn
    290                 295                 300

Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu Glu
305                 310                 315                 320
```

Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile
325 330 335

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

Val Ser Gly Trp Gly Arg Val Phe His Lys Gly Arg Ser Ala Leu Val
355 360 365

Leu Gln Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu Leu
370 375 380

Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe His
385 390 395 400

Gly Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly
405 410 415

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala
420 425 430

Thr Ser Gly Ser Glu Thr Pro Ala Ser Ser Glu Gly Gly Arg Asp Ser
435 440 445

Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr
450 455 460

Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys
465 470 475 480

Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile
485 490 495

Lys Glu Lys Thr Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr
500 505 510

Arg Ala Glu Thr Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln
515 520 525

Lys Leu Ile Ser Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His
530 535 540

His His His His His
545

<210> 74
<211> 549
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL136

<400> 74

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn

65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
180 185 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
195 200 205

Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe
210 215 220

Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp
225 230 235 240

Gln Val Val Leu Asn Gly Lys Val Asp Ala Phe Cys Gly Gly Ser Ile

245 250 255

Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly
260 265 270

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

His Thr Glu Gln Lys Arg Asn Val Ile Arg Ile Ile Pro His His Asn
290 295 300

Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu Glu
305 310 315 320

Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile
325 330 335

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

Val Ser Gly Trp Gly Arg Val Phe His Lys Gly Arg Ser Ala Leu Val
355 360 365

Leu Gln Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu Leu
370 375 380

Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe His
385 390 395 400

Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro His Val
405 410 415

Thr Glu Val Glu Gly Thr Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly

420 425 430

Glu Glu Cys Ala Met Lys Gly Ala Pro Gly Ser Pro Ala Gly Ser Pro
435 440 445

Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly
450 455 460

Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Ala Ser Ser
465 470 475 480

Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile
485 490 495

Lys Glu Lys Thr Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr
500 505 510

Arg Ala Glu Thr Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln
515 520 525

Lys Leu Ile Ser Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His
530 535 540

His His His His His
545

<210> 75
<211> 549
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL137

<400> 75

```
Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1               5                  10                  15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
            20                  25                  30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
        35                  40                  45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
    50                  55                  60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65                  70                  75                  80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
                85                  90                  95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
            100                 105                 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
        115                 120                 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
    130                 135                 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145                 150                 155                 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
                165                 170                 175
```

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Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
            180                 185                 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
        195                 200                 205

Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe
    210                 215                 220

Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp
225                 230                 235                 240

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

Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly
            260                 265                 270

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

His Thr Glu Gln Lys Arg Asn Val Ile Arg Ile Ile Pro His His Asn
    290                 295                 300

Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu Glu
305                 310                 315                 320

Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile
                325                 330                 335

Ala Asp Lys Glu Tyr Thr Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr
            340                 345                 350
```

```
Val Ser Gly Trp Gly Arg Val Phe His Lys Gly Arg Ser Ala Leu Val
        355                 360                 365

Leu Gln Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu Leu
    370                 375                 380

Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe His
385                 390                 395                 400

Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro His Val
                405                 410                 415

Thr Glu Val Glu Gly Thr Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly
            420                 425                 430

Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser
        435                 440                 445

Arg Gly Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu
    450                 455                 460

Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro
465                 470                 475                 480

Ala Thr Ser Gly Ser Glu Thr Pro Ala Ser Ser Tyr Val Asn Trp Ile
                485                 490                 495

Lys Glu Lys Thr Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr
            500                 505                 510

Arg Ala Glu Thr Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln
        515                 520                 525
```

Lys Leu Ile Ser Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His
530 535 540

His His His His His
545

<210> 76
<211> 549
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL138

<400> 76

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile

100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
180 185 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
195 200 205

Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe
210 215 220

Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp
225 230 235 240

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

Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly
260 265 270

Val Lys Ile Thr Val Val Ala Gly Glu His Asn Ile Glu Glu Thr Glu

275 280 285

His Thr Glu Gln Lys Arg Asn Val Ile Arg Ile Ile Pro His His Asn
290 295 300

Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu Glu
305 310 315 320

Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile
325 330 335

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

Val Ser Gly Trp Gly Arg Val Phe His Lys Gly Arg Ser Ala Leu Val
355 360 365

Leu Gln Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu Leu
370 375 380

Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe His
385 390 395 400

Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro His Val
405 410 415

Thr Glu Val Glu Gly Thr Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly
420 425 430

Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser
435 440 445

Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr Lys Gly Ala Pro Gly Ser

```
    450                 455                 460

Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala
465                 470                 475                 480

Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu
                485                 490                 495

Thr Pro Ala Ser Ser Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr
            500                 505                 510

Arg Ala Glu Thr Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln
        515                 520                 525

Lys Leu Ile Ser Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His
    530                 535                 540

His His His His His
545
```

<210> 77
<211> 575
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL140

<400> 77

```
Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1               5                   10                  15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
            20                  25                  30
```

```
Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
        35                  40                  45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
    50                  55                  60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65                  70                  75                  80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
                85                  90                  95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
            100                 105                 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
        115                 120                 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
    130                 135                 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145                 150                 155                 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
                165                 170                 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
            180                 185                 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
        195                 200                 205
```

```
Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe
    210                 215                 220

Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp
225                 230                 235                 240

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

Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly
            260                 265                 270

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

His Thr Glu Gln Lys Arg Asn Val Ile Arg Ile Ile Pro His His Asn
    290                 295                 300

Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu Glu
305                 310                 315                 320

Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile
                325                 330                 335

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

Val Ser Gly Trp Gly Arg Val Phe His Lys Gly Arg Ser Ala Leu Val
        355                 360                 365

Leu Gln Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu Leu
    370                 375                 380
```

Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe His
385 390 395 400

Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro His Val
405 410 415

Thr Glu Val Glu Gly Thr Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly
420 425 430

Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser
435 440 445

Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr Lys Leu Thr Gly Ala Gly
450 455 460

Ser Pro Gly Ala Glu Thr Ala Leu Val Pro Arg Ser Phe Leu Leu Arg
465 470 475 480

Asn Pro Asn Asp Lys Tyr Glu Pro Phe Trp Glu Asp Glu Glu Ser Gly
485 490 495

Ala Gly Ser Pro Gly Ala Glu Thr Ala Gly Ala Pro Gly Ser Pro Ala
500 505 510

Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro
515 520 525

Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro
530 535 540

Ala Ser Ser Gly Ala Glu Thr Ala Glu Gln Lys Leu Ile Ser Glu Glu
545 550 555 560

Asp Leu Ser Pro Ala Thr Gly His His His His His His His His
565 570 575

<210> 78
<211> 549
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL141

<400> 78

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Gly Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu
100 105 110

Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu

115 120 125

Pro Ala Thr Ser Gly Ser Glu Thr Pro Ala Ser Ser Ser Asn Pro Cys
130 135 140

Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile Asn Ser Tyr Glu Cys Trp
145 150 155 160

Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys Glu Leu Asp Val Thr Cys
165 170 175

Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe Cys Lys Asn Ser Ala Asp
180 185 190

Asn Lys Val Val Cys Ser Cys Thr Glu Gly Tyr Arg Leu Ala Glu Asn
195 200 205

Gln Lys Ser Cys Glu Pro Ala Val Pro Phe Pro Cys Gly Arg Val Ser
210 215 220

Val Ser Gln Thr Ser Lys Leu Thr Arg Ala Glu Thr Val Phe Pro Asp
225 230 235 240

Val Asp Tyr Val Asn Ser Thr Glu Ala Glu Thr Ile Leu Asp Asn Ile
245 250 255

Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe Thr Arg Val Val Gly Gly
260 265 270

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

Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile

290 295 300

Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val
305 310 315 320

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

Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn
340 345 350

Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val
355 360 365

Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr
370 375 380

Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg
385 390 395 400

Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val
405 410 415

Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile
420 425 430

Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser
435 440 445

Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr
450 455 460

Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys

465 470 475 480

Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile
485 490 495

Lys Glu Lys Thr Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr
500 505 510

Arg Ala Glu Thr Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln
515 520 525

Lys Leu Ile Ser Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His
530 535 540

His His His His His
545

<210> 79
<211> 549
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL142

<400> 79

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

```
Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
    50                  55                  60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65                  70                  75                  80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
                85                  90                  95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ala Pro Gly Ser Pro Ala
            100                 105                 110

Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro
        115                 120                 125

Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro
    130                 135                 140

Ala Ser Ser Gly Ser Cys Lys Asp Asp Ile Asn Ser Tyr Glu Cys Trp
145                 150                 155                 160

Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys Glu Leu Asp Val Thr Cys
                165                 170                 175

Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe Cys Lys Asn Ser Ala Asp
            180                 185                 190

Asn Lys Val Val Cys Ser Cys Thr Glu Gly Tyr Arg Leu Ala Glu Asn
        195                 200                 205

Gln Lys Ser Cys Glu Pro Ala Val Pro Phe Pro Cys Gly Arg Val Ser
    210                 215                 220
```

```
Val Ser Gln Thr Ser Lys Leu Thr Arg Ala Glu Thr Val Phe Pro Asp
225                 230                 235                 240

Val Asp Tyr Val Asn Ser Thr Glu Ala Glu Thr Ile Leu Asp Asn Ile
                245                 250                 255

Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe Thr Arg Val Val Gly Gly
            260                 265                 270

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

Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile
    290                 295                 300

Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val
305                 310                 315                 320

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

Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn
            340                 345                 350

Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val
        355                 360                 365

Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr
    370                 375                 380

Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg
385                 390                 395                 400
```

Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val
405 410 415

Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile
420 425 430

Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser
435 440 445

Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr
450 455 460

Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys
465 470 475 480

Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile
485 490 495

Lys Glu Lys Thr Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr
500 505 510

Arg Ala Glu Thr Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln
515 520 525

Lys Leu Ile Ser Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His
530 535 540

His His His His His
545

<210> 80
<211> 549
<212> PRT

<213> Artificial Sequence

<220>
<223> pNL143

<400> 80

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Gly Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly
115 120 125

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala
130 135 140

Thr Ser Gly Ser Glu Thr Pro Ala Ser Ser Asn Ser Tyr Glu Cys Trp

145 150 155 160

Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys Glu Leu Asp Val Thr Cys
165 170 175

Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe Cys Lys Asn Ser Ala Asp
180 185 190

Asn Lys Val Val Cys Ser Cys Thr Glu Gly Tyr Arg Leu Ala Glu Asn
195 200 205

Gln Lys Ser Cys Glu Pro Ala Val Pro Phe Pro Cys Gly Arg Val Ser
210 215 220

Val Ser Gln Thr Ser Lys Leu Thr Arg Ala Glu Thr Val Phe Pro Asp
225 230 235 240

Val Asp Tyr Val Asn Ser Thr Glu Ala Glu Thr Ile Leu Asp Asn Ile
245 250 255

Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe Thr Arg Val Val Gly Gly
260 265 270

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

Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile
290 295 300

Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val
305 310 315 320

Ala Gly Glu His Asn Ile Glu Glu Thr Glu His Thr Glu Gln Lys Arg

325 330 335

Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn
340 345 350

Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val
355 360 365

Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr
370 375 380

Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg
385 390 395 400

Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val
405 410 415

Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile
420 425 430

Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser
435 440 445

Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr
450 455 460

Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys
465 470 475 480

Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile
485 490 495

Lys Glu Lys Thr Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr

500 505 510

Arg Ala Glu Thr Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln
515 520 525

Lys Leu Ile Ser Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His
530 535 540

His His His His His
545

<210> 81
<211> 549
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL144

<400> 81

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

```
Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
                85                  90                  95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
            100                 105                 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Gly Ala
        115                 120                 125

Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser
    130                 135                 140

Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser
145                 150                 155                 160

Gly Ser Glu Thr Pro Ala Ser Ser Asn Cys Glu Leu Asp Val Thr Cys
                165                 170                 175

Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe Cys Lys Asn Ser Ala Asp
            180                 185                 190

Asn Lys Val Val Cys Ser Cys Thr Glu Gly Tyr Arg Leu Ala Glu Asn
        195                 200                 205

Gln Lys Ser Cys Glu Pro Ala Val Pro Phe Pro Cys Gly Arg Val Ser
    210                 215                 220

Val Ser Gln Thr Ser Lys Leu Thr Arg Ala Glu Thr Val Phe Pro Asp
225                 230                 235                 240

Val Asp Tyr Val Asn Ser Thr Glu Ala Glu Thr Ile Leu Asp Asn Ile
                245                 250                 255
```

```
Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe Thr Arg Val Val Gly Gly
            260                 265                 270

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

Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile
    290                 295                 300

Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val
305                 310                 315                 320

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

Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn
            340                 345                 350

Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val
        355                 360                 365

Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr
    370                 375                 380

Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg
385                 390                 395                 400

Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val
                405                 410                 415

Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile
            420                 425                 430
```

Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser
435 440 445

Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr
450 455 460

Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys
465 470 475 480

Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile
485 490 495

Lys Glu Lys Thr Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr
500 505 510

Arg Ala Glu Thr Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln
515 520 525

Lys Leu Ile Ser Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His
530 535 540

His His His His His
545

<210> 82
<211> 549
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL145

<400> 82

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr

```
1               5                   10                  15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
            20                  25                  30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
        35                  40                  45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
    50                  55                  60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65                  70                  75                  80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
                85                  90                  95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
            100                 105                 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
        115                 120                 125

Glu Leu Asp Gly Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr
    130                 135                 140

Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser
145                 150                 155                 160

Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Ala Ser Ser Val Thr Cys
                165                 170                 175

Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe Cys Lys Asn Ser Ala Asp
```

180 185 190

Asn Lys Val Val Cys Ser Cys Thr Glu Gly Tyr Arg Leu Ala Glu Asn
195 200 205

Gln Lys Ser Cys Glu Pro Ala Val Pro Phe Pro Cys Gly Arg Val Ser
210 215 220

Val Ser Gln Thr Ser Lys Leu Thr Arg Ala Glu Thr Val Phe Pro Asp
225 230 235 240

Val Asp Tyr Val Asn Ser Thr Glu Ala Glu Thr Ile Leu Asp Asn Ile
245 250 255

Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe Thr Arg Val Val Gly Gly
260 265 270

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

Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile
290 295 300

Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val
305 310 315 320

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

Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn
340 345 350

Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val

355 360 365

Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr
370 375 380

Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg
385 390 395 400

Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val
405 410 415

Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile
420 425 430

Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser
435 440 445

Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr
450 455 460

Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys
465 470 475 480

Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile
485 490 495

Lys Glu Lys Thr Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr
500 505 510

Arg Ala Glu Thr Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln
515 520 525

Lys Leu Ile Ser Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His

530 535 540

His His His His His
545

<210> 83
<211> 683
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL164

<400> 83

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
180 185 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
195 200 205

Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe
210 215 220

Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp
225 230 235 240

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

Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly
260 265 270

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

```
His Thr Glu Gln Lys Arg Asn Val Ile Arg Ile Ile Pro His His Asn
    290                 295                 300

Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu Glu
305                 310                 315                 320

Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile
                325                 330                 335

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

Val Ser Gly Trp Gly Arg Val Phe His Lys Gly Arg Ser Ala Leu Val
        355                 360                 365

Leu Gln Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu Leu
    370                 375                 380

Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe His
385                 390                 395                 400

Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro His Val
                405                 410                 415

Thr Glu Val Glu Gly Thr Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly
            420                 425                 430

Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser
        435                 440                 445

Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr Lys Leu Thr Gly Ala Gly
    450                 455                 460
```

Ser Pro Gly Ala Glu Thr Ala Leu Val Pro Arg Ser Phe Leu Leu Arg
465 470 475 480

Asn Pro Asn Asp Lys Tyr Glu Pro Phe Trp Glu Asp Glu Glu Ser Gly
485 490 495

Ala Gly Ser Pro Gly Ala Glu Thr Ala Gly Ala Pro Thr Ser Thr Glu
500 505 510

Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
515 520 525

Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
530 535 540

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala
545 550 555 560

Thr Ser Gly Ser Glu Thr Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser
565 570 575

Glu Thr Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly
580 585 590

Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu
595 600 605

Pro Ser Glu Gly Ser Ala Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser
610 615 620

Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
625 630 635 640

Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ala Ser Ser Gly
645 650 655

Ala Glu Thr Ala Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Ser Pro
660 665 670

Ala Thr Gly His His His His His His His His
675 680

<210> 84
<211> 827
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL165

<400> 84

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln

85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
180 185 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
195 200 205

Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe
210 215 220

Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp
225 230 235 240

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

Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly

260 265 270

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

His Thr Glu Gln Lys Arg Asn Val Ile Arg Ile Ile Pro His His Asn
290 295 300

Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu Glu
305 310 315 320

Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile
325 330 335

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

Val Ser Gly Trp Gly Arg Val Phe His Lys Gly Arg Ser Ala Leu Val
355 360 365

Leu Gln Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu Leu
370 375 380

Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe His
385 390 395 400

Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro His Val
405 410 415

Thr Glu Val Glu Gly Thr Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly
420 425 430

Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser

435 440 445

Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr Lys Leu Thr Gly Ala Gly
450 455 460

Ser Pro Gly Ala Glu Thr Ala Leu Val Pro Arg Ser Phe Leu Leu Arg
465 470 475 480

Asn Pro Asn Asp Lys Tyr Glu Pro Phe Trp Glu Asp Glu Glu Ser Gly
485 490 495

Ala Gly Ser Pro Gly Ala Glu Thr Ala Gly Ala Pro Gly Thr Ser Glu
500 505 510

Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly
515 520 525

Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
530 535 540

Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu
545 550 555 560

Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu
565 570 575

Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu
580 585 590

Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro
595 600 605

Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro

610 615 620

Glu Ser Gly Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu
625 630 635 640

Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr
645 650 655

Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro
660 665 670

Glu Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
675 680 685

Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro
690 695 700

Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Glu Pro Ala Thr Ser Gly
705 710 715 720

Ser Glu Thr Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu
725 730 735

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr
740 745 750

Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Glu Pro Ala Thr Ser Gly
755 760 765

Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
770 775 780

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Ala Ser Ser Gly

785 790 795 800

Ala Glu Thr Ala Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Ser Pro
805 810 815

Ala Thr Gly His His His His His His His His
820 825

<210> 85
<211> 1403
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL166

<400> 85

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

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Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
            100                 105                 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
        115                 120                 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
    130                 135                 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145                 150                 155                 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
                165                 170                 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
            180                 185                 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
        195                 200                 205

Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe
    210                 215                 220

Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp
225                 230                 235                 240

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

Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly
            260                 265                 270
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Val Lys Ile Thr Val Val Ala Gly Glu His Asn Ile Glu Glu Thr Glu
        275                 280                 285

His Thr Glu Gln Lys Arg Asn Val Ile Arg Ile Ile Pro His His Asn
    290                 295                 300

Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu Glu
305                 310                 315                 320

Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile
                325                 330                 335

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

Val Ser Gly Trp Gly Arg Val Phe His Lys Gly Arg Ser Ala Leu Val
        355                 360                 365

Leu Gln Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu Leu
    370                 375                 380

Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe His
385                 390                 395                 400

Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro His Val
                405                 410                 415

Thr Glu Val Glu Gly Thr Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly
            420                 425                 430

Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser
        435                 440                 445
```

Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr Lys Leu Thr Gly Ala Gly
450 455 460

Ser Pro Gly Ala Glu Thr Ala Leu Val Pro Arg Ser Phe Leu Leu Arg
465 470 475 480

Asn Pro Asn Asp Lys Tyr Glu Pro Phe Trp Glu Asp Glu Glu Ser Gly
485 490 495

Ala Gly Ser Pro Gly Ala Glu Thr Ala Gly Ala Pro Gly Ser Pro Ala
500 505 510

Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro
515 520 525

Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
530 535 540

Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr
545 550 555 560

Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu
565 570 575

Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
580 585 590

Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Glu Pro
595 600 605

Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Pro Ala Gly Ser Pro Thr
610 615 620

Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
625 630 635 640

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr
645 650 655

Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr
660 665 670

Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
675 680 685

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu
690 695 700

Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu
705 710 715 720

Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
725 730 735

Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Thr
740 745 750

Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu
755 760 765

Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
770 775 780

Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Pro Ala
785 790 795 800

Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro
805 810 815

Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro
820 825 830

Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr
835 840 845

Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu
850 855 860

Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
865 870 875 880

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr
885 890 895

Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu
900 905 910

Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu
915 920 925

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu
930 935 940

Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly
945 950 955 960

Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
965 970 975

Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu
980 985 990

Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu
995 1000 1005

Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly
1010 1015 1020

Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Ser
1025 1030 1035

Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Ser Pro Ala Gly
1040 1045 1050

Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro
1055 1060 1065

Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala
1070 1075 1080

Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser
1085 1090 1095

Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser
1100 1105 1110

Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly
1115 1120 1125

Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly
1130 1135 1140

```
Pro Gly  Thr Ser Thr Glu Pro  Ser Glu Gly Ser Ala  Pro Gly Ser
    1145                 1150                 1155

Pro Ala  Gly Ser Pro Thr Ser  Thr Glu Glu Gly Thr  Ser Glu Ser
    1160                 1165                 1170

Ala Thr  Pro Glu Ser Gly Pro  Gly Ser Glu Pro Ala  Thr Ser Gly
    1175                 1180                 1185

Ser Glu  Thr Pro Gly Thr Ser  Glu Ser Ala Thr Pro  Glu Ser Gly
    1190                 1195                 1200

Pro Gly  Ser Pro Ala Gly Ser  Pro Thr Ser Thr Glu  Glu Gly Ser
    1205                 1210                 1215

Pro Ala  Gly Ser Pro Thr Ser  Thr Glu Glu Gly Thr  Ser Thr Glu
    1220                 1225                 1230

Pro Ser  Glu Gly Ser Ala Pro  Gly Thr Ser Glu Ser  Ala Thr Pro
    1235                 1240                 1245

Glu Ser  Gly Pro Gly Thr Ser  Glu Ser Ala Thr Pro  Glu Ser Gly
    1250                 1255                 1260

Pro Gly  Thr Ser Glu Ser Ala  Thr Pro Glu Ser Gly  Pro Gly Ser
    1265                 1270                 1275

Glu Pro  Ala Thr Ser Gly Ser  Glu Thr Pro Gly Ser  Glu Pro Ala
    1280                 1285                 1290

Thr Ser  Gly Ser Glu Thr Pro  Gly Ser Pro Ala Gly  Ser Pro Thr
    1295                 1300                 1305
```

Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala
1310 1315 1320

Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser
1325 1330 1335

Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser
1340 1345 1350

Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu
1355 1360 1365

Gly Ser Ala Pro Ala Ser Ser Gly Ala Glu Thr Ala Glu Gln Lys
1370 1375 1380

Leu Ile Ser Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His
1385 1390 1395

His His His His His
1400

<210> 86
<211> 585
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL167

<400> 86

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu

20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Gly Ala Pro Ser
180 185 190

Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala

195 200 205

Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu
210 215 220

Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr
225 230 235 240

Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro
245 250 255

Ser Glu Gly Ser Ala Pro Gly Ala Ser Ser Leu Thr Arg Ala Glu Thr
260 265 270

Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu Thr Ile
275 280 285

Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe Thr Arg
290 295 300

Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp Gln Val
305 310 315 320

Val Leu Asn Gly Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn
325 330 335

Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys
340 345 350

Ile Thr Val Val Ala Gly Glu His Asn Ile Glu Glu Thr Glu His Thr
355 360 365

Glu Gln Lys Arg Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn

370 375 380

Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp
385 390 395 400

Glu Pro Leu Val Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp
405 410 415

Lys Glu Tyr Thr Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser
420 425 430

Gly Trp Gly Arg Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln
435 440 445

Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr
450 455 460

Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly
465 470 475 480

Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu
485 490 495

Val Glu Gly Thr Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu
500 505 510

Cys Ala Met Lys Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr
515 520 525

Val Asn Trp Ile Lys Glu Lys Thr Lys Leu Thr Gly Pro Glu Gly Pro
530 535 540

Ser Lys Leu Thr Arg Ala Glu Thr Gly Ala Gly Ser Pro Gly Ala Glu

545 550 555 560

Thr Ala Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Ser Pro Ala Thr
565 570 575

Gly His His His His His His His His
580 585

<210> 87
<211> 657
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL168

<400> 87

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

```
Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
            100                 105                 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
        115                 120                 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
    130                 135                 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145                 150                 155                 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
                165                 170                 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Gly Ala Pro Ser
            180                 185                 190

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

Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu
    210                 215                 220

Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr
225                 230                 235                 240

Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro
                245                 250                 255

Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser
            260                 265                 270
```

```
Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr
        275                 280                 285

Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro
    290                 295                 300

Ser Glu Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr
305                 310                 315                 320

Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ala
                325                 330                 335

Ser Ser Leu Thr Arg Ala Glu Thr Val Phe Pro Asp Val Asp Tyr Val
            340                 345                 350

Asn Ser Thr Glu Ala Glu Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr
        355                 360                 365

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

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

Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile Val Thr Ala Ala
                405                 410                 415

His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val Ala Gly Glu His
            420                 425                 430

Asn Ile Glu Glu Thr Glu His Thr Glu Gln Lys Arg Asn Val Ile Arg
        435                 440                 445
```

```
Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His
    450                 455                 460

Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr
465                 470                 475                 480

Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr Asn Ile Phe Leu
                485                 490                 495

Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg Val Phe His Lys
            500                 505                 510

Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val Pro Leu Val Asp
        515                 520                 525

Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met
    530                 535                 540

Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp
545                 550                 555                 560

Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr Ser Phe Leu Thr
                565                 570                 575

Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly
            580                 585                 590

Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr
        595                 600                 605

Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr Arg Ala Glu Thr
    610                 615                 620
```

Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln Lys Leu Ile Ser
625 630 635 640

Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His His His His His
645 650 655

His

<210> 88
<211> 801
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL169

<400> 88

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln

85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Gly Ala Pro Gly
180 185 190

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

Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
210 215 220

Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly
225 230 235 240

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu
245 250 255

Pro Ser Glu Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser

260 265 270

Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
275 280 285

Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser
290 295 300

Ala Thr Pro Glu Ser Gly Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser
305 310 315 320

Thr Glu Glu Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly
325 330 335

Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser
340 345 350

Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
355 360 365

Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
370 375 380

Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Glu Pro Ala
385 390 395 400

Thr Ser Gly Ser Glu Thr Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser
405 410 415

Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly
420 425 430

Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Glu Pro Ala

435 440 445

Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
450 455 460

Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Ala
465 470 475 480

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

Asn Ser Thr Glu Ala Glu Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr
500 505 510

Gln Ser Phe Asn Asp Phe Thr Arg Val Val Gly Gly Glu Asp Ala Lys
515 520 525

Pro Gly Gln Phe Pro Trp Gln Val Val Leu Asn Gly Lys Val Asp Ala
530 535 540

Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile Val Thr Ala Ala
545 550 555 560

His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val Ala Gly Glu His
565 570 575

Asn Ile Glu Glu Thr Glu His Thr Glu Gln Lys Arg Asn Val Ile Arg
580 585 590

Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His
595 600 605

Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr

610 615 620

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

Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg Val Phe His Lys
645 650 655

Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val Pro Leu Val Asp
660 665 670

Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met
675 680 685

Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp
690 695 700

Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr Ser Phe Leu Thr
705 710 715 720

Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly
725 730 735

Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr
740 745 750

Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr Arg Ala Glu Thr
755 760 765

Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln Lys Leu Ile Ser
770 775 780

Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His His His His His

785 790 795 800

His

<210> 89
<211> 585
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL170

<400> 89

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
180 185 190

Glu Thr Val Gly Ala Pro Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu
195 200 205

Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu
210 215 220

Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr
225 230 235 240

Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala
245 250 255

Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ala Ser
260 265 270

Ser Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu Thr Ile
275 280 285

```
Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe Thr Arg
    290                 295                 300

Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp Gln Val
305                 310                 315                 320

Val Leu Asn Gly Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn
                325                 330                 335

Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys
            340                 345                 350

Ile Thr Val Val Ala Gly Glu His Asn Ile Glu Glu Thr Glu His Thr
        355                 360                 365

Glu Gln Lys Arg Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn
    370                 375                 380

Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp
385                 390                 395                 400

Glu Pro Leu Val Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp
                405                 410                 415

Lys Glu Tyr Thr Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser
            420                 425                 430

Gly Trp Gly Arg Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln
        435                 440                 445

Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr
    450                 455                 460
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```
Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly
465                 470                 475                 480

Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu
                485                 490                 495

Val Glu Gly Thr Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu
            500                 505                 510

Cys Ala Met Lys Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr
        515                 520                 525

Val Asn Trp Ile Lys Glu Lys Thr Lys Leu Thr Gly Pro Glu Gly Pro
    530                 535                 540

Ser Lys Leu Thr Arg Ala Glu Thr Gly Ala Gly Ser Pro Gly Ala Glu
545                 550                 555                 560

Thr Ala Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Ser Pro Ala Thr
                565                 570                 575

Gly His His His His His His His His
            580                 585
```

<210> 90
<211> 657
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL171

<400> 90

```
Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
```

```
1               5                   10                  15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
            20                  25                  30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
        35                  40                  45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
    50                  55                  60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65                  70                  75                  80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
                85                  90                  95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
            100                 105                 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
        115                 120                 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
    130                 135                 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145                 150                 155                 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
                165                 170                 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
```

180 185 190

Glu Thr Val Gly Ala Pro Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu
195 200 205

Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu
210 215 220

Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr
225 230 235 240

Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala
245 250 255

Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser
260 265 270

Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser
275 280 285

Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala
290 295 300

Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Pro
305 310 315 320

Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser
325 330 335

Glu Gly Ser Ala Pro Gly Ala Ser Ser Phe Pro Asp Val Asp Tyr Val
340 345 350

Asn Ser Thr Glu Ala Glu Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr

355 360 365

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

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

Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile Val Thr Ala Ala
405 410 415

His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val Ala Gly Glu His
420 425 430

Asn Ile Glu Glu Thr Glu His Thr Glu Gln Lys Arg Asn Val Ile Arg
435 440 445

Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His
450 455 460

Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr
465 470 475 480

Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr Asn Ile Phe Leu
485 490 495

Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg Val Phe His Lys
500 505 510

Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val Pro Leu Val Asp
515 520 525

Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met

530 535 540

Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp
545 550 555 560

Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr Ser Phe Leu Thr
565 570 575

Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly
580 585 590

Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr
595 600 605

Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr Arg Ala Glu Thr
610 615 620

Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln Lys Leu Ile Ser
625 630 635 640

Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His His His His His
645 650 655

His

<210> 91
<211> 801
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL172

<400> 91

```
Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1               5                  10                  15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
            20                  25                  30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
        35                  40                  45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
    50                  55                  60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65                  70                  75                  80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
                85                  90                  95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
            100                 105                 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
        115                 120                 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
    130                 135                 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145                 150                 155                 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
                165                 170                 175
```

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
180 185 190

Glu Thr Val Gly Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser
195 200 205

Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr
210 215 220

Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr
225 230 235 240

Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser
245 250 255

Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser
260 265 270

Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala
275 280 285

Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu
290 295 300

Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser
305 310 315 320

Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Ser Pro Ala Gly Ser
325 330 335

Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser
340 345 350

Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr
355 360 365

Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Glu Ser Ala
370 375 380

Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu
385 390 395 400

Thr Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser
405 410 415

Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro
420 425 430

Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser
435 440 445

Ala Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr
450 455 460

Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro
465 470 475 480

Ser Glu Gly Ser Ala Pro Ala Ser Ser Phe Pro Asp Val Asp Tyr Val
485 490 495

Asn Ser Thr Glu Ala Glu Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr
500 505 510

Gln Ser Phe Asn Asp Phe Thr Arg Val Val Gly Gly Glu Asp Ala Lys
515 520 525

```
Pro Gly Gln Phe Pro Trp Gln Val Val Leu Asn Gly Lys Val Asp Ala
    530                 535                 540

Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile Val Thr Ala Ala
545                 550                 555                 560

His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val Ala Gly Glu His
                565                 570                 575

Asn Ile Glu Glu Thr Glu His Thr Glu Gln Lys Arg Asn Val Ile Arg
            580                 585                 590

Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His
        595                 600                 605

Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr
    610                 615                 620

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

Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg Val Phe His Lys
                645                 650                 655

Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val Pro Leu Val Asp
            660                 665                 670

Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met
        675                 680                 685

Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp
    690                 695                 700
```

```
Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr Ser Phe Leu Thr
705                 710                 715                 720

Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly
                725                 730                 735

Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr
            740                 745                 750

Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr Arg Ala Glu Thr
        755                 760                 765

Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln Lys Leu Ile Ser
    770                 775                 780

Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His His His His His
785                 790                 795                 800

His
```

<210> 92
<211> 585
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL173

<400> 92

```
Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1               5                   10                  15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
```

20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
180 185 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu

195 200 205

Gly Ala Pro Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr
210 215 220

Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr
225 230 235 240

Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser
245 250 255

Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr
260 265 270

Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ala Ser Ser Thr Ile
275 280 285

Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe Thr Arg
290 295 300

Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp Gln Val
305 310 315 320

Val Leu Asn Gly Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn
325 330 335

Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys
340 345 350

Ile Thr Val Val Ala Gly Glu His Asn Ile Glu Glu Thr Glu His Thr
355 360 365

Glu Gln Lys Arg Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn

370 375 380

Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp
385 390 395 400

Glu Pro Leu Val Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp
405 410 415

Lys Glu Tyr Thr Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser
420 425 430

Gly Trp Gly Arg Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln
435 440 445

Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr
450 455 460

Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly
465 470 475 480

Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu
485 490 495

Val Glu Gly Thr Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu
500 505 510

Cys Ala Met Lys Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr
515 520 525

Val Asn Trp Ile Lys Glu Lys Thr Lys Leu Thr Gly Pro Glu Gly Pro
530 535 540

Ser Lys Leu Thr Arg Ala Glu Thr Gly Ala Gly Ser Pro Gly Ala Glu

545 550 555 560

Thr Ala Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Ser Pro Ala Thr
565 570 575

Gly His His His His His His His His
580 585

<210> 93
<211> 657
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL174

<400> 93

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

```
Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
            100                 105                 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
        115                 120                 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
    130                 135                 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145                 150                 155                 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
                165                 170                 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
            180                 185                 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
        195                 200                 205

Gly Ala Pro Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr
    210                 215                 220

Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr
225                 230                 235                 240

Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser
                245                 250                 255

Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr
            260                 265                 270
```

Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro
275 280 285

Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser
290 295 300

Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr
305 310 315 320

Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser
325 330 335

Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser
340 345 350

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

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

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

Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile Val Thr Ala Ala
405 410 415

His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val Ala Gly Glu His
420 425 430

Asn Ile Glu Glu Thr Glu His Thr Glu Gln Lys Arg Asn Val Ile Arg
435 440 445

```
Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His
    450                 455                 460

Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr
465                 470                 475                 480

Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr Asn Ile Phe Leu
                485                 490                 495

Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg Val Phe His Lys
            500                 505                 510

Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val Pro Leu Val Asp
        515                 520                 525

Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met
    530                 535                 540

Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp
545                 550                 555                 560

Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr Ser Phe Leu Thr
                565                 570                 575

Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly
            580                 585                 590

Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr
        595                 600                 605

Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr Arg Ala Glu Thr
    610                 615                 620
```

Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln Lys Leu Ile Ser
625 630 635 640

Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His His His His His
645 650 655

His

<210> 94
<211> 801
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL175

<400> 94

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln

85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
180 185 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
195 200 205

Gly Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
210 215 220

Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser
225 230 235 240

Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser
245 250 255

Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly

260 265 270

Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Pro Ala Gly
275 280 285

Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu
290 295 300

Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly
305 310 315 320

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Pro Ala Gly
325 330 335

Ser Pro Thr Ser Thr Glu Glu Gly Ser Pro Ala Gly Ser Pro Thr Ser
340 345 350

Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly
355 360 365

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Glu Ser
370 375 380

Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
385 390 395 400

Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly
405 410 415

Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Pro Ala Gly
420 425 430

Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly

435 440 445

Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly
450 455 460

Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser
465 470 475 480

Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly
485 490 495

Ser Ala Pro Ala Ser Ser Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr
500 505 510

Gln Ser Phe Asn Asp Phe Thr Arg Val Val Gly Gly Glu Asp Ala Lys
515 520 525

Pro Gly Gln Phe Pro Trp Gln Val Val Leu Asn Gly Lys Val Asp Ala
530 535 540

Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile Val Thr Ala Ala
545 550 555 560

His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val Ala Gly Glu His
565 570 575

Asn Ile Glu Glu Thr Glu His Thr Glu Gln Lys Arg Asn Val Ile Arg
580 585 590

Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His
595 600 605

Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr

610 615 620

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

Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg Val Phe His Lys
645 650 655

Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val Pro Leu Val Asp
660 665 670

Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met
675 680 685

Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp
690 695 700

Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr Ser Phe Leu Thr
705 710 715 720

Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly
725 730 735

Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr
740 745 750

Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr Arg Ala Glu Thr
755 760 765

Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln Lys Leu Ile Ser
770 775 780

Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His His His His His

785 790 795 800

His

<210> 95
<211> 585
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL176

<400> 95

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
180 185 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
195 200 205

Thr Ile Leu Asp Gly Ala Pro Ser Pro Ala Gly Ser Pro Thr Ser Thr
210 215 220

Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser
225 230 235 240

Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala
245 250 255

Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser
260 265 270

Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ala
275 280 285

```
Ser Ser Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe Thr Arg
    290                 295                 300

Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp Gln Val
305                 310                 315                 320

Val Leu Asn Gly Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn
                325                 330                 335

Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys
            340                 345                 350

Ile Thr Val Val Ala Gly Glu His Asn Ile Glu Glu Thr Glu His Thr
        355                 360                 365

Glu Gln Lys Arg Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn
    370                 375                 380

Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp
385                 390                 395                 400

Glu Pro Leu Val Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp
                405                 410                 415

Lys Glu Tyr Thr Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser
            420                 425                 430

Gly Trp Gly Arg Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln
        435                 440                 445

Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr
    450                 455                 460
```

```
Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly
465                 470                 475                 480

Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu
                485                 490                 495

Val Glu Gly Thr Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu
            500                 505                 510

Cys Ala Met Lys Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr
        515                 520                 525

Val Asn Trp Ile Lys Glu Lys Thr Lys Leu Thr Gly Pro Glu Gly Pro
    530                 535                 540

Ser Lys Leu Thr Arg Ala Glu Thr Gly Ala Gly Ser Pro Gly Ala Glu
545                 550                 555                 560

Thr Ala Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Ser Pro Ala Thr
                565                 570                 575

Gly His His His His His His His His
            580                 585
```

<210> 96
<211> 657
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL177

<400> 96

```
Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
```

```
1               5                   10                  15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
            20                  25                  30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
        35                  40                  45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
    50                  55                  60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65                  70                  75                  80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
                85                  90                  95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
            100                 105                 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
        115                 120                 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
    130                 135                 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145                 150                 155                 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
                165                 170                 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
```

180 185 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
195 200 205

Thr Ile Leu Asp Gly Ala Pro Ser Pro Ala Gly Ser Pro Thr Ser Thr
210 215 220

Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser
225 230 235 240

Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala
245 250 255

Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser
260 265 270

Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr
275 280 285

Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro
290 295 300

Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser
305 310 315 320

Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser
325 330 335

Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro
340 345 350

Ser Glu Gly Ser Ala Pro Gly Ala Ser Ser Asn Ile Thr Gln Ser Thr

355 360 365

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

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

Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile Val Thr Ala Ala
405 410 415

His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val Ala Gly Glu His
420 425 430

Asn Ile Glu Glu Thr Glu His Thr Glu Gln Lys Arg Asn Val Ile Arg
435 440 445

Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His
450 455 460

Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr
465 470 475 480

Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr Asn Ile Phe Leu
485 490 495

Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg Val Phe His Lys
500 505 510

Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val Pro Leu Val Asp
515 520 525

Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met

530 535 540

Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp
545 550 555 560

Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr Ser Phe Leu Thr
565 570 575

Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly
580 585 590

Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr
595 600 605

Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr Arg Ala Glu Thr
610 615 620

Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln Lys Leu Ile Ser
625 630 635 640

Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His His His His His
645 650 655

His

<210> 97
<211> 801
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL178

<400> 97

```
Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1               5                  10                  15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
            20                  25                  30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
        35                  40                  45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
    50                  55                  60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65                  70                  75                  80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
                85                  90                  95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
            100                 105                 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
        115                 120                 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
    130                 135                 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145                 150                 155                 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
                165                 170                 175
```

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
180 185 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
195 200 205

Thr Ile Leu Asp Gly Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
210 215 220

Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly
225 230 235 240

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala
245 250 255

Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
260 265 270

Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly
275 280 285

Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser
290 295 300

Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser
305 310 315 320

Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
325 330 335

Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Ser Pro Ala Gly
340 345 350

Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly
355 360 365

Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
370 375 380

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Glu Ser
385 390 395 400

Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser
405 410 415

Glu Thr Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly
420 425 430

Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu
435 440 445

Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly
450 455 460

Ser Ala Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly
465 470 475 480

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu
485 490 495

Pro Ser Glu Gly Ser Ala Pro Ala Ser Ser Asn Ile Thr Gln Ser Thr
500 505 510

Gln Ser Phe Asn Asp Phe Thr Arg Val Val Gly Gly Glu Asp Ala Lys
515 520 525

```
Pro Gly Gln Phe Pro Trp Gln Val Val Leu Asn Gly Lys Val Asp Ala
    530                 535                 540

Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile Val Thr Ala Ala
545                 550                 555                 560

His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val Ala Gly Glu His
                565                 570                 575

Asn Ile Glu Glu Thr Glu His Thr Glu Gln Lys Arg Asn Val Ile Arg
            580                 585                 590

Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His
        595                 600                 605

Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr
    610                 615                 620

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

Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg Val Phe His Lys
                645                 650                 655

Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val Pro Leu Val Asp
            660                 665                 670

Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met
        675                 680                 685

Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp
    690                 695                 700
```

```
Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr Ser Phe Leu Thr
705                 710                 715                 720

Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly
                725                 730                 735

Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr
            740                 745                 750

Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr Arg Ala Glu Thr
        755                 760                 765

Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln Lys Leu Ile Ser
    770                 775                 780

Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His His His His His
785                 790                 795                 800

His
```

<210> 98
<211> 585
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL179

<400> 98

```
Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1               5                   10                  15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
```

20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
180 185 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu

195 200 205

Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Gly Ala Pro Ser
210 215 220

Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala
225 230 235 240

Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu
245 250 255

Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr
260 265 270

Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro
275 280 285

Ser Glu Gly Ser Ala Pro Gly Ala Ser Ser Phe Asn Asp Phe Thr Arg
290 295 300

Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp Gln Val
305 310 315 320

Val Leu Asn Gly Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn
325 330 335

Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys
340 345 350

Ile Thr Val Val Ala Gly Glu His Asn Ile Glu Glu Thr Glu His Thr
355 360 365

Glu Gln Lys Arg Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn

370 375 380

Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp
385 390 395 400

Glu Pro Leu Val Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp
405 410 415

Lys Glu Tyr Thr Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser
420 425 430

Gly Trp Gly Arg Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln
435 440 445

Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr
450 455 460

Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly
465 470 475 480

Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu
485 490 495

Val Glu Gly Thr Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu
500 505 510

Cys Ala Met Lys Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr
515 520 525

Val Asn Trp Ile Lys Glu Lys Thr Lys Leu Thr Gly Pro Glu Gly Pro
530 535 540

Ser Lys Leu Thr Arg Ala Glu Thr Gly Ala Gly Ser Pro Gly Ala Glu

545 550 555 560

Thr Ala Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Ser Pro Ala Thr
565 570 575

Gly His His His His His His His His
580 585

<210> 99
<211> 657
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL180

<400> 99

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

```
Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
            100                 105                 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
        115                 120                 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
    130                 135                 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145                 150                 155                 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
                165                 170                 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
            180                 185                 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
        195                 200                 205

Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Gly Ala Pro Ser
    210                 215                 220

Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala
225                 230                 235                 240

Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu
                245                 250                 255

Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr
            260                 265                 270
```

Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro
275 280 285

Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser
290 295 300

Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr
305 310 315 320

Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro
325 330 335

Ser Glu Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr
340 345 350

Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ala
355 360 365

Ser Ser Phe Asn Asp Phe Thr Arg Val Val Gly Gly Glu Asp Ala Lys
370 375 380

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

Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile Val Thr Ala Ala
405 410 415

His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val Ala Gly Glu His
420 425 430

Asn Ile Glu Glu Thr Glu His Thr Glu Gln Lys Arg Asn Val Ile Arg
435 440 445

```
Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His
    450                 455                 460

Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr
465                 470                 475                 480

Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr Asn Ile Phe Leu
                485                 490                 495

Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg Val Phe His Lys
            500                 505                 510

Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val Pro Leu Val Asp
        515                 520                 525

Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met
    530                 535                 540

Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp
545                 550                 555                 560

Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr Ser Phe Leu Thr
                565                 570                 575

Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly
            580                 585                 590

Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr
        595                 600                 605

Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr Arg Ala Glu Thr
    610                 615                 620
```

Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln Lys Leu Ile Ser
625 630 635 640

Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His His His His His
645 650 655

His

<210> 100
<211> 801
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL181

<400> 100

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln

85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
180 185 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
195 200 205

Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Gly Ala Pro Gly
210 215 220

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala
225 230 235 240

Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
245 250 255

Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly

260 265 270

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu
275 280 285

Pro Ser Glu Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser
290 295 300

Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
305 310 315 320

Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser
325 330 335

Ala Thr Pro Glu Ser Gly Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser
340 345 350

Thr Glu Glu Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly
355 360 365

Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser
370 375 380

Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
385 390 395 400

Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
405 410 415

Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Glu Pro Ala
420 425 430

Thr Ser Gly Ser Glu Thr Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser

435 440 445

Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly
450 455 460

Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Glu Pro Ala
465 470 475 480

Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
485 490 495

Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Ala
500 505 510

Ser Ser Phe Asn Asp Phe Thr Arg Val Val Gly Gly Glu Asp Ala Lys
515 520 525

Pro Gly Gln Phe Pro Trp Gln Val Val Leu Asn Gly Lys Val Asp Ala
530 535 540

Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile Val Thr Ala Ala
545 550 555 560

His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val Ala Gly Glu His
565 570 575

Asn Ile Glu Glu Thr Glu His Thr Glu Gln Lys Arg Asn Val Ile Arg
580 585 590

Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His
595 600 605

Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr

610 615 620

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

Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg Val Phe His Lys
645 650 655

Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val Pro Leu Val Asp
660 665 670

Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met
675 680 685

Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp
690 695 700

Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr Ser Phe Leu Thr
705 710 715 720

Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly
725 730 735

Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr
740 745 750

Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr Arg Ala Glu Thr
755 760 765

Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln Lys Leu Ile Ser
770 775 780

Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His His His His His

785 790 795 800

His

<210> 101
<211> 585
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL182

<400> 101

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
180 185 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
195 200 205

Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe
210 215 220

Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp
225 230 235 240

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

Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Gly Ala
260 265 270

Pro Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu
275 280 285

Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly
290 295 300

Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
305 310 315 320

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr
325 330 335

Glu Pro Ser Glu Gly Ser Ala Pro Gly Ala Ser Ser Thr Gly Val Lys
340 345 350

Ile Thr Val Val Ala Gly Glu His Asn Ile Glu Glu Thr Glu His Thr
355 360 365

Glu Gln Lys Arg Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn
370 375 380

Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp
385 390 395 400

Glu Pro Leu Val Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp
405 410 415

Lys Glu Tyr Thr Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser
420 425 430

Gly Trp Gly Arg Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln
435 440 445

Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr
450 455 460

```
Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly
465                 470                 475                 480

Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu
                485                 490                 495

Val Glu Gly Thr Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu
            500                 505                 510

Cys Ala Met Lys Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr
        515                 520                 525

Val Asn Trp Ile Lys Glu Lys Thr Lys Leu Thr Gly Pro Glu Gly Pro
    530                 535                 540

Ser Lys Leu Thr Arg Ala Glu Thr Gly Ala Gly Ser Pro Gly Ala Glu
545                 550                 555                 560

Thr Ala Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Ser Pro Ala Thr
                565                 570                 575

Gly His His His His His His His His
            580                 585
```

<210> 102
<211> 657
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL183

<400> 102

```
Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
```

```
1               5                   10                  15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
            20                  25                  30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
        35                  40                  45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
    50                  55                  60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65                  70                  75                  80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
                85                  90                  95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
            100                 105                 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
        115                 120                 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
    130                 135                 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145                 150                 155                 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
                165                 170                 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
```

180 185 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
195 200 205

Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe
210 215 220

Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp
225 230 235 240

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

Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Gly Ala
260 265 270

Pro Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu
275 280 285

Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly
290 295 300

Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
305 310 315 320

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr
325 330 335

Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu
340 345 350

Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro

355 360 365

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr
370 375 380

Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr
385 390 395 400

Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
405 410 415

Gly Ala Ser Ser Thr Gly Val Lys Ile Thr Val Val Ala Gly Glu His
420 425 430

Asn Ile Glu Glu Thr Glu His Thr Glu Gln Lys Arg Asn Val Ile Arg
435 440 445

Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His
450 455 460

Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr
465 470 475 480

Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr Asn Ile Phe Leu
485 490 495

Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg Val Phe His Lys
500 505 510

Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val Pro Leu Val Asp
515 520 525

Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met

530 535 540

Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp
545 550 555 560

Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr Ser Phe Leu Thr
565 570 575

Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly
580 585 590

Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr
595 600 605

Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr Arg Ala Glu Thr
610 615 620

Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln Lys Leu Ile Ser
625 630 635 640

Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His His His His His
645 650 655

His

<210> 103
<211> 801
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL184

<400> 103

```
Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1               5                  10                  15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
            20                  25                  30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
        35                  40                  45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
    50                  55                  60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65                  70                  75                  80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
                85                  90                  95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
            100                 105                 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
        115                 120                 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
    130                 135                 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145                 150                 155                 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
                165                 170                 175
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Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
            180                 185                 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
        195                 200                 205

Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe
    210                 215                 220

Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp
225                 230                 235                 240

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

Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Gly Ala
            260                 265                 270

Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu
        275                 280                 285

Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr
    290                 295                 300

Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr
305                 310                 315                 320

Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser
                325                 330                 335

Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro
            340                 345                 350
```

Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly
355 360 365

Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser
370 375 380

Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Pro Ala Gly Ser Pro
385 390 395 400

Thr Ser Thr Glu Glu Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu
405 410 415

Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser
420 425 430

Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr
435 440 445

Pro Glu Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly
450 455 460

Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Glu
465 470 475 480

Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Pro Ala Gly Ser Pro
485 490 495

Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala
500 505 510

Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Glu
515 520 525

```
Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr
    530                 535                 540

Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala
545                 550                 555                 560

Pro Ala Ser Ser Thr Gly Val Lys Ile Thr Val Val Ala Gly Glu His
                565                 570                 575

Asn Ile Glu Glu Thr Glu His Thr Glu Gln Lys Arg Asn Val Ile Arg
            580                 585                 590

Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His
        595                 600                 605

Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr
    610                 615                 620

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

Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg Val Phe His Lys
                645                 650                 655

Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val Pro Leu Val Asp
            660                 665                 670

Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met
        675                 680                 685

Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp
    690                 695                 700
```

Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr Ser Phe Leu Thr
705 710 715 720

Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly
725 730 735

Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr
740 745 750

Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr Arg Ala Glu Thr
755 760 765

Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln Lys Leu Ile Ser
770 775 780

Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His His His His His
785 790 795 800

His

<210> 104
<211> 585
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL185

<400> 104

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu

20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
180 185 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu

195 200 205

Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe
210 215 220

Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp
225 230 235 240

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

Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly
260 265 270

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

His Thr Glu Gln Lys Arg Asn Val Ile Arg Ile Ile Pro His His Asn
290 295 300

Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu Glu
305 310 315 320

Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile
325 330 335

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

Val Ser Gly Trp Gly Arg Val Phe His Lys Gly Arg Ser Ala Leu Val
355 360 365

Leu Gln Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu Leu

370 375 380

Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe His
385 390 395 400

Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro His Val
405 410 415

Thr Glu Val Glu Gly Thr Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly
420 425 430

Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser
435 440 445

Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr Lys Gly Ala Pro Ser Pro
450 455 460

Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr
465 470 475 480

Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr
485 490 495

Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser
500 505 510

Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser
515 520 525

Glu Gly Ser Ala Pro Gly Ala Ser Ser Leu Thr Gly Pro Glu Gly Pro
530 535 540

Ser Lys Leu Thr Arg Ala Glu Thr Gly Ala Gly Ser Pro Gly Ala Glu

545 550 555 560

Thr Ala Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Ser Pro Ala Thr
565 570 575

Gly His His His His His His His His
580 585

<210> 105
<211> 657
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL186

<400> 105

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

```
Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
            100                 105                 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
        115                 120                 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
    130                 135                 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145                 150                 155                 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
                165                 170                 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
            180                 185                 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
        195                 200                 205

Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe
    210                 215                 220

Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp
225                 230                 235                 240

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

Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly
            260                 265                 270
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```
Val Lys Ile Thr Val Val Ala Gly Glu His Asn Ile Glu Glu Thr Glu
        275                 280                 285

His Thr Glu Gln Lys Arg Asn Val Ile Arg Ile Ile Pro His His Asn
    290                 295                 300

Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu Glu
305                 310                 315                 320

Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile
                325                 330                 335

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

Val Ser Gly Trp Gly Arg Val Phe His Lys Gly Arg Ser Ala Leu Val
        355                 360                 365

Leu Gln Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu Leu
    370                 375                 380

Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe His
385                 390                 395                 400

Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro His Val
                405                 410                 415

Thr Glu Val Glu Gly Thr Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly
            420                 425                 430

Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser
        435                 440                 445
```

```
Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr Lys Gly Ala Pro Ser Pro
    450                 455                 460

Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr
465                 470                 475                 480

Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr
                485                 490                 495

Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser
            500                 505                 510

Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser
        515                 520                 525

Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala
    530                 535                 540

Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser
545                 550                 555                 560

Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser
                565                 570                 575

Glu Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu
            580                 585                 590

Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ala Ser
        595                 600                 605

Ser Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr Arg Ala Glu Thr
    610                 615                 620
```

Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln Lys Leu Ile Ser
625 630 635 640

Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His His His His His
645 650 655

His

<210> 106
<211> 801
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL187

<400> 106

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln

85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
180 185 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
195 200 205

Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe
210 215 220

Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp
225 230 235 240

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

Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly

260 265 270

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

His Thr Glu Gln Lys Arg Asn Val Ile Arg Ile Ile Pro His His Asn
290 295 300

Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu Glu
305 310 315 320

Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile
325 330 335

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

Val Ser Gly Trp Gly Arg Val Phe His Lys Gly Arg Ser Ala Leu Val
355 360 365

Leu Gln Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu Leu
370 375 380

Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe His
385 390 395 400

Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro His Val
405 410 415

Thr Glu Val Glu Gly Thr Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly
420 425 430

Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser

435 440 445

Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr Lys Gly Ala Pro Gly Thr
450 455 460

Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr
465 470 475 480

Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser
485 490 495

Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr
500 505 510

Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro
515 520 525

Ser Glu Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr
530 535 540

Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser
545 550 555 560

Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala
565 570 575

Thr Pro Glu Ser Gly Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr
580 585 590

Glu Glu Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr
595 600 605

Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala

610 615 620

Thr Pro Glu Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser
625 630 635 640

Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser
645 650 655

Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Glu Pro Ala Thr
660 665 670

Ser Gly Ser Glu Thr Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr
675 680 685

Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr
690 695 700

Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Glu Pro Ala Thr
705 710 715 720

Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser
725 730 735

Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Ala Ser
740 745 750

Ser Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr Arg Ala Glu Thr
755 760 765

Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln Lys Leu Ile Ser
770 775 780

Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His His His His His

785 790 795 800

His

<210> 107
<211> 585
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL188

<400> 107

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Gly Ala Pro Ser Pro Ala Gly Ser Pro Thr Ser
145 150 155 160

Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
165 170 175

Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser
180 185 190

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

Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly
210 215 220

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

Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe Pro Cys
245 250 255

Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala Glu Thr
260 265 270

Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu Thr Ile
275 280 285

```
Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe Thr Arg
    290                 295                 300

Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp Gln Val
305                 310                 315                 320

Val Leu Asn Gly Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn
                325                 330                 335

Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys
            340                 345                 350

Ile Thr Val Val Ala Gly Glu His Asn Ile Glu Glu Thr Glu His Thr
        355                 360                 365

Glu Gln Lys Arg Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn
    370                 375                 380

Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp
385                 390                 395                 400

Glu Pro Leu Val Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp
                405                 410                 415

Lys Glu Tyr Thr Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser
            420                 425                 430

Gly Trp Gly Arg Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln
        435                 440                 445

Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr
    450                 455                 460
```

```
Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly
465                 470                 475                 480

Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu
                485                 490                 495

Val Glu Gly Thr Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu
            500                 505                 510

Cys Ala Met Lys Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr
        515                 520                 525

Val Asn Trp Ile Lys Glu Lys Thr Lys Leu Thr Gly Pro Glu Gly Pro
    530                 535                 540

Ser Lys Leu Thr Arg Ala Glu Thr Gly Ala Gly Ser Pro Gly Ala Glu
545                 550                 555                 560

Thr Ala Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Ser Pro Ala Thr
                565                 570                 575

Gly His His His His His His His His
            580                 585
```

<210> 108
<211> 657
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL189

<400> 108

```
Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
```

1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Gly Ala Pro Ser Pro Ala Gly Ser Pro Thr Ser
145 150 155 160

Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
165 170 175

Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser

180 185 190

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

Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly
210 215 220

Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu
225 230 235 240

Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly
245 250 255

Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly
260 265 270

Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu
275 280 285

Pro Ser Glu Gly Ser Ala Pro Gly Ala Ser Ser Asp Asn Lys Val Val
290 295 300

Cys Ser Cys Thr Glu Gly Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys
305 310 315 320

Glu Pro Ala Val Pro Phe Pro Cys Gly Arg Val Ser Val Ser Gln Thr
325 330 335

Ser Lys Leu Thr Arg Ala Glu Thr Val Phe Pro Asp Val Asp Tyr Val
340 345 350

Asn Ser Thr Glu Ala Glu Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr

355 360 365

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

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

Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile Val Thr Ala Ala
405 410 415

His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val Ala Gly Glu His
420 425 430

Asn Ile Glu Glu Thr Glu His Thr Glu Gln Lys Arg Asn Val Ile Arg
435 440 445

Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His
450 455 460

Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr
465 470 475 480

Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr Asn Ile Phe Leu
485 490 495

Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg Val Phe His Lys
500 505 510

Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val Pro Leu Val Asp
515 520 525

Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met

530 535 540

Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp
545 550 555 560

Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr Ser Phe Leu Thr
565 570 575

Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly
580 585 590

Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr
595 600 605

Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr Arg Ala Glu Thr
610 615 620

Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln Lys Leu Ile Ser
625 630 635 640

Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His His His His His
645 650 655

His

<210> 109
<211> 801
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL190

<400> 109

```
Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1               5                  10                  15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
            20                  25                  30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
        35                  40                  45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
    50                  55                  60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65                  70                  75                  80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
                85                  90                  95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
            100                 105                 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
        115                 120                 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
    130                 135                 140

Cys Lys Asn Ser Ala Gly Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro
145                 150                 155                 160

Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro
                165                 170                 175
```

Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro
180 185 190

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

Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
210 215 220

Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu
225 230 235 240

Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly
245 250 255

Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
260 265 270

Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Ser Pro Ala
275 280 285

Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu
290 295 300

Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
305 310 315 320

Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Glu
325 330 335

Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly
340 345 350

Ser Glu Thr Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro
355 360 365

Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr
370 375 380

Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu
385 390 395 400

Gly Ser Ala Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro
405 410 415

Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr
420 425 430

Glu Pro Ser Glu Gly Ser Ala Pro Ala Ser Ser Asp Asn Lys Val Val
435 440 445

Cys Ser Cys Thr Glu Gly Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys
450 455 460

Glu Pro Ala Val Pro Phe Pro Cys Gly Arg Val Ser Val Ser Gln Thr
465 470 475 480

Ser Lys Leu Thr Arg Ala Glu Thr Val Phe Pro Asp Val Asp Tyr Val
485 490 495

Asn Ser Thr Glu Ala Glu Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr
500 505 510

Gln Ser Phe Asn Asp Phe Thr Arg Val Val Gly Gly Glu Asp Ala Lys
515 520 525

```
Pro Gly Gln Phe Pro Trp Gln Val Val Leu Asn Gly Lys Val Asp Ala
    530                 535                 540

Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile Val Thr Ala Ala
545                 550                 555                 560

His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val Ala Gly Glu His
                565                 570                 575

Asn Ile Glu Glu Thr Glu His Thr Glu Gln Lys Arg Asn Val Ile Arg
            580                 585                 590

Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His
        595                 600                 605

Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr
    610                 615                 620

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

Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg Val Phe His Lys
                645                 650                 655

Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val Pro Leu Val Asp
            660                 665                 670

Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met
        675                 680                 685

Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp
    690                 695                 700
```

```
Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr Ser Phe Leu Thr
705                 710                 715                 720

Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly
                725                 730                 735

Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr
            740                 745                 750

Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr Arg Ala Glu Thr
        755                 760                 765

Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln Lys Leu Ile Ser
    770                 775                 780

Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His His His His His
785                 790                 795                 800

His
```

<210> 110
<211> 549
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL195

<400> 110

```
Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1               5                   10                  15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
```

20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
180 185 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu

195 200 205

Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe
210 215 220

Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp
225 230 235 240

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

Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly
260 265 270

Gly Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly
275 280 285

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala
290 295 300

Thr Ser Gly Ser Glu Thr Pro Ala Ser Ser Val Lys Ile Thr Val Val
305 310 315 320

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

Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn
340 345 350

Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val
355 360 365

Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr

370 375 380

Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg
385 390 395 400

Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val
405 410 415

Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile
420 425 430

Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser
435 440 445

Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr
450 455 460

Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys
465 470 475 480

Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile
485 490 495

Lys Glu Lys Thr Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr
500 505 510

Arg Ala Glu Thr Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln
515 520 525

Lys Leu Ile Ser Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His
530 535 540

His His His His His

545

<210> 111
<211> 549
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL196

<400> 111

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

```
Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
    130                 135                 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145                 150                 155                 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
                165                 170                 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
            180                 185                 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
        195                 200                 205

Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe
    210                 215                 220

Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp
225                 230                 235                 240

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

Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly
            260                 265                 270

Val Lys Gly Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu
        275                 280                 285

Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu
    290                 295                 300
```

```
Pro Ala Thr Ser Gly Ser Glu Thr Pro Ala Ser Ser Ile Thr Val Val
305                 310                 315                 320

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

Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn
            340                 345                 350

Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val
        355                 360                 365

Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr
    370                 375                 380

Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg
385                 390                 395                 400

Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val
                405                 410                 415

Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile
            420                 425                 430

Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser
        435                 440                 445

Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr
    450                 455                 460

Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys
465                 470                 475                 480
```

```
Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile
                485                 490                 495

Lys Glu Lys Thr Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr
            500                 505                 510

Arg Ala Glu Thr Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln
        515                 520                 525

Lys Leu Ile Ser Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His
    530                 535                 540

His His His His His
545
```

<210> 112
<211> 549
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL197

<400> 112

```
Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1               5                   10                  15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
            20                  25                  30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
        35                  40                  45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
```

50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
180 185 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
195 200 205

Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe
210 215 220

Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp

225 230 235 240

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

Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly
260 265 270

Val Lys Ile Thr Gly Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser
275 280 285

Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
290 295 300

Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Ala Ser Ser Val Val
305 310 315 320

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

Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn
340 345 350

Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val
355 360 365

Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr
370 375 380

Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg
385 390 395 400

Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val

405 410 415

Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile
420 425 430

Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser
435 440 445

Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr
450 455 460

Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys
465 470 475 480

Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile
485 490 495

Lys Glu Lys Thr Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr
500 505 510

Arg Ala Glu Thr Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln
515 520 525

Lys Leu Ile Ser Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His
530 535 540

His His His His His
545

<210> 113
<211> 549
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL198

<400> 113

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Gly Ala Pro Gly Ser Pro Ala Gly Ser
145 150 155 160

Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser
165 170 175

Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Ala Ser
180 185 190

Ser Lys Val Val Cys Ser Cys Thr Glu Gly Tyr Arg Leu Ala Glu Asn
195 200 205

Gln Lys Ser Cys Glu Pro Ala Val Pro Phe Pro Cys Gly Arg Val Ser
210 215 220

Val Ser Gln Thr Ser Lys Leu Thr Arg Ala Glu Thr Val Phe Pro Asp
225 230 235 240

Val Asp Tyr Val Asn Ser Thr Glu Ala Glu Thr Ile Leu Asp Asn Ile
245 250 255

Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe Thr Arg Val Val Gly Gly
260 265 270

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

Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile
290 295 300

Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val
305 310 315 320

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

```
Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn
            340                 345                 350

Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val
        355                 360                 365

Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr
    370                 375                 380

Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg
385                 390                 395                 400

Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val
                405                 410                 415

Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile
            420                 425                 430

Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser
        435                 440                 445

Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr
    450                 455                 460

Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys
465                 470                 475                 480

Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile
                485                 490                 495

Lys Glu Lys Thr Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr
            500                 505                 510
```

Arg Ala Glu Thr Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln
515 520 525

Lys Leu Ile Ser Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His
530 535 540

His His His His His
545

<210> 114
<211> 549
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL199

<400> 114

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln

85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
180 185 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
195 200 205

Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe
210 215 220

Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp
225 230 235 240

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

Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly

260 265 270

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

His Thr Glu Gln Lys Arg Asn Val Ile Arg Ile Ile Pro His His Asn
290 295 300

Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu Glu
305 310 315 320

Leu Asp Glu Pro Leu Val Leu Asn Ser Gly Ala Pro Gly Ser Pro Ala
325 330 335

Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro
340 345 350

Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro
355 360 365

Ala Ser Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr
370 375 380

Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg
385 390 395 400

Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val
405 410 415

Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile
420 425 430

Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser

435 440 445

Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr
450 455 460

Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys
465 470 475 480

Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile
485 490 495

Lys Glu Lys Thr Lys Leu Thr Gly Pro Glu Gly Pro Ser Lys Leu Thr
500 505 510

Arg Ala Glu Thr Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Glu Gln
515 520 525

Lys Leu Ile Ser Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His
530 535 540

His His His His His
545

<210> 115
<211> 611
<212> PRT
<213> Artificial Sequence

<220>
<223> pNL202

<400> 115

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

```
Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
            20                  25                  30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
        35                  40                  45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
    50                  55                  60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65                  70                  75                  80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
                85                  90                  95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
            100                 105                 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
        115                 120                 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
    130                 135                 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145                 150                 155                 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
                165                 170                 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
            180                 185                 190
```

```
Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
        195                 200                 205

Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe
    210                 215                 220

Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp
225                 230                 235                 240

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

Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly
            260                 265                 270

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

His Thr Glu Gln Lys Arg Asn Val Ile Arg Ile Ile Pro His His Asn
    290                 295                 300

Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu Glu
305                 310                 315                 320

Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile
                325                 330                 335

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

Val Ser Gly Trp Gly Arg Val Phe His Lys Gly Arg Ser Ala Leu Val
        355                 360                 365
```

```
Leu Gln Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu Leu
    370                 375                 380

Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe His
385                 390                 395                 400

Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro His Val
                405                 410                 415

Thr Glu Val Glu Gly Thr Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly
            420                 425                 430

Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser
        435                 440                 445

Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr Lys Leu Thr Gly Ala Gly
    450                 455                 460

Ser Pro Gly Ala Glu Thr Ala Leu Val Pro Arg Ser Phe Leu Leu Arg
465                 470                 475                 480

Asn Pro Asn Asp Lys Tyr Glu Pro Phe Trp Glu Asp Glu Glu Ser Gly
                485                 490                 495

Ala Gly Ser Pro Gly Ala Glu Thr Ala Gly Ala Pro Ser Pro Ala Gly
            500                 505                 510

Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu
        515                 520                 525

Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly
    530                 535                 540
```

```
Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu
545                 550                 555                 560

Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly
                565                 570                 575

Ser Ala Pro Gly Ala Ser Ser Gly Ala Glu Thr Ala Glu Gln Lys Leu
            580                 585                 590

Ile Ser Glu Glu Asp Leu Ser Pro Ala Thr Gly His His His His His
        595                 600                 605

His His His
    610
```

<210> 116
<211> 1345
<212> PRT
<213> Artificial Sequence

<220>
<223> FIX-092

<400> 116

```
Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1               5                   10                  15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
            20                  25                  30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
        35                  40                  45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
```

50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
180 185 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
195 200 205

Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe
210 215 220

Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp

225 230 235 240

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

Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly
260 265 270

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

His Thr Glu Gln Lys Arg Asn Val Ile Arg Ile Ile Pro His His Asn
290 295 300

Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu Glu
305 310 315 320

Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile
325 330 335

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

Val Ser Gly Trp Gly Arg Val Phe His Lys Gly Arg Ser Ala Leu Val
355 360 365

Leu Gln Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu Arg
370 375 380

Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe His
385 390 395 400

Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro His Val

405 410 415

Thr Glu Val Glu Gly Thr Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly
420 425 430

Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser
435 440 445

Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr Lys Leu Thr Gly Pro Glu
450 455 460

Gly Pro Ser Lys Leu Thr Arg Ala Glu Thr Gly Ser Pro Gly Ser Pro
465 470 475 480

Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr
485 490 495

Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala
500 505 510

Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser
515 520 525

Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser
530 535 540

Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly
545 550 555 560

Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Glu
565 570 575

Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Pro Ala Gly Ser Pro

580 585 590

Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly
595 600 605

Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser
610 615 620

Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro
625 630 635 640

Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala
645 650 655

Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser
660 665 670

Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser
675 680 685

Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly
690 695 700

Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser
705 710 715 720

Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser
725 730 735

Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly
740 745 750

Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Pro

755 760 765

Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr
770 775 780

Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr
785 790 795 800

Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser
805 810 815

Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser
820 825 830

Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala
835 840 845

Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser
850 855 860

Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser
865 870 875 880

Glu Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu
885 890 895

Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser
900 905 910

Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser
915 920 925

Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly

930 935 940

Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser
945 950 955 960

Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser
965 970 975

Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly
980 985 990

Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Ser Pro
995 1000 1005

Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Ser Pro Ala Gly Ser
1010 1015 1020

Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu
1025 1030 1035

Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
1040 1045 1050

Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu
1055 1060 1065

Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala
1070 1075 1080

Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser
1085 1090 1095

Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro

1100 1105 1110

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Pro
1115 1120 1125

Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala
1130 1135 1140

Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser
1145 1150 1155

Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
1160 1165 1170

Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Ser Pro
1175 1180 1185

Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro
1190 1195 1200

Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
1205 1210 1215

Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
1220 1225 1230

Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu
1235 1240 1245

Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Glu Pro Ala Thr
1250 1255 1260

Ser Gly Ser Glu Thr Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser

1265 1270 1275

Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
1280 1285 1290

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Glu
1295 1300 1305

Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala
1310 1315 1320

Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly
1325 1330 1335

Ser Ala Pro Gly Ser Ser Ser
1340 1345

<210> 117
<211> 655
<212> PRT
<213> Artificial Sequence

<220>
<223> pJH0131

<400> 117

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
180 185 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
195 200 205

Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe
210 215 220

```
Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp
225                 230                 235                 240

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

Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly
            260                 265                 270

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

His Thr Glu Gln Lys Arg Asn Val Ile Arg Ile Ile Pro His His Asn
    290                 295                 300

Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu Glu
305                 310                 315                 320

Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile
                325                 330                 335

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

Val Ser Gly Trp Gly Arg Val Phe His Lys Gly Arg Ser Ala Leu Val
        355                 360                 365

Leu Gln Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu Leu
    370                 375                 380

Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe His
385                 390                 395                 400
```

Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro His Val
405 410 415

Thr Glu Val Glu Gly Thr Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly
420 425 430

Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser
435 440 445

Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr Lys Leu Thr Gly Ala Gly
450 455 460

Ser Pro Gly Ala Glu Thr Ala Leu Val Pro Arg Ser Phe Leu Leu Arg
465 470 475 480

Asn Pro Asn Asp Lys Tyr Glu Pro Phe Trp Glu Asp Glu Glu Ser Gly
485 490 495

Ala Gly Ser Pro Gly Ala Glu Thr Ala Gly Ala Pro Ser Pro Ala Gly
500 505 510

Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu
515 520 525

Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly
530 535 540

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu
545 550 555 560

Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly
565 570 575

Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly
580 585 590

Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu
595 600 605

Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly
610 615 620

Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly
625 630 635 640

Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ala Ser Ser
645 650 655

<210> 118
<211> 503
<212> PRT
<213> Artificial Sequence

<220>
<223> pJH44

<400> 118

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys

```
    50                  55                  60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65                  70                  75                  80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
                85                  90                  95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
            100                 105                 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
        115                 120                 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
    130                 135                 140

Cys Lys Asn Ser Ala Asp Asn Gly Ala Pro Gly Ser Pro Ala Gly Ser
145                 150                 155                 160

Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser
                165                 170                 175

Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Ala Ser
            180                 185                 190

Ser Lys Val Val Cys Ser Cys Thr Glu Gly Tyr Arg Leu Ala Glu Asn
        195                 200                 205

Gln Lys Ser Cys Glu Pro Ala Val Pro Phe Pro Cys Gly Arg Val Ser
    210                 215                 220

Val Ser Gln Thr Ser Lys Leu Thr Arg Ala Glu Thr Val Phe Pro Asp
```

225 230 235 240

Val Asp Tyr Val Asn Ser Thr Glu Ala Glu Thr Ile Leu Asp Asn Ile
245 250 255

Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe Thr Arg Val Val Gly Gly
260 265 270

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

Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile
290 295 300

Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val
305 310 315 320

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

Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn
340 345 350

Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val
355 360 365

Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr
370 375 380

Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg
385 390 395 400

Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val

405 410 415

Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile
420 425 430

Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser
435 440 445

Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr
450 455 460

Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys
465 470 475 480

Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile
485 490 495

Lys Glu Lys Thr Lys Leu Thr
500

<210> 119
<211> 539
<212> PRT
<213> Artificial Sequence

<220>
<223> pJH46

<400> 119

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

```
Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
        35                  40                  45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
    50                  55                  60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65                  70                  75                  80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
                85                  90                  95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
            100                 105                 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
        115                 120                 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
    130                 135                 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145                 150                 155                 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
                165                 170                 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
            180                 185                 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
        195                 200                 205
```

Thr Ile Leu Asp Gly Ala Pro Ser Pro Ala Gly Ser Pro Thr Ser Thr
210 215 220

Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser
225 230 235 240

Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala
245 250 255

Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser
260 265 270

Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ala
275 280 285

Ser Ser Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe Thr Arg
290 295 300

Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp Gln Val
305 310 315 320

Val Leu Asn Gly Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn
325 330 335

Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys
340 345 350

Ile Thr Val Val Ala Gly Glu His Asn Ile Glu Glu Thr Glu His Thr
355 360 365

Glu Gln Lys Arg Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn
370 375 380

```
Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp
385                 390                 395                 400

Glu Pro Leu Val Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp
                405                 410                 415

Lys Glu Tyr Thr Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser
            420                 425                 430

Gly Trp Gly Arg Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln
        435                 440                 445

Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr
    450                 455                 460

Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly
465                 470                 475                 480

Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu
                485                 490                 495

Val Glu Gly Thr Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu
            500                 505                 510

Cys Ala Met Lys Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr
        515                 520                 525

Val Asn Trp Ile Lys Glu Lys Thr Lys Leu Thr
    530                 535
```

<210> 120
<211> 611
<212> PRT

<213> Artificial Sequence

<220>
<223> pJH47

<400> 120

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly

145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
180 185 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
195 200 205

Thr Ile Leu Asp Gly Ala Pro Ser Pro Ala Gly Ser Pro Thr Ser Thr
210 215 220

Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser
225 230 235 240

Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala
245 250 255

Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser
260 265 270

Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr
275 280 285

Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro
290 295 300

Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser
305 310 315 320

Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser

325 330 335

Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro
340 345 350

Ser Glu Gly Ser Ala Pro Gly Ala Ser Ser Asn Ile Thr Gln Ser Thr
355 360 365

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

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

Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile Val Thr Ala Ala
405 410 415

His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val Ala Gly Glu His
420 425 430

Asn Ile Glu Glu Thr Glu His Thr Glu Gln Lys Arg Asn Val Ile Arg
435 440 445

Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His
450 455 460

Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr
465 470 475 480

Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr Asn Ile Phe Leu
485 490 495

Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg Val Phe His Lys

500 505 510

Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val Pro Leu Val Asp
515 520 525

Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met
530 535 540

Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp
545 550 555 560

Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr Ser Phe Leu Thr
565 570 575

Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly
580 585 590

Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr
595 600 605

Lys Leu Thr
610

<210> 121
<211> 655
<212> PRT
<213> Artificial Sequence

<220>
<223> pJH50

<400> 121

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

```
Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
            20                  25                  30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
        35                  40                  45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
    50                  55                  60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65                  70                  75                  80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
                85                  90                  95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
            100                 105                 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
        115                 120                 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
    130                 135                 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145                 150                 155                 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
                165                 170                 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
            180                 185                 190
```

```
Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
        195                 200                 205

Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe
    210                 215                 220

Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp
225                 230                 235                 240

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

Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly
            260                 265                 270

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

His Thr Glu Gln Lys Arg Asn Val Ile Arg Ile Ile Pro His His Asn
    290                 295                 300

Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu Glu
305                 310                 315                 320

Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile
                325                 330                 335

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

Val Ser Gly Trp Gly Arg Val Phe His Lys Gly Arg Ser Ala Leu Val
        355                 360                 365
```

```
Leu Gln Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu Leu
    370                 375                 380

Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe His
385                 390                 395                 400

Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro His Val
                405                 410                 415

Thr Glu Val Glu Gly Thr Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly
            420                 425                 430

Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser
        435                 440                 445

Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr Lys Leu Thr Gly Ala Gly
    450                 455                 460

Ser Pro Gly Ala Glu Thr Ala Leu Val Pro Arg Ser Phe Leu Leu Arg
465                 470                 475                 480

Asn Pro Asn Asp Lys Tyr Glu Pro Phe Trp Glu Asp Glu Glu Ser Gly
                485                 490                 495

Ala Gly Ser Pro Gly Ala Glu Thr Ala Gly Ala Pro Thr Ser Thr Glu
            500                 505                 510

Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
        515                 520                 525

Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
    530                 535                 540
```

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala
545 550 555 560

Thr Ser Gly Ser Glu Thr Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser
565 570 575

Glu Thr Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly
580 585 590

Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu
595 600 605

Pro Ser Glu Gly Ser Ala Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser
610 615 620

Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
625 630 635 640

Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ala Ser Ser
645 650 655

<210> 122
<211> 799
<212> PRT
<213> Artificial Sequence

<220>
<223> pJH51

<400> 122

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu

20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
180 185 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu

195 200 205

Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe
210 215 220

Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp
225 230 235 240

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

Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly
260 265 270

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

His Thr Glu Gln Lys Arg Asn Val Ile Arg Ile Ile Pro His His Asn
290 295 300

Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu Glu
305 310 315 320

Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile
325 330 335

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

Val Ser Gly Trp Gly Arg Val Phe His Lys Gly Arg Ser Ala Leu Val
355 360 365

Leu Gln Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu Leu

370 375 380

Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe His
385 390 395 400

Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro His Val
405 410 415

Thr Glu Val Glu Gly Thr Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly
420 425 430

Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser
435 440 445

Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr Lys Leu Thr Gly Ala Gly
450 455 460

Ser Pro Gly Ala Glu Thr Ala Leu Val Pro Arg Ser Phe Leu Leu Arg
465 470 475 480

Asn Pro Asn Asp Lys Tyr Glu Pro Phe Trp Glu Asp Glu Glu Ser Gly
485 490 495

Ala Gly Ser Pro Gly Ala Glu Thr Ala Gly Ala Pro Gly Thr Ser Glu
500 505 510

Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly
515 520 525

Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
530 535 540

Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu

545 550 555 560

Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu
565 570 575

Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu
580 585 590

Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro
595 600 605

Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro
610 615 620

Glu Ser Gly Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu
625 630 635 640

Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr
645 650 655

Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro
660 665 670

Glu Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
675 680 685

Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro
690 695 700

Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Glu Pro Ala Thr Ser Gly
705 710 715 720

Ser Glu Thr Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu

725 730 735

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr
740 745 750

Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Glu Pro Ala Thr Ser Gly
755 760 765

Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
770 775 780

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Ala Ser Ser
785 790 795

<210> 123
<211> 583
<212> PRT
<213> Artificial Sequence

<220>
<223> pJH52

<400> 123

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

```
Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65                  70                  75                  80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
                85                  90                  95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
            100                 105                 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
        115                 120                 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
    130                 135                 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145                 150                 155                 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
                165                 170                 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
            180                 185                 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
        195                 200                 205

Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe
    210                 215                 220

Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp
225                 230                 235                 240
```

```
Gln Val Val Leu Asn Gly Lys Val Asp Ala Phe Cys Gly Gly Ser Ile
               245                 250                 255

Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly
            260                 265                 270

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

His Thr Glu Gln Lys Arg Asn Val Ile Arg Ile Ile Pro His His Asn
    290                 295                 300

Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu Glu
305                 310                 315                 320

Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile
               325                 330                 335

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

Val Ser Gly Trp Gly Arg Val Phe His Lys Gly Arg Ser Ala Leu Val
        355                 360                 365

Leu Gln Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu Leu
    370                 375                 380

Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe His
385                 390                 395                 400

Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro His Val
               405                 410                 415
```

Thr Glu Val Glu Gly Thr Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly
420 425 430

Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser
435 440 445

Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr Lys Leu Thr Gly Ala Gly
450 455 460

Ser Pro Gly Ala Glu Thr Ala Leu Val Pro Arg Ser Phe Leu Leu Arg
465 470 475 480

Asn Pro Asn Asp Lys Tyr Glu Pro Phe Trp Glu Asp Glu Glu Ser Gly
485 490 495

Ala Gly Ser Pro Gly Ala Glu Thr Ala Gly Ala Pro Thr Ser Glu Ser
500 505 510

Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser
515 520 525

Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
530 535 540

Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser
545 550 555 560

Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly
565 570 575

Ser Ala Pro Gly Ala Ser Ser
580

<210> 124
<211> 503
<212> PRT
<213> Artificial Sequence

<220>
<223> pJH54

<400> 124

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe

130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
180 185 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
195 200 205

Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe
210 215 220

Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp
225 230 235 240

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

Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Gly Ala
260 265 270

Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser
275 280 285

Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser
290 295 300

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

305 310 315 320

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

Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn
340 345 350

Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val
355 360 365

Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr
370 375 380

Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg
385 390 395 400

Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val
405 410 415

Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile
420 425 430

Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser
435 440 445

Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr
450 455 460

Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys
465 470 475 480

Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile

485 490 495

Lys Glu Lys Thr Lys Leu Thr
500

<210> 125
<211> 503
<212> PRT
<213> Artificial Sequence

<220>
<223> pJH55

<400> 125

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

```
Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
        115                 120                 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
    130                 135                 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145                 150                 155                 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
                165                 170                 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
            180                 185                 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
        195                 200                 205

Thr Ile Leu Asp Gly Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser
    210                 215                 220

Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
225                 230                 235                 240

Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Ala Ser Ser Asn Ile
                245                 250                 255

Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe Thr Arg Val Val Gly Gly
            260                 265                 270

Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp Gln Val Val Leu Asn Gly
        275                 280                 285
```

```
Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile
    290                 295                 300

Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val
305                 310                 315                 320

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

Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn
            340                 345                 350

Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val
        355                 360                 365

Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr
    370                 375                 380

Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg
385                 390                 395                 400

Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val
                405                 410                 415

Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile
            420                 425                 430

Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser
        435                 440                 445

Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr
    450                 455                 460
```

```
Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys
465                 470                 475                 480

Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile
                485                 490                 495

Lys Glu Lys Thr Lys Leu Thr
            500
```

<210> 126
<211> 625
<212> PRT
<213> Artificial Sequence

<220>
<223> pJH59

<400> 126

```
Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1               5                   10                  15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
            20                  25                  30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
        35                  40                  45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
    50                  55                  60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65                  70                  75                  80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
```

85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
180 185 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
195 200 205

Thr Ile Leu Asp Gly Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser
210 215 220

Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
225 230 235 240

Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Ala Ser Ser Asn Ile
245 250 255

Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe Thr Arg Val Val Gly Gly

260 265 270

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

Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile
290 295 300

Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val
305 310 315 320

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

Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn
340 345 350

Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val
355 360 365

Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr
370 375 380

Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg
385 390 395 400

Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val
405 410 415

Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile
420 425 430

Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser

435 440 445

Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr
450 455 460

Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys
465 470 475 480

Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile
485 490 495

Lys Glu Lys Thr Lys Leu Thr Gly Ala Gly Ser Pro Gly Ala Glu Thr
500 505 510

Ala Leu Val Pro Arg Ser Phe Leu Leu Arg Asn Pro Asn Asp Lys Tyr
515 520 525

Glu Pro Phe Trp Glu Asp Glu Glu Ser Gly Ala Gly Ser Pro Gly Ala
530 535 540

Glu Thr Ala Gly Ala Pro Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly
545 550 555 560

Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser
565 570 575

Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser
580 585 590

Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly
595 600 605

Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ala Ser

610 615 620

Ser
625

<210> 127
<211> 697
<212> PRT
<213> Artificial Sequence

<220>
<223> pJH60

<400> 127

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

```
Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
        115                 120                 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
    130                 135                 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145                 150                 155                 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
                165                 170                 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
            180                 185                 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
        195                 200                 205

Thr Ile Leu Asp Gly Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser
    210                 215                 220

Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
225                 230                 235                 240

Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Ala Ser Ser Asn Ile
                245                 250                 255

Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe Thr Arg Val Val Gly Gly
            260                 265                 270

Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp Gln Val Val Leu Asn Gly
        275                 280                 285
```

```
Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile
    290                 295                 300

Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val
305                 310                 315                 320

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

Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn
            340                 345                 350

Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val
        355                 360                 365

Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr
    370                 375                 380

Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg
385                 390                 395                 400

Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val
                405                 410                 415

Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile
            420                 425                 430

Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser
        435                 440                 445

Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr
    450                 455                 460
```

```
Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys
465                 470                 475                 480

Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile
                485                 490                 495

Lys Glu Lys Thr Lys Leu Thr Gly Ala Gly Ser Pro Gly Ala Glu Thr
            500                 505                 510

Ala Leu Val Pro Arg Ser Phe Leu Leu Arg Asn Pro Asn Asp Lys Tyr
        515                 520                 525

Glu Pro Phe Trp Glu Asp Glu Glu Ser Gly Ala Gly Ser Pro Gly Ala
    530                 535                 540

Glu Thr Ala Gly Ala Pro Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala
545                 550                 555                 560

Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser
                565                 570                 575

Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr
            580                 585                 590

Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr
        595                 600                 605

Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Pro
    610                 615                 620

Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser
625                 630                 635                 640
```

Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala
645 650 655

Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser
660 665 670

Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser
675 680 685

Glu Gly Ser Ala Pro Gly Ala Ser Ser
690 695

<210> 128
<211> 841
<212> PRT
<213> Artificial Sequence

<220>
<223> pJH61

<400> 128

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn

65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
180 185 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
195 200 205

Thr Ile Leu Asp Gly Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser
210 215 220

Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
225 230 235 240

Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Ala Ser Ser Asn Ile

245 250 255

Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe Thr Arg Val Val Gly Gly
260 265 270

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

Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile
290 295 300

Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val
305 310 315 320

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

Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn
340 345 350

Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val
355 360 365

Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr
370 375 380

Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg
385 390 395 400

Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val
405 410 415

Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile

420 425 430

Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser
435 440 445

Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr
450 455 460

Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys
465 470 475 480

Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile
485 490 495

Lys Glu Lys Thr Lys Leu Thr Gly Ala Gly Ser Pro Gly Ala Glu Thr
500 505 510

Ala Leu Val Pro Arg Ser Phe Leu Leu Arg Asn Pro Asn Asp Lys Tyr
515 520 525

Glu Pro Phe Trp Glu Asp Glu Glu Ser Gly Ala Gly Ser Pro Gly Ala
530 535 540

Glu Thr Ala Gly Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser
545 550 555 560

Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr
565 570 575

Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr
580 585 590

Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser

595 600 605

Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser
610 615 620

Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala
625 630 635 640

Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu
645 650 655

Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser
660 665 670

Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Ser Pro Ala Gly Ser
675 680 685

Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser
690 695 700

Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr
705 710 715 720

Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Glu Ser Ala
725 730 735

Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu
740 745 750

Thr Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser
755 760 765

Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro

770 775 780

Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser
785 790 795 800

Ala Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr
805 810 815

Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro
820 825 830

Ser Glu Gly Ser Ala Pro Ala Ser Ser
835 840

<210> 129
<211> 661
<212> PRT
<213> Artificial Sequence

<220>
<223> pJH62

<400> 129

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

```
Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65                  70                  75                  80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
                85                  90                  95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
            100                 105                 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
        115                 120                 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
    130                 135                 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145                 150                 155                 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
                165                 170                 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
            180                 185                 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
        195                 200                 205

Thr Ile Leu Asp Gly Ala Pro Ser Pro Ala Gly Ser Pro Thr Ser Thr
    210                 215                 220

Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser
225                 230                 235                 240
```

```
Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala
                245                 250                 255

Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser
            260                 265                 270

Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ala
        275                 280                 285

Ser Ser Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe Thr Arg
    290                 295                 300

Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp Gln Val
305                 310                 315                 320

Val Leu Asn Gly Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn
                325                 330                 335

Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys
            340                 345                 350

Ile Thr Val Val Ala Gly Glu His Asn Ile Glu Glu Thr Glu His Thr
        355                 360                 365

Glu Gln Lys Arg Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn
    370                 375                 380

Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp
385                 390                 395                 400

Glu Pro Leu Val Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp
                405                 410                 415
```

Lys Glu Tyr Thr Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser
420 425 430

Gly Trp Gly Arg Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln
435 440 445

Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr
450 455 460

Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly
465 470 475 480

Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu
485 490 495

Val Glu Gly Thr Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu
500 505 510

Cys Ala Met Lys Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr
515 520 525

Val Asn Trp Ile Lys Glu Lys Thr Lys Leu Thr Gly Ala Gly Ser Pro
530 535 540

Gly Ala Glu Thr Ala Leu Val Pro Arg Ser Phe Leu Leu Arg Asn Pro
545 550 555 560

Asn Asp Lys Tyr Glu Pro Phe Trp Glu Asp Glu Glu Ser Gly Ala Gly
565 570 575

Ser Pro Gly Ala Glu Thr Ala Gly Ala Pro Thr Ser Glu Ser Ala Thr
580 585 590

Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr
595 600 605

Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu
610 615 620

Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr
625 630 635 640

Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala
645 650 655

Pro Gly Ala Ser Ser
660

<210> 130
<211> 733
<212> PRT
<213> Artificial Sequence

<220>
<223> pJH63

<400> 130

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys

```
    50                  55                  60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65                  70                  75                  80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
                85                  90                  95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
            100                 105                 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
        115                 120                 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
    130                 135                 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145                 150                 155                 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
                165                 170                 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
            180                 185                 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
        195                 200                 205

Thr Ile Leu Asp Gly Ala Pro Ser Pro Ala Gly Ser Pro Thr Ser Thr
    210                 215                 220

Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser
```

225 230 235 240

Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala
245 250 255

Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser
260 265 270

Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ala
275 280 285

Ser Ser Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe Thr Arg
290 295 300

Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp Gln Val
305 310 315 320

Val Leu Asn Gly Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn
325 330 335

Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys
340 345 350

Ile Thr Val Val Ala Gly Glu His Asn Ile Glu Glu Thr Glu His Thr
355 360 365

Glu Gln Lys Arg Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn
370 375 380

Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp
385 390 395 400

Glu Pro Leu Val Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp

405 410 415

Lys Glu Tyr Thr Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser
420 425 430

Gly Trp Gly Arg Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln
435 440 445

Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr
450 455 460

Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly
465 470 475 480

Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu
485 490 495

Val Glu Gly Thr Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu
500 505 510

Cys Ala Met Lys Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr
515 520 525

Val Asn Trp Ile Lys Glu Lys Thr Lys Leu Thr Gly Ala Gly Ser Pro
530 535 540

Gly Ala Glu Thr Ala Leu Val Pro Arg Ser Phe Leu Leu Arg Asn Pro
545 550 555 560

Asn Asp Lys Tyr Glu Pro Phe Trp Glu Asp Glu Glu Ser Gly Ala Gly
565 570 575

Ser Pro Gly Ala Glu Thr Ala Gly Ala Pro Thr Ser Thr Glu Pro Ser

580 585 590

Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly
595 600 605

Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser
610 615 620

Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser
625 630 635 640

Gly Ser Glu Thr Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr
645 650 655

Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser
660 665 670

Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser
675 680 685

Glu Gly Ser Ala Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr
690 695 700

Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser
705 710 715 720

Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ala Ser Ser
725 730

<210> 131
<211> 877
<212> PRT
<213> Artificial Sequence

<220>
<223> pJH64

<400> 131

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
180 185 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
195 200 205

Thr Ile Leu Asp Gly Ala Pro Ser Pro Ala Gly Ser Pro Thr Ser Thr
210 215 220

Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser
225 230 235 240

Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala
245 250 255

Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser
260 265 270

Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ala
275 280 285

Ser Ser Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe Thr Arg
290 295 300

Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp Gln Val
305 310 315 320

Val Leu Asn Gly Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn
325 330 335

Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys
340 345 350

Ile Thr Val Val Ala Gly Glu His Asn Ile Glu Glu Thr Glu His Thr
355 360 365

Glu Gln Lys Arg Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn
370 375 380

Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp
385 390 395 400

Glu Pro Leu Val Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp
405 410 415

Lys Glu Tyr Thr Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser
420 425 430

Gly Trp Gly Arg Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln
435 440 445

Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr
450 455 460

Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly
465 470 475 480

Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu
485 490 495

Val Glu Gly Thr Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu
500 505 510

Cys Ala Met Lys Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr
515 520 525

Val Asn Trp Ile Lys Glu Lys Thr Lys Leu Thr Gly Ala Gly Ser Pro
530 535 540

Gly Ala Glu Thr Ala Leu Val Pro Arg Ser Phe Leu Leu Arg Asn Pro
545 550 555 560

Asn Asp Lys Tyr Glu Pro Phe Trp Glu Asp Glu Glu Ser Gly Ala Gly
565 570 575

Ser Pro Gly Ala Glu Thr Ala Gly Ala Pro Gly Thr Ser Glu Ser Ala
580 585 590

Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu
595 600 605

Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser
610 615 620

Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala
625 630 635 640

Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser
645 650 655

Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr
660 665 670

Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr
675 680 685

Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser
690 695 700

Gly Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Ser
705 710 715 720

Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro
725 730 735

Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser
740 745 750

Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr
755 760 765

Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr
770 775 780

Ser Gly Ser Glu Thr Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu
785 790 795 800

Thr Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr
805 810 815

Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro
820 825 830

Ser Glu Gly Ser Ala Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu
835 840 845

Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr
850 855 860

Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Ala Ser Ser
865 870 875

<210> 132
<211> 733
<212> PRT
<213> Artificial Sequence

<220>
<223> pJH65

<400> 132

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys

115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
180 185 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
195 200 205

Thr Ile Leu Asp Gly Ala Pro Ser Pro Ala Gly Ser Pro Thr Ser Thr
210 215 220

Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser
225 230 235 240

Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala
245 250 255

Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser
260 265 270

Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr
275 280 285

Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro

290 295 300

Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser
305 310 315 320

Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser
325 330 335

Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro
340 345 350

Ser Glu Gly Ser Ala Pro Gly Ala Ser Ser Asn Ile Thr Gln Ser Thr
355 360 365

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

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

Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile Val Thr Ala Ala
405 410 415

His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val Ala Gly Glu His
420 425 430

Asn Ile Glu Glu Thr Glu His Thr Glu Gln Lys Arg Asn Val Ile Arg
435 440 445

Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His
450 455 460

Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr

```
465                 470                 475                 480

Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr Asn Ile Phe Leu
                485                 490                 495

Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg Val Phe His Lys
            500                 505                 510

Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val Pro Leu Val Asp
        515                 520                 525

Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met
    530                 535                 540

Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp
545                 550                 555                 560

Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr Ser Phe Leu Thr
                565                 570                 575

Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly
            580                 585                 590

Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr
        595                 600                 605

Lys Leu Thr Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Leu Val Pro
    610                 615                 620

Arg Ser Phe Leu Leu Arg Asn Pro Asn Asp Lys Tyr Glu Pro Phe Trp
625                 630                 635                 640

Glu Asp Glu Glu Ser Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Gly
```

645 650 655

Ala Pro Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu
660 665 670

Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr
675 680 685

Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr
690 695 700

Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser
705 710 715 720

Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ala Ser Ser
725 730

<210> 133
<211> 805
<212> PRT
<213> Artificial Sequence

<220>
<223> pJH66

<400> 133

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

```
Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
    50                  55                  60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65                  70                  75                  80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
                85                  90                  95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
            100                 105                 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
        115                 120                 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
    130                 135                 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145                 150                 155                 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
                165                 170                 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
            180                 185                 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
        195                 200                 205

Thr Ile Leu Asp Gly Ala Pro Ser Pro Ala Gly Ser Pro Thr Ser Thr
    210                 215                 220
```

```
Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser
225                 230                 235                 240

Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala
                245                 250                 255

Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser
            260                 265                 270

Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr
        275                 280                 285

Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro
    290                 295                 300

Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser
305                 310                 315                 320

Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser
                325                 330                 335

Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro
            340                 345                 350

Ser Glu Gly Ser Ala Pro Gly Ala Ser Ser Asn Ile Thr Gln Ser Thr
        355                 360                 365

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

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

Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile Val Thr Ala Ala
405 410 415

His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val Ala Gly Glu His
420 425 430

Asn Ile Glu Glu Thr Glu His Thr Glu Gln Lys Arg Asn Val Ile Arg
435 440 445

Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His
450 455 460

Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr
465 470 475 480

Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr Asn Ile Phe Leu
485 490 495

Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg Val Phe His Lys
500 505 510

Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val Pro Leu Val Asp
515 520 525

Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met
530 535 540

Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp
545 550 555 560

Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr Ser Phe Leu Thr
565 570 575

Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly
580 585 590

Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr
595 600 605

Lys Leu Thr Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Leu Val Pro
610 615 620

Arg Ser Phe Leu Leu Arg Asn Pro Asn Asp Lys Tyr Glu Pro Phe Trp
625 630 635 640

Glu Asp Glu Glu Ser Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Gly
645 650 655

Ala Pro Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser
660 665 670

Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr
675 680 685

Pro Glu Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly
690 695 700

Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Glu
705 710 715 720

Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Pro Ala Gly Ser Pro
725 730 735

Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala
740 745 750

```
Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Glu
        755                 760                 765

Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr
    770                 775                 780

Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala
785                 790                 795                 800

Pro Gly Ala Ser Ser
                805
```

<210> 134
<211> 949
<212> PRT
<213> Artificial Sequence

<220>
<223> pJH67

<400> 134

```
Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1               5                   10                  15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
            20                  25                  30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
        35                  40                  45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
    50                  55                  60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
```

65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
180 185 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
195 200 205

Thr Ile Leu Asp Gly Ala Pro Ser Pro Ala Gly Ser Pro Thr Ser Thr
210 215 220

Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser
225 230 235 240

Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala

245 250 255

Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser
260 265 270

Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr
275 280 285

Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro
290 295 300

Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser
305 310 315 320

Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser
325 330 335

Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro
340 345 350

Ser Glu Gly Ser Ala Pro Gly Ala Ser Ser Asn Ile Thr Gln Ser Thr
355 360 365

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

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

Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile Val Thr Ala Ala
405 410 415

His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val Ala Gly Glu His

420 425 430

Asn Ile Glu Glu Thr Glu His Thr Glu Gln Lys Arg Asn Val Ile Arg
435 440 445

Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His
450 455 460

Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr
465 470 475 480

Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr Asn Ile Phe Leu
485 490 495

Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg Val Phe His Lys
500 505 510

Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val Pro Leu Val Asp
515 520 525

Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met
530 535 540

Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp
545 550 555 560

Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr Ser Phe Leu Thr
565 570 575

Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly
580 585 590

Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr

595 600 605

Lys Leu Thr Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Leu Val Pro
610 615 620

Arg Ser Phe Leu Leu Arg Asn Pro Asn Asp Lys Tyr Glu Pro Phe Trp
625 630 635 640

Glu Asp Glu Glu Ser Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Gly
645 650 655

Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser
660 665 670

Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala
675 680 685

Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu
690 695 700

Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr
705 710 715 720

Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser
725 730 735

Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser
740 745 750

Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr
755 760 765

Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Pro Ala Gly Ser

770 775 780

Pro Thr Ser Thr Glu Glu Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr
785 790 795 800

Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr
805 810 815

Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Glu Ser Ala
820 825 830

Thr Pro Glu Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser
835 840 845

Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser
850 855 860

Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Pro Ala Gly Ser
865 870 875 880

Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser
885 890 895

Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser
900 905 910

Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala
915 920 925

Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser
930 935 940

Ala Pro Ala Ser Ser

945

<210> 135
<211> 545
<212> PRT
<213> Artificial Sequence

<220>
<223> pJH68

<400> 135

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

```
Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
    130                 135                 140

Cys Lys Asn Ser Ala Asp Asn Gly Ala Pro Gly Ser Pro Ala Gly Ser
145                 150                 155                 160

Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser
                165                 170                 175

Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Ala Ser
            180                 185                 190

Ser Lys Val Val Cys Ser Cys Thr Glu Gly Tyr Arg Leu Ala Glu Asn
        195                 200                 205

Gln Lys Ser Cys Glu Pro Ala Val Pro Phe Pro Cys Gly Arg Val Ser
    210                 215                 220

Val Ser Gln Thr Ser Lys Leu Thr Arg Ala Glu Thr Val Phe Pro Asp
225                 230                 235                 240

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

Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser
            260                 265                 270

Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser
        275                 280                 285

Gly Ser Glu Thr Pro Ala Ser Ser Asn Ile Thr Gln Ser Thr Gln Ser
    290                 295                 300
```

```
Phe Asn Asp Phe Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly
305                 310                 315                 320

Gln Phe Pro Trp Gln Val Val Leu Asn Gly Lys Val Asp Ala Phe Cys
                325                 330                 335

Gly Gly Ser Ile Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys
            340                 345                 350

Val Glu Thr Gly Val Lys Ile Thr Val Val Ala Gly Glu His Asn Ile
        355                 360                 365

Glu Glu Thr Glu His Thr Glu Gln Lys Arg Asn Val Ile Arg Ile Ile
    370                 375                 380

Pro His His Asn Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His Asp Ile
385                 390                 395                 400

Ala Leu Leu Glu Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr Val Thr
                405                 410                 415

Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr Asn Ile Phe Leu Lys Phe
            420                 425                 430

Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg Val Phe His Lys Gly Arg
        435                 440                 445

Ser Ala Leu Val Leu Gln Tyr Leu Arg Val Pro Leu Val Asp Arg Ala
    450                 455                 460

Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys
465                 470                 475                 480
```

Ala Gly Phe His Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly
485 490 495

Gly Pro His Val Thr Glu Val Glu Gly Thr Ser Phe Leu Thr Gly Ile
500 505 510

Ile Ser Trp Gly Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly Ile Tyr
515 520 525

Thr Lys Val Ser Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr Lys Leu
530 535 540

Thr
545

<210> 136
<211> 581
<212> PRT
<213> Artificial Sequence

<220>
<223> pJH69

<400> 136

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys

50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Gly Ala Pro Gly Ser Pro Ala Gly Ser
145 150 155 160

Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser
165 170 175

Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Ala Ser
180 185 190

Ser Lys Val Val Cys Ser Cys Thr Glu Gly Tyr Arg Leu Ala Glu Asn
195 200 205

Gln Lys Ser Cys Glu Pro Ala Val Pro Phe Pro Cys Gly Arg Val Ser
210 215 220

Val Ser Gln Thr Ser Lys Leu Thr Arg Ala Glu Thr Val Phe Pro Asp

225 230 235 240

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

Pro Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu
260 265 270

Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly
275 280 285

Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
290 295 300

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr
305 310 315 320

Glu Pro Ser Glu Gly Ser Ala Pro Gly Ala Ser Ser Asn Ile Thr Gln
325 330 335

Ser Thr Gln Ser Phe Asn Asp Phe Thr Arg Val Val Gly Gly Glu Asp
340 345 350

Ala Lys Pro Gly Gln Phe Pro Trp Gln Val Val Leu Asn Gly Lys Val
355 360 365

Asp Ala Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile Val Thr
370 375 380

Ala Ala His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val Ala Gly
385 390 395 400

Glu His Asn Ile Glu Glu Thr Glu His Thr Glu Gln Lys Arg Asn Val

405 410 415

Ile Arg Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn Lys Tyr
420 425 430

Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val Leu Asn
435 440 445

Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr Asn Ile
450 455 460

Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg Val Phe
465 470 475 480

His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val Pro Leu
485 490 495

Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile Tyr Asn
500 505 510

Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser Cys Gln
515 520 525

Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr Ser Phe
530 535 540

Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys Gly Lys
545 550 555 560

Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile Lys Glu
565 570 575

Lys Thr Lys Leu Thr

580

<210> 137
<211> 653
<212> PRT
<213> Artificial Sequence

<220>
<223> pJH70

<400> 137

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

```
Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
    130                 135                 140

Cys Lys Asn Ser Ala Asp Asn Gly Ala Pro Gly Ser Pro Ala Gly Ser
145                 150                 155                 160

Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser
                165                 170                 175

Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Ala Ser
            180                 185                 190

Ser Lys Val Val Cys Ser Cys Thr Glu Gly Tyr Arg Leu Ala Glu Asn
        195                 200                 205

Gln Lys Ser Cys Glu Pro Ala Val Pro Phe Pro Cys Gly Arg Val Ser
    210                 215                 220

Val Ser Gln Thr Ser Lys Leu Thr Arg Ala Glu Thr Val Phe Pro Asp
225                 230                 235                 240

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

Pro Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu
            260                 265                 270

Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly
        275                 280                 285

Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
    290                 295                 300
```

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr
305 310 315 320

Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu
325 330 335

Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
340 345 350

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr
355 360 365

Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr
370 375 380

Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
385 390 395 400

Gly Ala Ser Ser Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe
405 410 415

Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp
420 425 430

Gln Val Val Leu Asn Gly Lys Val Asp Ala Phe Cys Gly Gly Ser Ile
435 440 445

Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly
450 455 460

Val Lys Ile Thr Val Val Ala Gly Glu His Asn Ile Glu Glu Thr Glu
465 470 475 480

```
His Thr Glu Gln Lys Arg Asn Val Ile Arg Ile Ile Pro His His Asn
               485                 490                 495

Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu Glu
            500                 505                 510

Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile
        515                 520                 525

Ala Asp Lys Glu Tyr Thr Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr
    530                 535                 540

Val Ser Gly Trp Gly Arg Val Phe His Lys Gly Arg Ser Ala Leu Val
545                 550                 555                 560

Leu Gln Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu Leu
               565                 570                 575

Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe His
            580                 585                 590

Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro His Val
        595                 600                 605

Thr Glu Val Glu Gly Thr Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly
    610                 615                 620

Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser
625                 630                 635                 640

Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr Lys Leu Thr
               645                 650
```

<210> 138
<211> 625
<212> PRT
<213> Artificial Sequence

<220>
<223> pJH71

<400> 138

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe

130 135 140

Cys Lys Asn Ser Ala Asp Asn Gly Ala Pro Gly Ser Pro Ala Gly Ser
145 150 155 160

Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser
165 170 175

Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Ala Ser
180 185 190

Ser Lys Val Val Cys Ser Cys Thr Glu Gly Tyr Arg Leu Ala Glu Asn
195 200 205

Gln Lys Ser Cys Glu Pro Ala Val Pro Phe Pro Cys Gly Arg Val Ser
210 215 220

Val Ser Gln Thr Ser Lys Leu Thr Arg Ala Glu Thr Val Phe Pro Asp
225 230 235 240

Val Asp Tyr Val Asn Ser Thr Glu Ala Glu Thr Ile Leu Asp Asn Ile
245 250 255

Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe Thr Arg Val Val Gly Gly
260 265 270

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

Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile
290 295 300

Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val

305 310 315 320

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

Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn
340 345 350

Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val
355 360 365

Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr
370 375 380

Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg
385 390 395 400

Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val
405 410 415

Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile
420 425 430

Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser
435 440 445

Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr
450 455 460

Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys
465 470 475 480

Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile

485 490 495

Lys Glu Lys Thr Lys Leu Thr Gly Ala Gly Ser Pro Gly Ala Glu Thr
500 505 510

Ala Leu Val Pro Arg Ser Phe Leu Leu Arg Asn Pro Asn Asp Lys Tyr
515 520 525

Glu Pro Phe Trp Glu Asp Glu Glu Ser Gly Ala Gly Ser Pro Gly Ala
530 535 540

Glu Thr Ala Gly Ala Pro Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly
545 550 555 560

Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser
565 570 575

Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser
580 585 590

Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly
595 600 605

Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ala Ser
610 615 620

Ser
625

<210> 139
<211> 697
<212> PRT
<213> Artificial Sequence

<220>
<223> pJH72

<400> 139

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Gly Ala Pro Gly Ser Pro Ala Gly Ser
145 150 155 160

Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser
165 170 175

Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Ala Ser
180 185 190

Ser Lys Val Val Cys Ser Cys Thr Glu Gly Tyr Arg Leu Ala Glu Asn
195 200 205

Gln Lys Ser Cys Glu Pro Ala Val Pro Phe Pro Cys Gly Arg Val Ser
210 215 220

Val Ser Gln Thr Ser Lys Leu Thr Arg Ala Glu Thr Val Phe Pro Asp
225 230 235 240

Val Asp Tyr Val Asn Ser Thr Glu Ala Glu Thr Ile Leu Asp Asn Ile
245 250 255

Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe Thr Arg Val Val Gly Gly
260 265 270

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

Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile
290 295 300

Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val
305 310 315 320

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

```
Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn
            340                 345                 350

Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val
        355                 360                 365

Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr
    370                 375                 380

Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg
385                 390                 395                 400

Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val
                405                 410                 415

Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile
            420                 425                 430

Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser
        435                 440                 445

Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr
    450                 455                 460

Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys
465                 470                 475                 480

Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile
                485                 490                 495

Lys Glu Lys Thr Lys Leu Thr Gly Ala Gly Ser Pro Gly Ala Glu Thr
            500                 505                 510
```

Ala Leu Val Pro Arg Ser Phe Leu Leu Arg Asn Pro Asn Asp Lys Tyr
515 520 525

Glu Pro Phe Trp Glu Asp Glu Glu Ser Gly Ala Gly Ser Pro Gly Ala
530 535 540

Glu Thr Ala Gly Ala Pro Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala
545 550 555 560

Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser
565 570 575

Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr
580 585 590

Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr
595 600 605

Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Pro
610 615 620

Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser
625 630 635 640

Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala
645 650 655

Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser
660 665 670

Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser
675 680 685

Glu Gly Ser Ala Pro Gly Ala Ser Ser
690 695

<210> 140
<211> 841
<212> PRT
<213> Artificial Sequence

<220>
<223> pJH73

<400> 140

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys

115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Gly Ala Pro Gly Ser Pro Ala Gly Ser
145 150 155 160

Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser
165 170 175

Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Ala Ser
180 185 190

Ser Lys Val Val Cys Ser Cys Thr Glu Gly Tyr Arg Leu Ala Glu Asn
195 200 205

Gln Lys Ser Cys Glu Pro Ala Val Pro Phe Pro Cys Gly Arg Val Ser
210 215 220

Val Ser Gln Thr Ser Lys Leu Thr Arg Ala Glu Thr Val Phe Pro Asp
225 230 235 240

Val Asp Tyr Val Asn Ser Thr Glu Ala Glu Thr Ile Leu Asp Asn Ile
245 250 255

Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe Thr Arg Val Val Gly Gly
260 265 270

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

Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile

290 295 300

Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val
305 310 315 320

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

Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn
340 345 350

Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val
355 360 365

Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr
370 375 380

Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg
385 390 395 400

Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val
405 410 415

Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile
420 425 430

Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser
435 440 445

Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr
450 455 460

Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys

465 470 475 480

Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile
485 490 495

Lys Glu Lys Thr Lys Leu Thr Gly Ala Gly Ser Pro Gly Ala Glu Thr
500 505 510

Ala Leu Val Pro Arg Ser Phe Leu Leu Arg Asn Pro Asn Asp Lys Tyr
515 520 525

Glu Pro Phe Trp Glu Asp Glu Glu Ser Gly Ala Gly Ser Pro Gly Ala
530 535 540

Glu Thr Ala Gly Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser
545 550 555 560

Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr
565 570 575

Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr
580 585 590

Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser
595 600 605

Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser
610 615 620

Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala
625 630 635 640

Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu

645 650 655

Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser
660 665 670

Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Ser Pro Ala Gly Ser
675 680 685

Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser
690 695 700

Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr
705 710 715 720

Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Glu Ser Ala
725 730 735

Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu
740 745 750

Thr Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser
755 760 765

Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro
770 775 780

Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser
785 790 795 800

Ala Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr
805 810 815

Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro

820 825 830

Ser Glu Gly Ser Ala Pro Ala Ser Ser
835 840

<210> 141
<211> 545
<212> PRT
<213> Artificial Sequence

<220>
<223> pJH74

<400> 141

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

```
Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
        115                 120                 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
    130                 135                 140

Cys Lys Asn Ser Ala Asp Asn Gly Ala Pro Gly Ser Pro Ala Gly Ser
145                 150                 155                 160

Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser
                165                 170                 175

Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Ala Ser
            180                 185                 190

Ser Lys Val Val Cys Ser Cys Thr Glu Gly Tyr Arg Leu Ala Glu Asn
        195                 200                 205

Gln Lys Ser Cys Glu Pro Ala Val Pro Phe Pro Cys Gly Arg Val Ser
    210                 215                 220

Val Ser Gln Thr Ser Lys Leu Thr Arg Ala Glu Thr Val Phe Pro Asp
225                 230                 235                 240

Val Asp Tyr Val Asn Ser Thr Glu Ala Glu Thr Ile Leu Asp Asn Ile
                245                 250                 255

Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe Thr Arg Val Val Gly Gly
            260                 265                 270

Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp Gln Val Val Leu Asn Gly
        275                 280                 285
```

```
Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile
    290                 295                 300

Val Thr Ala Ala His Cys Val Glu Gly Ala Pro Gly Ser Pro Ala Gly
305                 310                 315                 320

Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu
                325                 330                 335

Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Ala
            340                 345                 350

Ser Ser Thr Gly Val Lys Ile Thr Val Val Ala Gly Glu His Asn Ile
        355                 360                 365

Glu Glu Thr Glu His Thr Glu Gln Lys Arg Asn Val Ile Arg Ile Ile
    370                 375                 380

Pro His His Asn Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His Asp Ile
385                 390                 395                 400

Ala Leu Leu Glu Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr Val Thr
                405                 410                 415

Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr Asn Ile Phe Leu Lys Phe
            420                 425                 430

Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg Val Phe His Lys Gly Arg
        435                 440                 445

Ser Ala Leu Val Leu Gln Tyr Leu Arg Val Pro Leu Val Asp Arg Ala
    450                 455                 460
```

Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys
465 470 475 480

Ala Gly Phe His Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly
485 490 495

Gly Pro His Val Thr Glu Val Glu Gly Thr Ser Phe Leu Thr Gly Ile
500 505 510

Ile Ser Trp Gly Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly Ile Tyr
515 520 525

Thr Lys Val Ser Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr Lys Leu
530 535 540

Thr
545

<210> 142
<211> 545
<212> PRT
<213> Artificial Sequence

<220>
<223> pJH75

<400> 142

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn

```
         35                  40                  45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
    50                  55                  60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65                  70                  75                  80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
                85                  90                  95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
            100                 105                 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
        115                 120                 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
    130                 135                 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145                 150                 155                 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
                165                 170                 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
            180                 185                 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
        195                 200                 205

Thr Ile Leu Asp Gly Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser
```

210 215 220

Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
225 230 235 240

Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Ala Ser Ser Asn Ile
245 250 255

Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe Thr Arg Val Val Gly Gly
260 265 270

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

Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile
290 295 300

Val Thr Ala Ala His Cys Val Glu Gly Ala Pro Gly Ser Pro Ala Gly
305 310 315 320

Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu
325 330 335

Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Ala
340 345 350

Ser Ser Thr Gly Val Lys Ile Thr Val Val Ala Gly Glu His Asn Ile
355 360 365

Glu Glu Thr Glu His Thr Glu Gln Lys Arg Asn Val Ile Arg Ile Ile
370 375 380

Pro His His Asn Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His Asp Ile

385 390 395 400

Ala Leu Leu Glu Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr Val Thr
405 410 415

Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr Asn Ile Phe Leu Lys Phe
420 425 430

Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg Val Phe His Lys Gly Arg
435 440 445

Ser Ala Leu Val Leu Gln Tyr Leu Arg Val Pro Leu Val Asp Arg Ala
450 455 460

Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys
465 470 475 480

Ala Gly Phe His Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly
485 490 495

Gly Pro His Val Thr Glu Val Glu Gly Thr Ser Phe Leu Thr Gly Ile
500 505 510

Ile Ser Trp Gly Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly Ile Tyr
515 520 525

Thr Lys Val Ser Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr Lys Leu
530 535 540

Thr
545

<210> 143

<211> 581
<212> PRT
<213> Artificial Sequence

<220>
<223> pJH76

<400> 143

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

```
Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145                 150                 155                 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
                165                 170                 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
            180                 185                 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
        195                 200                 205

Thr Ile Leu Asp Gly Ala Pro Ser Pro Ala Gly Ser Pro Thr Ser Thr
    210                 215                 220

Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser
225                 230                 235                 240

Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala
                245                 250                 255

Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser
            260                 265                 270

Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ala
        275                 280                 285

Ser Ser Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe Thr Arg
    290                 295                 300

Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp Gln Val
305                 310                 315                 320
```

Val Leu Asn Gly Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn
325 330 335

Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Gly Ala Pro Gly
340 345 350

Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser
355 360 365

Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser
370 375 380

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

Glu His Asn Ile Glu Glu Thr Glu His Thr Glu Gln Lys Arg Asn Val
405 410 415

Ile Arg Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn Lys Tyr
420 425 430

Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val Leu Asn
435 440 445

Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr Asn Ile
450 455 460

Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg Val Phe
465 470 475 480

His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val Pro Leu
485 490 495

```
Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile Tyr Asn
            500                 505                 510

Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser Cys Gln
        515                 520                 525

Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr Ser Phe
    530                 535                 540

Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys Gly Lys
545                 550                 555                 560

Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile Lys Glu
                565                 570                 575

Lys Thr Lys Leu Thr
            580
```

<210> 144
<211> 653
<212> PRT
<213> Artificial Sequence

<220>
<223> pJH77

<400> 144

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Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1               5                   10                  15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
            20                  25                  30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
```

35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
180 185 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
195 200 205

Thr Ile Leu Asp Gly Ala Pro Ser Pro Ala Gly Ser Pro Thr Ser Thr

210 215 220

Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser
225 230 235 240

Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala
245 250 255

Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser
260 265 270

Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr
275 280 285

Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro
290 295 300

Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser
305 310 315 320

Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser
325 330 335

Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro
340 345 350

Ser Glu Gly Ser Ala Pro Gly Ala Ser Ser Asn Ile Thr Gln Ser Thr
355 360 365

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

Pro Gly Gln Phe Pro Trp Gln Val Val Leu Asn Gly Lys Val Asp Ala

385 390 395 400

Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile Val Thr Ala Ala
405 410 415

His Cys Val Glu Gly Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser
420 425 430

Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
435 440 445

Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Ala Ser Ser Thr Gly
450 455 460

Val Lys Ile Thr Val Val Ala Gly Glu His Asn Ile Glu Glu Thr Glu
465 470 475 480

His Thr Glu Gln Lys Arg Asn Val Ile Arg Ile Ile Pro His His Asn
485 490 495

Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu Glu
500 505 510

Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile
515 520 525

Ala Asp Lys Glu Tyr Thr Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr
530 535 540

Val Ser Gly Trp Gly Arg Val Phe His Lys Gly Arg Ser Ala Leu Val
545 550 555 560

Leu Gln Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu Leu

565 570 575

Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe His
580 585 590

Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro His Val
595 600 605

Thr Glu Val Glu Gly Thr Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly
610 615 620

Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser
625 630 635 640

Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr Lys Leu Thr
645 650

<210> 145
<211> 625
<212> PRT
<213> Artificial Sequence

<220>
<223> pJH78

<400> 145

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
180 185 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
195 200 205

Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe
210 215 220

```
Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp
225                 230                 235                 240

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

Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Gly Ala
            260                 265                 270

Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser
        275                 280                 285

Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser
    290                 295                 300

Gly Ser Glu Thr Pro Ala Ser Ser Thr Gly Val Lys Ile Thr Val Val
305                 310                 315                 320

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

Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn
            340                 345                 350

Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val
        355                 360                 365

Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr
    370                 375                 380

Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg
385                 390                 395                 400
```

Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val
405 410 415

Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile
420 425 430

Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser
435 440 445

Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr
450 455 460

Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys
465 470 475 480

Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile
485 490 495

Lys Glu Lys Thr Lys Leu Thr Gly Ala Gly Ser Pro Gly Ala Glu Thr
500 505 510

Ala Leu Val Pro Arg Ser Phe Leu Leu Arg Asn Pro Asn Asp Lys Tyr
515 520 525

Glu Pro Phe Trp Glu Asp Glu Glu Ser Gly Ala Gly Ser Pro Gly Ala
530 535 540

Glu Thr Ala Gly Ala Pro Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly
545 550 555 560

Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser
565 570 575

Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser
580 585 590

Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly
595 600 605

Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ala Ser
610 615 620

Ser
625

<210> 146
<211> 697
<212> PRT
<213> Artificial Sequence

<220>
<223> pJH79

<400> 146

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn

65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
180 185 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
195 200 205

Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe
210 215 220

Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp
225 230 235 240

Gln Val Val Leu Asn Gly Lys Val Asp Ala Phe Cys Gly Gly Ser Ile

245 250 255

Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Gly Ala
260 265 270

Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser
275 280 285

Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser
290 295 300

Gly Ser Glu Thr Pro Ala Ser Ser Thr Gly Val Lys Ile Thr Val Val
305 310 315 320

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

Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn
340 345 350

Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val
355 360 365

Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr
370 375 380

Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg
385 390 395 400

Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val
405 410 415

Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile

420 425 430

Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser
435 440 445

Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr
450 455 460

Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys
465 470 475 480

Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile
485 490 495

Lys Glu Lys Thr Lys Leu Thr Gly Ala Gly Ser Pro Gly Ala Glu Thr
500 505 510

Ala Leu Val Pro Arg Ser Phe Leu Leu Arg Asn Pro Asn Asp Lys Tyr
515 520 525

Glu Pro Phe Trp Glu Asp Glu Glu Ser Gly Ala Gly Ser Pro Gly Ala
530 535 540

Glu Thr Ala Gly Ala Pro Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala
545 550 555 560

Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser
565 570 575

Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr
580 585 590

Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr

595 600 605

Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Pro
610 615 620

Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser
625 630 635 640

Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala
645 650 655

Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser
660 665 670

Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser
675 680 685

Glu Gly Ser Ala Pro Gly Ala Ser Ser
690 695

<210> 147
<211> 841
<212> PRT
<213> Artificial Sequence

<220>
<223> pJH80

<400> 147

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

```
Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
        35                  40                  45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
    50                  55                  60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65                  70                  75                  80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
                85                  90                  95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
            100                 105                 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
        115                 120                 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
    130                 135                 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145                 150                 155                 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
                165                 170                 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
            180                 185                 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
        195                 200                 205
```

```
Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe
    210                 215                 220

Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp
225                 230                 235                 240

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

Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Gly Ala
            260                 265                 270

Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser
        275                 280                 285

Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser
    290                 295                 300

Gly Ser Glu Thr Pro Ala Ser Ser Thr Gly Val Lys Ile Thr Val Val
305                 310                 315                 320

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

Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn
            340                 345                 350

Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val
        355                 360                 365

Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr
    370                 375                 380
```

```
Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg
385                 390                 395                 400

Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val
                405                 410                 415

Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile
            420                 425                 430

Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser
        435                 440                 445

Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr
    450                 455                 460

Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys
465                 470                 475                 480

Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile
                485                 490                 495

Lys Glu Lys Thr Lys Leu Thr Gly Ala Gly Ser Pro Gly Ala Glu Thr
            500                 505                 510

Ala Leu Val Pro Arg Ser Phe Leu Leu Arg Asn Pro Asn Asp Lys Tyr
        515                 520                 525

Glu Pro Phe Trp Glu Asp Glu Glu Ser Gly Ala Gly Ser Pro Gly Ala
    530                 535                 540

Glu Thr Ala Gly Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser
545                 550                 555                 560
```

Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr
565 570 575

Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr
580 585 590

Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser
595 600 605

Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser
610 615 620

Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala
625 630 635 640

Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu
645 650 655

Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser
660 665 670

Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Ser Pro Ala Gly Ser
675 680 685

Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser
690 695 700

Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr
705 710 715 720

Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Glu Ser Ala
725 730 735

Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu
740 745 750

Thr Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser
755 760 765

Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro
770 775 780

Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser
785 790 795 800

Ala Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr
805 810 815

Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro
820 825 830

Ser Glu Gly Ser Ala Pro Ala Ser Ser
835 840

<210> 148
<211> 977
<212> PRT
<213> Artificial Sequence

<220>
<223> pJH81

<400> 148

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu

20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Gly Ala Pro Gly Ser Pro Ala Gly Ser
145 150 155 160

Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser
165 170 175

Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Ala Ser
180 185 190

Ser Lys Val Val Cys Ser Cys Thr Glu Gly Tyr Arg Leu Ala Glu Asn

195 200 205

Gln Lys Ser Cys Glu Pro Ala Val Pro Phe Pro Cys Gly Arg Val Ser
210 215 220

Val Ser Gln Thr Ser Lys Leu Thr Arg Ala Glu Thr Val Phe Pro Asp
225 230 235 240

Val Asp Tyr Val Asn Ser Thr Glu Ala Glu Thr Ile Leu Asp Asn Ile
245 250 255

Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe Thr Arg Val Val Gly Gly
260 265 270

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

Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile
290 295 300

Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val
305 310 315 320

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

Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn
340 345 350

Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val
355 360 365

Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr

370 375 380

Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg
385 390 395 400

Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val
405 410 415

Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile
420 425 430

Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser
435 440 445

Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr
450 455 460

Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys
465 470 475 480

Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile
485 490 495

Lys Glu Lys Thr Lys Leu Thr Asp Lys Thr His Thr Cys Pro Pro Cys
500 505 510

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
515 520 525

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
530 535 540

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp

545 550 555 560

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
565 570 575

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
580 585 590

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
595 600 605

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
610 615 620

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu
625 630 635 640

Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
645 650 655

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
660 665 670

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
675 680 685

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
690 695 700

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
705 710 715 720

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly

725 730 735

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Lys
740 745 750

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
755 760 765

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
770 775 780

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
785 790 795 800

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
805 810 815

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
820 825 830

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
835 840 845

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
850 855 860

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
865 870 875 880

Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr
885 890 895

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu

900 905 910

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
915 920 925

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
930 935 940

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
945 950 955 960

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
965 970 975

Lys

<210> 149
<211> 977
<212> PRT
<213> Artificial Sequence

<220>
<223> pJH81

<400> 149

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
180 185 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
195 200 205

Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe
210 215 220

```
Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp
225                 230                 235                 240

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

Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Gly Ala
            260                 265                 270

Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser
        275                 280                 285

Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser
    290                 295                 300

Gly Ser Glu Thr Pro Ala Ser Ser Thr Gly Val Lys Ile Thr Val Val
305                 310                 315                 320

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

Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn
            340                 345                 350

Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val
        355                 360                 365

Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr
    370                 375                 380

Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg
385                 390                 395                 400
```

Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val
405 410 415

Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile
420 425 430

Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser
435 440 445

Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr
450 455 460

Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys
465 470 475 480

Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile
485 490 495

Lys Glu Lys Thr Lys Leu Thr Asp Lys Thr His Thr Cys Pro Pro Cys
500 505 510

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
515 520 525

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
530 535 540

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
545 550 555 560

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
565 570 575

```
Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
            580                 585                 590

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
        595                 600                 605

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
    610                 615                 620

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu
625                 630                 635                 640

Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
                645                 650                 655

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
            660                 665                 670

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
        675                 680                 685

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
    690                 695                 700

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
705                 710                 715                 720

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly
                725                 730                 735

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Lys
            740                 745                 750
```

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
755 760 765

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
770 775 780

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
785 790 795 800

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
805 810 815

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
820 825 830

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
835 840 845

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
850 855 860

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
865 870 875 880

Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr
885 890 895

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
900 905 910

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
915 920 925

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
930 935 940

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
945 950 955 960

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
965 970 975

Lys

<210> 150
<211> 977
<212> PRT
<213> Artificial Sequence

<220>
<223> pJH82

<400> 150

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn

65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
180 185 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
195 200 205

Thr Ile Leu Asp Gly Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser
210 215 220

Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
225 230 235 240

Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Ala Ser Ser Asn Ile

245 250 255

Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe Thr Arg Val Val Gly Gly
260 265 270

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

Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile
290 295 300

Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val
305 310 315 320

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

Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn
340 345 350

Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val
355 360 365

Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr
370 375 380

Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg
385 390 395 400

Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val
405 410 415

Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile

420 425 430

Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser
435 440 445

Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr
450 455 460

Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys
465 470 475 480

Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile
485 490 495

Lys Glu Lys Thr Lys Leu Thr Asp Lys Thr His Thr Cys Pro Pro Cys
500 505 510

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
515 520 525

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
530 535 540

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
545 550 555 560

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
565 570 575

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
580 585 590

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn

595 600 605

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
610 615 620

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu
625 630 635 640

Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
645 650 655

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
660 665 670

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
675 680 685

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
690 695 700

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
705 710 715 720

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly
725 730 735

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Lys
740 745 750

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
755 760 765

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser

770 775 780

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
785 790 795 800

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
805 810 815

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
820 825 830

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
835 840 845

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
850 855 860

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
865 870 875 880

Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr
885 890 895

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
900 905 910

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
915 920 925

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
930 935 940

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu

945 950 955 960

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
965 970 975

Lys

<210> 151
<211> 1013
<212> PRT
<213> Artificial Sequence

<220>
<223> pJH84

<400> 151

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

```
Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
            100                 105                 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
        115                 120                 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
    130                 135                 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145                 150                 155                 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
                165                 170                 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
            180                 185                 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
        195                 200                 205

Thr Ile Leu Asp Gly Ala Pro Ser Pro Ala Gly Ser Pro Thr Ser Thr
    210                 215                 220

Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser
225                 230                 235                 240

Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala
                245                 250                 255

Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser
            260                 265                 270
```

Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ala
275 280 285

Ser Ser Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe Thr Arg
290 295 300

Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp Gln Val
305 310 315 320

Val Leu Asn Gly Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn
325 330 335

Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys
340 345 350

Ile Thr Val Val Ala Gly Glu His Asn Ile Glu Glu Thr Glu His Thr
355 360 365

Glu Gln Lys Arg Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn
370 375 380

Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp
385 390 395 400

Glu Pro Leu Val Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp
405 410 415

Lys Glu Tyr Thr Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr Val Ser
420 425 430

Gly Trp Gly Arg Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln
435 440 445

```
Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr
    450                 455                 460

Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly
465                 470                 475                 480

Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu
                485                 490                 495

Val Glu Gly Thr Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu
            500                 505                 510

Cys Ala Met Lys Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr
        515                 520                 525

Val Asn Trp Ile Lys Glu Lys Thr Lys Leu Thr Asp Lys Thr His Thr
    530                 535                 540

Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe
545                 550                 555                 560

Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro
                565                 570                 575

Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val
            580                 585                 590

Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
        595                 600                 605

Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val
    610                 615                 620
```

```
Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
625                 630                 635                 640

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

Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro
            660                 665                 670

Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val
        675                 680                 685

Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
    690                 695                 700

Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp
705                 710                 715                 720

Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp
                725                 730                 735

Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His
            740                 745                 750

Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Gly Gly
        755                 760                 765

Gly Gly Ser Gly Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
    770                 775                 780

Gly Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
785                 790                 795                 800
```

Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
805 810 815

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
820 825 830

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
835 840 845

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
850 855 860

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
865 870 875 880

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
885 890 895

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
900 905 910

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
915 920 925

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
930 935 940

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
945 950 955 960

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
965 970 975

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
980 985 990

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
995 1000 1005

Leu Ser Pro Gly Lys
1010

<210> 152
<211> 1085
<212> PRT
<213> Artificial Sequence

<220>
<223> pJH85

<400> 152

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln

85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
180 185 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
195 200 205

Thr Ile Leu Asp Gly Ala Pro Ser Pro Ala Gly Ser Pro Thr Ser Thr
210 215 220

Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser
225 230 235 240

Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala
245 250 255

Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser

260 265 270

Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr
275 280 285

Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro
290 295 300

Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser
305 310 315 320

Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser
325 330 335

Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro
340 345 350

Ser Glu Gly Ser Ala Pro Gly Ala Ser Ser Asn Ile Thr Gln Ser Thr
355 360 365

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

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

Phe Cys Gly Gly Ser Ile Val Asn Glu Lys Trp Ile Val Thr Ala Ala
405 410 415

His Cys Val Glu Thr Gly Val Lys Ile Thr Val Val Ala Gly Glu His
420 425 430

Asn Ile Glu Glu Thr Glu His Thr Glu Gln Lys Arg Asn Val Ile Arg

435 440 445

Ile Ile Pro His His Asn Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His
450 455 460

Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr
465 470 475 480

Val Thr Pro Ile Cys Ile Ala Asp Lys Glu Tyr Thr Asn Ile Phe Leu
485 490 495

Lys Phe Gly Ser Gly Tyr Val Ser Gly Trp Gly Arg Val Phe His Lys
500 505 510

Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu Arg Val Pro Leu Val Asp
515 520 525

Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met
530 535 540

Phe Cys Ala Gly Phe His Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp
545 550 555 560

Ser Gly Gly Pro His Val Thr Glu Val Glu Gly Thr Ser Phe Leu Thr
565 570 575

Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly
580 585 590

Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr
595 600 605

Lys Leu Thr Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu

610 615 620

Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
625 630 635 640

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
645 650 655

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
660 665 670

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
675 680 685

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
690 695 700

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
705 710 715 720

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
725 730 735

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
740 745 750

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
755 760 765

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
770 775 780

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys

785 790 795 800

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
805 810 815

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
820 825 830

Ser Leu Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
835 840 845

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Lys Thr His Thr Cys
850 855 860

Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu
865 870 875 880

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
885 890 895

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
900 905 910

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
915 920 925

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
930 935 940

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
945 950 955 960

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys

965 970 975

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
980 985 990

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

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
1010 1015 1020

Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
1025 1030 1035

Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
1040 1045 1050

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
1055 1060 1065

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
1070 1075 1080

Gly Lys
1085

<210> 153
<211> 935
<212> PRT
<213> Artificial Sequence

<220>
<223> pJH56

<400> 153

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Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1               5                  10                  15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
            20                  25                  30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
        35                  40                  45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
    50                  55                  60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65                  70                  75                  80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
                85                  90                  95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
            100                 105                 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
        115                 120                 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
    130                 135                 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145                 150                 155                 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
                165                 170                 175
```

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Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
            180                 185                 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
        195                 200                 205

Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe
    210                 215                 220

Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp
225                 230                 235                 240

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

Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly
            260                 265                 270

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

His Thr Glu Gln Lys Arg Asn Val Ile Arg Ile Ile Pro His His Asn
    290                 295                 300

Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu Glu
305                 310                 315                 320

Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile
                325                 330                 335

Ala Asp Lys Glu Tyr Thr Asn Ile Phe Leu Lys Phe Gly Ser Gly Tyr
            340                 345                 350
```

Val Ser Gly Trp Gly Arg Val Phe His Lys Gly Arg Ser Ala Leu Val
355 360 365

Leu Gln Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu Leu
370 375 380

Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe His
385 390 395 400

Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro His Val
405 410 415

Thr Glu Val Glu Gly Thr Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly
420 425 430

Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser
435 440 445

Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr Lys Leu Thr Asp Lys Thr
450 455 460

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
465 470 475 480

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
485 490 495

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
500 505 510

Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
515 520 525

```
Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
    530                 535                 540

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
545                 550                 555                 560

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
                565                 570                 575

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
            580                 585                 590

Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys
        595                 600                 605

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
    610                 615                 620

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
625                 630                 635                 640

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
                645                 650                 655

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
            660                 665                 670

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
        675                 680                 685

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    690                 695                 700
```

```
Gly Gly Gly Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
705                 710                 715                 720

Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
                725                 730                 735

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
            740                 745                 750

Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
        755                 760                 765

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
    770                 775                 780

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
785                 790                 795                 800

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
                805                 810                 815

Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
            820                 825                 830

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys
        835                 840                 845

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
    850                 855                 860

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
865                 870                 875                 880
```

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
885 890 895

Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
900 905 910

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
915 920 925

Leu Ser Leu Ser Pro Gly Lys
930 935

<210> 154
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> PAS peptide

<400> 154

Ala Ser Pro Ala Ala Pro Ala Pro Ala Ser Pro Ala Ala Pro Ala Pro
1 5 10 15

Ser Ala Pro Ala
20

<210> 155
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> PAS peptide

<400> 155

Ala Ala Pro Ala Ser Pro Ala Pro Ala Ala Pro Ser Ala Pro Ala Pro
1 5 10 15

Ala Ala Pro Ser
20

<210> 156
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> PAS peptide

<400> 156

Ala Pro Ser Ser Pro Ser Pro Ser Ala Pro Ser Ser Pro Ser Pro Ala
1 5 10 15

Ser Pro Ser Ser
20

<210> 157
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> PAS peptide

<400> 157

Ala Pro Ser Ser Pro Ser Pro Ser Ala Pro Ser Ser Pro Ser Pro Ala
1 5 10 15

Ser Pro Ser

<210> 158
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> PAS peptide

<400> 158

Ser Ser Pro Ser Ala Pro Ser Pro Ser Ser Pro Ala Ser Pro Ser Pro
1 5 10 15

Ser Ser Pro Ala
20

<210> 159
<211> 24
<212> PRT
<213> Artificial Sequence

<220>
<223> PAS peptide

<400> 159

Ala Ala Ser Pro Ala Ala Pro Ser Ala Pro Pro Ala Ala Ala Ser Pro
1 5 10 15

Ala Ala Pro Ser Ala Pro Pro Ala
20

<210> 160
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> PAS peptide

<400> 160

Ala Ser Ala Ala Ala Pro Ala Ala Ala Ser Ala Ala Ala Ser Ala Pro
1 5 10 15

Ser Ala Ala Ala
20

<210> 161
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Gly-Ser peptide linker

<400> 161

Gly Gly Gly Ser
1

<210> 162
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Gly-Ser peptide linker

<400> 162

Gly Gly Gly Ser Gly Gly Gly Ser
1 5

<210> 163
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> albumin-binding peptide core sequence

<400> 163

Asp Ile Cys Leu Pro Arg Trp Gly Cys Leu Trp
1 5 10

<210> 164
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> CTP Peptide

<400> 164

Asp Pro Arg Phe Gln Asp Ser Ser Ser Ser Lys Ala Pro Pro Pro Ser
1 5 10 15

Leu Pro Ser Pro Ser Arg Leu Pro Gly Pro Ser Asp Thr Pro Ile Leu
20 25 30

<210> 165
<211> 28
<212> PRT
<213> Artificial Sequence

<220>
<223> CTP Peptide

<400> 165

Ser Ser Ser Ser Lys Ala Pro Pro Pro Ser Leu Pro Ser Pro Ser Arg
1 5 10 15

Leu Pro Gly Pro Ser Asp Thr Pro Ile Leu Pro Gln
20 25

<210> 166
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> FXIa cleavage site

<400> 166

Thr Gln Ser Phe Asn Asp Phe Thr Arg
1 5

<210> 167
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> FXIa cleavage site

<400> 167

Ser Val Ser Gln Thr Ser Lys Leu Thr Arg
1 5 10

<210> 168
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> thrombin cleavage site

<400> 168

Asp Phe Leu Ala Glu Gly Gly Gly Val Arg
1 5 10

<210> 169

<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> thrombin cleavage site

<400> 169

Thr Thr Lys Ile Lys Pro Arg
1 5

<210> 170
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> thrombin cleavage site

<400> 170

Leu Val Pro Arg Gly
1 5

<210> 171
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> thrombin cleavage site

<400> 171

Ala Leu Arg Pro Arg
1 5

<210> 172
<211> 12
<212> PRT

<213> Artificial Sequence

<220>
<223> Gly-Ser peptide linker

<400> 172

Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser
1 5 10

<210> 173
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Gly-Ser peptide linker

<400> 173

Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser
1 5 10 15

<210> 174
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Gly-Ser peptide linker

<400> 174

Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser
1 5 10 15

Gly Gly Gly Ser
20

<210> 175

<211> 24
<212> PRT
<213> Artificial Sequence

<220>
<223> Gly-Ser peptide linker

<400> 175

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 Gly Gly Ser
20

<210> 176
<211> 28
<212> PRT
<213> Artificial Sequence

<220>
<223> Gly-Ser peptide linker

<400> 176

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 Gly Gly Ser Gly Gly Gly Ser
20 25

<210> 177
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> Gly-Ser peptide linker

<400> 177

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 Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser
20 25 30

<210> 178
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> Gly-Ser peptide linker

<400> 178

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 Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser
20 25 30

Gly Gly Gly Ser
35

<210> 179
<211> 40
<212> PRT
<213> Artificial Sequence

<220>
<223> Gly-Ser peptide linker

<400> 179

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 Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser
20 25 30

Gly Gly Gly Ser Gly Gly Gly Ser
35 40

<210> 180
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Gly-Ser peptide linker

<400> 180

Ser Gly Gly Gly Ser
1 5

<210> 181
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Gly-Ser peptide linker

<400> 181

Ser Gly Gly Gly Ser Gly Gly Gly Ser
1 5

<210> 182
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> Gly-Ser peptide linker

<400> 182

Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser
1 5 10

<210> 183
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Gly-Ser peptide linker

<400> 183

Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
1 5 10 15

Ser

<210> 184
<211> 21
<212> PRT
<213> Artificial Sequence

<220>
<223> Gly-Ser peptide linker

<400> 184

Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
1 5 10 15

Ser Gly Gly Gly Ser
20

<210> 185

<211> 25
<212> PRT
<213> Artificial Sequence

<220>
<223> Gly-Ser peptide linker

<400> 185

Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
1 5 10 15

Ser Gly Gly Gly Ser Gly Gly Gly Ser
20 25

<210> 186
<211> 29
<212> PRT
<213> Artificial Sequence

<220>
<223> Gly-Ser peptide linker

<400> 186

Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
1 5 10 15

Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser
20 25

<210> 187
<211> 33
<212> PRT
<213> Artificial Sequence

<220>
<223> Gly-Ser peptide linker

<400> 187

Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
1 5 10 15

Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
20 25 30

Ser

<210> 188
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Gly-Ser peptide linker

<400> 188

Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
1 5 10 15

Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
20 25 30

Ser Gly Gly Gly Ser
35

<210> 189
<211> 41
<212> PRT
<213> Artificial Sequence

<220>
<223> Gly-Ser peptide linker

<400> 189

Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
1 5 10 15

Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
20 25 30

Ser Gly Gly Gly Ser Gly Gly Gly Ser
35 40

<210> 190
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> PAR1 Linker Motif

<400> 190

Ser Phe Leu Leu Arg Asn
1 5

<210> 191
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> PAR1 Linker Motif

<400> 191

Pro Asn Asp Lys
1

<210> 192
<211> 5
<212> PRT

<213> Artificial Sequence

<220>
<223> PAR1 Linker Motif

<400> 192

Pro Asn Asp Lys Tyr
1 5

<210> 193
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> PAR1 Linker Motif

<400> 193

Pro Asn Asp Lys Tyr Glu
1 5

<210> 194
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> PAR1 Linker Motif

<400> 194

Pro Asn Asp Lys Tyr Glu Pro
1 5

<210> 195
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> PAR1 Linker Motif

<400> 195

Pro Asn Asp Lys Tyr Glu Pro Phe
1 5

<210> 196
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> PAR1 Linker Motif

<400> 196

Pro Asn Asp Lys Tyr Glu Pro Phe Trp
1 5

<210> 197
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> PAR1 Linker Motif

<400> 197

Pro Asn Asp Lys Tyr Glu Pro Phe Trp Glu
1 5 10

<210> 198
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> PAR1 Linker Motif

<400> 198

Pro Asn Asp Lys Tyr Glu Pro Phe Trp Glu Asp
1 5 10

<210> 199
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> PAR1 Linker Motif

<400> 199

Pro Asn Asp Lys Tyr Glu Pro Phe Trp Glu Asp Glu
1 5 10

<210> 200
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> PAR1 Linker Motif

<400> 200

Pro Asn Asp Lys Tyr Glu Pro Phe Trp Glu Asp Glu Glu
1 5 10

<210> 201
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> PAR1 Linker Motif

<400> 201

Pro Asn Asp Lys Tyr Glu Pro Phe Trp Glu Asp Glu Glu Ser
1 5 10

<210> 202
<211> 72
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN_AE72_2A_1

<400> 202

Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Pro Ala Gly
1 5 10 15

Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly
20 25 30

Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly
35 40 45

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu
50 55 60

Pro Ser Glu Gly Ser Ala Pro Gly
65 70

<210> 203
<211> 72
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN_AE72_2A_2

<400> 203

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala
1 5 10 15

Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly
20 25 30

Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly
35 40 45

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Glu Ser
50 55 60

Ala Thr Pro Glu Ser Gly Pro Gly
65 70

<210> 204
<211> 72
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN_AE72_3B_1

<400> 204

Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser
1 5 10 15

Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser
20 25 30

Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
35 40 45

Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu

50 55 60

Pro Ser Glu Gly Ser Ala Pro Gly
65 70

<210> 205
<211> 72
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN_AE72_3B_2

<400> 205

Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu
1 5 10 15

Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly
20 25 30

Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly
35 40 45

Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu
50 55 60

Pro Ser Glu Gly Ser Ala Pro Gly
65 70

<210> 206
<211> 72
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN_AE72_4A_2

<400> 206

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Pro Ala Gly
1 5 10 15

Ser Pro Thr Ser Thr Glu Glu Gly Ser Pro Ala Gly Ser Pro Thr Ser
20 25 30

Thr Glu Glu Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly
35 40 45

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu
50 55 60

Pro Ser Glu Gly Ser Ala Pro Gly
65 70

<210> 207
<211> 72
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN_AE72_5A_2

<400> 207

Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser
1 5 10 15

Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser
20 25 30

Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
35 40 45

Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Ser Pro Ala Gly
    50   55   60

Ser Pro Thr Ser Thr Glu Glu Gly
65   70

<210> 208
<211> 72
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN_AE72_6B_1

<400> 208

Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser
1   5   10   15

Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
            20   25   30

Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
        35   40   45

Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Glu Pro Ala
    50   55   60

Thr Ser Gly Ser Glu Thr Pro Gly
65   70

<210> 209
<211> 72
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN_AE72_6B_2

<400> 209

Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu
1 5 10 15

Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly
20 25 30

Ser Ala Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly
35 40 45

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu
50 55 60

Pro Ser Glu Gly Ser Ala Pro Gly
65 70

<210> 210
<211> 72
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN_AE72_1A_1

<400> 210

Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser
1 5 10 15

Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly
20 25 30

Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly

35 40 45

Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu
50 55 60

Pro Ser Glu Gly Ser Ala Pro Gly
65 70

<210> 211
<211> 72
<212> PRT
<213> Artificial Sequence

<220>
<223> XTEN_AE72_1A_2

<400> 211

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala
1 5 10 15

Thr Ser Gly Ser Glu Thr Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser
20 25 30

Glu Thr Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly
35 40 45

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu
50 55 60

Pro Ser Glu Gly Ser Ala Pro Gly
65 70

<210> 212
<211> 144
<212> PRT

<213> Artificial Sequence

<220>
<223> XTEN_AE144_1A

<400> 212

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Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser
1               5                   10                  15


Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly
            20                  25                  30


Ser Ala Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly
        35                  40                  45


Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Thr Glu
    50                  55                  60


Pro Ser Glu Gly Ser Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
65                  70                  75                  80


Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly
                85                  90                  95


Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Pro Ala Gly
            100                 105                 110


Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu
        115                 120                 125


Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly
    130                 135                 140
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<210> 213

<211> 150
<212> PRT
<213> Artificial Sequence

<220>
<223> AE150

<400> 213

Gly Ala Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly
1 5 10 15

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala
20 25 30

Thr Ser Gly Ser Glu Thr Pro Gly Ser Pro Ala Gly Ser Pro Thr Ser
35 40 45

Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly
50 55 60

Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Glu Pro Ala
65 70 75 80

Thr Ser Gly Ser Glu Thr Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser
85 90 95

Glu Thr Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly
100 105 110

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala
115 120 125

Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly
130 135 140

Ser Ala Pro Ala Ser Ser
145 150

<210> 214
<211> 150
<212> PRT
<213> Artificial Sequence

<220>
<223> AG150

<400> 214

Gly Ala Pro Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro Gly
1 5 10 15

Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser Pro Ser
20 25 30

Ala Ser Thr Gly Thr Gly Pro Gly Ser Ser Pro Ser Ala Ser Thr Gly
35 40 45

Thr Gly Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly
50 55 60

Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Ser Ser Thr Pro
65 70 75 80

Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser Pro Ser Ala Ser Thr Gly
85 90 95

Thr Gly Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly
100 105 110

Ser Ser Pro Ser Ala Ser Thr Gly Thr Gly Pro Gly Thr Pro Gly Ser

115 120 125

Gly Thr Ala Ser Ser Ser Pro Gly Ser Ser Thr Pro Ser Gly Ala Thr
130 135 140

Gly Ser Pro Ala Ser Ser
145 150

<210> 215
<211> 294
<212> PRT
<213> Artificial Sequence

<220>
<223> AE294

<400> 215

Gly Ala Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
1 5 10 15

Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser
20 25 30

Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser
35 40 45

Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly
50 55 60

Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Pro Ala Gly
65 70 75 80

Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro Glu
85 90 95

Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly
100 105 110

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Pro Ala Gly
115 120 125

Ser Pro Thr Ser Thr Glu Glu Gly Ser Pro Ala Gly Ser Pro Thr Ser
130 135 140

Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly
145 150 155 160

Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Glu Ser
165 170 175

Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu
180 185 190

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

Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Pro Ala Gly
210 215 220

Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly
225 230 235 240

Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly
245 250 255

Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser
260 265 270

Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly
275 280 285

Ser Ala Pro Ala Ser Ser
290

<210> 216
<211> 294
<212> PRT
<213> Artificial Sequence

<220>
<223> AG294

<400> 216

Gly Ala Pro Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro
1 5 10 15

Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Thr Pro Gly
20 25 30

Ser Gly Thr Ala Ser Ser Ser Pro Gly Ser Ser Thr Pro Ser Gly Ala
35 40 45

Thr Gly Ser Pro Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro
50 55 60

Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro Gly Thr Pro Gly
65 70 75 80

Ser Gly Thr Ala Ser Ser Ser Pro Gly Ser Ser Thr Pro Ser Gly Ala
85 90 95

Thr Gly Ser Pro Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro

100 105 110

Gly Ser Ser Pro Ser Ala Ser Thr Gly Thr Gly Pro Gly Ser Ser Pro
115 120 125

Ser Ala Ser Thr Gly Thr Gly Pro Gly Ala Ser Pro Gly Thr Ser Ser
130 135 140

Thr Gly Ser Pro Gly Thr Pro Gly Ser Gly Thr Ala Ser Ser Ser Pro
145 150 155 160

Gly Ser Ser Thr Pro Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser Pro
165 170 175

Ser Ala Ser Thr Gly Thr Gly Pro Gly Ser Ser Pro Ser Ala Ser Thr
180 185 190

Gly Thr Gly Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro
195 200 205

Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro Gly Ser Ser Thr
210 215 220

Pro Ser Gly Ala Thr Gly Ser Pro Gly Ser Ser Pro Ser Ala Ser Thr
225 230 235 240

Gly Thr Gly Pro Gly Ala Ser Pro Gly Thr Ser Ser Thr Gly Ser Pro
245 250 255

Gly Ser Ser Pro Ser Ala Ser Thr Gly Thr Gly Pro Gly Thr Pro Gly
260 265 270

Ser Gly Thr Ala Ser Ser Ser Pro Gly Ser Ser Thr Pro Ser Gly Ala

275 280 285

Thr Gly Ser Ala Ser Ser
290

<210> 217
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> AE36

<400> 217

Gly Ser Pro Ala Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu
1 5 10 15

Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly
20 25 30

Ser Glu Thr Pro
35

<210> 218
<211> 78
<212> PRT
<213> Artificial Sequence

<220>
<223> AE78

<400> 218

Gly Ala Pro Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser
1 5 10 15

Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala

20 25 30

Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu
35 40 45

Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr
50 55 60

Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ala Ser Ser
65 70 75

<210> 219
<211> 46
<212> PRT
<213> Artificial Sequence

<220>
<223> linker

<400> 219

Gly Pro Glu Gly Pro Ser Lys Leu Thr Arg Ala Glu Thr Gly Ala Gly
1 5 10 15

Ser Pro Gly Ala Glu Thr Ala Glu Gln Lys Leu Ile Ser Glu Glu Asp
20 25 30

Leu Ser Pro Ala Thr Gly His His His His His His His His
35 40 45

<210> 220
<211> 25
<212> PRT
<213> Artificial Sequence

<220>
<223> linker

<400> 220

Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Leu Val Pro Arg Gly Ala
1 5 10 15

Gly Ser Pro Gly Ala Glu Thr Ala Gly
20 25

<210> 221
<211> 44
<212> PRT
<213> Artificial Sequence

<220>
<223> linker

<400> 221

Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala Leu Val Pro Arg Ser Phe
1 5 10 15

Leu Leu Arg Asn Pro Asn Asp Lys Tyr Glu Pro Phe Trp Glu Asp Glu
20 25 30

Glu Ser Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala
35 40

<210> 222
<211> 23
<212> PRT
<213> Artificial Sequence

<220>
<223> linker

<400> 222

Gly Pro Glu Gly Pro Ser Lys Leu Thr Arg Ala Glu Thr Gly Ala Gly

1 5 10 15

Ser Pro Gly Ala Glu Thr Ala
20

<210> 223
<211> 22
<212> PRT
<213> Artificial Sequence

<220>
<223> linker

<400> 223

Gly Gly Gly Gly Ala Leu Arg Pro Arg Val Val Gly Gly Ala Gly Ser
1 5 10 15

Pro Gly Ala Glu Thr Ala
20

<210> 224
<211> 40
<212> PRT
<213> Artificial Sequence

<220>
<223> linker

<400> 224

Gly Gly Gly Gly Thr Leu Asp Pro Arg Ser Phe Leu Leu Arg Asn Pro
1 5 10 15

Asn Asp Lys Tyr Glu Pro Phe Trp Glu Asp Glu Glu Lys Gly Gly Ala
20 25 30

Gly Ser Pro Gly Ala Glu Thr Ala

35 40

<210> 225
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> linker

<400> 225

Gly Gly Ala Gly Ser Pro Gly Ala Glu Thr Ala
1 5 10

<210> 226
<211> 798
<212> PRT
<213> Artificial Sequence

<220>
<223> pSYN-FIX-102

<400> 226

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn

65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
115 120 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
130 135 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145 150 155 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
165 170 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
180 185 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
195 200 205

Thr Ile Leu Asp Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe
210 215 220

Thr Arg Val Val Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp
225 230 235 240

Gln Val Val Leu Asn Gly Lys Val Asp Ala Phe Cys Gly Gly Ser Ile

245 250 255

Val Asn Glu Lys Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly
260 265 270

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

His Thr Glu Gln Lys Arg Asn Val Ile Arg Ile Ile Pro His His Asn
290 295 300

Tyr Asn Ala Ala Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu Glu
305 310 315 320

Leu Asp Glu Pro Leu Val Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile
325 330 335

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

Val Ser Gly Trp Gly Arg Val Phe His Lys Gly Arg Ser Ala Leu Val
355 360 365

Leu Gln Tyr Leu Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu Leu
370 375 380

Ser Thr Lys Phe Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe His
385 390 395 400

Glu Gly Gly Arg Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro His Val
405 410 415

Thr Glu Val Glu Gly Thr Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly

420 425 430

Glu Glu Cys Ala Met Lys Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser
435 440 445

Arg Tyr Val Asn Trp Ile Lys Glu Lys Thr Lys Leu Thr Gly Pro Glu
450 455 460

Gly Pro Ser Lys Leu Thr Arg Ala Glu Thr Gly Ala Gly Ser Pro Gly
465 470 475 480

Ala Glu Thr Ala Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
485 490 495

Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu
500 505 510

Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly
515 520 525

Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro
530 535 540

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ser Pro Ala
545 550 555 560

Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Glu Ser Ala Thr Pro
565 570 575

Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro
580 585 590

Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Pro Ala

595 600 605

Gly Ser Pro Thr Ser Thr Glu Glu Gly Ser Pro Ala Gly Ser Pro Thr
610 615 620

Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
625 630 635 640

Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Glu
645 650 655

Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Glu Ser Ala Thr Pro
660 665 670

Glu Ser Gly Pro Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro
675 680 685

Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Ser Pro Ala
690 695 700

Gly Ser Pro Thr Ser Thr Glu Glu Gly Thr Ser Thr Glu Pro Ser Glu
705 710 715 720

Gly Ser Ala Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
725 730 735

Gly Ser Glu Pro Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu
740 745 750

Ser Ala Thr Pro Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu
755 760 765

Gly Ser Ala Pro Gly Ala Glu Thr Ala Glu Gln Lys Leu Ile Ser Glu

770 775 780

Glu Asp Leu Ser Pro Ala Thr Gly His His His His His His
785 790 795

<210> 227
<211> 763
<212> PRT
<213> Artificial Sequence

<220>
<223> pSYN-FIX-216

<400> 227

Met Gln Arg Val Asn Met Ile Met Ala Glu Ser Pro Gly Leu Ile Thr
1 5 10 15

Ile Cys Leu Leu Gly Tyr Leu Leu Ser Ala Glu Cys Thr Val Phe Leu
20 25 30

Asp His Glu Asn Ala Asn Lys Ile Leu Asn Arg Pro Lys Arg Tyr Asn
35 40 45

Ser Gly Lys Leu Glu Glu Phe Val Gln Gly Asn Leu Glu Arg Glu Cys
50 55 60

Met Glu Glu Lys Cys Ser Phe Glu Glu Ala Arg Glu Val Phe Glu Asn
65 70 75 80

Thr Glu Arg Thr Thr Glu Phe Trp Lys Gln Tyr Val Asp Gly Asp Gln
85 90 95

Cys Glu Ser Asn Pro Cys Leu Asn Gly Gly Ser Cys Lys Asp Asp Ile
100 105 110

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Asn Ser Tyr Glu Cys Trp Cys Pro Phe Gly Phe Glu Gly Lys Asn Cys
        115                 120                 125

Glu Leu Asp Val Thr Cys Asn Ile Lys Asn Gly Arg Cys Glu Gln Phe
    130                 135                 140

Cys Lys Asn Ser Ala Asp Asn Lys Val Val Cys Ser Cys Thr Glu Gly
145                 150                 155                 160

Tyr Arg Leu Ala Glu Asn Gln Lys Ser Cys Glu Pro Ala Val Pro Phe
                165                 170                 175

Pro Cys Gly Arg Val Ser Val Ser Gln Thr Ser Lys Leu Thr Arg Ala
            180                 185                 190

Glu Thr Val Phe Pro Asp Val Asp Tyr Val Asn Ser Thr Glu Ala Glu
        195                 200                 205

Thr Ile Leu Asp Gly Pro Ser Pro Gly Ser Pro Thr Ser Thr Glu Glu
    210                 215                 220

Gly Thr Ser Glu Ser Ala Thr Pro Glu Ser Gly Pro Gly Ser Glu Pro
225                 230                 235                 240

Ala Thr Ser Gly Ser Glu Thr Pro Gly Thr Ser Glu Ser Ala Thr Pro
                245                 250                 255

Glu Ser Gly Pro Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro
            260                 265                 270

Gly Thr Ser Thr Glu Pro Ser Glu Gly Ser Ala Pro Gly Ala Ser Ser
        275                 280                 285
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Asn Ile Thr Gln Ser Thr Gln Ser Phe Asn Asp Phe Thr Arg Val Val
    290                 295                 300

Gly Gly Glu Asp Ala Lys Pro Gly Gln Phe Pro Trp Gln Val Val Leu
305                 310                 315                 320

Asn Gly Lys Val Asp Ala Phe Cys Gly Gly Ser Ile Val Asn Glu Lys
                325                 330                 335

Trp Ile Val Thr Ala Ala His Cys Val Glu Thr Gly Val Lys Ile Thr
            340                 345                 350

Val Val Ala Gly Glu His Asn Ile Glu Glu Thr Glu His Thr Glu Gln
        355                 360                 365

Lys Arg Asn Val Ile Arg Ile Ile Pro His His Asn Tyr Asn Ala Ala
    370                 375                 380

Ile Asn Lys Tyr Asn His Asp Ile Ala Leu Leu Glu Leu Asp Glu Pro
385                 390                 395                 400

Leu Val Leu Asn Ser Tyr Val Thr Pro Ile Cys Ile Ala Asp Lys Glu
                405                 410                 415

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

Gly Arg Val Phe His Lys Gly Arg Ser Ala Leu Val Leu Gln Tyr Leu
        435                 440                 445

Arg Val Pro Leu Val Asp Arg Ala Thr Cys Leu Leu Ser Thr Lys Phe
    450                 455                 460
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Thr Ile Tyr Asn Asn Met Phe Cys Ala Gly Phe His Glu Gly Gly Arg
465                 470                 475                 480

Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro His Val Thr Glu Val Glu
                485                 490                 495

Gly Thr Ser Phe Leu Thr Gly Ile Ile Ser Trp Gly Glu Glu Cys Ala
            500                 505                 510

Met Lys Gly Lys Tyr Gly Ile Tyr Thr Lys Val Ser Arg Tyr Val Asn
        515                 520                 525

Trp Ile Lys Glu Lys Thr Lys Leu Thr Asp Lys Thr His Thr Cys Pro
    530                 535                 540

Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe
545                 550                 555                 560

Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val
                565                 570                 575

Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe
            580                 585                 590

Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro
        595                 600                 605

Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr
    610                 615                 620

Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val
625                 630                 635                 640
```

Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala
645 650 655

Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg
660 665 670

Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly
675 680 685

Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro
690 695 700

Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser
705 710 715 720

Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln
725 730 735

Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His
740 745 750

Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
755 760

<210> 228
<211> 226
<212> PRT
<213> Artificial Sequence

<220>
<223> pSYN-FIX-216-Fc

<400> 228

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly

1 5 10 15

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
20 25 30

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
35 40 45

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
50 55 60

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
65 70 75 80

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
85 90 95

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
100 105 110

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
115 120 125

Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
130 135 140

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
145 150 155 160

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
165 170 175

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val

180 185 190

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
195 200 205

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
210 215 220

Pro Gly
225

摘要

本发明提供包含至少一个诸如 XTEN 之异源部分的因子 IX(FIX)融合蛋白。本发明另外揭示制备及使用该等 FIX 融合蛋白之方法。