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(71) Applicant(s)
The Regents of the University of California

(72) Inventor(s)
Taunton, John W.;Lim, Wendell A.;Wu, Chia-Yung

(74) Agent / Attorney
FB Rice Pty Ltd, Level 23 44 Market Street, Sydney, NSW, 2000, AU

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(71) Applicant: **THE REGENTS OF THE UNIVERSITY OF CALIFORNIA** [US/US]; 1111 Franklin Street, 12th Floor, Oakland, California 94607 (US).

(72) Inventors: **TAUNTON, John W.**; 600 16th Street, San Francisco, California 94158 (US). **LIM, Wendell A.**; 600 16th Street, San Francisco, California 94158 (US). **WU, Chia-Yung**; 1 Hawthorne St., Unit 4F, San Francisco, California 94105 (US).

(74) Agent: **GUEDELHOEFER, Otto C.**; 201 Redwood Shores Parkway, Suite 200, Redwood City, California 94065 (US).

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FIG. 1A

Mineralocorticoid receptor (*Homo sapiens*)

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   1 metkgyhslp egldmerrwg qvsqaverss lgptertden nymelvnvsc vagaiprnst
  61 qgesskekqel ipc_qqdnnr pgiltsdikt eleskelsat vaesmglymd svroadysye
 121 qqnqqgsmsp akiyqnveql vkfykgnghr pstlscvnrp lrsfmsdsgs svngqvmrav
 181 vksoimchek spsvcsplnm tssvcspagi nsvsstasf qsfpvhspit qgtpltcspn
 241 venrgsrshs pahasnvgsp lsspissmks sisspposhcs vkspvsspnn vtlrssvssp
 301 aninnsrcsv sspsntnnrs tlsspaastv gsicspvnna fsyrasgtsa gsstlrdvvp
 361 spdtqekgaq evpfpkteev esaisngvtg qlnivqyikp epdgafsssc lggnskinsd
 421 ssfsvpikqe stkhscsgts fkgnptvnpf pfmdgsyfsf mddxdyysls gilgppvpgf
 481 dgncegsgfp vgikqepddg syypeasips saivgvnsgg qsfhyrigaq gtislsrsar
 541 dqsfghlssf ppvntivesw kshgdlssrr sdgypvleyi penvssstlr svstgssrps
 601 kiclvcgdea sgchygvvtc gsckvffkra vegqhnylca grndcilidki rrkncpacrl
 661 qkclqagmnl garkskklgk lkgiheeqpq qqqppppppp pqspeegtpy iapakepsvn
 721 talvpqlsni sraltpspvm vleniepeiv yagydsskpd taenllstln rlagkqmiqv
 781 vkwakvlpgf knlpledqit liqyswmcls sfalswrsyk htnsqflyfa pdlvfneekm
 841 hqsamyelcq gmhqislqfv rlqltfeeyt imkvllllst ipkdglksqa afeemrtnyi
 901 kelrkmvtkc pnnsgqswqr fyqltkllds mhdlvsdlle fcfytfresh alkvefpaml
 961 veiisdqlpk vesgnakply fhrk
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(57) Abstract: The present disclosure provides conditionally active, heterodimeric polypeptides. The conditionally active, heterodimeric polypeptides are active in the presence of a dimerizing agent that induces dimerization of the polypeptides of the heterodimer. A conditionally active, heterodimeric polypeptide of the present disclosure is useful in a variety of research and treatment methods, which are also provided.

WO 2017/120546 A1

CONDITIONALLY ACTIVE HETERODIMERIC POLYPEPTIDES AND METHODS OF USE THEREOF

CROSS-REFERENCE

[0001] This application claims the benefit of U.S. Provisional Patent Application No. 62/276,725, filed January 8, 2016, which application is incorporated herein by reference in its entirety.

STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH

[0002] This invention was made with government support under Grant Nos. R01 CA196277, P50 GM081879, and R01 GM055040 awarded by the National Institutes of Health. The government has certain rights in the invention.

INCORPORATION BY REFERENCE OF SEQUENCE LISTING PROVIDED AS A TEXT FILE

[0003] A Sequence Listing is provided herewith as a text file, "UCSF-524WO_seqlist_ST25.txt" created on January 6, 2017 and having a size of 2,005 KB. The contents of the text file are incorporated by reference herein in their entirety.

INTRODUCTION

[0004] In cell-based adoptive immunotherapy, immune cells isolated from a patient can be modified to express synthetic proteins that enable the cells to perform new therapeutic functions after they are subsequently transferred back into the patient. Examples of such synthetic proteins are chimeric antigen receptors (CARs) and engineered T cell Receptors (TCR). An example of a currently used CAR is a fusion of an extracellular recognition domain (e.g., an antigen-binding domain), a transmembrane domain, and one or more intracellular signaling domains. Upon antigen engagement, the intracellular signaling portion of the CAR can initiate an activation-related response in an immune cell, such as release of cytolytic molecules to induce tumor cell death, etc. However, such CARs are not capable of being pharmacologically controlled. Safe human testing and clinical use of such CARs and engineered TCR requires fine control of the powerful stimulating activity of these highly engineered proteins and protein complexes. In some cases, control is required in order to inhibit, halt or otherwise modulate immune cell activation when activation from the designer stimulating receptor is unwanted, becomes undesirable or is no longer necessary.

SUMMARY

[0005] The present disclosure provides conditionally active, heterodimeric polypeptides. The conditionally active, heterodimeric polypeptides are active in the presence of a dimerizing agent that induces dimerization of the polypeptides of the heterodimer. A conditionally active, heterodimeric polypeptide of the present disclosure is useful in a variety of research and treatment methods, which are also provided.

[0006] The present disclosure provides a heterodimeric, conditionally active polypeptide comprising: a) a first chimeric polypeptide comprising a first member of a dimerization pair and a first heterologous polypeptide; and b) a second chimeric polypeptide comprising a second member of a dimerization pair and a second heterologous polypeptide, wherein the first member of the dimerization pair comprises a ligand-binding domain (LBD) of a nuclear hormone receptor, and the second member of the dimerization pair comprises a co-regulator of the nuclear hormone receptor, or wherein the first member of the dimerization pair is a co-regulator of a nuclear hormone receptor, and the second member of the dimerization pair comprises an LBD of the nuclear hormone receptor; and wherein the first chimeric polypeptide and the second chimeric polypeptide are dimerized in the presence of a dimerization agent that induces binding of the LBD to the co-regulator. In some cases, a) the first heterologous polypeptide is a T-cell receptor (TCR) alpha chain; and b) the second heterologous polypeptide is a TCR beta chain. In some cases: a) the first heterologous polypeptide is a first polypeptide of a chimeric antigen receptor (CAR) heterodimer; and b) the second heterologous polypeptide is a second polypeptide of a CAR heterodimer. In some cases: a) the first heterologous polypeptide is an N-terminal portion of an RNA-guided endonuclease; and b) the second heterologous polypeptide is a C-terminal portion of the RNA-guided endonuclease, wherein dimerization of the first chimeric polypeptide and the second chimeric polypeptide, mediated by the dimerization agent that induces binding of the LBD to the co-regulator, restores enzymatic function of the RNA-guided endonuclease. In some cases, the RNA-guided endonuclease is a class 2 CRISPR/Cas endonuclease. In some cases, the class 2 CRISPR/Cas endonuclease is a type II CRISPR/Cas protein, a type V CRISPR/Cas protein, or a type VI CRISPR/Cas protein. In some cases: a) the first heterologous polypeptide is an N-terminal portion of an enzyme; and b) the second heterologous polypeptide is a C-terminal portion of the enzyme, wherein dimerization of the first chimeric polypeptide and the second chimeric polypeptide restore enzymatic activity of the enzyme. In some cases, the enzyme is a kinase, a protease, a phosphatase, or a caspase. In some cases, the first polypeptide and the second polypeptide exhibit an activity when brought into proximity upon dimerization mediated by the dimerization agent, but do not exhibit the activity individually. In some cases: a) the first heterologous polypeptide is an N-terminal portion of an antigen receptor; and b) the second heterologous polypeptide is a C-terminal portion of the antigen receptor, wherein dimerization of the first chimeric polypeptide and the second chimeric polypeptide restore signaling activity of the antigen receptor. In some cases: a) the first heterologous polypeptide is an N-terminal portion of a

receptor; and b) the second heterologous polypeptide is a C-terminal portion of the antigen receptor, wherein dimerization of the first chimeric polypeptide and the second chimeric polypeptide mediated by the dimerization agent restores signaling activity of the receptor. In some cases, the LBD of the nuclear hormone binding member of the dimerization pair is an LBD of a nuclear hormone receptor selected from an estrogen receptor, an ecdysone receptor, a PPARγ receptor, a glucocorticoid receptor, an androgen receptor, a thyroid hormone receptor, a mineralocorticoid receptor, a progesterone receptor, a vitamin D receptor, a PPARβ receptor, a PPARα receptor, a pregnane X receptor, a liver X receptor, a farnesoid X receptor, a retinoid X receptor, a RAR-related orphan receptor, and a retinoic acid receptor. In some cases, the co-regulator of the nuclear hormone receptor is selected from SRC1, GRIP1, AIB1, PGC1a, PGC1b, PRC, TRAP220, ASC2, CBP, P300, CIA, ARA70, TIF1, NSD1, SMAP, Tip60, ERAP140, Nix1, LCoR, N-CoR, SMRT, RIP140, and PRIC285. In some cases, the co-regulator of the nuclear hormone receptor is selected from: a) SRC1: CPSSHSSLTERHKILHRLLQEGSPS (SEQ ID NO:1); b) SRC1–2: SLTARHKILHRLLQEGSPSDI (SEQ ID NO:2); c) SRC3-1: ESKGHKKLLQLLTCSSDDR (SEQ ID NO:3); d) SRC3: PKKENNALLRYLLDRDDPSDV (SEQ ID NO:4); e) PGC-1: AEEPSLLKKLLLAPANT (SEQ ID NO:5); f) PGC1a: QEAEEPSLLKKLLLAPANTQL (SEQ ID NO:6); g) TRAP220–1: SKVSQNPILTSLLQITGNGGS (SEQ ID NO:7); h) NCoR (2051–2075): GHSFADPASNLGLEDIIRKALMGSF (SEQ ID NO:8); i) NR0B1: PRQGSILYSMLTSAKQT (SEQ ID NO:9); j) NRIP1: AANNSLLLHLLKSQTIP (SEQ ID NO:10); k) TIF2: PKKKENALLRYLLDKDDTKDI (SEQ ID NO:11); l) CoRNR Box: DAFQLRQLILRGLQDD (SEQ ID NO:12); m) αβV: SPGSREWFKDMLS (SEQ ID NO:13); n) TRAP220-2: GNTKNHPMLMNLLKDNPAQDF (SEQ ID NO:14); o) EA2: SSKGVLWRMLAEPVSR (SEQ ID NO:15); p) TA1: SRTLQLDWGTLYWSR (SEQ ID NO:16); q) EAB1: SSNHQSSRLIELLSR (SEQ ID NO:17); r) SRC2: LKEKHKILHRLLQDSSSPV (SEQ ID NO:18); s) SRC1-3: QAQQKSLLQQLLTE (SEQ ID NO:19); t) SRC1–1: KYSQTSHKLVQLLTTTAEQQL (SEQ ID NO:20); u) SRC1–2: SLTARHKILHRLLQEGSPSDI (SEQ ID NO:21); v) SRC1–3: KESKDHQLLRYLLDKDEKDLR (SEQ ID NO:22); w) SRC1–4a: PQAQQKSLLQQLLTE (SEQ ID NO:23); x) SRC1–4b: PQAQQKSLRQQLLTE (SEQ ID NO:24); y) GRIP1–1: HDSKGQTKLLQLLTTKSDQME (SEQ ID NO:25); z) GRIP1–2: SLKEKHKILHRLLQDSSSPVD (SEQ ID NO:26); aa) GRIP1–3: PKKKENALLRYLLDKDDTKDI (SEQ ID NO:27); bb) AIB1–1: LESKGHKKLLQLLTCSSDDRG (SEQ ID NO:28); cc) AIB1–2: LLQEKHRILHKLLQNGNSPAE (SEQ ID NO:29); dd) AIB1–3: KKKENNALLRYLLDRDDPSDA (SEQ ID NO:30); ee) PGC1a: QEAEEPSLLKKLLLAPANTQL (SEQ ID NO:31); ff) PGC1b: PEVDELSLLQKLLLATSYPTS (SEQ ID NO:32); gg) PRC: VSPREGSSLHKLLTLSRTPPE (SEQ ID NO:33); hh) TRAP220–1: SKVSQNPILTSLLQITGNGGS (SEQ ID NO:34); ii) TRAP220–2: GNTKNHPMLMNLLKDNPAQDF (SEQ ID NO:35); jj) ASC2–1: DVTLTSPLLVNLLQSDISAGH (SEQ ID NO:36); kk) ASC2–2:

AMREAPTSLSQLLDNSGAPNV (SEQ ID NO:37); ll) CBP-1: DAASKHKQLSELLRGGSGSSI (SEQ ID NO:38); mm) CBP-2: KRKLIQQQLVLLLHAHKCQRR (SEQ ID NO:39); nn) P300: DAASKHKQLSELLRSGSSPNL (SEQ ID NO:40); oo) CIA: GHPPAIQSLINLLADNRYLTA (SEQ ID NO:41); pp) ARA70–1: TLQQQAQQLYSLLGQFNCLTH (SEQ ID NO:42); qq) ARA70–2: GSRETSEKFKLLFQSYNVNDW (SEQ ID NO:43); rr) TIF1: NANYPRSILTSLLLNSSQSST (SEQ ID NO:44); ss) NSD1: IPIEPDYKFSTLLMMLKDMHD (SEQ ID NO:45); tt) SMAP: ATPPPSPLLSELLKKGSLLPT (SEQ ID NO:46); uu) Tip60: VDGHERAMLKRLLRIDSKCLH (SEQ ID NO:47); vv) ERAP140: HEDLDKVKLIEYYLTKNKEGP (SEQ ID NO:48); ww) Nix1: ESPEFCLGLQTLLSLKCCIDL (SEQ ID NO:49); xx) LCoR: AATTQNPVLSKLLMADQDSPL (SEQ ID NO:50); yy) CoRNR1 (N-CoR): MGQVPRTHRLITLADHICQIITQDFARNQV (SEQ ID NO:51); zz) CoRNR2 (N-CoR): NLGLEDIIRKALMG (SEQ ID NO:52); aaa) CoRNR1 (SMRT): APGVKGHQRVVTLAQHISEVITQDTYRHHPQQLSAPLPAP (SEQ ID NO:53); bbb) CoRNR2 (SMRT): NMGLEAIIRKALMG (SEQ ID NO:54); ccc) RIP140-C: RLTKTNPILYYMLQKGGNSVA (SEQ ID NO:55); ddd) RIP140-1: QDSIVLTYLEGLLMHQAAGGS (SEQ ID NO:56); eee) RIP140-2: KGKQDSTLLASLLQSFSSRLQ (SEQ ID NO:57); fff) RIP140-3: CYGVASSHLKTLLKKSKVKDQ (SEQ ID NO:58); ggg) RIP140-4: KPSVACSQLALLLSSEAHLQQ (SEQ ID NO:59); hhh) RIP140-5: KQAANNSLLLHLLKSQTIPKP (SEQ ID NO:60); iii) RIP140-6: NSHQKVTLLQLLLGHKNEENV (SEQ ID NO:61); jjj) RIP140-7: NLLERRTVLQLLLGNPTKGRV (SEQ ID NO:62); kkk) RIP140-8: FSFSKNGLLSRLLRQNQDSYL (SEQ ID NO:63); lll) RIP140-9: RESKSFNVLKQLLLSENCVRD (SEQ ID NO:64); mmm) PRIC285-1: ELNADDAILRELLDESQKVMV (SEQ ID NO:65); nnn) PRIC285-2: YENLPPAALRKLLRAEPERYR (SEQ ID NO:66); ooo) PRIC285-3: MAFAGDEVLVQLLSGDKAPEG (SEQ ID NO:67); ppp) PRIC285-4: SCCYLCIRLEGLLAPTASPRP (SEQ ID NO:68); and qqq) PRIC285-5: PSNKSVDVLAGLLLRRMELKP (SEQ ID NO:69).

[0007] The present disclosure provides a heterodimeric, conditionally active receptor comprising: a) a first chimeric polypeptide comprising: i) a first member of a specific binding pair; ii) a first modulatory domain; iii) a first member of a dimerization pair; and iv) a transmembrane domain interposed between the first member of a specific binding pair and the first modulatory domain; and b) a second chimeric polypeptide comprising: i) a transmembrane domain; ii) a second modulatory domain; iii) a second member of the dimerization pair; and iv) an intracellular signaling domain; or comprising: a) a first chimeric polypeptide comprising: i) a first member of a specific binding pair; ii) a modulatory domain; iii) a first member of a dimerization pair; iv) a transmembrane domain interposed between the first member of a specific binding pair and the modulatory domain; and b) a second chimeric polypeptide comprising: i) a second member of the dimerization pair; and ii) an intracellular signaling domain, wherein the first member of the dimerization pair comprises a ligand-binding domain (LBD) of a nuclear hormone receptor, and the second member of the dimerization pair comprises a co-regulator of the

nuclear hormone receptor, or wherein the first member of the dimerization pair is a co-regulator of a nuclear hormone receptor, and the second member of the dimerization pair comprises an LBD of the nuclear hormone receptor, wherein the first chimeric polypeptide and the second chimeric polypeptide are dimerized in the presence of a dimerizer that induces binding of the LBD to the co-regulator. In some cases, the first polypeptide comprises a hinge region interposed between the first member of the specific binding pair and the transmembrane domain. In some cases, the first member of the specific binding pair is an antibody or antibody fragment, a ligand, a receptor, or a non-antibody-based recognition scaffold. In some cases, the hinge region is an immunoglobulin IgG hinge region or a hinge derived from CD8. In some cases, the first and second modulatory domains are selected from 4-1BB (CD137), CD28, ICOS, BTLA, OX-40, CD27, CD30, GITR, HVEM, DAP10, DAP12, and CD28. In some cases, the intracellular signaling domain is selected from ZAP70 and CD3-zeta. In some cases, the intracellular signaling domain comprises an immunoreceptor tyrosine-based activation motif (ITAM). In some cases, the LBD of the nuclear hormone binding member of the dimerization pair is an LBD of a nuclear hormone receptor selected from estrogen receptor, an ecdysone receptor, a PPARγ receptor, a glucocorticoid receptor, an androgen receptor, a thyroid hormone receptor, a mineralocorticoid receptor, a progesterone receptor, a vitamin D receptor, a PPARβ receptor, a PPARα receptor, a pregnane X receptor, a liver X receptor, a farnesoid X receptor, a retinoid X receptor, a RAR-related orphan receptor, and a retinoic acid receptor. In some cases, the co-regulator of the nuclear hormone receptor is selected from SRC1, GRIP1, AIB1, PGC1a, PGC1b, PRC, TRAP220, ASC2, CBP, P300, CIA, ARA70, TIF1, NSD1, SMAP, Tip60, ERAP140, Nix1, LCoR, N-CoR, SMRT, RIP140, and PRIC285. In some cases, the co-regulator of the nuclear hormone receptor is a peptide selected from a) SRC1: CPSSHSSLTERHKILHRLLQEGSPS (SEQ ID NO:1); b) SRC1–2: SLTARHKILHRLLQEGSPSDI (SEQ ID NO:2); c) SRC3-1: ESKGHKKLLQLLTCSSDDR (SEQ ID NO:3); d) SRC3: PKKENNALLRYLLDRDDPSDV (SEQ ID NO:4); e) PGC-1: AEEPSLLKKLLLAPANT (SEQ ID NO:5); f) PGC1a: QEAEEPSLLKKLLLAPANTQL (SEQ ID NO:6); g) TRAP220–1: SKVSQNPILTSLLQITGNGGS (SEQ ID NO:7); h) NCoR (2051–2075): GHSFADPASNLGLEDIIRKALMGSF (SEQ ID NO:8); i) NR0B1: PRQGSILYSMLTSAKQT (SEQ ID NO:9); j) NRIP1: AANNSLLLHLLKSQTIP (SEQ ID NO:10); k) TIF2: PKKKENALLRYLLDKDDTKDI (SEQ ID NO:11); l) CoRNR Box: DAFQLRQLILRGLQDD (SEQ ID NO:12); m) αβV: SPGSREWFKDMLS (SEQ ID NO:13); n) TRAP220-2: GNTKNHPMLMNLLKDNPAQDF (SEQ ID NO:14); o) EA2: SSKGVLWRMLAEPVSR (SEQ ID NO:15); p) TA1: SRTLQLDWGTLYWSR (SEQ ID NO:16); q) EAB1: SSNHQSSRLIELLSR (SEQ ID NO:17); r) SRC2: LKEKHKILHRLLQDSSSPV (SEQ ID NO:18); s) SRC1-3: QAQQKSLLQQLLTE (SEQ ID NO:19); t) SRC1–1: KYSQTSHKLVQLLTTTAEQQL (SEQ ID NO:20); u) SRC1–2: SLTARHKILHRLLQEGSPSDI (SEQ ID NO:21); v) SRC1–3: KESKDHQLLRYLLDKDEKDLR (SEQ

ID NO:22); w) SRC1–4a: PQAQQKSLLQQLLTE (SEQ ID NO:23); x) SRC1–4b: PQAQQKSLRQQLLTE (SEQ ID NO:24); y) GRIP1–1: HDSKGQTKLLQLLTTKSDQME (SEQ ID NO:25); z) GRIP1–2: SLKEKHKILHRLLQDSSSPVD (SEQ ID NO:26); aa) GRIP1–3: PKKKENALLRYLLDKDDTKDI (SEQ ID NO:27); bb) AIB1–1: LESKGHKKLLQLLTCSSDDRG (SEQ ID NO:28); cc) AIB1–2: LLQEKHRILHKLLQNGNSPAE (SEQ ID NO:29); dd) AIB1–3: KKKENNALLRYLLDRDDPSDA (SEQ ID NO:30); ee) PGC1a: QEAEEPSLLKKLLLAPANTQL (SEQ ID NO:31); ff) PGC1b: PEVDELSLLQKLLLATSYPTS (SEQ ID NO:32); gg) PRC: VSPREGSSLHKLLTLSRTPPE (SEQ ID NO:33); hh) TRAP220–1: SKVSQNPILTSLLQITGNGGS (SEQ ID NO:34); ii) TRAP220–2: GNTKNHPMLMNLLKDNPAQDF (SEQ ID NO:35); jj) ASC2–1: DVTLTSPLLVNLLQSDISAGH (SEQ ID NO:36); kk) ASC2–2: AMREAPTSLSQLLDNSGAPNV (SEQ ID NO:37); ll) CBP-1: DAASKHKQLSELLRGGSGSSI (SEQ ID NO:38); mm) CBP-2: KRKLIQQQLVLLLHAHKCQRR (SEQ ID NO:39); nn) P300: DAASKHKQLSELLRSGSSPNL (SEQ ID NO:40); oo) CIA: GHPPAIQSLINLLADNRYLTA (SEQ ID NO:41); pp) ARA70–1: TLQQQAQQLYSLLGQFNCLTH (SEQ ID NO:42); qq) ARA70–2: GSRETSEKFKLLFQSYNVNDW (SEQ ID NO:43); rr) TIF1: NANYPRSILTSLLLNSSQSST (SEQ ID NO:44); ss) NSD1: IPIEPDYKFSTLLMMLKDMHD (SEQ ID NO:45); tt) SMAP: ATPPPSPLLSELLKKGSLLPT (SEQ ID NO:46); uu) Tip60: VDGHERAMLKRLLRIDSKCLH (SEQ ID NO:47); vv) ERAP140: HEDLDKVKLIEYYLTKNKEGP (SEQ ID NO:48); ww) Nix1: ESPEFCLGLQTLLSLKCCIDL (SEQ ID NO:49); xx) LCoR: AATTQNPVLSKLLMADQDSPL (SEQ ID NO:50); yy) CoRNR1 (N-CoR): MGQVPRTHRLITLADHICQIITQDFARNQV (SEQ ID NO:51); zz) CoRNR2 (N-CoR): NLGLEDIIRKALMG (SEQ ID NO:52); aaa) CoRNR1 (SMRT): APGVKGHQRVVTLAQHISEVITQDTYRHHPQQLSAPLPAP (SEQ ID NO:53); bbb) CoRNR2 (SMRT): NMGLEAIIRKALMG (SEQ ID NO:54); ccc) RIP140-C: RLTKTNPILYYMLQKGGNSVA (SEQ ID NO:55); ddd) RIP140-1: QDSIVLTYLEGLLMHQAAGGS (SEQ ID NO:56); eee) RIP140-2: KGKQDSTLLASLLQSFSSRLQ (SEQ ID NO:57); fff) RIP140-3: CYGVASSHLKTLLKKSKVKDQ (SEQ ID NO:58); ggg) RIP140-4: KPSVACSQLALLLSSEAHLQQ (SEQ ID NO:59); hhh) RIP140-5: KQAANNSLLLHLLKSQTIPKP (SEQ ID NO:60); iii) RIP140-6: NSHQKVTLLQLLLGHKNEENV (SEQ ID NO:61); jjj) RIP140-7: NLLERRTVLQLLLGNPTKGRV (SEQ ID NO:62); kkk) RIP140-8: FSFSKNGLLSRLLRQNQDSYL (SEQ ID NO:63); lll) RIP140-9: RESKSFNVLKQLLLSENCVRD (SEQ ID NO:64); mmm) PRIC285-1: ELNADDAILRELLDESQKVMV (SEQ ID NO:65); nnn) PRIC285-2: YENLPPAALRKLLRAEPERYR (SEQ ID NO:66); ooo) PRIC285-3: MAFAGDEVLVQLLSGDKAPEG (SEQ ID NO:67); ppp) PRIC285-4: SCCYLCIRLEGLLAPTASPRP (SEQ ID NO:68); and qqq) PRIC285-5: PSNKSVDVLAGLLLRRMELKP (SEQ ID NO:69). In some cases: i) the first and second modulatory domains are derived from 4-1BB; ii) the first and second members of the dimerization pair are PPARγ and SRC3; and ii) the signaling domain comprises an

ITAM. In some cases, the first member of the specific binding pair is a single-chain Fv. In some cases, the first member of the specific binding pair binds an epitope present on a cell, on a solid surface, or a lipid bilayer. In some cases, the cell is a cancer cell. In some cases, the intracellular signaling domain is an intracellular inhibitory domain. In some cases, the intracellular inhibitory domain is derived from a protein selected from the group consisting of: PD-1, CTLA4, HPK1, SHP1, SHP2, Sts1, and Csk.

[0008] The present disclosure provides a heterodimeric, conditionally repressible synthetic immune cell receptor (ICR) comprising: a synthetic stimulatory ICR comprising a first member of a dimerization pair linked to the synthetic stimulatory ICR; and a synthetic ICR repressor comprising a second member of the dimerization pair linked to an intracellular inhibitory domain, wherein the first member of the dimerization pair comprises a ligand-binding domain (LBD) of a nuclear hormone receptor, and the second member of the dimerization pair comprises a co-regulator of the nuclear hormone receptor, or wherein the first member of the dimerization pair is a co-regulator of a nuclear hormone receptor, and the second member of the dimerization pair comprises an LBD of the nuclear hormone receptor, wherein the synthetic stimulatory ICR and the synthetic ICR repressor are dimerized in the presence of a dimerizer that induces binding of the LBD to the co-regulator. In some cases, the synthetic stimulatory ICR comprises an intracellular co-stimulatory domain. In some cases, the intracellular co-stimulatory domain is selected from the group consisting of: 4-1BB (CD137), CD28, ICOS, OX-40, BTLA, CD27, CD30, GITR, and HVEM. In some cases, the first member of a dimerization pair is linked intracellularly to the synthetic stimulatory ICR and the second member of the dimerization pair is linked intracellularly to the intracellular inhibitory domain. In some cases, the synthetic ICR repressor further comprises a transmembrane domain. In some cases, the second member of the dimerization pair is linked intracellularly to the transmembrane domain. In some cases, the second member of the dimerization pair is extracellular and linked to the intracellular inhibitory domain by way of the transmembrane domain. In some cases, the stimulatory ICR binds a soluble antigen. In some cases, the stimulatory ICR binds a cell surface antigen. In some cases, the intracellular inhibitory domain is an inhibitory domain derived from a protein selected from the group consisting of: PD-1, CTLA4, HPK1, SHP1, SHP2, Sts1 and Csk. In some cases, the synthetic stimulatory ICR comprises an intracellular signaling domain selected from the group consisting of: a CD3-zeta signaling domain, a ZAP70 signaling domain and an immunoreceptor tyrosine-based activation motif (ITAM). In some cases, the LBD of the nuclear hormone binding member of the dimerization pair is an LBD of a nuclear hormone receptor selected from estrogen receptor, an ecdysone receptor, a PPARγ receptor, a glucocorticoid receptor, an androgen receptor, a thyroid hormone receptor, a mineralocorticoid receptor, a progesterone receptor, a vitamin D receptor, a PPARβ receptor, a PPARα receptor, a pregnane X receptor, a liver X receptor, a farnesoid X receptor, a retinoid X receptor, a RAR-related orphan receptor, and a retinoic acid receptor. In some cases, the co-regulator of the nuclear hormone receptor is selected from SRC1, GRIP1, AIB1, PGC1a, PGC1b, PRC,

TRAP220, ASC2, CBP, P300, CIA, ARA70, TIF1, NSD1, SMAP, Tip60, ERAP140, Nix1, LCoR, N-CoR, SMRT, RIP140, and PRIC285. In some cases, the co-regulator of the nuclear hormone receptor is selected from: a) SRC1: CPSSHSSLTERHKILHRLLQEGSPS (SEQ ID NO:1); b) SRC1–2: SLTARHKILHRLLQEGSPSDI (SEQ ID NO:2); c) SRC3-1: ESKGHKKLLQLLTCSSDDR (SEQ ID NO:3); d) SRC3: PKKENNALLRYLLDRDDPSDV (SEQ ID NO:4); e) PGC-1: AEEPSLLKKLLLAPANT (SEQ ID NO:5); f) PGC1a: QEAEEPSLLKKLLLAPANTQL (SEQ ID NO:6); g) TRAP220–1: SKVSQNPILTSLLQITGNGGS (SEQ ID NO:7); h) NCoR (2051–2075): GHSFADPASNLGLEDIIRKALMGSF (SEQ ID NO:8); i) NR0B1: PRQGSILYSMLTSAKQT (SEQ ID NO:9); j) NRIP1: AANNSLLLHLLKSQTIP (SEQ ID NO:10); k) TIF2: PKKKENALLRYLLDKDDTKDI (SEQ ID NO:11); l) CoRNR Box: DAFQLRQLILRGLQDD (SEQ ID NO:12); m) αβV: SPGSREWFKDMLS (SEQ ID NO:13); n) TRAP220-2: GNTKNHPMLMNLLKDNPAQDF (SEQ ID NO:14); o) EA2: SSKGVLWRMLAEPVSR (SEQ ID NO:15); p) TA1: SRTLQLDWGTLYWSR (SEQ ID NO:16); q) EAB1: SSNHQSSRLIELLSR (SEQ ID NO:17); r) SRC2: LKEKHKILHRLLQDSSSPV (SEQ ID NO:18); s) SRC1-3: QAQQKSLLQQLLTE (SEQ ID NO:19); t) SRC1–1: KYSQTSHKLVQLLTTTAEQQL (SEQ ID NO:20); u) SRC1–2: SLTARHKILHRLLQEGSPSDI (SEQ ID NO:21); v) SRC1–3: KESKDHQLLRYLLDKDEKDLR (SEQ ID NO:22); w) SRC1–4a: PQAQQKSLLQQLLTE (SEQ ID NO:23); x) SRC1–4b: PQAQQKSLRQQLLTE (SEQ ID NO:24); y) GRIP1–1: HDSKGQTKLLQLLTTKSDQME (SEQ ID NO:25); z) GRIP1–2: SLKEKHKILHRLLQDSSSPVD (SEQ ID NO:26); aa) GRIP1–3: PKKKENALLRYLLDKDDTKDI (SEQ ID NO:27); bb) AIB1–1: LESKGHKKLLQLLTCSSDDRG (SEQ ID NO:28); cc) AIB1–2: LLQEKHRILHKLLQNGNSPAE (SEQ ID NO:29); dd) AIB1–3: KKKENNALLRYLLDRDDPSDA (SEQ ID NO:30); ee) PGC1a: QEAEEPSLLKKLLLAPANTQL (SEQ ID NO:31); ff) PGC1b: PEVDELSLLQKLLLATSYPTS (SEQ ID NO:32); gg) PRC: VSPREGSSLHKLLTLSRTPPE (SEQ ID NO:33); hh) TRAP220–1: SKVSQNPILTSLLQITGNGGS (SEQ ID NO:34); ii) TRAP220–2: GNTKNHPMLMNLLKDNPAQDF (SEQ ID NO:35); jj) ASC2–1: DVTLTSPLLVNLLQSDISAGH (SEQ ID NO:36); kk) ASC2–2: AMREAPTSLSQLLDNSGAPNV (SEQ ID NO:37); ll) CBP-1: DAASKHKQLSELLRGGSGSSI (SEQ ID NO:38); mm) CBP-2: KRKLIQQQLVLLLHAHKCQRR (SEQ ID NO:39); nn) P300: DAASKHKQLSELLRSGSSPNL (SEQ ID NO:40); oo) CIA: GHPPAIQSLINLLADNRYLTA (SEQ ID NO:41); pp) ARA70–1: TLQQQAQQLYSLLGQFNCLTH (SEQ ID NO:42); qq) ARA70–2: GSRETSEKFKLLFQSYNVNDW (SEQ ID NO:43); rr) TIF1: NANYPRSILTSLLLNSSQSST (SEQ ID NO:44); ss) NSD1: IPIEPDYKFSTLLMMLKDMHD (SEQ ID NO:45); tt) SMAP: ATPPPSPLLSELLKKGSLLPT (SEQ ID NO:46); uu) Tip60: VDGHERAMLKRLLRIDSKCLH (SEQ ID NO:47); vv) ERAP140: HEDLDKVKLIEYYLTKNKEGP (SEQ ID NO:48); ww) Nix1: ESPEFCLGLQTLLSLKCCIDL (SEQ ID NO:49); xx) LCoR: AATTQNPVLSKLLMADQDSPL (SEQ ID NO:50); yy) CoRNR1 (N-CoR):

MGQVPRTHRLITLADHICQIITQDFARNQV (SEQ ID NO:51); zz) CoRNR2 (N-CoR): NLGLEDIIRKALMG (SEQ ID NO:52); aaa) CoRNR1 (SMRT): APGVKGHQRVVTLAQHISEVITQDTYRHHPQQLSAPLPAP (SEQ ID NO:53); bbb) CoRNR2 (SMRT): NMGLEAIIRKALMG (SEQ ID NO:54); ccc) RIP140-C: RLTKTNPILYYMLQKGGNSVA (SEQ ID NO:55); ddd) RIP140-1: QDSIVLTYLEGLLMHQAAGGS (SEQ ID NO:56); eee) RIP140-2: KGKQDSTLLASLLQSFSSRLQ (SEQ ID NO:57); fff) RIP140-3: CYGVASSHLKTLLKKSKVKDQ (SEQ ID NO:58); ggg) RIP140-4: KPSVACSQLALLLSSEAHLQQ (SEQ ID NO:59); hhh) RIP140-5: KQAANNSLLLHLLKSQTIPKP (SEQ ID NO:60); iii) RIP140-6: NSHQKVTLLQLLLGHKNEENV (SEQ ID NO:61); jjj) RIP140-7: NLLERRTVLQLLLGNPTKGRV (SEQ ID NO:62); kkk) RIP140-8: FSFSKNGLLSRLLRQNQDSYL (SEQ ID NO:63); lll) RIP140-9: RESKSFNVLKQLLLSENCVRD (SEQ ID NO:64); mmm) PRIC285-1: ELNADDAILRELLDESQKVMV (SEQ ID NO:65); nnn) PRIC285-2: YENLPPAALRKLLRAEPERYR (SEQ ID NO:66); ooo) PRIC285-3: MAFAGDEVLVQLLSGDKAPEG (SEQ ID NO:67); ppp) PRIC285-4: SCCYLCIRLEGLLAPTASPRP (SEQ ID NO:68); and qqq) PRIC285-5: PSNKSVDVLAGLLLRRMELKP (SEQ ID NO:69). In some cases, the synthetic stimulatory ICR is a synthetic chimeric antigen receptor (CAR) or portion thereof. In some cases, the synthetic stimulatory ICR is a synthetic T cell receptor (TCR) or portion thereof.

[0009] The present disclosure provides a heterodimeric, conditionally repressible synthetic chimeric antigen receptor (CAR) comprising: a) a synthetic stimulatory CAR comprising: i) a extracellular recognition domain; ii) a transmembrane domain linked to the extracellular recognition domain; iii) a first member of a dimerization pair linked to the transmembrane domain; and iv) an intracellular stimulation domain; and b) a synthetic CAR repressor comprising: i) a second member of the dimerization pair; and ii) an intracellular inhibitory domain linked to the second member of the dimerization pair, wherein the first member of the dimerization pair comprises a ligand-binding domain (LBD) of a nuclear hormone receptor, and the second member of the dimerization pair comprises a co-regulator of the nuclear hormone receptor, or wherein the first member of the dimerization pair is a co-regulator of a nuclear hormone receptor, and the second member of the dimerization pair comprises an LBD of the nuclear hormone receptor; and wherein the synthetic stimulatory CAR and the synthetic CAR repressor are dimerized in the presence of a ligand that induces binding of the LBD to the co-regulator. In some cases, the synthetic CAR repressor further comprises a transmembrane domain linked to the second member of the dimerization pair, the intracellular inhibitory domain or both. In some cases, the LBD of the nuclear hormone binding member of the dimerization pair is an LBD of a nuclear hormone receptor selected from estrogen receptor, an ecdysone receptor, a PPARγ receptor, a glucocorticoid receptor, an androgen receptor, a thyroid hormone receptor, a mineralocorticoid receptor, a progesterone receptor, a vitamin D receptor, a PPARβ receptor, a PPARα receptor, a pregnane X receptor, a liver X receptor, a farnesoid X receptor, a retinoid X receptor, a RAR-related orphan receptor, and a retinoic acid receptor. In some

cases, the co-regulator of the nuclear hormone receptor is selected from SRC1, GRIP1, AIB1, PGC1a, PGC1b, PRC, TRAP220, ASC2, CBP, P300, CIA, ARA70, TIF1, NSD1, SMAP, Tip60, ERAP140, Nix1, LCoR, N-CoR, SMRT, RIP140, and PRIC285. In some cases, the co-regulator of the nuclear hormone receptor is selected from: a) SRC1: CPSSHSSLTERHKILHRLLQEGSPS (SEQ ID NO:1); b) SRC1–2: SLTARHKILHRLLQEGSPSDI (SEQ ID NO:2); c) SRC3-1: ESKGHKKLLQLLTCSSDDR (SEQ ID NO:3); d) SRC3: PKKENNALLRYLLDRDDPSDV (SEQ ID NO:4); e) PGC-1: AEEPSLLKKLLLAPANT (SEQ ID NO:5); f) PGC1a: QEAEEPSLLKKLLLAPANTQL (SEQ ID NO:6); g) TRAP220–1: SKVSQNPILTSLLQITGNGGS (SEQ ID NO:7); h) NCoR (2051–2075): GHSFADPASNLGLEDIIRKALMGSF (SEQ ID NO:8); i) NR0B1: PRQGSILYSMLTSAKQT (SEQ ID NO:9); j) NRIP1: AANNSLLLHLLKSQTIP (SEQ ID NO:10); k) TIF2: PKKKENALLRYLLDKDDTKDI (SEQ ID NO:11); l) CoRNR Box: DAFQLRQLILRGLQDD (SEQ ID NO:12); m) αβV: SPGSREWFKDMLS (SEQ ID NO:13); n) TRAP220-2: GNTKNHPMLMNLLKDNPAQDF (SEQ ID NO:14); o) EA2: SSKGVLWRMLAEPVSR (SEQ ID NO:15); p) TA1: SRTLQLDWGTLYWSR (SEQ ID NO:16); q) EAB1: SSNHQSSRLIELLSR (SEQ ID NO:17); r) SRC2: LKEKHKILHRLLQDSSSPV (SEQ ID NO:18); s) SRC1-3: QAQQKSLLQQLLTE (SEQ ID NO:19); t) SRC1–1: KYSQTSHKLVQLLTTTAEQQL (SEQ ID NO:20); u) SRC1–2: SLTARHKILHRLLQEGSPSDI (SEQ ID NO:21); v) SRC1–3: KESKDHQLLRYLLDKDEKDLR (SEQ ID NO:22); w) SRC1–4a: PQAQQKSLLQQLLTE (SEQ ID NO:23); x) SRC1–4b: PQAQQKSLRQQLLTE (SEQ ID NO:24); y) GRIP1–1: HDSKGQTKLLQLLTTKSDQME (SEQ ID NO:25); z) GRIP1–2: SLKEKHKILHRLLQDSSSPVD (SEQ ID NO:26); aa) GRIP1–3: PKKKENALLRYLLDKDDTKDI (SEQ ID NO:27); bb) AIB1–1: LESKGHKKLLQLLTCSSDDRG (SEQ ID NO:28); cc) AIB1–2: LLQEKHRILHKLLQNGNSPAE (SEQ ID NO:29); dd) AIB1–3: KKKENNALLRYLLDRDDPSDA (SEQ ID NO:30); ee) PGC1a: QEAEEPSLLKKLLLAPANTQL (SEQ ID NO:31); ff) PGC1b: PEVDELSLLQKLLLATSYPTS (SEQ ID NO:32); gg) PRC: VSPREGSSLHKLLTLSRTPPE (SEQ ID NO:33); hh) TRAP220–1: SKVSQNPILTSLLQITGNGGS (SEQ ID NO:34); ii) TRAP220–2: GNTKNHPMLMNLLKDNPAQDF (SEQ ID NO:35); jj) ASC2–1: DVTLTSPLLVNLLQSDISAGH (SEQ ID NO:36); kk) ASC2–2: AMREAPTSLSQLLDNSGAPNV (SEQ ID NO:37); ll) CBP-1: DAASKHKQLSELLRGGSGSSI (SEQ ID NO:38); mm) CBP-2: KRKLIQQQLVLLLHAHKCQRR (SEQ ID NO:39); nn) P300: DAASKHKQLSELLRSGSSPNL (SEQ ID NO:40); oo) CIA: GHPPAIQSLINLLADNRYLTA (SEQ ID NO:41); pp) ARA70–1: TLQQQAQQLYSLLGQFNCLTH (SEQ ID NO:42); qq) ARA70–2: GSRETSEKFKLLFQSYNVNDW (SEQ ID NO:43); rr) TIF1: NANYPRSILTSLLLNSSQSST (SEQ ID NO:44); ss) NSD1: IPIEPDYKFSTLLMMLKDMHD (SEQ ID NO:45); tt) SMAP: ATPPPSPLLSELLKKGSLLPT (SEQ ID NO:46); uu) Tip60: VDGHERAMLKRLLRIDSKCLH (SEQ ID NO:47); vv) ERAP140: HEDLDKVKLIEYYLTKNKEGP (SEQ ID NO:48); ww) Nix1: ESPEFCLGLQTLLSLKCCIDL (SEQ

ID NO:49); xx) LCoR: AATTQNPVLSKLLMADQDSPL (SEQ ID NO:50); yy) CoRNR1 (N-CoR): MGQVPRTHRLITLADHICQIITQDFARNQV (SEQ ID NO:51); zz) CoRNR2 (N-CoR): NLGLEDIIRKALMG (SEQ ID NO:52); aaa) CoRNR1 (SMRT): APGVKGHQRVVTLAQHISEVITQDTYRHHPQQLSAPLPAP (SEQ ID NO:53); bbb) CoRNR2 (SMRT): NMGLEAIIRKALMG (SEQ ID NO:54); ccc) RIP140-C: RLTKTNPILYYMLQKGGNSVA (SEQ ID NO:55); ddd) RIP140-1: QDSIVLTYLEGLLMHQAAGGS (SEQ ID NO:56); eee) RIP140-2: KGKQDSTLLASLLQSFSSRLQ (SEQ ID NO:57); fff) RIP140-3: CYGVASSHLKTLLKKSKVKDQ (SEQ ID NO:58); ggg) RIP140-4: KPSVACSQLALLLSSEAHLQQ (SEQ ID NO:59); hhh) RIP140-5: KQAANNSLLLHLLKSQTIPKP (SEQ ID NO:60); iii) RIP140-6: NSHQKVTLLQLLLGHKNEENV (SEQ ID NO:61); jjj) RIP140-7: NLLERRTVLQLLLGNPTKGRV (SEQ ID NO:62); kkk) RIP140-8: FSFSKNGLLSRLLRQNQDSYL (SEQ ID NO:63); lll) RIP140-9: RESKSFNVLKQLLLSENCVRD (SEQ ID NO:64); mmm) PRIC285-1: ELNADDAILRELLDESQKVMV (SEQ ID NO:65); nnn) PRIC285-2: YENLPPAALRKLLRAEPERYR (SEQ ID NO:66); ooo) PRIC285-3: MAFAGDEVLVQLLSGDKAPEG (SEQ ID NO:67); ppp) PRIC285-4: SCCYLCIRLEGLLAPTASPRP (SEQ ID NO:68); and qqq) PRIC285-5: PSNKSVDVLAGLLLRRMELKP (SEQ ID NO:69).

[0010] The present disclosure provides a heterodimeric, conditionally repressible synthetic T cell receptor (TCR) comprising: a) a synthetic stimulatory TCR comprising: i) a transmembrane domain; ii) a first member of a dimerization pair linked to the transmembrane domain; iii) an engineered TCR polypeptide comprising at least one TCR alpha or beta chain, wherein the at least one TCR alpha or beta chain is linked to the transmembrane domain or the first member of a dimerization pair; and b) a synthetic TCR repressor comprising: i) a second member of the dimerization pair; and ii) an intracellular inhibitory domain linked to the second member of the dimerization pair, wherein the first member of the dimerization pair comprises a ligand-binding domain (LBD) of a nuclear hormone receptor, and the second member of the dimerization pair comprises a co-regulator of the nuclear hormone receptor, or wherein the first member of the dimerization pair is a co-regulator of a nuclear hormone receptor, and the second member of the dimerization pair comprises an LBD of the nuclear hormone receptor; and wherein the synthetic stimulatory TCR and the synthetic TCR repressor are dimerized in the presence of a dimerization agent that induces binding of the LBD to the co-regulator. In some cases, the synthetic TCR repressor further comprises a transmembrane domain linked to the second member of the dimerization pair, the intracellular inhibitory domain or both. In some cases, the engineered TCR polypeptide further comprises a TCR gamma chain. In some cases, the LBD of the nuclear hormone binding member of the dimerization pair is an LBD of a nuclear hormone receptor selected from estrogen receptor, an ecdysone receptor, a PPARγ receptor, a glucocorticoid receptor, an androgen receptor, a thyroid hormone receptor, a mineralocorticoid receptor, a progesterone receptor, a vitamin D receptor, a PPARβ receptor, a PPARα receptor, a pregnane X receptor, a liver X receptor, a farnesoid X receptor, a

retinoid X receptor, a RAR-related orphan receptor, and a retinoic acid receptor. In some cases, the co-regulator of the nuclear hormone receptor is selected from SRC1, GRIP1, AIB1, PGC1a, PGC1b, PRC, TRAP220, ASC2, CBP, P300, CIA, ARA70, TIF1, NSD1, SMAP, Tip60, ERAP140, Nix1, LCoR, N-CoR, SMRT, RIP140, and PRIC285. In some cases, the co-regulator of the nuclear hormone receptor is selected from: a) SRC1: CPSSHSSLTERHKILHRLLQEGSPS (SEQ ID NO:1); b) SRC1–2: SLTARHKILHRLLQEGSPSDI (SEQ ID NO:2); c) SRC3-1: ESKGHKKLLQLLTCSSDDR (SEQ ID NO:3); d) SRC3: PKKENNALLRYLLDRDDPSDV (SEQ ID NO:4); e) PGC-1: AEEPSLLKKLLLAPANT (SEQ ID NO:5); f) PGC1a: QEAEEPSLLKKLLLAPANTQL (SEQ ID NO:6); g) TRAP220–1: SKVSQNPILTSLLQITGNGGS (SEQ ID NO:7); h) NCoR (2051–2075): GHSFADPASNLGLEDIIRKALMGSF (SEQ ID NO:8); i) NR0B1: PRQGSILYSMLTSAKQT (SEQ ID NO:9); j) NRIP1: AANNSLLLHLLKSQTIP (SEQ ID NO:10); k) TIF2: PKKKENALLRYLLDKDDTKDI (SEQ ID NO:11); l) CoRNR Box: DAFQLRQLILRGLQDD (SEQ ID NO:12); m) αβV: SPGSREWFKDMLS (SEQ ID NO:13); n) TRAP220-2: GNTKNHPMLMNLLKDNPAQDF (SEQ ID NO:14); o) EA2: SSKGVLWRMLAEPVSR (SEQ ID NO:15); p) TA1: SRTLQLDWGTLYWSR (SEQ ID NO:16); q) EAB1: SSNHQSSRLIELLSR (SEQ ID NO:17); r) SRC2: LKEKHKILHRLLQDSSSPV (SEQ ID NO:18); s) SRC1-3: QAQQKSLLQQLLTE (SEQ ID NO:19); t) SRC1–1: KYSQTSHKLVQLLTTTAEQQL (SEQ ID NO:20); u) SRC1–2: SLTARHKILHRLLQEGSPSDI (SEQ ID NO:21); v) SRC1–3: KESKDHQLLRYLLDKDEKDLR (SEQ ID NO:22); w) SRC1–4a: PQAQQKSLLQQLLTE (SEQ ID NO:23); x) SRC1–4b: PQAQQKSLRQQLLTE (SEQ ID NO:24); y) GRIP1–1: HDSKGQTKLLQLLTTKSDQME (SEQ ID NO:25); z) GRIP1–2: SLKEKHKILHRLLQDSSSPVD (SEQ ID NO:26); aa) GRIP1–3: PKKKENALLRYLLDKDDTKDI (SEQ ID NO:27); bb) AIB1–1: LESKGHKKLLQLLTCSSDDRG (SEQ ID NO:28); cc) AIB1–2: LLQEKHRILHKLLQNGNSPAE (SEQ ID NO:29); dd) AIB1–3: KKKENNALLRYLLDRDDPSDA (SEQ ID NO:30); ee) PGC1a: QEAEEPSLLKKLLLAPANTQL (SEQ ID NO:31); ff) PGC1b: PEVDELSLLQKLLLATSYPTS (SEQ ID NO:32); gg) PRC: VSPREGSSLHKLLTLSRTPPE (SEQ ID NO:33); hh) TRAP220–1: SKVSQNPILTSLLQITGNGGS (SEQ ID NO:34); ii) TRAP220–2: GNTKNHPMLMNLLKDNPAQDF (SEQ ID NO:35); jj) ASC2–1: DVTLTSPLLVNLLQSDISAGH (SEQ ID NO:36); kk) ASC2–2: AMREAPTSLSQLLDNSGAPNV (SEQ ID NO:37); ll) CBP-1: DAASKHKQLSELLRGGSGSSI (SEQ ID NO:38); mm) CBP-2: KRKLIQQQLVLLLHAHKCQRR (SEQ ID NO:39); nn) P300: DAASKHKQLSELLRSGSSPNL (SEQ ID NO:40); oo) CIA: GHPPAIQSLINLLADNRYLTA (SEQ ID NO:41); pp) ARA70–1: TLQQQAQQLYSLLGQFNCLTH (SEQ ID NO:42); qq) ARA70–2: GSRETSEKFKLLFQSYNVNDW (SEQ ID NO:43); rr) TIF1: NANYPRSILTSLLLNSSQSST (SEQ ID NO:44); ss) NSD1: IPIEPDYKFSTLLMMLKDMHD (SEQ ID NO:45); tt) SMAP: ATPPPSPLLSELLKKGSLLPT (SEQ ID NO:46); uu) Tip60: VDGHERAMLKRLLRIDSKCLH (SEQ ID NO:47); vv) ERAP140:

HEDLDKVKLIEYYLTKNKEGP (SEQ ID NO:48); ww) Nix1: ESPEFCLGLQTLLSLKCCIDL (SEQ ID NO:49); xx) LCoR: AATTQNPVLSKLLMADQDSPL (SEQ ID NO:50); yy) CoRNR1 (N-CoR): MGQVPRTHRLITLADHICQIITQDFARNQV (SEQ ID NO:51); zz) CoRNR2 (N-CoR): NLGLEDIIRKALMG (SEQ ID NO:52); aaa) CoRNR1 (SMRT): APGVKGHQRVVTLAQHISEVITQDTYRHHPQQLSAPLPAP (SEQ ID NO:53); bbb) CoRNR2 (SMRT): NMGLEAIIRKALMG (SEQ ID NO:54); ccc) RIP140-C: RLTKTNPILYYMLQKGGNSVA (SEQ ID NO:55); ddd) RIP140-1: QDSIVLTYLEGLLMHQAAGGS (SEQ ID NO:56); eee) RIP140-2: KGKQDSTLLASLLQSFSSRLQ (SEQ ID NO:57); fff) RIP140-3: CYGVASSHLKTLLKKSKVKDQ (SEQ ID NO:58); ggg) RIP140-4: KPSVACSQLALLLSSEAHLQQ (SEQ ID NO:59); hhh) RIP140-5: KQAANNSLLLHLLKSQTIPKP (SEQ ID NO:60); iii) RIP140-6: NSHQKVTLLQLLLGHKNEENV (SEQ ID NO:61); jjj) RIP140-7: NLLERRTVLQLLLGNPTKGRV (SEQ ID NO:62); kkk) RIP140-8: FSFSKNGLLSRLLRQNQDSYL (SEQ ID NO:63); lll) RIP140-9: RESKSFNVLKQLLLSENCVRD (SEQ ID NO:64); mmm) PRIC285-1: ELNADDAILRELLDESQKVMV (SEQ ID NO:65); nnn) PRIC285-2: YENLPPAALRKLLRAEPERYR (SEQ ID NO:66); ooo) PRIC285-3: MAFAGDEVLVQLLSGDKAPEG (SEQ ID NO:67); ppp) PRIC285-4: SCCYLCIRLEGLLAPTASPRP (SEQ ID NO:68); and qqq) PRIC285-5: PSNKSVDVLAGLLLRRMELKP (SEQ ID NO:69).

[0011] The present disclosure provides a heterodimeric, conditionally active chimeric antigen receptor (CAR) comprising: a) a first polypeptide comprising: i) a first member of a specific binding pair; ii) a first modulatory domain; iii) a first member of a dimerization pair; and iv) a transmembrane domain interposed between the first member of a specific binding pair and the first modulatory domain; and b) a second polypeptide comprising: i) a transmembrane domain; ii) a second modulatory domain; iii) a second member of the dimerization pair; and iv) an intracellular signaling domain; or comprising: a) a first polypeptide comprising: i) a first member of a specific binding pair; ii) a modulatory domain; iii) a first member of a dimerization pair; iv) a transmembrane domain interposed between the first member of a specific binding pair and the modulatory domain; and b) a second polypeptide comprising: i) a second member of the dimerization pair; and ii) an intracellular signaling domain, wherein the first member of the dimerization pair comprises a ligand-binding domain (LBD) of a nuclear hormone receptor, and the second member of the dimerization pair comprises a co-regulator of the nuclear hormone receptor, or wherein the first member of the dimerization pair is a co-regulator of a nuclear hormone receptor, and the second member of the dimerization pair comprises an LBD of the nuclear hormone receptor; and wherein the first polypeptide and the second polypeptide are dimerized in the presence of a dimerizing agent that induces binding of the LBD to the co-regulator.In some cases, the first polypeptide comprises a hinge region interposed between the first member of the specific binding pair and the transmembrane domain. In some cases, the first member of the specific binding pair is an antibody or antibody fragment, a ligand, or a receptor. In some cases, the hinge region is an immunoglobulin IgG hinge region or a hinge

derived from CD8. In some cases, the first and second modulatory domains are selected from 4-1BB (CD137), CD28, ICOS, BTLA, OX-40, CD27, CD30, GITR, HVEM, DAP10, DAP12, and CD28. In some cases, the intracellular signaling domain is selected from ZAP70 and CD3-zeta. In some cases, the intracellular signaling domain comprises an immunoreceptor tyrosine-based activation motif (ITAM). In some cases, the LBD of the nuclear hormone binding member of the dimerization pair is an LBD of a nuclear hormone receptor selected from estrogen receptor, an ecdysone receptor, a PPARγ receptor, a glucocorticoid receptor, an androgen receptor, a thyroid hormone receptor, a mineralocorticoid receptor, a progesterone receptor, a vitamin D receptor, a PPARβ receptor, a PPARα receptor, a pregnane X receptor, a liver X receptor, a farnesoid X receptor, a retinoid X receptor, a RAR-related orphan receptor, and a retinoic acid receptor. In some cases, the LBD of the nuclear hormone binding member of the dimerization pair is an LBD of a nuclear hormone receptor selected from estrogen receptor, an ecdysone receptor, a PPARγ receptor, a glucocorticoid receptor, an androgen receptor, a thyroid hormone receptor, a mineralocorticoid receptor, a progesterone receptor, a vitamin D receptor, a PPARβ receptor, a PPARα receptor, a pregnane X receptor, a liver X receptor, a farnesoid X receptor, a retinoid X receptor, a RAR-related orphan receptor, and a retinoic acid receptor. In some cases, the co-regulator of the nuclear hormone receptor is selected from SRC1, GRIP1, AIB1, PGC1a, PGC1b, PRC, TRAP220, ASC2, CBP, P300, CIA, ARA70, TIF1, NSD1, SMAP, Tip60, ERAP140, Nix1, LCoR, N-CoR, SMRT, RIP140, and PRIC285. In some cases, the co-regulator of the nuclear hormone receptor is selected from: a) SRC1: CPSSHSSLTERHKILHRLLQEGSPS (SEQ ID NO:1); b) SRC1–2: SLTARHKILHRLLQEGSPSDI (SEQ ID NO:2); c) SRC3-1: ESKGHKKLLQLLTCSSDDR (SEQ ID NO:3); d) SRC3: PKKENNALLRYLLDRDDPSDV (SEQ ID NO:4); e) PGC-1: AEEPSLLKKLLLAPANT (SEQ ID NO:5); f) PGC1a: QEAEEPSLLKKLLLAPANTQL (SEQ ID NO:6); g) TRAP220–1: SKVSQNPILTSLLQITGNGGS (SEQ ID NO:7); h) NCoR (2051–2075): GHSFADPASNLGLEDIIRKALMGSF (SEQ ID NO:8); i) NR0B1: PRQGSILYSMLTSAKQT (SEQ ID NO:9); j) NRIP1: AANNSLLLHLLKSQTIP (SEQ ID NO:10); k) TIF2: PKKKENALLRYLLDKDDTKDI (SEQ ID NO:11); l) CoRNR Box: DAFQLRQLILRGLQDD (SEQ ID NO:12); m) αβV: SPGSREWFKDMLS (SEQ ID NO:13); n) TRAP220-2: GNTKNHPMLMNLLKDNPAQDF (SEQ ID NO:14); o) EA2: SSKGVLWRMLAEPVSR (SEQ ID NO:15); p) TA1: SRTLQLDWGTLYWSR (SEQ ID NO:16); q) EAB1: SSNHQSSRLIELLSR (SEQ ID NO:17); r) SRC2: LKEKHKILHRLLQDSSSPV (SEQ ID NO:18); s) SRC1-3: QAQQKSLLQQLLTE (SEQ ID NO:19); t) SRC1–1: KYSQTSHKLVQLLTTTAEQQL (SEQ ID NO:20); u) SRC1–2: SLTARHKILHRLLQEGSPSDI (SEQ ID NO:21); v) SRC1–3: KESKDHQLLRYLLDKDEKDLR (SEQ ID NO:22); w) SRC1–4a: PQAQQKSLLQQLLTE (SEQ ID NO:23); x) SRC1–4b: PQAQQKSLRQQLLTE (SEQ ID NO:24); y) GRIP1–1: HDSKGQTKLLQLLTTKSDQME (SEQ ID NO:25); z) GRIP1–2: SLKEKHKILHRLLQDSSSPVD (SEQ ID NO:26); aa) GRIP1–3:

PKKKENALLRYLLDKDDTKDI (SEQ ID NO:27); bb) AIB1–1: LESKGHKKLLQLLTCSSDDRG (SEQ ID NO:28); cc) AIB1–2: LLQEKHRILHKLLQNGNSPAE (SEQ ID NO:29); dd) AIB1–3: KKKENNALLRYLLDRDDPSDA (SEQ ID NO:30); ee) PGC1a: QEAEEPSLLKKLLLAPANTQL (SEQ ID NO:31); ff) PGC1b: PEVDELSLLQKLLLATSYPTS (SEQ ID NO:32); gg) PRC: VSPREGSSLHKLLTLSRTPPE (SEQ ID NO:33); hh) TRAP220–1: SKVSQNPILTSLLQITGNGGS (SEQ ID NO:34); ii) TRAP220–2: GNTKNHPMLMNLLKDNPAQDF (SEQ ID NO:35); jj) ASC2–1: DVTLTSPLLVNLLQSDISAGH (SEQ ID NO:36); kk) ASC2–2: AMREAPTSLSQLLDNSGAPNV (SEQ ID NO:37); ll) CBP-1: DAASKHKQLSELLRGGSGSSI (SEQ ID NO:38); mm) CBP-2: KRKLIQQQLVLLLHAHKCQRR (SEQ ID NO:39); nn) P300: DAASKHKQLSELLRSGSSPNL (SEQ ID NO:40); oo) CIA: GHPPAIQSLINLLADNRYLTA (SEQ ID NO:41); pp) ARA70–1: TLQQQAQQLYSLLGQFNCLTH (SEQ ID NO:42); qq) ARA70–2: GSRETSEKFKLLFQSYNVNDW (SEQ ID NO:43); rr) TIF1: NANYPRSILTSLLLNSSQSST (SEQ ID NO:44); ss) NSD1: IPIEPDYKFSTLLMMLKDMHD (SEQ ID NO:45); tt) SMAP: ATPPPSPLLSELLKKGSLLPT (SEQ ID NO:46); uu) Tip60: VDGHERAMLKRLLRIDSKCLH (SEQ ID NO:47); vv) ERAP140: HEDLDKVKLIEYYLTKNKEGP (SEQ ID NO:48); ww) Nix1: ESPEFCLGLQTLLSLKCCIDL (SEQ ID NO:49); xx) LCoR: AATTQNPVLSKLLMADQDSPL (SEQ ID NO:50); yy) CoRNR1 (N-CoR): MGQVPRTHRLITLADHICQIITQDFARNQV (SEQ ID NO:51); zz) CoRNR2 (N-CoR): NLGLEDIIRKALMG (SEQ ID NO:52); aaa) CoRNR1 (SMRT): APGVKGHQRVVTLAQHISEVITQDTYRHHPQQLSAPLPAP (SEQ ID NO:53); bbb) CoRNR2 (SMRT): NMGLEAIIRKALMG (SEQ ID NO:54); ccc) RIP140-C: RLTKTNPILYYMLQKGGNSVA (SEQ ID NO:55); ddd) RIP140-1: QDSIVLTYLEGLLMHQAAGGS (SEQ ID NO:56); eee) RIP140-2: KGKQDSTLLASLLQSFSSRLQ (SEQ ID NO:57); fff) RIP140-3: CYGVASSHLKTLLKKSKVKDQ (SEQ ID NO:58); ggg) RIP140-4: KPSVACSQLALLLSSEAHLQQ (SEQ ID NO:59); hhh) RIP140-5: KQAANNSLLLHLLKSQTIPKP (SEQ ID NO:60); iii) RIP140-6: NSHQKVTLLQLLLGHKNEENV (SEQ ID NO:61); jjj) RIP140-7: NLLERRTVLQLLLGNPTKGRV (SEQ ID NO:62); kkk) RIP140-8: FSFSKNGLLSRLLRQNQDSYL (SEQ ID NO:63); lll) RIP140-9: RESKSFNVLKQLLLSENCVRD (SEQ ID NO:64); mmm) PRIC285-1: ELNADDAILRELLDESQKVMV (SEQ ID NO:65); nnn) PRIC285-2: YENLPPAALRKLLRAEPERYR (SEQ ID NO:66); ooo) PRIC285-3: MAFAGDEVLVQLLSGDKAPEG (SEQ ID NO:67); ppp) PRIC285-4: SCCYLCIRLEGLLAPTASPRP (SEQ ID NO:68); and qqq) PRIC285-5: PSNKSVDVLAGLLLRRMELKP (SEQ ID NO:69). In some cases, the first member of the specific binding pair is a single-chain Fv. In some cases, the first member of the specific binding pair binds an epitope present on a cell, on a solid surface, or a lipid bilayer. In some cases, the cell is a cancer cell.

[0012] The present disclosure provides a mammalian cell genetically modified to produce the heterodimeric, conditionally active polypeptide or receptor as described above or elsewhere herein. In some cases, the

cell is a stem cell, a progenitor cell, or a cell derived from a stem cell or a progenitor cell. In some cases, the cell is a T lymphocyte or an NK cell.

[0013] The present disclosure provides a nucleic acid comprising nucleotide sequences encoding the heterodimeric, conditionally active receptor or polypeptide as described above or elsewhere herein. In some cases, the nucleotide sequences are operably linked to a promoter. In some cases, the promoter is an inducible promoter. In some cases, the promoter is a cell type-specific or tissue-specific promoter. In some cases, the promoter is a T lymphocyte-specific promoter or an NK cell-specific promoter. In some cases, the nucleic acid is *in vitro* transcribed RNA. The present disclosure provides a recombinant expression vector comprising the nucleic acid. In some cases, the recombinant expression vector is a viral vector, e.g., a lentiviral vector, a retroviral vector, or an adeno-associated viral vector.

[0014] The present disclosure provides a method of modulating an activity of a eukaryotic cell, the method comprising: a) expressing the heterodimeric, conditionally active polypeptide or receptor as described above, or elsewhere herein, in the eukaryotic cell; and b) contacting the cell with the ligand.

[0015] The present disclosure provides a method of modulating an activity of a T lymphocyte, the method comprising contacting the T lymphocyte with a dimerizing agent and a second member of a specific binding pair, wherein the T lymphocyte is genetically modified to produce a heterodimeric, conditionally active receptor as described above, or elsewhere herein, and wherein, in the presence of the dimerizing agent and the second member of a specific binding pair, the heterodimeric, conditionally active receptor dimerizes and modulates an activity of the T lymphocyte, thereby producing a modulated T lymphocyte. In some cases, the second member of a specific binding pair is an antigen. In some cases, the contacting occurs *in vivo*. In some cases, the T lymphocyte is activated, thereby producing an activated T lymphocyte. In some cases, the activated T lymphocyte mediates killing of a target cell. In some cases, the activated T lymphocyte produces IL-2 and/or IFN-γ. In some cases, the target cell is a cancer cell.

[0016] The present disclosure provides a method of making the cell of any one of claims 66-68, the method comprising genetically modifying a mammalian cell with an expression vector comprising nucleotide sequences encoding the heterodimeric, conditionally active receptor or polypeptide as described above or elsewhere herein, or genetically modifying a mammalian cell with an RNA comprising nucleotide sequences encoding the heterodimeric, conditionally active receptor as described above or elsewhere herein. In some cases, the genetic modification is carried out *ex vivo*. In some cases, the cell is a T lymphocyte, a stem cell, an NK cell, a progenitor cell, a cell derived from a stem cell, or a cell derived from a progenitor cell.

[0017] The present disclosure provides a method of treating a cancer in an individual, the method comprising: i) genetically modifying T lymphocytes obtained from the individual with an expression vector comprising nucleotide sequences encoding the heterodimeric, conditionally active chimeric

antigen receptor (CAR) as described above or elsewhere herein, wherein the antigen-binding domain of the heterodimeric, conditionally active CAR is specific for an epitope on a cancer cell in the individual, and wherein said genetic modification is carried out *ex vivo*; ii) introducing the genetically modified T lymphocytes into the individual; and iii) administering to the individual an effective amount of a dimerizing agent, wherein the dimerizing agent induces dimerization of the heterodimeric, conditionally active receptor, wherein said dimerization provides for activation of the genetically modified T lymphocytes and killing of the cancer cell, thereby treating the cancer. In some cases, the dimerizing agent is a nuclear hormone that binds the LBD of the nuclear hormone receptor and the co-regulator.

[0018] The present disclosure provides a method of modulating the activity of a host cell, the method comprising contacting the host cell with a dimerizing agent and a second member of a specific binding pair, wherein the T lymphocyte is genetically modified to produce a heterodimeric, conditionally active receptor as described above or elsewhere herein, and wherein, in the presence of the dimerizing agent and the second member of a specific binding pair, the heterodimeric, conditionally active receptor dimerizes and modulates at least one activity of the host cell. In some cases, the activity is proliferation, cell survival, apoptosis, gene expression, or immune activation. In some cases, the second member of a specific binding pair is an antigen.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1A-1F depict amino acid sequences of mineralocorticoid receptors (MR). FIG. 1A: full-length MR amino acid sequence; FIG. 1B-1E: amino acid sequences of ligand-binding domain (LBD) of MR; FIG. 1F: multiple sequence alignment of LBD of MR of various species. (SEQ ID NOs:70-84).

FIG. 2A-2I depict amino acid sequences of androgen receptors (AR). FIG. 2A: full-length AR amino acid sequence; FIG. 2B-2I: amino acid sequences of LBD of AR. (SEQ ID NOs:85-93).

FIG. 3A-3D depict amino acid sequences of progesterone receptors (PR). FIG. 3A: full-length PR amino acid sequence; FIG. 3B-3C: amino acid sequences of LBD of PR; FIG. 3D: multiple sequence alignment of LBD of PR of various species. (SEQ ID NOs:94-103).

FIG. 4A-4D depict amino acid sequences of thyroid hormone receptor-beta (TRβ). FIG. 3A: full-length PR amino acid sequence; FIG. 3B-3C: amino acid sequences of LBD of TRβ; FIG. 3D: multiple sequence alignment of LBD of TRβ of various species. (SEQ ID NO:104-118).

FIG. 5A-5H depict amino acid sequences of estrogen receptor-alpha (ERα). FIG. 5A: full-length ERα amino acid sequence; FIG. 5B-5G: amino acid sequences of LBD of ERα; FIG. 5H; multiple sequence alignment of LBD of ERα of various species. (SEQ ID NO:119-133).

FIG. 6A-6C depict amino acid sequences of estrogen receptor-beta (ERβ). FIG. 6A: full-length ERβ amino acid sequence; FIG. 6B: amino acid sequence of LBD of ERβ; FIG. 6C; multiple sequence alignment of LBD of ERβ of various species. (SEQ ID NO:134-143).

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FIG. 7A-7E depict amino acid sequences of peroxisome proliferator-activated receptor-gamma (PPAR-γ). FIG. 7A: full-length PPAR-γ amino acid sequence; FIG. 7B-7D: amino acid sequences of LBD of PPAR-γ; FIG. 7E: multiple sequence alignment of LBD of PPAR-γ of various species. (SEQ ID NOs:144-157).

FIG. 8A-8C depict amino acid sequences of glucocorticoid receptor (GR). FIG. 8A: full-length GR amino acid sequence; FIG. 8B: amino acid sequence of LBD of GR; FIG. 8C; multiple sequence alignment of LBD of GR of various species. (SEQ ID NOs:158-166).

FIG. 9A-9C depict amino acid sequences of vitamin D receptor (VDR). FIG. 9A: full-length VDR amino acid sequence; FIG. 9B: amino acid sequence of LBD of VDR; FIG. 9C; multiple sequence alignment of LBD of VDR of various species. (SEQ ID NOs:167-172).

FIG. 10A-10C depict amino acid sequences of thyroid hormone receptor-alpha (TRα). FIG. 10A: full-length TRα amino acid sequence; FIG. 10B: amino acid sequence of LBD of TRα; FIG. 10C; multiple sequence alignment of LBD of TRα of various species. (SEQ ID NOs:173-185).

FIG. 11A-11C depict amino acid sequences of retinoic acid receptor-beta (RARβ). FIG. 11A: full-length RARβ amino acid sequence; FIG. 11B: amino acid sequence of LBD of RARβ; FIG. 11C; multiple sequence alignment of LBD of RARβ of various species. (SEQ ID NOs:186-196).

FIG. 12 is a schematic diagram of an ON-switch CAR featuring the Ligand Binding Domain (LBD) of a Nuclear Hormone Receptor, a co-regulator peptide, and a small molecule as the ternary hetero-dimerizing module.

FIG. 13 is a schematic diagram of a PPARγ-based ON-switch CAR construct.

FIG. 14 depicts IL-2 cytokine production by ON-switch CAR+ Jurkat cells (transduced with the indicated lentiviral constructs) after 18 hours of co-culturing with K562 target cells (+/- CD19 Ag, as indicated), in the presence or absence of rosiglitazone dimerizer (10 micromolar).

FIGs. 16A-16B depict CD69 upregulation by ER CAR+ Jurkat cells after 24 hours of co-culturing with K562 target cells expressing CD19 or an irrelevant antigen ("meso"), in the presence or absence of a small-molecule dimerizer (4-hydroxytamoxifen or rapalog AP21967). CD69 expression in ER CAR+ Jurkat cells is strongly induced by 4- hydroxytamoxifen (EC50 ~100 nM) only in the presence of K562 cells expressing CD19. Rapamycin CAR and dead rapamycin CAR were tested as positive and negative controls, respectively. Dead rapamycin CAR comprises a mutation in the ITAM domain such that it does not signal. The data series presented in FIG. 16B from back to front are CD19 antigen + 4-hydroxytamoxifen 10 μM, 1 μM, 100 nM, 10 nM, 1 nM, 0 nM, meso antigen + 10 μM rapalog, and meso antigen + 0 μM rapalog.

FIG. 17 provides a schematic diagram of an estrogen receptor beta-based ON-switch CAR construct.

FIGs. 18A-18B depict CD69 upregulation by primary human T cells expressing ER-beta/CoRNR-based on-switch CAR measured after 24 hours of co-culturing with K562 target cells expressing CD19 or an irrelevant antigen ("meso"), in the presence or absence of a small-molecule dimerizer (4-hydroxytamoxifen or rapalog). CD69 expression is induced in a dimerizer dose dependent manner. The data series presented in FIG. 18B from back to front are CD19 antigen + 4-hydroxytamoxifen 10 μM, 1 μM, 100 nM, 10 nM, 1 nM, 0 nM, meso antigen + 10 μM rapalog, and meso antigen + 0 μM rapalog.

FIG. 19 provides a table showing various possible combinations of LBD, co-regulator, and dimerization agent.

FIG. 20A-20C depict amino acid sequences of Lyn kinase (FIG. 20A), an N-terminal portion of a Lyn kinase (FIG. 20B), and a C-terminal portion of a Lyn kinase (FIG. 20C). (SEQ ID NOs:197-199)

FIG. 21 provides an amino acid sequence of a Fak kinase. (SEQ ID NO:200)

FIG. 22A-22B depict amino acid sequences of an FXR (FIG. 22A) and a LBD of an FXR (FIG. 22B). (SEQ ID NOs:201-202)

FIG. 23A-23B depict amino acid sequences of an LXRα (FIG. 23A) and a LBD of an LXRα (FIG. 23B). (SEQ ID NOs:203-204)

FIG. 24A-24B depict amino acid sequences of an RORγ (FIG. 24A) and a LBD of an RORγ (FIG. 24B). (SEQ ID NOs:205-206)

FIG. 25A-25B depict amino acid sequences of an RXRα (FIG. 25A) and a LBD of an RXRα (FIG. 25B). (SEQ ID NOs:207-208)

FIG. 26A-26B depict amino acid sequences of a PXR (FIG. 26A) and a LBD of a PXR (FIG. 26B). (SEQ ID NOs:209-210)

FIG. 27 provides Table 1 (SEQ ID NOs:211-278).

FIG. 28 provides the amino acid sequence of *S. pyogenes* Cas9 (SEQ ID NO:279).

FIG. 29-51B provide amino acid sequences of various co-regulator polypeptides (SEQ ID NOs:280-302).

FIG. 52 depicts target cell killing by primary human CD8+ T cells expressing a CD19 specific ER-beta/CoRNR ON-switch CAR.

FIG. 53 provide the amino acid sequences of exemplary IL-2 family receptors (SEQ ID NOs:303-313).

FIG. 54 provide the amino acid sequences of exemplary IL-3 family receptors (SEQ ID NOs:314-317).

FIG. 55 provide the amino acid sequences of exemplary IL-6 family receptors (SEQ ID NOs:318-326).

FIG. 56 provide the amino acid sequences of exemplary IL-12 family receptors (SEQ ID NOs:327-329).

FIG. 57 provide the amino acid sequences of exemplary prolactin family receptors (SEQ ID NOs:330-334).

FIG. 58 provide the amino acid sequences of exemplary interferon family receptors (SEQ ID NOs:335-338).

FIG. 59 provide the amino acid sequences of exemplary IL-10 family receptors (SEQ ID NOs:339-345).

FIG. 60 provide the amino acid sequences of exemplary IL-17 family receptors (SEQ ID NOs:346-350).

FIG. 61 provide the amino acid sequences of exemplary immunoglobulin-like superfamily receptors (SEQ ID NOs:351-361).

FIG. 62 provide the amino acid sequences of exemplary tumor necrosis factor family receptors (SEQ ID NOs:362-392).

FIG. 63 provide the amino acid sequences of exemplary chemokine receptors (SEQ ID NOs:393-409).

FIG. 64 provide the amino acid sequences of exemplary TGF-beta family receptors (SEQ ID NOs:410-412).

FIG. 65 provide the amino acid sequences of exemplary receptor tyrosine kinases (RTKs) (SEQ ID NOs:413-469).

DEFINITIONS

[0019] The terms “polynucleotide” and “nucleic acid,” used interchangeably herein, refer to a polymeric form of nucleotides of any length, either ribonucleotides or deoxyribonucleotides. Thus, this term includes, but is not limited to, single-, double-, or multi-stranded DNA or RNA, genomic DNA, cDNA, DNA-RNA hybrids, or a polymer comprising purine and pyrimidine bases or other natural, chemically or biochemically modified, non-natural, or derivatized nucleotide bases.

[0020] "Operably linked" refers to a juxtaposition wherein the components so described are in a relationship permitting them to function in their intended manner. For instance, a promoter is operably linked to a coding sequence if the promoter affects its transcription or expression.

[0021] A "vector" or "expression vector" is a replicon, such as plasmid, phage, virus, or cosmid, to which another DNA segment, i.e. an "insert", may be attached so as to bring about the replication of the attached segment in a cell.

[0022] Heterologous," as used herein, means a nucleotide or polypeptide sequence that is not found in the native (e.g., naturally-occurring) nucleic acid or protein, respectively.

[0023] The terms "antibodies" and “immunoglobulin” include antibodies or immunoglobulins of any isotype, fragments of antibodies that retain specific binding to antigen, including, but not limited to, Fab, Fv, scFv, and Fd fragments, chimeric antibodies, humanized antibodies, single-chain antibodies (scAb), single domain antibodies (dAb), single domain heavy chain antibodies, a single domain light chain antibodies, bi-specific antibodies, multi-specific antibodies, and fusion proteins comprising an antigen-binding (also referred to herein as antigen binding) portion of an antibody and a non-antibody protein. The antibodies can be detectably labeled, *e.g.*, with a radioisotope, an enzyme that generates a detectable product, a fluorescent protein, and the like. The antibodies can be further conjugated to other moieties,

such as members of specific binding pairs, *e.g.*, biotin (member of biotin-avidin specific binding pair), and the like. The antibodies can also be bound to a solid support, including, but not limited to, polystyrene plates or beads, and the like. Also encompassed by the term are Fab', Fv, $F(ab')_2$, and or other antibody fragments that retain specific binding to antigen, and monoclonal antibodies. As used herein, a monoclonal antibody is an antibody produced by a group of identical cells, all of which were produced from a single cell by repetitive cellular replication. That is, the clone of cells only produces a single antibody species. While a monoclonal antibody can be produced using hybridoma production technology, other production methods known to those skilled in the art can also be used (e.g., antibodies derived from antibody phage display libraries). An antibody can be monovalent or bivalent. An antibody can be an Ig monomer, which is a "Y-shaped" molecule that consists of four polypeptide chains: two heavy chains and two light chains connected by disulfide bonds.

[0024] The term "humanized immunoglobulin" as used herein refers to an immunoglobulin comprising portions of immunoglobulins of different origin, wherein at least one portion comprises amino acid sequences of human origin. For example, the humanized antibody can comprise portions derived from an immunoglobulin of nonhuman origin with the requisite specificity, such as a mouse, and from immunoglobulin sequences of human origin (e.g., chimeric immunoglobulin), joined together chemically by conventional techniques (e.g., synthetic) or prepared as a contiguous polypeptide using genetic engineering techniques (e.g., DNA encoding the protein portions of the chimeric antibody can be expressed to produce a contiguous polypeptide chain). Another example of a humanized immunoglobulin is an immunoglobulin containing one or more immunoglobulin chains comprising a CDR derived from an antibody of nonhuman origin and a framework region derived from a light and/or heavy chain of human origin (e.g., CDR-grafted antibodies with or without framework changes). Chimeric or CDR-grafted single chain antibodies are also encompassed by the term humanized immunoglobulin. See, e.g., Cabilly et al., U.S. Pat. No. 4,816,567; Cabilly et al., European Patent No. 0,125,023 B1; Boss et al., U.S. Pat. No. 4,816,397; Boss et al., European Patent No. 0,120,694 B1; Neuberger, M. S. et al., WO 86/01533; Neuberger, M. S. et al., European Patent No. 0,194,276 B1; Winter, U.S. Pat. No. 5,225,539; Winter, European Patent No. 0,239,400 B1; Padlan, E. A. et al., European Patent Application No. 0,519,596 A1. See also, Ladner et al., U.S. Pat. No. 4,946,778; Huston, U.S. Pat. No. 5,476,786; and Bird, R. E. et al., Science, 242: 423-426 (1988)), regarding single chain antibodies.

[0025] The term "nanobody" (Nb), as used herein, refers to the smallest antigen binding fragment or single variable domain (V_{HH}) derived from naturally occurring heavy chain antibody and is known to the person skilled in the art. They are derived from heavy chain only antibodies, seen in camelids (Hamers-Casterman et al., 1993; Desmyter et al., 1996). In the family of "camelids" immunoglobulins devoid of light polypeptide chains are found. "Camelids" comprise old world camelids (*Camelus bactrianus* and

Camelus dromedarius) and new world camelids (for example, *Llama paccos*, *Llama glama*, *Llama guanicoe* and *Llama vicugna*). A single variable domain heavy chain antibody is referred to herein as a nanobody or a V_{HH} antibody.

[0026] "Antibody fragments" comprise a portion of an intact antibody, for example, the antigen binding or variable region of the intact antibody. Examples of antibody fragments include Fab, Fab', $F(ab')_2$, and Fv fragments; diabodies; linear antibodies (Zapata et al., Protein Eng. 8(10): 1057-1062 (1995)); domain antibodies (dAb; Holt et al. (2003) *Trends Biotechnol.* 21:484); single-chain antibody molecules; and multi-specific antibodies formed from antibody fragments. Papain digestion of antibodies produces two identical antigen-binding fragments, called "Fab" fragments, each with a single antigen-binding site, and a residual "Fc" fragment, a designation reflecting the ability to crystallize readily. Pepsin treatment yields an $F(ab')_2$ fragment that has two antigen combining sites and is still capable of cross-linking antigen.

[0027] "Fv" is the minimum antibody fragment that contains a complete antigen-recognition and -binding site. This region consists of a dimer of one heavy- and one light-chain variable domain in tight, non-covalent association. It is in this configuration that the three CDRS of each variable domain interact to define an antigen-binding site on the surface of the V_H-V_L dimer. Collectively, the six CDRs confer antigen-binding specificity to the antibody. However, even a single variable domain (or half of an Fv comprising only three CDRs specific for an antigen) has the ability to recognize and bind antigen, although at a lower affinity than the entire binding site.

[0028] The "Fab" fragment also contains the constant domain of the light chain and the first constant domain (CH_1) of the heavy chain. Fab fragments differ from Fab' fragments by the addition of a few residues at the carboxyl terminus of the heavy chain CH_1 domain including one or more cysteines from the antibody hinge region. Fab'-SH is the designation herein for Fab' in which the cysteine residue(s) of the constant domains bear a free thiol group. $F(ab')_2$ antibody fragments originally were produced as pairs of Fab' fragments which have hinge cysteines between them. Other chemical couplings of antibody fragments are also known.

[0029] The "light chains" of antibodies (immunoglobulins) from any vertebrate species can be assigned to one of two clearly distinct types, called kappa and lambda, based on the amino acid sequences of their constant domains. Depending on the amino acid sequence of the constant domain of their heavy chains, immunoglobulins can be assigned to different classes. There are five major classes of immunoglobulins: IgA, IgD, IgE, IgG, and IgM, and several of these classes can be further divided into subclasses (isotypes), e.g., IgG1, IgG2, IgG3, IgG4, IgA, and IgA2. The subclasses can be further divided into types, e.g., IgG2a and IgG2b.

[0030] "Single-chain Fv" or "sFv" or "scFv" antibody fragments comprise the V_H and V_L domains of antibody, wherein these domains are present in a single polypeptide chain. In some embodiments, the Fv

polypeptide further comprises a polypeptide linker between the V_H and V_L domains, which enables the sFv to form the desired structure for antigen binding. For a review of sFv, see *Pluckthun in The Pharmacology of Monoclonal Antibodies, vol. 113, Rosenburg and Moore eds., Springer-Verlag, New York, pp. 269-315 (1994)*.

[0031] The term "diabodies" refers to small antibody fragments with two antigen-binding sites, which fragments comprise a heavy-chain variable domain (V_H) connected to a light-chain variable domain (V_L) in the same polypeptide chain (V_H-V_L). By using a linker that is too short to allow pairing between the two domains on the same chain, the domains are forced to pair with the complementary domains of another chain and create two antigen-binding sites. Diabodies are described more fully in, for example, EP 404,097; WO 93/11161; and Hollinger et al. (1993) *Proc. Natl. Acad. Sci. USA* 90:6444-6448.

[0032] As used herein, the term “hinge region” refers to a flexible polypeptide connector region (also referred to herein as “hinge” or “spacer”) providing structural flexibility and spacing to flanking polypeptide regions and can consist of natural or synthetic polypeptides. A "hinge region" derived from an immunoglobulin (e.g., IgG1) is generally defined as stretching from Glu216 to Pro230 of human IgG1 (Burton (1985) Molec. Immunol., 22:161-206). Hinge regions of other IgG isotypes may be aligned with the IgG1 sequence by placing the first and last cysteine residues forming inter-heavy chain disulfide (S-S) bonds in the same positions. The hinge region may be of natural occurrence or non-natural occurrence, including but not limited to an altered hinge region as described in U.S. Pat. No. 5,677,425. The hinge region can include complete hinge region derived from an antibody of a different class or subclass from that of the CH1 domain. The term “hinge region” can also include regions derived from CD8 and other receptors that provide a similar function in providing flexibility and spacing to flanking regions.

[0033] As used herein, the term "affinity" refers to the equilibrium constant for the reversible binding of two agents (e.g., an antibody and an antigen) and is expressed as a dissociation constant (K_D). Affinity can be at least 1-fold greater, at least 2-fold greater, at least 3-fold greater, at least 4-fold greater, at least 5-fold greater, at least 6-fold greater, at least 7-fold greater, at least 8-fold greater, at least 9-fold greater, at least 10-fold greater, at least 20-fold greater, at least 30-fold greater, at least 40-fold greater, at least 50-fold greater, at least 60-fold greater, at least 70-fold greater, at least 80-fold greater, at least 90-fold greater, at least 100-fold greater, or at least 1,000-fold greater, or more, than the affinity of an antibody for unrelated amino acid sequences. Affinity of an antibody to a target protein can be, for example, from about 100 nanomolar (nM) to about 0.1 nM, from about 100 nM to about 1 picomolar (pM), or from about 100 nM to about 1 femtomolar (fM) or more. As used herein, the term “avidity” refers to the resistance of a complex of two or more agents to dissociation after dilution. The terms “immunoreactive” and “preferentially binds” are used interchangeably herein with respect to antibodies and/or antigen-binding fragments.

[0034] The term "binding" refers to a direct association between two molecules, due to, for example, covalent, electrostatic, hydrophobic, and ionic and/or hydrogen-bond interactions, including interactions such as salt bridges and water bridges. In some cases, the first member of a specific binding pair present in the extracellular domain of a conditionally active heterodimeric polypeptide of the present disclosure binds specifically to a second member of the specific binding pair. "Specific binding" refers to binding with an affinity of at least about 10^{-7} M or greater, e.g., 5x 10^{-7} M, 10^{-8} M, 5 x 10^{-8} M, and greater. "Non-specific binding" refers to binding with an affinity of less than about 10^{-7} M, e.g., binding with an affinity of 10^{-6} M, 10^{-5} M, 10^{-4} M, etc.

[0035] The terms "polypeptide," "peptide," and "protein", used interchangeably herein, refer to a polymeric form of amino acids of any length, which can include genetically coded and non-genetically coded amino acids, chemically or biochemically modified or derivatized amino acids, and polypeptides having modified peptide backbones. The term includes fusion proteins, including, but not limited to, fusion proteins with a heterologous amino acid sequence, fusions with heterologous and homologous leader sequences, with or without N-terminal methionine residues; immunologically tagged proteins; and the like.

[0036] An "isolated" polypeptide is one that has been identified and separated and/or recovered from a component of its natural environment. Contaminant components of its natural environment are materials that would interfere with diagnostic or therapeutic uses for the polypeptide, and may include enzymes, hormones, and other proteinaceous or nonproteinaceous solutes. In some embodiments, the polypeptide will be purified (1) to greater than 90%, greater than 95%, or greater than 98%, by weight of antibody as determined by the Lowry method, for example, more than 99% by weight, (2) to a degree sufficient to obtain at least 15 residues of N-terminal or internal amino acid sequence by use of a spinning cup sequenator, or (3) to homogeneity by sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) under reducing or nonreducing conditions using Coomassie blue or silver stain. Isolated polypeptide includes the polypeptide in situ within recombinant cells since at least one component of the polypeptide's natural environment will not be present. In some instances, isolated polypeptide will be prepared by at least one purification step.

[0037] The term "module", as used herein, refers to a contiguous polypeptide sequence, or fragment thereof, that is associated with some function, particularly a biological function.

[0038] The terms "domain" and "motif", used interchangeably herein, refer to both structured domains having one or more particular functions and unstructured segments of a polypeptide that, although unstructured, retain one or more particular functions. For example, a structured domain may encompass but is not limited to a continuous or discontinuous plurality of amino acids, or portions thereof, in a folded polypeptide that comprise a three-dimensional structure which contributes to a particular function

of the polypeptide. In other instances, a domain may include an unstructured segment of a polypeptide comprising a plurality of two or more amino acids, or portions thereof, that maintains a particular function of the polypeptide unfolded or disordered. Also encompassed within this definition are domains that may be disordered or unstructured but become structured or ordered upon association with a target or binding partner. Non-limiting examples of intrinsically unstructured domains and domains of intrinsically unstructured proteins are described, e.g., in Dyson & Wright. *Nature Reviews Molecular Cell Biology* 6:197-208.

[0039] The terms "chimeric antigen receptor" and "CAR", used interchangeably herein, refer to artificial multi-module molecules capable of triggering or inhibiting the activation of an immune cell which generally but not exclusively comprise an extracellular domain (e.g., a ligand/antigen binding domain), a transmembrane domain and one or more intracellular signaling domains. The term "CAR" is not limited specifically to CAR molecules but also includes CAR variants. CAR variants include split CARs wherein the extracellular portion (e.g., the ligand binding portion) and the intracellular portion (e.g., the intracellular signaling portion) of a CAR are present on two separate molecules. CAR variants also include ON-switch CARs which are conditionally activatable CARs, e.g., comprising a split CAR wherein conditional hetero-dimerization of the two portions of the split CAR is pharmacologically controlled. CAR variants also include bispecific CARs, which include a secondary CAR binding domain that can either amplify or inhibit the activity of a primary CAR. CAR variants also include inhibitory chimeric antigen receptors (iCARs) which may, e.g., be used as a component of a bispecific CAR system, where binding of a secondary CAR binding domain results in inhibition of primary CAR activation. CAR molecules and derivatives thereof (i.e., CAR variants) are described, e.g., in PCT Application No. US2014/016527; Fedorov et al. *Sci Transl Med* (2013) ;5(215):215ra172; Glienke et al. *Front Pharmacol* (2015) 6:21; Kakarla & Gottschalk 52 *Cancer J* (2014) 20(2):151-5; Riddell et al. *Cancer J* (2014) 20(2):141-4; Pegram et al. *Cancer J* (2014) 20(2):127-33; Cheadle et al. *Immunol Rev* (2014) 257(1):91-106; Barrett et al. *Annu Rev Med* (2014) 65:333-47; Sadelain et al. *Cancer Discov* (2013) 3(4):388-98; Cartellieri et al., *J Biomed Biotechnol* (2010) 956304; the disclosures of which are incorporated herein by reference in their entirety.

[0040] As used herein, the term "immune cells" generally includes white blood cells (leukocytes) which are derived from hematopoietic stem cells (HSC) produced in the bone marrow. "Immune cells" includes, e.g., lymphocytes (T cells, B cells, natural killer (NK) cells) and myeloid-derived cells (neutrophil, eosinophil, basophil, monocyte, macrophage, dendritic cells).

[0041] "T cell" includes all types of immune cells expressing CD3 including T-helper cells ($CD4^+$ cells), cytotoxic T-cells ($CD8^+$ cells), T-regulatory cells (Treg) and gamma-delta T cells.

[0042] A "cytotoxic cell" includes $CD8^+$ T cells, natural-killer (NK) cells, and neutrophils, which cells are capable of mediating cytotoxicity responses.

[0043] As used herein, the term “stem cell” generally includes pluripotent or multipotent stem cells. “Stem cells” includes, e.g., embryonic stem cells (ES); mesenchymal stem cells (MSC); induced-pluripotent stem cells (iPS); and committed progenitor cells (hematopoietic stem cells (HSC); bone marrow derived cells, neural progenitor cells, etc.).

[0044] As used herein, the terms "treatment," "treating," “treat” and the like, refer to obtaining a desired pharmacologic and/or physiologic effect. The effect can be prophylactic in terms of completely or partially preventing a disease or symptom thereof and/or can be therapeutic in terms of a partial or complete cure for a disease and/or adverse effect attributable to the disease. "Treatment," as used herein, covers any treatment of a disease in a mammal, particularly in a human, and includes: (a) preventing the disease from occurring in a subject which can be predisposed to the disease but has not yet been diagnosed as having it; (b) inhibiting the disease, i.e., arresting its development; and (c) relieving the disease, i.e., causing regression of the disease.

[0045] The terms “individual,” “subject,” “host,” and “patient,” used interchangeably herein, refer to a mammal, including, but not limited to, murines (rats, mice), non-human primates, humans, canines, felines, ungulates (e.g., equines, bovines, ovines, porcines, caprines), lagomorphs, etc. In some cases, the individual is a human. In some cases, the individual is a non-human primate. In some cases, the individual is a rodent, e.g., a rat or a mouse. In some cases, the individual is a lagomorph, e.g., a rabbit.

[0046] A “therapeutically effective amount” or “efficacious amount” refers to the amount of an agent, or combined amounts of two agents, that, when administered to a mammal or other subject for treating a disease, is sufficient to effect such treatment for the disease. The “therapeutically effective amount” will vary depending on the agent(s), the disease and its severity and the age, weight, etc., of the subject to be treated.

[0047] As used herein, the term “heteromeric” refers to a polypeptide or protein that contains more than one kind of subunit. Such heteromeric polypeptides may, in some instances, be referred to as “a heteromer”. Heteromeric polypeptides may contain two or more different polypeptides, wherein different polypeptides are defined at least as two polypeptides that are not identical, however, such different polypeptides may or may not include one or more portions of similar and/or identical amino acid sequence. In some instances, the two or more polypeptides of a heteromer share no identical amino acid sequence or share no identical domains. A heteromer may, in some instances, consist of two different polypeptides or two different types of polypeptides and may be referred to as a heterodimer. In some instances, a heteromer may consist of three different polypeptides or three different types of polypeptides and may be referred to as a heterotrimer. In some instances, a heteromer may consist of two or more different polypeptides or two or more different types of polypeptides, including but not limited to, e.g., three or more different polypeptides, four or more different polypeptides, five or more different

polypeptides, six or more different polypeptides, seven or more different polypeptides, eight or more different polypeptides, etc.

[0048] The term "synthetic" as used herein generally refers to an artificially derived polypeptide or polypeptide encoding nucleic acid that is not naturally occurring. Such synthetic polypeptides and/or nucleic acids may be assembled de novo from basic subunits including, e.g., single amino acids, single nucleotides, etc., or may be derived from pre-existing polypeptides or polynucleotides, whether naturally or artificially derived, e.g., as through recombinant methods.

[0049] The term "recombinant", as used herein describes a nucleic acid molecule, e.g., a polynucleotide of genomic, cDNA, viral, semisynthetic, and/or synthetic origin, which, by virtue of its origin or manipulation, is not associated with all or a portion of the polynucleotide sequences with which it is associated in nature. The term recombinant as used with respect to a protein or polypeptide means a polypeptide produced by expression from a recombinant polynucleotide. The term recombinant as used with respect to a host cell or a virus means a host cell or virus into which a recombinant polynucleotide has been introduced. Recombinant is also used herein to refer to, with reference to material (e.g., a cell, a nucleic acid, a protein, or a vector) that the material has been modified by the introduction of a heterologous material (e.g., a cell, a nucleic acid, a protein, or a vector).

[0050] A "biological sample" encompasses a variety of sample types obtained from an individual or a population of individuals and can be used in a diagnostic, monitoring or screening assay. The definition encompasses blood and other liquid samples of biological origin, solid tissue samples such as a biopsy specimen or tissue cultures or cells derived therefrom and the progeny thereof. The definition also includes samples that have been manipulated in any way after their procurement, such as by mixing or pooling of individual samples, treatment with reagents, solubilization, or enrichment for certain components, such as cells, polynucleotides, polypeptides, etc. The term "biological sample" encompasses a clinical sample, and also includes cells in culture, cell supernatants, cell lysates, serum, plasma, biological fluid, and tissue samples. The term "biological sample" includes urine, saliva, cerebrospinal fluid, interstitial fluid, ocular fluid, synovial fluid, blood fractions such as plasma and serum, and the like. The term "biological sample" also includes solid tissue samples, tissue culture samples, and cellular samples.

[0051] Before the present invention is further described, it is to be understood that this invention is not limited to particular embodiments described, as such may, of course, vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only, and is not intended to be limiting, since the scope of the present invention will be limited only by the appended claims.

[0052] Where a range of values is provided, it is understood that each intervening value, to the tenth of the unit of the lower limit unless the context clearly dictates otherwise, between the upper and lower limit of that range and any other stated or intervening value in that stated range, is encompassed within the invention. The upper and lower limits of these smaller ranges may independently be included in the smaller ranges, and are also encompassed within the invention, subject to any specifically excluded limit in the stated range. Where the stated range includes one or both of the limits, ranges excluding either or both of those included limits are also included in the invention.

[0053] 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 invention belongs. Although any methods and materials similar or equivalent to those described herein can also be used in the practice or testing of the present invention, the preferred methods and materials are now described. All publications mentioned herein are incorporated herein by reference to disclose and describe the methods and/or materials in connection with which the publications are cited.

[0054] It must be noted that as used herein and in the appended claims, the singular forms "a," "an," and "the" include plural referents unless the context clearly dictates otherwise. Thus, for example, reference to "a dimerizing agent" includes a plurality of such dimerizing agents and reference to "the antigen-binding domain" includes reference to one or more antigen-binding domains and equivalents thereof known to those skilled in the art, and so forth. It is further noted that the claims may be drafted to exclude any optional element. As such, this statement is intended to serve as antecedent basis for use of such exclusive terminology as "solely," "only" and the like in connection with the recitation of claim elements, or use of a "negative" limitation.

[0055] It is appreciated that certain features of the invention, which are, for clarity, described in the context of separate embodiments, may also be provided in combination in a single embodiment. Conversely, various features of the invention, which are, for brevity, described in the context of a single embodiment, may also be provided separately or in any suitable sub-combination. All combinations of the embodiments pertaining to the invention are specifically embraced by the present invention and are disclosed herein just as if each and every combination was individually and explicitly disclosed. In addition, all sub-combinations of the various embodiments and elements thereof are also specifically embraced by the present invention and are disclosed herein just as if each and every such sub-combination was individually and explicitly disclosed herein.

[0056] The publications discussed herein are provided solely for their disclosure prior to the filing date of the present application. Nothing herein is to be construed as an admission that the present invention is not entitled to antedate such publication by virtue of prior invention. Further, the dates of publication

provided may be different from the actual publication dates which may need to be independently confirmed.

DETAILED DESCRIPTION

[0057] The present disclosure provides conditionally active, heterodimeric polypeptides. The conditionally active, heterodimeric polypeptides are active in the presence of a dimerizing agent that induces dimerization of the polypeptides of the heterodimer. A conditionally active, heterodimeric polypeptide of the present disclosure is useful in a variety of research and treatment methods, which are also provided.

CONDITIONALLY ACTIVE HETERODIMERIC POLYPEPTIDES

[0058] The present disclosure provides a heterodimeric, conditionally active polypeptide comprising: a) a first chimeric polypeptide comprising a first member of a dimerization pair and a first heterologous polypeptide; and b) a second chimeric polypeptide comprising a second member of a dimerization pair and a second heterologous polypeptide. In some cases, the first member of the dimerization pair comprises a ligand-binding domain (LBD) of a nuclear hormone receptor, and the second member of the dimerization pair comprises a co-regulator of the nuclear hormone receptor. In other cases, the first member of the dimerization pair is a co-regulator of a nuclear hormone receptor, and the second member of the dimerization pair comprises an LBD of the nuclear hormone receptor. The first chimeric polypeptide and the second chimeric polypeptide are dimerized in the presence of a dimerization agent that induces binding of the LBD to the co-regulator.

[0059] In some instances, the function of a conditionally active heterodimeric polypeptide of the present disclosure does not utilize a DNA-binding function or a transcription activating function of the nuclear hormone receptor from which the LBD is derived. Put another way, the function of the conditionally active heterodimeric polypeptide of the present disclosure may be independent of any DNA-binding function of the nuclear hormone receptor from which the LBD is derived. In some instances, activation of a conditionally active heterodimeric polypeptide of the present disclosure does not result in a transcription activating function attributable to a domain (e.g., a DNA-binding domain) of the nuclear hormone receptor from which a LBD of the conditionally active heterodimeric polypeptide is derived. In some instances, a conditionally active heterodimeric polypeptide of the present disclosure does not contain a DNA-binding domain of a nuclear hormone receptor, including e.g., the DNA-binding domain of the nuclear hormone receptor from which a LBD of a conditionally active heterodimeric polypeptide is derived.

[0060] A conditionally active heterodimeric polypeptide of the present disclosure can, in some instances, be activating. A conditionally active heterodimeric polypeptide of the present disclosure can, in some instances, have repressor activity. For example, where a conditionally active heterodimeric polypeptide of the present disclosure is present in the membrane of a cell, and the cell is contacted with a dimerizing

agent that induces binding of the LBD to the co-regulator, in some cases, the conditionally active heterodimeric polypeptide activates the cell. For example, where a conditionally active heterodimeric polypeptide of the present disclosure is present in the membrane of a cell, and the cell is contacted with a dimerizing agent that induces binding of the LBD to the co-regulator, in some cases, the conditionally active heterodimeric polypeptide represses an activity in or by the cell. In some cases, activation of a conditionally active heterodimeric polypeptide of the present disclosure depends on the presence of a dimerization agent. In some cases, activation of a conditionally active heterodimeric polypeptide of the present disclosure depends on the presence of a dimerization agent and a second agent (e.g., an antigen). Depending on the nature of the conditionally active heterodimeric polypeptide and/or depending on the nature of the dimerization agent, activation of a conditionally active heterodimeric polypeptide of the present disclosure can result in activation of an activity of a cell (where the conditionally active heterodimeric polypeptide is present in the cell), or repression of an activity of a cell (where the conditionally active heterodimeric polypeptide is present in the cell). Depending on the nature of the conditionally active heterodimeric polypeptide and/or depending on the nature of the dimerization agent, activation of a conditionally active heterodimeric polypeptide of the present disclosure can result in activation of an activity of a heterologous polypeptide present in the conditionally active heterodimeric polypeptide, or can result in inhibition of an activity of a heterologous polypeptide present in the conditionally active heterodimeric polypeptide.

[0061] By "conditionally active" is meant that the activity attributaible to the relevant heterodimeric polypeptide is dependent upon a condition, such as e.g., dimerization of the heterodimeric parts of the polypeptide. For instance, the activity of a heterodimeric polypeptide of the present disclosure may be conditionally dependent upon the presence of a dimerizing agent. In such instances, in the presence of the dimerizing agent, the heterodimeric polypeptide is "activatable", i.e., may be activated (e.g., through binding of the second member of a specific binding pair of the polypeptide, such as an antigen). Conditionally activatable polypeptides will generally not be activatable in the absesnce of dimerizing agent, i.e., the relevant polypeptide cannot be activated in the absence of the dimerizing agent regardless of whether some additional condition for function is met, e.g., the second member of a specific binding pair of the polypeptide (such as an antigen) is present and/or bound.

[0062] The activities attributaible to the relevant polypeptides that may be conditionally dependent, e.g., on the presence of the relevant dimerizing agent, may vary and will generally include any activity including both activating activities and repressive activities as noted above and described in greater detail below. As an example, a conditionally active on-switch chimeric antigen receptor (CAR), as described in more detail below, may be activatable in the presence of the relevant dimerization agent such that, in the presence of both the dimerization agent and the relevant member of the specific binding pair to which the polypeptide binds, signal transduction resulting from the on-switch CAR may activate a cell (e.g., an

immune cell) in which the on-switch CAR resides. In the contrary case, in the absence of the relevant dimerization agent, signal transduction which would lead to activation of a cell expressing the on-switch CAR does not occur regardless of the presence of the relevant member of the specific binding pair to which the on-switch CAR binds. As another example, the repression attributable to a conditionally active off-switch CAR, as described in more detail below, may be activatable in the presence of the relevant dimerization agent such that, in the presence of both the dimerization agent and the relevant member of the specific binding pair to which the polypeptide binds, the off-switch CAR may repress activation of a cell (e.g., an immune cell) in which the off-switch CAR resides. In the contrary case, in the absence of the relevant dimerization agent, activation of the off-switch CAR which would lead to repression of that activation of a cell expressing the off-switch CAR does not occur regardless of the presence of the relevant member of the specific binding pair to which the off-switch CAR binds.

Interacting polypeptides

[0063] The first heterologous polypeptide and the second heterologous polypeptide of the subject conditionally active heterodimeric polypeptides can be any polypeptides that exhibit an activity when brought into proximity to one another, e.g., when the first chimeric polypeptide and the second chimeric polypeptide are dimerized by the dimerization agent that induces binding of the LBD to the co-regulator. The first and the second heterologous polypeptides do not exhibit that activity individually, e.g., when not in proximity to one another. In other words, activity of the first heterologous polypeptide and the second heterologous polypeptide is dependent upon assembly of the two polypeptides. For example, in some cases, the first heterologous polypeptide is a receptor and the second heterologous polypeptide is a co-receptor. In some cases, the first heterologous polypeptide is a T-cell receptor (TCR) alpha chain; and the second heterologous polypeptide is a TCR beta chain. In some cases, the first heterologous polypeptide is a first polypeptide of a chimeric antigen receptor (CAR) heterodimer; and the second heterologous polypeptide is a second polypeptide of the CAR heterodimer. In some cases, the first heterologous polypeptide and the second heterologous polypeptide are caspases. In some cases, the first heterologous polypeptide is a first subunit of a polypeptide; and the second heterologous polypeptide is a second subunit of the polypeptide. In some cases, the first heterologous polypeptide is an enzyme; and the second heterologous polypeptide is a polypeptide substrate of the enzyme. In some cases, the first heterologous polypeptide is a scaffold polypeptide (e.g., LAT; SLP76; and the like); and the second heterologous polypeptide is a polypeptide that conditionally binds to the scaffold polypeptide. In some cases, the first heterologous polypeptide is a signal transducing adaptor protein (e.g., MyD88; Grb2; SHC1); and the second heterologous polypeptide is a polypeptide that conditionally binds the signal transducing adaptor protein. In some cases, the first and second heterologous polypeptides are dimerization-dependent cell-surface receptors (e.g., cytokine receptors, receptor tyrosine kinases (RTK), and the like) or a portion thereof. In some cases, the first and the second heterologous polypeptides are

the same dimerization-dependent cell-surface receptor (e.g., the same cytokine receptor, the same RTK, etc.) or the same portions of a dimerization-dependent cell-surface receptor.

[0064] In some cases, the first heterologous polypeptide and the second heterologous polypeptide have the same amino acid sequence. In some cases, the first heterologous polypeptide and the second heterologous polypeptide have different amino acid sequences.

Split products

[0065] In some cases, the first heterologous polypeptide and the second heterologous polypeptide are split products of a single parent polypeptide that exhibit an activity of the parent polypeptide when brought into proximity to one another, e.g., when the first chimeric polypeptide and the second chimeric polypeptide are dimerized by the dimerization agent that induces binding of the LBD to the co-regulator. For example, in some cases, the first heterologous polypeptide is an N-terminal portion of a parent polypeptide; and the second heterologous polypeptide is the C-terminal portion of the parent polypeptide. The N-terminal portion and the C-terminal portion of the parent polypeptide, when split such that they are not in proximity to one another, do not individual exhibit the activity of the parent polypeptide. For example, in some cases, the first heterologous polypeptide and the second heterologous polypeptide are split products of a kinase. As another example, in some cases, the first heterologous polypeptide and the second heterologous polypeptide are split products of a protease. As another example, in some cases, the first heterologous polypeptide and the second heterologous polypeptide are split products of a fluorescent protein; see, e.g., Ghosh et al. (2000) *J. Am. Chem. Soc.*122:5658. As another example, in some cases, the first heterologous polypeptide and the second heterologous polypeptide are split products of ubiquitin; see, e.g., Johnsson and Varshavsky (1994) *Proc. Natl. Acad. Sci. USA* 91:10340. As another example, in some cases, the first heterologous polypeptide and the second heterologous polypeptide are split products of a lactamase polypeptide; see, e.g., Galarneau et al. (2002) *Nat. Biotechnol.* 20:619. As another example, in some cases, the first heterologous polypeptide and the second heterologous polypeptide are split products of luciferase; see, e.g., Luker et al. (2004) *Proc. Natl. Acad. Sci. USA* 101:12288; Remy and Michnick (2006) *Nat. Methods* 3:977; and Paulmurugan and Gambhir (2003) *Anal. Chem.* 75:1584. As another example, in some cases, the first heterologous polypeptide and the second heterologous polypeptide are split products of a caspase. As another example, in some cases, the first heterologous polypeptide and the second heterologous polypeptide are split products of a phosphatase. As another example, in some cases, the first heterologous polypeptide and the second heterologous polypeptide are split products of an endonuclease. As another example, in some cases, the first heterologous polypeptide and the second heterologous polypeptide are split products of an RNA-guided endonuclease. As another example, in some cases, the first heterologous polypeptide and the second heterologous polypeptide are split products of a Tobacco etch virus (TEV) protease; see, e.g., Gray et al. (2010) *Cell* 142:637. As another example, in some cases, the first heterologous polypeptide

and the second heterologous polypeptide are split products of a tyrosine phosphatase; see, e.g., Camacho-Soto et al. (2014) *J. Am. Chem. Soc.* 136:17078. As another example, in some cases, the first heterologous polypeptide and the second heterologous polypeptide are split products of a Cas9 polypeptide; see, e.g., Zetche et al. (2015) *Nat. Biotechnol.* 33:139.

[0066] As noted above, in some cases, the first heterologous polypeptide and the second heterologous polypeptide are split products of a kinase.As a non-limiting example, a tyrosine kinase can be the parent polypeptide; and split product of the parent tyrosine kinase can be the first heterologous polypeptide and the second heterologous polypeptide. For example, a tyrosine kinase can be split between amino acids E393 and D394 of the amino acid sequence depicted in FIG. 20A, or a corresponding site in a different tyrosine kinase, such that the first heterologous polypeptide is an N-terminal portion of the tyrosine kinase ending with E393, and the second heterologous polypeptide is a C-terminal portion of the tyrosine kinase beginning with D394. As an example, the first heterologous polypeptide can comprise the amino acid sequence depicted in FIG. 20B; and the second heterologous polypeptide can comprise the amino acid sequence depicted in FIG. 20C. As another example, a tyrosine kinase can be split between amino acids E572 and D573 of the amino acid sequence depicted in FIG. 21, or a corresponding site in a different tyrosine kinase, such that the first heterologous polypeptide is an N-terminal portion of the tyrosine kinase ending with E572, and the second heterologous polypeptide is a C-terminal portion of the tyrosine kinase beginning with D573. See, e.g., Camacho-Soto et al. (2014) J. Am. Chem. Soc. 136:3995. Tyrosine kinases include, e.g., Lyn, Fak, Src, and PKA. Tyrosine kinases include, e.g., ABL1, ABL1 (T315I), ACVR1, AKT1, ALK, AURKA, AXL, BTK, CAMK2D, CDK1B, CDK2A, CDK4D1, CSK, CSNK1G3, EGFR, EPHA4, EPHB4, ERBB4, FGFR1, FGFR2, FGFR3, FGFR3 (K650E), FGFR4, FLT3 (D835Y), IGF1R, GSK3B, INSR, IRAK4, JAK1, JAK2, JAK3, KDR, KIT, LCK, LYN, MAP3K8, MAPK1, MAPK10, MAPK14, MAPKAPK2, MAPKAPK5, MET, MKNK1, MKNK2, PAK2, PDGFRa, PDPK1, PIM2, PKN1, PKN2, PLK1, PRKACA, PRKCA, PRKCQ, RET, ROCK2, RPS6 KB1, SRC, SYK, TYK2, WNK1, ZAP70, PIKSCD, PIK3CG, MTOR, PIK3C3, PIK3CA, PIK3CB and PIK4CB. Suitable tyrosine kinases include SYK, LCK, IRK (=INSR=Insulin receptor), IGF-1 receptor, MK2, ZAP-70, Aurora-2, PRAK, ROCK, CAK, cMET, IRAK1, IRAK2, BLK, BMX, BTK, FRK, FGR, FYN, HCK, ITK, LYN, TEC, TXK, YES, ABL, SRC, EGF-R (=ErbB-1), ErbB-2 (=NEU=HER 2), ErbB-3, ErbB-4, FAK, FGF1R (=FGR-1), FGF2R (=FGR-2), IKK-1 (=IKK-α=CHUK), IKK-2 (=IKKβ), MET (=c-Met), NIK, PGDF receptor α, PDGF receptor β, TIE1, TIE2 (=TEK), VEGFR 1 (=FLT-1), VEGFR 2 (=KDR), FLT-3, FLT-4, KIT, CSK, JAK1, JAK2, JAK3, TYK2, RIP, RIP-2, LOK, TAKI, RET, ALK, MLK3, COT, TRKA, PYK2, EPHB4, RON, GSK3, UL13, ORF47, ATM, CDK (including all subtypes), PKA, PKB (including all PKB subtypes) (=AKT-1, AKT-2, AKT-3), PKC (including all PKC subtypes), REDK, SAPK, PIM, PDK, PIM, ERK and BARK, and all subtypes of these kinases.

[0067] As noted above, in some cases, the first heterologous polypeptide and the second heterologous polypeptide are split products of a caspase. Chelur and Chalfie (2007) *Proc. Natl. Acad. Sci. USA* 104:2283. In some cases, the caspase is an apoptotic caspase.

[0068] As noted above, in some cases, the first heterologous polypeptide and the second heterologous polypeptide are split products of a Cas9 polypeptide. A Cas9 polypeptide can comprise an amino acid sequence having at least 50%, at least 60%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 28. In some cases, the Cas9 is a catalytically inactive Cas9 ("dCas9"); e.g., where the dCas9 comprises a D10A and an H840A substitution relative to the amino acid sequence depicted in FIG. 28, or corresponding amino acids of another Cas9 polypeptide.

Specific binding pairs and extracellular recognition domains

[0069] The present disclosure provides conditionally active, heterodimeric polypeptides. The conditionally active, heterodimeric polypeptides, when expressed on the plasma membrane of a cell, are active in the presence of: 1) an antigen or other moiety that interacts with the extracellular domain; and 2) a dimerizing agent that induces dimerization of the polypeptides of the heterodimer.

[0070] In some cases, a conditionally active heterodimeric polypeptide of the present disclosure comprises: a) a first polypeptide comprising: i) a first member of a specific binding pair; ii) a first modulatory domain; iii) a first member of a dimerization pair; and iv) a transmembrane domain interposed between the first member of a specific binding pair and the first modulatory domain; and b) a second polypeptide comprising: i) a transmembrane domain; ii) a second modulatory domain; iii) a second member of the dimerization pair; and iv) an intracellular signaling domain. In some cases, the first member of the dimerization pair comprises a ligand-binding domain (LBD) of a nuclear hormone receptor, and the second member of the dimerization pair comprises a co-regulator of the nuclear hormone receptor. In some cases, the first member of the dimerization pair comprises a co-regulator of a nuclear hormone receptor, and the second member of the dimerization pair comprises an LBD of the nuclear hormone receptor.

[0071] Thus, in some cases, a conditionally active heterodimeric polypeptide of the present disclosure comprises: a) a first polypeptide comprising: i) a first member of a specific binding pair; ii) a first modulatory domain; iii) a first member of a dimerization pair, wherein the first member of the dimerization pair comprises an LBD of a nuclear hormone receptor; and iv) a transmembrane domain interposed between the first member of a specific binding pair and the first modulatory domain; and b) a second polypeptide comprising: i) a transmembrane domain; ii) a second modulatory domain; iii) a second member of the dimerization pair, wherein the second member of the dimerization pair comprises a co-regulator of the nuclear hormone receptor; and iv) an intracellular signaling domain. In other cases, a conditionally active heterodimeric polypeptide of the present disclosure comprises: a) a first

polypeptide comprising: i) a first member of a specific binding pair; ii) a first modulatory domain; iii) a first member of a dimerization pair, wherein the first member of the dimerization pair comprises a co-regulator of a nuclear hormone receptor; and iv) a transmembrane domain interposed between the first member of a specific binding pair and the first modulatory domain; and b) a second polypeptide comprising: i) a transmembrane domain; ii) a second modulatory domain; iii) a second member of the dimerization pair, wherein the second member of the dimerization pair comprises an LBD of the nuclear hormone receptor; and iv) an intracellular signaling domain.

[0072] In some cases, a conditionally active heterodimeric polypeptide of the present disclosure comprises: a) a first polypeptide comprising: i) a first member of a specific binding pair; ii) a modulatory domain; iii) a first member of a dimerization pair; iv) a transmembrane domain interposed between the first member of a specific binding pair and the modulatory domain; and b) a second polypeptide comprising: i) a second member of the dimerization pair; and ii) an intracellular signaling domain. In some cases, the first member of the dimerization pair comprises an LBD of a nuclear hormone receptor, and the second member of the dimerization pair is a co-regulator of the nuclear hormone receptor. In some cases, the first member of the dimerization pair is a co-regulator of a nuclear hormone receptor, and the second member of the dimerization pair comprises an LBD of the nuclear hormone receptor.

[0073] In some cases, a conditionally active heterodimeric polypeptide of the present disclosure is a conditionally active on-switch chimeric antigen receptor (CAR). In some cases, a conditionally active heterodimeric polypeptide of the present disclosure is a conditionally active off-switch CAR. In some cases, a conditionally active heterodimeric polypeptide of the present disclosure is a conditionally active T-cell receptor (TCR).

[0074] The present disclosure provides a heterodimeric, conditionally repressible synthetic immune cell receptor (ICR) comprising: a synthetic stimulatory ICR comprising a first member of a dimerization pair linked to the synthetic stimulatory ICR; and a synthetic ICR repressor comprising a second member of the dimerization pair linked to an intracellular inhibitory domain, wherein the first member of the dimerization pair comprises an LBD of a nuclear hormone receptor, and the second member of the dimerization pair comprises a co-activator of the nuclear hormone receptor, or wherein the first member of the dimerization pair is a co-activator of a nuclear hormone receptor, and the second member of the dimerization pair comprises an LBD of the nuclear hormone receptor. The synthetic stimulatory ICR and the synthetic ICR repressor are dimerized in the presence of a ligand (dimerization agent) that induces binding of the LBD to the co-regulator.

[0075] The present disclosure provides a heterodimeric, conditionally repressible synthetic chimeric antigen receptor (CAR) comprising: a) a synthetic stimulatory CAR comprising: i) a extracellular recognition domain; ii) a transmembrane domain linked to the extracellular recognition domain; iii) a first member of a dimerization pair linked to the transmembrane domain; and iv) an intracellular stimulation domain;

and b) a synthetic CAR repressor comprising: i) a second member of the dimerization pair; and ii) an intracellular inhibitory domain linked to the second member of the dimerization pair. The first member of the dimerization pair comprises an LBD of a nuclear hormone receptor, and the second member of the dimerization pair comprises a co-activator of the nuclear hormone receptor; or the first member of the dimerization pair is a co-activator of a nuclear hormone receptor, and the second member of the dimerization pair comprises an LBD of the nuclear hormone receptor. The synthetic stimulatory CAR and the synthetic CAR repressor are dimerized in the presence of a dimerization agent that induces binding of the LBD to the co-regulator.

[0076] The present disclosure provides a heterodimeric, conditionally repressible synthetic T cell receptor (TCR) comprising: a) a synthetic stimulatory TCR comprising: i) a transmembrane domain; ii) a first member of a dimerization pair linked to the transmembrane domain; iii) an engineered TCR polypeptide comprising at least one TCR alpha or beta chain, wherein the at least one TCR alpha or beta chain is linked to the transmembrane domain or the first member of a dimerization pair; and b) a synthetic TCR repressor comprising: i) a second member of the dimerization pair; and ii) an intracellular inhibitory domain linked to the second member of the dimerization pair. The first member of the dimerization pair comprises an LBD of a nuclear hormone receptor, and the second member of the dimerization pair comprises a co-activator of the nuclear hormone receptor; or the first member of the dimerization pair is a co-activator of a nuclear hormone receptor, and the second member of the dimerization pair comprises an LBD of the nuclear hormone receptor. The synthetic stimulatory TCR and the synthetic TCR repressor are dimerized in the presence of a dimerization agent that induces binding of the LBD to the co-regulator.

[0077] The present disclosure provides a heterodimeric, conditionally active chimeric antigen receptor (CAR) comprising: I) a) a first polypeptide comprising: i) a first member of a specific binding pair; ii) a first modulatory domain; iii) a first member of a dimerization pair; and iv) a transmembrane domain interposed between the first member of a specific binding pair and the first modulatory domain; and b) a second polypeptide comprising: i) a transmembrane domain; ii) a second modulatory domain; iii) a second member of the dimerization pair; and iv) an intracellular signaling domain; or II) a) a first polypeptide comprising: i) a first member of a specific binding pair; ii) a modulatory domain; iii) a first member of a dimerization pair; iv) a transmembrane domain interposed between the first member of a specific binding pair and the modulatory domain; and b) a second polypeptide comprising: i) a second member of the dimerization pair; and ii) an intracellular signaling domain. The first member of the dimerization pair comprises an LBD of a nuclear hormone receptor, and the second member of the dimerization pair comprises a co-activator of the nuclear hormone receptor; or the first member of the dimerization pair is a co-activator of a nuclear hormone receptor, and the second member of the dimerization pair comprises an LBD of the nuclear hormone receptor. The first polypeptide and the

second polypeptide are dimerized in the presence of a dimerization agent that induces binding of the LBD to the co-regulator.

CONDITIONALLY ACTIVE ON-SWITCH CAR

[0078] In some cases, a conditionally active heterodimeric polypeptide of the present disclosure is a conditionally active on-switch chimeric antigen receptor (CAR).

Member of a specific binding pair

[0079] As noted above, a conditionally active heterodimeric polypeptide of the present disclosure comprises a first polypeptide comprising a first member of a specific binding pair. The second member of the specific binding pair can be present on the surface of a cell. The second member of the specific binding pair can be immobilized on an insoluble support, expressed on the surface of a cell (e.g., a target cell, a non-target cell, etc.), or the like. The second member of the specific binding pair can be soluble. The second member of the specific binding pair can be present in an extracellular environment (e.g., extracellular matrix). The second member of the specific binding pair can be present in an artificial matrix. The second member of the specific binding pair can be present in an acellular environment.

[0080] Suitable first members of a specific binding pairs include, but are not limited to, antibody-based recognition scaffolds; antibodies (i.e., an antibody-based recognition scaffold, including antigen-binding antibody fragments); non-antibody-based recognition scaffolds; antigens (e.g., endogenous antigens; exogenous antigens; etc.); a ligand for a receptor; a receptor; a target of a non-antibody-based recognition scaffold; an Fc receptor (e.g., FcγRIIIa; FcγRIIIb; etc.); an extracellular matrix component; and the like.

[0081] Specific binding pairs include, e.g., antigen-antibody specific binding pairs, where the first member is an antibody (or antibody-based recognition scaffold) that binds specifically to the second member, which is an antigen, or where the first member is an antigen and the second member is an antibody (or antibody-based recognition scaffold) that binds specifically to the antigen; ligand-receptor specific binding pairs, where the first member is a ligand and the second member is a receptor to which the ligand binds, or where the first member is a receptor, and the second member is a ligand that binds to the receptor; non-antibody-based recognition scaffold-target specific binding pairs, where the first member is a non-antibody-based recognition scaffold and the second member is a target that binds to the non-antibody-based recognition scaffold, or where the first member is a target and the second member is a non-antibody-based recognition scaffold that binds to the target; adhesion molecule-extracellular matrix binding pairs; Fc receptor-Fc binding pairs, where the first member comprises an immunoglobulin Fc that binds to the second member, which is an Fc receptor, or where the first member is an Fc receptor that binds to the second member which comprises an immunoglobulin Fc; and receptor-co-receptor binding pairs, where the first member is a receptor that binds specifically to the second member which is

a co-receptor, or where the first member is a co-receptor that binds specifically to the second member which is a receptor.

Antigen-binding domain

[0082] An antigen-binding domain suitable for use in a conditionally active heterodimeric polypeptide of the present disclosure can be any antigen-binding polypeptide, a wide variety of which are known in the art. In some instances, the antigen-binding domain is a single chain Fv (scFv). Other antibody based recognition domains (cAb VHH (camelid antibody variable domains) and humanized versions, IgNAR VH (shark antibody variable domains) and humanized versions, sdAb VH (single domain antibody variable domains) and "camelized" antibody variable domains are suitable for use. In some instances, T-cell receptor (TCR) based recognition domains such as single chain TCR (scTv, single chain two-domain TCR containing VαVβ) are also suitable for use.

[0083] An antigen-binding domain suitable for use in a conditionally active heterodimeric polypeptide of the present disclosure can have a variety of antigen-binding specificities. In some cases, the antigen-binding domain is specific for an epitope present in an antigen that is expressed by (synthesized by) a cancer cell, i.e., a cancer cell associated antigen. The cancer cell associated antigen can be an antigen associated with, e.g., a breast cancer cell, a B cell lymphoma, a Hodgkin lymphoma cell, an ovarian cancer cell, a prostate cancer cell, a mesothelioma, a lung cancer cell (e.g., a small cell lung cancer cell), a non-Hodgkin B-cell lymphoma (B-NHL) cell, an ovarian cancer cell, a prostate cancer cell, a mesothelioma cell, a lung cancer cell (e.g., a small cell lung cancer cell), a melanoma cell, a chronic lymphocytic leukemia cell, an acute lymphocytic leukemia cell, a neuroblastoma cell, a glioma, a glioblastoma, a medulloblastoma, a colorectal cancer cell, etc. A cancer cell associated antigen may also be expressed by a non-cancerous cell.

[0084] Non-limiting examples of antigens to which an antigen-binding domain of a conditionally active heterodimeric polypeptide of the present disclosure can bind include, e.g., CD19, CD20, CD38, CD30, Her2/neu/ERBB2, CA125, MUC-1, prostate-specific membrane antigen (PSMA), CD44 surface adhesion molecule, mesothelin, carcinoembryonic antigen (CEA), epidermal growth factor receptor (EGFR), EGFRvIII, vascular endothelial growth factor receptor-2 (VEGFR2), high molecular weight-melanoma associated antigen (HMW-MAA), MAGE-A1, IL-13R-a2, GD2, and the like.

[0085] In some instances, an antigen-binding domain of a conditionally active heterodimeric polypeptide of the instant disclosure may target a cancer-associated antigen. In some instances, an antigen-binding domain of the instant disclosure may include an antibody or portion thereof specific for a cancer associated antigen. Non-limiting examples of cancer associated antigens include but are not limited to e.g., CD19, CD20, CD38, CD30, Her2/neu, ERBB2, CA125, MUC-1, prostate-specific membrane antigen (PSMA), CD44 surface adhesion molecule, mesothelin, carcinoembryonic antigen (CEA), epidermal growth factor receptor (EGFR), EGFRvIII, vascular endothelial growth factor receptor-2

(VEGFR2), high molecular weight-melanoma associated antigen (HMW-MAA), MAGE-A1, IL-13R-a2, GD2, and the like. Cancer-associated antigens also include, e.g., 4-1BB, 5T4, adenocarcinoma antigen, alpha-fetoprotein, BAFF, B-lymphoma cell, C242 antigen, CA-125, carbonic anhydrase 9 (CA-IX), C-MET, CCR4, CD152, CD19, CD20, CD200, CD22, CD221, CD23 (IgE receptor), CD28, CD30 (TNFRSF8), CD33, CD4, CD40, CD44 v6, CD51, CD52, CD56, CD74, CD80, CEA, CNTO888, CTLA-4, DRS, EGFR, EpCAM, CD3, FAP, fibronectin extra domain-B, folate receptor 1, GD2, GD3 ganglioside, glycoprotein 75, GPNMB, HER2/neu, HGF, human scatter factor receptor kinase, IGF-1 receptor, IGF-I, IgG1, L1-CAM, IL-13, IL-6, insulin-like growth factor I receptor, integrin α5β1, integrin αvβ3, MORAb-009, MS4A1, MUC1, mucin CanAg, N-glycolylneuraminic acid, NPC-1C, PDGF-R α, PDL192, phosphatidylserine, prostatic carcinoma cells, RANKL, RON, ROR1, SCH 900105, SDC1, SLAMF7, TAG-72, tenascin C, TGF beta 2, TGF-β, TRAIL-R1, TRAIL-R2, tumor antigen CTAA16.88, VEGF-A, VEGFR-1, VEGFR2, and vimentin.

[0086] In some instances, an antigen-binding domain may specifically bind a target comprising a fragment of a protein (e.g., a peptide) in conjunction with a major histocompatibility complex (MHC) molecule. As MHC molecules present peptide fragments of both intracellularly expressed and extracellularly expressed proteins, specific binding members directed to MHC-peptide complexes allows for the targeting of intracellular antigens as well as extracellularly expressed antigens.

[0087] Intracellularly expressed target proteins (e.g., cytoplasmically expressed (i.e., cytoplasmic proteins), nuclearly expressed (i.e., nuclear proteins), etc.) may be referred to as intracellular antigens (e.g., cytoplasmic antigens, nuclear antigens, etc.). Accordingly, antigen-binding domains of the subject disclosure may, in some instances, be specific for intracellular antigen fragments complexed with MHC, e.g., a peptide-MHC complex, also, in some instances, described as a human leukocyte antigen (HLA)-peptide complex.

[0088] Exemplary protein targets to which an antigen-binding domain targeting a peptide-MHC complex may be directed as well as exemplary peptides in the context of MHC for each protein target are provided in **Table 2** below.

Table 2: anti-peptide-MHC targets

Target	Exemplary Peptides	HLA	References
WT1	RMFPNAPYL (SEQ ID NO:470)	HLA-A2	Leukemia. (2015) 29(11):2238-47
KRAS and KRAS mutants (e.g., G12V & G12C)	KLVVVGAGGV (SEQ ID NO:471); KLVVVGAVGV (SEQ ID NO:742); KLVVVGACGV (SEQ ID NO:473); KLVVVGADGV (SEQ ID NO:744); VVGAVGVGK (SEQ ID NO:745); VVGACGVGK (SEQ ID NO:476); VVGAGGVGK (SEQ ID NO:477)	HLA-A2; HLA-A3	Proc Natl Acad Sci U S A. (2015) 112(32)
EGFP and EGFP	KITDFGLAK (SEQ ID NO:478);	HLA-A3	Proc Natl Acad Sci U S A. (2015)

mutants (e.g., L858R)	KITDFGRAK (SEQ ID NO:479);		112(32)
PR1	VLQELNVTV (SEQ ID NO:480)	HLA-A2	Cytotherapy. (2016) 18(8):985-94
MAGE-A1	EADPTGHSY (SEQ ID NO:481)	HLA-A1	Blood. (2011) 117(16):4262-4272
P53	LLGRNSFEV (SEQ ID NO:482); STTPPPGTRV (SEQ ID NO:483)	HLA-A2	Gene Ther. (2001) 8(21):1601-8
MART-1	ELAGIGILTV (SEQ ID NO:484)	HLA-A2	Biomark Med. (2010) 4(4):496-7
gp100	IMDQVPFSV (SEQ ID NO:485)	HLA-A2	Biomark Med. (2010) 4(4):496-7
CMV pp65	NLVPMVATV (SEQ ID NO:486)	HLA-A2	Biomark Med. (2010) 4(4):496-7
HIV Vpr	AIIRILQQL (SEQ ID NO:487)	HLA-A2	Biomark Med. (2010) 4(4):496-7
HA-1H	VLHDDLLEA (SEQ ID NO:488); VLRDDLLEA (SEQ ID NO:489)	HLA-A2	Biomark Med. (2010) 4(4):496-7
NY-ESO-1	SLLMWITQV (SEQ ID NO:490)	HLA-A2	Gene Ther. (2014) 21(6):575-84
EBNA3C	LLDFVRFMGV (SEQ ID NO:491)	HLA-A2	Proc Natl Acad Sci U S A. (2009) 106(14):5784-8
AFP	FMNKFIYEI (SEQ ID NO:492)	HLA-A2	Cancer Gene Ther. (2012) 19(2):84-100
Her2	KIFGSLAFL (SEQ ID NO:493)	HLA-A2	Clin Cancer Res. (2016) pii: clincanres 1203.2016
hCG-beta	GVLPALPQV (SEQ ID NO:494)	HLA-A2	J Natl Cancer Inst. (2013) 105(3):202-18
HBV Env183-91	FLLTRILTI (SEQ ID NO:495)	HLA-A2	J Immunol. (2006) 177(6):4187-95

[0089] In some instances, the antigen-binding domain of a conditionally active heterodimeric polypeptide of the instant disclosure is or includes a portion of an antibody (e.g., a scFv) that specifically binds a peptide-MHC having an intracellular cancer antigen peptide of **Table 2**.

[0090] In some instances, the antigen-binding domain of a conditionally active heterodimeric polypeptide of the instant disclosure is or includes a portion of an antibody (e.g., a scFv) that specifically binds a peptide-MHC described in Dhanik et al. *BMC Bioinformatics* (2016) 17:286, the disclosure of which is incorporated herein by reference in its entirety, including but not limited to e.g., a NLRP4 peptide (e.g., HLSPIDCEV (SEQ ID NO:496))-MHC complex, a UMODL1 peptide (e.g., LTSMWSPAV (SEQ ID NO:497))-MHC complex, a NLRP4 peptide (e.g., HLDHPHPAV (SEQ ID NO:498))-MHC complex, a MAGEC2 peptide (e.g., SLSVMSSNV (SEQ ID NO:499))-MHC complex, a NLRP4 peptide (e.g., MMAWSDNKI (SEQ ID NO:500))-MHC complex, a COX7B2 peptide (e.g., TQIGIEWNL (SEQ ID NO:501))-MHC complex, a NLRP4 peptide (e.g., CLFEMQDPA (SEQ ID NO:502))-MHC complex, a UMODL1 peptide (e.g., YLSHPSCNV (SEQ ID NO:503))-MHC complex, a COX7B2 peptide (e.g., GIEWNLSPV (SEQ ID NO:504))-MHC complex, a MAGEA11 peptide (e.g., GLGCSPASI (SEQ ID NO:505))-MHC complex, a RPE65 peptide (e.g., RQAFEFPQI (SEQ ID NO:506))-MHC complex, a RPE65 peptide (e.g., RQAFEFPQI (SEQ ID NO:507))-MHC complex, a NLRP4 peptide (e.g., GMWTDTFEF (SEQ ID NO:508))-MHC complex, a TRIM51 peptide (e.g., YLNWQDTAV (SEQ ID NO:509))-MHC complex, a MAGEA11 peptide (e.g., VLWGPITQI (SEQ ID NO:510))-MHC complex, a NLRP4 peptide (e.g., TLDHTGVVV (SEQ ID NO:511))-MHC complex, a RPE65 peptide (e.g., TMGVWLHIA (SEQ ID NO:512))-MHC complex, a RPE65 peptide (e.g., TMGVWLHIA (SEQ ID

NO:513))-MHC complex, a MAGEC2 peptide (e.g., KVWVQGHYL (SEQ ID NO:514))-MHC complex, a UMODL1 peptide (e.g., KINCNNFRL (SEQ ID NO:515))-MHC complex, etc.

Ligand

[0091] In some cases, a member of a specific binding pair suitable for use in a subject conditionally active heterodimeric polypeptide is a ligand for a receptor. Ligands include, but are not limited to, cytokines (e.g., IL-13, etc.); growth factors (e.g., heregulin; vascular endothelial growth factor (VEGF); and the like); an integrin-binding peptide (e.g., a peptide comprising the sequence Arg-Gly-Asp); and the like.

[0092] Where the member of a specific binding pair in a subject conditionally active heterodimeric polypeptide is a ligand, the conditionally active heterodimeric polypeptide can be activated in the presence of both a dimerizer agent and a second member of the specific binding pair, where the second member of the specific binding pair is a receptor for the ligand. For example, where the ligand is VEGF, the second member of the specific binding pair can be a VEGF receptor, including a soluble VEGF receptor. As another example, where the ligand is heregulin, the second member of the specific binding pair can be Her2.

Receptors

[0093] As noted above, in some cases, the member of a specific binding pair that is included in a subject conditionally active heterodimeric polypeptide is a receptor, e.g., a receptor for a ligand, a co-receptor, etc. The receptor can be a ligand-binding fragment of a receptor. Suitable receptors include, but are not limited to, a growth factor receptor (e.g., a VEGF receptor); a killer cell lectin-like receptor subfamily K, member 1 (NKG2D) polypeptide (receptor for MICA, MICB, and ULB6); a cytokine receptor (e.g., an IL-13 receptor; an IL-2 receptor; etc.); Her2; CD27; a natural cytotoxicity receptor (NCR) (e.g., NKP30 (NCR3/CD337) polypeptide (receptor for HLA-B–associated transcript 3 (BAT3) and B7-H6); etc.); etc.

Antibody-based recognition scaffolds

[0094] In some cases, the first member of the specific binding pair is an antibody. The antibody can be any antigen-binding antibody-based polypeptide, a wide variety of which are known in the art. In some instances, the antigen-binding domain is a single chain Fv (scFv). Other antibody based recognition domains (cAb VHH (camelid antibody variable domains) and humanized versions, IgNAR VH (shark antibody variable domains) and humanized versions, sdAb VH (single domain antibody variable domains) and "camelized" antibody variable domains are suitable for use. In some instances, T-cell receptor (TCR) based recognition domains such as single chain TCR (scTv, single chain two-domain TCR containing VαVβ) are also suitable for use.

[0095] Where the member of a specific binding pair in a conditionally active heterodimeric polypeptide of the present disclosure is an antibody-based recognition scaffold, the conditionally active heterodimeric polypeptide can be activated in the presence of a second member of the specific binding pair, where the

second member of the specific binding pair is an antigen that binds to the antibody-based recognition scaffold.

[0096] An antibody suitable for inclusion in a conditionally active heterodimeric polypeptide of the present disclosure can have a variety of antigen-binding specificities.

[0097] In some cases, the antigen-binding domain is specific for an epitope present in an antigen that is expressed by (synthesized by) a cancer cell, i.e., a cancer cell associated antigen. The cancer cell associated antigen can be an antigen associated with, e.g., a breast cancer cell, a B cell lymphoma, a pancreatic cancer, a Hodgkin lymphoma cell, an ovarian cancer cell, a prostate cancer cell, a mesothelioma, a lung cancer cell (e.g., a small cell lung cancer cell), a non-Hodgkin B-cell lymphoma (B-NHL) cell, an ovarian cancer cell, a prostate cancer cell, a mesothelioma cell, a lung cancer cell (e.g., a small cell lung cancer cell), a melanoma cell, a chronic lymphocytic leukemia cell, an acute lymphocytic leukemia cell, a neuroblastoma cell, a glioma, a glioblastoma, a medulloblastoma, a colorectal cancer cell, etc. A cancer cell associated antigen may also be expressed by a non-cancerous cell.

[0098] In some cases, the antigen-binding domain is specific for an epitope present in a tissue-specific antigen, including e.g., those antigens described herein. In some cases, the antigen-binding domain is specific for an epitope present in a disease-associated antigen, including e.g., those antigens described herein.

[0099] Non-limiting examples of antigens to which an antigen-binding domain of a subject conditionally active heterodimeric polypeptide can bind include, e.g., CD19, CD20, CD38, CD30, Her2/neu/ERBB2, CA125, MUC-1, prostate-specific membrane antigen (PSMA), CD44 surface adhesion molecule, mesothelin, carcinoembryonic antigen (CEA), epidermal growth factor receptor (EGFR), EGFRvIII, vascular endothelial growth factor receptor-2 (VEGFR2), high molecular weight-melanoma associated antigen (HMW-MAA), MAGE-A1, IL-13R-a2, GD2, and the like.

[00100] Non-limiting examples of antigens to which an antigen-binding domain of a subject conditionally active heterodimeric polypeptide can bind include, e.g., Cadherins (CDH1-20), Integrins (alpha and beta isoforms), Ephrins, NCAMs, connexins, CD44, syndecan, CD47, DGalpha/beta, SV2, protocadherin, Fas, Dectin-1, CD7, CD40, Neuregulin, KIR, BTLA, Tim-2, Lag-3, CD19, CTLA4, CD28, TIGIT, and ICOS.

[00101] In some cases, the antibody is specific for a cytokine. In some cases, the antibody is specific for a cytokine receptor. In some cases, the antibody is specific for a growth factor. In some cases, the antibody is specific for a growth factor receptor. In some cases, the antibody is specific for a cell-surface receptor.

[00102] In some cases, the antibody is specific for a cell surface target, where non-limiting examples of cell surface targets include CD19, CD30, Her2, CD22, ENPP3, EGFR, CD20, CD52, CD 11a, and alpha-integrin.

[00103] In some cases, the antigen (second member of the specific binding pair) bound by the antibody-based scaffold is soluble. In some cases, the antigen is membrane-bound, e.g., in some cases, the antigen is present on the surface of a cell. In some cases, the antigen is immobilized on an insoluble support, where an insoluble support can comprise any of a variety of materials (e.g., polyethylene, polystyrene, polyvinylpyrrolidone, polycarbonate, nitrocellulose, and the like); and where an insoluble support can take a variety of forms, e.g., a plate, a tissue culture dish, a column, and the like. In some cases, the antigen is present in an extracellular matrix (ECM) (e.g., the antigen is an ECM component). In some cases, the antigen is present in an artificial matrix. In some cases, the antigen is present in an acellular environment.

Non-antibody-based recognition scaffolds

[00104] In some cases, the first member of the specific binding pair is a non-antibody-based recognition scaffold. Where the member of a specific binding pair in a conditionally active heterodimeric polypeptide of the present disclosure is a non-antibody-based recognition scaffold, the conditionally active heterodimeric polypeptide can be activated in the presence of a second member of the specific binding pair, where the second member of the specific binding pair is a target that binds to the non-antibody-based recognition scaffold.

[00105] Non-antibody-based recognition scaffolds include, e.g., affibodies; engineered Kunitz domains; monobodies (adnectins); anticalins; designed ankyrin repeat domains (DARPins); a binding site of a cysteine-rich polypeptide (e.g., cysteine-rich knottin peptides); avimers; afflins; and the like. See, e.g., Gebauer and Skerra (2009) *Curr. Opin. Chem. Biol.* 13:245.

[00106] Non-antibody-based scaffolds (also referred to herein as "antibody mimic molecules") may be identified by selection or isolation of a target-binding variant from a library of binding molecules having artificially diversified binding sites. Diversified libraries can be generated using completely random approaches (e.g., error-prone polymerase chain reaction (PCR), exon shuffling, or directed evolution) or aided by art-recognized design strategies. For example, amino acid positions that are usually involved when the binding site interacts with its cognate target molecule can be randomized by insertion of degenerate codons, trinucleotides, random peptides, or entire loops at corresponding positions within the nucleic acid which encodes the binding site (see e.g., U.S. Pub. No. 20040132028). The location of the amino acid positions can be identified by investigation of the crystal structure of the binding site in protein entity with the target molecule. Candidate positions for randomization include loops, flat surfaces, helices, and binding cavities of the binding site. In certain embodiments, amino acids within the

binding site that are likely candidates for diversification can be identified by their homology with the immunoglobulin fold. For example, residues within the CDR-like loops of fibronectin may be randomized to generate a library of fibronectin binding molecules (see, e.g., Koide et al., J. Mol. Biol., 284: 1141-1151 (1998)). Other portions of the binding site which may be randomized include flat surfaces. Following randomization, the diversified library may then be subjected to a selection or screening procedure to obtain binding molecules with the desired binding characteristics. For example, selection can be achieved by art-recognized methods such as phage display, yeast display, or ribosome display.

[00107] For example, in some cases, the non-antibody-based scaffold comprises a binding site from a fibronectin binding molecule. Fibronectin binding molecules (e.g., molecules comprising the Fibronectin type I, II, or III domains) display CDR-like loops which, in contrast to immunoglobulins, do not rely on intra-chain disulfide bonds. The FnIII loops comprise regions that may be subjected to random mutation and directed evolutionary schemes of iterative rounds of target binding, selection, and further mutation in order to develop useful therapeutic tools. Fibronectin-based "addressable" therapeutic binding molecules ("FATBIM") can be developed to specifically bind the target antigen or epitope. Methods for making fibronectin binding polypeptides are described, for example, in WO 01/64942 and in U.S. Pat. Nos. 6,673,901, 6,703,199, 7,078,490, and 7,119,171.

[00108] As another example, in some cases, the non-antibody-based scaffold comprises a binding site from an affibody. Affibodies are derived from the immunoglobulin binding domains of staphylococcal Protein A (SPA) (see e.g., Nord et al., Nat. Biotechnol., 15: 772-777 (1997)). An affibody is an antibody mimic that has unique binding sites that bind specific targets. Affibodies can be small (e.g., consisting of three alpha helices with 58 amino acids and having a molar mass of about 6 kDa), have an inert format (no Fc function), and have been successfully tested in humans as targeting moieties. Affibody binding sites can be synthesized by mutagenizing an SPA-related protein (e.g., Protein Z) derived from a domain of SPA (e.g., domain B) and selecting for mutant SPA-related polypeptides having binding affinity for a target antigen or epitope. Other methods for making affibody binding sites are described in U.S. Pat. Nos. 6,740,734 and 6,602,977 and in WO 00/63243.

[00109] As another example, in some cases, the non-antibody-based scaffold comprises a binding site from an anticalin. An anticalin is an antibody functional mimetic derived from a human lipocalin. Lipocalins are a family of naturally-occurring binding proteins that bind and transport small hydrophobic molecules such as steroids, bilins, retinoids, and lipids. The main structure of an anticalin is similar to wild type lipocalins. The central element of this protein architecture is a beta-barrel structure of eight antiparallel strands, which supports four loops at its open end. These loops form the natural binding site of the lipocalins and can be reshaped in vitro by extensive amino acid replacement, thus creating novel binding specificities. Anticalins possess high affinity and specificity for their ligands as well as fast binding

kinetics, so that their functional properties are similar to those of antibodies. Anticalins are described in, e.g., U.S. Pat. No. 7,723,476.

[00110] As another example, in some cases, the non-antibody-based scaffold comprises a binding site from a cysteine-rich polypeptide. Cysteine-rich domains in some cases do not form an alpha-helix, a beta-sheet, or a beta-barrel structure. In some cases, the disulfide bonds promote folding of the domain into a three-dimensional structure. In some cases, cysteine-rich domains have at least two disulfide bonds, e.g., at least three disulfide bonds. An exemplary cysteine-rich polypeptide is an A domain protein. A-domains (sometimes called "complement-type repeats") contain about 30-50 or 30-65 amino acids. In some cases, the domains comprise about 35-45 amino acids and in some cases about 40 amino acids. Within the 30-50 amino acids, there are about 6 cysteine residues. Of the six cysteines, disulfide bonds typically are found between the following cysteines: C1 and C3, C2 and C5, C4 and C6. The A domain constitutes a ligand binding moiety. The cysteine residues of the domain are disulfide linked to form a compact, stable, functionally independent moiety. Clusters of these repeats make up a ligand binding domain, and differential clustering can impart specificity with respect to the ligand binding. Exemplary proteins containing A-domains include, e.g., complement components (e.g., C6, C7, C8, C9, and Factor I), serine proteases (e.g., enteropeptidase, matriptase, and corin), transmembrane proteins (e.g., ST7, LRP3, LRP5 and LRP6) and endocytic receptors (e.g. Sortilin-related receptor, LDL-receptor, VLDLR, LRP1, LRP2, and ApoER2). Methods for making A-domain proteins of a desired binding specificity are disclosed, for example, in WO 02/088171 and WO 04/044011.

[00111] As another example, in some cases, the non-antibody-based scaffold comprises a binding site from a repeat protein. Repeat proteins are proteins that contain consecutive copies of small (e.g., about 20 to about 40 amino acid residues) structural units or repeats that stack together to form contiguous domains. Repeat proteins can be modified to suit a particular target binding site by adjusting the number of repeats in the protein. Exemplary repeat proteins include designed ankyrin repeat proteins (i.e., a DARPins) (see e.g., Binz et al., Nat. Biotechnol., 22: 575-582 (2004)) or leucine-rich repeat proteins (i.e., LRRPs) (see e.g., Pancer et al., Nature, 430: 174-180 (2004)). As another example, in some cases, the non-antibody-based scaffold comprises a DARPin.

[00112] As used herein, the term "DARPin" refers to a genetically engineered antibody mimetic protein that typically exhibits highly specific and high-affinity target protein binding. DARPins were first derived from natural ankyrin proteins. In some cases, DARPins comprise three, four or five repeat motifs of an ankyrin protein. In some cases, a unit of an ankyrin repeat consists of 30-34 amino acid residues and functions to mediate protein-protein interactions. In some cases, each ankyrin repeat exhibits a helix-turn-helix conformation, and strings of such tandem repeats are packed in a nearly linear array to form helix-turn-helix bundles connected by relatively flexible loops. In some cases, the global structure of an ankyrin repeat protein is stabilized by intra- and inter-repeat hydrophobic and hydrogen bonding

interactions. The repetitive and elongated nature of the ankyrin repeats provides the molecular bases for the unique characteristics of ankyrin repeat proteins in protein stability, folding and unfolding, and binding specificity. The molecular mass of a DARPin domain can be from about 14 or 18 kDa for four- or five-repeat DARPins, respectively. DARPins are described in, e.g., U.S. Pat. No. 7,417,130. In some cases, tertiary structures of ankyrin repeat units share a characteristic composed of a beta-hairpin followed by two antiparallel alpha-helices and ending with a loop connecting the repeat unit with the next one. Domains built of ankyrin repeat units can be formed by stacking the repeat units to an extended and curved structure. LRRP binding sites from part of the adaptive immune system of sea lampreys and other jawless fishes and resemble antibodies in that they are formed by recombination of a suite of leucine-rich repeat genes during lymphocyte maturation. Methods for making DARpin or LRRP binding sites are described in WO 02/20565 and WO 06/083275.

[00113] As another example, in some cases, the non-antibody-based scaffold comprises a binding site derived from Src homology domains (e.g. SH2 or SH3 domains), PDZ domains, beta-lactamase, high affinity protease inhibitors, or small disulfide binding protein scaffolds such as scorpion toxins. Methods for making binding sites derived from these molecules have been disclosed in the art, see e.g., Panni et al., J. Biol. Chem., 277: 21666-21674 (2002), Schneider et al., Nat. Biotechnol., 17: 170-175 (1999); Legendre et al., Protein Sci., 11:1506-1518 (2002); Stoop et al., Nat. Biotechnol., 21: 1063-1068 (2003); and Vita et al., PNAS, 92: 6404-6408 (1995). Yet other binding sites may be derived from a binding domain selected from the group consisting of an EGF-like domain, a Kringle-domain, a PAN domain, a Gla domain, a SRCR domain, a Kunitz/Bovine pancreatic trypsin Inhibitor domain, a Kazal-type serine protease inhibitor domain, a Trefoil (P-type) domain, a von Willebrand factor type C domain, an Anaphylatoxin-like domain, a CUB domain, a thyroglobulin type I repeat, LDL-receptor class A domain, a Sushi domain, a Link domain, a Thrombospondin type I domain, an Immunoglobulin-like domain, a C-type lectin domain, a MAM domain, a von Willebrand factor type A domain, a Somatomedin B domain, a WAP-type four disulfide core domain, a F5/8 type C domain, a Hemopexin domain, a Laminin-type EGF-like domain, a C2 domain, a binding domain derived from tetranectin in its monomeric or trimeric form, and other such domains known to those of ordinary skill in the art, as well as derivatives and/or variants thereof. Exemplary non-antibody-based scaffolds, and methods of making the same, can also be found in Stemmer et al., "Protein scaffolds and uses thereof", U.S. Patent Publication No. 20060234299 (Oct. 19, 2006) and Hey, et al., Artificial, Non-Antibody Binding Proteins for Pharmaceutical and Industrial Applications, TRENDS in Biotechnology, vol. 23, No. 10, Table 2 and pp. 514-522 (October 2005).

[00114] As another example, in some cases, the non-antibody-based scaffold comprises a Kunitz domain. The term "Kunitz domains" as used herein, refers to conserved protein domains that inhibit certain proteases, e.g., serine proteases. Kunitz domains are relatively small, typically being about 50 to 60

amino acids long and having a molecular weight of about 6 kDa. Kunitz domains typically carry a basic charge and are characterized by the placement of two, four, six or eight or more that form disulfide linkages that contribute to the compact and stable nature of the folded peptide. For example, many Kunitz domains have six conserved cysteine residues that form three disulfide linkages. The disulfide-rich α/β fold of a Kunitz domain can include two, three (typically), or four or more disulfide bonds.

[00115] Kunitz domains have a pear-shaped structure that is stabilized the, e.g., three disulfide bonds, and that contains a reactive site region featuring the principal determinant P1 residue in a rigid confirmation. These inhibitors competitively prevent access of a target protein (e.g., a serine protease) for its physiologically relevant macromolecular substrate through insertion of the P1 residue into the active site cleft. The P1 residue in the proteinase-inhibitory loop provides the primary specificity determinant and dictates much of the inhibitory activity that particular Kunitz protein has toward a targeted proteinase. In general, the N-terminal side of the reactive site (P) is energetically more important that the P' C-terminal side. In most cases, lysine or arginine occupy the P1 position to inhibit proteinases that cleave adjacent to those residues in the protein substrate. Other residues, particularly in the inhibitor loop region, contribute to the strength of binding. Generally, about 10-12 amino acid residues in the target protein and 20-25 residues in the proteinase are in direct contact in the formation of a stable proteinase-inhibitor protein entity and provide a buried area of about 600 to 900 A. By modifying the residues in the P site and surrounding residues Kunitz domains can be designed to target a protein of choice. Kunitz domains are described in, e.g., U.S. Pat. No. 6,057,287.

[00116] As another example, in some cases, the non-antibody-based scaffold is an affilin. Affilins are small antibody-mimic proteins which are designed for specific affinities towards proteins and small compounds. New affilins can be very quickly selected from two libraries, each of which is based on a different human derived scaffold protein. Affilins do not show any structural homology to immunoglobulin proteins. There are two commonly-used affilin scaffolds, one of which is gamma crystalline, a human structural eye lens protein and the other is "ubiquitin" superfamily proteins. Both human scaffolds are very small, show high temperature stability and are almost resistant to pH changes and denaturing agents. This high stability is mainly due to the expanded beta sheet structure of the proteins. Examples of gamma crystalline derived proteins are described in WO200104144 and examples of "ubiquitin-like" proteins are described in WO2004106368.

[00117] As another example, in some cases, the non-antibody-based scaffold is an Avimer. Avimers are evolved from a large family of human extracellular receptor domains by in vitro exon shuffling and phage display, generating multidomain proteins with binding and inhibitory properties. Linking multiple independent binding domains has been shown to create avidity and results in improved affinity and specificity compared with conventional single-epitope binding proteins. In certain embodiments, Avimers consist of two or more peptide sequences of 30 to 35 amino acids each, connected by spacer

region peptides. The individual sequences are derived from A domains of various membrane receptors and have a rigid structure, stabilized by disulfide bonds and calcium. Each A domain can bind to a certain epitope of the target protein. The combination of domains binding to different epitopes of the same protein increases affinity to this protein, an effect known as avidity (hence the name). Avimers with sub-nanomolar affinities have been obtained against a variety of targets. Alternatively, the domains can be directed against epitopes on different target proteins. Additional information regarding avimers can be found in U.S. patent application Publication Nos. 2006/0286603, 2006/0234299, 2006/0223114, 2006/0177831, 2006/0008844, 2005/0221384, 2005/0164301, 2005/0089932, 2005/0053973, 2005/0048512, 2004/0175756.

[00118] Suitable targets of a non-antibody-based scaffold include any of the above-mentioned antigens to which an antibody-based scaffold can bind.

[00119] In some cases, the target (second member of the specific binding pair) bound by the non-antibody-based scaffold is soluble. In some cases, the target is membrane-bound, e.g., in some cases, the target is present on the surface of a cell. In some cases, the target is immobilized on an insoluble support, where an insoluble support can comprise any of a variety of materials (e.g., polyethylene, polystyrene, polyvinylpyrrolidone, polycarbonate, nitrocellulose, and the like); and where an insoluble support can take a variety of forms, e.g., a plate, a tissue culture dish, a column, and the like. In some cases, the target is present in an extracellular matrix (ECM) (e.g., the antigen is an ECM component). In some cases, the target is present in an artificial matrix. In some cases, the target is present in an acellular environment.

Cell adhesion molecules

[00120] In some cases, the first member of the specific binding pair is a cell adhesion molecule (CAM), i.e., a polypeptide that binds a component of an extracellular matrix (ECM) or that binds a cell surface molecule. For example, in some cases, the first member of the specific binding pair is the extracellular region of a CAM. In some cases, the CAM is a calcium-independent adhesion molecule; for example, in some cases, the CAM is an immunoglobulin superfamily CAM. In some cases, the CAM is a calcium-dependent adhesion molecule; e.g., the CAM is an integrin, a cadherin, or a selectin. In some cases, the first member of the specific binding pair is an integrin. In some cases, the first member of the specific binding pair is a cadherin, e.g., an E-cadherin, a P-cadherin, an N-cadherin, an R-cadherin, an M-cadherin, etc. In some cases, the first member of the specific binding pair is a selectin, e.g., an E-selectin, an L-selectin, or a P-selectin. Binding fragments of a CAM can be used as the first member of the specific binding pair.

[00121] Where the first member of the specific binding pair is a CAM, the second member of the specific binding pair is a component of ECM or a cell surface molecule that binds the CAM. For example, where the first member of the specific binding pair is an integrin, the second member of the specific binding pair is a component of collagen, fibrinogen, fibronectin, or vitronectin. As another example, where the

first member of the specific binding pair is cadherin, the second member of the specific binding pair is cell surface antigen bound by the cadherin. As another example, where the first member of the specific binding pair is a selectin, the second member of the specific binding pair is a fucosylated carbohydrate.

Ligands

[00122] In some cases, the first member of the specific binding pair is a ligand for a receptor. Ligands include polypeptides, nucleic acids, glycoproteins, small molecules, carbohydrates, lipids, glycolipids, lipoproteins, lipopolysaccharides, etc. In some cases, the ligand is soluble.

[00123] Ligands include, but are not limited to, cytokines (e.g., IL-13, etc.); growth factors (e.g., heregulin; vascular endothelial growth factor (VEGF); and the like); peptide hormones; an integrin-binding peptide (e.g., a peptide comprising the sequence Arg-Gly-Asp); an N-glycan; and the like.

[00124] Where the member of a specific binding pair in a conditionally active heterodimeric polypeptide of the present disclosure is a ligand, the conditionally active heterodimeric polypeptide can be activated in the presence of a second member of the specific binding pair, where the second member of the specific binding pair is a receptor for the ligand. For example, where the ligand is VEGF, the second member of the specific binding pair can be a VEGF receptor, including a soluble VEGF receptor. Alternatively, the first member of the specific binding pair can be a VEGF receptor; and the first member of the specific binding pair can be VEGF. As another example, where the ligand is heregulin, the second member of the specific binding pair can be Her2.

[00125] Where the first member of the specific binding pair is a ligand, the second member of the specific binding pair is a molecule that binds the ligand, e.g., the second member of the specific binding pair is an antibody that specifically binds the ligand, a receptor for the ligand, etc.

[00126] Where the first member of the specific binding pair is a ligand, in some cases, the second member of the specific binding pair (the molecule that binds the ligand) is soluble. In some cases, the second member of the specific binding pair is membrane-bound, e.g., in some cases, the second member of the specific binding pair is present on the surface of a cell. In some cases, the second member of the specific binding pair is immobilized on an insoluble support, where an insoluble support can comprise any of a variety of materials (e.g., polyethylene, polystyrene, polyvinylpyrrolidone, polycarbonate, nitrocellulose, and the like); and where an insoluble support can take a variety of forms, e.g., a plate, a tissue culture dish, a column, and the like. In some cases, the second member of the specific binding pair is present in an acellular environment.

Antigens

[00127] In some cases, the first member of the specific binding pair is an antigen to which an antibody specifically binds. The antigen can be any antigen, e.g., a naturally-occurring (endogenous) antigen; a

synthetic (e.g., modified in such a way that it is no longer the same as a naturally-occurring antigen; modified from its natural state; etc.) antigen; etc.

[00128] Where the member of a specific binding pair in a conditionally active heterodimeric polypeptide of the present disclosure is an antigen, the conditionally active heterodimeric polypeptide can be activated in the presence of a second member of the specific binding pair, where the second member of the specific binding pair is an antibody (antibody-based recognition scaffold) that binds to the antigen.

[00129] In some cases, the antigen is a disease-associated antigen, e.g., a cancer-associated antigen, an autoimmune disease-associated antigen, a pathogen-associated antigen, an inflammation-associated antigen, or the like.

[00130] For example, where the second member of the specific binding pair is an antibody specific for a cancer-associated antigen, the antigen can be a cancer-associated antigen, where cancer-associated antigens include, e.g., CD19, CD20, CD38, CD30, Her2/neu/ERBB2, CA125, MUC-1, prostate-specific membrane antigen (PSMA), CD44 surface adhesion molecule, mesothelin, carcinoembryonic antigen (CEA), epidermal growth factor receptor (EGFR), EGFRvIII, vascular endothelial growth factor receptor-2 (VEGFR2), high molecular weight-melanoma associated antigen (HMW-MAA), MAGE-A1, IL-13R-a2, GD2, and the like. Cancer-associated antigens also include, e.g., 4-1BB, 5T4, adenocarcinoma antigen, alpha-fetoprotein, BAFF, B-lymphoma cell, C242 antigen, CA-125, carbonic anhydrase 9 (CA-IX), C-MET, CCR4, CD152, CD19, CD20, CD200, CD22, CD221, CD23 (IgE receptor), CD28, CD30 (TNFRSF8), CD33, CD4, CD40, CD44 v6, CD51, CD52, CD56, CD74, CD80, CEA, CNTO888, CTLA-4, DRS, EGFR, EpCAM, CD3, FAP, fibronectin extra domain-B, folate receptor 1, GD2, GD3 ganglioside, glycoprotein 75, GPNMB, HER2/neu, HGF, human scatter factor receptor kinase, IGF-1 receptor, IGF-I, IgG1, L1-CAM, IL-13, IL-6, insulin-like growth factor I receptor, integrin $\alpha 5\beta 1$, integrin $\alpha v\beta 3$, MORAb-009, MS4A1, MUC1, mucin CanAg, N-glycolylneuraminic acid, NPC-1C, PDGF-R α, PDL192, phosphatidylserine, prostatic carcinoma cells, RANKL, RON, ROR1, SCH 900105, SDC1, SLAMF7, TAG-72, tenascin C, TGF beta 2, TGF-β, TRAIL-R1, TRAIL-R2, tumor antigen CTAA16.88, VEGF-A, VEGFR-1, VEGFR2, and vimentin.

[00131] The antigen can be associated with an inflammatory disease. Non-limiting examples of antigens associated with inflammatory disease include, e.g., AOC3 (VAP-1), CAM-3001, CCL11 (eotaxin-1), CD125, CD147 (basigin), CD154 (CD40L), CD2, CD20, CD23 (IgE receptor), CD25 (α chain of IL-2 receptor), CD3, CD4, CD5, IFN-α, IFN-γ, IgE, IgE Fc region, IL-1, IL-12, IL-23, IL-13, IL-17, IL-17A, IL-22, IL-4, IL-5, IL-5, IL-6, IL-6 receptor, integrin $\alpha 4$, integrin $\alpha 4\beta 7$, LFA-1 (CD11a), myostatin, OX-40, scleroscin, SOST, TGF beta 1, TNF-α, and VEGF-A.

[00132] Where the first member of the specific binding pair is an antigen, the second member of the specific binding pair can be an antibody-based scaffold (e.g., an antibody) or a non-antibody-based scaffold. In

some cases, the second member of the specific binding pair is present on the surface of a cell. In some cases, the second member of the specific binding pair is immobilized on an insoluble support. In some cases, the second member of the specific binding pair is soluble. In some cases, the second member of the specific binding pair is present in an extracellular environment (e.g., extracellular matrix). In some cases, the second member of the specific binding pair is present in an artificial matrix. In some cases, the second member of the specific binding pair is present in an acellular environment.

Targets of non-antibody-based recognition scaffolds

[00133] In some cases, the first member of the specific binding pair is a target of a non-antibody-based scaffold. Targets include, e.g., polypeptides, nucleic acids, glycoproteins, small molecules, carbohydrates, lipids, glycolipids, lipoproteins, lipopolysaccharides, etc.

[00134] Where the first member of the specific binding pair is a target of a non-antibody-based scaffold, the second member of the specific binding pair is a non-antibody-based scaffold.

Receptors

[00135] In some cases, the first member of the specific binding pair is a receptor. In some cases, the receptor is a growth factor receptor. In some cases, the receptor is a cytokine receptor. In some cases, the receptor is a cell surface receptor that binds to a co-receptor on a cell. In some cases, the receptor is a neurotransmitter receptor. In some cases, the receptor binds to an extracellular matrix component. In some cases, the receptor is an immunoglobulin Fc receptor.

[00136] Suitable receptors include, but are not limited to, a growth factor receptor (e.g., a VEGF receptor); a killer cell lectin-like receptor subfamily K, member 1 (NKG2D) polypeptide (receptor for MICA, MICB, and ULB6); a cytokine receptor (e.g., an IL-13 receptor; an IL-2 receptor; etc.); an epidermal growth factor (EGF) receptor; Her2; CD27; a natural cytotoxicity receptor (NCR) (e.g., NKP30 (NCR3/CD337) polypeptide (receptor for HLA-B–associated transcript 3 (BAT3) and B7-H6); etc.); a T cell antigen receptor; a dihydrofolate receptor; a chimeric cytokine receptor; an Fc receptor; an extracellular matrix receptor (e.g. an integrin); a cell adhesion receptor (e.g. a cadherin); an immunoregulatory receptor including both positive co-receptors (e.g. CD28) and negative (immunosuppressive) co-receptors (e.g., PD1); a cytokine receptor; and a receptor for a immunoregulatory molecule (e.g. TGFβ), etc. In some cases, the receptor is truncated, relative to the wild-type receptor.

[00137] Where the first member of the specific binding pair is a receptor, the second member of the specific binding pair is target of the receptor, where the target can be a ligand for the receptor, or a co-receptor. In some cases, the second member of the specific binding pair is present on the surface of a cell. In some cases, the second member of the specific binding pair is immobilized on an insoluble support. In some cases, the second member of the specific binding pair is soluble. In some cases, the second member of the specific binding pair is present in an extracellular environment (e.g., extracellular matrix). In some

cases, the second member of the specific binding pair is present in an artificial matrix. In some cases, the second member of the specific binding pair is present in an acellular environment.

Hinge region

[00138] In some cases, the first polypeptide of a subject conditionally active heterodimeric polypeptide comprises a hinge region (also referred to herein as a "spacer"), where the hinge region is interposed between the antigen-binding domain and the transmembrane domain. In some cases, the hinge region is an immunoglobulin heavy chain hinge region. In some cases, the hinge region is a hinge region polypeptide derived from a receptor (e.g., a CD8-derived hinge region).

[00139] The hinge region can have a length of from about 4 amino acids to about 50 amino acids, e.g., from about 4 aa to about 10 aa, from about 10 aa to about 15 aa, from about 15 aa to about 20 aa, from about 20 aa to about 25 aa, from about 25 aa to about 30 aa, from about 30 aa to about 40 aa, or from about 40 aa to about 50 aa.

[00140] Suitable spacers can be readily selected and can be of any of a number of suitable lengths, such as from 1 amino acid (e.g., Gly) to 20 amino acids, from 2 amino acids to 15 amino acids, from 3 amino acids to 12 amino acids, including 4 amino acids to 10 amino acids, 5 amino acids to 9 amino acids, 6 amino acids to 8 amino acids, or 7 amino acids to 8 amino acids, and can be 1, 2, 3, 4, 5, 6, or 7 amino acids.

[00141] Exemplary spacers include glycine polymers $(G)_n$, glycine-serine polymers (including, for example, $(GS)_n$, $(GSGGS)_n$ (SEQ ID NO:516) and $(GGGS)_n$ (SEQ ID NO:517), where n is an integer of at least one), glycine-alanine polymers, alanine-serine polymers, and other flexible linkers known in the art. Glycine and glycine-serine polymers can be used; both Gly and Ser are relatively unstructured, and therefore can serve as a neutral tether between components. Glycine polymers can be used; glycine accesses significantly more phi-psi space than even alanine, and is much less restricted than residues with longer side chains (see Scheraga, *Rev. Computational Chem.* 11173-142 (1992)). Exemplary spacers can comprise amino acid sequences including, but not limited to, GGSG (SEQ ID NO:518), GGSGG (SEQ ID NO:519), GSGSG (SEQ ID NO:520), GSGGG (SEQ ID NO:521), GGGSG (SEQ ID NO:522), GSSSG (SEQ ID NO:523), and the like.

[00142] In some cases, the hinge region in the first polypeptide of a subject conditionally active heterodimeric polypeptide includes at least one cysteine. For example, in some cases, the hinge region can include the sequence Cys-Pro-Pro-Cys. If present, a cysteine in the hinge region of a first conditionally active heterodimeric polypeptide can be available to form a disulfide bond with a hinge region in a second conditionally active heterodimeric polypeptide.

[00143] Immunoglobulin hinge region amino acid sequences are known in the art; see, e.g., Tan et al. (1990) *Proc. Natl. Acad. Sci. USA* 87:162; and Huck et al. (1986) *Nucl. Acids Res.* 14:1779. As non-limiting examples, an immunoglobulin hinge region can include one of the following amino acid sequences:

DKTHT (SEQ ID NO:524); CPPC (SEQ ID NO:525); CPEPKSCDTPPPCPR (SEQ ID NO:526) (see, e.g., Glaser et al. (2005) *J. Biol. Chem.* 280:41494); ELKTPLGDTTHT (SEQ ID NO:527); KSCDKTHTCP (SEQ ID NO:528); KCCVDCP (SEQ ID NO:529); KYGPPCP (SEQ ID NO:530); EPKSCDKTHTCPPCP (SEQ ID NO:531) (human IgG1 hinge); ERKCCVECPPCP (SEQ ID NO:532) (human IgG2 hinge); ELKTPLGDTTHTCPRCP (SEQ ID NO:533) (human IgG3 hinge); SPNMVPHAHHAQ (SEQ ID NO:534) (human IgG4 hinge); and the like.

[00144] The hinge region can comprise an amino acid sequence of a human IgG1, IgG2, IgG3, or IgG4, hinge region. The hinge region can include one or more amino acid substitutions and/or insertions and/or deletions compared to a wild-type (naturally-occurring) hinge region. For example, His_{229} of human IgG1 hinge can be substituted with Tyr, so that the hinge region comprises the sequence EPKSCDKTYTCPPCP (SEQ ID NO:535); see, e.g., Yan et al. (2012) *J. Biol. Chem.* 287:5891.

[00145] The hinge region can comprise an amino acid sequence derived from human CD8; e.g., the hinge region can comprise the amino acid sequence: TTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACD (SEQ ID NO:536), or a variant thereof.

Transmembrane domain

[00146] The first and the second polypeptides of a CAR of the present disclosure include transmembrane domains for insertion into a eukaryotic cell membrane. The transmembrane domain of the first polypeptide is interposed between the antigen-binding domain and the co-stimulatory domain. Where the first polypeptide includes a hinge region, the transmembrane domain is interposed between the hinge region and the co-stimulatory domain, such that the first polypeptide comprises, in order from the amino terminus (N-terminus) to the carboxyl terminus (C-terminus): an antigen-binding domain; a hinge region; a transmembrane domain; a first co-stimulatory domain; and a first member of a dimerizer-binding pair.

[00147] The transmembrane domain of the second polypeptide is at or near the N-terminus of the polypeptide, such that the second polypeptide comprises, in order from N-terminus to C-terminus: a transmembrane domain; a second co-stimulatory domain; a second member of the dimerizer-binding pair; and an intracellular signaling domain.

[00148] Any transmembrane (TM) domain that provides for insertion of a polypeptide into the cell membrane of a eukaryotic (e.g., mammalian) cell is suitable for use. As one non-limiting example, the TM sequence IYIWAPLAGTCGVLLLSLVITLYC (SEQ ID NO:537) can be used. Additional non-limiting examples of suitable TM sequences include: a) CD8 beta derived : LGLLVAGVLVLLVSLGVAIHLCC (SEQ ID NO:538); b) CD4 derived: ALIVLGGVAGLLLFIGLGIFFCVRC (SEQ ID NO:539); c) CD3 zeta derived: LCYLLDGILFIYGVILTALFLRV (SEQ ID NO:540); d) CD28 derived: WVLVVVGGVLACYSLLVTVAFIIFWV (SEQ ID NO:541); e) CD134 (OX40) derived:

VAAILGLGLVLGLLGPLAILLALYLL (SEQ ID NO:542); and f) CD7 derived: ALPAALAVISFLLGLGLGVACVLA (SEQ ID NO:543).

Linkers

[00149] In some cases, a first polypeptide of a subject CAR includes a linker between any two adjacent domains. For example, a linker can be disposed between the transmembrane domain and the first co-stimulatory domain of the first polypeptide. As another example, a linker can be disposed between the first co-stimulatory domain and the first member of a dimerizer-binding pair of the first polypeptide. As another example, a linker can be disposed between the transmembrane domain and the second co-stimulatory domain of the second polypeptide. As another example, a linker can be disposed between the second co-stimulatory domain and the second member of the dimerizer-binding pair of the second polypeptide. As another example, a linker can be disposed between the second member of the dimerizer-binding pair and the intracellular signaling domain of the second polypeptide.

[00150] The linker peptide may have any of a variety of amino acid sequences. Proteins can be joined by a spacer peptide, generally of a flexible nature, although other chemical linkages are not excluded. A linker can be a peptide of between about 6 and about 40 amino acids in length, or between about 6 and about 25 amino acids in length. These linkers can be produced by using synthetic, linker-encoding oligonucleotides to couple the proteins. Peptide linkers with a degree of flexibility can be used. The linking peptides may have virtually any amino acid sequence, bearing in mind that suitable linkers will have a sequence that results in a generally flexible peptide. The use of small amino acids, such as glycine and alanine, are of use in creating a flexible peptide. The creation of such sequences is routine to those of skill in the art.

[00151] Suitable linkers can be readily selected and can be of any of a suitable of different lengths, such as from 1 amino acid (e.g., Gly) to 20 amino acids, from 2 amino acids to 15 amino acids, from 3 amino acids to 12 amino acids, including 4 amino acids to 10 amino acids, 5 amino acids to 9 amino acids, 6 amino acids to 8 amino acids, or 7 amino acids to 8 amino acids, and may be 1, 2, 3, 4, 5, 6, or 7 amino acids.

[00152] Exemplary flexible linkers include glycine polymers $(G)_n$, glycine-serine polymers (including, for example, $(GS)_n$, $GSGGS_n$ (SEQ ID NO:516) and $GGGS_n$ (SEQ ID NO:517), where n is an integer of at least one), glycine-alanine polymers, alanine-serine polymers, and other flexible linkers known in the art. Glycine and glycine-serine polymers are of interest since both of these amino acids are relatively unstructured, and therefore may serve as a neutral tether between components. Glycine polymers are of particular interest since glycine accesses significantly more phi-psi space than even alanine, and is much less restricted than residues with longer side chains (see Scheraga, *Rev. Computational Chem.* 11173-142 (1992)). Exemplary flexible linkers include, but are not limited GGSG (SEQ ID NO:518), GGSGG (SEQ ID NO:519), GSGSG (SEQ ID NO:520), GSGGG (SEQ ID NO:521), GGGSG (SEQ ID NO:522),

GSSSG (SEQ ID NO:523), and the like. The ordinarily skilled artisan will recognize that design of a peptide conjugated to any elements described above can include linkers that are all or partially flexible, such that the linker can include a flexible linker as well as one or more portions that confer less flexible structure.

Modulatory domains

[00153] Modulatory domains suitable for use in a CAR of the present disclosure include co-stimulatory domains. Modulatory domains may be present or absent in a subject conditionally acitive heterodimeric polypeptide of the present disclosure. As such, a particular conditionally acitive heterodimeric polypeptide of the present disclosure (or one or more polypeptide chains of a multichain conditionally acitive heterodimeric polypeptide of the present disclosure) may include anywhere from 0 to 6 or more modulatory domains. For example, in some instances, the polypeptide chains of a conditionally acitive heterodimeric polypeptide of the present disclosure may collectively include 0, 1, 2, 3, 4, 5, 6 or more modulatory domains. In some instances, a polypeptide chain of a conditionally acitive heterodimeric polypeptide of the present disclosure may individually include 0, 1, 2, 3, 4, 5, 6 or more modulatory domains. A particular modulatory domain may be present in one polypeptide chain of a conditionally acitive heterodimeric polypeptide but absent from another. In some instances, a particular modulatory domain may be present in both chains of a two chain conditionally acitive heterodimeric polypeptide. Furthermore, position of a modulatory domains on or within a polypeptide may vary greatly as a particular modulatory domain may be positioned at an end (e.g., the N-termal or C-terminal end) of the polypeptide or essentially any appropriate position within the polypeptide, e.g., adjacent to a transmembrane domain, adjacent to an intracellular signaling domain, adjacent to one or more other modulatory domains, etc.

[00154] In some cases, the modulatory domain on the first polypeptide of a subject CAR has substantially the same amino acid sequence as the modulatory domain on the second polypeptide of the CAR. For example, in some cases, the modulatory domain on the first polypeptide of a CAR comprises an amino acid sequence that is at least about 90%, at least about 95%, at least about 98%, at least about 99%, or 100%, identical to the amino acid sequence of the modulatory domain on the second polypeptide of the CAR. The modulatory domain of the first polypeptide of a subject CAR can have substantially the same length as the modulatory domain of the second polypeptide of a subject CAR; e.g., the first and second modulatory domains can differ in length from one another by fewer than 10 amino acids, or fewer than 5 amino acids. In some cases, the first and second modulatory domains have the same length.

[00155] A modulatory domain suitable for inclusion in the first and the second polypeptide of a subject CAR can have a length of from about 30 amino acids to about 70 amino acids (aa), e.g., a modulatory domain can have a length of from about 30 aa to about 35 aa, from about 35 aa to about 40 aa, from about 40 aa to about 45 aa, from about 45 aa to about 50 aa, from about 50 aa to about 55 aa, from about 55 aa to

about 60 aa, from about 60 aa to about 65 aa, or from about 65 aa to about 70 aa. In other cases, modulatory domain can have a length of from about 70 aa to about 100 aa, from about 100 aa to about 200 aa, or greater than 200 aa.

[00156] Co-stimulatory domains suitable for use in a CAR of the present disclosure are generally polypeptides derived from receptors. In some embodiments, co-stimulatory domains homodimerize. A subject co-stimulatory domain can be an intracellular portion of a transmembrane protein (i.e., the co-stimulatory domain can be derived from a transmembrane protein). Non-limiting examples of suitable co-stimulatory polypeptides include, but are not limited to, 4-1BB (CD137), CD28, ICOS, OX-40, BTLA, CD27, CD30, GITR, and HVEM.

[00157] In some cases, the co-stimulatory domain on the first polypeptide of a subject CAR has substantially the same amino acid sequence as the co-stimulatory domain on the second polypeptide of the CAR. For example, in some cases, the co-stimulatory domain on the first polypeptide of a CAR comprises an amino acid sequence that is at least about 90%, at least about 95%, at least about 98%, at least about 99%, or 100%, identical to the amino acid sequence of the co-stimulatory domain on the second polypeptide of the CAR. The co-stimulatory domain of the first polypeptide of a subject CAR can have substantially the same length as the co-stimulatory domain of the second polypeptide of a subject CAR; e.g., the first and second co-stimulatory domains can differ in length from one another by fewer than 10 amino acids, or fewer than 5 amino acids. In some cases, the first and second co-stimulatory domains have the same length.

[00158] A co-stimulatory domain suitable for inclusion in the first and the second polypeptide of a subject CAR can have a length of from about 30 amino acids to about 70 amino acids (aa), e.g., a co-stimulatory domain can have a length of from about 30 aa to about 35 aa, from about 35 aa to about 40 aa, from about 40 aa to about 45 aa, from about 45 aa to about 50 aa, from about 50 aa to about 55 aa, from about 55 aa to about 60 aa, from about 60 aa to about 65 aa, or from about 65 aa to about 70 aa. In other cases, the co-stimulatory domain can have a length of from about 70 aa to about 100 aa, from about 100 aa to about 200 aa, or greater than 200 aa.

[00159] In some cases, the co-stimulatory domain is derived from an intracellular portion of the transmembrane protein 4-1BB (also known as TNFRSF9; CD137; 4-1BB; CDw137; ILA; etc.). For example, a suitable co-stimulatory domain can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100% amino acid sequence identity to the following amino acid sequence: KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCEL (SEQ ID NO:544). In some of these embodiments, the co-stimulatory domain of both the first and the second polypeptide has a length of from about 30 aa to about 35 aa, from about 35 aa to about 40 aa, from about 40 aa to about 45 aa, from

about 45 aa to about 50 aa, from about 50 aa to about 55 aa, from about 55 aa to about 60 aa, from about 60 aa to about 65 aa, or from about 65 aa to about 70 aa.

[00160] In some cases, the co-stimulatory domain is derived from an intracellular portion of the transmembrane protein CD28 (also known as Tp44). For example, a suitable co-stimulatory domain can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100% amino acid sequence identity to the following amino acid sequence: FWVRSKRSRLLHSDYMNMTPRRPGPTRKHYQPYAPPRDFAAYRS (SEQ ID NO:545). In some of these embodiments, the co-stimulatory domain of both the first and the second polypeptide has a length of from about 30 aa to about 35 aa, from about 35 aa to about 40 aa, from about 40 aa to about 45 aa, from about 45 aa to about 50 aa, from about 50 aa to about 55 aa, from about 55 aa to about 60 aa, from about 60 aa to about 65 aa, or from about 65 aa to about 70 aa.

[00161] In some cases, the co-stimulatory domain is derived from an intracellular portion of the transmembrane protein ICOS (also known as AILIM, CD278, and CVID1). For example, a suitable co-stimulatory domain can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100% amino acid sequence identity to the following amino acid sequence: TKKKYSSSVHDPNGEYMFMRAVNTAKKSRLTDVTL (SEQ ID NO:546). In some of these embodiments, the co-stimulatory domain of both the first and the second polypeptide has a length of from about 30 aa to about 35 aa, from about 35 aa to about 40 aa, from about 40 aa to about 45 aa, from about 45 aa to about 50 aa, from about 50 aa to about 55 aa, from about 55 aa to about 60 aa, from about 60 aa to about 65 aa, or from about 65 aa to about 70 aa.

[00162] In some cases, the co-stimulatory domain is derived from an intracellular portion of the transmembrane protein OX-40 (also known as TNFRSF4, RP5-902P8.3, ACT35, CD134, OX40, TXGP1L). For example, a suitable co-stimulatory domain can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100% amino acid sequence identity to the following amino acid sequence: RRDQRLPPDAHKPPGGGSFRTPIQEEQADAHSTLAKI (SEQ ID NO:547). In some of these embodiments, the co-stimulatory domain of both the first and the second polypeptide has a length of from about 30 aa to about 35 aa, from about 35 aa to about 40 aa, from about 40 aa to about 45 aa, from about 45 aa to about 50 aa, from about 50 aa to about 55 aa, from about 55 aa to about 60 aa, from about 60 aa to about 65 aa, or from about 65 aa to about 70 aa.

[00163] In some cases, the co-stimulatory domain is derived from an intracellular portion of the transmembrane protein BTLA (also known as BTLA1 and CD272). For example, a suitable co-stimulatory domain can comprise an amino acid sequence having at least about 75%, at least about 80%,

at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100% amino acid sequence identity to the following amino acid sequence: CCLRRHQGKQNELSDTAGREINLVDAHLKSEQTEASTRQNSQVLLSETGIYDNDPDLCFRMQEG SEVYSNPCLEENKPGIVYASLNHSVIGPNSRLARNVKEAPTEYASICVRS (SEQ ID NO:548).

[00164] In some cases, the co-stimulatory domain is derived from an intracellular portion of the transmembrane protein CD27 (also known as S152, T14, TNFRSF7, and Tp55). For example, a suitable co-stimulatory domain can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100% amino acid sequence identity to the following amino acid sequence: HQRRKYRSNKGESPVEPAEPCRYSCPREEEGSTIPIQEDYRKPEPACSP (SEQ ID NO:549). In some of these embodiments, the co-stimulatory domain of both the first and the second polypeptide has a length of from about 30 aa to about 35 aa, from about 35 aa to about 40 aa, from about 40 aa to about 45 aa, from about 45 aa to about 50 aa, from about 50 aa to about 55 aa, from about 55 aa to about 60 aa, from about 60 aa to about 65 aa, or from about 65 aa to about 70 aa.

[00165] In some cases, the co-stimulatory domain is derived from an intracellular portion of the transmembrane protein CD30 (also known as TNFRSF8, D1S166E, and Ki-1). For example, a suitable co-stimulatory domain can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100% amino acid sequence identity to a contiguous stretch of from about 100 amino acids to about 110 amino acids (aa), from about 110 aa to about 115 aa, from about 115 aa to about 120 aa, from about 120 aa to about 130 aa, from about 130 aa to about 140 aa, from about 140 aa to about 150 aa, from about 150 aa to about 160 aa, or from about 160 aa to about 185 aa of the following amino acid sequence: RRACRKRIRQKLHLCYPVQTSQPKLELVDSRPRRSSTQLRSGASVTEPVAEERGLMSQPLMETC HSVGAAYLESLPLQDASPAGGPSSPRDLPEPRVSTEHTNNKIEKIYIMKADTVIVGTVKAELPEG RGLAGPAEPELEEELEADHTPHYPEQETEPPLGSCSDVMLSVEEEGKEDPLPTAASGK (SEQ ID NO:550).

[00166] In some cases, the co-stimulatory domain is derived from an intracellular portion of the transmembrane protein GITR (also known as TNFRSF18, RP5-902P8.2, AITR, CD357, and GITR-D). For example, a suitable co-stimulatory domain can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100% amino acid sequence identity to the following amino acid sequence: HIWQLRSQCMWPRETQLLLEVPPSTEDARSCQFPEEERGERSAEEKGRLGDLWV (SEQ ID NO:551). In some of these embodiments, the co-stimulatory domain of both the first and the second polypeptide has a length of from about 30 aa to about 35 aa, from about 35 aa to about 40 aa, from about

40 aa to about 45 aa, from about 45 aa to about 50 aa, from about 50 aa to about 55 aa, from about 55 aa to about 60 aa, from about 60 aa to about 65 aa, or from about 65 aa to about 70 aa.

[00167] In some cases, the co-stimulatory domain derived from an intracellular portion of the transmembrane protein HVEM (also known as TNFRSF14, RP3-395M20.6, ATAR, CD270, HVEA, HVEM, LIGHTR, and TR2). For example, a suitable co-stimulatory domain can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100% amino acid sequence identity to the following amino acid sequence: CVKRRKPRGDVVKVIVSVQRKRQEAEGEATVIEALQAPPDVTTVAVEETIPSFTGRSPNH (SEQ ID NO:552). In some of these embodiments, the co-stimulatory domain of both the first and the second polypeptide has a length of from about 30 aa to about 35 aa, from about 35 aa to about 40 aa, from about 40 aa to about 45 aa, from about 45 aa to about 50 aa, from about 50 aa to about 55 aa, from about 55 aa to about 60 aa, from about 60 aa to about 65 aa, or from about 65 aa to about 70 aa.

Dimerization pairs

[00168] As noted above, a conditionally active, heterodimeric polypeptide of the present disclosure comprises two polypeptide chains, one of which comprises a first member of a dimerization pair, and the second of which comprises a second member of a dimerization pair. One of the members of the dimerization pair will comprise a ligand-binding domain (LBD) of a nuclear hormone receptor; the other member of the dimerization pair will comprise a co-regulator peptide of the same nuclear hormone receptor. In the presence of a dimerization agent (e.g., a nuclear hormone, or a functional derivative or analog of the nuclear hormone; also referred to herein as a "dimerizer"), the first and second members of the dimerization pair will bind to one another, and will effect dimerization of the two polypeptide chains of the conditionally active, heterodimeric polypeptide of the present disclosure. A first member of a dimerization pair, or a second member of a dimerization pair, can also be referred to as a "dimerization domain."

Ligand-binding domain (LBD)

[00169] A ligand-binding domain of a nuclear hormone receptor can be from any of a variety of nuclear hormone receptors, including, but not limited to, ERα, ERβ, PR, AR, GR, MR, RARα, RARβ, RARγ, TRα, TRβ, VDR, EcR, RXRα, RXRβ, RXRγ, PPARα, PPARβ, PPARγ, LXRα, LXRβ, FXR, PXR, SXR, CAR, SF-1, LRH-1, DAX-1, SHP, TLX, PNR, NGF1-Bα, NGF1-Bβ, NGF1-Bγ, RORα, RORβ, RORγ, ERRα, ERRβ, ERRγ, GCNF, TR2/4, HNF-4, COUP-TFα, COUP-TFβ and COUP-TFγ.

[00170] Abbreviations for nuclear hormone receptors are as follows. ER: Estrogen Receptor; PR: Progesterone Receptor; AR: Androgen Receptor; GR: Glucocorticoid Receptor; MR: Mineralocorticoid Receptor; RAR: Retinoic Acid Receptor; TRα, β: Thyroid Receptor; VDR: Vitamin D3 Receptor; EcR: Ecdysone Receptor; RXR: Retinoic Acid X Receptor; PPAR: Peroxisome Proliferator Activated Receptor; LXR: Liver X Receptor; FXR: Farnesoid X Receptor; PXR/SXR: Pregnane X

Receptor/Steroid and Xenobiotic Receptor; CAR: Constitutive Adrostrane Receptor; SF-1: Steroidogenic Factor 1; DAX-1: Dosage sensitive sex reversal-adrenal hypoplasia congenital critical region on the X chromosome, gene 1; LRH-1: Liver Receptor Homolog 1; SHP: Small Heterodimer Partner; TLX: Tail-less Gene; PNR: Photoreceptor-Specific Nuclear Receptor; NGF1-B: Nerve Growth Factor; ROR: RAR related orphan receptor; ERR: Estrogen Related Receptor; GCNF: Germ Cell Nuclear Factor; TR2/4: Testicular Receptor; HNF-4: Hepatocyte Nuclear Factor; COUP-TF: Chicken Ovalbumin Upstream Promoter, Transcription Factor.

[00171] In some cases, a polypeptide chain of a heterodimeric polypeptide of the present disclosure comprises a single LBD of a nuclear hormone receptor. In some cases, a polypeptide chain of a heterodimeric polypeptide of the present disclosure comprises multiple (two or more) LBD of a nuclear hormone receptor. In some cases, a polypeptide chain of a heterodimeric polypeptide of the present disclosure comprises two LBD of a nuclear hormone receptor. In some cases, a polypeptide chain of a heterodimeric polypeptide of the present disclosure comprises three LBD of a nuclear hormone receptor. Where a polypeptide chain of a heterodimeric polypeptide of the present disclosure comprises multiple (two or more) LBD of a nuclear hormone receptor, in some cases the multiple LBD comprise identical amino acid sequences. In some cases, the two or more LBD are in tandem, either directly or separated by a linker.

Mineralocorticoid receptor

[00172] In some cases, an LBD suitable for inclusion as a member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a mineralocorticoid receptor (MR). For example, in some cases, the LBD comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the LBD of an MR having the amino acid sequence depicted in FIG. 1A.

[00173] As one non-limiting example, the LBD of a MR can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to an amino acid sequence depicted in FIG. 1F; and has a length of from about 200 amino acids to 250 amino acids (e.g., has a length of from 200 amino acids to 225 amino acids, or from 225 amino acids to 250 amino acids; e.g., has a length of 248 amino acids).

[00174] As one non-limiting example, the LBD of a MR can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 1B; and has a length of from about 250 amino acids to 299 amino acids (e.g., has a length of from 250 amino acids to 275 amino acids, or from 275 amino acids to 299 amino acids).

[00175] As one non-limiting example, the LBD of a MR can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 1C; and has a length of from about 200 amino acids to 250 amino acids (e.g., has a length of from 200 amino acids to 225 amino acids, or from 225 amino acids to 250 amino acids; e.g., has a length of 248 amino acids).

[00176] As another non-limiting example, the LBD of a MR can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 1D, and has an S810L substitution (where the amino acid numbering is based on the amino acid sequence depicted in FIG. 1A); and has a length of from about 250 amino acids to 299 amino acids (e.g., has a length of from 250 amino acids to 275 amino acids, or from 275 amino acids to 299 amino acids).

[00177] As one non-limiting example, the LBD of a MR can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 1C, and has an S810L substitution (where the amino acid numbering is based on the amino acid sequence depicted in FIG. 1A); and has a length of from about 200 amino acids to 250 amino acids (e.g., has a length of from 200 amino acids to 225 amino acids, or from 225 amino acids to 250 amino acids; e.g., has a length of 248 amino acids).

[00178] In some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of an MR, the second member of the dimerization pair is a co-regulator peptide comprising the amino acid sequence SLTARHKILHRLLQEGSPSDI (SEQ ID NO:2), where the co-regulator peptide has a length of from about 21 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from 21 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids). In some cases, where the second member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of an MR, the first member of the dimerization pair is a co-regulator peptide comprising the amino acid sequence SLTARHKILHRLLQEGSPSDI (SEQ ID NO:2), where the co-regulator peptide has a length of from about 21 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from 21 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids).

[00179] In some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of an MR, the second member of the dimerization pair is

a co-regulator peptide comprising the amino acid sequence QEAEEPSLLKKLLLAPANTQL (SEQ ID NO:6), where the co-regulator peptide has a length of from about 21 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from 21 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids). In some cases, where the second member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of an MR, the first member of the dimerization pair is a co-regulator peptide comprising the amino acid sequence QEAEEPSLLKKLLLAPANTQL (SEQ ID NO:6), where the co-regulator peptide has a length of from about 21 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from 21 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids).

[00180] In some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of an MR, the second member of the dimerization pair is a co-regulator peptide comprising the amino acid sequence SKVSQNPILTSLLQITGNGGS (SEQ ID NO:7), where the co-regulator peptide has a length of from about 21 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from 21 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids). In some cases, where the second member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of an MR, the first member of the dimerization pair is a co-regulator peptide comprising the amino acid sequence SKVSQNPILTSLLQITGNGGS (SEQ ID NO:7), where the co-regulator peptide has a length of from about 21 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from 21 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids).

Androgen receptor

[00181] In some cases, an LBD suitable for inclusion as a member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of an androgen receptor (AR). For example, in some cases, the LBD comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the LBD of an AR having the amino acid sequence depicted in FIG. 2A.

[00182] As one non-limiting example, the LBD of an AR can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 2B; and has a length of from

about 250 amino acids to 301 amino acids (e.g., has a length of from 250 amino acids to 275 amino acids, or from 275 amino acids to 301 amino acids).

[00183] As one non-limiting example, the LBD of an AR can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 2C; and has a length of from about 190 amino acids to 230 amino acids (e.g., has a length of from 190 amino acids to 210 amino acids, or from 210 amino acids to 230 amino acids).

[00184] As one non-limiting example, the LBD of an AR can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 2B, and has a T877A substitution (where the amino acid numbering is based on the amino acid sequence depicted in FIG. 2A); and has a length of from about 250 amino acids to 301 amino acids (e.g., has a length of from 250 amino acids to 275 amino acids, or from 275 amino acids to 301 amino acids).

[00185] As one non-limiting example, the LBD of an AR can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 2C, and has a T877A substitution (where the amino acid numbering is based on the amino acid sequence depicted in FIG. 2A); and has a length of from about 190 amino acids to 230 amino acids (e.g., has a length of from 190 amino acids to 210 amino acids, or from 210 amino acids to 230 amino acids).

[00186] As one non-limiting example, the LBD of an AR can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 2B, and has an F876L substitution (where the amino acid numbering is based on the amino acid sequence depicted in FIG. 2A); and has a length of from about 250 amino acids to 301 amino acids (e.g., has a length of from 250 amino acids to 275 amino acids, or from 275 amino acids to 301 amino acids).

[00187] As one non-limiting example, the LBD of an AR can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 2C, and has an F876L substitution (where the amino acid numbering is based on the amino acid sequence depicted in FIG. 2A); and has a length of from about 190 amino acids to 230 amino acids (e.g., has a length of from 190 amino acids to 210 amino acids, or from 210 amino acids to 230 amino acids).

[00188] As one non-limiting example, the LBD of an AR can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 2B, and has a T877A and an

F876L substitution (where the amino acid numbering is based on the amino acid sequence depicted in FIG. 2A); and has a length of from about 250 amino acids to 301 amino acids (e.g., has a length of from 250 amino acids to 275 amino acids, or from 275 amino acids to 301 amino acids).

[00189] As one non-limiting example, the LBD of an AR can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 2C, and has a T877A and an F876L substitution (where the amino acid numbering is based on the amino acid sequence depicted in FIG. 2A); and has a length of from about 190 amino acids to 230 amino acids (e.g., has a length of from 190 amino acids to 210 amino acids, or from 210 amino acids to 230 amino acids).

[00190] In some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of an AR, the second member of the dimerization pair is a co-regulator peptide comprising the amino acid sequence ESKGHKKLLQLLTCSSDDR (SEQ ID NO:3), where the co-regulator peptide has a length of from about 19 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from 19 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids). In some cases, where the second member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of an AR, the first member of the dimerization pair is a co-regulator peptide comprising the amino acid sequence ESKGHKKLLQLLTCSSDDR (SEQ ID NO:3), where the co-regulator peptide has a length of from about 19 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from 19 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids).

Progesterone receptor

[00191] In some cases, an LBD suitable for inclusion as a member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a progesterone receptor (PR). For example, in some cases, the LBD comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the LBD of a PR having the amino acid sequence depicted in FIG. 3A.

[00192] As one non-limiting example, the LBD of a PR can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to an amino acid sequence depicted in FIG. 3D; and has a length of from about 200 amino acids to 250 amino acids (e.g., has a length of from 200 amino acids to 225 amino acids, or from 225 amino acids to 250 amino acids; e.g., has a length of 248 amino acids).

[00193] As one non-limiting example, the LBD of a PR can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 3B; and has a length of from about 200 amino acids to 256 amino acids (e.g., has a length of from 200 amino acids to 225 amino acids, or from 225 amino acids to 256 amino acids; e.g., has a length of 256 amino acids).

[00194] As one non-limiting example, the LBD of a PR can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 3C; and has a length of from about 200 amino acids to 250 amino acids (e.g., has a length of from 200 amino acids to 225 amino acids, or from 225 amino acids to 250 amino acids; e.g., has a length of 248 amino acids).

[00195] In some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a PR, the second member of the dimerization pair is a co-regulator peptide comprising the amino acid sequence GHSFADPASNLGLEDIIRKALMGSF (SEQ ID NO:8), where the co-regulator peptide has a length of from about 25 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids). In some cases, where the second member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a PR, the first member of the dimerization pair is a co-regulator peptide comprising the amino acid sequence GHSFADPASNLGLEDIIRKALMGSF (SEQ ID NO:8), where the co-regulator peptide has a length of from about 25 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids).

Thyroid hormone receptor-β

[00196] In some cases, an LBD suitable for inclusion as a member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of thyroid hormone receptor-beta (TRβ). For example, in some cases, the LBD comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the LBD of a TRβ having the amino acid sequence depicted in FIG. 4A.

[00197] As one non-limiting example, the LBD of a TRβ can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to one of the amino acid sequences depicted in FIG. 4D; and has a length of from about 200 amino acids to 250 amino acids (e.g., has a length of from 200 amino acids to 225 amino

acids, from 225 amino acids to 230 amino acids, from 230 amino acids to 240 amino acids, or from 240 amino acids to 250 amino acids).

[00198] As one non-limiting example, the LBD of a TRβ can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 4B; and has a length of from about 200 amino acids to 260 amino acids (e.g., has a length of from 200 amino acids to 225 amino acids, or from 225 amino acids to 260 amino acids; e.g., has a length of 260 amino acids).

[00199] As one non-limiting example, the LBD of a TRβ can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 4B; and has a length of from about 200 amino acids to 246 amino acids (e.g., has a length of from 200 amino acids to 225 amino acids, or from 225 amino acids to 246 amino acids; e.g., has a length of 246 amino acids).

[00200] In some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a TRβ, the second member of the dimerization pair is an NCOA3/SRC3 polypeptide. For example, in some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a TRβ, the second member of the dimerization pair is a co-regulator peptide comprises the amino acid sequence CSSDDRGHSSLTNSPLDSSCKESSVSVTSPSGVSSSTSGGVSSTSNMHGSLLQEKHRILHKLLQNG NSPAEVAKITAEATGKDTSSITSCGDGNVVKQEQLSPKKKENNALLRYLLDRDDPSDALSKELQ PQVEGVDNKMSQCTSSTIPSSSQEKDPKIKTETSEEGSGDLDNLDAILGDLTSSDFYNNSISSNGS HLGTKQQ (SEQ ID NO:553). In other cases, where the second member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a TRβ, the first member of the dimerization pair is an NCOA3/SRC3 polypeptide. In some cases, the co-regulator peptide comprises the amino acid sequence: MHGSLLQEKHRILHKLLQNGNSPAEVAKITAEATGKDTSSITSCGDGNVVKQEQLSPKKKENNA LLRYLLDRDDPSDA (SEQ ID NO:554).

[00201] In some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a TRβ, the second member of the dimerization pair is an NCOA2/SRC2 polypeptide. For example, in some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a TRβ, the second member of the dimerization pair is a co-regulator peptide comprises the amino acid sequence STAPGSEVTIKQEPVSPKKKENALLRYLLDKDDTKDIGLPEITPKLERLDSKTDPASNTKLIAMKT EKEEMSFEPGDQPGSELDNLEEILDDLQNSQLPQLFPDTRPGAPAGSVDKQAIINDLMQLTAENS PVTPVGAQKTALRISQSTFNNPRPGQLGRLLPNQNLPLDITLQSPTGAGPFPPIRNSSPYSVIPQPG MMGNQGMIGNQGNLGNSSTGMIGNSASRPTMPSGEWAPQSSAVRVTCAATTSAMNRPVQGG

MIRNPAASIPMRPSSQPGQRQTLQSQVMNIGPSELEMNMGGP (SEQ ID NO:555). In some cases, where the second member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a TRβ, the first member of the dimerization pair is an NCOA2/SRC2 polypeptide.

Estrogen receptor-alpha

[00202] In some cases, an LBD suitable for inclusion as a member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of estrogen receptor-alpha (ERα). For example, in some cases, the LBD comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the LBD of an ERα having the amino acid sequence depicted in FIG. 5A.

[00203] As one non-limiting example, the LBD of an ERα can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to an amino acid sequence depicted in FIG. 5H; and has a length of from about 200 amino acids to 240 amino acids (e.g., has a length of from 200 amino acids to 225 amino acids, from 225 amino acids to 230 amino acids, from 230 amino acids to 235 amino acids, or from 235 amino acids to 240 amino acids).

[00204] As one non-limiting example, the LBD of an ERα can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 5B; and has a length of from about 180 amino acids to 229 amino acids (e.g., has a length of from 180 amino acids to 200 amino acids, or from 200 amino acids to 229 amino acids; e.g., has a length of 229 amino acids).

[00205] As one non-limiting example, the LBD of an ERα can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 5C; and has a length of from about 250 amino acids to 314 amino acids (e.g., has a length of from 250 amino acids to 275 amino acids, from 275 amino acids to 300 amino acids, or from 300 amino acids to 314 amino acids; e.g., has a length of 314 amino acids).

[00206] As one non-limiting example, the LBD of an ERα can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 5D; and has a length of from about 190 amino acids to 238 amino acids (e.g., has a length of from 190 amino acids to 220 amino acids, or from 220 amino acids to 238 amino acids; e.g., has a length of 238 amino acids).

[00207] As one non-limiting example, the LBD of an ERα can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%,

amino acid sequence identity to the amino acid sequence depicted in FIG. 5E, and has a D351Y substitution (where the amino acid numbering is based on the amino acid sequence depicted in FIG. 5A); and has a length of from about 180 amino acids to 229 amino acids (e.g., has a length of from 180 amino acids to 200 amino acids, or from 200 amino acids to 229 amino acids; e.g., has a length of 229 amino acids).

[00208] As one non-limiting example, the LBD of an ERα can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 5F, and has a D351Y substitution (where the amino acid numbering is based on the amino acid sequence depicted in FIG. 5A); and has a length of from about 250 amino acids to 314 amino acids (e.g., has a length of from 250 amino acids to 275 amino acids, from 275 amino acids to 300 amino acids, or from 300 amino acids to 314 amino acids; e.g., has a length of 314 amino acids).

[00209] As one non-limiting example, the LBD of an ERα can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 5G, and has a D351Y substitution (where the amino acid numbering is based on the amino acid sequence depicted in FIG. 5A); and has a length of from about 190 amino acids to 238 amino acids (e.g., has a length of from 190 amino acids to 220 amino acids, or from 220 amino acids to 238 amino acids; e.g., has a length of 238 amino acids).

[00210] In some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of an ERα, the second member of the dimerization pair is a co-regulator peptide comprising the amino acid sequence DAFQLRQLILRGLQDD (SEQ ID NO:12), where the co-regulator peptide has a length of from about 16 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from 16 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids). In some cases, where the second member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of an ERα, the first member of the dimerization pair is a co-regulator peptide comprising the amino acid sequence DAFQLRQLILRGLQDD (SEQ ID NO:12), where the co-regulator peptide has a length of from about from about 16 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from 16 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids).

[00211] In some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of an ERα, the second member of the dimerization pair is a co-regulator peptide comprising the amino acid sequence SPGSREWFKDMLS (SEQ ID NO:13), where the co-regulator peptide has a length of from about 13 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from 13 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids). In some cases, where the second member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of an ERα, the first member of the dimerization pair is a co-regulator peptide comprising the amino acid sequence SPGSREWFKDMLS (SEQ ID NO:13), where the co-regulator peptide has a length of from about from about 13 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from 13 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids).

Estrogen receptor-beta (ERβ)

[00212] In some cases, an LBD suitable for inclusion as a member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of estrogen receptor-alpha (ERβ). For example, in some cases, the LBD comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the LBD of an ERβ having the amino acid sequence depicted in FIG. 6A.

[00213] As one non-limiting example, the LBD of an ERβ can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to an amino acid sequence depicted in FIG. 6C; and has a length of from about 200 amino acids to 243 amino acids (e.g., has a length of from 200 amino acids to 225 amino acids, from 225 amino acids to 230 amino acids, from 230 amino acids to 235 amino acids, or from 235 amino acids to 243 amino acids).

[00214] As one non-limiting example, the LBD of an ERβ can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 6B; and has a length of from about 200 amino acids to 243 amino acids (e.g., has a length of from 200 amino acids to 225 amino acids, from 225 amino acids to 230 amino acids, from 230 amino acids to 235 amino acids, or from 235 amino acids to 243 amino acids).

[00215] In some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of an ERβ, the second member of the dimerization pair is a co-regulator peptide comprising the amino acid sequence PRQGSILYSMLTSAKQT (SEQ ID NO:9), where the co-regulator peptide has a length of from about 17 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from 17 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids). In some cases, where the second member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of an ERβ, the first member of the dimerization pair is a co-regulator peptide comprising the amino acid sequence PRQGSILYSMLTSAKQT (SEQ ID NO:9), where the co-regulator peptide has a length of from about from about 17 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from 17 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids).

Peroxisome proliferator-activated receptor-gamma

[00216] In some cases, an LBD suitable for inclusion as a member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of peroxisome proliferator-activated receptor-gamma (PPAR-γ). For example, in some cases, the LBD comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the LBD of a PPAR-γ having the amino acid sequence depicted in FIG. 7A.

[00217] As one non-limiting example, the LBD of a PPAR-γ can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to one of the amino acid sequences depicted in FIG. 7E; and has a length of from about 200 amino acids to 269 amino acids (e.g., has a length of from 200 amino acids to 225 amino acids, from 225 amino acids to 250 amino acids, or from 250 amino acids to 269 amino acids).

[00218] As one non-limiting example, the LBD of a PPAR-γ can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 7B; and has a length of from about 150 amino acids to 202 amino acids (e.g., has a length of from 150 amino acids to 160 amino acids, from 160 amino acids to 170 amino acids, from 170 amino acids to 190 amino acids, or from 190 amino acids to 202 amino acids).

[00219] As one non-limiting example, the LBD of a PPAR-γ can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 7C; and has a length of from about 200 amino acids to 269 amino acids (e.g., has a length of from 200 amino acids to 225 amino acids, from 225 amino acids to 250 amino acids, or from 250 amino acids to 269 amino acids).

[00220] As one non-limiting example, the LBD of a PPAR-γ can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 7D; and has a length of from about 200 amino acids to 269 amino acids (e.g., has a length of from 200 amino acids to 225 amino acids, from 225 amino acids to 250 amino acids, or from 250 amino acids to 271 amino acids).

[00221] In some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a PPAR-γ, the second member of the dimerization pair is a co-regulator peptide comprising the amino acid sequence CPSSHSSLTERHKILHRLLQEGSPS (SEQ ID NO:1), where the co-regulator peptide has a length of from about 25 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from 25 amino acids to 28 amino acids, from 28 amino acids to 29 amino acids, from 29 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids). In some cases, where the second member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a PPAR-γ, the first member of the dimerization pair is a co-regulator peptide comprising the amino acid sequence CPSSHSSLTERHKILHRLLQEGSPS (SEQ ID NO:1), where the co-regulator peptide has a length of from about from about 17 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from about 25 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from 25 amino acids to 28 amino acids, from 28 amino acids to 29 amino acids, from 29 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids).

[00222] In some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a PPAR-γ, the second member of the dimerization pair is a co-regulator peptide comprising the amino acid sequence PKKENNALLRYLLDRDDPSDV (SEQ ID NO:4), where the co-regulator peptide has a length of from about 21 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from 21 amino acids to 23 amino acids, from 23 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids). In some cases, where the second member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a PPAR-γ, the first

member of the dimerization pair is a co-regulator peptide comprising the amino acid sequence PKKENNALLRYLLDRDDPSDV (SEQ ID NO:4), where the co-regulator peptide has a length of from about from about 17 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from about 21 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from 21 amino acids to 23 amino acids, from 23 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids).

[00223] In some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a PPAR-γ, the second member of the dimerization pair is a co-regulator peptide comprising the amino acid sequence PKKKENALLRYLLDKDDTKDI (SEQ ID NO:11), where the co-regulator peptide has a length of from about 21 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from 21 amino acids to 23 amino acids, from 23 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids). In some cases, where the second member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a PPAR-γ, the first member of the dimerization pair is a co-regulator peptide comprising the amino acid sequence PKKKENALLRYLLDKDDTKDI (SEQ ID NO:11), where the co-regulator peptide has a length of from about from about 21 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from about 21 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from 21 amino acids to 23 amino acids, from 23 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids).

Glucocorticoid receptor

[00224] In some cases, an LBD suitable for inclusion as a member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of glucocorticoid receptor (GR). For example, in some cases, the LBD comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the LBD of a GR having the amino acid sequence depicted in FIG. 8A.

[00225] As one non-limiting example, the LBD of a GR can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to one of the amino acid sequences depicted in FIG. 8C; and has a length of from about 200 amino acids to 247 amino acids (e.g., has a length of from 200 amino acids to 225 amino acids, from 225 amino acids to 230 amino acids, from 230 amino acids to 240 amino acids, or from 240 amino acids to 247 amino acids).

[00226] As one non-limiting example, the LBD of a GR can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 8B; and has a length of from about 200 amino acids to 247 amino acids (e.g., has a length of from 200 amino acids to 225 amino acids, or from 225 amino acids to 247 amino acids; e.g., has a length of 247 amino acids).

[00227] In some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a GR, the second member of the dimerization pair is an NCOA1/SRC1 polypeptide. For example, in some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a GR, the second member of the dimerization pair is an NCOA1/SRC1 polypeptide comprising the amino acid sequence NYGTNPGTPPASTSPFSQLAANPEASLANRNSMVSRGMTGNIGGQFGTGINPQMQQNVFQYPG AGMVPQGEANFAPSLSPGSSMVPMPIPPPQSSLLQQTPPASGYQSPDMKAWQQGAIGNNNVFSQ AVQNQPTPAQPGVYNNMSITVSMAGGNTNVQNMNPMMAQMQMSSLQMPGMNTVCPEQIND PALRHTGLYCNQLSSTDLLKTEADGTQQVQQVQVFADVQCTVNLVGGDPYLNQPGPLGTQKP TSGPQTPQAQQKSLLQQLLTE (SEQ ID NO:556) or a fragment thereof. In some cases, where the second member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a GR, the first member of the dimerization pair is an NCOA1/SRC1 polypeptide.

[00228] In some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a GR, the second member of the dimerization pair is an NCOA2/SRC2 polypeptide. For example, in some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a GR, the second member of the dimerization pair is an NCOA2/SRC2 polypeptide comprising the amino acid sequence KRHHHEVLRQGLAFSQIYRFSLSDGTLVAAQTKSKLIRSQTTNEPQLVISLHMLHREQNVCVMN PDLTGQTMGKPLNPISSNSPAHQALCSGNPGQDMTLSSNINFPINGPKEQMGMPMGRFGGSGG MNHVSGMQATTPQGSNYALKMNSPSQSSPGMNPGQPTSMLSPRHRMSPGVAGSPRIPPSQFSPA GSLHSPVGVCSSTGNSHSYTNSSLNALQALSEGHGVSLGSSLASPDLKMGNLQNSPVNMNPPPL SKMGSLDSKDCFGLYGEPSEGTTGQAESSCHPGEQKETNDPNLPPAVSSERADGQSRLHDSKGQ TKLLQLLTTKSDQMEPSPLASSLSDTNKDSTGSLPGSGSTHGTSLKEKHKILHRLLQDSSSPVDL AKLTAEATGKDLSQESSSTAPGSEVTIKQEPVSPKKKENALLRYLLDKDDTKDIGLPEITPKLERL DSKTDPASNTKLIAMKTEKEEMSFEPGDQPGSELDNLEEILDDLQNSQLPQLFPDTRPGAPAGSV DKQAIINDLMQLTAENSPVTPVGAQKTALRISQSTFNNPRPGQLGRLLPNQNLPLDITLQSPTGA GPFPPIRNSSPYSVIPQPGMMGNQGMIGNQGNLGNSSTGMIGNSASRPTMPSGEWAPQSSAVRV TCAATTSAMNRPVQGGMIRNPAASIPMRPSSQPGQRQTLQSQVMNIGPSELEMNMGGP (SEQ ID

NO:557) or a fragment thereof. In some cases, where the second member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a GR, the first member of the dimerization pair is an NCOA2/SRC2 polypeptide.

Vitamin D receptor

[00229] In some cases, an LBD suitable for inclusion as a member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of vitamin D receptor (VDR). For example, in some cases, the LBD comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the LBD of a VDR having the amino acid sequence depicted in FIG. 9A.

[00230] As one non-limiting example, the LBD of a VDR can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to one of the amino acid sequences depicted in FIG. 9C; and has a length of from about 250 amino acids to 310 amino acids (e.g., has a length of from 250 amino acids to 275 amino acids, from 275 amino acids to 300 amino acids, or from 300 amino acids to 310 amino acids).

[00231] As one non-limiting example, the LBD of a VDR can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 9B; and has a length of from about 250 amino acids to 303 amino acids (e.g., has a length of from 250 amino acids to 275 amino acids, from 275 amino acids to 300 amino acids, or from 300 amino acids to 303 amino acids).

[00232] In some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a VDR, the second member of the dimerization pair is an NCOA1/SRC1 polypeptide. For example, in some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a VDR, the second member of the dimerization pair is an NCOA1/SRC1 polypeptide comprising the amino acid sequence NYGTNPGTPPASTSPFSQLAANPEASLANRNSMVSRGMTGNIGGQFGTGINPQMQQNVFQYPG AGMVPQGEANFAPSLSPGSSMVPMPIPPPQSSLLQQTPPASGYQSPDMKAWQQGAIGNNNVFSQ AVQNQPTPAQPGVYNNMSITVSMAGGNTNVQNMNPMMAQMQMSSLQMPGMNTVCPEQIND PALRHTGLYCNQLSSTDLLKTEADGTQQVQQVQVFADVQCTVNLVGGDPYLNQPGPLGTQKP TSGPQTPQAQQKSLLQQLLTE (SEQ ID NO:558) or a fragment thereof. In some cases, where the second member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a VDR, the first member of the dimerization pair is an NCOA1/SRC1 polypeptide.

[00233] In some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a VDR, the second member of the dimerization pair is an NCOA2/SRC2 polypeptide. For example, in some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a VDR, the second member of the dimerization pair is an NCOA2/SRC2 polypeptide comprising the amino acid sequence KRHHHEVLRQGLAFSQIYRFSLSDGTLVAAQTKSKLIRSQTTNEPQLVISLHMLHREQNVCVMN PDLTGQTMGKPLNPISSNSPAHQALCSGNPGQDMTLSSNINFPINGPKEQMGMPMGRFGGSGG MNHVSGMQATTPQGSNYALKMNSPSQSSPGMNPGQPTSMLSPRHRMSPGVAGSPRIPPSQFSPA GSLHSPVGVCSSTGNSHSYTNSSLNALQALSEGHGVSLGSSLASPDLKMGNLQNSPVNMNPPPL SKMGSLDSKDCFGLYGEPSEGTTGQAESSCHPGEQKETNDPNLPPAVSSERADGQSRLHDSKGQ TKLLQLLTTKSDQMEPSPLASSLSDTNKDSTGSLPGSGSTHGTSLKEKHKILHRLLQDSSSPVDL AKLTAEATGKDLSQESSSTAPGSEVTIKQEPVSPKKKENALLRYLLDKDDTKDIGLPEITPKLERL DSKTDPASNTKLIAMKTEKEEMSFEPGDQPGSELDNLEEILDDLQNSQLPQLFPDTRPGAPAGSV DKQAIINDLMQLTAENSPVTPVGAQKTALRISQSTFNNPRPGQLGRLLPNQNLPLDITLQSPTGA GPFPPIRNSSPYSVIPQPGMMGNQGMIGNQGNLGNSSTGMIGNSASRPTMPSGEWAPQSSAVRV TCAATTSAMNRPVQGGMIRNPAASIPMRPSSQPGQRQTLQSQVMNIGPSELEMNMGGP (SEQ ID NO:559) or a fragment thereof. For example, in some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a VDR, the second member of the dimerization pair is an NCOA2/SRC2 polypeptide comprising the amino acid sequence LLRYLLDK (SEQ ID NO:560), where the co-regulator peptide has a length of from about from about 8 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from about 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 23 amino acids, from 23 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids). In some cases, where the second member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a VDR, the first member of the dimerization pair is an NCOA2/SRC2 polypeptide.

Thyroid hormone receptor-alpha

[00234] In some cases, an LBD suitable for inclusion as a member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of thyroid hormone receptor-alpha (TRα). For example, in some cases, the LBD comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the LBD of a TRα having the amino acid sequence depicted in FIG. 10A.

[00235] As one non-limiting example, the LBD of a TRα can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to one of the amino acid sequences depicted in FIG. 10C; and has a length of from about 190 amino acids to about 245 amino acids (e.g., has a length of from 190 amino acids to 210 amino acids, from 210 amino acids to 230 amino acids, or from 230 amino acids to 245 amino acids).

[00236] As one non-limiting example, the LBD of a TRα can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 10B; and has a length of from about 190 amino acids to about 243 amino acids (e.g., has a length of from 190 amino acids to 210 amino acids, from 210 amino acids to 230 amino acids, or from 230 amino acids to 243 amino acids).

[00237] A suitable co-regulator peptide for TRα is an SRC1 polypeptide, or a fragment thereof (e.g., a peptide of from 8 amino acids to 50 amino acids in length, derived from an SRC1 polypeptide).

Retinoic acid receptor-beta

[00238] In some cases, an LBD suitable for inclusion as a member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of retinoic acid receptor-beta (RARβ). For example, in some cases, the LBD comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the LBD of a RARβ having the amino acid sequence depicted in FIG. 11A.

[00239] As one non-limiting example, the LBD of a RARβ can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to one of the amino acid sequences depicted in FIG. 11C; and has a length of from about 180 amino acids to about 235 amino acids (e.g., has a length of from 180 amino acids to 200 amino acids, from 200 amino acids to 220 amino acids, or from 220 amino acids to 235 amino acids).

[00240] As one non-limiting example, the LBD of a RARβ can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 11B; and has a length of from about 180 amino acids to about 231 amino acids (e.g., has a length of from 180 amino acids to 200 amino acids, from 200 amino acids to 220 amino acids, or from 220 amino acids to 231 amino acids).

[00241] A suitable co-regulator peptide for RARβ is an SRC1 polypeptide, or a fragment thereof (e.g., a peptide of from 8 amino acids to 50 amino acids in length, derived from an SRC1 polypeptide).

[00242] In some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a RARβ, the second member of the dimerization pair

is an NCOA1/SRC1 polypeptide. For example, in some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a RARβ, the second member of the dimerization pair is an NCOA1/SRC1 polypeptide comprising the amino acid sequence

NYGTNPGTPPASTSPFSQLAANPEASLANRNSMVSRGMTGNIGGQFGTGINPQMQQNVFQYPG AGMVPQGEANFAPSLSPGSSMVPMPIPPPQSSLLQQTPPASGYQSPDMKAWQQGAIGNNNVFSQ AVQNQPTPAQPGVYNNMSITVSMAGGNTNVQNMNPMMAQMQMSSLQMPGMNTVCPEQIND PALRHTGLYCNQLSSTDLLKTEADGTQQVQQVQVFADVQCTVNLVGGDPYLNQPGPLGTQKP TSGPQTPQAQQKSLLQQLLTE (SEQ ID NO:561) or a fragment thereof. In some cases, where the second member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a RARβ, the first member of the dimerization pair is an NCOA1/SRC1 polypeptide.

[00243] In some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a RARβ, the second member of the dimerization pair is an NCOA2/SRC2 polypeptide. For example, in some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a RARβ, the second member of the dimerization pair is an NCOA2/SRC2 polypeptide comprising the amino acid sequence

KRHHHEVLRQGLAFSQIYRFSLSDGTLVAAQTKSKLIRSQTTNEPQLVISLHMLHREQNVCVMN PDLTGQTMGKPLNPISSNSPAHQALCSGNPGQDMTLSSNINFPINGPKEQMGMPMGRFGGSGG MNHVSGMQATTPQGSNYALKMNSPSQSSPGMNPGQPTSMLSPRHRMSPGVAGSPRIPPSQFSPA GSLHSPVGVCSSTGNSHSYTNSSLNALQALSEGHGVSLGSSLASPDLKMGNLQNSPVNMNPPPL SKMGSLDSKDCFGLYGEPSEGTTGQAESSCHPGEQKETNDPNLPPAVSSERADGQSRLHDSKGQ TKLLQLLTTKSDQMEPSPLASSLSDTNKDSTGSLPGSGSTHGTSLKEKHKILHRLLQDSSSPVDL AKLTAEATGKDLSQESSSTAPGSEVTIKQEPVSPKKKENALLRYLLDKDDTKDIGLPEITPKLERL DSKTDPASNTKLIAMKTEKEEMSFEPGDQPGSELDNLEEILDDLQNSQLPQLFPDTRPGAPAGSV DKQAIINDLMQLTAENSPVTPVGAQKTALRISQSTFNNPRPGQLGRLLPNQNLPLDITLQSPTGA GPFPPIRNSSPYSVIPQPGMMGNQGMIGNQGNLGNSSTGMIGNSASRPTMPSGEWAPQSSAVRV TCAATTSAMNRPVQGGMIRNPAASIPMRPSSQPGQRQTLQSQVMNIGPSELEMNMGGP (SEQ ID NO:562) or a fragment thereof. In some cases, where the second member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a RARβ, the first member of the dimerization pair is an NCOA2/SRC2 polypeptide.

Farnesoid X receptor

[00244] In some cases, an LBD suitable for inclusion as a member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of farnesoid X receptor (FXR. For

example, in some cases, the LBD comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the LBD of an FXR having the amino acid sequence depicted in FIG. 22A.

[00245] As one non-limiting example, the LBD of an FXR can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 22B; and has a length of from about 100 amino acids to about 136 amino acids (e.g., has a length of from 100 amino acids to 110 amino acids, from 110 amino acids to 120 amino acids, or from 120 amino acids to 136 amino acids).

[00246] A suitable co-regulator peptide for an FXR is an SRC1 polypeptide, or a fragment thereof (e.g., a peptide of from 8 amino acids to 50 amino acids in length, derived from an SRC1 polypeptide).

LXR-alpha

[00247] In some cases, an LBD suitable for inclusion as a member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of liver X receptor-alpha (LRXα). For example, in some cases, the LBD comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the LBD of an LRXα having the amino acid sequence depicted in FIG. 23A.

[00248] As one non-limiting example, the LBD of an LRXα can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 23B; and has a length of from about 200 amino acids to about 266 amino acids (e.g., has a length of from 200 amino acids to 220 amino acids, from 220 amino acids to 240 amino acids, or from 240 amino acids to 266 amino acids).

[00249] A suitable co-regulator peptide for an LRXα is an SRC1 polypeptide, or a fragment thereof (e.g., a peptide of from 8 amino acids to 50 amino acids in length, derived from an SRC1 polypeptide).

RORgamma

[00250] In some cases, an LBD suitable for inclusion as a member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a retinoid-related orphan receptor gamma (RORγ). For example, in some cases, the LBD comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the LBD of an RORγ having the amino acid sequence depicted in FIG. 24A.

[00251] As one non-limiting example, the LBD of an RORγ can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 24B; and has a length of from

about 200 amino acids to about 261 amino acids (e.g., has a length of from 200 amino acids to 220 amino acids, from 220 amino acids to 240 amino acids, or from 240 amino acids to 261 amino acids).

[00252] A suitable co-regulator for an RORγ is an NCORNR peptide (CDPASNLGLEDIIRKALMGSFDDK, SEQ ID NO:563).

[00253] A suitable co-regulator peptide for an RORγ is an SRC1 polypeptide, or a fragment thereof (e.g., a peptide of from 8 amino acids to 50 amino acids in length, derived from an SRC1 polypeptide).

RXR-alpha

[00254] In some cases, an LBD suitable for inclusion as a member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a retinoid-X receptor-alpha (RXRα). For example, in some cases, the LBD comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the LBD of an RXRα having the amino acid sequence depicted in FIG. 25A.

[00255] As one non-limiting example, the LBD of an RORγ can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 25B; and has a length of from about 190 amino acids to about 238 amino acids (e.g., has a length of from 190 amino acids to 200 amino acids, from 200 amino acids to 210 amino acids, or from 210 amino acids to 238 amino acids).

[00256] A suitable co-regulator peptide for an RXRα is an SRC1 polypeptide, or a fragment thereof (e.g., a peptide of from 8 amino acids to 50 amino acids in length, derived from an SRC1 polypeptide).

PXR

[00257] In some cases, an LBD suitable for inclusion as a member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a Pregnane X Receptor (PXR). For example, in some cases, the LBD comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the LBD of a PXR having the amino acid sequence depicted in FIG. 26A. In some cases, the LBD comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to amino acids 143-428 of the amino acid sequence depicted in FIG. 26A. In some cases, the LBD comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to amino acids 205-434 of the amino acid sequence depicted in FIG. 26A.

[00258] As one non-limiting example, the LBD of a PXR can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 26B; and has a length of from

about 250 amino acids to about 302 amino acids (e.g., has a length of from 250 amino acids to 275 amino acids, from 275 amino acids to 290 amino acids, or from 290 amino acids to 302 amino acids).

[00259] A suitable co-regulator peptide for a PXR is an SRC1 polypeptide, or a fragment thereof (e.g., a peptide of from 8 amino acids to 50 amino acids in length, derived from an SRC1 polypeptide).

Co-regulator polypeptides

[00260] Suitable co-regulator polypeptides include full-length naturally-occurring nuclear hormone co-regulator polypeptides. Suitable co-regulator polypeptides include fragments of naturally-occurring nuclear hormone co-regulator polypeptides. Suitable co-regulator polypeptides include synthetic or recombinant nuclear hormone co-regulator polypeptides.

[00261] Suitable co-regulator polypeptides can have a length of from 8 amino acids to 2000 amino acids. Suitable co-regulator polypeptides can have a length of from 8 amino acids to 50 amino acids, e.g., from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids. Suitable co-regulator polypeptides can have a length of from 50 amino acids to 100 amino acids, e.g., from 50 amino acids to 60 amino acids, from 60 amino acids to 70 amino acids, from 70 amino acids to 80 amino acids, from 80 amino acids to 90 amino acids, or from 90 amino acids to 100 amino acids. Suitable co-regulator polypeptides can have a length of from 100 amino acids to 200 amino acids, from 200 amino acids to 300 amino acids, from 300 amino acids to 400 amino acids, from 400 amino acids to 500 amino acids, from 500 amino acids to 600 amino acids, from 600 amino acids to 700 amino acids, from 700 amino acids to 800 amino acids, from 800 amino acids to 900 amino acids, or from 900 amino acids to 1000 amino acids. Suitable co-regulator polypeptides can have a length of from 1000 amino acids to 2000 amino acids.

[00262] Suitable co-regulator polypeptides include, but are not limited to, SRC1, GRIP1, AIB1, PGC1a, PGC1b, PRC, TRAP220, ASC2, CBP, P300, CIA, ARA70, TIF1, NSD1, SMAP, Tip60, ERAP140, Nix1, LCoR, N-CoR, SMRT, RIP140, and PRIC285.

[00263] National Center for Biotechnology Information (NCBI) accession numbers for such co-regulators include the following: SRC1 (NP_003734), GRIP1 (NP_006531), AIB1 (NP_006525), PGC1a (NP_037393), PGC1b (NP_573570), PRC (NP_055877), TRAP220 (NP_004765), ASC2 (NP_054790), CBP (NP_004371), P300 (NP_001420), CIA (NP_066018), ARA70 (NP_005428), TIF1 (NP_003843), NSD1 (NP_071900), SMAP (NP_006687), Tip60 (NP_006379), ERAP140 (NP_861447), Nix1 (NP_113662), LCoR (NP_115816), N-CoR (NP_006302), SMRT (NP_006303), RIP140 (NP_003480) and PRIC285 (NP_208384).

[00264] Examples of suitable co-regulator polypeptides are provided in FIGs. 29-51B.

[00265] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 29.

[00266] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 30.

[00267] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 31.

[00268] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 32.

[00269] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at

least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 33.

[00270] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 34.

[00271] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 35.

[00272] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 36A-36B.

[00273] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 37A-37B.

[00274] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino

acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 36A-36B.

[00275] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 39.

[00276] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 40.

[00277] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 41.

[00278] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 42A-42B.

[00279] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino

acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 43.

[00280] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 44.

[00281] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 45.

[00282] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 46.

[00283] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 47.

[00284] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20

amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 48A-48B.

[00285] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 49A-49B.

[00286] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 50.

[00287] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 51A-51B.

[00288] Suitable co-regulator peptides include, but are not limited to, Steroid Receptor Coactivator (SRC)-1, SRC-2, SRC-3, TRAP220-1, TRAP220-2, NR0B1, NRIP1, CoRNR box, αβV, TIF1, TIF2, EA2, TA1, EAB1, SRC1-1, SRC1-2, SRC1-3, SRC1-4a, SRC1-4b, GRIP1-1, GRIP1-2, GRIP1-3, AIB1-1, AIB1-2, AIB1-3, PGC1a, PGC1b, PRC, ASC2-1, ASC2-2, CBP-1, CBP-2, P300, CIA, ARA70-1, ARA70-2, NSD1, SMAP, Tip60, ERAP140, Nix1, LCoR, CoRNR1 (N-CoR), CoRNR2, SMRT, RIP140-C, RIP140-1, RIP140-2, RIP140-3, RIP140-4, RIP140-5, RIP140-6, RIP140-7, RIP140-8, RIP140-9, PRIC285-1, PRIC285-2, PRIC285-3, PRIC285-4, and PRIC285-5.

[00289] In some cases, a suitable co-regulator peptide comprises an LXXLL motif, where X is any amino acid; where the co-regulator peptide has a length of from 8 amino acids to 50 amino acids, e.g., from 8 amino acids to 10 amino acids, from 10 amino acids to 12 amino acids, from 12 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids.

[00290] Non-limiting examples of suitable co-regulator peptides are as follows:

SRC1: CPSSHSSLTERHKILHRLLQEGSPS (SEQ ID NO:1);

SRC1–2: SLTARHKILHRLLQEGSPSDI (SEQ ID NO:2);

SRC3-1: ESKGHKKLLQLLTCSSDDR (SEQ ID NO:3);

SRC3: PKKENNALLRYLLDRDDPSDV (SEQ ID NO:4);

PGC-1: AEEPSLLKKLLLAPANT (SEQ ID NO:5);

PGC1a: QEAEEPSLLKKLLLAPANTQL (SEQ ID NO:6);

TRAP220–1: SKVSQNPILTSLLQITGNGGS (SEQ ID NO:7);

NCoR (2051–2075): GHSFADPASNLGLEDIIRKALMGSF (SEQ ID NO:8);

NR0B1: PRQGSILYSMLTSAKQT (SEQ ID NO:9);

NRIP1: AANNSLLLHLLKSQTIP (SEQ ID NO:10);

TIF2: PKKKENALLRYLLDKDDTKDI (SEQ ID NO:11);

CoRNR Box: DAFQLRQLILRGLQDD (SEQ ID NO:12);

abV: SPGSREWFKDMLS (SEQ ID NO:13);

TRAP220-2: GNTKNHPMLMNLLKDNPAQDF (SEQ ID NO:14);

EA2: SSKGVLWRMLAEPVSR (SEQ ID NO:15);

TA1: SRTLQLDWGTLYWSR (SEQ ID NO:16);

EAB1: SSNHQSSRLIELLSR (SEQ ID NO:17);

SRC2: LKEKHKILHRLLQDSSSPV (SEQ ID NO:18);

SRC1-3: QAQQKSLLQQLLTE (SEQ ID NO:19);

SRC1–1: KYSQTSHKLVQLLTTTAEQQL (SEQ ID NO:20);

SRC1–2: SLTARHKILHRLLQEGSPSDI (SEQ ID NO:21);

SRC1–3: KESKDHQLLRYLLDKDEKDLR (SEQ ID NO:22);

SRC1–4a: PQAQQKSLLQQLLTE (SEQ ID NO:23);

SRC1–4b: PQAQQKSLRQQLLTE (SEQ ID NO:24);

GRIP1–1: HDSKGQTKLLQLLTTKSDQME (SEQ ID NO:25);

GRIP1–2: SLKEKHKILHRLLQDSSSPVD (SEQ ID NO:26);

GRIP1–3: PKKKENALLRYLLDKDDTKDI (SEQ ID NO:27);

AIB1–1: LESKGHKKLLQLLTCSSDDRG (SEQ ID NO:28);

AIB1–2: LLQEKHRILHKLLQNGNSPAE (SEQ ID NO:29);
AIB1–3: KKKENNALLRYLLDRDDPSDA (SEQ ID NO:30);
PGC1a: QEAEEPSLLKKLLLAPANTQL (SEQ ID NO:31);
PGC1b: PEVDELSLLQKLLLATSYPTS (SEQ ID NO:32);
PRC: VSPREGSSLHKLLTLSRTPPE (SEQ ID NO:33);
TRAP220–1: SKVSQNPILTSLLQITGNGGS (SEQ ID NO:34);
TRAP220–2: GNTKNHPMLMNLLKDNPAQDF (SEQ ID NO:35);
ASC2–1: DVTLTSPLLVNLLQSDISAGH (SEQ ID NO:36);
ASC2–2: AMREAPTSLSQLLDNSGAPNV (SEQ ID NO:37);
CBP-1: DAASKHKQLSELLRGGSGSSI (SEQ ID NO:38);
CBP-2: KRKLIQQQLVLLLHAHKCQRR (SEQ ID NO:39);
P300: DAASKHKQLSELLRSGSSPNL (SEQ ID NO:40);
CIA: GHPPAIQSLINLLADNRYLTA (SEQ ID NO:41);
ARA70–1: TLQQQAQQLYSLLGQFNCLTH (SEQ ID NO:42);
ARA70–2: GSRETSEKFKLLFQSYNVNDW (SEQ ID NO:43);
TIF1: NANYPRSILTSLLLNSSQSST (SEQ ID NO:44);
NSD1: IPIEPDYKFSTLLMMLKDMHD (SEQ ID NO:45);
SMAP: ATPPPSPLLSELLKKGSLLPT (SEQ ID NO:46);
Tip60: VDGHERAMLKRLLRIDSKCLH (SEQ ID NO:47);
ERAP140: HEDLDKVKLIEYYLTKNKEGP (SEQ ID NO:48);
Nix1: ESPEFCLGLQTLLSLKCCIDL (SEQ ID NO:49);
LCoR: AATTQNPVLSKLLMADQDSPL (SEQ ID NO:50);
CoRNR1 (N-CoR): MGQVPRTHRLITLADHICQIITQDFARNQV (SEQ ID NO:51);
CoRNR2 (N-CoR): NLGLEDIIRKALMG (SEQ ID NO:52);
CoRNR1 (SMRT): APGVKGHQRVVTLAQHISEVITQDTYRHHPQQLSAPLPAP (SEQ ID NO:53);
CoRNR2 (SMRT): NMGLEAIIRKALMG (SEQ ID NO:54);
RIP140-C: RLTKTNPILYYMLQKGGNSVA (SEQ ID NO:55);
RIP140-1: QDSIVLTYLEGLLMHQAAGGS (SEQ ID NO:56);
RIP140-2: KGKQDSTLLASLLQSFSSRLQ (SEQ ID NO:57);
RIP140-3: CYGVASSHLKTLLKKSKVKDQ (SEQ ID NO:58);
RIP140-4: KPSVACSQLALLLSSEAHLQQ (SEQ ID NO:59);
RIP140-5: KQAANNSLLLHLLKSQTIPKP (SEQ ID NO:60);
RIP140-6: NSHQKVTLLQLLLGHKNEENV (SEQ ID NO:61);
RIP140-7: NLLERRTVLQLLLGNPTKGRV (SEQ ID NO:62);
RIP140-8: FSFSKNGLLSRLLRQNQDSYL (SEQ ID NO:63);

RIP140-9: RESKSFNVLKQLLLSENCVRD (SEQ ID NO:64);

PRIC285-1: ELNADDAILRELLDESQKVMV (SEQ ID NO:65);

PRIC285-2: YENLPPAALRKLLRAEPERYR (SEQ ID NO:66);

PRIC285-3: MAFAGDEVLVQLLSGDKAPEG (SEQ ID NO:67);

PRIC285-4: SCCYLCIRLEGLLAPTASPRP (SEQ ID NO:68); and

PRIC285-5: PSNKSVDVLAGLLLRRMELKP (SEQ ID NO:69).

[00291] Further examples are provided in Example 1, Example 2 and Example 3.

[00292] In some cases, a given LBD can be paired with two or more different co-regulator polypeptides. For example, as depicted in FIG. 19, PPARγ can be paired with SRC1, SRC2, SRC3, or TRAP220. As another example, ERα can be paired with CoRNR, αβV, or TA1. As another example, ERβ can be paired with CoRNR, αβV, or TA1. As another example, AR can be paired with SRC1, SRC2, SRC3, or TRAP220. As another example, PR can be paired with SRC1, SRC2, SRC3, TRAP220, NR0B1, PGC1B, NRIP1, EA2, or EAB1. As another example, TRβ can be paired with SRC1, SRC2, SRC3, or TRAP220.

[00293] In some cases, a heterodimeric polypeptide of the present disclosure comprises a polypeptide chain comprising multiple (two or more) co-regulator peptides. Where a heterodimeric polypeptide of the present disclosure comprises a polypeptide chain comprising multiple (two or more) co-regulator peptides, the multiple co-regulator peptides can be in tandem, directly or separated by a linker. In some cases, the two or more co-regulator peptides present in the polypeptide chain are identical in amino acid sequence to one another. In some cases, where a heterodimeric polypeptide of the present disclosure comprises a polypeptide chain comprising multiple (two or more) co-regulator peptides, the polypeptide chain comprises two co-regulator peptides. In some cases, where a heterodimeric polypeptide of the present disclosure comprises a polypeptide chain comprising multiple (two or more) co-regulator peptides, the polypeptide chain comprises three co-regulator peptides. In such cases, the second polypeptide chain can comprise multiple (two or more) LBD of a nuclear hormone receptor. For example, where the second polypeptide chain comprises two LBD of a nuclear hormone receptor, the two LBD can be identical in amino acid sequence to one another.

Intracellular signaling domain

[00294] Intracellular signaling domains suitable for use in a conditionally active heterodimeric polypeptide of the present disclosure include any desired signaling domain that provides a distinct and detectable signal (e.g., increased production of one or more cytokines by the cell; change in transcription of a target gene; change in activity of a protein; change in cell behavior, e.g., cell death; cellular proliferation; cellular differentiation; cell survival; modulation of cellular signaling responses; etc.) in response to activation of the conditionally active heterodimeric polypeptide (i.e., activated by antigen and dimerizing agent). In some instances, the intracellular signaling domain(s) of a conditionally active heterodimeric polypeptide

of the present disclosure provides a signal transduction function when activated and may thus, in some instances, be referred to as a signal transducing domain. In some embodiments, the intracellular signaling domain includes at least one (e.g., one, two, three, four, five, six, etc.) ITAM motifs as described below. In some embodiments, the intracellular signaling domain includes DAP10/CD28 type signaling chains. In some embodiments, the intracellular signaling domain is not covalently attached to the membrane bound conditionally active heterodimeric polypeptide, but is instead diffused in the cytoplasm.

ITAM

[00295] Intracellular signaling domains suitable for use in a conditionally active heterodimeric polypeptide of the present disclosure include immunoreceptor tyrosine-based activation motif (ITAM)-containing intracellular signaling polypeptides. An ITAM motif is YX_1X_2L/I, where X_1 and X_2 are independently any amino acid (SEQ ID NO:564). In some cases, the intracellular signaling domain of a subject CAR comprises 1, 2, 3, 4, or 5 ITAM motifs. In some cases, an ITAM motif is repeated twice in an intracellular signaling domain, where the first and second instances of the ITAM motif are separated from one another by 6 to 8 amino acids, e.g., $(YX_1X_2L/I)(X_3)_n(YX_1X_2L/I)$, where n is an integer from 6 to 8, and each of the 6-8 X_3 can be any amino acid (SEQ ID NO:565). In some cases, the intracellular signaling domain of a subject CAR comprises 3 ITAM motifs.

[00296] A suitable intracellular signaling domain can be an ITAM motif-containing portion that is derived from a polypeptide that contains an ITAM motif. For example, a suitable intracellular signaling domain can be an ITAM motif-containing domain from any ITAM motif-containing protein. Thus, a suitable intracellular signaling domain need not contain the entire sequence of the entire protein from which it is derived. Examples of suitable ITAM motif-containing polypeptides include, but are not limited to: DAP12; FCER1G (Fc epsilon receptor I gamma chain); CD3D (CD3 delta); CD3E (CD3 epsilon); CD3G (CD3 gamma); CD3Z (CD3 zeta); and CD79A (antigen receptor complex-associated protein alpha chain).

[00297] In some cases, the intracellular signaling domain is derived from DAP12 (also known as TYROBP; TYRO protein tyrosine kinase binding protein; KARAP; PLOSL; DNAX-activation protein 12; KAR-associated protein; TYRO protein tyrosine kinase-binding protein; killer activating receptor associated protein; killer-activating receptor-associated protein; etc.). For example, a suitable intracellular signaling domain polypeptide can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100%, amino acid sequence identity to any of the following amino acid sequences (4 isoforms):
MGGLEPCSRLLLLPLLLAVSGLRPVQAQAQSDCSCSTVSPGVLAGIVMGDLVLTVLIALAVYFL GRLVPRGRGAAEAATRKQRITETESP**YQEL**QGQRSDV**YSDL**NTQRPYYK (SEQ ID NO:566);
MGGLEPCSRLLLLPLLLAVSGLRPVQAQAQSDCSCSTVSPGVLAGIVMGDLVLTVLIALAVYFL GRLVPRGRGAAEATRKQRITETESP**YQEL**QGQRSDV**YSDL**NTQRPYYK (SEQ ID NO:567);

MGGLEPCSRLLLLPLLLAVSDCSCSTVSPGVLAGIVMGDLVLTVLIALAVYFLGRLVPRGRGAA EAATRKQRITETESP**YQEL**QGQRSDV**YSDL**NTQRPYYK (SEQ ID NO:568); or MGGLEPCSRLLLLPLLLAVSDCSCSTVSPGVLAGIVMGDLVLTVLIALAVYFLGRLVPRGRGAA EATRKQRITETESP**YQEL**QGQRSDV**YSDL**NTQRPYYK (SEQ ID NO:569), where the ITAM motifs are in bold and are underlined.

[00298] Likewise, a suitable intracellular signaling domain polypeptide can comprise an ITAM motif-containing portion of the full length DAP12 amino acid sequence. Thus, a suitable intracellular signaling domain polypeptide can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100%, amino acid sequence identity to the following amino acid sequence: ESP**YQEL**QGQRSDV**YSDL**NTQ (SEQ ID NO:570), where the ITAM motifs are in bold and are underlined.

[00299] In some cases, the intracellular signaling domain is derived from FCER1G (also known as FCRG; Fc epsilon receptor I gamma chain; Fc receptor gamma-chain; fc-epsilon RI-gamma; fcRgamma; fceRI gamma; high affinity immunoglobulin epsilon receptor subunit gamma; immunoglobulin E receptor, high affinity, gamma chain; etc.). For example, a suitable intracellular signaling domain polypeptide can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100% amino acid sequence identity to the following amino acid sequence: MIPAVVLLLLLLVEQAAALGEPQLCYILDAILFLYGIVLTLLYCRLKIQVRKAAITSYEKSDGV**YT GL**STRNQET**YETL**KHEKPPQ (SEQ ID NO:571), where the ITAM motifs are in bold and are underlined.

[00300] Likewise, a suitable intracellular signaling domain polypeptide can comprise an ITAM motif-containing portion of the full length FCER1G amino acid sequence. Thus, a suitable intracellular signaling domain polypeptide can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100%, amino acid sequence identity to the following amino acid sequence: DGV**YTGL**STRNQET**YETL**KHE (SEQ ID NO:572), where the ITAM motifs are in bold and are underlined.

[00301] In some cases, the intracellular signaling domain is derived from T-cell surface glycoprotein CD3 delta chain (also known as CD3D; CD3-DELTA; T3D; CD3 antigen, delta subunit; CD3 delta; CD3d antigen, delta polypeptide (TiT3 complex); OKT3, delta chain; T-cell receptor T3 delta chain; T-cell surface glycoprotein CD3 delta chain; etc.). For example, a suitable intracellular signaling domain polypeptide can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100%, amino acid sequence

identity to a contiguous stretch of from about 100 amino acids to about 110 amino acids (aa), from about 110 aa to about 115 aa, from about 115 aa to about 120 aa, from about 120 aa to about 130 aa, from about 130 aa to about 140 aa, from about 140 aa to about 150 aa, or from about 150 aa to about 170 aa, of either of the following amino acid sequences (2 isoforms):
MEHSTFLSGLVLATLLSQVSPFKIPIEELEDRVFVNCNTSITWVEGTVGTLLSDITRLDLGKRILDP
RGIYRCNGTDIYKDKESTVQVHYRMCQSCVELDPATVAGIIVTDVIATLLLALGVFCFAGHETG
RLSGAADTQALLRNDQV**YQPL**RDRDDAQ**YSHL**GGNWARNK (SEQ ID NO:573) or
MEHSTFLSGLVLATLLSQVSPFKIPIEELEDRVFVNCNTSITWVEGTVGTLLSDITRLDLGKRILDP
RGIYRCNGTDIYKDKESTVQVHYRTADTQALLRNDQV**YQPL**RDRDDAQ**YSHL**GGNWARNK
(SEQ ID NO:574) , where the ITAM motifs are in bold and are underlined.

[00302] Likewise, a suitable intracellular signaling domain polypeptide can comprise an ITAM motif-containing portion of the full length CD3 delta amino acid sequence. Thus, a suitable intracellular signaling domain polypeptide can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100%, amino acid sequence identity to the following amino acid sequence:
DQV**YQPL**RDRDDAQ**YSHL**GGN (SEQ ID NO:575), where the ITAM motifs are in bold and are underlined.

[00303] In some cases, the intracellular signaling domain is derived from T-cell surface glycoprotein CD3 epsilon chain (also known as CD3e, T-cell surface antigen T3/Leu-4 epsilon chain, T-cell surface glycoprotein CD3 epsilon chain, AI504783, CD3, CD3epsilon, T3e, etc.). For example, a suitable intracellular signaling domain polypeptide can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100%, amino acid sequence identity to a contiguous stretch of from about 100 amino acids to about 110 amino acids (aa), from about 110 aa to about 115 aa, from about 115 aa to about 120 aa, from about 120 aa to about 130 aa, from about 130 aa to about 140 aa, from about 140 aa to about 150 aa, or from about 150 aa to about 205 aa, of the following amino acid sequence:
MQSGTHWRVLGLCLLSVGVWGQDGNEEMGGITQTPYKVSISGTTVILTCPQYPGSEILWQHND
KNIGGDEDDKNIGSDEDHLSLKEFSELEQSGYYVCYPRGSKPEDANFYLYLRARVCENCMEMD
VMSVATIVIVDICITGGLLLLVYYWSKNRKAKAKPVTRGAGAGGRQRGQNKERPPPVPNPD**YE**
PIRKGQRDL**YSGL**NQRRI (SEQ ID NO:576), where the ITAM motifs are in bold and are underlined.

[00304] Likewise, a suitable intracellular signaling domain polypeptide can comprise an ITAM motif-containing portion of the full length CD3 epsilon amino acid sequence. Thus, a suitable intracellular signaling domain polypeptide can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100%, amino acid sequence identity to the following amino acid sequence:

NPD**YEPI**RKGQRDL**YSGL**NQR (SEQ ID NO:577), where the ITAM motifs are in bold and are underlined.

[00305] In some cases, the intracellular signaling domain is derived from T-cell surface glycoprotein CD3 gamma chain (also known as CD3G, T-cell receptor T3 gamma chain, CD3-GAMMA, T3G, gamma polypeptide (TiT3 complex), etc.). For example, a suitable intracellular signaling domain polypeptide can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100%, amino acid sequence identity to a contiguous stretch of from about 100 amino acids to about 110 amino acids (aa), from about 110 aa to about 115 aa, from about 115 aa to about 120 aa, from about 120 aa to about 130 aa, from about 130 aa to about 140 aa, from about 140 aa to about 150 aa, or from about 150 aa to about 180 aa, of the following amino acid sequence:
MEQGKGLAVLILAIILLQGTLAQSIKGNHLVKVYDYQEDGSVLLTCDAEAKNITWFKDGKMIGF
LTEDKKKWNLGSNAKDPRGMYQCKGSQNKSKPLQVYYRMCQNCIELNAATISGFLFAEIVSIFV
LAVGVYFIAGQDGVRQSRASDKQTLLPNDQL**YQPL**KDREDDQ**YSHL**QGNQLRRN (SEQ ID NO:578), where the ITAM motifs are in bold and are underlined.

[00306] Likewise, a suitable intracellular signaling domain polypeptide can comprise an ITAM motif-containing portion of the full length CD3 gamma amino acid sequence. Thus, a suitable intracellular signaling domain polypeptide can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100%, amino acid sequence identity to the following amino acid sequence:
DQL**YQPL**KDREDDQ**YSHL**QGN (SEQ ID NO:579), where the ITAM motifs are in bold and are underlined.

[00307] In some cases, the intracellular signaling domain is derived from T-cell surface glycoprotein CD3 zeta chain (also known as CD3Z, T-cell receptor T3 zeta chain, CD247, CD3-ZETA, CD3H, CD3Q, T3Z, TCRZ, etc.). For example, a suitable intracellular signaling domain polypeptide can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100%, amino acid sequence identity to a contiguous stretch of from about 100 amino acids to about 110 amino acids (aa), from about 110 aa to about 115 aa, from about 115 aa to about 120 aa, from about 120 aa to about 130 aa, from about 130 aa to about 140 aa, from about 140 aa to about 150 aa, or from about 150 aa to about 160 aa, of either of the following amino acid sequences (2 isoforms):
MKWKALFTAAILQAQLPITEAQSFGLLDPKLCYLLDGILFIYGVILTALFLRVKFSRSADAPAYQ
QGQNQL**YNEL**NLGRREE**YDVL**DKRRGRDPEMGGKPRRKNPQEGL**YNEL**QKDKMAEA**YSEI**G
MKGERRRGKGHDGL**YQGL**STATKDT**YDAL**HMQALPPR (SEQ ID NO:580) or
MKWKALFTAAILQAQLPITEAQSFGLLDPKLCYLLDGILFIYGVILTALFLRVKFSRSADAPAYQ

QGQNQL**YNEL**NLGRREE**YDVL**DKRRGRDPEMGGKPQRRKNPQEGL**YNEL**QKDKMAEA**YSEI**GMKGERRRGKGHDGL**YQGL**STATKDT**YDAL**HMQALPPR(SEQ ID NO:581), where the ITAM motifs are in bold and are underlined.

[00308] Likewise, a suitable intracellular signaling domain polypeptide can comprise an ITAM motif-containing portion of the full length CD3 zeta amino acid sequence. Thus, a suitable intracellular signaling domain polypeptide can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100%, amino acid sequence identity to any of the following amino acid sequences: RVKFSRSADAPAYQQGQNQL**YNEL**NLGRREE**YDVL**DKRRGRDPEMGGKPRRKNPQEGL**YNEL**QKDKMAEA**YSEI**GMKGERRRGKGHDGL**YQGL**STATKDT**YDAL**HMQALPPR (SEQ ID NO:582); NQL**YNEL**NLGRREE**YDVL**DKR (SEQ ID NO:583); EGL**YNEL**QKDKMAEA**YSEI**GMK (SEQ ID NO:534); or DGL**YQGL**STATKDT**YDAL**HMQ (SEQ ID NO:585), where the ITAM motifs are in bold and are underlined.

[00309] In some cases, the intracellular signaling domain is derived from CD79A (also known as B-cell antigen receptor complex-associated protein alpha chain; CD79a antigen (immunoglobulin-associated alpha); MB-1 membrane glycoprotein; ig-alpha; membrane-bound immunoglobulin-associated protein; surface IgM-associated protein; etc.). For example, a suitable intracellular signaling domain polypeptide can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100%, amino acid sequence identity to a contiguous stretch of from about 100 amino acids to about 110 amino acids (aa), from about 110 aa to about 115 aa, from about 115 aa to about 120 aa, from about 120 aa to about 130 aa, from about 130 aa to about 150 aa, from about 150 aa to about 200 aa, or from about 200 aa to about 220 aa, of either of the following amino acid sequences (2 isoforms):

[00310] MPGGPGVLQALPATIFLLFLLSAVYLGPGCQALWMHKVPASLMVSLGEDAHFQCPHNSSN NANVTWWRVLHGNYTWPPEFLGPGEDPNGTLIIQNVNKSHGGIYVCRVQEGNESYQQSCGTYL RVRQPPPRPFLDMGEGTKNRIITAEGIILLFCAVVPGTLLLFRKRWQNEKLGLDAGDEYEDENL**Y EGL**NLDDCSM**YEDI**SRGLQGTYQDVGSLNIGDVQLEKP (SEQ ID NO:586); or

[00311] MPGGPGVLQALPATIFLLFLLSAVYLGPGCQALWMHKVPASLMVSLGEDAHFQCPHNSSN NANVTWWRVLHGNYTWPPEFLGPGEDPNEPPPRPFLDMGEGTKNRIITAEGIILLFCAVVPGTLL LFRKRWQNEKLGLDAGDEYEDENLYEGLNLDDCSMYEDISRGLQGTYQDVGSLNIGDVQLEKP (SEQ ID NO:587), where the ITAM motifs are in bold and are underlined.

[00312] Likewise, a suitable intracellular signaling domain polypeptide can comprise an ITAM motif-containing portion of the full length CD79A amino acid sequence. Thus, a suitable intracellular signaling domain polypeptide can comprise an amino acid sequence having at least about 75%, at least about 80%,

at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100%, amino acid sequence identity to the following amino acid sequence: ENL**YEGL**NLDDCSM**YEDI**SRG (SEQ ID NO:588), where the ITAM motifs are in bold and are underlined.

DAP10/CD28

[00313] Intracellular signaling domains suitable for use in a conditionally active heterodimeric polypeptide of the present disclosure include a DAP10/CD28 type signaling chain.

[00314] An example of a DAP10 signaling chain is the amino acid sequence is: RPRRSPAQDGKV**YINM**PGRG (SEQ ID NO:589). In some embodiments, a suitable intracellular signaling domain comprises an amino acid sequence having at least about 85%, at least about 90%, at least about 95%, at least about 98%, or at least about 99%, amino acid sequence identity to the entire length of the amino acid sequence RPRRSPAQDGKV**YINM**PGRG (SEQ ID NO:590).

[00315] An example of a CD28 signaling chain is the amino acid sequence is FWVLVVVGGVLACYSLLVTVAFIIFWVRSKRSRLLHSD**YMNM**TPRRPGPTRKHYQPYAPPRDF AAYRS (SEQ ID NO:591). In some embodiments, a suitable intracellular signaling domain comprises an amino acid sequence having at least about 85%, at least about 90%, at least about 95%, at least about 98%, or at least about 99%, amino acid sequence identity to the entire length of the amino acid sequence FWVLVVVGGVLACYSLLVTVAFIIFWVRSKRSRLLHSD**YMNM**TPRRPGPTRKHYQPYAPPRDF AAYRS (SEQ ID NO:592).

ZAP70

[00316] Intracellular signaling domains suitable for use in a conditionally active heterodimeric polypeptide of the present disclosure include a ZAP70 polypeptide, e.g., a polypeptide comprising an amino acid sequence having at least about 85%, at least about 90%, at least about 95%, at least about 98%, at least about 99%, or 100%, amino acid sequence identity to a contiguous stretch of from about 300 amino acids to about 400 amino acids, from about 400 amino acids to about 500 amino acids, or from about 500 amino acids to 619 amino acids, of the following amino acid sequence:

[00317] MPDPAAHLPFFYGSISRAEAEEHLKLAGMADGLFLLRQCLRSLGGYVLSLVHDVRFHHFPIE RQLNGTYAIAGGKAHCGPAELCEFYSRDPDGLPCNLRKPCNRPSGLEPQPGVFDCLRDAMVRD YVRQTWKLEGEALEQAIISQAPQVEKLIATTAHERMPWYHSSLTREEAERKLYSGAQTDGKFLL RPRKEQGTYALSLIYGKTVYHYLISQDKAGKYCIPEGTKFDTLWQLVEYLKLKADGLIYCLKEA CPNSSASNASGAAAPTLPAHPSTLTHPQRRIDTLNSDGYTPEPARITSPDKPRPMPMDTSVYESPY SDPEELKDKKLFLKRDNLLIADIELGCGNFGSVRQGVYRMRKKQIDVAIKVLKQGTEKADTEE MMREAQIMHQLDNPYIVRLIGVCQAEALMLVMEMAGGGPLHKFLVGKREEIPVSNVAELLHQ VSMGMKYLEEKNFVHRDLAARNVLLVNRHYAKISDFGLSKALGADDSYYTARSAGKWPLKW YAPECINFRKFSSRSDVWSYGVTMWEALSYGQKPYKKMKGPEVMAFIEQGKRMECPPECPPEL

YALMSDCWIYKWEDRPDFLTVEQRMRACYYSLASKVEGPPGSTQKAEAACA (SEQ ID NO:593).

Additional sequences

[00318] The first and/or the second polypeptide of a subject conditionally active heterodimeric polypeptide can further include one or more additional polypeptide domains, where such domains include, but are not limited to, a signal sequence; an epitope tag; an affinity domain; and a polypeptide that produces a detectable signal.

Signal sequences

[00319] Signal sequences that are suitable for use in a subject CAR, e.g., in the first polypeptide of a subject CAR, include any eukaryotic signal sequence, including a naturally-occurring signal sequence, a synthetic (e.g., man-made) signal sequence, etc.

Epitope tag

[00320] Suitable epitope tags include, but are not limited to, hemagglutinin (HA; e.g., YPYDVPDYA (SEQ ID NO:594); FLAG (e.g., DYKDDDDK (SEQ ID NO:595); c-myc (e.g., EQKLISEEDL; SEQ ID NO:596), and the like.

Affinity domain

[00321] Affinity domains include peptide sequences that can interact with a binding partner, e.g., such as one immobilized on a solid support, useful for identification or purification. DNA sequences encoding multiple consecutive single amino acids, such as histidine, when fused to the expressed protein, may be used for one-step purification of the recombinant protein by high affinity binding to a resin column, such as nickel sepharose. Exemplary affinity domains include His5 (HHHHH) (SEQ ID NO:597), HisX6 (HHHHHH) (SEQ ID NO:598), C-myc (EQKLISEEDL) (SEQ ID NO:599), Flag (DYKDDDDK) (SEQ ID NO:600), StrepTag (WSHPQFEK) (SEQ ID NO:601), hemagglutinin, e.g., HA Tag (YPYDVPDYA) (SEQ ID NO:602), GST, thioredoxin, cellulose binding domain, RYIRS (SEQ ID NO:603), Phe-His-His-Thr (SEQ ID NO:064), chitin binding domain, S-peptide, T7 peptide, SH2 domain, C-end RNA tag, WEAAAREACCRECCARA (SEQ ID NO:605), metal binding domains, e.g., zinc binding domains or calcium binding domains such as those from calcium-binding proteins, e.g., calmodulin, troponin C, calcineurin B, myosin light chain, recoverin, S-modulin, visinin, VILIP, neurocalcin, hippocalcin, frequenin, caltractin, calpain large-subunit, S100 proteins, parvalbumin, calbindin D9K, calbindin D28K, and calretinin, inteins, biotin, streptavidin, MyoD, Id, leucine zipper sequences, and maltose binding protein.

Detectable signal-producing polypeptides

[00322] Suitable detectable signal-producing proteins include, e.g., fluorescent proteins; enzymes that catalyze a reaction that generates a detectable signal as a product; and the like.

[00323] Suitable fluorescent proteins include, but are not limited to, green fluorescent protein (GFP) or variants thereof, blue fluorescent variant of GFP (BFP), cyan fluorescent variant of GFP (CFP), yellow fluorescent variant of GFP (YFP), enhanced GFP (EGFP), enhanced CFP (ECFP), enhanced YFP (EYFP), GFPS65T, Emerald, Topaz (TYFP), Venus, Citrine, mCitrine, GFPuv, destabilized EGFP (dEGFP), destabilized ECFP (dECFP), destabilized EYFP (dEYFP), mCFPm, Cerulean, T-Sapphire, CyPet, YPet, mKO, HcRed, t-HcRed, DsRed, DsRed2, DsRed-monomer, J-Red, dimer2, t-dimer2(12), mRFP1, pocilloporin, Renilla GFP, Monster GFP, paGFP, Kaede protein and kindling protein, Phycobiliproteins and Phycobiliprotein conjugates including B-Phycoerythrin, R-Phycoerythrin and Allophycocyanin. Other examples of fluorescent proteins include mHoneydew, mBanana, mOrange, dTomato, tdTomato, mTangerine, mStrawberry, mCherry, mGrape1, mRaspberry, mGrape2, mPlum (Shaner et al. (2005) *Nat. Methods* 2:905-909), and the like. Any of a variety of fluorescent and colored proteins from Anthozoan species, as described in, e.g., Matz et al. (1999) *Nature Biotechnol.* 17:969-973, is suitable for use.

[00324] Suitable enzymes include, but are not limited to, horse radish peroxidase (HRP), alkaline phosphatase (AP), beta-galactosidase (GAL), glucose-6-phosphate dehydrogenase, beta-N-acetylglucosaminidase, β-glucuronidase, invertase, Xanthine Oxidase, firefly luciferase, glucose oxidase (GO), and the like.

Exemplary conditionally active heterodimeric polypeptides

[00325] In some cases, a conditionally active, heterodimeric polypeptide of the present disclosure comprises: a) a first chimeric polypeptide comprising: i) a first member of a specific binding pair; ii) a first modulatory domain; iii) a first member of a dimerization pair; and iv) a transmembrane domain interposed between the first member of a specific binding pair and the first modulatory domain; and b) a second chimeric polypeptide comprising: i) a transmembrane domain; ii) a second modulatory domain; iii) a second member of the dimerization pair; and iv) an intracellular signaling domain, where i) the first and second modulatory domains are derived from 4-1BB; ii) the first and second members of the dimerization pair are SRC3 and a PPARγ LBD, respectively; and iii) the signaling domain comprises an ITAM. In some cases, the first member of the dimerization pair comprises one copy of an SRC3 co-regulator peptide. In some cases, the SRC3 co-regulator peptide has a length of from 20 amino acids to 25 amino acids. In some cases, the SRC3 co-regulator peptide has a length of from 75 amino acids to 80 amino acids. In some cases, the first chimeric polypeptide comprises a single SRC3 co-regulator peptide. In some cases, the first chimeric polypeptide comprises 2 copies of an SRC3 co-regulator peptide. In some cases, the first chimeric polypeptide comprises 3 copies of an SRC3 co-regulator peptide. In some cases, each of the copies of the SRC3 co-regulator peptide has a length of from 20 amino acids to 25 amino acids.

[00326] For example, in some cases, a conditionally active, heterodimeric polypeptide of the present disclosure comprises a first polypeptide chain comprising: i) a single chain Fv; ii) a transmembrane polypeptide; and iii) a polypeptide comprising the amino acid sequence: ***KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCEL***SRGSGSGSTSPKKENNALLRYLLDRDDPSDAGS* (SEQ ID NO:606), where the 4-1BB sequence is in italics and bold text, and the co-regulator peptide is underlined (single underline). In some cases, the second polypeptide chain comprises the following amino acid sequence:

[00327] IYIWAPLAGTCGVLLLSLVITLYCSL**KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCEL**GSGSGSGSGSGSGSTSESADLRALAKHLYDSYIKSFPLTKAKARAILTGKTTDKSPFVIYDMNSLMMGEDKIKFKHITPLQEQSKEVAIRIFQGCQFRSVEAVQEITEYAKSIPGFVNLDLNDQVTLLKYGVHEIIYTMLASLMNKDGVLISEGQGFMTREFLKSLRKPFGDFMEPKFEFAVKFNALELDDSDLAIFIAVIILSGDRPGLLNVKPIEDIQDNLLQALELQLKLNHPESSQLFAKLLQKMTDLRQIVTEHVQLLQVIKKTETDMSLHPLLQEIYKDLYGSGSGSGSSL***RVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR*** (SEQ ID NO:607), where the PPARγ LBD is underlined (single underline); the CD8α TM domain is double underlined; 4-1BB is in bold text; and CD3 zeta is in bold and italics.

[00328] In some cases, the first member of a specific binding pair is an scFv specific for CD19, and the first polypeptide chain comprises a transmembrane domain between the anti-CD19 scFv and the first modulatory domain, where the first modulatory domain is 4-1BB. For example, in some cases, a conditionally active, heterodimeric polypeptide of the present disclosure comprises a first polypeptide chain comprising the following amino acid sequence:

[00329] DIQMTQTTSSLSASLGDRVTISCRASQDISKYLNWYQQKPDGTVKLLIYHTSRLHSGVPSRFSGSGSGTDYSLTISNLEQEDIATYFCQQGNTLPYTFGGGTKLEITGGGGSGGGGSGGGGSEVKLQESGPGLVAPSQSLSVTCTVSGVSLPDYGVSWIRQPPRKGLEWLGVIWGSETTYYNSALKSRLTIIKDNSKSQVFLKMNSLQTDDTAIYYCAKHYYYGGSYAMDYWGQGTSVTVSSTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCSL*KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCEL*SRGSGSGSTSPKKENNALLRYLLDRDDPSDAGS* (SEQ ID NO:608), where the anti-CD19 sequence is in bold, the CD8α transmembrane (TM) domain is double underlined, the 4-1BB sequence is in italics and bold text, and the co-regulator peptide is underlined (single underline). In some cases, the second polypeptide chain comprises the following amino acid sequence:

[00330] IYIWAPLAGTCGVLLLSLVITLYCSL**KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCEL**GSGSGSGSGSGSGSTSESADLRALAKHLYDSYIKSFPLTKAKARAILTGKTTDKSPF

VIYDMNSLMMGEDKIKFKHITPLQEQSKEVAIRIFQGCQFRSVEAVQEITEYAKSIPGFVNLDLN DQVTLLKYGVHEIIYTMLASLMNKDGVLISEGQGFMTREFLKSLRKPFGDFMEPKFEFAVKFNA LELDDSDLAIFIAVIILSGDRPGLLNVKPIEDIQDNLLQALELQLKLNHPESSQLFAKLLQKMTDL RQIVTEHVQLLQVIKKTETDMSLHPLLQEIYKDLYGSGSGSGSSL***RVKFSRSADAPAYQQGQNQL YNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRR GKGHDGLYQGLSTATKDTYDALHMQALPPR*** (SEQ ID NO:609), where the PPARγ LBD is underlined (single underline); the CD8α TM domain is double underlined; 4-1BB is in bold text; and CD3 zeta is in bold and italics.

[00331] As another example, in some cases, a conditionally active, heterodimeric polypeptide of the present disclosure comprises a first polypeptide chain comprising the following amino acid sequence: **DIQMTQTTSSLSASLGDRVTISCRASQDISKYLNWYQQKPDGTVKLLIYHTSRLHSGVPSRF SGSGSGTDYSLTISNLEQEDIATYFCQQGNTLPYTFGGGTKLEITGGGGSGGGGSGGGGSE VKLQESGPGLVAPSQSLSVTCTVSGVSLPDYGVSWIRQPPRKGLEWLGVIWGSETTYYNSA LKSRLTIIKDNSKSQVFLKMNSLQTDDTAIYYCAKHYYYGGSYAMDYWGQGTSVTVSSTT TPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACD**IYIWAPLAGTCGVLLLSLVIT LYCSL***KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCEL***SRGSGSGSTSMHGSLLQ EKHRILHKLLQNGNSPAEVAKITAEATGKDTSSITSCGDGNVVKQEQLSPKKKENNALLRYLLD RDDPSDAGS* (SEQ ID NO:610), where the anti-CD19 sequence is in bold, the CD8α transmembrane (TM) domain is double underlined, the 4-1BB sequence is in italics and bold text, and the co-regulator peptide is underlined (single underline). In some cases, the second polypeptide chain comprises the following amino acid sequence:

[00332] IYIWAPLAGTCGVLLLSLVITLYCSL**KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPE EEEGGCEL**GSGSGSGSGSGSGSTSESADLRALAKHLYDSYIKSFPLTKAKARAILTGKTTDKSPF VIYDMNSLMMGEDKIKFKHITPLQEQSKEVAIRIFQGCQFRSVEAVQEITEYAKSIPGFVNLDLN DQVTLLKYGVHEIIYTMLASLMNKDGVLISEGQGFMTREFLKSLRKPFGDFMEPKFEFAVKFNA LELDDSDLAIFIAVIILSGDRPGLLNVKPIEDIQDNLLQALELQLKLNHPESSQLFAKLLQKMTDL RQIVTEHVQLLQVIKKTETDMSLHPLLQEIYKDLYGSGSGSGSSL***RVKFSRSADAPAYQQGQNQL YNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRR GKGHDGLYQGLSTATKDTYDALHMQALPPR*** (SEQ ID NO:611), where the PPARγ LBD is underlined (single underline); the CD8α TM domain is double underlined; 4-1BB is in bold text; and CD3 zeta is in bold and italics.

[00333] As another example, in some cases, a conditionally active, heterodimeric polypeptide of the present disclosure comprises a first polypeptide chain comprising the following amino acid sequence: **DIQMTQTTSSLSASLGDRVTISCRASQDISKYLNWYQQKPDGTVKLLIYHTSRLHSGVPSRF SGSGSGTDYSLTISNLEQEDIATYFCQQGNTLPYTFGGGTKLEITGGGGSGGGGSGGGGSE**

VKLQESGPGLVAPSQSLSVTCTVSGVSLPDYGVSWIRQPPRKGLEWLGVIWGSETTYYNSA LKSRLTIIKDNSKSQVFLKMNSLQTDDTAIYYCAKHYYYGGSYAMDYWGQGTSVTVSSTT TPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVIT LYCSL***KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEEGGCEL***SRGSGSGSTSPKKENNA LLRYLLDRDDPSDAGGGSGGGSPKKENNALLRYLLDRDDPSDAGGGSGGGSKKENNALLRYLL DRDDPSDAGS* (SEQ ID NO:612), where the anti-CD19 sequence is in bold, the CD8α transmembrane (TM) domain is double underlined, the 4-1BB sequence is in italics and bold text, and the co-regulator peptide is underlined (single underline). In some cases, the second polypeptide chain comprises the following amino acid sequence:

[00334] IYIWAPLAGTCGVLLLSLVITLYCSL**KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPE EEEGGCEL**GSGSGSGSGSGSGSTSESADLRALAKHLYDSYIKSFPLTKAKARAILTGKTTDKSPF VIYDMNSLMMGEDKIKFKHITPLQEQSKEVAIRIFQGCQFRSVEAVQEITEYAKSIPGFVNLDLN DQVTLLKYGVHEIIYTMLASLMNKDGVLISEGQGFMTREFLKSLRKPFGDFMEPKFEFAVKFNA LELDDSDLAIFIAVIILSGDRPGLLNVKPIEDIQDNLLQALELQLKLNHPESSQLFAKLLQKMTDL RQIVTEHVQLLQVIKKTETDMSLHPLLQEIYKDLYGSGSGSGSSL***RVKFSRSADAPAYQQGQNQL YNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRR GKGHDGLYQGLSTATKDTYDALHMQALPPR*** (SEQ ID NO:613), where the PPARγ LBD is underlined (single underline); the CD8α TM domain is double underlined; 4-1BB is in bold text; and CD3 zeta is in bold and italics.

[00335] As another example, in some cases, a conditionally active, heterodimeric polypeptide of the present disclosure comprises: a) a first chimeric polypeptide comprising: i) a first member of a specific binding pair; ii) a first modulatory domain; iii) a first member of a dimerization pair; and iv) a transmembrane domain interposed between the first member of a specific binding pair and the first modulatory domain; and b) a second chimeric polypeptide comprising: i) a transmembrane domain; ii) a second modulatory domain; iii) a second member of the dimerization pair; and iv) an intracellular signaling domain, where i) the first and second modulatory domains are derived from 4-1BB; ii) the first and second members of the dimerization pair are CoRNR and an ERα LBD, respectively; and iii) the signaling domain comprises an ITAM. In some cases, the first member of the dimerization pair comprises one copy of a CoRNR co-regulator peptide. In some cases, the CoRNR co-regulator peptide has a length of from 60 amino acids to 70 amino acids. In some cases, the first chimeric polypeptide comprises a single CoRNR co-regulator peptide. In some cases, the first chimeric polypeptide comprises 2 copies of a CoRNR co-regulator peptide. In some cases, the first chimeric polypeptide comprises 3 copies of a CoRNR co-regulator peptide. In some cases, each of the copies of the CoRNR co-regulator peptide has a length of from 15 amino acids to 20 amino acids.

[00336] For example, in some cases, a conditionally active, heterodimeric polypeptide of the present disclosure comprises a first polypeptide chain comprising: i) a single chain Fv; ii) a transmembrane polypeptide; and iii) a polypeptide comprising the amino acid sequence: ***KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCEL***SRGSGSGSTSDAFQLRQLILRG LQDDGGGSGGGSDAFQLRQLILRGLQDDGGGSGGGSDAFQLRQLILRGLQDDG (SEQ ID NO:614), where the 4-1BB amino acid sequence is in bold and italics, and the 3x CoRNR co-regulator peptide is underlined. In some cases, the second polypeptide chain comprises the following amino acid sequence: IYIWAPLAGTCGVLLLSLVITLYCSL***KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGG CEL***GSGSGSGSGSGSGSTSDRRGGRMLKHKRQRDDGEGRGEVGSAGDMRAANLWPSPLMIKR SKKNSLALSLTADQMVSALLDAEPPILYSEYDPTRPFSEASMMGLLTNLADRELVHMINWAKR VPGFVDLTLHDQVHLLECAWLEILMIGLVWRSMEHPGKLLFAPNLLLDRNQGKCVEGMVEIFD MLLATSSRFRMMNLQGEEFVCLKSIILLNSGVYTFLSSTLKSLEEKDHIHRVLDKITDTLIHLMAK AGLTLQQQHQRLAQLLLILSHIRHMSNKGMEHLYSMKCKNVVPLYDLLLEMLDAHRLHAPTS (SEQ ID NO:615), where the TM polypeptide is double underlined, the 4-1BB amino acid sequence is in bold and italics, and the ER LBD is underlined (single underlined).

[00337] In some cases, the first member of a specific binding pair is an scFv specific for CD19, and the first polypeptide chain comprises a transmembrane domain between the anti-CD19 scFv and the first modulatory domain, where the first modulatory domain is 4-1BB. For example, in some cases, a conditionally active, heterodimeric polypeptide of the present disclosure comprises a first polypeptide chain comprising the following amino acid sequence:

[00338] DIQMTQTTSSLSASLGDRVTISCRASQDISKYLNWYQQKPDGTVKLLIYHTSRLHSGVPSRFS GSGSGTDYSLTISNLEQEDIATYFCQQGNTLPYTFGGGTKLEITGGGGSGGGGSGGGGSEVKLQE SGPGLVAPSQSLSVTCTVSGVSLPDYGVSWIRQPPRKGLEWLGVIWGSETTYYNSALKSRLTIIK DNSKSQVFLKMNSLQTDDTAIYYCAKHYYYGGSYAMDYWGQGTSVTVSSTTTPAPRPPTPAPT IASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCSL*KRGRKKLLY IFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCEL*SRGSGSGSTSDAFQLRQLILRGLQDDGGGSGG GSDAFQLRQLILRGLQDDGGGSGGGSDAFQLRQLILRGLQDDGS (SEQ ID NO:616), where the anti-CD19 scFv is in bold, the TM region is double underlined, the 4-1BB polypeptide is in bold and italics, and the 3x CoRNR co-regulator peptide is underlined (single underlined). In some cases, the second polypeptide chain comprises the following amino acid sequence: MIHLGHILFLLLLPVAAAQTTPGERSSLPAFYPGTSGSCSGCGSLSLPIYIWAPLAGTCGVLLLSL VITLYCSL*KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCEL*GSGSGSGSGSGSTSD RRGGRMLKHKRQRDDGEGRGEVGSAGDMRAANLWPSPLMIKRSKKNSLALSLTADQMVSAL LDAEPPILYSEYDPTRPFSEASMMGLLTNLADRELVHMINWAKRVPGFVDLTLHDQVHLLECA

WLEILMIGLVWRSMEHPGKLLFAPNLLLDRNQGKCVEGMVEIFDMLLATSSRFRMMNLQGEEF VCLKSIILLNSGVYTFLSSTLKSLEEKDHIHRVLDKITDTLIHLMAKAGLTLQQQHQRLAQLLLIL SHIRHMSNKGMEHLYSMKCKNVVPLYDLLLEMLDAHRLHAPTS (SEQ ID NO:617), where the TM polypeptide is double underlined, the 4-1BB amino acid sequence is in bold and italics, and the ER LBD is underlined (single underlined).

Dimerization agents

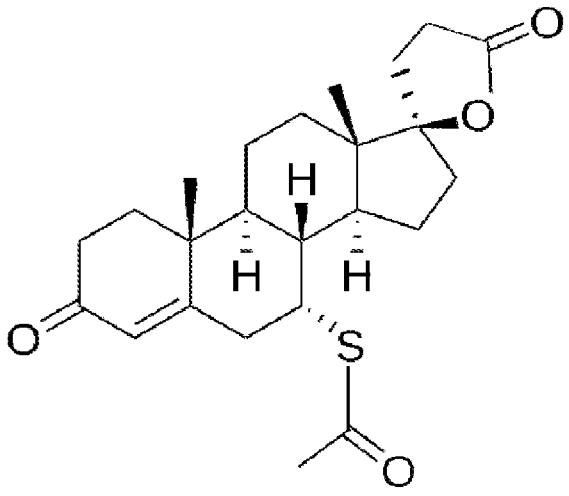
[00339] Suitable dimerization agents (also referred to as dimerizing agents; dimerizers) bind the LBD of a nuclear hormone receptor in a first polypeptide of a conditionally active, heterodimeric polypeptide of the present disclosure, and bind the co-regulator peptide in a second polypeptide of the conditionally active, heterodimeric polypeptide. Binding of to dimerization agent to the LBD and the co-regulator peptide functions to dimerize the first and second polypeptides of a conditionally active, heterodimeric polypeptide of the present disclosure.

[00340] Suitable dimerization agents are known in the art; any known dimerization agent can be used.

[00341] Examples of dimerization agents include corticosterone (11beta,21-dihydroxy-4-pregnene-3,20-dione); deoxycorticosterone (21-hydroxy-4-pregnene-3,20-dione); cortisol (11beta,17,21-trihydroxy-4-pregnene-3,20-dione); 11-deoxycortisol (17,21-dihydroxy-4-pregnene-3,20-dione); cortisone (17,21-dihydroxy-4-pregnene-3,11,20-trione); 18-hydroxycorticosterone (11beta,18,21-trihydroxy-4-pregnene-3,20-dione); 1.alpha.-hydroxycorticosterone (1alpha,11beta,21-trihydroxy-4-pregnene-3,20-dione); aldosterone 18,11-hemiacetal of 11beta,21-dihydroxy-3,20-dioxo-4-pregnen-18-al, androstenedione (4-androstene-3,17-dione); 4-hydroxy-androstenedione; 11β-hydroxyandrostenedione (11 beta-4-androstene-3,17-dione); androstanediol (3-beta,17-beta-Androstanediol); androsterone (3alpha-hydroxy-5alpha-androstan-17-one); epiandrosterone (3beta-hydroxy-5alpha-androstan-17-one); adrenosterone (4-androstene-3,11,17-trione); dehydroepiandrosterone (3beta-hydroxy-5-androsten-17-one); dehydroepiandrosterone sulphate (3beta-sulfoxy-5-androsten-17-one); testosterone (17beta-hydroxy-4-androsten-3-one); epitestosterone (17alpha-hydroxy-4-androsten-3-one); 5α-dihydrotestosterone (17beta-hydroxy-5alpha-androstan-3-one 5β-dihydrotestosterone; 5-beta-dihydroxy testosterone (17beta-hydroxy-5beta-androstan-3-one); 11β-hydroxytestosterone (11beta,17beta-dihydroxy-4-androsten-3-one); 11-ketotestosterone (17beta-hydroxy-4-androsten-3,17-dione), estrone (3-hydroxy-1,3,5(10)-estratrien-17-one); estradiol (1,3,5(10)-estratriene-3,17beta-diol); estriol 1,3,5(10)-estratriene-3,16alpha,17beta-triol; pregnenolone (3-beta-hydroxy-5-pregnen-20-one); 17-hydroxypregnenolone (3-beta,17-dihydroxy-5-pregnen-20-one); progesterone (4-pregnene-3,20-dione); 17-hydroxyprogesterone (17-hydroxy-4-pregnene-3,20-dione); progesterone (pregn-4-ene-3,20-dione); T3 and T4.

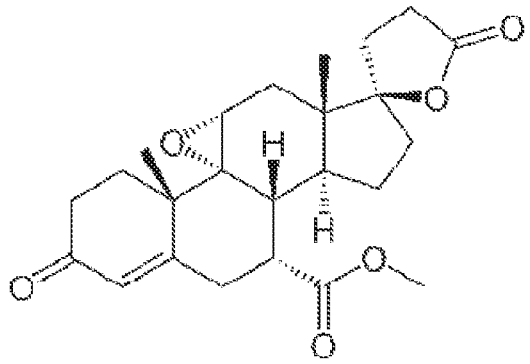
[00342] Where a conditionally active, heterodimeric polypeptide of the present disclosure comprises an LBD of a mineralocorticoid receptor (MR) and a corresponding co-regulator peptide, a suitable dimerization agent includes, but is not limited to, spironolactone, and eplerenone.

[00343] Spironolactone is a compound of the following structure:



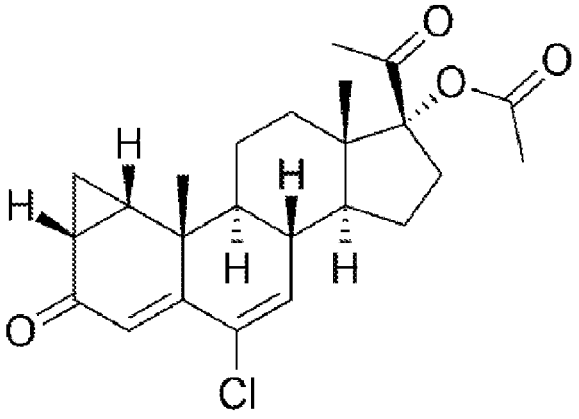
[00344] Spironolactone can be administered at a dose ranging from 10 to 35 mg per day, e.g., 25 mg per day.

[00345] Eplerenone is a compound of the following structure:

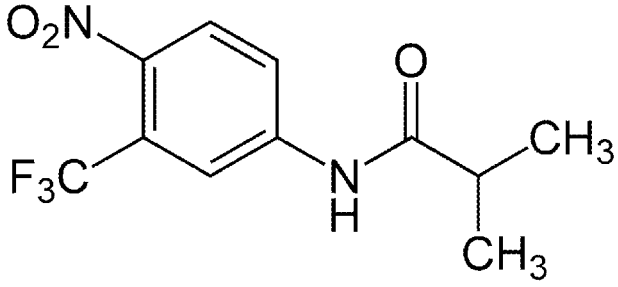


[00346] Where a conditionally active, heterodimeric polypeptide of the present disclosure comprises an LBD of an androgen receptor (AR) and a corresponding co-regulator peptide, a suitable dimerization agent includes, but is not limited to, cyproterone acetate, hydroxyflutamide, enzalutamide, ARN-509, 3,3'-diindolylmethane (DIM), bexlosteride, bicalutamide, N-butylbenzene-sulfonamide (NBBS), dutasteride, epristeride, finasteride, flutamide, izonsteride, ketoconazole, N-butylbenzene-sulfonamide, nilutamide, megestrol, a steroidal antiandrogen, and turosteride.

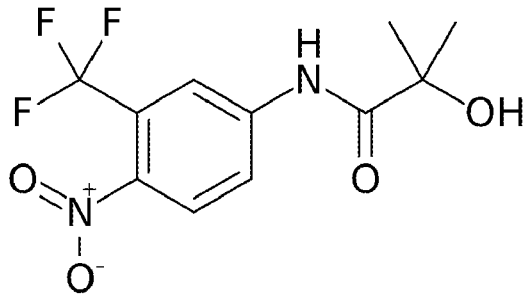
[00347] Cyproterone acetate is a compound of the formula:



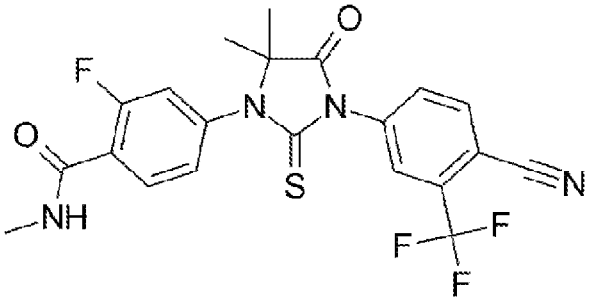
[00348] Flutamide is a compound of the formula:



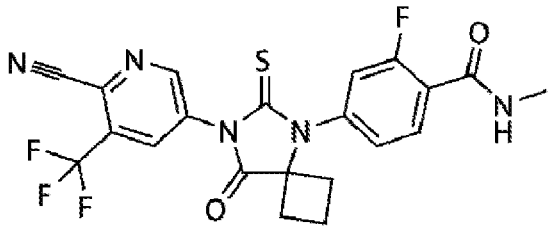
[00349] Hydroxyflutamide is a compound of the formula:



[00350] Enzalutamide is a compound of the formula:



[00351] ARN-509 is a compound of the formula:

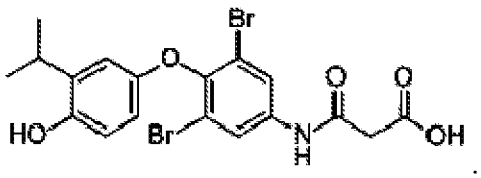


[00352] Where a conditionally active, heterodimeric polypeptide of the present disclosure comprises an LBD of progesterone receptor (PR) and a corresponding co-regulator peptide, a suitable dimerization agent includes, but is not limited to, mifepristone (RU-486; 11β-[4 N,N-dimethylaminophenyl]-17β -hydroxy-17-(1-propynyl)-estra-4,9-dien-- 3-one); Lilopristone (11β-(4 N,N-dimethylaminophenyl)-17β-hydroxy-17-((Z)-3-hydroxypropenyl)estra-4,9-dien-3-one); onapristone (11β-(4 N,N-dimethylaminophenyl)-17α-hydroxy-17-(3-hydroxypropyl)-13α- estra-4,9-dien-3-one); asoprisnil (benzaldehyde, 4-[(11β,17β)-17-methoxy-17-(methoxymethyl)-3-oxoestra-4,9-dien- 11-yl]-1-(E)-oxim; J867); J912 (4-[17β-Hydroxy-17α-(methoxymethyl)-3-oxoestra-4,9-dien-11β-yl]benzaldehyd-(1E)-oxim); and CDB-2914 (17α-acetoxy-11β-(4-N,N-dimethylaminophenyl)-19-norpregna-4,9- dien-3,20-dione). Other suitable dimerization agents include, e.g., JNJ-1250132, (6α,11β,17β)-11-(4-dimethylaminophenyl)-6-methyl-4',5'-dihydrospiro[estra-4,9-diene-17,2'(3'H)-furan]-3-one (ORG-31710); (11β,17α)-11-(4-acetylphenyl)-17,23-epoxy-19,24-dinorchola-4,9-,20-trien-3-one (ORG-33628); (7β,11β,17β)-11-(4-dimethylaminophenyl-7-methyl]-4',5'-dihydrospiro[estra-4,9-diene-17,2'(3'H)-furan]-3-one (ORG-31806); ZK-112993; ORG-31376; ORG-33245; ORG-31167; ORG-31343; RU-2992; RU-1479; RU-25056; RU-49295; RU-46556; RU-26819; LG1127; LG120753; LG120830; LG1447; LG121046; CGP-19984A; RTI-3021-012; RTI-3021-022; RTI-3021-020; RWJ-25333; ZK-136796; ZK-114043; ZK-230211; ZK-136798; ZK-98229; ZK-98734; ZK-137316; 4-[17β-Methoxy-17α-(methoxymethyl)-3-oxoestra-4,9-dien-11β-yl]benzaldehyde-1-(E)-oxime; 4-[17β-Methoxy-17α-(methoxymethyl)-3-oxoestra-4,9-dien-11β-yl]benzaldehyde-1-(E)-[O-(ethylamino)carbonyl]oxime; 4-[17β-Methoxy-17α-(methoxymethyl)-3-oxoestra-4,9-dien-11β-yl]benzaldehyde-1-(E)-[O-(ethylthio)carbonyl]oxime; (Z)-6'-(4-cyanophenyl)-9,11α-dihydro-17β-hydroxy-17α-[4--(1-oxo-3-methylbutoxy)-1-butenyl]4'H-naphtho[3',2',1';10,9,11]estr-4-en-3- one; 11β-(4-acetylphenyl)-17β-hydroxy-17α-(1,1,2,2,2-penta-fluoroethyl)estra-4,9-dien-3-one; 11β-(4-Acetylphenyl)-19,24-dinor-17,23-epoxy-17alpha-chola-4,9,20-trie- n-3-one; (Z)-11beta,19-[4-(3-Pyridinyl)-o-phenylene]-17beta-hydroxy-17α-[3-hydroxy-1-propenyl]-4-androsten-3-one; 11beta-[4-(1-methylethenyl)phenyl]-17α-hydroxy-17beta-β-hydroxypropyl)-13α-

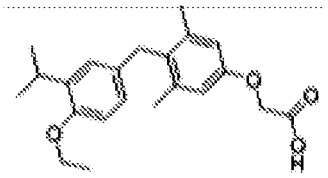
estra-4,9-dien-3-one; 4',5'-Dihydro-11beta-[4-(dimethylamino)phenyl]-6beta-methylspiro[estra-4,- 9-dien-17beta,2'(3'H)-furan]-3-one, and drospirenone.

[00353] Where a conditionally active, heterodimeric polypeptide of the present disclosure comprises an LBD of thyroid receptor-beta (TRβ) and a corresponding co-regulator peptide, a suitable dimerization agent includes, but is not limited to, T_3 (3,5,3'-triiodo-L-thyronine); KB-141 (3,5-dichloro-4-(4-hydroxy-3-isopropylphenoxy)phenylacetic acid); sobetirome (also known as GC-1) (3,5-dimethyl-4-(4'-hydroxy-3'-isopropylbenzyl)-phenoxy acetic acid); GC-24 (3,5-dimethyl-4-(4'-hydroxy-3'-benzyl)benzylphenoxyacetic acid); 4-OH-PCB106 (4-OH-2',3,3',4',5'-pentachlorobiphenyl); eprotirome; MB07811 ((2*R*,4*S*)-4-(3-chlorophenyl)-2-[(3,5-dimethyl-4-(4′-hydroxy-3′-isopropylbenzyl)phenoxy)methyl]-2-oxido-[1,3,2]-dioxaphosphonane); QH2; and (3,5-dimethyl-4-(4′-hydroxy-3′-isopropylbenzyl)phenoxy)methylphosphonic acid (MB07344).

[00354] Eprotirome has the following structure:



[00355] QH2 has the following structure:



[00356] Where a conditionally active, heterodimeric polypeptide of the present disclosure comprises an LBD of estrogen receptor-alpha (ERα) and a corresponding co-regulator peptide, a suitable dimerization agent includes, but is not limited to, tamoxifen, 4-OH-tamoxifen, raloxifene, lasofoxifene, bazedoxifene, falsodex, clomifene, femarelle, ormeloxifene, toremifiene, ospemifene, and ethinyl estradiol.

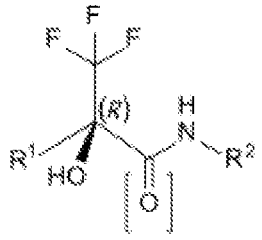
[00357] Where a conditionally active, heterodimeric polypeptide of the present disclosure comprises an LBD of estrogen receptor-beta (ERβ) and a corresponding co-regulator peptide, a suitable dimerization agent includes, but is not limited to, estradiol (E2; or 17-beta-estradiol), and ethinyl estradiol.

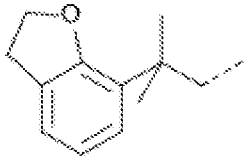
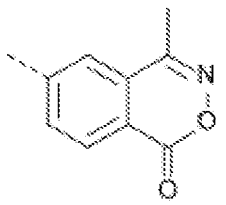
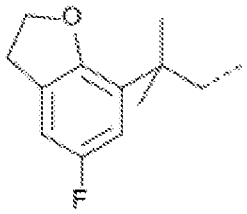
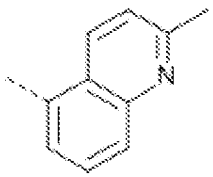
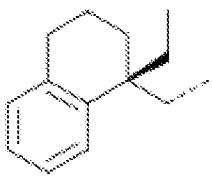
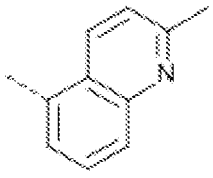
[00358] Where a conditionally active, heterodimeric polypeptide of the present disclosure comprises an LBD of a PPARγ and a corresponding co-regulator peptide, a suitable dimerization agent includes, but is not limited to, a thiazolidinedione (e.g., rosiglitazone, pioglitazone, lobeglitazone, troglitazone), farglitazar, aleglitazar, and fenofibric acid.

[00359] Where a conditionally active, heterodimeric polypeptide of the present disclosure comprises an LBD of a GR and a corresponding co-regulator peptide, a suitable dimerization agent can be a selective GR

agonist (SEGRA) or a selective GR modulator (SEGRM). Where a conditionally active, heterodimeric polypeptide of the present disclosure comprises an LBD of a GR and a corresponding co-regulator peptide, a suitable dimerization agent includes, but is not limited to, benzopyranoquinoline A 276575, Mapracorat, ZK 216348, 55D1E1, dexamethasone, prednisolone, prednisone, methylprednisolone, fluticasone propionate, beclomethasone-17-monopropionate, betamethasone, rimexolone, paramethasone, and hydrocortisone.

[00360] Non-limiting examples are shown below.



designation	R^1	R^2	
ZK 216348			amide
Mapracorat			amine
55D1E1			amine

[00361] Where a conditionally active, heterodimeric polypeptide of the present disclosure comprises an LBD of a VDR and a corresponding co-regulator peptide, a suitable dimerization agent can be 1,25-dihydroxyvitamin D3 (calcitriol), paricalitol, doxercalciferol, 25-hydroxyvitamin D3 (calcifediol), cholecalciferol, ergocalciferol, tacalciol, 22-dihydroergocalciferol, (6Z)-Tacalciol, 2-methylene-19-nor-

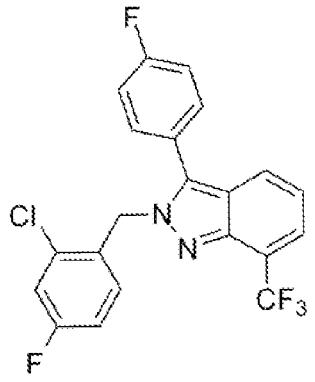
20(S)-1α-hydroxy-bishomopregnacalciferol, 19-nor-26,27-dimethylene-20(S)-2-methylene-1α,25-dihydroxyvitamin D3, 2-methylene-1α,25-dihydroxy-(17E)-17(20)-dehydro-19-nor-vi- tamin D3, 2-methylene-19-nor-(24R)-1α,25-dihydroxyvitamin D2, 2-methylene-(20R,25S)-19,26-dinor-1α,25-dihydroxyvitamin D3, 2-methylene-19-nor-1α-hydroxy-pregnacalciferol, 1α-hydroxy-2-methylene-19-nor-homopregnacalciferol, (20R)-1α-hydroxy-2-methylene-19-nor-bishomopregnacalciferol, 2-methylene-19-nor-(20S)-1α-hydroxy-trishomopregnacalciferol, 2-methylene-23,23-difluoro-1α-hydroxy-19-nor-bishomopregnacalcifero- l, 2-methylene-(20S)-23,23-difluoro-1α-hydroxy-19-nor-bishomopregnan- calciferol, (2-(3' hydroxypropyl-1',2'-idene)-19,23,24-trinor-(20S)-1α-hydroxyvitamin D3, 2-methylene-18,19-dinor-(20S)-1α,25-dihydroxyvitamin D3, and the like.

[00362] Where a conditionally active, heterodimeric polypeptide of the present disclosure comprises an LBD of a RARβ and a corresponding co-regulator peptide, a suitable dimerization agent can be retinoic acid, all-trans-retinoic acid, 9-cis-retinoic acid, tamibarotene, 13-cis-retinoic acid, (2E,4E,6Z,8E)-3,7-dimethyl-9-(2,6,6-trimethyl-1-cyclohexeneyl)nona-2,4,6,- 8-tetraenoic acid, 9-(4-methoxy-2,3,6-trimethyl-phenyl)-3,7-dimethyl-nona-2,4,6,8-tetraenoic acid, 6-[3-(1-adamantyl)-4-methoxyphenyl]-2-napthoic acid, 4-[1-(3,5,5,8,8-pentamethyl-tetralin-2-yl)ethenyl]benzoic acid, retinobenzoic acid, ethyl 6-[2-(4,4-dimethylthiochroman-6-yl)ethynyl]pyridine-3-carboxylate, retinoyl t-butyrate, retinoyl pinacol, and retinoyl cholesterol.

[00363] Where a conditionally active, heterodimeric polypeptide of the present disclosure comprises an LBD of an FXR and a corresponding co-regulator peptide, a suitable dimerization agent includes, but is not limited to, obeticholic acid, LY2562175 (6-(4-((5-cyclopropyl-3-(2,6-dichlorophenyl)isoxazol-4-yl)methoxy)piperidin-1-yl)-1-methyl-1H-indole-3-carboxylic acid), and GW4064 (3-[2-[2-Chloro-4-[[3-(2,6-dichlorophenyl)-5-(1-methylethyl)-4-isoxazolyl]methoxy]phenyl]ethenyl]benzoic acid).

[00364] Where a conditionally active, heterodimeric polypeptide of the present disclosure comprises an LBD of an LXRα and a corresponding co-regulator peptide, a suitable dimerization agent includes, but is not limited to, T0901317 (*N*-(2,2,2-Trifluoroethyl)-*N*-[4-[2,2,2-trifluoro-1-hydroxy-1-(trifluoromethyl)ethyl]phenyl]benzenesulfonamide), GW3965 (3-[3-[[[2-Chloro-3-(trifluoromethyl)phenyl]methyl](2,2-diphenylethyl)amino]propoxy]benzeneacetic acid hydrochloride), and LXR-623.

[00365] LXR-632 has the following structure:

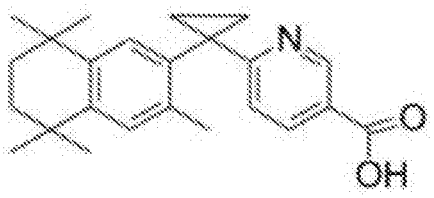


[00366] Where a conditionally active, heterodimeric polypeptide of the present disclosure comprises an LBD of an RORγ and a corresponding co-regulator peptide, a suitable dimerization agent includes, but is not limited to, GNE-3500 (27, 1-{4-[3-fluoro-4-((3S,6R)-3-methyl-1,1-dioxo-6-phenyl-[1,2]thiazinan-2-ylmethyl)-phenyl]-piperazin-1-yl}-ethanone).

[00367] Where a conditionally active, heterodimeric polypeptide of the present disclosure comprises an LBD of an RORγ and a corresponding co-regulator peptide, a suitable dimerization agent includes, but is not limited to, 7β, 27-dihydroxycholesterol, and 7α, 27-dihydroxycholesterol.

[00368] Where a conditionally active, heterodimeric polypeptide of the present disclosure comprises an LBD of an RXRα and a corresponding co-regulator peptide, a suitable dimerization agent includes, but is not limited to, 9-cis retinoic acid, LGD100268, CD3254 (3-[4-Hydroxy-3-(5,6,7,8-tetrahydro-3,5,5,8,8-pentamethyl-2-naphthalenyl)phenyl]-2-propenoic acid), and CD2915 (Sorensen et al. (1997) *Skin Pharmacol.* 10:144).

[00369] LGD100268 has the following structure:



[00370] Where a conditionally active, heterodimeric polypeptide of the present disclosure comprises an LBD of a PXR and a corresponding co-regulator peptide, a suitable dimerization agent can be rifampicin, chlotrimazole, and lovastatin.

CONDITIONALLY ACTIVE OFF-SWITCH CAR

[00371] In some cases, a conditionally active heterodimeric polypeptide of the present disclosure is a conditionally active off-switch CAR. A conditionally active off-switch CAR of the present disclosure is also referred to as a heteromeric, conditionally repressible synthetic immune cell receptor (ICR). A conditionally active off-switch CAR of the present disclosure comprises: a synthetic stimulatory ICR comprising a first member of a dimerization pair linked to the synthetic stimulatory ICR; and a synthetic

ICR repressor comprising a second member of the dimerization pair linked to an intracellular inhibitory domain. A heteromeric, conditionally repressible synthetic ICR of the present disclosure will generally include a synthetic stimulatory ICR and a synthetic ICR repressor configured such that upon introduction of a dimerizing agent, the synthetic ICR repressor dimerizes with the synthetic stimulatory ICR to repress activation due to the synthetic stimulatory ICR. Examples of heterodimeric conditionally active off-switch CAR polypeptides include but are not limited to e.g., those described in PCT International Application No. PCT/US2016/062612; the disclosure of which is incorporated herein by reference in its entirety.

[00372] The configuration of the heteromeric, conditionally repressible synthetic ICR will vary depending on the particular context within which repression of a synthetic stimulatory ICR is desired. In some instances, the stimulatory portion of the heteromeric, conditionally repressible synthetic ICR may be referred to as Part 1 of the heteromeric, conditionally repressible synthetic ICR. In some instances, the repressor portion of the heteromeric, conditionally repressible synthetic ICR may be referred to as Part 2 of the heteromeric, conditionally repressible synthetic ICR. Thus, a heteromeric, conditionally repressible synthetic ICR collectively refers to a multi-modular protein or protein complex that includes various modules including the stimulatory portion (e.g., synthetic stimulatory ICR, Part 1, etc.) and the repressor portion (e.g., synthetic ICR repressor, Part 2, etc.) whether or not the various modules are or are not present or were or were not present at some point within the same protein and whether or not the various modules are expressed from the same or different nucleic acid constructs.

[00373] One of skill in the art will readily recognize from the instant disclosure that first and second parts (e.g., stimulatory and inhibitory parts) will individually include first and second portions of a dimerizing pair and that such portions of the dimerizing pair may be interchangeable between the first and second parts of the heteromeric, conditionally repressible synthetic ICR. One of skill in the art will also readily recognize from the instant disclosure that individual domains of heteromeric, conditionally repressible synthetic ICR may be rearranged in many instances, in order and/or orientation, while maintaining the functions of being activatable and repressible as described herein. As such, description of a particular configuration of a heteromeric, conditionally repressible synthetic ICR described herein also includes wherein the modules of the heteromeric, conditionally repressible synthetic ICR are rearranged without abolishing the primary functions of the heteromeric, conditionally repressible synthetic ICR. Such rearrangements may also include the inclusion or exclusion of particular optional modules (including e.g., linkers, reporters, etc.) that do not result in abolishment of the primary functions of the heteromeric, conditionally repressible synthetic ICR due to their inclusion or exclusion from the heteromeric, conditionally repressible synthetic ICR.

Synthetic Stimulatory ICR

[00374] As described herein, a heteromeric, conditionally repressible synthetic ICR includes a synthetic stimulatory ICR, also referred to herein as a "stimulatory ICR" or "stimulatory part" for simplicity. Such stimulatory ICRs will vary depending on the particular context of immune cell stimulation to which the construct is directed and will generally function to mediate activation of the immune cell expressing the stimulatory ICR. Thus, a stimulatory ICR includes an extracellular domain that upon reception of a specific signal functions to transduce the signal to intracellularly to activate the immune cell expressing the stimulatory ICR.

[00375] In some instances, the extracellular component of a stimulatory ICR therefore may include an extracellular recognition domain, described in more detail below, which contains one member of a specific binding pair. Specific binding pairs include, but are not limited to, antigen-antibody binding pairs; ligand-receptor binding pairs; and the like. Thus, a member of a specific binding pair suitable for use in an extracellular recognition domain of the present disclosure includes an antigen; an antibody; a ligand; and a ligand-binding receptor. Suitable extracellular recognition domains for use in a stimulatory ICR include but are not limited to e.g., members of specific binding pairs (e.g., antigen-binding domain containing members of specific binding pairs) including e.g., those described above with relationship to conditionally acitive heterodimeric On-switch CARs above.

[00376] A stimulatory ICR further includes one or more intracellular stimulation domains that, upon activation of one or more extracellular domains, mediates intracellular signaling leading to activation of the immune cell expressing the stimulatory ICR. Domains useful as signaling domains will vary depending on the particular context of immune cell activation, including e.g., the particular type of cell to be activated and the desired degree of activation. Exemplary non-limited examples of stimulatory domains, described in greater detail below, include but are not limited to domains and motifs thereof derived from immune stimulatory molecules including, e.g., co-stimulatory molecules, immune receptors and the like. Suitable intracellular stimulation domains for use in a stimulatory ICR include but are not limited to e.g., modulatory domains and portions thereof including e.g., those described above with relationship to conditionally acitive heterodimeric On-switch CARs above.

[00377] In some instances, stimulatory ICRs may be or may be derived from engineered or synthetic immune regulatory constructs designed for therapeutic immune system modulation including but not limited to e.g., chimeric antigen receptors (CARs) and derivatives, engineered T cell receptors (TCRs) and derivatives and the like. Engineered CARs, TCRs and derivatives thereof useful as the basis for a synthetic ICR include those CARs, TCRs and derivatives thereof that are activatable, e.g., are activated upon binding of a binding partner to the CAR, TCR or derivative thereof, and upon activation transduce the signal intracellularly to activate the immune cell expressing the CAR, TCR or derivative thereof. In some instances, a stimulatory ICR may be conditionally activatable such that activation upon binding of

a binding partner to the stimulatory ICR requires an additional event for transduction of the activation signal including e.g., dimerization of components of the stimulatory ICR.

[00378] A stimulatory ICR further includes, as described in more detail below, a domain (e.g., a first member or a second member) of a dimerization pair. Useful dimerization pairs will vary depending on the desired dimerizer and the desired relative position of the member of the dimerization pair within the stimulatory ICR. Generally, the presence of a first member of a dimerization pair within the stimulatory ICR mediates the dimerization, upon introduction of the dimerizer, with a second member of the dimerization pair present in the ICR repressor such that upon dimerization the ICR repressor represses any immune cell activation due to the stimulatory ICR.

[00379] In some instances, a stimulatory ICR may further include additional domains. Such additional domains may be functional, e.g., they directly contribute to the immune cell activation function of the stimulatory ICR, or non-functional, e.g., they do not directly contribute to the activation function of the stimulatory ICR. Non-functional additional domains may include domains having various purposes that do not directly affect the ability of the stimulatory ICR to activate immune cell function including, but not limited to, e.g., structural functions, linker functions, etc.

Chimeric Antigen Receptor (CAR)

[00380] In some instances, a heteromeric, conditionally repressible synthetic ICR may include, in part or in whole, a CAR or may essentially be a modified CAR such that by modification the CAR is conditionally repressible. In such instances, the CAR containing heteromeric, conditionally repressible synthetic ICR may be referred to as a heterodimeric, conditionally repressible synthetic CAR or, for simplicity, a repressible CAR. Any CAR having immune cell activation function may find use in a heteromeric, conditionally repressible synthetic ICR as described herein including but not limited to, e.g., those CAR variants described herein.

[00381] In some instances, a CAR may be modified for use as a component of a heterodimeric, conditionally repressible synthetic ICR through introduction or insertion of a dimerization domain (e.g., a member of a dimerization pair) into the CAR and, in such instances, following modification, the CAR may be referred to as a dimerizer-domain containing CAR or a dimerizable CAR.

[00382] A dimerizer domain may be inserted into the CAR amino acid sequence, e.g., by introducing a coding sequence for the dimerizer domain into the coding sequence of the CAR, at any convenient location provided the insertion does not negatively impact the primary functional domains of the CAR (including e.g., the extracellular recognition domain, the immune activation domain(s), etc.) and/or the negatively impact the dimerization function of the dimerizer domain.

[00383] In some instances, the dimerizer may be inserted into an extracellular portion of the CAR. In some instances the dimerizer may be inserted into an intracellular portion of the CAR. In some instances, the

dimerizer may be inserted such that following insertion the dimerizer is linked to an extracellular recognition domain of the CAR. In some instances, the dimerizer may be inserted such that following insertion the dimerizer is linked to a transmembrane domain of the CAR. In some instances, the dimerizer may be inserted such that following insertion the dimerizer is linked to the extracellular side of a transmembrane domain of the CAR. In some instances, the dimerizer may be inserted such that following insertion the dimerizer is linked to the intracellular side of a transmembrane domain of the CAR. In some instances, the dimerizer may be inserted such that following insertion the dimerizer is linked to an immune stimulatory domain of the CAR. In some instances, the dimerizer may be inserted such that following insertion the dimerizer is linked to a co-stimulation domain of the CAR. In some instances, the dimerizer may be inserted such that following insertion the dimerizer is at the N-terminal end of the CAR. In some instances, the dimerizer may be inserted such that following insertion the dimerizer is at the C-terminal end of the CAR.

[00384] In instances where a heteromeric, conditionally repressible synthetic ICR includes, in part or in whole, or the heteromeric, conditionally repressible synthetic ICR is essentially a modified CAR, the CAR may contain an extracellular recognition domain, a stimulatory domain and a transmembrane domain. Such a CAR may optionally include linker regions and/or hinge regions. CARs as part of a heteromeric, conditionally repressible synthetic ICR may be encompassed within a single polypeptide or may be "split" across two or more polypeptides.

Extracellular Recognition Domain

[00385] A repressible CAR includes a member of a specific binding pair. Specific binding pairs include, but are not limited to, antigen-antibody binding pairs; ligand-receptor binding pairs; and the like. Thus, a member of a specific binding pair suitable for use in a repressible CAR of the present disclosure includes an antigen; an antibody; a ligand; and a ligand-binding receptor.

Antigen binding domain

[00386] An antigen-binding domain suitable for use in a repressible CAR of the present disclosure can be any antigen-binding polypeptide, a wide variety of which are known in the art. In some instances, the antigen-binding domain is a single chain Fv (scFv). Other antibody based recognition domains (cAb VHH (camelid antibody variable domains) and humanized versions, IgNAR VH (shark antibody variable domains) and humanized versions, sdAb VH (single domain antibody variable domains) and "camelized" antibody variable domains are suitable for use. In some instances, T-cell receptor (TCR) based recognition domains such as single chain TCR (scTv, single chain two-domain TCR containing VαVβ) are also suitable for use. Such TCR recognition domains when present as a repressible engineered TCR rather than a component of a repressible CAR as described in more detail below.

[00387] An antigen-binding domain suitable for use in a repressible CAR of the present disclosure can have a variety of antigen-binding specificities. In some cases, the antigen-binding domain is specific for an

epitope present in an antigen that is expressed by (synthesized by) a cancer cell, i.e., a cancer cell associated antigen. The cancer cell associated antigen can be an antigen associated with, e.g., a breast cancer cell, a B cell lymphoma, a Hodgkin lymphoma cell, an ovarian cancer cell, a prostate cancer cell, a mesothelioma, a lung cancer cell (e.g., a small cell lung cancer cell), a non-Hodgkin B-cell lymphoma (B-NHL) cell, an ovarian cancer cell, a prostate cancer cell, a mesothelioma cell, a lung cancer cell (e.g., a small cell lung cancer cell), a melanoma cell, a chronic lymphocytic leukemia cell, an acute lymphocytic leukemia cell, a neuroblastoma cell, a glioma, a glioblastoma, a medulloblastoma, a colorectal cancer cell, etc. A cancer cell associated antigen may also be expressed by a non-cancerous cell.

[00388] Non-limiting examples of antigens to which an antigen-binding domain of a subject repressible CAR can bind include, e.g., CD19, CD20, CD38, CD30, Her2/neu/ERBB2, CA125, MUC-1, prostate-specific membrane antigen (PSMA), CD44 surface adhesion molecule, mesothelin, carcinoembryonic antigen (CEA), epidermal growth factor receptor (EGFR), EGFRvIII, vascular endothelial growth factor receptor-2 (VEGFR2), high molecular weight-melanoma associated antigen (HMW-MAA), MAGE-A1, IL-13R-a2, GD2, and the like. Further examples of antigens to which an antigen-binding domain of a subject repressible CAR can bind include but are not limited to those described above with relevance to conditionally active on-switch CARs.

Ligand

[00389] In some cases, a member of a specific binding pair suitable for use in a subject repressible CAR is a ligand for a receptor. Ligands include, but are not limited to, cytokines (e.g., IL-13, etc.); growth factors (e.g., heregulin; vascular endothelial growth factor (VEGF); and the like); an integrin-binding peptide (e.g., a peptide comprising the sequence Arg-Gly-Asp); and the like.

[00390] Where the member of a specific binding pair in a subject repressible CAR is a ligand, the repressible CAR can be activated in the presence of both a dimerizer agent and a second member of the specific binding pair, where the second member of the specific binding pair is a receptor for the ligand. For example, where the ligand is VEGF, the second member of the specific binding pair can be a VEGF receptor, including a soluble VEGF receptor. As another example, where the ligand is heregulin, the second member of the specific binding pair can be Her2.

Receptors

[00391] As noted above, in some cases, the member of a specific binding pair that is included in a subject repressible CAR is a receptor, e.g., a receptor for a ligand, a co-receptor, etc. The receptor can be a ligand-binding fragment of a receptor. Suitable receptors include, but are not limited to, a growth factor receptor (e.g., a VEGF receptor); a killer cell lectin-like receptor subfamily K, member 1 (NKG2D) polypeptide (receptor for MICA, MICB, and ULB6); a cytokine receptor (e.g., an IL-13 receptor; an IL-2

receptor; etc.); Her2; CD27; a natural cytotoxicity receptor (NCR) (e.g., NKP30 (NCR3/CD337) polypeptide (receptor for HLA-B–associated transcript 3 (BAT3) and B7-H6); etc.); etc.

Stimulatory Domain

[00392] A stimulatory domain suitable for use in a stimulatory CAR of a subject repressible ICR may be any functional unit of a polypeptide as short as a 3 amino acid linear motif and as long as an entire protein, where size of the stimulatory domain is restricted only in that the domain must be sufficiently large as to retain its function and sufficiently small so as to be compatible with the other components of the repressible CAR. Accordingly, a stimulatory domain may range in size from 3 amino acids in length to 1000 amino acids or more and, in some instances, can have a length of from about 30 amino acids to about 70 amino acids (aa), e.g., a stimulatory domain can have a length of from about 30 aa to about 35 aa, from about 35 aa to about 40 aa, from about 40 aa to about 45 aa, from about 45 aa to about 50 aa, from about 50 aa to about 55 aa, from about 55 aa to about 60 aa, from about 60 aa to about 65 aa, or from about 65 aa to about 70 aa. In other cases, stimulatory domain can have a length of from about 70 aa to about 100 aa, from about 100 aa to about 200 aa, or greater than 200 aa.

[00393] In some instances, "co-stimulatory domains" find use as stimulatory domains of a repressible CAR of the present disclosure. Co-stimulation generally refers to a secondary non-specific activation mechanism through which a primary specific stimulation is propagated. Examples of co-stimulation include antigen nonspecific T cell co-stimulation following antigen specific signaling through the T cell receptor and antigen nonspecific B cell co-stimulation following signaling through the B cell receptor. Co-stimulation, e.g., T cell co-stimulation, and the factors involved have been described in Chen & Flies. *Nat Rev Immunol* (2013) 13(4):227-42, the disclosure of which are incorporated herein by reference in their entirety. Co-stimulatory domains are generally polypeptides derived from receptors. In some embodiments, co-stimulatory domains homodimerize. A subject co-stimulatory domain can be an intracellular portion of a transmembrane protein (i.e., the co-stimulatory domain can be derived from a transmembrane protein). Non-limiting examples of suitable co-stimulatory polypeptides include, but are not limited to, 4-1BB (CD137), CD28, ICOS, OX-40, BTLA, CD27, CD30, GITR, and HVEM. In some instances, a co-stimulatory domain, e.g., as used in repressible CAR of the instant disclosure may include a co-stimulatory domain listed in **Table 1**. In some instances, a co-stimulatory domain of a repressible CAR comprises a an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100% amino acid sequence identity to a co-stimulatory domain as described herein.

[00394] In some instances, a stimulatory CAR may contain an intracellular signaling domain, e.g., a co-stimulatory domain, derived from an intracellular portion of a transmembrane protein listed in **Table 1**. For example, a suitable co-stimulatory domain can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about

98%, or 100% amino acid sequence identity to an amino acid sequence listed in **Table 1**. In some of these embodiments, the co-stimulatory domain has a length of from about 30 aa to about 35 aa, from about 35 aa to about 40 aa, from about 40 aa to about 45 aa, from about 45 aa to about 50 aa, from about 50 aa to about 55 aa, from about 55 aa to about 60 aa, from about 60 aa to about 65 aa, or from about 65 aa to about 70 aa, from about 70 aa to about 75 aa, from about 75 aa to about 80 aa, from about 80 aa to about 85 aa, from about 85 aa to about 90 aa, from about 90 aa to about 95 aa, from about 95 aa to about 100 aa, from about 100 aa to about 105 aa, from about 105 aa to about 110 aa, from about 110 aa to about 115 aa, from about 115 aa to about 120 aa, from about 120 aa to about 125 aa, from about 125 aa to about 130 aa, from about 130 aa to about 135 aa, from about 135 aa to about 140 aa, from about 140 aa to about 145 aa, from about 145 aa to about 150 aa, from about 150 aa to about 155 aa, from about 155 aa to about 160 aa, from about 160 aa to about 165, aa from about 165 aa to about 170 aa, from about 170 aa to about 175 aa, from about 175 aa to about 180 aa, from about 180 aa to about 185 aa, or from about 185 aa to about 190 aa.

[00395] In some cases, a repressible CAR may contain two more stimulatory domains, present on the same or different polypeptides. In some instances, where the repressible CAR contains two more stimulatory domains, the stimulatory domains may have substantially the same amino acid sequences. For example, in some cases, the first stimulatory domain comprises an amino acid sequence that is at least about 90%, at least about 95%, at least about 98%, at least about 99%, or 100%, identical to the amino acid sequence of the second stimulatory domain. In some instances, where the repressible CAR contains two more stimulatory domains, the stimulatory domains of the subject repressible CAR can have substantially the same length; e.g., the first and second stimulatory domains can differ in length from one another by fewer than 10 amino acids, or fewer than 5 amino acids. In some instances, where the repressible CAR contains two more stimulatory domains, the first and second stimulatory domains have the same length. In some instances, where the repressible CAR contains two more stimulatory domains, the two stimulatory domains are the same.

[00396] In some instances, a repressible CAR may contain an intracellular signaling domain, e.g., a co-stimulatory domain, derived from an intracellular portion of the transmembrane protein 4-1BB (also known as TNFRSF9; CD137; 4-1BB; CDw137; ILA; etc.). For example, a suitable co-stimulatory domain can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100% amino acid sequence identity to the following amino acid sequence: KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCEL (SEQ ID NO:618). In some of these embodiments, the co-stimulatory domain has a length of from about 30 aa to about 35 aa, from about 35 aa to about 40 aa, from about 40 aa to about 45 aa, from about 45 aa to about 50 aa, from about 50 aa to

about 55 aa, from about 55 aa to about 60 aa, from about 60 aa to about 65 aa, or from about 65 aa to about 70 aa.

[00397] In some instances, a repressible CAR may contain an intracellular signaling domain, e.g., a co-stimulatory domain, derived from an intracellular portion of the transmembrane protein CD28 (also known as Tp44). For example, a suitable co-stimulatory domain can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100% amino acid sequence identity to the following amino acid sequence: FWVRSKRSRLLHSDYMNMTPRRPGPTRKHYQPYAPPRDFAAYRS (SEQ ID NO:619). In some of these embodiments, the co-stimulatory domain has a length of from about 30 aa to about 35 aa, from about 35 aa to about 40 aa, from about 40 aa to about 45 aa, from about 45 aa to about 50 aa, from about 50 aa to about 55 aa, from about 55 aa to about 60 aa, from about 60 aa to about 65 aa, or from about 65 aa to about 70 aa.

[00398] In some instances, a repressible CAR may contain an intracellular signaling domain, e.g., a co-stimulatory domain, derived from an intracellular portion of the transmembrane protein ICOS (also known as AILIM, CD278, and CVID1). For example, a suitable co-stimulatory domain can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100% amino acid sequence identity to the following amino acid sequence: TKKKYSSSVHDPNGEYMFMRAVNTAKKSRLTDVTL (SEQ ID NO:620). In some of these embodiments, the co-stimulatory domain has a length of from about 30 aa to about 35 aa, from about 35 aa to about 40 aa, from about 40 aa to about 45 aa, from about 45 aa to about 50 aa, from about 50 aa to about 55 aa, from about 55 aa to about 60 aa, from about 60 aa to about 65 aa, or from about 65 aa to about 70 aa.

[00399] In some instances, a repressible CAR may contain an intracellular signaling domain, e.g., a co-stimulatory domain, derived from an intracellular portion of the transmembrane protein OX-40 (also known as TNFRSF4, RP5-902P8.3, ACT35, CD134, OX40, TXGP1L). For example, a suitable co-stimulatory domain can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100% amino acid sequence identity to the following amino acid sequence: RRDQRLPPDAHKPPGGGSFRTPIQEEQADAHSTLAKI (SEQ ID NO:621). In some of these embodiments, the co-stimulatory domain has a length of from about 30 aa to about 35 aa, from about 35 aa to about 40 aa, from about 40 aa to about 45 aa, from about 45 aa to about 50 aa, from about 50 aa to about 55 aa, from about 55 aa to about 60 aa, from about 60 aa to about 65 aa, or from about 65 aa to about 70 aa.

[00400] In some instances, a repressible CAR may contain an intracellular signaling domain, e.g., a co-stimulatory domain, derived from an intracellular portion of the transmembrane protein BTLA (also

known as BTLA1 and CD272). For example, a suitable co-stimulatory domain can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100% amino acid sequence identity to the following amino acid sequence:
CCLRRHQGKQNELSDTAGREINLVDAHLKSEQTEASTRQNSQVLLSETGIYDNDPDLCFRMQEG
SEVYSNPCLEENKPGIVYASLNHSVIGPNSRLARNVKEAPTEYASICVRS (SEQ ID NO:622).

[00401] In some instances, a repressible CAR may contain an intracellular signaling domain, e.g., a co-stimulatory domain, derived from an intracellular portion of the transmembrane protein CD27 (also known as S152, T14, TNFRSF7, and Tp55). For example, a suitable co-stimulatory domain can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100% amino acid sequence identity to the following amino acid sequence:
HQRRKYRSNKGESPVEPAEPCRYSCPREEEGSTIPIQEDYRKPEPACSP (SEQ ID NO:623). In some of these embodiments, the co-stimulatory domain has a length of from about 30 aa to about 35 aa, from about 35 aa to about 40 aa, from about 40 aa to about 45 aa, from about 45 aa to about 50 aa, from about 50 aa to about 55 aa, from about 55 aa to about 60 aa, from about 60 aa to about 65 aa, or from about 65 aa to about 70 aa.

[00402] In some instances, a repressible CAR may contain an intracellular signaling domain, e.g., a co-stimulatory domain, derived from an intracellular portion of the transmembrane protein CD30 (also known as TNFRSF8, D1S166E, and Ki-1). For example, a suitable co-stimulatory domain can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100% amino acid sequence identity to a contiguous stretch of from about 100 amino acids to about 110 amino acids (aa), from about 110 aa to about 115 aa, from about 115 aa to about 120 aa, from about 120 aa to about 130 aa, from about 130 aa to about 140 aa, from about 140 aa to about 150 aa, from about 150 aa to about 160 aa, or from about 160 aa to about 185 aa of the following amino acid sequence:
RRACRKRIRQKLHLCYPVQTSQPKLELVDSRPRRSSTQLRSGASVTEPVAEERGLMSQPLMETC
HSVGAAYLESLPLQDASPAGGPSSPRDLPEPRVSTEHTNNKIEKIYIMKADTVIVGTVKAELPEG
RGLAGPAEPELEEELEADHTPHYPEQETEPPLGSCSDVMLSVEEEGKEDPLPTAASGK (SEQ ID NO:624).

[00403] In some instances, a repressible CAR may contain an intracellular signaling domain, e.g., a co-stimulatory domain, derived from an intracellular portion of the transmembrane protein GITR (also known as TNFRSF18, RP5-902P8.2, AITR, CD357, and GITR-D). For example, a suitable co-stimulatory domain can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100% amino acid

sequence identity to the following amino acid sequence: HIWQLRSQCMWPRETQLLLEVPPSTEDARSCQFPEEERGERSAEEKGRLGDLWV (SEQ ID NO:625). In some of these embodiments, the co-stimulatory domain has a length of from about 30 aa to about 35 aa, from about 35 aa to about 40 aa, from about 40 aa to about 45 aa, from about 45 aa to about 50 aa, from about 50 aa to about 55 aa, from about 55 aa to about 60 aa, from about 60 aa to about 65 aa, or from about 65 aa to about 70 aa.

[00404] In some instances, a repressible CAR may contain an intracellular signaling domain, e.g., a co-stimulatory domain, derived from an intracellular portion of the transmembrane protein HVEM (also known as TNFRSF14, RP3-395M20.6, ATAR, CD270, HVEA, HVEM, LIGHTR, and TR2). For example, a suitable co-stimulatory domain can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100% amino acid sequence identity to the following amino acid sequence: CVKRRKPRGDVVKVIVSVQRKRQEAEGEATVIEALQAPPDVTTVAVEETIPSFTGRSPNH (SEQ ID NO:626). In some of these embodiments, the co-stimulatory domain has a length of from about 30 aa to about 35 aa, from about 35 aa to about 40 aa, from about 40 aa to about 45 aa, from about 45 aa to about 50 aa, from about 50 aa to about 55 aa, from about 55 aa to about 60 aa, from about 60 aa to about 65 aa, or from about 65 aa to about 70 aa.

[00405] In some instances, a repressible CAR may contain an intracellular signaling domain that includes at least one (e.g., one, two, three, four, five, six, etc.) intracellular signaling motif. In some instances, the intracellular signaling motif may be an immunoreceptor tyrosine-based activation motif (ITAM). In some instances, the intracellular signaling motif, e.g., an ITAM motif is within an intracellular signaling domain derived from a signaling molecule that contains one or more ITAM motifs. In other instances, the ITAM is derived, e.g., synthetically produced, within an amino acid sequence de novo, e.g., through mutation of the amino acid sequence.

[00406] An ITAM motif is YX_1X_2L/I, where X_1 and X_2 are independently any amino acid (SEQ ID NO:564). In some cases, the intracellular signaling domain of a subject repressible CAR comprises 1, 2, 3, 4, or 5 ITAM motifs. In some cases, an ITAM motif is repeated twice in an intracellular signaling domain, where the first and second instances of the ITAM motif are separated from one another by 6 to 8 amino acids, e.g., $(YX_1X_2L/I)(X_3)_n(YX_1X_2L/I)$, where n is an integer from 6 to 8, and each of the 6-8 X_3 can be any amino acid (SEQ ID NO:565). In some cases, the intracellular signaling domain of a subject repressible CAR comprises 3 ITAM motifs.

[00407] A suitable intracellular signaling domain can be an ITAM motif-containing portion that is derived from a polypeptide that contains an ITAM motif. For example, a suitable intracellular signaling domain can be an ITAM motif-containing domain from any ITAM motif-containing protein. Thus, a suitable intracellular signaling domain need not contain the entire sequence of the entire protein from which it is

derived. Examples of suitable ITAM motif-containing polypeptides include, but are not limited to: DAP12; FCER1G (Fc epsilon receptor I gamma chain); CD3D (CD3 delta); CD3E (CD3 epsilon); CD3G (CD3 gamma); CD3Z (CD3 zeta); and CD79A (antigen receptor complex-associated protein alpha chain).

[00408] In some cases, the intracellular signaling domain is derived from DAP12 (also known as TYROBP; TYRO protein tyrosine kinase binding protein; KARAP; PLOSL; DNAX-activation protein 12; KAR-associated protein; TYRO protein tyrosine kinase-binding protein; killer activating receptor associated protein; killer-activating receptor-associated protein; etc.). For example, a suitable intracellular signaling domain can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100%, amino acid sequence identity to any of the following amino acid sequences (4 isoforms): MGGLEPCSRLLLLPLLLAVSGLRPVQAQAQSDCSCSTVSPGVLAGIVMGDLVLTVLIALAVYFL GRLVPRGRGAAEAATRKQRITETESP**YQEL**QGQRSDV**YSDL**NTQRPYYK (SEQ ID NO:627); MGGLEPCSRLLLLPLLLAVSGLRPVQAQAQSDCSCSTVSPGVLAGIVMGDLVLTVLIALAVYFL GRLVPRGRGAAEATRKQRITETESP**YQEL**QGQRSDV**YSDL**NTQRPYYK (SEQ ID NO:628); MGGLEPCSRLLLLPLLLAVSDCSCSTVSPGVLAGIVMGDLVLTVLIALAVYFLGRLVPRGRGAA EAATRKQRITETESP**YQEL**QGQRSDV**YSDL**NTQRPYYK (SEQ ID NO:629); or MGGLEPCSRLLLLPLLLAVSDCSCSTVSPGVLAGIVMGDLVLTVLIALAVYFLGRLVPRGRGAA EATRKQRITETESP**YQEL**QGQRSDV**YSDL**NTQRPYYK (SEQ ID NO:630), where the ITAM motifs are in bold and are underlined.

[00409] Likewise, a suitable intracellular signaling domain can comprise an ITAM motif-containing portion of the full length DAP12 amino acid sequence. Thus, a suitable intracellular signaling domain can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100%, amino acid sequence identity to the following amino acid sequence: ESP**YQEL**QGQRSDV**YSDL**NTQ (SEQ ID NO:631), where the ITAM motifs are in bold and are underlined.

[00410] In some cases, the intracellular signaling domain is derived from FCER1G (also known as FCRG; Fc epsilon receptor I gamma chain; Fc receptor gamma-chain; fc-epsilon RI-gamma; fcRgamma; fceRI gamma; high affinity immunoglobulin epsilon receptor subunit gamma; immunoglobulin E receptor, high affinity, gamma chain; etc.). For example, a suitable intracellular signaling domain can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100% amino acid sequence identity to the following amino acid sequence: MIPAVVLLLLLLVEQAAALGEPQLCYILDAILFLYGIVLTLLYCRLKIQVRKAAITSYEKSDGV**YT**

GLSTRNQET**YETL**KHEKPPQ (SEQ ID NO:632), where the ITAM motifs are in bold and are underlined.

[00411] Likewise, a suitable intracellular signaling domain can comprise an ITAM motif-containing portion of the full length FCER1G amino acid sequence. Thus, a suitable intracellular signaling domain can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100%, amino acid sequence identity to the following amino acid sequence: DGV**YTGL**STRNQET**YETL**KHE (SEQ ID NO:633), where the ITAM motifs are in bold and are underlined.

[00412] In some cases, the intracellular signaling domain is derived from T-cell surface glycoprotein CD3 delta chain (also known as CD3D; CD3-DELTA; T3D; CD3 antigen, delta subunit; CD3 delta; CD3d antigen, delta polypeptide (TiT3 complex); OKT3, delta chain; T-cell receptor T3 delta chain; T-cell surface glycoprotein CD3 delta chain; etc.). For example, a suitable intracellular signaling domain can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100%, amino acid sequence identity to a contiguous stretch of from about 100 amino acids to about 110 amino acids (aa), from about 110 aa to about 115 aa, from about 115 aa to about 120 aa, from about 120 aa to about 130 aa, from about 130 aa to about 140 aa, from about 140 aa to about 150 aa, or from about 150 aa to about 170 aa, of either of the following amino acid sequences (2 isoforms):
MEHSTFLSGLVLATLLSQVSPFKIPIEELEDRVFVNCNTSITWVEGTVGTLLSDITRLDLGKRILDP
RGIYRCNGTDIYKDKESTVQVHYRMCQSCVELDPATVAGIIVTDVIATLLLALGVFCFAGHETG
RLSGAADTQALLRNDQV**YQPL**RDRDDAQ**YSHL**GGNWARNK (SEQ ID NO:634) or
MEHSTFLSGLVLATLLSQVSPFKIPIEELEDRVFVNCNTSITWVEGTVGTLLSDITRLDLGKRILDP
RGIYRCNGTDIYKDKESTVQVHYRTADTQALLRNDQV**YQPL**RDRDDAQ**YSHL**GGNWARNK
(SEQ ID NO:635) , where the ITAM motifs are in bold and are underlined.

[00413] Likewise, a suitable intracellular signaling domain can comprise an ITAM motif-containing portion of the full length CD3 delta amino acid sequence. Thus, a suitable intracellular signaling domain can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100%, amino acid sequence identity to the following amino acid sequence: DQV**YQPL**RDRDDAQ**YSHL**GGN (SEQ ID NO:636), where the ITAM motifs are in bold and are underlined.

[00414] In some cases, the intracellular signaling domain is derived from T-cell surface glycoprotein CD3 epsilon chain (also known as CD3e, T-cell surface antigen T3/Leu-4 epsilon chain, T-cell surface glycoprotein CD3 epsilon chain, AI504783, CD3, CD3epsilon, T3e, etc.). For example, a suitable intracellular signaling domain can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100%,

amino acid sequence identity to a contiguous stretch of from about 100 amino acids to about 110 amino acids (aa), from about 110 aa to about 115 aa, from about 115 aa to about 120 aa, from about 120 aa to about 130 aa, from about 130 aa to about 140 aa, from about 140 aa to about 150 aa, or from about 150 aa to about 205 aa, of the following amino acid sequence:

[00415] MQSGTHWRVLGLCLLSVGVWGQDGNEEMGGITQTPYKVSISGTTVILTCPQYPGSEILWQH NDKNIGGDEDDKNIGSDEDHLSLKEFSELEQSGYYVCYPRGSKPEDANFYLYLRARVCENCME MDVMSVATIVIVDICITGGLLLLVYYWSKNRKAKAKPVTRGAGAGGRQRGQNKERPPPVPNPD **YEPI**RKGQRDL**YSGL**NQRRI (SEQ ID NO:637), where the ITAM motifs are in bold and are underlined.

[00416] Likewise, a suitable intracellular signaling domain can comprise an ITAM motif-containing portion of the full length CD3 epsilon amino acid sequence. Thus, a suitable intracellular signaling domain can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100%, amino acid sequence identity to the following amino acid sequence: NPD**YEPI**RKGQRDL**YSGL**NQR (SEQ ID NO:638), where the ITAM motifs are in bold and are underlined.

[00417] In some cases, the intracellular signaling domain is derived from T-cell surface glycoprotein CD3 gamma chain (also known as CD3G, T-cell receptor T3 gamma chain, CD3-GAMMA, T3G, gamma polypeptide (TiT3 complex), etc.). For example, a suitable intracellular signaling domain can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100%, amino acid sequence identity to a contiguous stretch of from about 100 amino acids to about 110 amino acids (aa), from about 110 aa to about 115 aa, from about 115 aa to about 120 aa, from about 120 aa to about 130 aa, from about 130 aa to about 140 aa, from about 140 aa to about 150 aa, or from about 150 aa to about 180 aa, of the following amino acid sequence:

MEQGKGLAVLILAIILLQGTLAQSIKGNHLVKVYDYQEDGSVLLTCDAEAKNITWFKDGKMIGF LTEDKKKWNLGSNAKDPRGMYQCKGSQNKSKPLQVYYRMCQNCIELNAATISGFLFAEIVSIFV LAVGVYFIAGQDGVRQSRASDKQTLLPNDQL**YQPL**KDREDDQ**YSHL**QGNQLRRN (SEQ ID NO:639), where the ITAM motifs are in bold and are underlined.

[00418] Likewise, a suitable intracellular signaling domain can comprise an ITAM motif-containing portion of the full length CD3 gamma amino acid sequence. Thus, a suitable intracellular signaling domain can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100%, amino acid sequence identity to the following amino acid sequence: DQL**YQPL**KDREDDQ**YSHL**QGN (SEQ ID NO:640), where the ITAM motifs are in bold and are underlined.

[00419] In some cases, the intracellular signaling domain is derived from T-cell surface glycoprotein CD3 zeta chain (also known as CD3Z, T-cell receptor T3 zeta chain, CD247, CD3-ZETA, CD3H, CD3Q, T3Z, TCRZ, etc.). For example, a suitable intracellular signaling domain can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100%, amino acid sequence identity to a contiguous stretch of from about 100 amino acids to about 110 amino acids (aa), from about 110 aa to about 115 aa, from about 115 aa to about 120 aa, from about 120 aa to about 130 aa, from about 130 aa to about 140 aa, from about 140 aa to about 150 aa, or from about 150 aa to about 160 aa, of either of the following amino acid sequences (2 isoforms):
MKWKALFTAAILQAQLPITEAQSFGLLDPKLCYLLDGILFIYGVILTALFLRVKFSRSADAPAYQ QGQNQL**YNEL**NLGRREE**YDVL**DKRRGRDPEMGGKPRRKNPQEGL**YNEL**QKDKMAEA**YSEI**G MKGERRRGKGHDGL**YQGL**STATKDT**YDAL**HMQALPPR (SEQ ID NO:641) or
MKWKALFTAAILQAQLPITEAQSFGLLDPKLCYLLDGILFIYGVILTALFLRVKFSRSADAPAYQ QGQNQL**YNEL**NLGRREE**YDVL**DKRRGRDPEMGGKPQRRKNPQEGL**YNEL**QKDKMAEA**YSEI** GMKGERRRGKGHDGL**YQGL**STATKDT**YDAL**HMQALPPR(SEQ ID NO:642) , where the ITAM motifs are in bold and are underlined.

[00420] Likewise, a suitable intracellular signaling domain can comprise an ITAM motif-containing portion of the full length CD3 zeta amino acid sequence. Thus, a suitable intracellular signaling domain can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100%, amino acid sequence identity to any of the following amino acid sequences:
RVKFSRSADAPAYQQGQNQL**YNEL**NLGRREE**YDVL**DKRRGRDPEMGGKPRRKNPQEGL**YNE L**QKDKMAEA**YSEI**GMKGERRRGKGHDGL**YQGL**STATKDT**YDAL**HMQALPPR (SEQ ID NO:643); NQL**YNEL**NLGRREE**YDVL**DKR (SEQ ID NO:644); EGL**YNEL**QKDKMAEA**YSEI**GMK (SEQ ID NO:645); or DGL**YQGL**STATKDT**YDAL**HMQ (SEQ ID NO:646), where the ITAM motifs are in bold and are underlined.

[00421] In some cases, the intracellular signaling domain is derived from CD79A (also known as B-cell antigen receptor complex-associated protein alpha chain; CD79a antigen (immunoglobulin-associated alpha); MB-1 membrane glycoprotein; ig-alpha; membrane-bound immunoglobulin-associated protein; surface IgM-associated protein; etc.). For example, a suitable intracellular signaling domain can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100%, amino acid sequence identity to a contiguous stretch of from about 100 amino acids to about 110 amino acids (aa), from about 110 aa to about 115 aa, from about 115 aa to about 120 aa, from about 120 aa to about 130 aa, from about 130 aa to about 150 aa, from about 150 aa to about 200 aa, or from about 200 aa to about 220 aa, of either of the

following amino acid sequences (2 isoforms):
MPGGPGVLQALPATIFLLFLLSAVYLGPGCQALWMHKVPASLMVSLGEDAHFQCPHNSSNNAN
VTWWRVLHGNYTWPPEFLGPGEDPNGTLIIQNVNKSHGGIYVCRVQEGNESYQQSCGTYLRVR
QPPPRPFLDMGEGTKNRIITAEGIILLFCAVVPGTLLLFRKRWQNEKLGLDAGDEYEDENL**YEGL**
NLDDCSM**YEDI**SRGLQGTYQDVGSLNIGDVQLEKP (SEQ ID NO:647); or
MPGGPGVLQALPATIFLLFLLSAVYLGPGCQALWMHKVPASLMVSLGEDAHFQCPHNSSNNAN
VTWWRVLHGNYTWPPEFLGPGEDPNEPPPRPFLDMGEGTKNRIITAEGIILLFCAVVPGTLLLFR
KRWQNEKLGLDAGDEYEDENLYEGLNLDDCSMYEDISRGLQGTYQDVGSLNIGDVQLEKP
(SEQ ID NO:648) , where the ITAM motifs are in bold and are underlined.

[00422] Likewise, a suitable intracellular signaling domain can comprise an ITAM motif-containing portion of the full length CD79A amino acid sequence. Thus, a suitable intracellular signaling domain can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100%, amino acid sequence identity to the following amino acid sequence: ENL**YEGL**NLDDCSM**YEDI**SRG (SEQ ID NO:649), where the ITAM motifs are in bold and are underlined.

[00423] In some instances, a repressible CAR may contain an intracellular signaling domain derived from a DAP10/CD28 type signaling chain. Intracellular signaling domains suitable for use in a repressible CAR of the present disclosure include a DAP10/CD28 type signaling chain.

[00424] An example of a DAP10 signaling chain is the amino acid sequence is: RPRRSPAQDGKV**YINM**PGRG (SEQ ID NO:650). In some embodiments, a suitable intracellular signaling domain comprises an amino acid sequence having at least about 85%, at least about 90%, at least about 95%, at least about 98%, or at least about 99%, amino acid sequence identity to the entire length of the amino acid sequence RPRRSPAQDGKV**YINM**PGRG (SEQ ID NO:651).

[00425] An example of a CD28 signaling chain is the amino acid sequence is FWVLVVVGGVLACYSLLVTVAFIIFWVRSKRSRLLHSD**YMNM**TPRRPGPTRKHYQPYAPPRDF AAYRS (SEQ ID NO:652). In some embodiments, a suitable intracellular signaling domain comprises an amino acid sequence having at least about 85%, at least about 90%, at least about 95%, at least about 98%, or at least about 99%, amino acid sequence identity to the entire length of the amino acid sequence FWVLVVVGGVLACYSLLVTVAFIIFWVRSKRSRLLHSD**YMNM**TPRRPGPTRKHYQPYAPPRDF AAYRS (SEQ ID NO:653).

[00426] Intracellular signaling domains suitable for use in a CAR of the present disclosure include a ZAP70 polypeptide, e.g., a polypeptide comprising an amino acid sequence having at least about 85%, at least about 90%, at least about 95%, at least about 98%, at least about 99%, or 100%, amino acid sequence identity to a contiguous stretch of from about 300 amino acids to about 400 amino acids, from about 400

amino acids to about 500 amino acids, or from about 500 amino acids to 619 amino acids, of the following amino acid sequence:

MPDPAAHLPFFYGSISRAEAEEHLKLAGMADGLFLLRQCLRSLGGYVLSLVHDVRFHHFPIERQ LNGTYAIAGGKAHCGPAELCEFYSRDPDGLPCNLRKPCNRPSGLEPQPGVFDCLRDAMVRDYV RQTWKLEGEALEQAIISQAPQVEKLIATTAHERMPWYHSSLTREEAERKLYSGAQTDGKFLLRP RKEQGTYALSLIYGKTVYHYLISQDKAGKYCIPEGTKFDTLWQLVEYLKLKADGLIYCLKEACP NSSASNASGAAAPTLPAHPSTLTHPQRRIDTLNSDGYTPEPARITSPDKPRPMPMDTSVYESPYSD PEELKDKKLFLKRDNLLIADIELGCGNFGSVRQGVYRMRKKQIDVAIKVLKQGTEKADTEEMM REAQIMHQLDNPYIVRLIGVCQAEALMLVMEMAGGGPLHKFLVGKREEIPVSNVAELLHQVSM GMKYLEEKNFVHRDLAARNVLLVNRHYAKISDFGLSKALGADDSYYTARSAGKWPLKWYAP ECINFRKFSSRSDVWSYGVTMWEALSYGQKPYKKMKGPEVMAFIEQGKRMECPPECPPELYAL MSDCWIYKWEDRPDFLTVEQRMRACYYSLASKVEGPPGSTQKAEAACA (SEQ ID NO:654).

Transmembrane Domain

[00427] Any transmembrane (TM) domain that provides for insertion of a polypeptide into the cell membrane of a eukaryotic (e.g., mammalian) cell is suitable for use. As one non-limiting example, the TM sequence IYIWAPLAGTCGVLLLSLVITLYC (SEQ ID NO:655) can be used. Additional non-limiting examples of suitable TM sequences include: a) CD8 beta derived : LGLLVAGVLVLLVSLGVAIHLCC (SEQ ID NO:656); b) CD4 derived: ALIVLGGVAGLLLFIGLGIFFCVRC (SEQ ID NO:657); c) CD3 zeta derived: LCYLLDGILFIYGVILTALFLRV (SEQ ID NO:658); d) CD28 derived: WVLVVVGGVLACYSLLVTVAFIIFWV (SEQ ID NO:659); e) CD134 (OX40) derived: VAAILGLGLVLGLLGPLAILLALYLL (SEQ ID NO:660); and f) CD7 derived: ALPAALAVISFLLGLGLGVACVLA (SEQ ID NO:661).

Linkers

[00428] In some cases, a subject repressible CAR includes a linker between any two adjacent domains. For example, a linker can be disposed between the transmembrane domain and the first intracellular functional domain, e.g., a co-stimulatory domain, of the repressible CAR. As another example, a linker can be disposed between a first intracellular functional domain and the member of the dimerization domain of the repressible CAR. As another example, a linker can be disposed between the member of the dimerization domain and a second intracellular functional domain, e.g., an immune cell activation domain. As another example, a linker can be disposed between any domain of the repressible CAR and any additional domain including e.g., a domain not involved in the primary immune activation functions of the CAR including but not limited to e.g., a reporter domain, a tag domain, etc.

[00429] Linkers may be utilized in a suitable configuration in the repressible CAR provided they do not abolish the primary activities of the repressible CAR including, e.g., the ability of the repressible CAR to

become activated upon extracellular binding, the ability of the dimerization domain of the repressible CAR to bind the dimerization domain of the ICR repressor.

[00430] A linker peptide may have any of a variety of amino acid sequences. Proteins can be joined by a spacer peptide, generally of a flexible nature, although other chemical linkages are not excluded. A linker can be a peptide of between about 6 and about 40 amino acids in length, or between about 6 and about 25 amino acids in length. These linkers can be produced by using synthetic, linker-encoding oligonucleotides to couple the proteins. Peptide linkers with a degree of flexibility can be used. The linking peptides may have virtually any amino acid sequence, bearing in mind that suitable linkers will have a sequence that results in a generally flexible peptide. The use of small amino acids, such as glycine and alanine, are of use in creating a flexible peptide. The creation of such sequences is routine to those of skill in the art.

[00431] Suitable linkers can be readily selected and can be of any of a suitable of different lengths, such as from 1 amino acid (e.g., Gly) to 20 amino acids, from 2 amino acids to 15 amino acids, from 3 amino acids to 12 amino acids, including 4 amino acids to 10 amino acids, 5 amino acids to 9 amino acids, 6 amino acids to 8 amino acids, or 7 amino acids to 8 amino acids, and may be 1, 2, 3, 4, 5, 6, or 7 amino acids.

[00432] Exemplary flexible linkers include glycine polymers $(G)_n$, glycine-serine polymers (including, for example, $(GS)_n$, $GSGGS_n$ (SEQ ID NO:516) and $GGGS_n$ (SEQ ID NO:517), where n is an integer of at least one), glycine-alanine polymers, alanine-serine polymers, and other flexible linkers known in the art. Glycine and glycine-serine polymers are of interest since both of these amino acids are relatively unstructured, and therefore may serve as a neutral tether between components. Glycine polymers are of particular interest since glycine accesses significantly more phi-psi space than even alanine, and is much less restricted than residues with longer side chains (see Scheraga, *Rev. Computational Chem.* 11173-142 (1992)). Exemplary flexible linkers include, but are not limited GGSG (SEQ ID NO:518), GGSGG (SEQ ID NO:519), GSGSG (SEQ ID NO:520), GSGGG (SEQ ID NO:521), GGGSG (SEQ ID NO:522), GSSSG (SEQ ID NO:523), and the like. The ordinarily skilled artisan will recognize that design of a peptide conjugated to any elements described above can include linkers that are all or partially flexible, such that the linker can include a flexible linker as well as one or more portions that confer less flexible structure.

Hinge Regions

[00433] In some cases, the first polypeptide of a subject repressible CAR comprises a hinge region (also referred to herein as a "spacer"), where the hinge region is interposed between the antigen-binding domain and the transmembrane domain. In some cases, the hinge region is an immunoglobulin heavy chain hinge region. In some cases, the hinge region is a hinge region polypeptide derived from a receptor (e.g., a CD8-derived hinge region).

[00434] The hinge region can have a length of from about 4 amino acids to about 50 amino acids, e.g., from about 4 aa to about 10 aa, from about 10 aa to about 15 aa, from about 15 aa to about 20 aa, from about 20 aa to about 25 aa, from about 25 aa to about 30 aa, from about 30 aa to about 40 aa, or from about 40 aa to about 50 aa.

[00435] Suitable spacers can be readily selected and can be of any of a number of suitable lengths, such as from 1 amino acid (e.g., Gly) to 20 amino acids, from 2 amino acids to 15 amino acids, from 3 amino acids to 12 amino acids, including 4 amino acids to 10 amino acids, 5 amino acids to 9 amino acids, 6 amino acids to 8 amino acids, or 7 amino acids to 8 amino acids, and can be 1, 2, 3, 4, 5, 6, or 7 amino acids.

[00436] Exemplary spacers include glycine polymers $(G)_n$, glycine-serine polymers (including, for example, $(GS)_n$, $(GSGGS)_n$ (SEQ ID NO:516) and $(GGGS)_n$ (SEQ ID NO:517), where n is an integer of at least one), glycine-alanine polymers, alanine-serine polymers, and other flexible linkers known in the art. Glycine and glycine-serine polymers can be used; both Gly and Ser are relatively unstructured, and therefore can serve as a neutral tether between components. Glycine polymers can be used; glycine accesses significantly more phi-psi space than even alanine, and is much less restricted than residues with longer side chains (see Scheraga, *Rev. Computational Chem.* 11173-142 (1992)). Exemplary spacers can comprise amino acid sequences including, but not limited to, GGSG (SEQ ID NO:518), GGSGG (SEQ ID NO:519), GSGSG (SEQ ID NO:520), GSGGG (SEQ ID NO:521), GGGSG (SEQ ID NO:522), GSSSG (SEQ ID NO:523), and the like.

[00437] In some cases, e.g., when the stimulatory ICR portion of a repressible CAR is split between two or more polypeptides the repressible CAR may include a hinge region that includes at least one cysteine. For example, in some cases, the hinge region can include the sequence Cys-Pro-Pro-Cys. If present, a cysteine in the hinge region of a first polypeptide, e.g., a first portion of a repressible CAR, can be available to form a disulfide bond with a hinge region in a second polypeptide, e.g., a second portion of a repressible CAR.

[00438] Immunoglobulin hinge region amino acid sequences are known in the art; see, e.g., Tan et al. (1990) *Proc. Natl. Acad. Sci. USA* 87:162; and Huck et al. (1986) *Nucl. Acids Res.* 14:1779. As non-limiting examples, an immunoglobulin hinge region can include one of the following amino acid sequences: DKTHT (SEQ ID NO:524); CPPC (SEQ ID NO:525); CPEPKSCDTPPPCPR (SEQ ID NO:526) (see, e.g., Glaser et al. (2005) *J. Biol. Chem.* 280:41494); ELKTPLGDTTHT (SEQ ID NO:527); KSCDKTHTCP (SEQ ID NO:528); KCCVDCP (SEQ ID NO:529); KYGPPCP (SEQ ID NO:530); EPKSCDKTHTCPPCP (SEQ ID NO:531) (human IgG1 hinge); ERKCCVECPPCP (SEQ ID NO:532) (human IgG2 hinge); ELKTPLGDTTHTCPRCP (SEQ ID NO:533) (human IgG3 hinge); SPNMVPHAHHAQ (SEQ ID NO:534) (human IgG4 hinge); and the like.

[00439] The hinge region can comprise an amino acid sequence of a human IgG1, IgG2, IgG3, or IgG4, hinge region. The hinge region can include one or more amino acid substitutions and/or insertions and/or deletions compared to a wild-type (naturally-occurring) hinge region. For example, His_{229} of human IgG1 hinge can be substituted with Tyr, so that the hinge region comprises the sequence EPKSCDKTYTCPPCP (SEQ ID NO:535); see, e.g., Yan et al. (2012) *J. Biol. Chem.* 287:5891.

[00440] The hinge region can comprise an amino acid sequence derived from human CD8; e.g., the hinge region can comprise the amino acid sequence: TTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACD (SEQ ID NO:536), or a variant thereof.

Dimerization domain

[00441] As noted above, heterodimeric, conditionally repressible synthetic immune cell receptor (ICR) of the present disclosure comprises a first member of a dimerization pair, and a second member of a dimerization pair. One of the members of the dimerization pair will comprise an LBD of a nuclear hormone receptor; the other member of the dimerization pair will comprise a co-regulator peptide of the same nuclear hormone receptor. In the presence of a dimerization agent (e.g., a nuclear hormone, or a functional derivative or analog of the nuclear hormone), the members of the dimerization pair will bind to one another, and will effect dimerization of the two polypeptide chains of the conditionally repressible synthetic ICR of the present disclosure. A first member of a dimerization pair, or a second member of a dimerization pair, can also be referred to as a "dimerization domain."

Ligand-binding domain (LBD)

[00442] A ligand-binding domain of a nuclear hormone receptor can be from any of a variety of nuclear hormone receptors, including, but not limited to, ERα, ERβ, PR, AR, GR, MR, RARα, RARβ, RARγ, TRα, TRβ, VDR, EcR, RXRα, RXRβ, RXRγ, PPARα, PPARβ, PPARγ, LXRα, LXRβ, FXR, PXR, SXR, CAR, SF-1, LRH-1, DAX-1, SHP, TLX, PNR, NGF1-Bα, NGF1-Bβ, NGF1-Bγ, RORα, RORβ, RORγ, ERRα, ERRβ, ERRγ, GCNF, TR2/4, HNF-4, COUP-TFα, COUP-TFβ and COUP-TFγ.

[00443] Abbreviations for nuclear hormone receptors are as follows. ER: Estrogen Receptor; PR: Progesterone Receptor; AR: Androgen Receptor; GR: Glucocorticoid Receptor; MR: Mineralocorticoid Receptor; RAR: Retinoic Acid Receptor; TRα, β: Thyroid Receptor; VDR: Vitamin D3 Receptor; EcR: Ecdysone Receptor; RXR: Retinoic Acid X Receptor; PPAR: Peroxisome Proliferator Activated Receptor; LXR: Liver X Receptor; FXR: Farnesoid X Receptor; PXR/SXR: Pregnane X Receptor/Steroid and Xenobiotic Receptor; CAR: Constitutive Adrostrane Receptor; SF-1: Steroidogenic Factor 1; DAX-1: Dosage sensitive sex reversal-adrenal hypoplasia congenital critical region on the X chromosome, gene 1; LRH-1: Liver Receptor Homolog 1; SHP: Small Heterodimer Partner; TLX: Tail-less Gene; PNR: Photoreceptor-Specific Nuclear Receptor; NGF1-B: Nerve Growth Factor; ROR: RAR

related orphan receptor; ERR: Estrogen Related Receptor; GCNF: Germ Cell Nuclear Factor; TR2/4: Testicular Receptor; HNF-4: Hepatocyte Nuclear Factor; COUP-TF: Chicken Ovalbumin Upstream Promoter, Transcription Factor.

[00444] In some cases, a polypeptide chain of a heterodimeric polypeptide of the present disclosure comprises a single LBD of a nuclear hormone receptor. In some cases, a polypeptide chain of a heterodimeric polypeptide of the present disclosure comprises multiple (two or more) LBD of a nuclear hormone receptor. In some cases, a polypeptide chain of a heterodimeric polypeptide of the present disclosure comprises two LBD of a nuclear hormone receptor. In some cases, a polypeptide chain of a heterodimeric polypeptide of the present disclosure comprises three LBD of a nuclear hormone receptor. Where a polypeptide chain of a heterodimeric polypeptide of the present disclosure comprises multiple (two or more) LBD of a nuclear hormone receptor, in some cases the multiple LBD comprise identical amino acid sequences. In some cases, the two or more LBD are in tandem, either directly or separated by a linker.

Mineralocorticoid receptor

[00445] In some cases, an LBD suitable for inclusion as a member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a mineralocorticoid receptor (MR). For example, in some cases, the LBD comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the LBD of an MR having the amino acid sequence depicted in FIG. 1A.

[00446] As one non-limiting example, the LBD of a MR can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to an amino acid sequence depicted in FIG. 1F; and has a length of from about 200 amino acids to 250 amino acids (e.g., has a length of from 200 amino acids to 225 amino acids, or from 225 amino acids to 250 amino acids; e.g., has a length of 248 amino acids).

[00447] As one non-limiting example, the LBD of a MR can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 1B; and has a length of from about 250 amino acids to 299 amino acids (e.g., has a length of from 250 amino acids to 275 amino acids, or from 275 amino acids to 299 amino acids).

[00448] As one non-limiting example, the LBD of a MR can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 1C; and has a length of from about 200 amino acids to 250 amino acids (e.g., has a length of from 200 amino acids to 225 amino acids, or from 225 amino acids to 250 amino acids; e.g., has a length of 248 amino acids).

[00449] As another non-limiting example, the LBD of a MR can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 1D, and has an S810L substitution (where the amino acid numbering is based on the amino acid sequence depicted in FIG. 1A); and has a length of from about 250 amino acids to 299 amino acids (e.g., has a length of from 250 amino acids to 275 amino acids, or from 275 amino acids to 299 amino acids).

[00450] As one non-limiting example, the LBD of a MR can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 1C, and has an S810L substitution (where the amino acid numbering is based on the amino acid sequence depicted in FIG. 1A); and has a length of from about 200 amino acids to 250 amino acids (e.g., has a length of from 200 amino acids to 225 amino acids, or from 225 amino acids to 250 amino acids; e.g., has a length of 248 amino acids).

[00451] In some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of an MR, the second member of the dimerization pair is a co-regulator peptide comprising the amino acid sequence SLTARHKILHRLLQEGSPSDI (SEQ ID NO:2), where the co-regulator peptide has a length of from about 21 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from 21 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids). In some cases, where the second member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of an MR, the first member of the dimerization pair is a co-regulator peptide comprising the amino acid sequence SLTARHKILHRLLQEGSPSDI (SEQ ID NO:2), where the co-regulator peptide has a length of from about 21 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from 21 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids).

[00452] In some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of an MR, the second member of the dimerization pair is a co-regulator peptide comprising the amino acid sequence QEAEEPSLLKKLLLAPANTQL (SEQ ID NO:6), where the co-regulator peptide has a length of from about 21 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from 21 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids). In some cases, where the second member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the

present disclosure is an LBD of an MR, the first member of the dimerization pair is a co-regulator peptide comprising the amino acid sequence QEAEEPSLLKKLLLAPANTQL (SEQ ID NO:6), where the co-regulator peptide has a length of from about 21 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from 21 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids).

[00453] In some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of an MR, the second member of the dimerization pair is a co-regulator peptide comprising the amino acid sequence SKVSQNPILTSLLQITGNGGS (SEQ ID NO:7), where the co-regulator peptide has a length of from about 21 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from 21 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids). In some cases, where the second member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of an MR, the first member of the dimerization pair is a co-regulator peptide comprising the amino acid sequence SKVSQNPILTSLLQITGNGGS (SEQ ID NO:7), where the co-regulator peptide has a length of from about 21 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from 21 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids).

Androgen receptor

[00454] In some cases, an LBD suitable for inclusion as a member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of an androgen receptor (AR). For example, in some cases, the LBD comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the LBD of an AR having the amino acid sequence depicted in FIG. 2A.

[00455] As one non-limiting example, the LBD of an AR can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 2B; and has a length of from about 250 amino acids to 301 amino acids (e.g., has a length of from 250 amino acids to 275 amino acids, or from 275 amino acids to 301 amino acids).

[00456] As one non-limiting example, the LBD of an AR can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 2C; and has a length of from

about 190 amino acids to 230 amino acids (e.g., has a length of from 190 amino acids to 210 amino acids, or from 210 amino acids to 230 amino acids).

[00457] As one non-limiting example, the LBD of an AR can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 2B, and has a T877A substitution (where the amino acid numbering is based on the amino acid sequence depicted in FIG. 2A); and has a length of from about 250 amino acids to 301 amino acids (e.g., has a length of from 250 amino acids to 275 amino acids, or from 275 amino acids to 301 amino acids).

[00458] As one non-limiting example, the LBD of an AR can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 2C, and has a T877A substitution (where the amino acid numbering is based on the amino acid sequence depicted in FIG. 2A); and has a length of from about 190 amino acids to 230 amino acids (e.g., has a length of from 190 amino acids to 210 amino acids, or from 210 amino acids to 230 amino acids).

[00459] As one non-limiting example, the LBD of an AR can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 2B, and has an F876L substitution (where the amino acid numbering is based on the amino acid sequence depicted in FIG. 2A); and has a length of from about 250 amino acids to 301 amino acids (e.g., has a length of from 250 amino acids to 275 amino acids, or from 275 amino acids to 301 amino acids).

[00460] As one non-limiting example, the LBD of an AR can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 2C, and has an F876L substitution (where the amino acid numbering is based on the amino acid sequence depicted in FIG. 2A); and has a length of from about 190 amino acids to 230 amino acids (e.g., has a length of from 190 amino acids to 210 amino acids, or from 210 amino acids to 230 amino acids).

[00461] As one non-limiting example, the LBD of an AR can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 2B, and has a T877A and an F876L substitution (where the amino acid numbering is based on the amino acid sequence depicted in FIG. 2A); and has a length of from about 250 amino acids to 301 amino acids (e.g., has a length of from 250 amino acids to 275 amino acids, or from 275 amino acids to 301 amino acids).

[00462] As one non-limiting example, the LBD of an AR can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%,

amino acid sequence identity to the amino acid sequence depicted in FIG. 2C, and has a T877A and an F876L substitution (where the amino acid numbering is based on the amino acid sequence depicted in FIG. 2A); and has a length of from about 190 amino acids to 230 amino acids (e.g., has a length of from 190 amino acids to 210 amino acids, or from 210 amino acids to 230 amino acids).

[00463] In some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of an AR, the second member of the dimerization pair is a co-regulator peptide comprising the amino acid sequence ESKGHKKLLQLLTCSSDDR (SEQ ID NO:3), where the co-regulator peptide has a length of from about 19 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from 19 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids). In some cases, where the second member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of an AR, the first member of the dimerization pair is a co-regulator peptide comprising the amino acid sequence ESKGHKKLLQLLTCSSDDR (SEQ ID NO:3), where the co-regulator peptide has a length of from about 19 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from 19 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids).

Progesterone receptor

[00464] In some cases, an LBD suitable for inclusion as a member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a progesterone receptor (PR). For example, in some cases, the LBD comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the LBD of a PR having the amino acid sequence depicted in FIG. 3A.

[00465] As one non-limiting example, the LBD of a PR can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to an amino acid sequence depicted in FIG. 3D; and has a length of from about 200 amino acids to 250 amino acids (e.g., has a length of from 200 amino acids to 225 amino acids, or from 225 amino acids to 250 amino acids; e.g., has a length of 248 amino acids).

[00466] As one non-limiting example, the LBD of a PR can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 3B; and has a length of from about 200 amino acids to 256 amino acids (e.g., has a length of from 200 amino acids to 225 amino acids, or from 225 amino acids to 256 amino acids; e.g., has a length of 256 amino acids).

[00467] As one non-limiting example, the LBD of a PR can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 3C; and has a length of from about 200 amino acids to 250 amino acids (e.g., has a length of from 200 amino acids to 225 amino acids, or from 225 amino acids to 250 amino acids; e.g., has a length of 248 amino acids).

[00468] In some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a PR, the second member of the dimerization pair is a co-regulator peptide comprising the amino acid sequence GHSFADPASNLGLEDIIRKALMGSF (SEQ ID NO:8), where the co-regulator peptide has a length of from about 25 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids). In some cases, where the second member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a PR, the first member of the dimerization pair is a co-regulator peptide comprising the amino acid sequence GHSFADPASNLGLEDIIRKALMGSF (SEQ ID NO:8), where the co-regulator peptide has a length of from about 25 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids).

Thyroid hormone receptor-β

[00469] In some cases, an LBD suitable for inclusion as a member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of thyroid hormone receptor-beta (TRβ). For example, in some cases, the LBD comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the LBD of a TRβ having the amino acid sequence depicted in FIG. 4A.

[00470] As one non-limiting example, the LBD of a TRβ can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to one of the amino acid sequences depicted in FIG. 4D; and has a length of from about 200 amino acids to 250 amino acids (e.g., has a length of from 200 amino acids to 225 amino acids, from 225 amino acids to 230 amino acids, from 230 amino acids to 240 amino acids, or from 240 amino acids to 250 amino acids).

[00471] As one non-limiting example, the LBD of a TRβ can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 4B; and has a length of from

about 200 amino acids to 260 amino acids (e.g., has a length of from 200 amino acids to 225 amino acids, or from 225 amino acids to 260 amino acids; e.g., has a length of 260 amino acids).

[00472] As one non-limiting example, the LBD of a TRβ can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 4B; and has a length of from about 200 amino acids to 246 amino acids (e.g., has a length of from 200 amino acids to 225 amino acids, or from 225 amino acids to 246 amino acids; e.g., has a length of 246 amino acids).

[00473] In some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a TRβ, the second member of the dimerization pair is an NCOA3/SRC3 polypeptide. For example, in some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a TRβ, the second member of the dimerization pair is a co-regulator peptide comprises the amino acid sequence CSSDDRGHSSLTNSPLDSSCKESSVSVTSPSGVSSSTSGGVSSTSNMHGSLLQEKHRILHKLLQNG NSPAEVAKITAEATGKDTSSITSCGDGNVVKQEQLSPKKKENNALLRYLLDRDDPSDALSKELQ PQVEGVDNKMSQCTSSTIPSSSQEKDPKIKTETSEEGSGDLDNLDAILGDLTSSDFYNNSISSNGS HLGTKQQ (SEQ ID NO:662). In other cases, where the second member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a TRβ, the first member of the dimerization pair is an NCOA3/SRC3 polypeptide.

[00474] In some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a TRβ, the second member of the dimerization pair is an NCOA2/SRC2 polypeptide. For example, in some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a TRβ, the second member of the dimerization pair is a co-regulator peptide comprises the amino acid sequence STAPGSEVTIKQEPVSPKKKENALLRYLLDKDDTKDIGLPEITPKLERLDSKTDPASNTKLIAMKT EKEEMSFEPGDQPGSELDNLEEILDDLQNSQLPQLFPDTRPGAPAGSVDKQAIINDLMQLTAENS PVTPVGAQKTALRISQSTFNNPRPGQLGRLLPNQNLPLDITLQSPTGAGPFPPIRNSSPYSVIPQPG MMGNQGMIGNQGNLGNSSTGMIGNSASRPTMPSGEWAPQSSAVRVTCAATTSAMNRPVQGG MIRNPAASIPMRPSSQPGQRQTLQSQVMNIGPSELEMNMGGP (SEQ ID NO:663). In some cases, where the second member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a TRβ, the first member of the dimerization pair is an NCOA2/SRC2 polypeptide.

Estrogen receptor-alpha

[00475] In some cases, an LBD suitable for inclusion as a member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of estrogen receptor-alpha (ERα). For example, in some cases, the LBD comprises an amino acid sequence having at least 75%, at least

80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the LBD of an ERα having the amino acid sequence depicted in FIG. 5A.

[00476] As one non-limiting example, the LBD of an ERα can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to an amino acid sequence depicted in FIG. 5H; and has a length of from about 200 amino acids to 240 amino acids (e.g., has a length of from 200 amino acids to 225 amino acids, from 225 amino acids to 230 amino acids, from 230 amino acids to 235 amino acids, or from 235 amino acids to 240 amino acids).

[00477] As one non-limiting example, the LBD of an ERα can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 5B; and has a length of from about 180 amino acids to 229 amino acids (e.g., has a length of from 180 amino acids to 200 amino acids, or from 200 amino acids to 229 amino acids; e.g., has a length of 229 amino acids).

[00478] As one non-limiting example, the LBD of an ERα can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 5C; and has a length of from about 250 amino acids to 314 amino acids (e.g., has a length of from 250 amino acids to 275 amino acids, from 275 amino acids to 300 amino acids, or from 300 amino acids to 314 amino acids; e.g., has a length of 314 amino acids).

[00479] As one non-limiting example, the LBD of an ERα can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 5D; and has a length of from about 190 amino acids to 238 amino acids (e.g., has a length of from 190 amino acids to 220 amino acids, or from 220 amino acids to 238 amino acids; e.g., has a length of 238 amino acids).

[00480] As one non-limiting example, the LBD of an ERα can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 5E, and has a D351Y substitution (where the amino acid numbering is based on the amino acid sequence depicted in FIG. 5A); and has a length of from about 180 amino acids to 229 amino acids (e.g., has a length of from 180 amino acids to 200 amino acids, or from 200 amino acids to 229 amino acids; e.g., has a length of 229 amino acids).

[00481] As one non-limiting example, the LBD of an ERα can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 5F, and has a D351Y

substitution (where the amino acid numbering is based on the amino acid sequence depicted in FIG. 5A); and has a length of from about 250 amino acids to 314 amino acids (e.g., has a length of from 250 amino acids to 275 amino acids, from 275 amino acids to 300 amino acids, or from 300 amino acids to 314 amino acids; e.g., has a length of 314 amino acids).

[00482] As one non-limiting example, the LBD of an ERα can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 5G, and has a D351Y substitution (where the amino acid numbering is based on the amino acid sequence depicted in FIG. 5A); and has a length of from about 190 amino acids to 238 amino acids (e.g., has a length of from 190 amino acids to 220 amino acids, or from 220 amino acids to 238 amino acids; e.g., has a length of 238 amino acids).

[00483] In some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of an ERα, the second member of the dimerization pair is a co-regulator peptide comprising the amino acid sequence DAFQLRQLILRGLQDD (SEQ ID NO:12), where the co-regulator peptide has a length of from about 16 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from 16 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids). In some cases, where the second member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of an ERα, the first member of the dimerization pair is a co-regulator peptide comprising the amino acid sequence DAFQLRQLILRGLQDD (SEQ ID NO:12), where the co-regulator peptide has a length of from about from about 16 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from 16 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids).

[00484] In some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of an ERα, the second member of the dimerization pair is a co-regulator peptide comprising the amino acid sequence SPGSREWFKDMLS (SEQ ID NO:13), where the co-regulator peptide has a length of from about 13 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from 13 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids). In some cases, where the second member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD

of an ERα, the first member of the dimerization pair is a co-regulator peptide comprising the amino acid sequence SPGSREWFKDMLS (SEQ ID NO:13), where the co-regulator peptide has a length of from about from about 13 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from 13 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids).

Estrogen receptor-beta (ERβ)

[00485] In some cases, an LBD suitable for inclusion as a member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of estrogen receptor-alpha (ERβ). For example, in some cases, the LBD comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the LBD of an ERβ having the amino acid sequence depicted in FIG. 6A.

[00486] As one non-limiting example, the LBD of an ERβ can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to an amino acid sequence depicted in FIG. 6C; and has a length of from about 200 amino acids to 243 amino acids (e.g., has a length of from 200 amino acids to 225 amino acids, from 225 amino acids to 230 amino acids, from 230 amino acids to 235 amino acids, or from 235 amino acids to 243 amino acids).

[00487] As one non-limiting example, the LBD of an ERβ can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 6B; and has a length of from about 200 amino acids to 243 amino acids (e.g., has a length of from 200 amino acids to 225 amino acids, from 225 amino acids to 230 amino acids, from 230 amino acids to 235 amino acids, or from 235 amino acids to 243 amino acids).

[00488] In some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of an ERβ, the second member of the dimerization pair is a co-regulator peptide comprising the amino acid sequence PRQGSILYSMLTSAKQT (SEQ ID NO:9), where the co-regulator peptide has a length of from about 17 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from 17 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids). In some cases, where the second member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of an ERβ, the first member of the dimerization pair is a co-regulator peptide comprising the amino acid sequence

PRQGSILYSMLTSAKQT (SEQ ID NO:9), where the co-regulator peptide has a length of from about from about 17 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from 17 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids).

Peroxisome proliferator-activated receptor-gamma

[00489] In some cases, an LBD suitable for inclusion as a member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of peroxisome proliferator-activated receptor-gamma (PPAR-γ). For example, in some cases, the LBD comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the LBD of a PPAR-γ having the amino acid sequence depicted in FIG. 7A.

[00490] As one non-limiting example, the LBD of a PPAR-γ can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to one of the amino acid sequences depicted in FIG. 7E; and has a length of from about 200 amino acids to 269 amino acids (e.g., has a length of from 200 amino acids to 225 amino acids, from 225 amino acids to 250 amino acids, or from 250 amino acids to 269 amino acids).

[00491] As one non-limiting example, the LBD of a PPAR-γ can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 7B; and has a length of from about 150 amino acids to 202 amino acids (e.g., has a length of from 150 amino acids to 160 amino acids, from 160 amino acids to 170 amino acids, from 170 amino acids to 190 amino acids, or from 190 amino acids to 202 amino acids).

[00492] As one non-limiting example, the LBD of a PPAR-γ can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 7C; and has a length of from about 200 amino acids to 269 amino acids (e.g., has a length of from 200 amino acids to 225 amino acids, from 225 amino acids to 250 amino acids, or from 250 amino acids to 269 amino acids).

[00493] As one non-limiting example, the LBD of a PPAR-γ can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 7D; and has a length of from about 200 amino acids to 269 amino acids (e.g., has a length of from 200 amino acids to 225 amino acids, from 225 amino acids to 250 amino acids, or from 250 amino acids to 271 amino acids).

[00494] In some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a PPAR-γ, the second member of the dimerization pair is a co-regulator peptide comprising the amino acid sequence CPSSHSSLTERHKILHRLLQEGSPS (SEQ ID NO:1), where the co-regulator peptide has a length of from about 25 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from 25 amino acids to 28 amino acids, from 28 amino acids to 29 amino acids, from 29 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids). In some cases, where the second member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a PPAR-γ, the first member of the dimerization pair is a co-regulator peptide comprising the amino acid sequence CPSSHSSLTERHKILHRLLQEGSPS (SEQ ID NO:1), where the co-regulator peptide has a length of from about from about 17 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from about 25 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from 25 amino acids to 28 amino acids, from 28 amino acids to 29 amino acids, from 29 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids).

[00495] In some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a PPAR-γ, the second member of the dimerization pair is a co-regulator peptide comprising the amino acid sequence PKKENNALLRYLLDRDDPSDV (SEQ ID NO:4), where the co-regulator peptide has a length of from about 21 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from 21 amino acids to 23 amino acids, from 23 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids). In some cases, where the second member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a PPAR-γ, the first member of the dimerization pair is a co-regulator peptide comprising the amino acid sequence PKKENNALLRYLLDRDDPSDV (SEQ ID NO:4), where the co-regulator peptide has a length of from about from about 17 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from about 21 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from 21 amino acids to 23 amino acids, from 23 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids).

[00496] In some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a PPAR-γ, the second member of the dimerization pair is a co-regulator peptide comprising the amino acid sequence PKKKENALLRYLLDKDDTKDI

(SEQ ID NO:11), where the co-regulator peptide has a length of from about 21 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from 21 amino acids to 23 amino acids, from 23 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids). In some cases, where the second member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a PPAR-γ, the first member of the dimerization pair is a co-regulator peptide comprising the amino acid sequence PKKKENALLRYLLDKDDTKDI (SEQ ID NO:11), where the co-regulator peptide has a length of from about from about 21 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from about 21 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from 21 amino acids to 23 amino acids, from 23 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids).

Glucocorticoid receptor

[00497] In some cases, an LBD suitable for inclusion as a member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of glucocorticoid receptor (GR). For example, in some cases, the LBD comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the LBD of a GR having the amino acid sequence depicted in FIG. 8A.

[00498] As one non-limiting example, the LBD of a GR can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to one of the amino acid sequences depicted in FIG. 8C; and has a length of from about 200 amino acids to 247 amino acids (e.g., has a length of from 200 amino acids to 225 amino acids, from 225 amino acids to 230 amino acids, from 230 amino acids to 240 amino acids, or from 240 amino acids to 247 amino acids).

[00499] As one non-limiting example, the LBD of a GR can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 8B; and has a length of from about 200 amino acids to 247 amino acids (e.g., has a length of from 200 amino acids to 225 amino acids, or from 225 amino acids to 247 amino acids; e.g., has a length of 247 amino acids).

[00500] In some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a GR, the second member of the dimerization pair is an NCOA1/SRC1 polypeptide. For example, in some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a GR, the second member of the dimerization pair is an NCOA1/SRC1 polypeptide comprising the amino acid

sequence
NYGTNPGTPPASTSPFSQLAANPEASLANRNSMVSRGMTGNIGGQFGTGINPQMQQNVFQYPG
AGMVPQGEANFAPSLSPGSSMVPMPIPPPQSSLLQQTPPASGYQSPDMKAWQQGAIGNNNVFSQ
AVQNQPTPAQPGVYNNMSITVSMAGGNTNVQNMNPMMAQMQMSSLQMPGMNTVCPEQIND
PALRHTGLYCNQLSSTDLLKTEADGTQQVQQVQVFADVQCTVNLVGGDPYLNQPGPLGTQKP
TSGPQTPQAQQKSLLQQLLTE (SEQ ID NO:664) or a fragment thereof. In some cases, where the second member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a GR, the first member of the dimerization pair is an NCOA1/SRC1 polypeptide.

[00501] In some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a GR, the second member of the dimerization pair is an NCOA2/SRC2 polypeptide. For example, in some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a GR, the second member of the dimerization pair is an NCOA2/SRC2 polypeptide comprising the amino acid sequence
KRHHHEVLRQGLAFSQIYRFSLSDGTLVAAQTKSKLIRSQTTNEPQLVISLHMLHREQNVCVMN
PDLTGQTMGKPLNPISSNSPAHQALCSGNPGQDMTLSSNINFPINGPKEQMGMPMGRFGGSGG
MNHVSGMQATTPQGSNYALKMNSPSQSSPGMNPGQPTSMLSPRHRMSPGVAGSPRIPPSQFSPA
GSLHSPVGVCSSTGNSHSYTNSSLNALQALSEGHGVSLGSSLASPDLKMGNLQNSPVNMNPPPL
SKMGSLDSKDCFGLYGEPSEGTTGQAESSCHPGEQKETNDPNLPPAVSSERADGQSRLHDSKGQ
TKLLQLLTTKSDQMEPSPLASSLSDTNKDSTGSLPGSGSTHGTSLKEKHKILHRLLQDSSSPVDL
AKLTAEATGKDLSQESSSTAPGSEVTIKQEPVSPKKKENALLRYLLDKDDTKDIGLPEITPKLERL
DSKTDPASNTKLIAMKTEKEEMSFEPGDQPGSELDNLEEILDDLQNSQLPQLFPDTRPGAPAGSV
DKQAIINDLMQLTAENSPVTPVGAQKTALRISQSTFNNPRPGQLGRLLPNQNLPLDITLQSPTGA
GPFPPIRNSSPYSVIPQPGMMGNQGMIGNQGNLGNSSTGMIGNSASRPTMPSGEWAPQSSAVRV
TCAATTSAMNRPVQGGMIRNPAASIPMRPSSQPGQRQTLQSQVMNIGPSELEMNMGGP (SEQ ID NO:665) or a fragment thereof. In some cases, where the second member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a GR, the first member of the dimerization pair is an NCOA2/SRC2 polypeptide.

Vitamin D receptor

[00502] In some cases, an LBD suitable for inclusion as a member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of vitamin D receptor (VDR). For example, in some cases, the LBD comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the LBD of a VDR having the amino acid sequence depicted in FIG. 9A.

[00503] As one non-limiting example, the LBD of a VDR can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to one of the amino acid sequences depicted in FIG. 9C; and has a length of from about 250 amino acids to 310 amino acids (e.g., has a length of from 250 amino acids to 275 amino acids, from 275 amino acids to 300 amino acids, or from 300 amino acids to 310 amino acids).

[00504] As one non-limiting example, the LBD of a VDR can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 9B; and has a length of from about 250 amino acids to 303 amino acids (e.g., has a length of from 250 amino acids to 275 amino acids, from 275 amino acids to 300 amino acids, or from 300 amino acids to 303 amino acids).

[00505] In some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a VDR, the second member of the dimerization pair is an NCOA1/SRC1 polypeptide. For example, in some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a VDR, the second member of the dimerization pair is an NCOA1/SRC1 polypeptide comprising the amino acid sequence NYGTNPGTPPASTSPFSQLAANPEASLANRNSMVSRGMTGNIGGQFGTGINPQMQQNVFQYPG AGMVPQGEANFAPSLSPGSSMVPMPIPPPQSSLLQQTPPASGYQSPDMKAWQQGAIGNNNVFSQ AVQNQPTPAQPGVYNNMSITVSMAGGNTNVQNMNPMMAQMQMSSLQMPGMNTVCPEQIND PALRHTGLYCNQLSSTDLLKTEADGTQQVQQVQVFADVQCTVNLVGGDPYLNQPGPLGTQKP TSGPQTPQAQQKSLLQQLLTE (SEQ ID NO:666) or a fragment thereof. In some cases, where the second member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a VDR, the first member of the dimerization pair is an NCOA1/SRC1 polypeptide.

[00506] In some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a VDR, the second member of the dimerization pair is an NCOA2/SRC2 polypeptide. For example, in some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a VDR, the second member of the dimerization pair is an NCOA2/SRC2 polypeptide comprising the amino acid sequence KRHHHEVLRQGLAFSQIYRFSLSDGTLVAAQTKSKLIRSQTTNEPQLVISLHMLHREQNVCVMN PDLTGQTMGKPLNPISSNSPAHQALCSGNPGQDMTLSSNINFPINGPKEQMGMPMGRFGGSGG MNHVSGMQATTPQGSNYALKMNSPSQSSPGMNPGQPTSMLSPRHRMSPGVAGSPRIPPSQFSPA GSLHSPVGVCSSTGNSHSYTNSSLNALQALSEGHGVSLGSSLASPDLKMGNLQNSPVNMNPPPL SKMGSLDSKDCFGLYGEPSEGTTGQAESSCHPGEQKETNDPNLPPAVSSERADGQSRLHDSKGQ

TKLLQLLTTKSDQMEPSPLASSLSDTNKDSTGSLPGSGSTHGTSLKEKHKILHRLLQDSSSPVDL AKLTAEATGKDLSQESSSTAPGSEVTIKQEPVSPKKKENALLRYLLDKDDTKDIGLPEITPKLERL DSKTDPASNTKLIAMKTEKEEMSFEPGDQPGSELDNLEEILDDLQNSQLPQLFPDTRPGAPAGSV DKQAIINDLMQLTAENSPVTPVGAQKTALRISQSTFNNPRPGQLGRLLPNQNLPLDITLQSPTGA GPFPPIRNSSPYSVIPQPGMMGNQGMIGNQGNLGNSSTGMIGNSASRPTMPSGEWAPQSSAVRV TCAATTSAMNRPVQGGMIRNPAASIPMRPSSQPGQRQTLQSQVMNIGPSELEMNMGGP (SEQ ID NO:667) or a fragment thereof. For example, in some cases, where the first member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a VDR, the second member of the dimerization pair is an NCOA2/SRC2 polypeptide comprising the amino acid sequence LLRYLLDK (SEQ ID NO:668), where the co-regulator peptide has a length of from about from about 8 amino acids to about 50 amino acids (e.g., the co-regulator peptide has a length of from about 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 23 amino acids, from 23 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids). In some cases, where the second member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a VDR, the first member of the dimerization pair is an NCOA2/SRC2 polypeptide.

Thyroid hormone receptor-alpha

[00507] In some cases, an LBD suitable for inclusion as a member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of thyroid hormone receptor-alpha (TRα). For example, in some cases, the LBD comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the LBD of a TRα having the amino acid sequence depicted in FIG. 10A.

[00508] As one non-limiting example, the LBD of a TRα can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to one of the amino acid sequences depicted in FIG. 10C; and has a length of from about 190 amino acids to about 245 amino acids (e.g., has a length of from 190 amino acids to 210 amino acids, from 210 amino acids to 230 amino acids, or from 230 amino acids to 245 amino acids).

[00509] As one non-limiting example, the LBD of a TRα can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 10B; and has a length of from about 190 amino acids to about 243 amino acids (e.g., has a length of from 190 amino acids to 210 amino acids, from 210 amino acids to 230 amino acids, or from 230 amino acids to 243 amino acids).

Retinoic acid receptor-beta

[00510] In some cases, an LBD suitable for inclusion as a member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of retinoic acid receptor-beta (RARβ). For example, in some cases, the LBD comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the LBD of a RARβ having the amino acid sequence depicted in FIG. 11A.

[00511] As one non-limiting example, the LBD of a RARβ can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to one of the amino acid sequences depicted in FIG. 11C; and has a length of from about 180 amino acids to about 235 amino acids (e.g., has a length of from 180 amino acids to 200 amino acids, from 200 amino acids to 220 amino acids, or from 220 amino acids to 235 amino acids).

[00512] As one non-limiting example, the LBD of a RARβ can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 11B; and has a length of from about 180 amino acids to about 231 amino acids (e.g., has a length of from 180 amino acids to 200 amino acids, from 200 amino acids to 220 amino acids, or from 220 amino acids to 231 amino acids).

[00513] A suitable co-regulator peptide for a RARβ is an SRC1 polypeptide, or a fragment thereof (e.g., a peptide of from 8 amino acids to 50 amino acids in length, derived from an SRC1 polypeptide).

Farnesoid X receptor

[00514] In some cases, an LBD suitable for inclusion as a member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of farnesoid X receptor (FXR. For example, in some cases, the LBD comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the LBD of an FXR having the amino acid sequence depicted in FIG. 22A.

[00515] As one non-limiting example, the LBD of an FXR can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 22B; and has a length of from about 100 amino acids to about 136 amino acids (e.g., has a length of from 100 amino acids to 110 amino acids, from 110 amino acids to 120 amino acids, or from 120 amino acids to 136 amino acids).

[00516] A suitable co-regulator peptide for an FXR is an SRC1 polypeptide, or a fragment thereof (e.g., a peptide of from 8 amino acids to 50 amino acids in length, derived from an SRC1 polypeptide).

LXR-alpha

[00517] In some cases, an LBD suitable for inclusion as a member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of liver X receptor-alpha (LRXα). For example, in some cases, the LBD comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the LBD of an LRXα having the amino acid sequence depicted in FIG. 23A.

[00518] As one non-limiting example, the LBD of an LRXα can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 23B; and has a length of from about 200 amino acids to about 266 amino acids (e.g., has a length of from 200 amino acids to 220 amino acids, from 220 amino acids to 240 amino acids, or from 240 amino acids to 266 amino acids).

[00519] A suitable co-regulator peptide for an LXRα is an SRC1 polypeptide, or a fragment thereof (e.g., a peptide of from 8 amino acids to 50 amino acids in length, derived from an SRC1 polypeptide).

RORgamma

[00520] In some cases, an LBD suitable for inclusion as a member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a retinoid-related orphan receptor gamma (RORγ). For example, in some cases, the LBD comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the LBD of an RORγ having the amino acid sequence depicted in FIG. 24A.

[00521] As one non-limiting example, the LBD of an RORγ can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 24B; and has a length of from about 200 amino acids to about 261 amino acids (e.g., has a length of from 200 amino acids to 220 amino acids, from 220 amino acids to 240 amino acids, or from 240 amino acids to 261 amino acids).

[00522] A suitable co-regulator for an RORγ is an NCORNR peptide (CDPASNLGLEDIIRKALMGSFDDK, SEQ ID NO:669).

[00523] A suitable co-regulator peptide for an RORγ is an SRC1 polypeptide, or a fragment thereof (e.g., a peptide of from 8 amino acids to 50 amino acids in length, derived from an SRC1 polypeptide).

RXR-alpha

[00524] In some cases, an LBD suitable for inclusion as a member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a retinoid-X receptor-alpha (RXRα). For example, in some cases, the LBD comprises an amino acid sequence having at least 75%, at

least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the LBD of an RXRα having the amino acid sequence depicted in FIG. 25A.

[00525] As one non-limiting example, the LBD of an RORγ can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 25B; and has a length of from about 190 amino acids to about 238 amino acids (e.g., has a length of from 190 amino acids to 200 amino acids, from 200 amino acids to 210 amino acids, or from 210 amino acids to 238 amino acids).

[00526] A suitable co-regulator peptide for an RXRα is an SRC1 polypeptide, or a fragment thereof (e.g., a peptide of from 8 amino acids to 50 amino acids in length, derived from an SRC1 polypeptide).

PXR

[00527] In some cases, an LBD suitable for inclusion as a member of a dimerization pair of a conditionally active, heterodimeric polypeptide of the present disclosure is an LBD of a Pregnane X Receptor (PXR). For example, in some cases, the LBD comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the LBD of a PXR having the amino acid sequence depicted in FIG. 26A. In some cases, the LBD comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to amino acids 143-428 of the amino acid sequence depicted in FIG. 26A. In some cases, the LBD comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to amino acids 205-434 of the amino acid sequence depicted in FIG. 26A.

[00528] As one non-limiting example, the LBD of a PXR can comprise an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in FIG. 26B; and has a length of from about 250 amino acids to about 302 amino acids (e.g., has a length of from 250 amino acids to 275 amino acids, from 275 amino acids to 290 amino acids, or from 290 amino acids to 302 amino acids).

[00529] A suitable co-regulator peptide for a PXR is an SRC1 polypeptide, or a fragment thereof (e.g., a peptide of from 8 amino acids to 50 amino acids in length, derived from an SRC1 polypeptide).

Co-regulator peptides

[00530] Suitable co-regulator polypeptides include full-length naturally-occurring nuclear hormone co-regulator polypeptides. Suitable co-regulator polypeptides include fragments of naturally-occurring nuclear hormone co-regulator polypeptides. Suitable co-regulator polypeptides include synthetic or recombinant nuclear hormone co-regulator polypeptides.

[00531] Suitable co-regulator polypeptides can have a length of from 8 amino acids to 2000 amino acids. Suitable co-regulator polypeptides can have a length of from 8 amino acids to 50 amino acids, e.g., from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids. Suitable co-regulator polypeptides can have a length of from 50 amino acids to 100 amino acids, e.g., from 50 amino acids to 60 amino acids, from 60 amino acids to 70 amino acids, from 70 amino acids to 80 amino acids, from 80 amino acids to 90 amino acids, or from 90 amino acids to 100 amino acids. Suitable co-regulator polypeptides can have a length of from 100 amino acids to 200 amino acids, from 200 amino acids to 300 amino acids, from 300 amino acids to 400 amino acids, from 400 amino acids to 500 amino acids, from 500 amino acids to 600 amino acids, from 600 amino acids to 700 amino acids, from 700 amino acids to 800 amino acids, from 800 amino acids to 900 amino acids, or from 900 amino acids to 1000 amino acids. Suitable co-regulator polypeptides can have a length of from 1000 amino acids to 2000 amino acids.

[00532] Suitable co-regulator polypeptides include, but are not limited to, SRC1, GRIP1, AIB1, PGC1a, PGC1b, PRC, TRAP220, ASC2, CBP, P300, CIA, ARA70, TIF1, NSD1, SMAP, Tip60, ERAP140, Nix1, LCoR, N-CoR, SMRT, RIP140, and PRIC285.

[00533] National Center for Biotechnology Information (NCBI) accession numbers for such co-regulators include the following: SRC1 (NP_003734), GRIP1 (NP_006531), AIB1 (NP_006525), PGC1a (NP_037393), PGC1b (NP_573570), PRC (NP_055877), TRAP220 (NP_004765), ASC2 (NP_054790), CBP (NP_004371), P300 (NP_001420), CIA (NP_066018), ARA70 (NP_005428), TIF1 (NP_003843), NSD1 (NP_071900), SMAP (NP_006687), Tip60 (NP_006379), ERAP140 (NP_861447), Nix1 (NP_113662), LCoR (NP_115816), N-CoR (NP_006302), SMRT (NP_006303), RIP140 (NP_003480) and PRIC285 (NP_208384).

[00534] Examples of suitable co-regulator polypeptides are provided in FIGs. 29-51B.

[00535] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 29.

[00536] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20

amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 30.

[00537] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 31.

[00538] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 32.

[00539] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 33.

[00540] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 34.

[00541] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 35.

[00542] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 36A-36B.

[00543] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 37A-37B.

[00544] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 36A-36B.

[00545] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at

least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 39.

[00546] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 40.

[00547] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 41.

[00548] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 42A-42B.

[00549] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 43.

[00550] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino

acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 44.

[00551] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 45.

[00552] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 46.

[00553] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 47.

[00554] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 48A-48B.

[00555] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino

acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 49A-49B.

[00556] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 50.

[00557] In some cases, a suitable suitable co-regulator polypeptide has a length of from 8 amino acids to 10 amino acids, from 10 amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids; and has at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to a stretch of from 8 to 50 contiguous amino acids of the amino acid sequence depicted in FIG. 51A-51B.

[00558] Suitable co-regulator peptides include, but are not limited to, Steroid Receptor Coactivator (SRC)-1, SRC-2, SRC-3, TRAP220-1, TRAP220-2, NR0B1, NRIP1, CoRNR box, abV, TIF1, TIF2, EA2, TA1, EAB1, SRC1-1, SRC1-2, SRC1-3, SRC1-4a, SRC1-4b, GRIP1-1, GRIP1-2, GRIP1-3, AIB1-1, AIB1-2, AIB1-3, PGC1a, PGC1b, PRC, ASC2-1, ASC2-2, CBP-1, CBP-2, P300, CIA, ARA70-1, ARA70-2, NSD1, SMAP, Tip60, ERAP140, Nix1, LCoR, CoRNR1 (N-CoR), CoRNR2, SMRT, RIP140-C, RIP140-1, RIP140-2, RIP140-3, RIP140-4, RIP140-5, RIP140-6, RIP140-7, RIP140-8, RIP140-9, PRIC285-1, PRIC285-2, PRIC285-3, PRIC285-4, and PRIC285-5.

[00559] National Center for Biotechnology Information (NCBI) accession numbers for such co-regulators include the following: SRC1 (NP_003734), GRIP1 (NP_006531), AIB1 (NP_006525), PGC1a (NP_037393), PGC1b (NP_573570), PRC (NP_055877), TRAP220 (NP_004765), ASC2 (NP_054790), CBP (NP_004371), P300 (NP_001420), CIA (NP_066018), ARA70 (NP_005428), TIF1 (NP_003843), NSD1 (NP_071900), SMAP (NP_006687), Tip60 (NP_006379), ERAP140 (NP_861447), Nix1 (NP_113662), LCoR (NP_115816), N-CoR (NP_006302), SMRT (NP_006303), RIP140 (NP_003480) and PRIC285 (NP_208384).

[00560] In some cases, a suitable co-regulator peptide comprises an LXXLL motif, where X is any amino acid; where the co-regulator peptide has a length of from 12 amino acids to 50 amino acids, e.g., from 12

amino acids to 15 amino acids, from 15 amino acids to 20 amino acids, from 20 amino acids to 25 amino acids, from 25 amino acids to 30 amino acids, from 30 amino acids to 35 amino acids, from 35 amino acids to 40 amino acids, from 40 amino acids to 45 amino acids, or from 45 amino acids to 50 amino acids.

[00561] Non-limiting examples of suitable co-regulator peptides are as follows:

SRC1: CPSSHSSLTERHKILHRLLQEGSPS (SEQ ID NO:1);

SRC1–2: SLTARHKILHRLLQEGSPSDI (SEQ ID NO:2);

SRC3-1: ESKGHKKLLQLLTCSSDDR (SEQ ID NO:3);

SRC3: PKKENNALLRYLLDRDDPSDV (SEQ ID NO:4);

PGC-1: AEEPSLLKKLLLAPANT (SEQ ID NO:5);

PGC1a: QEAEEPSLLKKLLLAPANTQL (SEQ ID NO:6);

TRAP220–1: SKVSQNPILTSLLQITGNGGS (SEQ ID NO:7);

NCoR (2051–2075): GHSFADPASNLGLEDIIRKALMGSF (SEQ ID NO:8);

NR0B1: PRQGSILYSMLTSAKQT (SEQ ID NO:9);

NRIP1: AANNSLLLHLLKSQTIP (SEQ ID NO:10);

TIF2: PKKKENALLRYLLDKDDTKDI (SEQ ID NO:11);

CoRNR Box: DAFQLRQLILRGLQDD (SEQ ID NO:12);

abV: SPGSREWFKDMLS (SEQ ID NO:13);

TRAP220-2: GNTKNHPMLMNLLKDNPAQDF (SEQ ID NO:14);

EA2: SSKGVLWRMLAEPVSR (SEQ ID NO:15);

TA1: SRTLQLDWGTLYWSR (SEQ ID NO:16);

EAB1: SSNHQSSRLIELLSR (SEQ ID NO:17);

SRC2: LKEKHKILHRLLQDSSSPV (SEQ ID NO:18);

SRC1-3: QAQQKSLLQQLLTE (SEQ ID NO:19);

SRC1–1: KYSQTSHKLVQLLTTTAEQQL (SEQ ID NO:20);

SRC1–2: SLTARHKILHRLLQEGSPSDI (SEQ ID NO:21);

SRC1–3: KESKDHQLLRYLLDKDEKDLR (SEQ ID NO:22);

SRC1–4a: PQAQQKSLLQQLLTE (SEQ ID NO:23);

SRC1–4b: PQAQQKSLRQQLLTE (SEQ ID NO:24);

GRIP1–1: HDSKGQTKLLQLLTTKSDQME (SEQ ID NO:25);

GRIP1–2: SLKEKHKILHRLLQDSSSPVD (SEQ ID NO:26);

GRIP1–3: PKKKENALLRYLLDKDDTKDI (SEQ ID NO:27);

AIB1–1: LESKGHKKLLQLLTCSSDDRG (SEQ ID NO:28);

AIB1–2: LLQEKHRILHKLLQNGNSPAE (SEQ ID NO:29);

AIB1–3: KKKENNALLRYLLDRDDPSDA (SEQ ID NO:30);

PGC1a: QEAEEPSLLKKLLLAPANTQL (SEQ ID NO:31);
PGC1b: PEVDELSLLQKLLLATSYPTS (SEQ ID NO:32);
PRC: VSPREGSSLHKLLTLSRTPPE (SEQ ID NO:33);
TRAP220–1: SKVSQNPILTSLLQITGNGGS (SEQ ID NO:34);
TRAP220–2: GNTKNHPMLMNLLKDNPAQDF (SEQ ID NO:35);
ASC2–1: DVTLTSPLLVNLLQSDISAGH (SEQ ID NO:36);
ASC2–2: AMREAPTSLSQLLDNSGAPNV (SEQ ID NO:37);
CBP-1: DAASKHKQLSELLRGGSGSSI (SEQ ID NO:38);
CBP-2: KRKLIQQQLVLLLHAHKCQRR (SEQ ID NO:39);
P300: DAASKHKQLSELLRSGSSPNL (SEQ ID NO:40);
CIA: GHPPAIQSLINLLADNRYLTA (SEQ ID NO:41);
ARA70–1: TLQQQAQQLYSLLGQFNCLTH (SEQ ID NO:42);
ARA70–2: GSRETSEKFKLLFQSYNVNDW (SEQ ID NO:43);
TIF1: NANYPRSILTSLLLNSSQSST (SEQ ID NO:44);
NSD1: IPIEPDYKFSTLLMMLKDMHD (SEQ ID NO:45);
SMAP: ATPPPSPLLSELLKKGSLLPT (SEQ ID NO:46);
Tip60: VDGHERAMLKRLLRIDSKCLH (SEQ ID NO:47);
ERAP140: HEDLDKVKLIEYYLTKNKEGP (SEQ ID NO:48);
Nix1: ESPEFCLGLQTLLSLKCCIDL (SEQ ID NO:49);
LCoR: AATTQNPVLSKLLMADQDSPL (SEQ ID NO:50);
CoRNR1 (N-CoR): MGQVPRTHRLITLADHICQIITQDFARNQV (SEQ ID NO:51);
CoRNR2 (N-CoR): NLGLEDIIRKALMG (SEQ ID NO:52);
CoRNR1 (SMRT): APGVKGHQRVVTLAQHISEVITQDTYRHHPQQLSAPLPAP (SEQ ID NO:53);
CoRNR2 (SMRT): NMGLEAIIRKALMG (SEQ ID NO:54);
RIP140-C: RLTKTNPILYYMLQKGGNSVA (SEQ ID NO:55);
RIP140-1: QDSIVLTYLEGLLMHQAAGGS (SEQ ID NO:56);
RIP140-2: KGKQDSTLLASLLQSFSSRLQ (SEQ ID NO:57);
RIP140-3: CYGVASSHLKTLLKKSKVKDQ (SEQ ID NO:58);
RIP140-4: KPSVACSQLALLLSSEAHLQQ (SEQ ID NO:59);
RIP140-5: KQAANNSLLLHLLKSQTIPKP (SEQ ID NO:60);
RIP140-6: NSHQKVTLLQLLLGHKNEENV (SEQ ID NO:61);
RIP140-7: NLLERRTVLQLLLGNPTKGRV (SEQ ID NO:62);
RIP140-8: FSFSKNGLLSRLLRQNQDSYL (SEQ ID NO:63);
RIP140-9: RESKSFNVLKQLLLSENCVRD (SEQ ID NO:64);
PRIC285-1: ELNADDAILRELLDESQKVMV (SEQ ID NO:65);

PRIC285-2: YENLPPAALRKLLRAEPERYR (SEQ ID NO:66);

PRIC285-3: MAFAGDEVLVQLLSGDKAPEG (SEQ ID NO:67);

PRIC285-4: SCCYLCIRLEGLLAPTASPRP (SEQ ID NO:68); and

PRIC285-5: PSNKSVDVLAGLLLRRMELKP (SEQ ID NO:69).

[00562] In some cases, a given LBD can be paired with two or more different co-regulator polypeptides. For example, as depicted in FIG. 19, PPARγ can be paired with SRC1, SRC2, SRC3, or TRAP220. As another example, ERα can be paired with CoRNR, αβV, or TA1. As another example, ERβ can be paired with CoRNR, αβV, or TA1. As another example, AR can be paired with SRC1, SRC2, SRC3, or TRAP220. As another example, PR can be paired with SRC1, SRC2, SRC3, TRAP220, NR0B1, PGC1B, NRIP1, EA2, or EAB1. As another example, TRβ can be paired with SRC1, SRC2, SRC3, or TRAP220.

[00563] In some cases, a heterodimeric polypeptide of the present disclosure comprises a polypeptide chain comprising multiple (two or more) co-regulator peptides. Where a heterodimeric polypeptide of the present disclosure comprises a polypeptide chain comprising multiple (two or more) co-regulator peptides, the multiple co-regulator peptides can be in tandem, directly or separated by a linker. In some cases, the two or more co-regulator peptides present in the polypeptide chain are identical in amino acid sequence to one another. In some cases, where a heterodimeric polypeptide of the present disclosure comprises a polypeptide chain comprising multiple (two or more) co-regulator peptides, the polypeptide chain comprises two co-regulator peptides. In some cases, where a heterodimeric polypeptide of the present disclosure comprises a polypeptide chain comprising multiple (two or more) co-regulator peptides, the polypeptide chain comprises three co-regulator peptides. In such cases, the second polypeptide chain can comprise multiple (two or more) LBD of a nuclear hormone receptor. For example, where the second polypeptide chain comprises two LBD of a nuclear hormone receptor, the two LBD can be identical in amino acid sequence to one another.

[00564] Suitable dimerization agents are as described above.

Engineered T Cell Receptor (TCR)

[00565] In some instances, a heteromeric, conditionally repressible synthetic ICR may include, in part or in whole, an engineered T cell receptor (TCR) or may essentially be a modified engineered TCR such that by modification the engineered TCR is conditionally repressible. In such instances, the engineered TCR containing heteromeric, conditionally repressible synthetic ICR may be referred to as a heteromeric, conditionally repressible synthetic TCR or, for simplicity, a repressible TCR.

[00566] Any engineered TCR having immune cell activation function may find use in a heteromeric, conditionally repressible synthetic ICR as described herein including but not limited to, e.g., antigen-specific TCRs, Monoclonal TCRs (MTCRs), Single chain MTCRs, High Affinity CDR2 Mutant TCRs,

CD1-binding MTCRs, High Affinity NY-ESO TCRs, VYG HLA-A24 Telomerase TCRs, including e.g., those described in PCT Pub Nos. WO 2003/020763, WO 2004/033685, WO 2004/044004, WO 2005/114215, WO 2006/000830, WO 2008/038002, WO 2008/039818, WO 2004/074322, WO 2005/113595, WO 2006/125962; Strommes et al. Immunol Rev. 2014; 257(1):145-64; Schmitt et al. Blood. 2013; 122(3):348-56; Chapuls et al. Sci Transl Med. 2013; 5(174):174ra27; Thaxton et al. Hum Vaccin Immunother. 2014; 10(11):3313-21 (PMID:25483644); Gschweng et al. Immunol Rev. 2014; 257(1):237-49 (PMID:24329801); Hinrichs et al. Immunol Rev. 2014; 257(1):56-71 (PMID:24329789); Zoete et al. Front Immunol. 2013; 4:268 (PMID:24062738); Marr et al. Clin Exp Immunol. 2012; 167(2):216-25 (PMID:22235997); Zhang et al. Adv Drug Deliv Rev. 2012; 64(8):756-62 (PMID:22178904); Chhabra et al. Scientific World Journal. 2011; 11:121-9 (PMID:21218269); Boulter et al. Clin Exp Immunol. 2005; 142(3):454-60 (PMID:16297157); Sami et al. Protein Eng Des Sel. 2007; 20(8):397-403; Boulter et al. Protein Eng. 2003; 16(9):707-11; Ashfield et al. IDrugs. 2006; 9(8):554-9; Li et al. Nat Biotechnol. 2005; 23(3):349-54; Dunn et al. Protein Sci. 2006; 15(4):710-21; Liddy et al. Mol Biotechnol. 2010; 45(2); Liddy et al. Nat Med. 2012; 18(6):980-7; Oates, et al. Oncoimmunology. 2013; 2(2):e22891; McCormack, et al. Cancer Immunol Immunother. 2013 Apr;62(4):773-85; Bossi et al. Cancer Immunol Immunother. 2014; 63(5):437-48 and Oates, et al. Mol Immunol. 2015 Oct;67(2 Pt A):67-74; the disclosures of which are incorporated herein by reference in their entirety.

[00567] In some instances, an engineered TCR useful in a heteromeric, conditionally repressible synthetic ICR as described herein may include, e.g., a NY-ESO-1-binding TCR or a TCR that binds to NY-ESO-1 or a peptide derived therefrom. For example, in some instances a NY-ESO-1-binding TCR may be an engineered TCR that binds to a peptide having the amino acid sequence: SLLMWITQC (SEQ ID NO:670).

[00568] In some instances, an engineered TCR useful in a heteromeric, conditionally repressible synthetic ICR as described herein may be or may be derived from an engineered TCR having high affinity for its ligand including but not limited to, e.g., a K_D of less than or equal to 100 μM, including but not limited to e.g., a K_D of less than or equal to 10 μM or a K_D of less than or equal to 1 μM. In some instances, an engineered TCR useful in a heteromeric, conditionally repressible synthetic ICR as described herein may be or may be derived from an engineered TCR having high affinity for the peptide SLLMWITQC (SEQ ID NO:671), including but not limited to, e.g., a K_D of less than or equal to 100 μM, including but not limited to e.g., a K_D of less than or equal to 10 μM or a K_D of less than or equal to 1 μM for the peptide SLLMWITQC (SEQ ID NO:672). The K_D measurement can be made by any known method, including but not limited to e.g., Surface Plasmon Resonance (Biacore).

[00569] In some instances, an engineered TCR useful in a heteromeric, conditionally repressible synthetic ICR as described herein may be or may be derived from an engineered TCR having a slow off-rate (k_{off}) from its ligand including but not limited to, e.g., a k_{off} of 0.1 S^{-1} or slower, including but not limited to

e.g., a k_{off} of 1 x 10^{-2} S^{-1} or slower or a k_{off} of 1 x 10^{-3} S^{-1} or slower. In some instances, an engineered TCR useful in a heteromeric, conditionally repressible synthetic ICR as described herein may be or may be derived from an engineered TCR having a slow off-rate from the peptide SLLMWITQC (SEQ ID NO:673), including but not limited to, e.g., a K_D of less than or equal to 100 μM, including but not limited to e.g., a k_{off} of 0.1 S^{-1} or slower, including but not limited to e.g., a k_{off} of 1 x 10^{-2} S^{-1} or slower or a k_{off} of 1 x 10^{-3} S^{-1} or slower from the peptide SLLMWITQC (SEQ ID NO:674). The k_{off} measurement can be made by any known method, including but not limited to e.g., Surface Plasmon Resonance (Biacore).

[00570] In some instances, an engineered TCR may be modified for use as a component of a heteromeric, conditionally repressible synthetic ICR through introduction or insertion of a dimerization domain (e.g., a member of a dimerizer pair) into the engineered TCR and, in such instances, following modification, the engineered TCR may be referred to as a dimerizer-domain containing TCR or a dimerizable TCR.

[00571] A dimerizer domain may be inserted into the engineered TCR amino acid sequence, e.g., by introducing a coding sequence for the dimerizer domain into the coding sequence of the engineered TCR, at any convenient location provided the insertion does not negatively impact the primary functional domains of the engineered TCR (including e.g., a TCR alpha chain domain, a TCR beta chain domain, a TCR CD3 chain domain, a TCR zeta chain domain, a TCR CD3-zeta chain domain a TCR extracellular domain, a TCR intracellular domain, a TCR variable region domain, a TCR constant region domain, a TCR IgSF domain, etc., or a function thereof) and/or the negatively impact the dimerization function of the dimerizer domain.

[00572] An engineered TCR may include one or more epsilon, sigma, or gamma chains, or in some instances, an engineered TCR may not include one or more epsilon, sigma, or gamma chains and may instead rely upon endogenously expressed epsilon, sigma, or gamma chains. In some instances, an engineered TCR may not include one or more CD3-zeta chains and may instead rely on endogenously expressed CD3-zeta.

[00573] In some instances, the dimerizer domain may be inserted into an extracellular portion of the engineered TCR. In some instances the dimerizer domain (first or second member of the dimerization pair) may be inserted into an intracellular portion of the engineered TCR.

[00574] In some instances, the dimerizer domain may be inserted into or linked to an alpha chain of the engineered TCR. In some instances, the dimerizer domain is inserted or linked such that following the insertion or linking the dimerizer domain is linked intracellularly to the alpha chain including e.g., where the dimerizer domain is linked to the cytoplasmic side of the alpha chain transmembrane domain. In some instances, the dimerizer domain is inserted or linked such that following the insertion or linking the dimerizer domain is linked extracellularly to the alpha chain including e.g., where the dimerizer domain

is linked to the extracellular side of the alpha chain transmembrane domain, where the dimerizer domain is inserted between the alpha chain transmembrane domain and the alpha chain constant region domain, etc.

[00575] In some instances, the dimerizer domain may be inserted into or linked to a beta chain of the engineered TCR. In some instances, the dimerizer domain is inserted or linked such that following the insertion or linking the dimerizer domain is linked intracellularly to the beta chain including e.g., where the dimerizer domain is linked to the cytoplasmic side of the beta chain transmembrane. In some instances, the dimerizer domain is inserted or linked such that following the insertion or linking the dimerizer domain is linked extracellularly to the beta chain including e.g., where the dimerizer domain is linked to the extracellular side of the beta chain transmembrane domain, where the dimerizer domain is inserted between the beta chain transmembrane domain and the beta chain constant region domain, etc..

[00576] In some instances, the dimerizer domain may be inserted into or linked to a fused alpha-CD3-zeta chain, e.g., where the CD3-zeta chain is full-length CD3-zeta (e.g., a TCR:zeta fusion) of the engineered TCR. In some instances, the dimerizer domain is inserted or linked such that following the insertion or linking the dimerizer domain is linked intracellularly to the fused alpha-CD3-zeta chain including e.g., where the dimerizer domain is inserted between the CD3-zeta transmembrane domain and other intracellular domains of the fused alpha-CD3-zeta chain, including e.g., one or more intracellular ITAM domains. In some instances, the dimerizer domain is inserted or linked such that following the insertion or linking the dimerizer domain is linked extracellularly to the fused alpha-CD3-zeta chain including e.g., where the dimerizer domain is linked to the extracellular side of the CD3-zeta transmembrane domain, where the dimerizer domain is inserted between the extracellular alpha chain domain and the transmembrane domain of the fused CD3-zeta, etc.

[00577] In some instances, the dimerizer domain may be inserted into or linked to a fused beta-CD3-zeta chain, e.g., where the CD3-zeta chain is full-length CD3-zeta (e.g., a TCR:zeta fusion) of the engineered TCR. In some instances, the dimerizer domain is inserted or linked such that following the insertion or linking the dimerizer domain is linked intracellularly to the fused beta-CD3-zeta chain including e.g., where the dimerizer domain is inserted between the CD3-zeta transmembrane domain and other intracellular domains of the fused beta-CD3-zeta chain, including e.g., one or more intracellular ITAM domains. In some instances, the dimerizer domain is inserted or linked such that following the insertion or linking the dimerizer domain is linked extracellularly to the fused beta-CD3-zeta chain including e.g., where the dimerizer domain is linked to the extracellular side of the CD3-zeta transmembrane domain, where the dimerizer domain is inserted between the extracellular beta chain domain and the transmembrane domain of the fused CD3-zeta, etc.

[00578] In some instances, the dimerizer domain may be inserted into or linked to a fused alpha-CD3-zeta domain (e.g., in an engineered TCR alpha-zeta + beta-zeta fusion) of the engineered TCR. In some

instances, the dimerizer domain is inserted or linked such that following the insertion or linking the dimerizer domain is linked intracellularly to the fused alpha-CD3-zeta domain including e.g., where the dimerizer domain is inserted between one or more domains of the CD3-zeta domain and the transmembrane domain of the alpha chain. In some instances, the dimerizer domain is inserted or linked such that following the insertion or linking the dimerizer domain is linked extracellularly to the fused alpha-CD3-zeta domain including e.g., where the dimerizer domain is linked to the extracellular side of the alpha chain transmembrane domain, where the dimerizer domain is inserted between the alpha chain transmembrane domain and the alpha chain constant region domain, etc.

[00579] In some instances, the dimerizer domain may be inserted into or linked to a fused beta-CD3-zeta domain (e.g., in an engineered TCR alpha-zeta + beta-zeta fusion) of the engineered TCR. In some instances, the dimerizer domain is inserted or linked such that following the insertion or linking the dimerizer domain is linked intracellularly to the fused beta-CD3-zeta domain including e.g., where the dimerizer domain is inserted between one or more domains of the CD3-zeta domain and the transmembrane domain of the beta chain. In some instances, the dimerizer domain is inserted or linked such that following the insertion or linking the dimerizer domain is linked extracellularly to the fused beta-CD3-zeta domain including e.g., where the dimerizer domain is linked to the extracellular side of the beta chain transmembrane domain, where the dimerizer domain is inserted between the beta chain transmembrane domain and the beta chain constant region domain, etc..

[00580] In some instances, the dimerizer domain may be inserted into or linked to a chain of an engineered single chain TCR (e.g., in an engineered single chain TCR:zeta fusion, e.g., where a TCR alpha chain variable domain is linked to a TCR beta chain which is fused to a full-length CD3-zeta chain). In some instances, the dimerizer domain is inserted or linked such that following the insertion or linking the dimerizer domain is linked intracellularly to the engineered single chain TCR including e.g., where the dimerizer domain is inserted between one or more domains of the CD3-zeta chain and the transmembrane domain of the CD3-zeta chain. In some instances, the dimerizer domain is inserted or linked such that following the insertion or linking the dimerizer domain is linked extracellularly to the engineered single chain TCR including e.g., where the dimerizer domain is linked to the extracellular side of the CD3-zeta chain transmembrane domain, where the dimerizer domain is inserted between the CD3-zeta chain transmembrane domain and the beta chain constant region domain, etc..

[00581] In some instances, only a single dimerizer domain may be present in a conditionally repressible engineered TCR, e.g., where a single dimerizer domain is linked or inserted into an alpha chain of the engineered TCR, where a single dimerizer domain is linked or inserted into a beta chain of the engineered TCR, where a single dimerizer domain is linked or inserted into a CD3-zeta chain of the engineered TCR, etc.

[00582] In some instances, two or more dimerizer domains may be present in a conditionally repressible engineered TCR. For example, two dimerizer domains may be present in a conditionally repressible engineered TCR, e.g., where a first dimerizer domain is linked or inserted into an alpha chain of the engineered TCR and a second dimerizer domain is linked or inserted into a beta chain of the engineered TCR, where a first dimerizer domain is linked or inserted into a first CD3-zeta chain of the engineered TCR and a second dimerizer domain is linked or inserted into a second CD3-zeta chain of the engineered TCR, etc.

[00583] In some instances, the engineered TCR of a conditionally repressible TCR may be an engineered TCR variant including but not limited to, e.g., TCR variants that include one or more variant or mutant TCR chains. In some instances, the engineered TCR of a conditionally repressible TCR may include one or more non-modified chains, including but not limited to a non-modified alpha chain, a non-modified beta chain, etc. In some instances, the engineered TCR of a conditionally repressible TCR may include one or more murinized chains, including but not limited to, e.g., a murinized alpha chain, a murinized beta chain, etc. In some instances, the engineered TCR of a conditionally repressible TCR may include one or more cysteine modified chains, including but not limited to, e.g., a cysteine modified alpha chain, a cysteine modified beta chain, etc. In some instances, the engineered TCR of a conditionally repressible TCR may include a combination of variant TCR chains, including but not limited to a combination of murinized and cysteine-modified chains, including but not limited to, e.g., a murinized and cysteine-modified alpha chain, a murinized and cysteine-modified beta chain, a murinized alpha chain and cysteine-modified beta chain, a murinized beta chain and cysteine-modified alpha chain, etc.

[00584] In instances where a heteromeric, conditionally repressible synthetic ICR includes, in part or in whole, or the heteromeric, conditionally repressible synthetic ICR is essentially a modified TCR, the TCR may contain non-modified TRC chains having extracellular domains or the extracellular domains therefore present in modified TCR chains, one or more intracellular stimulatory domains present in non-modified or modified TCR chains and the transmembrane domains of such extracellular domain-containing or intracellular domain-containing chains. Such a TCR may optionally include linker regions and/or hinge regions. TCRs as part of a heteromeric, conditionally repressible synthetic ICR may be encompassed within a single polypeptide (e.g., as in engineered single chain TCRs) or various chains and portions thereof may be "split" across two or more polypeptides.

TCR Chains

[00585] Many native TCRs exist in heterodimeric αβ or γδ forms. However, recombinant or engineered TCR may include a single TCR α or TCR β chain and may bind to peptide MHC molecules. In certain embodiments, an engineered TCR of a repressible ICR includes both an α chain variable domain and an TCR β chain variable domain. The chains of an engineered TCR useful in a repressible ICR of the instant

disclosure may vary and may include any suitable native or synthetic or recombinant or mutant TCR chain or chains or combination thereof.

[00586] As will be apparent to those skilled in the art the mutation(s) in TCR chain sequence, including e.g., α chain sequence and/or TCR β chain sequence, may be one or more of substitution(s), deletion(s) or insertion(s). These mutations can be carried out using any appropriate method including, but not limited to, those based on polymerase chain reaction (PCR), restriction enzyme-based cloning, or ligation independent cloning (LIC) procedures. These methods are detailed in many standard molecular biology texts, including but not limited to e.g., Sambrook & Russell, (2001) Molecular Cloning—A Laboratory Manual (3rd Ed.) CSHL Press and Rashtchian, (1995) *Curr Opin Biotechnol* 6 (1): 30-6.

[00587] As used herein the term "variable domain" is understood to encompass all amino acids of a given TCR which are not included within the constant domain as encoded by the TRAC gene for TCR α chains and either the TRBC1 or TRBC2 for TCR β chains as described in, e.g., *T cell receptor Factsbook*, (2001) LeFranc and LeFranc, Academic Press.

[00588] In some instances, an engineered TCR has at least one TCR α chain domain having or derived from an amino acid sequence that is at least 70% identical, including at least 75% identical to, including at least 80% identical to, including at least 85% identical to, including at least 90% identical to, including at least 95% identical to or is 100% identical to the IG4 α chain amino acid sequence: METLLGLLILWLQLQWVSSKQEVTQIPAALSVPEGENLVLNCSFTDSAIYNLQWFRQDPGKGLT SLLLIQSSQREQTSGRLNASLDKSSGRSTLYIAASQPGDSATYLCAVRPTSGGSYIPTFGRGTSLIV HPPNIQNPDPAVYQLRDSKSSDKSVCLFTDFDSQTNVSQSKDSDVYITDKTVLDMRSMDFKSNS AVAWSNKSDFACANAFNNSIIPEDTFFPSPESSCDVKLVEKSFETDTNLNFQNLSVIGFRILLLKV AGFNLLMTLRLWSS (SEQ ID NO:675).

[00589] In some instances, an engineered TCR has at least one TCR α chain domain having or derived from an amino acid sequence that is at least 70% identical, including at least 75% identical to, including at least 80% identical to, including at least 85% identical to, including at least 90% identical to, including at least 95% identical to or is 100% identical to the IG4 α chain A95:LY mutant amino acid sequence: METLLGLLILWLQLQWVSSKQEVTQIPAALSVPEGENLVLNCSFTDSAIYNLQWFRQDPGKGLT SLLLIQSSQREQTSGRLNASLDKSSGRSTLYIAASQPGDSATYLCAVRPLYGGSYIPTFGRGTSLIV HPPNIQNPDPAVYQLRDSKSSDKSVCLFTDFDSQTNVSQSKDSDVYITDKTVLDMRSMDFKSNS AVAWSNKSDFACANAFNNSIIPEDTFFPSPESSCDVKLVEKSFETDTNLNFQNLSVIGFRILLLKV AGFNLLMTLRLWSS (SEQ ID NO:676).

[00590] In some instances, an engineered TCR has at least one TCR β chain domain having or derived from an amino acid sequence that is at least 70% identical, including at least 75% identical to, including at least 80% identical to, including at least 85% identical to, including at least 90% identical to, including at

least 95% identical to or is 100% identical to the IG4 β chain amino acid sequence: MSIGLLCCAALSLLWAGPVNAGVTQTPKFQVLKTGQSMTLQCAQDMNHEYMSWYRQDPGMG LRLIHYSVGAGITDQGEVPNGYNVSRSTTEDFPLRLLSAAPSQTSVYFCASSYVGNTGELFFGEG SRLTVLEDLNKVFPPEVAVFEPSEAEISHTQKATLVCLATGFFPDHVELSWWVNGKEVHSGVST DPQPLKEQPALNDSRYCLSSRLRVSATFWQNPRNHFRCQVQFYGLSENDEWTQDRAKPVTQIV SAEAWGRADCGFTSVSYQQGVLSATILYEILLGKATLYAVLVSALVLMAMVKRKDF (SEQ ID NO:677).

[00591] In some instances, an engineered TCR has at least one TCR β chain domain having or derived from an amino acid sequence that is at least 70% identical, including at least 75% identical to, including at least 80% identical to, including at least 85% identical to, including at least 90% identical to, including at least 95% identical to or is 100% identical to the IG4 β chain G51A mutant amino acid sequence: MSIGLLCCAALSLLWAGPVNAGVTQTPKFQVLKTGQSMTLQCAQDMNHEYMSWYRQDPGMG LRLIHYSVAAGITDQGEVPNGYNVSRSTTEDFPLRLLSAAPSQTSVYFCASSYVGNTGELFFGEG SRLTVLEDLNKVFPPEVAVFEPSEAEISHTQKATLVCLATGFFPDHVELSWWVNGKEVHSGVST DPQPLKEQPALNDSRYCLSSRLRVSATFWQNPRNHFRCQVQFYGLSENDEWTQDRAKPVTQIV SAEAWGRADCGFTSVSYQQGVLSATILYEILLGKATLYAVLVSALVLMAMVKRKDF (SEQ ID NO:678).

[00592] In some instances, a NY-ESO-1-binding TCR has at least one TCR α chain variable domain having an amino acid sequence that is at least 70% identical, including at least 75% identical to, including at least 80% identical to, including at least 85% identical to, including at least 90% identical to, including at least 95% identical to or is 100% identical to the α chain extracellular sequence: MQEVTQIPAALSVPEGENLVLNCSFTDSAIYNLQWFRQDPGKGLTSLLLIQSSQREQTSGRLNAS LDKSSGRSTLYIAASQPGDSATYLCAVRPTSGGSYIPTFGRGTSLIVHPYIQNPDPAVYQLRDSKS SDKSVCLFTDFDSQTNVSQSKDSDVYITDKTVLDMRSMDFKSNSAVAWSNKSDFACANAFNNS IIPEDTFFPSPESS (SEQ ID NO:679). In some instances, the α chain extracellular sequence contains one or more of the following amino acid substitutions: T95L and S96Y.

[00593] In some instances, a NY-ESO-1-binding TCR has at least one TCR β chain variable domain having an amino acid sequence that is at least 70% identical, including at least 75% identical to, including at least 80% identical to, including at least 85% identical to, including at least 90% identical to, including at least 95% identical to or is 100% identical to the β chain extracellular sequence: MGVTQTPKFQVLKTGQSMTLQCAQDMNHEYMSWYRQDPGMGLRLIHYSVGAGITDQGEVPN GYNVSRSTTEDFPLRLLSAAPSQTSVYFCASSYVGNTGELFFGEGSRLTVLEDLKNVFPPEVAVF EPSEAEISHTQKATLVCLATGFYPDHVELSWWVNGKEVHSGVSTDPQPLKEQPALNDSRYALSS RLRVSATFWQDPRNHFRCQVQFYGLSENDEWTQDRAKPVTQIVSAEAWGRAD (SEQ ID NO:680).

[00594] In some instances, the engineered TCR include an introduced disulfide bond between cysteines. For example, disulfide bond between cysteines may be introduced between substitute amino acids of two chains of the engineered including but not limited to, e.g., between an α chain and a β chain of the TCR. In some instances an engineered TCR may be a NY-ESO-1-binding TCR that includes a disulfide bond between cysteines of substitute amino acids of two chains of the engineered NY-ESO-1-binding TCR including but not limited to, e.g., between an α chain and a β chain of the engineered NY-ESO-1-binding TCR. For example, in some instances, an engineered NY-ESO-1-binding TCR may include a disulfide bond between cysteines substituted for alpha chain T162 and beta chain S169 of SEQ ID NOs:679-680. Linkers

[00595] In some cases, a subject conditionally repressible TCR includes a linker between any two adjacent domains or artificially linked chains. For example, a linker can be disposed between the intracellular potion of a transmembrane domain of an alpha chain and a dimerizer domain of the conditionally repressible TCR. In some instances, a linker can be disposed between the intracellular potion of a transmembrane domain of a beta chain and a dimerizer domain of the conditionally repressible TCR. In some instances, a linker can be disposed between the transmembrane domain of an alpha chain and the first intracellular functional domain of a linked CD3-zeta chain of the conditionally repressible TCR. In some instances, a linker can be disposed between the transmembrane domain of a beta chain and the first intracellular functional domain of a linked CD3-zeta chain of the conditionally repressible TCR. As another example, a linker can be disposed between any domain of the conditionally repressible TCR and any additional domain including e.g., a domain not involved in the primary immune activation functions of the conditionally repressible TCR including but not limited to e.g., a reporter domain, a tag domain, etc.

[00596] Linkers may be utilized in a suitable configuration in the conditionally repressible TCR provided they do not abolish the primary activities of the conditionally repressible TCR including, e.g., the ability of the conditionally repressible TCR to activate an immune cell, the ability of the dimerization domain of the conditionally repressible TCR to bind the dimerization domain of the synthetic ICR repressor, etc.

[00597] Any suitable linker, including two or more linkers (e.g., where the two or more linkers are the same or different and including where the multiple linkers are three or more, four or more , five or more, six or more, etc. and including where all the linkers are different and where the multiple linkers include an mix of some linkers utilized in more than one location and some linkers utilized specifically in only one location and the like) may be utilized in the subject conditionally repressible TCRs including e.g., those linkers described herein for acceptable use in a CAR.

Synthetic ICR Repressor

[00598] As described herein, a heteromeric, conditionally repressible synthetic ICR includes a synthetic ICR repressor, also referred to herein as an "ICR repressor" or "inhibitory part" for simplicity. Such

inhibitory ICRs will vary depending on the particular context of immune cell repression to which the construct is directed and will generally function to mediate repression of an activated or activatable immune cell expressing a stimulatory ICR and the ICR repressor. Thus, an ICR repressor includes an inhibitory domain that functions to repress immune cell activation attributed to the stimulatory ICR upon dimerization of reciprocal dimerizer domains present in the ICR repressor and the stimulatory ICR when dimerizer is present.

[00599] A ICR repressor therefore includes one or more intracellular inhibitory domains that mediates intracellular signaling leading to inhibition of immune cell activation in immune cells expressing the stimulatory ICR. Domains useful as inhibitory domains will vary depending on the particular context of immune cell activation and repression, including e.g., the particular type of activated cell to be repressed and the desired degree of repression. Exemplary non-limited examples of inhibitory domains, described in greater detail below, include but are not limited to domains and motifs thereof derived from immune receptors including, e.g., co-inhibitory molecules, immune checkpoint molecules, immune tolerance molecules, and the like.

[00600] An ICR repressor further includes, as described in more detail below, a domain of a dimerization pair. Useful dimerization domains will vary depending on the desired dimerizer and the desired relative position of the dimerization domain within the ICR repressor. Generally, the presence of a first domain of a dimerization pair within the stimulatory ICR mediates the dimerization, upon introduction of the dimerizer, with a second domain of the dimerization pair present in the ICR repressor such that upon dimerization the ICR repressor represses immune cell activation due to the stimulatory ICR.

[00601] An ICR repressor may, optionally, include a transmembrane domain. As such, ICR repressors as described herein may or may not be membrane tethered. As such, an ICR repressor may contain a transmembrane domain, or portion thereof, and thus may be a membrane-bound ICR repressor. In other instances, an ICR repressor may lack a transmembrane domain and thus may be a cytosolic ICR repressor. Such transmembrane domains useful in an ICR repressor of the instant disclosure are described further herein.

[00602] In some instances, an ICR repressor may further include additional domains. Such additional domains may be functional, e.g., they directly contribute to the immune cell activation inhibition function of the ICR repressor, or non-functional, e.g., they do not directly contribute to the repression function of the ICR repressor. Non-functional additional domains may include domains having various purposes that do not directly affect the ability of the ICR repressor to repress immune cell activation including, but not limited to, e.g., structural functions, linker functions, etc.

Intracellular Inhibitory Domain

[00603] A stimulatory domain suitable for use in a synthetic ICR repressor of a subject repressible ICR may be any functional unit of a polypeptide as short as a 3 amino acid linear motif and as long as an entire protein, where size of the stimulatory domain is restricted only in that the domain must be sufficiently large as to retain its function and sufficiently small so as to be compatible with the other components of the repressible ICR. Accordingly, an inhibitory domain may range in size from 3 amino acids in length to 1000 amino acids or more and, in some instances, can have a length of from about 30 amino acids to about 70 amino acids (aa), e.g., an inhibitory domain can have a length of from about 30 aa to about 35 aa, from about 35 aa to about 40 aa, from about 40 aa to about 45 aa, from about 45 aa to about 50 aa, from about 50 aa to about 55 aa, from about 55 aa to about 60 aa, from about 60 aa to about 65 aa, or from about 65 aa to about 70 aa. In other cases, stimulatory domain can have a length of from about 70 aa to about 100 aa, from about 100 aa to about 200 aa, or greater than 200 aa.

[00604] In some instances, "co-inhibitory domains" find use in the synthetic ICR repressor of the present disclosure. Such co- inhibitory domains are generally polypeptides derived from receptors. Co-inhibition generally refers to the secondary inhibition of primary antigen-specific activation mechanisms which prevents co-stimulation. Co-inhibition, e.g., T cell co-inhibition, and the factors involved have been described in Chen & Flies. *Nat Rev Immunol* (2013) 13(4):227-42 and Thaventhiran et al. *J Clin Cell Immunol* (2012) S12, the disclosures of which are incorporated herein by reference in their entirety. In some embodiments, co-inhibitory domains homodimerize. A subject co-inhibitory domain can be an intracellular portion of a transmembrane protein (i.e., the co-inhibitory domain can be derived from a transmembrane protein). Non-limiting examples of suitable co-inhibitory polypeptides include, but are not limited to, CTLA-4 and PD-1. In some instances, a co-inhibitory domain, e.g., as used in a synthetic ICR repressor of the instant disclosure may include a co-inhibitory domain listed in FIG. 27, which provides **Table 1**. In some instances, a co- inhibitory domain of a synthetic ICR repressor comprises an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100% amino acid sequence identity to a co-inhibitory domain as described herein.

[00605] In some instances, a synthetic ICR repressor may contain an intracellular signaling domain, e.g., a co-inhibitory domain, derived from an intracellular portion of the transmembrane protein PD-1 (also known as CD279, programed cell death 1; etc.). For example, a suitable co-inhibitory domain can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100% amino acid sequence identity to the following amino acid sequence:
ICSRAARGTIGARRTGQPLKEDPSAVPVFSVDYGELDFQWREKTPEPPVPCVPEQTEYATIVFPS
GMGTSSPARRGSADGPRSAQPLRPEDGHCSWPL (SEQ ID NO:681). In some of these

embodiments, the co-inhibitory domain has a length of from about 30 aa to about 35 aa, from about 35 aa to about 40 aa, from about 40 aa to about 45 aa, from about 45 aa to about 50 aa, from about 50 aa to about 55 aa, from about 55 aa to about 60 aa, from about 60 aa to about 65 aa, from about 65 aa to about 70 aa, from about 70 aa to about 75 aa, from about 75 aa to about 80 aa, from about 80 aa to about 85 aa, from about 85 aa to about 90 aa, from about 90 aa to about 95 aa, or from about 95 aa to about 100 aa.

[00606] In some instances, a synthetic ICR repressor may contain an intracellular signaling domain, e.g., a co-inhibitory domain, derived from an intracellular portion of the transmembrane protein CTLA4 (also known as CD152, Cytotoxic T-lymphocyte protein 4, Cytotoxic T-lymphocyte-associated antigen 4 ; etc.). For example, a suitable co-inhibitory domain can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100% amino acid sequence identity to the following amino acid sequence: SLSKMLKKRSPLTTGVYVKMPPTEPECEKQFQPYFIPIN (SEQ ID NO:682). In some of these embodiments, the co-inhibitory domain has a length of from about 30 aa to about 35 aa, from about 35 aa to about 40 aa, from about 40 aa to about 45 aa, from about 45 aa to about 50 aa, from about 50 aa to about 55 aa, from about 55 aa to about 60 aa, from about 60 aa to about 65 aa, or from about 65 aa to about 70 aa.

[00607] In some instances, a synthetic ICR repressor may contain an intracellular signaling domain, e.g., a co-inhibitory domain, derived from an intracellular portion of the transmembrane protein HPK1 (also known as MAP4K1, Mitogen-activated protein kinase kinase kinase kinase 1, Hematopoietic progenitor kinase, MAPK/ERK kinase kinase kinase 1, MEK kinase kinase 1, MEKKK 1; etc.). For example, a suitable co-inhibitory domain can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100% amino acid sequence identity to the following amino acid sequence: YDLLQRLGGGTYGEVFKARDKVSGDLVALKMVKMEPDDDVSTLQKEILILKTCRHANIVAYH GSYLWLQKLWICMEFCGAGSLQDIYQVTGSLSELQISYVCREVLQGLAYLHSQKKIHRDIKGAN ILINDAGEVRLADFGISAQIGATLARRLSFIGTPYWMAPEVAAVALKGGYNELCDIWSLGITAIEL AELQPPLFDVHPLRVLFLMTKSGYQPPRLKEKGKWSAAFHNFIKVTLTKSPKKRPSATKMLSHQ LV (SEQ ID NO:683). In some of these embodiments, the co-inhibitory domain has a length of from about 30 aa to about 35 aa, from about 35 aa to about 40 aa, from about 40 aa to about 45 aa, from about 45 aa to about 50 aa, from about 50 aa to about 55 aa, from about 55 aa to about 60 aa, from about 60 aa to about 65 aa, from about 65 aa to about 70 aa, from about 70 aa to about 75 aa, from about 75 aa to about 80 aa, from about 80 aa to about 85 aa, from about 85 aa to about 90 aa, from about 90 aa to about 95 aa, from about 95 aa to about 100 aa, from about 100 aa to about 105 aa, from about 105 aa to about 110 aa, from about 110 aa to about 115 aa, from about 115 aa to about 120 aa, from about 120 aa to about 125 aa, from about 125 aa to about 130 aa, from about 130 aa to about 135 aa, from about 135 aa

to about 140 aa, from about 140 aa to about 145 aa, from about 145 aa to about 150 aa, from about 150 aa to about 155 aa, from about 155 aa to about 160 aa, from about 160 aa to about 165 aa, from about 165 aa to about 170 aa, from about 170 aa to about 175 aa, from about 175 aa to about 180 aa, from about 180 aa to about 185 aa, from about 185 aa to about 190 aa, from about 190 aa to about 195 aa, from about 195 aa to about 200 aa, from about 200 aa to about 205 aa, from about 205 aa to about 210 aa, from about 210 aa to about 215 aa, from about 215 aa to about 220 aa, from about 220 aa to about 225 aa, from about 225 aa to about 230 aa, from about 230 aa to about 235 aa, from about 235 aa to about 240 aa, from about 240 aa to about 245 aa, from about 245 aa to about 250 aa, from about 250 aa to about 255 aa or from about 255 aa to about 258 aa.

[00608] In some instances, a synthetic ICR repressor may contain an intracellular signaling domain, e.g., a co-inhibitory domain, derived from an intracellular portion of the transmembrane protein SHP1 (also known as PTN6, Tyrosine-protein phosphatase non-receptor type 6, Hematopoietic cell protein-tyrosine phosphatase, Protein-tyrosine phosphatase 1C, PTP-1C, SH-PTP1, HCP, PTP1C; etc.). For example, a suitable co-inhibitory domain can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100% amino acid sequence identity to the following amino acid sequence: FWEEFESLQKQEVKNLHQRLEGQRPENKGKNRYKNILPFDHSRVILQGRDSNIPGSDYINANYIK NQLLGPDENAKTYIASQGCLEATVNDFWQMAWQENSRVIVMTTREVEKGRNKCVPYWPEVG MQRAYGPYSVTNCGEHDTTEYKLRTLQVSPLDNGDLIREIWHYQYLSWPDHGVPSEPGGVLSF LDQINQRQESLPHAGPIIVHCSAGIGRTGTIIVIDMLMENISTKGLDCDIDIQKTIQMVRAQRSGM VQTEAQYKFIYVAIAQF (SEQ ID NO:684). In some of these embodiments, the co-inhibitory domain has a length of from about 30 aa to about 35 aa, from about 35 aa to about 40 aa, from about 40 aa to about 45 aa, from about 45 aa to about 50 aa, from about 50 aa to about 55 aa, from about 55 aa to about 60 aa, from about 60 aa to about 65 aa, or from about 65 aa to about 70 aa, from about 70 aa to about 75 aa, from about 75 aa to about 80 aa, from about 80 aa to about 85 aa, from about 85 aa to about 90 aa, from about 90 aa to about 95 aa, from about 95 aa to about 100 aa, from about 100 aa to about 105 aa, from about 105 aa to about 110 aa, from about 110 aa to about 115 aa, from about 115 aa to about 120 aa, from about 120 aa to about 125 aa, from about 125 aa to about 130 aa, from about 130 aa to about 135 aa, from about 135 aa to about 140 aa, from about 140 aa to about 145 aa, from about 145 aa to about 150 aa, from about 150 aa to about 155 aa, from about 155 aa to about 160 aa, from about 160 aa to about 165 aa, from about 165 aa to about 170 aa, from about 170 aa to about 175 aa, from about 175 aa to about 180 aa, from about 180 aa to about 185 aa, from about 185 aa to about 190 aa, from about 190 aa to about 195 aa, from about 195 aa to about 200 aa, from about 200 aa to about 205 aa, from about 205 aa to about 210 aa, from about 210 aa to about 215 aa, from about 215 aa to about 220 aa, from about 220 aa to about 225 aa, from about 225 aa to about 230 aa, from about 230 aa to about 235

aa, from about 235 aa to about 240 aa, from about 240 aa to about 245 aa, from about 245 aa to about 250 aa, from about 250 aa to about 255 aa, from about 255 aa to about 260 aa, from about 260 aa to about 265 aa, from about 265 aa to about 270 aa or from about 270 aa to about 272 aa.

[00609] In some instances, a synthetic ICR repressor may contain an intracellular signaling domain, e.g., a co-inhibitory domain, derived from an intracellular portion of the transmembrane protein SHP2 (also known as PTN11, Tyrosine-protein phosphatase non-receptor type 11, Protein-tyrosine phosphatase 1D, PTP-1D, Protein-tyrosine phosphatase 2C, PTP-2C, SH-PTP2, SHP-2, SH-PTP3, PTP2C, SHPTP2; etc.). For example, a suitable co-inhibitory domain can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100% amino acid sequence identity to the following amino acid sequence: FWEEFETLQQQECKLLYSRKEGQRQENKNKNRYKNILPFDHTRVVLHDGDPNEPVSDYINANII MPEFETKCNNSKPKKSYIATQGCLQNTVNDFWRMVFQENSRVIVMTTKEVERGKSKCVKYWP DEYALKEYGVMRVRNVKESAAHDYTLRELKLSKVGQALLQGNTERTVWQYHFRTWPDHGVP SDPGGVLDFLEEVHHKQESIMDAGPVVVHCSAGIGRTGTFIVIDILIDIIREKGVDCDIDVPKTIQM VRSQRSGMVQTEAQYRFIYMA (SEQ ID NO:685). In some of these embodiments, the co-inhibitory domain has a length of from about 30 aa to about 35 aa, from about 35 aa to about 40 aa, from about 40 aa to about 45 aa, from about 45 aa to about 50 aa, from about 50 aa to about 55 aa, from about 55 aa to about 60 aa, from about 60 aa to about 65 aa, or from about 65 aa to about 70 aa, from about 70 aa to about 75 aa, from about 75 aa to about 80 aa, from about 80 aa to about 85 aa, from about 85 aa to about 90 aa, from about 90 aa to about 95 aa, from about 95 aa to about 100 aa, from about 100 aa to about 105 aa, from about 105 aa to about 110 aa, from about 110 aa to about 115 aa, from about 115 aa to about 120 aa, from about 120 aa to about 125 aa, from about 125 aa to about 130 aa, from about 130 aa to about 135 aa, from about 135 aa to about 140 aa, from about 140 aa to about 145 aa, from about 145 aa to about 150 aa, from about 150 aa to about 155 aa, from about 155 aa to about 160 aa, from about 160 aa to about 165 aa, from about 165 aa to about 170 aa, from about 170 aa to about 175 aa, from about 175 aa to about 180 aa, from about 180 aa to about 185 aa, from about 185 aa to about 190 aa, from about 190 aa to about 195 aa, from about 195 aa to about 200 aa, from about 200 aa to about 205 aa, from about 205 aa to about 210 aa, from about 210 aa to about 215 aa, from about 215 aa to about 220 aa, from about 220 aa to about 225 aa, from about 225 aa to about 230 aa, from about 230 aa to about 235 aa, from about 235 aa to about 240 aa, from about 240 aa to about 245 aa, from about 245 aa to about 250 aa, from about 250 aa to about 255 aa, from about 255 aa to about 260 aa, from about 260 aa to about 265 aa, from about 265 aa to about 270 aa or from about 270 aa to about 275 aa.

[00610] In some instances, a synthetic ICR repressor may contain an intracellular signaling domain, e.g., a co-inhibitory domain, derived from an intracellular portion of the transmembrane protein Sts1 (also known as UBS3B, Ubiquitin-associated and SH3 domain-containing protein B, Cbl-interacting protein

p70, Suppressor of T-cell receptor signaling 1, STS-1, T-cell ubiquitin ligand 2, TULA-2, Tyrosine-protein phosphatase STS1/TULA2, UBASH3B, KIAA1959; etc.). For example, a suitable co-inhibitory domain can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100% amino acid sequence identity to the following amino acid sequence:
GPQKRCLFVCRHGERMDVVFGKYWLSQCFDAKGRYIRTNLNMPHSLPQRSGGFRDYEKDAPIT
VFGCMQARLVGEALLESNTIIDHVYCSPSLRCVQTAHNILKGLQQENHLKIRVEPGLFEWTKWV
AGSTLPAWIPPSELAAANLSVDTTYRPHIPISKLVVSESYDTYISRSFQVTKEIISECKSKGNNILIV
AHASSLEACTCQLQGLSPQNSKDFVQMVRKIPYLGFCSCEELGETGIWQLTDPPILPLTHGPTGG
FNWRETLLQE (SEQ ID NO:686). In some of these embodiments, the co-inhibitory domain has a length of from about 30 aa to about 35 aa, from about 35 aa to about 40 aa, from about 40 aa to about 45 aa, from about 45 aa to about 50 aa, from about 50 aa to about 55 aa, from about 55 aa to about 60 aa, from about 60 aa to about 65 aa, or from about 65 aa to about 70 aa, from about 70 aa to about 75 aa, from about 75 aa to about 80 aa, from about 80 aa to about 85 aa, from about 85 aa to about 90 aa, from about 90 aa to about 95 aa, from about 95 aa to about 100 aa, from about 100 aa to about 105 aa, from about 105 aa to about 110 aa, from about 110 aa to about 115 aa, from about 115 aa to about 120 aa, from about 120 aa to about 125 aa, from about 125 aa to about 130 aa, from about 130 aa to about 135 aa, from about 135 aa to about 140 aa, from about 140 aa to about 145 aa, from about 145 aa to about 150 aa, from about 150 aa to about 155 aa, from about 155 aa to about 160 aa, from about 160 aa to about 165 aa, from about 165 aa to about 170 aa, from about 170 aa to about 175 aa, from about 175 aa to about 180 aa, from about 180 aa to about 185 aa, from about 185 aa to about 190 aa, from about 190 aa to about 195 aa, from about 195 aa to about 200 aa, from about 200 aa to about 205 aa, from about 205 aa to about 210 aa, from about 210 aa to about 215 aa, from about 215 aa to about 220 aa, from about 220 aa to about 225 aa, from about 225 aa to about 230 aa, from about 230 aa to about 235 aa, from about 235 aa to about 240 aa, from about 240 aa to about 245 aa, from about 245 aa to about 250 aa, from about 250 aa to about 255 aa, from about 255 aa to about 260 aa, from about 260 aa to about 265 aa or from about 265 aa to about 270 aa.

[00611] In some instances, a synthetic ICR repressor may contain an intracellular signaling domain, e.g., a co-inhibitory domain, derived from an intracellular portion of the transmembrane protein Csk (also known as Tyrosine-protein kinase CSK, C-Src kinase, Protein-tyrosine kinase CYL; etc.). For example, a suitable co-inhibitory domain can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100% amino acid sequence identity to the following amino acid sequence:
LKLLQTIGKGEFGDVMLGDYRGNKVAVKCIKNDATAQAFLAEASVMTQLRHSNLVQLLGVIVE
EKGGLYIVTEYMAKGSLVDYLRSRGRSVLGGDCLLKFSLDVCEAMEYLEGNNFVHRDLAARN

VLVSEDNVAKVSDFGLTKEASSTQDTGKLPVKWTAPEALREKKFSTKSDVWSFGILLWEIYSFG RVPYPRIPLKDVVPRVEKGYKMDAPDGCPPAVYEVMKNCWHLDAAMRPSFLQLREQLEHIKT HELH (SEQ ID NO:687). In some of these embodiments, the co-inhibitory domain has a length of from about 30 aa to about 35 aa, from about 35 aa to about 40 aa, from about 40 aa to about 45 aa, from about 45 aa to about 50 aa, from about 50 aa to about 55 aa, from about 55 aa to about 60 aa, from about 60 aa to about 65 aa, or from about 65 aa to about 70 aa, from about 70 aa to about 75 aa, from about 75 aa to about 80 aa, from about 80 aa to about 85 aa, from about 85 aa to about 90 aa, from about 90 aa to about 95 aa, from about 95 aa to about 100 aa, from about 100 aa to about 105 aa, from about 105 aa to about 110 aa, from about 110 aa to about 115 aa, from about 115 aa to about 120 aa, from about 120 aa to about 125 aa, from about 125 aa to about 130 aa, from about 130 aa to about 135 aa, from about 135 aa to about 140 aa, from about 140 aa to about 145 aa, from about 145 aa to about 150 aa, from about 150 aa to about 155 aa, from about 155 aa to about 160 aa, from about 160 aa to about 165 aa, from about 165 aa to about 170 aa, from about 170 aa to about 175 aa, from about 175 aa to about 180 aa, from about 180 aa to about 185 aa, from about 185 aa to about 190 aa, from about 190 aa to about 195 aa, from about 195 aa to about 200 aa, from about 200 aa to about 205 aa, from about 205 aa to about 210 aa, from about 210 aa to about 215 aa, from about 215 aa to about 220 aa, from about 220 aa to about 225 aa, from about 225 aa to about 230 aa, from about 230 aa to about 235 aa, from about 235 aa to about 240 aa, from about 240 aa to about 245 aa, from about 245 aa to about 250 aa or from about 250 aa to about 255 aa.

[00612] In some instances, a synthetic ICR repressor may contain an intracellular signaling domain, e.g., a co-inhibitory domain, derived from an intracellular portion of a transmembrane protein listed in **Table 1**. For example, a suitable co-inhibitory domain can comprise an amino acid sequence having at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or 100% amino acid sequence identity to an amino acid sequence listed in **Table 1**. In some of these embodiments, the co-inhibitory domain has a length of from about 30 aa to about 35 aa, from about 35 aa to about 40 aa, from about 40 aa to about 45 aa, from about 45 aa to about 50 aa, from about 50 aa to about 55 aa, from about 55 aa to about 60 aa, from about 60 aa to about 65 aa, or from about 65 aa to about 70 aa, from about 70 aa to about 75 aa, from about 75 aa to about 80 aa, from about 80 aa to about 85 aa, from about 85 aa to about 90 aa, from about 90 aa to about 95 aa, from about 95 aa to about 100 aa, from about 100 aa to about 105 aa, from about 105 aa to about 110 aa, from about 110 aa to about 115 aa, from about 115 aa to about 120 aa, from about 120 aa to about 125 aa, from about 125 aa to about 130 aa, from about 130 aa to about 135 aa, from about 135 aa to about 140 aa, from about 140 aa to about 145 aa, from about 145 aa to about 150 aa, from about 150 aa to about 155 aa, from about 155 aa to about 160 aa, from about 160 aa to about 165, aa from about 165 aa to about 170 aa, from about

170 aa to about 175 aa, from about 175 aa to about 180 aa, from about 180 aa to about 185 aa, or from about 185 aa to about 190 aa.

Transmembrane Domain

[00613] Any transmembrane (TM) domain that provides for insertion of a polypeptide into the cell membrane of a eukaryotic (e.g., mammalian) cell is suitable for use. As one non-limiting example, the TM sequence IYIWAPLAGTCGVLLLSLVITLYC (SEQ ID NO:688) can be used. Additional non-limiting examples of suitable TM sequences include: a) CD8 beta derived : LGLLVAGVLVLLVSLGVAIHLCC (SEQ ID NO:689); b) CD4 derived: ALIVLGGVAGLLLFIGLGIFFCVRC (SEQ ID NO:690); c) CD3 zeta derived: LCYLLDGILFIYGVILTALFLRV (SEQ ID NO:691); d) CD28 derived: WVLVVVGGVLACYSLLVTVAFIIFWV (SEQ ID NO:692); e) CD134 (OX40) derived: VAAILGLGLVLGLLGPLAILLALYLL (SEQ ID NO:693); and f) CD7 derived: ALPAALAVISFLLGLGLGVACVLA (SEQ ID NO:694).

Linkers

[00614] In some cases, a subject synthetic ICR repressor includes a linker between any two adjacent domains. For example, a linker can be disposed between the transmembrane domain, where present, and the first intracellular functional domain, e.g., a co-inhibitory domain, of the synthetic ICR repressor. As another example, a linker can be disposed between a first intracellular functional domain and the member of the dimerization domain of the synthetic ICR repressor. As another example, a linker can be disposed the transmembrane domain, where present, and the member of the dimerization domain of the synthetic ICR repressor. As another example, a linker can be disposed between the member of the dimerization domain and a second intracellular functional domain, e.g., an immune cell negative regulatory domain. As another example, a linker can be disposed between any domain of the synthetic ICR repressor and any additional domain including e.g., a domain not involved in the primary immune repression functions of the synthetic ICR repressor including but not limited to e.g., a reporter domain, a tag domain, etc.

[00615] Linkers may be utilized in a suitable configuration in the synthetic ICR repressor provided they do not abolish the primary activities of the synthetic ICR repressor including, e.g., the ability of the synthetic ICR repressor to repress an activated ICR, the ability of the dimerization domain of the synthetic ICR repressor to bind the dimerization domain of the repressible ICR.

[00616] Any suitable linker, including two or more linkers (e.g., where the two or more linkers are the same or different and including where the multiple linkers are three or more, four or more , five or more, six or more, etc. and including where all the linkers are different and where the multiple linkers include an mix of some linkers utilized in more than one location and some linkers utilized specifically in only one location and the like) may be utilized in the subject synthetic ICR repressors including e.g., those linkers described herein for acceptable use in a CAR.

Additional Sequences

[00617] The heteromeric, conditionally repressible synthetic ICR of the instant disclosure may further include one or more additional polypeptide domains, where such domains include, but are not limited to, a signal sequence; an epitope tag; an affinity domain; and a polypeptide that produces a detectable signal.

Signal sequences

[00618] Signal sequences that are suitable for use in a subject repressible synthetic ICR, e.g., in the stimulatory ICR or the ICR repressor, include any eukaryotic signal sequence, including a naturally-occurring signal sequence, a synthetic (e.g., man-made) signal sequence, etc.

Epitope tag

[00619] Suitable epitope tags include, but are not limited to, hemagglutinin (HA; e.g., YPYDVPDYA (SEQ ID NO:594); FLAG (e.g., DYKDDDDK (SEQ ID NO:595); c-myc (e.g., EQKLISEEDL; SEQ ID NO:596), and the like.

Affinity domain

[00620] Affinity domains include peptide sequences that can interact with a binding partner, e.g., such as one immobilized on a solid support, useful for identification or purification. DNA sequences encoding multiple consecutive single amino acids, such as histidine, when fused to the expressed protein, may be used for one-step purification of the recombinant protein by high affinity binding to a resin column, such as nickel sepharose. Exemplary affinity domains include His5 (HHHHH) (SEQ ID NO:597), HisX6 (HHHHHH) (SEQ ID NO:598), C-myc (EQKLISEEDL) (SEQ ID NO:599), Flag (DYKDDDDK) (SEQ ID NO:600), StrepTag (WSHPQFEK) (SEQ ID NO:601), hemagglutinin, e.g., HA Tag (YPYDVPDYA) (SEQ ID NO:602), GST, thioredoxin, cellulose binding domain, RYIRS (SEQ ID NO:603), Phe-His-His-Thr (SEQ ID NO:604), chitin binding domain, S-peptide, T7 peptide, SH2 domain, C-end RNA tag, WEAAAREACCRECCARA (SEQ ID NO:605), metal binding domains, e.g., zinc binding domains or calcium binding domains such as those from calcium-binding proteins, e.g., calmodulin, troponin C, calcineurin B, myosin light chain, recoverin, S-modulin, visinin, VILIP, neurocalcin, hippocalcin, frequenin, caltractin, calpain large-subunit, S100 proteins, parvalbumin, calbindin D9K, calbindin D28K, and calretinin, inteins, biotin, streptavidin, MyoD, Id, leucine zipper sequences, and maltose binding protein.

Detectable signal-producing polypeptides

[00621] Suitable detectable signal-producing proteins include, e.g., fluorescent proteins; enzymes that catalyze a reaction that generates a detectable signal as a product; and the like.

[00622] Suitable fluorescent proteins include, but are not limited to, green fluorescent protein (GFP) or variants thereof, blue fluorescent variant of GFP (BFP), cyan fluorescent variant of GFP (CFP), yellow fluorescent variant of GFP (YFP), enhanced GFP (EGFP), enhanced CFP (ECFP), enhanced YFP (EYFP), GFPS65T, Emerald, Topaz (TYFP), Venus, Citrine, mCitrine, GFPuv, destabilised EGFP

(dEGFP), destabilised ECFP (dECFP), destabilised EYFP (dEYFP), mCFPm, Cerulean, T-Sapphire, CyPet, YPet, mKO, HcRed, t-HcRed, DsRed, DsRed2, DsRed-monomer, J-Red, dimer2, t-dimer2(12), mRFP1, pocilloporin, Renilla GFP, Monster GFP, paGFP, Kaede protein and kindling protein, Phycobiliproteins and Phycobiliprotein conjugates including B-Phycoerythrin, R-Phycoerythrin and Allophycocyanin. Other examples of fluorescent proteins include mHoneydew, mBanana, mOrange, dTomato, tdTomato, mTangerine, mStrawberry, mCherry, mGrape1, mRaspberry, mGrape2, mPlum (Shaner et al. (2005) *Nat. Methods* 2:905-909), and the like. Any of a variety of fluorescent and colored proteins from Anthozoan species, as described in, e.g., Matz et al. (1999) *Nature Biotechnol.* 17:969-973, is suitable for use.

[00623] Suitable enzymes include, but are not limited to, horse radish peroxidase (HRP), alkaline phosphatase (AP), beta-galactosidase (GAL), glucose-6-phosphate dehydrogenase, beta-N-acetylglucosaminidase, β-glucuronidase, invertase, Xanthine Oxidase, firefly luciferase, glucose oxidase (GO), and the like.

CONDITIONALLY ACTIVE DIMERIZATION-DEPENDENT CELL-SURFACE RECEPTORS

[00624] In some cases, a conditionally active heterodimeric polypeptide of the present disclosure is a conditionally active dimerization-dependent cell-surface receptor. By "conditionally active dimerization-dependent cell-surface receptor" is meant a variant of a cell surface receptor that is naturally dependent on dimerization for signal propagation, e.g., through ligand-binding induced dimerization, where the variant comprises a modification (e.g., a modification of a naturally-occurring cell surface receptor or other parental cell surface receptor) such that it includes one member of a dimerization pair and is conditionally dependent on dimerization of the dimerization pair induced by the presence of a dimerizing agent. As such, a conditionally acitive dimerization-dependent cell-surface receptor of the present disclosure will generally include a cell-surface receptor polypeptide which comprises a first member of a dimerization pair paired with a cell-surface receptor polypeptide which comprises a second member of the dimerization pair. For example, in some embodiments, a first dimerization-dependent cell-surface receptor that naturally forms a dimer in the presence of a ligand is modified to include a LBD of a nuclear hormone receptor and a second dimerization-dependent cell-surface receptor is modified to include a co-regulator of the nuclear hormone receptor such that the first dimerization-dependent cell-surface receptor and the second dimerization-dependent cell-surface receptor are dimerized in the presence of a dimerization agent that induces binding of the LBD to the co-regulator.

[00625] In some cases, the first and second dimerization-dependent cell-surface receptor may be the same dimerization-dependent cell-surface receptor, i.e., the first and second dimerization-dependent cell-surface receptors naturally form a homodimer in the presence of a dimerizing ligand. Accordingly, in some instances, the first and second conditionally acitive dimerization-dependent cell-surface receptors

may only differ in that one includes a LBD of a nuclear hormone receptor and the other includes a co-regulator of the nuclear hormone receptor.

[00626] In some cases, the first and second dimerization-dependent cell-surface receptor may be different dimerization-dependent cell-surface receptors, i.e., the first and second dimerization-dependent cell-surface receptors naturally form a heterodimer in the presence of a dimerizing ligand. Accordingly, in some instances, the first and second conditionally acitive dimerization-dependent cell-surface receptors may differ in one or more domains besides the LBD of a nuclear hormone receptor present in one member and the co-regulator of the nuclear hormone receptor present in the other member.

[00627] By "dimerization-dependent cell-surface receptor" is meant any cell-surface receptor polypeptide which depends upon dimerization with a second polypeptide to propagate an intracellular signal. In its natural context, a dimerization-dependent cell-surface receptor will generally dimerize in response to binding a ligand of the receptor. Useful dimerization-dependent cell-surface receptors include those that dimerize to form homodimers, those that dimerize to form heterodimers, as well as those that dimerize to form homodimers or heterodimers depending on the context.

[00628] Conditionally active dimerization-dependent cell-surface receptors of the present disclosure may be constructed in various ways. In some cases, a LBD of a nuclear hormone receptor or a co-regulator of a nuclear hormone receptor is appended to or recombinantly inserted into the otherwise unmodified dimerization-dependent cell-surface receptor. In some cases, one or more domains of the dimerization-dependent cell-surface receptor are replaced with a nuclear hormone receptor or a co-regulator of a nuclear hormone receptor. In some cases, a LBD of a nuclear hormone receptor or a co-regulator of a nuclear hormone receptor may be appended to or recombinantly inserted into a modified dimerization-dependent cell-surface receptor, e.g., a dimerization-dependent cell-surface receptor that has been modified to remove its natural ligand binding activity or other render it unable to bind its natural receptor ligand (e.g., by deletion of all or a potion of the endogenous ligand binding domain, buy mutation of the ligand binding domain, etc.). In some cases, the endogenous ligand binding domain of a dimerization-dependent cell-surface receptor may be replaced with a LBD of a nuclear hormone receptor or a co-regulator of a nuclear hormone receptor.

[00629] For example, in some embodiments, the endogengous ligand binding domain of a cytokine receptor may be replaced with a LBD of a nuclear hormone receptor or a co-regulator of a nuclear hormone receptor of the subject disclosure to generate a conditionally active dimerization-dependent cytokine receptor. In some embodiments, the endogengous ligand binding domain of a cytokine receptor may be completely or partially removed and a LBD of a nuclear hormone receptor or a co-regulator of a nuclear hormone receptor of the subject disclosure may be appended to or inserted into the modified cytokine receptor to generate a conditionally active dimerization-dependent cytokine receptor.

[00630] In some embodiments, the endogengous ligand binding domain of a RTK may be replaced with a LBD of a nuclear hormone receptor or a co-regulator of a nuclear hormone receptor of the subject disclosure to generate a conditionally active dimerization-dependent RTK. In some embodiments, the endogengous ligand binding domain of a RTK may be completely or partially removed and a LBD of a nuclear hormone receptor or a co-regulator of a nuclear hormone receptor of the subject disclosure may be appended to or inserted into the modified RTK to generate a conditionally active dimerization-dependent RTK.

Cytokine receptors

[00631] As noted above, useful non-limiting examples of dimerization-dependent cell-surface receptors include cytokine receptors, including e.g., cytokine receptors that form homodimers and cytokine receptors that form heterodimers. Useful cytokine receptors include but are not limited to e.g., IL-2 family receptors, IL-3 family receptors, IL-6 family receptors, IL-12 family receptors, prolactin family receptors, interferon family receptors, IL-10 family receptors, IL-17 family receptors, immunoglobulin-like superfamily receptors, tumor necrosis factor family receptors, chemokine receptors, TGF-beta family receptors, and the like.

[00632] Non-limiting examples of IL-2 family receptors include Interleukin 13 receptor, α2; Interleukin-2 receptor subunit α; Interleukin-2 receptor subunit β; Interleukin-2 receptor subunit γ; Interleukin-4 receptor subunit α ; Interleukin-7 receptor subunit α; Interleukin 9 receptor; Interleukin-13 receptor subunit α1; Interleukin-15 receptor subunit α; Interleukin 21 receptor; Cytokine receptor-like factor 2, and the like. The amino acid sequences of such examples are provided in FIG. 53.

[00633] Non-limiting examples of IL-3 family receptors include Interleukin 3 receptor, α subunit ; Interleukin 5 receptor, α subunit; GM-CSF receptor, α subunit; Cytokine receptor common β subunit; and the like. The amino acid sequences of such examples are provided in FIG. 54.

[00634] Non-limiting examples of IL-6 family receptors include Leptin receptor; IL6R (Interleukin-6 receptor, α subunit / interleukin 6 receptor); IL6ST (Interleukin-6 receptor, β subunit / interleukin 6 signal transducer); Interleukin-11 receptor, α subunit; Interleukin 27 receptor, alpha; Interleukin-31 receptor, α subunit; Ciliary neurotrophic factor receptor α subunit; Leukemia inhibitory factor receptor; Oncostatin M-specific receptor, β subunit; and the like. The amino acid sequences of such examples are provided in FIG. 55.

[00635] Non-limiting examples of IL-12 family receptors include Interleukin-12 receptor, β1 subunit; Interleukin-12 receptor, β2 subunit; Interleukin 23 receptor; and the like. The amino acid sequences of such examples are provided in FIG. 56.

[00636] Non-limiting examples of prolactin family receptors include Eythropoietin receptor; Granulocyte colony-stimulating factor receptor; Growth hormone receptor; Prolactin receptor; Thrombopoietin receptor; and the like. The amino acid sequences of such examples are provided in FIG. 57.

[00637] Non-limiting examples of interferon family receptors include interferon α/β receptor 1; Interferon α/β receptor 2; Interferon γ receptor 1; Interferon γ receptor 2; and the like. The amino acid sequences of such examples are provided in FIG. 58.

[00638] Non-limiting examples of IL-10 family receptors include Interleukin-22 receptor α2; Interleukin 10 receptor, α subunit; Interleukin 10 receptor, β subunit; Interleukin 20 receptor, α subunit; Interleukin 20 receptor, β subunit; Interleukin 22 receptor, α1 subunit; Interferon-λ receptor subunit 1; and the like. The amino acid sequences of such examples are provided in FIG. 59.

[00639] Non-limiting examples of IL-17 family receptors include Interleukin 17 receptor A; Interleukin 17 receptor B; interleukin 17 receptor C; Interleukin-17 receptor D; Interleukin 17 receptor E; and the like. The amino acid sequences of such examples are provided in FIG. 60.

[00640] Non-limiting examples of immunoglobulin-like superfamily receptors include Interleukin 1 receptor, type I ; Interleukin 1 receptor, type II; Interleukin-1 receptor-like 1; Interleukin-1 receptor-like 2; Interleukin-18 1; IL-1 receptor accessory protein; IL-18 receptor accessory protein; PDGFRα (platelet derived growth factor receptor alpha); PDGFRβ (platelet derived growth factor receptor beta); KIT proto-oncogene receptor tyrosine kinase; CSFR (colony stimulating factor 1 receptor); and the like. The amino acid sequences of such examples are provided in FIG. 61.

[00641] Non-limiting examples of tumor necrosis factor family receptors include TNFR1 (tumor necrosis factor receptor 1 / TNFRSF1A); TNFR2 (tumor necrosis factor receptor 2 / TNFRSF1B); lymphotoxin β receptor / TNFRSF3; OX40 / TNFRSF4; CD40 / TNFRSF5; Fas / TNFRSF6; decoy receptor 3 / TNFRSF6B; CD27 / TNFRSF7; CD30 / TNFRSF8; 4-1BB / TNFRSF9; DR4 (death receptor 4 / TNFRSF10A); DR5 (death receptor 5 / TNFRSF10B); decoy receptor 1 / TNFRSF10C; decoy receptor 2 / TNFRSF10D; RANK (receptor activator of NF-kappa B / TNFRSF11A); OPG (osteoprotegerin / TNFRSF11B); DR3 (death receptor 3 / TNFRSF25); TWEAK receptor / TNFRSF12A; TACI / TNFRSF13B; BAFF-R (BAFF receptor / TNFRSF13C); HVEM (herpes virus entry mediator / TNFRSF14); nerve growth factor receptor / TNFRSF16; BCMA (B cell maturation antigen / TNFRSF17); GITR (glucocorticoid-induced TNF receptor / TNFRSF18); TAJ (toxicity and JNK inducer / TNFRSF19); RELT / TNFRSF19L; DR6 (death receptor 6 / TNFRSF21); TNFRSF22; TNFRSF23; ectodysplasin A2 isoform receptor / TNFRS27; ectodysplasin 1, anhidrotic receptor; and the like. The amino acid sequences of such examples are provided in FIG. 62.

[00642] Non-limiting examples of chemokine receptors include CCR1; CCR2; CCR3; CCR4; CCR5; CCR6; CCR7; CCR8; CCR9; CCR10; CXCR1 (IL8Ra); CXCR2 (IL8Rb); CXCR3; CXCR4; CXCR5; CXCR6; CX3CR1; and the like. The amino acid sequences of such examples are provided in FIG. 63.

[00643] Non-limiting examples of TGF-beta family receptors include transforming growth factor beta, receptor type I (TGFBR1 (ALK5)); transforming growth factor beta, receptor type II (TGFBR2 (MFS2))

and transforming growth factor beta, receptor type III (TGFBR3 (β-Glycan)). The amino acid sequences of such examples are provided in FIG. 64.

Receptor tyrosine kinases

[00644] As noted above, useful non-limiting examples of dimerization-dependent cell-surface receptors include receptor tyrosine kinases (RTKs), including e.g., RTKs that form homodimers and RTKs that form heterodimers. Useful RTKs include but are not limited to e.g., MERTK (RefSeq Accession NP_006334); LMTK3 (RefSeq Accession NP_001073903); CSF1R (RefSeq Accession NP_001275634); EGFR (RefSeq Accession NP_005219); EPHA2 (RefSeq Accession NP_004422); EPHA1 (RefSeq Accession NP_005223); EPHA3 (RefSeq Accession NP_005224); EPHA4 (RefSeq Accession NP_001291465); EPHA5 (RefSeq Accession NP_004430); EPHA7 (RefSeq Accession NP_004431); EPHA8 (RefSeq Accession NP_065387); EPHB1 (RefSeq Accession NP_004432); EPHB2 (RefSeq Accession NP_001296122); EPHB3 (RefSeq Accession NP_004434); EPHB4 (RefSeq Accession NP_004435); EPHB6 (RefSeq Accession NP_004436); ERBB2 (RefSeq Accession NP_004439); ERBB3 (RefSeq Accession NP_001973); ERBB4 (RefSeq Accession NP_005226); FGFR1 (RefSeq Accession NP_075598); FGFR3 (RefSeq Accession NP_000133); FGFR2 (RefSeq Accession NP_000132); FGFR4 (RefSeq Accession NP_002002); LMTK2 (RefSeq Accession NP_055731); FLT1 (RefSeq Accession NP_002010); FLT3 (RefSeq Accession NP_004110); FLT4 (RefSeq Accession NP_891555); ALK (RefSeq Accession NP_004295); EPHA10 (RefSeq Accession NP_001092909); EPHA6 (RefSeq Accession NP_001265229); IGF1R (RefSeq Accession NP_000866); INSR (RefSeq Accession NP_000199); INSRR (RefSeq Accession NP_055030); KDR (RefSeq Accession NP_002244); KIT (RefSeq Accession NP_000213); LTK (RefSeq Accession NP_002335); MET (RefSeq Accession NP_000236); MST1R (RefSeq Accession NP_002438); MUSK (RefSeq Accession NP_005583); NTRK1 (RefSeq Accession NP_002520); NTRK2 (RefSeq Accession NP_001018074); NTRK3 (RefSeq Accession NP_001012338); ROR1 (RefSeq Accession NP_005003); ROR2 (RefSeq Accession NP_004551); DDR2 (RefSeq Accession NP_001014796); PDGFRA (RefSeq Accession NP_006197); PDGFRB (RefSeq Accession NP_002600); AXL (RefSeq Accession NP_068713); PTK7 (RefSeq Accession NP_002812); RET (RefSeq Accession NP_066124); ROS1 (RefSeq Accession NP_002935); RYK (RefSeq Accession NP_002949); TEK (RefSeq Accession NP_000450); TIE1 (RefSeq Accession NP_005415); TYRO3 (RefSeq Accession NP_006284); DDR1 (RefSeq Accession NP_001284583); AATK (RefSeq Accession NP_001073864); and the like. The amino acid sequences of such examples are provided in FIG. 65.

Dimerization pairs

[00645] As noted above, conditionally active dimerization-dependent cell-surface receptor of the present disclosure will generally include a cell-surface receptor polypeptide that comprises a first member of a dimerization pair that is conditionally dimerizable with a second cell-surface receptor polypeptide that

comprises the second member of a dimerization pair. Thus, a conditionally active dimerization-dependent cell-surface receptor of the present disclosure will comprise a member of a dimerization pair that includes a LBD of a nuclear hormone receptor or a co-regulator peptide. Two conditionally active dimerization-dependent cell-surface receptors may be utilized as a system where one conditionally active dimerization-dependent cell-surface receptor comprises a first member of a dimerization pair that includes a LBD of a nuclear hormone receptor and the other conditionally active dimerization-dependent cell-surface receptor comprises the second member of the dimerization pair that includes a co-regulator peptide of the same nuclear hormone receptor. In the presence of a dimerization agent (e.g., a nuclear hormone, or a functional derivative or analog of the nuclear hormone; also referred to herein as a "dimerizer"), the first and second members of the dimerization pair will bind to one another, and will effect dimerization of the two conditionally active dimerization-dependent cell-surface receptor polypeptides. A first member of a dimerization pair, or a second member of a dimerization pair, can also be referred to as a "dimerization domain".

[00646] A ligand-binding domain of a nuclear hormone receptor can be from any of a variety of nuclear hormone receptors, including, but not limited to, those described above. Suitable co-regulator polypeptides include full-length naturally-occurring nuclear hormone co-regulator polypeptides. Suitable co-regulator polypeptides include fragments of naturally-occurring nuclear hormone co-regulator polypeptides. Suitable co-regulator polypeptides include synthetic or recombinant nuclear hormone co-regulator polypeptides. Non-limiting examples of suitable co-regulator polypeptides include those described above.

NUCLEIC ACIDS

[00647] The present disclosure provides a nucleic acid that comprises a nucleotide sequence encoding a heterodimeric, conditionally active polypeptide of the present disclosure. A single nucleic acid molecule may include multiple sequences encoding two or more portions of a heterodimeric, conditionally active polypeptide of the present disclosure. In some instances, two or more portions of a heterodimeric, conditionally active polypeptide of the present disclosure may be separated across multiple individual nucleic acid molecules (e.g., multiple nucleic acid vectors). A nucleic acid comprising a nucleotide sequence encoding a heterodimeric, conditionally active polypeptide of the present disclosure will in some embodiments be DNA, including, e.g., a recombinant expression vector. A nucleic acid comprising a nucleotide sequence encoding a heterodimeric, conditionally active polypeptide of the present disclosure will in some embodiments be RNA, e.g., *in vitro* synthesized RNA.

[00648] In some cases, a nucleic acid of the present disclosure comprises a nucleotide sequence encoding only a first portion, e.g., a first polypeptide chain of a heterodimeric, conditionally active polypeptide of the present disclosure. In some cases, a nucleic acid of the present disclosure comprises a nucleotide sequence encoding only a second portion, e.g., a second polypeptide chain, of a heterodimeric,

conditionally active polypeptide of the present disclosure. In some cases, a nucleic acid of the present disclosure comprises a nucleotide sequence encoding both polypeptide chains of a heterodimeric, conditionally active polypeptide of the present disclosure.

[00649] In some cases, a single nucleic acid of the present disclosure may comprise one or more nucleotide sequences encoding two or more conditionally active polypeptides of the present disclosure. For example, in some instances, a nucleic acid of the present disclosure may encode a first conditionally acitive polypeptide comprising a first member of a dimerization pair and a second conditionally acitive polypeptide comprising the second member of a dimerization pair. In some embodiments, a nucleic acid of the present disclosure may comprise a sequence or multiple sequences that encode a first conditionally active dimerization-dependent cell-surface receptor comprising a first member of a dimerization pair and a second conditionally active dimerization-dependent cell-surface receptor comprising the second member of a dimerization pair. In some embodiments, two conditionally active dimerization-dependent cell-surface receptors, although each containing half of a dimerization pair, may be encoded by sequences present on separate nucleic acids.

[00650] In some cases, a subject nucleic acid provides for production of a heterodimeric, conditionally active polypeptide of the present disclosure, e.g., in a mammalian cell. In other cases, a subject nucleic acid provides for amplification of the heterodimeric, conditionally active polypeptide-encoding nucleic acid.

[00651] A nucleotide sequence encoding a heterodimeric, conditionally active polypeptide of the present disclosure can be operably linked to a transcriptional control element, e.g., a promoter, and enhancer, etc. In some instances, the heterodimeric, conditionally active polypeptide encoding nucleic acid is operably linked to a tissue specific promoter for expression in a particular cell type of interest. For example, a heterodimeric, conditionally active polypeptide may be operably linked to an immune cell specific promoter for specific expression in one or more immune cell types. In other instances, a heterodimeric, conditionally active polypeptide may be operably linked to a general (i.e., non-immune cell specific) promoter including e.g., a ubiquitous promoter, a constitutive promoter, a heterologous promoter, a regulatable promoters (e.g., inducible promoters, reversible promoters, etc.), etc.

General Promoters

[00652] Suitable promoter and enhancer elements are known in the art. For expression in a bacterial cell, suitable promoters include, but are not limited to, lacI, lacZ, T3, T7, gpt, lambda P and trc. For expression in a eukaryotic cell, suitable promoters include, but are not limited to; cytomegalovirus immediate early promoter; herpes simplex virus thymidine kinase promoter; early and late SV40 promoters; promoter present in long terminal repeats from a retrovirus; mouse metallothionein-I promoter; and various art-known promoters.

[00653] Suitable promoters for use in prokaryotic host cells include, but are not limited to, a bacteriophage T7 RNA polymerase promoter; a trp promoter; a lac operon promoter; a hybrid promoter, e.g., a lac/tac hybrid promoter, a tac/trc hybrid promoter, a trp/lac promoter, a T7/lac promoter; a trc promoter; a tac promoter, and the like; an araBAD promoter; in vivo regulated promoters, such as an ssaG promoter or a related promoter (see, e.g., U.S. Patent Publication No. 20040131637), a pagC promoter (Pulkkinen and Miller, J. Bacteriol., 1991: 173(1): 86-93; Alpuche-Aranda et al., PNAS, 1992; 89(21): 10079-83), a nirB promoter (Harborne et al. (1992) Mol. Micro. 6:2805-2813), and the like (see, e.g., Dunstan et al. (1999) Infect. Immun. 67:5133-5141; McKelvie et al. (2004) Vaccine 22:3243-3255; and Chatfield et al. (1992) Biotechnol. 10:888-892); a sigma70 promoter, e.g., a consensus sigma70 promoter (see, e.g., GenBank Accession Nos. AX798980, AX798961, and AX798183); a stationary phase promoter, e.g., a dps promoter, an spv promoter, and the like; a promoter derived from the pathogenicity island SPI-2 (see, e.g., WO96/17951); an actA promoter (see, e.g., Shetron-Rama et al. (2002) Infect. Immun. 70:1087-1096); an rpsM promoter (see, e.g., Valdivia and Falkow (1996). Mol. Microbiol. 22:367); a tet promoter (see, e.g., Hillen,W. and Wissmann,A. (1989) In Saenger,W. and Heinemann,U. (eds), Topics in Molecular and Structural Biology, Protein–Nucleic Acid Interaction. Macmillan, London, UK, Vol. 10, pp. 143–162); an SP6 promoter (see, e.g., Melton et al. (1984) Nucl. Acids Res. 12:7035); and the like. Suitable strong promoters for use in prokaryotes such as Escherichia coli include, but are not limited to Trc, Tac, T5, T7, and PLambda. Non-limiting examples of operators for use in bacterial host cells include a lactose promoter operator (LacI repressor protein changes conformation when contacted with lactose, thereby preventing the LacI repressor protein from binding to the operator), a tryptophan promoter operator (when complexed with tryptophan, TrpR repressor protein has a conformation that binds the operator; in the absence of tryptophan, the TrpR repressor protein has a conformation that does not bind to the operator), and a tac promoter operator (see, for example, deBoer et al. (1983) Proc. Natl. Acad. Sci. U.S.A. 80:21-25).

[00654] Suitable reversible promoters, including reversible inducible promoters are known in the art. Such reversible promoters may be isolated and derived from many organisms, e.g., eukaryotes and prokaryotes. Modification of reversible promoters derived from a first organism for use in a second organism, e.g., a first prokaryote and a second a eukaryote, a first eukaryote and a second a prokaryote, etc., is well known in the art. Such reversible promoters, and systems based on such reversible promoters but also comprising additional control proteins, include, but are not limited to, alcohol regulated promoters (e.g., alcohol dehydrogenase I (alcA) gene promoter, promoters responsive to alcohol transactivator proteins (AlcR), etc.), tetracycline regulated promoters, (e.g., promoter systems including TetActivators, TetON, TetOFF, etc.), steroid regulated promoters (e.g., rat glucocorticoid receptor promoter systems, human estrogen receptor promoter systems, retinoid promoter systems, thyroid promoter systems, ecdysone promoter systems, mifepristone promoter systems, etc.), metal regulated

promoters (e.g., metallothionein promoter systems, etc.), pathogenesis-related regulated promoters (e.g., salicylic acid regulated promoters, ethylene regulated promoters, benzothiadiazole regulated promoters, etc.), temperature regulated promoters (e.g., heat shock inducible promoters (e.g., HSP-70, HSP-90, soybean heat shock promoter, etc.), light regulated promoters, synthetic inducible promoters, and the like.

[00655] In some embodiments, e.g., for expression in a yeast cell, a suitable promoter is a constitutive promoter such as an ADH1 promoter, a PGK1 promoter, an ENO promoter, a PYK1 promoter and the like; or a regulatable promoter such as a GAL1 promoter, a GAL10 promoter, an ADH2 promoter, a PHO5 promoter, a CUP1 promoter, a GAL7 promoter, a MET25 promoter, a MET3 promoter, a CYC1 promoter, a HIS3 promoter, an ADH1 promoter, a PGK promoter, a GAPDH promoter, an ADC1 promoter, a TRP1 promoter, a URA3 promoter, a LEU2 promoter, an ENO promoter, a TP1 promoter, and AOX1 (e.g., for use in Pichia). Selection of the appropriate vector and promoter is well within the level of ordinary skill in the art.

Immune Cell Promoters

[00656] In some instances, nucleic acids of the present disclosure include immune cell specific promoters that are expressed in one or more immune cell types, including but not limited to lymphocytes, hematopoietic stem cells and/or progeny thereof (i.e., immune cell progenitors), etc. Any convenient and appropriate promoter of an immune cell specific gene may find use in nucleic acids of the present disclosure. In some instances, an immune cell specific promoter of a nucleic acid of the present disclosure may be a T cell specific promoter. In some instances, an immune cell specific promoter of a nucleic acid of the present disclosure may be a light and/or heavy chain immunoglobulin gene promoter and may or may not include one or more related enhancer elements.

[00657] In some instances, an immune cell specific promoter of a nucleic acid of the present disclosure may be a promoter of a B29 gene promoter, a CD14 gene promoter, a CD43 gene promoter, a CD45 gene promoter, a CD68 gene promoter, a IFN-β gene promoter, a WASP gene promoter, a T-cell receptor β -chain gene promoter, a V9 γ (TRGV9) gene promoter, a V2 δ (TRDV2) gene promoter, and the like.

[00658] In some instances, an immune cell specific promoter of a nucleic acid of the present disclosure may be a viral promoter expressed in immune cells. As such, in some instances, viral promoters useful in nucleic acids of the present disclosure include viral promoters derived from immune cells viruses, including but not limited to, e.g., lentivirus promoters (e.g., HIV, SIV, FIV, EIAV, or Visna promoters) including e.g., LTR promoter, etc., Retroviridae promoters including, e.g., HTLV-I promoter, HTLV-II promoter, etc., and the like.

[00659] In some cases, the promoter is a CD8 cell-specific promoter, a CD4 cell-specific promoter, a neutrophil-specific promoter, or an NK-specific promoter. For example, a CD4 gene promoter can be

used; see, e.g., Salmon et al. (1993) Proc. Natl. Acad. Sci. USA 90:7739; and Marodon et al. (2003) Blood 101:3416. As another example, a CD8 gene promoter can be used. NK cell-specific expression can be achieved by use of an Ncr1 (p46) promoter; see, e.g., Eckelhart et al. (2011) Blood 117:1565.

Additional Nucleic Acid Components, Constructs and Use Thereof

[00660] In some instances, the locus or construct or transgene containing the suitable promoter is irreversibly switched through the induction of an inducible system. Suitable systems for induction of an irreversible switch are well known in the art, e.g., induction of an irreversible switch may make use of a Cre-lox-mediated recombination (see, e.g., Fuhrmann-Benzakein, et al., PNAS (2000) 28:e99, the disclosure of which is incorporated herein by reference). Any suitable combination of recombinase, endonuclease, ligase, recombination sites, etc. known to the art may be used in generating an irreversibly switchable promoter. Methods, mechanisms, and requirements for performing site-specific recombination, described elsewhere herein, find use in generating irreversibly switched promoters and are well known in the art, see, e.g., Grindley et al. (2006) Annual Review of Biochemistry, 567-605 and Tropp (2012) Molecular Biology (Jones & Bartlett Publishers, Sudbury, MA), the disclosures of which are incorporated herein by reference.

[00661] A nucleotide sequence encoding a subject heterodimeric, conditionally active polypeptide can be present in an expression vector and/or a cloning vector. Where a subject heterodimeric, conditionally active polypeptide is split between two or more separate polypeptides, nucleotide sequences encoding the two or more polypeptides can be cloned in the same or separate vectors. An expression vector can include a selectable marker, an origin of replication, and other features that provide for replication and/or maintenance of the vector. Suitable expression vectors include, e.g., plasmids, viral vectors, and the like.

[00662] Large numbers of suitable vectors and promoters are known to those of skill in the art; many are commercially available for generating a subject recombinant constructs. The following vectors are provided by way of example. Bacterial: pBs, phagescript, PsiX174, pBluescript SK, pBs KS, pNH8a, pNH16a, pNH18a, pNH46a (Stratagene, La Jolla, Calif., USA); pTrc99A, pKK223-3, pKK233-3, pDR540, and pRIT5 (Pharmacia, Uppsala, Sweden). Eukaryotic: pWLneo, pSV2cat, pOG44, PXR1, pSG (Stratagene) pSVK3, pBPV, pMSG and pSVL (Pharmacia).

[00663] Expression vectors generally have convenient restriction sites located near the promoter sequence to provide for the insertion of nucleic acid sequences encoding heterologous proteins. A selectable marker operative in the expression host may be present. Suitable expression vectors include, but are not limited to, viral vectors (e.g. viral vectors based on vaccinia virus; poliovirus; adenovirus (see, e.g., Li et al., Invest Opthalmol Vis Sci 35:2543 2549, 1994; Borras et al., Gene Ther 6:515 524, 1999; Li and Davidson, PNAS 92:7700 7704, 1995; Sakamoto et al., H Gene Ther 5:1088 1097, 1999; WO 94/12649, WO 93/03769; WO 93/19191; WO 94/28938; WO 95/11984 and WO 95/00655); adeno-associated virus (see, e.g., Ali et al., Hum Gene Ther 9:81 86, 1998, Flannery et al., PNAS 94:6916 6921, 1997; Bennett

et al., Invest Opthalmol Vis Sci 38:2857 2863, 1997; Jomary et al., Gene Ther 4:683 690, 1997, Rolling et al., Hum Gene Ther 10:641 648, 1999; Ali et al., Hum Mol Genet 5:591 594, 1996; Srivastava in WO 93/09239, Samulski et al., J. Vir. (1989) 63:3822-3828; Mendelson et al., Virol. (1988) 166:154-165; and Flotte et al., PNAS (1993) 90:10613-10617); SV40; herpes simplex virus; human immunodeficiency virus (see, e.g., Miyoshi et al., PNAS 94:10319 23, 1997; Takahashi et al., J Virol 73:7812 7816, 1999); a retroviral vector (e.g., Murine Leukemia Virus, spleen necrosis virus, and vectors derived from retroviruses such as Rous Sarcoma Virus, Harvey Sarcoma Virus, avian leukosis virus, human immunodeficiency virus, myeloproliferative sarcoma virus, and mammary tumor virus); and the like.

[00664] As noted above, in some embodiments, a nucleic acid comprising a nucleotide sequence encoding a heterodimeric, conditionally active polypeptide of the present disclosure will in some embodiments be RNA, e.g., in vitro synthesized RNA. Methods for in vitro synthesis of RNA are known in the art; any known method can be used to synthesize RNA comprising a nucleotide sequence encoding the first and/or the second polypeptide of a heterodimeric, conditionally active polypeptide of the present disclosure. Methods for introducing RNA into a host cell are known in the art. See, e.g., Zhao et al. (2010) Cancer Res. 15:9053. Introducing RNA comprising a nucleotide sequence encoding the first and/or the second polypeptide of a heterodimeric, conditionally active polypeptide of the present disclosure into a host cell can be carried out in vitro or ex vivo or in vivo. For example, a host cell (e.g., an NK cell, a cytotoxic T lymphocyte, etc.) can be electroporated in vitro or ex vivo with RNA comprising a nucleotide sequence encoding the first and/or the second polypeptide of a heterodimeric, conditionally active polypeptide of the present disclosure.

CELLS

[00665] The present disclosure provides a mammalian cell that is genetically modified to produce a heterodimeric, conditionally active polypeptide of the present disclosure.

[00666] Suitable mammalian cells include primary cells and immortalized cell lines. Suitable mammalian cell lines include human cell lines, non-human primate cell lines, rodent (e.g., mouse, rat) cell lines, and the like. Suitable mammalian cell lines include, but are not limited to, HeLa cells (e.g., American Type Culture Collection (ATCC) No. CCL-2), CHO cells (e.g., ATCC Nos. CRL9618, CCL61, CRL9096), 293 cells (e.g., ATCC No. CRL-1573), Vero cells, NIH 3T3 cells (e.g., ATCC No. CRL-1658), Huh-7 cells, BHK cells (e.g., ATCC No. CCL10), PC12 cells (ATCC No. CRL1721), COS cells, COS-7 cells (ATCC No. CRL1651), RAT1 cells, mouse L cells (ATCC No. CCLI.3), human embryonic kidney (HEK) cells (ATCC No. CRL1573), HLHepG2 cells, Hut-78, Jurkat, HL-60, NK cell lines (e.g., NKL, NK92, and YTS), and the like.

[00667] In some instances, suitable cells include those described in Themeli et al. Cell Stem Cell. 2015 Apr 2;16(4):357-66; the disclosure of which is incorporated herein by reference in its entirety.

[00668] In some instances, the cell is not an immortalized cell line, but is instead a cell (e.g., a primary cell) obtained from an individual. For example, in some cases, the cell is an immune cell, immune cell progenitor or immune stem cell obtained from an individual. As an example, the cell is a T lymphocyte, or progenitor thereof, obtained from an individual. As another example, the cell is a cytotoxic cell, or progenitor thereof, obtained from an individual. As another example, the cell is a stem cell or progenitor cell obtained from an individual.

UTILITY

[00669] A heterodimeric, conditionally active polypeptide of the present disclosure finds use in a variety of research and treatment methods, which are provided herein.

[00670] In some cases, where a heterodimeric, conditionally active polypeptide of the present disclosure comprises a first heterologous polypeptide and a second heterologous polypeptide that individually do not exhibit an activity but do exhibit the activity when present in a heterodimeric, conditionally active polypeptide of the present disclosure and in the presence of a dimerization agent that induces binding of the LBD to the co-regulator peptide in the heterodimeric, conditionally active polypeptide, the present disclosure provides a method of activating the activity. Thus, e.g., the present disclosure provides a method of activating a polypeptide (inducing an activity of a polypeptide), the method comprising contacting a heterodimeric, conditionally active polypeptide of the present disclosure with a dimerization agent, where the polypeptide is present in the heterodimeric polypeptide as a first heterologous polypeptide and a second heterologous polypeptide, where the first heterologous polypeptide and a second heterologous polypeptide that individually do not exhibit an activity but do exhibit the activity when present in a heterodimeric, conditionally active polypeptide of the present disclosure and in the presence of the dimerization agent. The activity that is induced depends on the nature of the first heterologous polypeptide and a second heterologous polypeptide. For example, where the first heterologous polypeptide and a second heterologous polypeptide are a receptor and a co-receptor, respectively, the activity can be binding of the receptor to the co-receptor, or a downstream activity that results from binding of the receptor to the co-receptor. In some cases, contacting a heterodimeric, conditionally active polypeptide of the present disclosure occurs *in vitro*, where the heterodimeric, conditionally active polypeptide of the present disclosure is not in a cell. In some cases, contacting a heterodimeric, conditionally active polypeptide of the present disclosure occurs in a cell *in vitro*, where the heterodimeric, conditionally active polypeptide of the present disclosure is in the cell. In some cases, contacting a heterodimeric, conditionally active polypeptide of the present disclosure occurs in a cell *in vivo*, where the heterodimeric, conditionally active polypeptide of the present disclosure is in the cell.

METHODS FOR MODULATING THE ACTIVITY OF A CELL

[00671] The present disclosure provides methods for modulating (activating; repressing) an activity of a cell. The methods generally involve contacting a cell that expresses a heterodimeric, conditionally active

polypeptide of the present disclosure with a dimerizing agent. In some cases, the methods involve contacting a cell that expresses a heterodimeric, conditionally active polypeptide of the present disclosure with a dimerizing agent and a second agent (e.g., an antigen).

METHODS OF ACTIVATING AN IMMUNE CELL

[00672] The present disclosure provides methods of activating an immune cell, where the immune cell expresses an On-switch CAR of the present disclosure. The present disclosure provides methods of activating an immune cell *in vitro*, *in vivo*, or *ex vivo*. The methods generally involve contacting an immune cell (*in vitro*, *in vivo*, or *ex vivo*) with a dimerizing agent and an antigen, where the immune cell is genetically modified to produce a heterodimeric, conditionally active CAR of the present disclosure. In the presence of the dimerizing agent and the antigen, the heterodimeric, conditionally active CAR dimerizes and activates the immune cell, thereby producing an activated immune cell. Immune cells include, e.g., a cytotoxic T lymphocyte, an NK cell, a $CD4^+$ T cell, a T regulatory (Treg) cell, etc.

[00673] Contacting the genetically modified immune cell (e.g., a T lymphocyte, an NK cell) with a dimerizing agent and a second member of a specific binding pair (e.g., an antigen, a ligand, a receptor) can increase production of a cytokine by the immune cell by at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 40%, at least about 50%, at least about 75%, at least about 2-fold, at least about 2.5-fold, at least about 5-fold, at least about 10-fold, or more than 10-fold, compared with the amount of cytokine produced by the immune cell in the absence of the second member of a specific binding pair and/or the dimerizing agent. Cytokines whose production can be increased include, but are not limited to, IL-2 and IFN-γ.

[00674] Contacting the genetically modified immune cell (e.g., a T lymphocyte, an NK cell) with a dimerizing agent and an antigen can increase production of a cytokine by the immune cell by at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 40%, at least about 50%, at least about 75%, at least about 2-fold, at least about 2.5-fold, at least about 5-fold, at least about 10-fold, or more than 10-fold, compared with the amount of cytokine produced by the immune cell in the absence of the antigen and/or the dimerizing agent. Cytokines whose production can be increased include, but are not limited to, IL-2 and IFN-γ.

[00675] Contacting a genetically modified cytotoxic cell (e.g., cytotoxic T lymphocyte) with a dimerizing agent and a second member of a specific binding pair (e.g., an antigen, a ligand, a receptor) can increase cytotoxic activity of the cytotoxic cell by at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 40%, at least about 50%, at least about 75%, at least about 2-fold, at least about 2.5-fold, at least about 5-fold, at least about 10-fold, or more than 10-fold, compared to the cytotoxic activity of the cytotoxic cell in the absence of the dimerizing agent.

[00676] Contacting a genetically modified cytotoxic cell (e.g., cytotoxic T lymphocyte) with a dimerizing agent and an antigen can increase cytotoxic activity of the cytotoxic cell by at least about 10%, at least

about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 40%, at least about 50%, at least about 75%, at least about 2-fold, at least about 2.5-fold, at least about 5-fold, at least about 10-fold, or more than 10-fold, compared to the cytotoxic activity of the cytotoxic cell in the absence of the dimerizing agent.

[00677] In other embodiments, e.g., depending on the host immune cell, contacting a genetically modified host cell with a dimerizing agent and an antigen can increase or decrease cell proliferation, cell survival, cell death, and the like.

[00678] The present disclosure provides a method of generating a conditionally activatable cell. The method generally involves genetically modifying a mammalian cell with an expression vector, or an RNA (e.g., *in vitro* transcribed RNA), comprising nucleotide sequences encoding a heterodimeric, conditionally active CAR of the present disclosure. The genetically modified cell is conditionally activatable in the presence of: a) an antigen to which the first polypeptide of the CAR binds; and b) a dimerizer (a dimerizing agent). The genetic modification can be carried out *in vivo*, *in vitro*, or *ex vivo*. The cell can be an immune cell (e.g., a T lymphocyte or NK cell), a stem cell, a progenitor cell, etc.

[00679] In some cases, the genetic modification is carried out *ex vivo*. For example, a T lymphocyte, a stem cell, or an NK cell is obtained from an individual; and the cell obtained from the individual is genetically modified to express a CAR of the present disclosure. The genetically modified cell is conditionally activatable in the presence of: a) an antigen to which the first polypeptide of the CAR binds; and b) a dimerizer. In some cases, the genetically modified cell is activated *ex vivo*. In other cases, the genetically modified cell is introduced into an individual (e.g., the individual from whom the cell was obtained); and the genetically modified cell is activated *in vivo*, e.g., by administering to the individual a dimerizer. For example, where the antigen is present on the surface of a cell in the individual, there is no need to administer the antigen. The genetically modified cell comes into contact with the antigen present on the surface of a cell in the individual; and, upon administration to the individual of a dimerizer, the genetically modified cell is activated. For example, where the genetically modified cell is a T lymphocyte, the genetically modified cell can exhibit cytotoxicity toward a cell that presents an antigen on its surface to which the CAR binds.

METHODS OF REPRESSING IMMUNE CELL ACTIVATION

[00680] The present disclosure provides methods of repressing immune cell activation, such methods being applicable in vitro, in vivo, or ex vivo. The methods generally involve contacting an immune cell (in vitro, in vivo, or ex vivo) with a dimerizing agent, where the immune cell is genetically modified to produce a heteromeric, conditionally repressible synthetic ICR of the present disclosure. In the presence of the dimerizing agent, the heteromeric, conditionally repressible ICR dimerizes and represses activation of the immune cell, thereby producing a repressed immune cell. Immune cells include, e.g., a cytotoxic T lymphocyte, an NK cell, a CD4+ T cell, a T regulatory (Treg) cell, etc.

[00681] Contacting the genetically modified immune cell (e.g., a T lymphocyte, an NK cell) with a dimerizing agent can repress the expression of a lymphocyte cell surface antigen, e.g., a cell surface antigen indicative of immune cell activation, T cell activation, etc., by the immune cell by at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 40%, at least about 50%, at least about 75%, at least about 2-fold, at least about 2.5-fold, at least about 5-fold, at least about 10-fold, or more than 10-fold, compared with the amount of the cell surface antigen expressed by the activated immune cell in the absence of the dimerizing agent. Lymphocyte cell surface antigens whose production can be repressed include, but are not limited to e.g., CD69.

[00682] Contacting the genetically modified immune cell (e.g., a T lymphocyte, an NK cell) with a dimerizing agent can repress the production of a cytokine by the immune cell by at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 40%, at least about 50%, at least about 75%, at least about 2-fold, at least about 2.5-fold, at least about 5-fold, at least about 10-fold, or more than 10-fold, compared with the amount of cytokine produced by the activated immune cell in the absence of the dimerizing agent. Cytokines whose production can be repressed include, but are not limited to, IL-2 and IFN-γ.

FORMULATIONS, DOSAGES, AND ROUTES OF ADMINISTRATION

[00683] As discussed above, a treatment method of the present disclosure involves administration to an individual in need thereof of an effective amount of a dimerizer agent, and may also involve administration of an antigen.

[00684] An "effective amount" of a dimerizer agent is in some cases an amount that, when administered in one or more doses to an individual in need thereof, increases the level of cytotoxic activity of a T lymphocyte expressing a subject CAR by at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 40%, at least about 50%, at least about 75%, at least about 2-fold, at least about 2.5-fold, at least about 5-fold, at least about 10-fold, or more than 10-fold, compared to the cytotoxic activity of the T lymphocyte in the absence of the dimerizing agent.

[00685] An "effective amount" of a dimerizer agent is in some cases an amount that, when administered in one or more doses to an individual in need thereof, increases the level of cytotoxic activity of an NK cell expressing a subject CAR by at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 40%, at least about 50%, at least about 75%, at least about 2-fold, at least about 2.5-fold, at least about 5-fold, at least about 10-fold, or more than 10-fold, compared to the cytotoxic activity of the NK cell in the absence of the dimerizing agent.

[00686] An "effective amount" of a dimerizer agent is in some cases an amount that, when administered in one or more doses to an individual in need thereof, reduces the number of cancer cells in the individual and/or reduces tumor mass in the individual, by at least about 10%, at least about 15%, at least about

20%, at least about 25%, at least about 30%, at least about 40%, at least about 50%, at least about 75%, or more than 75%, compared to the number of cancer cells and/or tumor mass in the absence of the dimerizing agent.

[00687] In some embodiments, an effective amount of a dimerizer is an amount that, when administered alone (e.g., in monotherapy) or in combination (e.g., in combination therapy) with one or more additional therapeutic agents, in one or more doses, is effective to reduce one or more of tumor growth rate, cancer cell number, and tumor mass, by at least about 5%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, 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 more, compared to the tumor growth rate, cancer cell number, or tumor mass in the absence of treatment with the dimerizer.

Formulations

[00688] In the subject methods, a dimerizer can be administered to the host using any convenient means capable of resulting in the desired therapeutic effect or diagnostic effect. Thus, the dimerizer can be incorporated into a variety of formulations for therapeutic administration. More particularly, a dimerizer can be formulated into pharmaceutical compositions by combination with appropriate, pharmaceutically acceptable carriers or diluents, and may be formulated into preparations in solid, semi-solid, liquid or gaseous forms, such as tablets, capsules, powders, granules, ointments, solutions, suppositories, injections, inhalants and aerosols.

[00689] In pharmaceutical dosage forms, a dimerizer can be administered in the form of their pharmaceutically acceptable salts, or they may also be used alone or in appropriate association, as well as in combination, with other pharmaceutically active compounds. The following methods and excipients are merely exemplary and are in no way limiting.

[00690] Suitable excipient vehicles are, for example, water, saline, dextrose, glycerol, ethanol, or the like, and combinations thereof. In addition, if desired, the vehicle may contain minor amounts of auxiliary substances such as wetting or emulsifying agents or pH buffering agents. Actual methods of preparing such dosage forms are known, or will be apparent, to those skilled in the art. See, e.g., Remington's Pharmaceutical Sciences, Mack Publishing Company, Easton, Pennsylvania, 17th edition, 1985. The composition or formulation to be administered will, in any event, contain a quantity of a dimerizer adequate to achieve the desired state in the subject being treated.

[00691] The pharmaceutically acceptable excipients, such as vehicles, adjuvants, carriers or diluents, are readily available to the public. Moreover, pharmaceutically acceptable auxiliary substances, such as pH adjusting and buffering agents, tonicity adjusting agents, stabilizers, wetting agents and the like, are readily available to the public.

[00692] For oral preparations, a dimerizer can be used alone or in combination with appropriate additives to make tablets, powders, granules or capsules, for example, with conventional additives, such as lactose,

mannitol, corn starch or potato starch; with binders, such as crystalline cellulose, cellulose derivatives, acacia, corn starch or gelatins; with disintegrators, such as corn starch, potato starch or sodium carboxymethylcellulose; with lubricants, such as talc or magnesium stearate; and if desired, with diluents, buffering agents, moistening agents, preservatives and flavoring agents.

[00693] A dimerizer can be formulated into preparations for injection by dissolving, suspending or emulsifying them in an aqueous or nonaqueous solvent, such as vegetable or other similar oils, synthetic aliphatic acid glycerides, esters of higher aliphatic acids or propylene glycol; and if desired, with conventional additives such as solubilizers, isotonic agents, suspending agents, emulsifying agents, stabilizers and preservatives.

[00694] Pharmaceutical compositions comprising a dimerizer are prepared by mixing the dimerizer having the desired degree of purity with optional physiologically acceptable carriers, excipients, stabilizers, surfactants, buffers and/or tonicity agents. Acceptable carriers, excipients and/or stabilizers are nontoxic to recipients at the dosages and concentrations employed, and include buffers such as phosphate, citrate, and other organic acids; antioxidants including ascorbic acid, glutathione, cysteine, methionine and citric acid; preservatives (such as ethanol, benzyl alcohol, phenol, m-cresol, p-chlor-m-cresol, methyl or propyl parabens, benzalkonium chloride, or combinations thereof); amino acids such as arginine, glycine, ornithine, lysine, histidine, glutamic acid, aspartic acid, isoleucine, leucine, alanine, phenylalanine, tyrosine, tryptophan, methionine, serine, proline and combinations thereof; monosaccharides, disaccharides and other carbohydrates; low molecular weight (less than about 10 residues) polypeptides; proteins, such as gelatin or serum albumin; chelating agents such as EDTA; sugars such as trehalose, sucrose, lactose, glucose, mannose, maltose, galactose, fructose, sorbose, raffinose, glucosamine, N-methylglucosamine, galactosamine, and neuraminic acid; and/or non-ionic surfactants such as Tween, Brij Pluronics, Triton-X, or polyethylene glycol (PEG).

[00695] The pharmaceutical composition may be in a liquid form, a lyophilized form or a liquid form reconstituted from a lyophilized form, wherein the lyophilized preparation is to be reconstituted with a sterile solution prior to administration. The standard procedure for reconstituting a lyophilized composition is to add back a volume of pure water (typically equivalent to the volume removed during lyophilization); however solutions comprising antibacterial agents may be used for the production of pharmaceutical compositions for parenteral administration; see also Chen (1992) Drug Dev Ind Pharm 18, 1311-54.

[00696] The term "unit dosage form," as used herein, refers to physically discrete units suitable as unitary dosages for human and animal subjects, each unit containing a predetermined quantity a dimerizer calculated in an amount sufficient to produce the desired effect in association with a pharmaceutically acceptable diluent, carrier or vehicle. The specifications for a given dimerizer may depend on the

particular dimerizer employed and the effect to be achieved, and the pharmacodynamics associated with each dimerizer in the host.

[00697] In some embodiments, a dimerizer is formulated in a controlled release formulation. Sustained-release preparations may be prepared using methods well known in the art. Suitable examples of sustained-release preparations include semipermeable matrices of solid hydrophobic polymers containing the dimerizer in which the matrices are in the form of shaped articles, e.g. films or microcapsules. Examples of sustained-release matrices include polyesters, copolymers of L-glutamic acid and ethyl-L-glutamate, non-degradable ethylene-vinyl acetate, hydrogels, polylactides, degradable lactic acid-glycolic acid copolymers and poly-D-(-)-3-hydroxybutyric acid. Possible loss of biological activity may be prevented by using appropriate additives, by controlling moisture content and by developing specific polymer matrix compositions.

Dosages

[00698] A suitable dosage can be determined by an attending physician or other qualified medical personnel, based on various clinical factors. As is well known in the medical arts, dosages for any one patient depend upon many factors, including the patient's size, body surface area, age, the particular dimerizer to be administered, sex of the patient, time, and route of administration, general health, and other drugs being administered concurrently. A dimerizer may be administered in amounts between 1 ng/kg body weight and 20 mg/kg body weight per dose, e.g. between 0.1 mg/kg body weight to 10 mg/kg body weight, e.g. between 0.5 mg/kg body weight to 5 mg/kg body weight; however, doses below or above this exemplary range are envisioned, especially considering the aforementioned factors. If the regimen is a continuous infusion, it can also be in the range of 1 μg to 10 mg per kilogram of body weight per minute.

[00699] Those of skill will readily appreciate that dose levels can vary as a function of the specific dimerizer, the severity of the symptoms and the susceptibility of the subject to side effects. Preferred dosages for a given compound are readily determinable by those of skill in the art by a variety of means.

Routes of administration

[00700] A dimerizer is administered to an individual using any available method and route suitable for drug delivery, including *in vivo* and *ex vivo* methods, as well as systemic and localized routes of administration.

[00701] Conventional and pharmaceutically acceptable routes of administration include intratumoral, peritumoral, intramuscular, intratracheal, intracranial, subcutaneous, intradermal, topical application, intravenous, intraarterial, rectal, nasal, oral, and other enteral and parenteral routes of administration. Routes of administration may be combined, if desired, or adjusted depending upon the dimerizer and/or the desired effect. A dimerizer can be administered in a single dose or in multiple doses. In some embodiments, a dimerizer is administered orally. In some embodiments, a dimerizer is administered via

an inhalational route. In some embodiments, a dimerizer is administered intranasally. In some embodiments, a dimerizer is administered locally. In some embodiments, a dimerizer is administered intratumorally. In some embodiments, a dimerizer is administered peritumorally. In some embodiments, a dimerizer is administered intracranially. In some embodiments, a dimerizer is administered intravenously.

[00702] The agent can be administered to a host using any available conventional methods and routes suitable for delivery of conventional drugs, including systemic or localized routes. In general, routes of administration contemplated by the invention include, but are not necessarily limited to, enteral, parenteral, or inhalational routes.

[00703] Parenteral routes of administration other than inhalation administration include, but are not necessarily limited to, topical, transdermal, subcutaneous, intramuscular, intraorbital, intracapsular, intraspinal, intrasternal, intratumoral, peritumoral, and intravenous routes, *i.e.*, any route of administration other than through the alimentary canal. Parenteral administration can be carried to effect systemic or local delivery of a dimerizer. Where systemic delivery is desired, administration typically involves invasive or systemically absorbed topical or mucosal administration of pharmaceutical preparations.

[00704] A dimerizer can also be delivered to the subject by enteral administration. Enteral routes of administration include, but are not necessarily limited to, oral and rectal (*e.g.*, using a suppository) delivery.

[00705] By treatment is meant at least an amelioration of the symptoms associated with the pathological condition afflicting the host, where amelioration is used in a broad sense to refer to at least a reduction in the magnitude of a parameter, *e.g.* symptom, associated with the pathological condition being treated, such as cancer. As such, treatment also includes situations where the pathological condition, or at least symptoms associated therewith, are completely inhibited, *e.g.* prevented from happening, or stopped, *e.g.* terminated, such that the host no longer suffers from the pathological condition, or at least the symptoms that characterize the pathological condition.

[00706] In some embodiments, a dimerizer is administered by injection and/or delivery, e.g., to a site in a brain artery or directly into brain tissue. A dimerizer can also be administered directly to a target site e.g., by direct injection, by implantation of a drug delivery device such as an osmotic pump or slow release particle, by biolistic delivery to the target site, etc.

[00707]

EXAMPLES OF NON-LIMITING ASPECTS OF THE DISCLOSURE

[00708] Aspects, including embodiments, of the present subject matter described above may be beneficial alone or in combination, with one or more other aspects or embodiments. Without limiting the foregoing

description, certain non-limiting aspects of the disclosure numbered 1-45 are provided below. As will be apparent to those of skill in the art upon reading this disclosure, each of the individually numbered aspects may be used or combined with any of the preceding or following individually numbered aspects. This is intended to provide support for all such combinations of aspects and is not limited to combinations of aspects explicitly provided below:

[00709] 1. A heterodimeric, conditionally active polypeptide comprising: a) a first chimeric polypeptide comprising a first member of a dimerization pair and a first heterologous polypeptide; and b) a second chimeric polypeptide comprising a second member of a dimerization pair and a second heterologous polypeptide, wherein the first member of the dimerization pair comprises a ligand-binding domain (LBD) of a nuclear hormone receptor, and the second member of the dimerization pair comprises a co-regulator of the nuclear hormone receptor, or wherein the first member of the dimerization pair is a co-regulator of a nuclear hormone receptor, and the second member of the dimerization pair comprises an LBD of the nuclear hormone receptor; and wherein the first chimeric polypeptide and the second chimeric polypeptide are dimerized in the presence of a dimerization agent that induces binding of the LBD to the co-regulator.

[00710] 2. The heterodimeric, conditionally active polypeptide of aspect 1, wherein: a) the first heterologous polypeptide is a T-cell receptor (TCR) alpha chain; and b) the second heterologous polypeptide is a TCR beta chain.

[00711] 3. The heterodimeric, conditionally active polypeptide of aspect 1, wherein: a) the first heterologous polypeptide is a first polypeptide of a chimeric antigen receptor (CAR) heterodimer; and b) the second heterologous polypeptide is a second polypeptide of a CAR heterodimer.

[00712] 4. The heterodimeric, conditionally active polypeptide of aspect 1, wherein: a) the first heterologous polypeptide is an N-terminal portion of an RNA-guided endonuclease; and b) the second heterologous polypeptide is a C-terminal portion of the RNA-guided endonuclease, wherein dimerization of the first chimeric polypeptide and the second chimeric polypeptide, mediated by the dimerization agent that induces binding of the LBD to the co-regulator, restores enzymatic function of the RNA-guided endonuclease.

[00713] 5. The heterodimeric, conditionally active polypeptide of aspect 4, wherein the RNA-guided endonuclease is a class 2 CRISPR/Cas endonuclease.

[00714] 6. The heterodimeric, conditionally active polypeptide of aspect 5, wherein the class 2 CRISPR/Cas endonuclease is a type II CRISPR/Cas protein, a type V CRISPR/Cas protein, or a type VI CRISPR/Cas protein.

[00715] 7. The heterodimeric, conditionally active polypeptide of aspect 1, wherein: a) the first heterologous polypeptide is an N-terminal portion of an enzyme; and b) the second heterologous

polypeptide is a C-terminal portion of the enzyme, wherein dimerization of the first chimeric polypeptide and the second chimeric polypeptide restore enzymatic activity of the enzyme.

[00716] 8. The heterodimeric, conditionally active polypeptide of aspect 7, wherein the enzyme is a kinase, a protease, a phosphatase, or a caspase.

[00717] 9. The heterodimeric, conditionally active polypeptide of aspect 1, wherein the first polypeptide and the second polypeptide exhibit an activity when brought into proximity upon dimerization mediated by the dimerization agent, but do not exhibit the activity individually.

[00718] 10. The heterodimeric, conditionally active polypeptide of aspect 1, wherein a) the first heterologous polypeptide is an N-terminal portion of an antigen receptor; and b) the second heterologous polypeptide is a C-terminal portion of the antigen receptor, wherein dimerization of the first chimeric polypeptide and the second chimeric polypeptide restore signaling activity of the antigen receptor.

[00719] 11. The heterodimeric, conditionally active polypeptide of aspect 1, wherein: a) the first heterologous polypeptide is an N-terminal portion of a receptor; and b) the second heterologous polypeptide is a C-terminal portion of the antigen receptor, wherein dimerization of the first chimeric polypeptide and the second chimeric polypeptide mediated by the dimerization agent restores signaling activity of the receptor.

[00720] 12. The heterodimeric, conditionally active polypeptide of any one of aspects 1-11, wherein LBD of the nuclear hormone binding member of the dimerization pair is an LBD of a nuclear hormone receptor selected from an estrogen receptor, an ecdysone receptor, a PPARγ receptor, a glucocorticoid receptor, an androgen receptor, a thyroid hormone receptor, a mineralocorticoid receptor, a progesterone receptor, a vitamin D receptor, a PPARβ receptor, a PPARα receptor, a pregnane X receptor, a liver X receptor, a farnesoid X receptor, a retinoid X receptor, a RAR-related orphan receptor, and a retinoic acid receptor.

[00721] 13. The heterodimeric, conditionally active polypeptide of any one of aspects 1-12, wherein the co-regulator of the nuclear hormone receptor is selected from SRC1, GRIP1, AIB1, PGC1a, PGC1b, PRC, TRAP220, ASC2, CBP, P300, CIA, ARA70, TIF1, NSD1, SMAP, Tip60, ERAP140, Nix1, LCoR, N-CoR, SMRT, RIP140, and PRIC285.

[00722] 14. The heterodimeric, conditionally active polypeptide of any one of aspects 1-12, wherein the co-regulator of the nuclear hormone receptor is selected from:

a) SRC1: CPSSHSSLTERHKILHRLLQEGSPS (SEQ ID NO:1);

b) SRC1–2: SLTARHKILHRLLQEGSPSDI (SEQ ID NO:2);

c) SRC3-1: ESKGHKKLLQLLTCSSDDR (SEQ ID NO:3);

d) SRC3: PKKENNALLRYLLDRDDPSDV (SEQ ID NO:4);

e) PGC-1: AEEPSLLKKLLLAPANT (SEQ ID NO:5);

f) PGC1a: QEAEEPSLLKKLLLAPANTQL (SEQ ID NO:6);

g) TRAP220–1: SKVSQNPILTSLLQITGNGGS (SEQ ID NO:7);

h) NCoR (2051–2075): GHSFADPASNLGLEDIIRKALMGSF (SEQ ID NO:8);

i) NR0B1: PRQGSILYSMLTSAKQT (SEQ ID NO:9);

j) NRIP1: AANNSLLLHLLKSQTIP (SEQ ID NO:10);

k) TIF2: PKKKENALLRYLLDKDDTKDI (SEQ ID NO:11);

l) CoRNR Box: DAFQLRQLILRGLQDD (SEQ ID NO:12);

m) αβV: SPGSREWFKDMLS (SEQ ID NO:13);

n) TRAP220-2: GNTKNHPMLMNLLKDNPAQDF (SEQ ID NO:14);

o) EA2: SSKGVLWRMLAEPVSR (SEQ ID NO:15);

p) TA1: SRTLQLDWGTLYWSR (SEQ ID NO:16);

q) EAB1: SSNHQSSRLIELLSR (SEQ ID NO:17);

r) SRC2: LKEKHKILHRLLQDSSSPV (SEQ ID NO:18);

s) SRC1-3: QAQQKSLLQQLLTE (SEQ ID NO:19);

t) SRC1–1: KYSQTSHKLVQLLTTTAEQQL (SEQ ID NO:20);

u) SRC1–2: SLTARHKILHRLLQEGSPSDI (SEQ ID NO:21);

v) SRC1–3: KESKDHQLLRYLLDKDEKDLR (SEQ ID NO:22);

w) SRC1–4a: PQAQQKSLLQQLLTE (SEQ ID NO:23);;

x) SRC1–4b: PQAQQKSLRQQLLTE (SEQ ID NO:24);

y) GRIP1–1: HDSKGQTKLLQLLTTKSDQME (SEQ ID NO:25);

z) GRIP1–2: SLKEKHKILHRLLQDSSSPVD (SEQ ID NO:26);

aa) GRIP1–3: PKKKENALLRYLLDKDDTKDI (SEQ ID NO:27);

bb) AIB1–1: LESKGHKKLLQLLTCSSDDRG (SEQ ID NO:28);

cc) AIB1–2: LLQEKHRILHKLLQNGNSPAE (SEQ ID NO:29);

dd) AIB1–3: KKKENNALLRYLLDRDDPSDA (SEQ ID NO:30);

ee) PGC1a: QEAEEPSLLKKLLLAPANTQL (SEQ ID NO:31);

ff) PGC1b: PEVDELSLLQKLLLATSYPTS (SEQ ID NO:32);

gg) PRC: VSPREGSSLHKLLTLSRTPPE (SEQ ID NO:33);

hh) TRAP220–1: SKVSQNPILTSLLQITGNGGS (SEQ ID NO:34);

ii) TRAP220–2: GNTKNHPMLMNLLKDNPAQDF (SEQ ID NO:35);

jj) ASC2–1: DVTLTSPLLVNLLQSDISAGH (SEQ ID NO:36);

kk) ASC2–2: AMREAPTSLSQLLDNSGAPNV (SEQ ID NO:37);

ll) CBP-1: DAASKHKQLSELLRGGSGSSI (SEQ ID NO:38);

mm) CBP-2: KRKLIQQQLVLLLHAHKCQRR (SEQ ID NO:39);

nn) P300: DAASKHKQLSELLRSGSSPNL (SEQ ID NO:40);

oo) CIA: GHPPAIQSLINLLADNRYLTA (SEQ ID NO:41);

pp) ARA70–1: TLQQQAQQLYSLLGQFNCLTH (SEQ ID NO:42);

qq) ARA70–2: GSRETSEKFKLLFQSYNVNDW (SEQ ID NO:43);

rr) TIF1: NANYPRSILTSLLLNSSQSST (SEQ ID NO:44);

ss) NSD1: IPIEPDYKFSTLLMMLKDMHD (SEQ ID NO:45);

tt) SMAP: ATPPPSPLLSELLKKGSLLPT (SEQ ID NO:46);

uu) Tip60: VDGHERAMLKRLLRIDSKCLH (SEQ ID NO:47);

vv) ERAP140: HEDLDKVKLIEYYLTKNKEGP (SEQ ID NO:48);

ww) Nix1: ESPEFCLGLQTLLSLKCCIDL (SEQ ID NO:49);

xx) LCoR: AATTQNPVLSKLLMADQDSPL (SEQ ID NO:50);

yy) CoRNR1 (N-CoR): MGQVPRTHRLITLADHICQIITQDFARNQV (SEQ ID NO:51);

zz) CoRNR2 (N-CoR): NLGLEDIIRKALMG (SEQ ID NO:52);

aaa) CoRNR1 (SMRT): APGVKGHQRVVTLAQHISEVITQDTYRHHPQQLSAPLPAP (SEQ ID NO:53);

bbb) CoRNR2 (SMRT): NMGLEAIIRKALMG (SEQ ID NO:54);

ccc) RIP140-C: RLTKTNPILYYMLQKGGNSVA (SEQ ID NO:55);

ddd) RIP140-1: QDSIVLTYLEGLLMHQAAGGS (SEQ ID NO:56);

eee) RIP140-2: KGKQDSTLLASLLQSFSSRLQ (SEQ ID NO:57);

fff) RIP140-3: CYGVASSHLKTLLKKSKVKDQ (SEQ ID NO:58);

ggg) RIP140-4: KPSVACSQLALLLSSEAHLQQ (SEQ ID NO:59);

hhh) RIP140-5: KQAANNSLLLHLLKSQTIPKP (SEQ ID NO:60);

iii) RIP140-6: NSHQKVTLLQLLLGHKNEENV (SEQ ID NO:61);

jjj) RIP140-7: NLLERRTVLQLLLGNPTKGRV (SEQ ID NO:62);

kkk) RIP140-8: FSFSKNGLLSRLLRQNQDSYL (SEQ ID NO:63);

lll) RIP140-9: RESKSFNVLKQLLLSENCVRD (SEQ ID NO:64);

mmm) PRIC285-1: ELNADDAILRELLDESQKVMV (SEQ ID NO:65);

nnn) PRIC285-2: YENLPPAALRKLLRAEPERYR (SEQ ID NO:66);

ooo) PRIC285-3: MAFAGDEVLVQLLSGDKAPEG (SEQ ID NO:67);

ppp) PRIC285-4: SCCYLCIRLEGLLAPTASPRP (SEQ ID NO:68); and

qqq) PRIC285-5: PSNKSVDVLAGLLLRRMELKP (SEQ ID NO:69).

[00723] 15. A heterodimeric, conditionally active receptor comprising: a) a first chimeric polypeptide comprising: i) a first member of a specific binding pair; ii) a first modulatory domain; iii) a first member of a dimerization pair; and iv) a transmembrane domain interposed between the first member of a specific binding pair and the first modulatory domain; and b) a second chimeric polypeptide comprising: i) a transmembrane domain; ii) a second modulatory domain; iii) a second member of the dimerization pair; and iv) an intracellular signaling domain; or comprising: a) a first chimeric polypeptide comprising:

i) a first member of a specific binding pair; ii) a modulatory domain; iii) a first member of a dimerization pair; iv) a transmembrane domain interposed between the first member of a specific binding pair and the modulatory domain; and b) a second chimeric polypeptide comprising: i) a second member of the dimerization pair; and ii) an intracellular signaling domain, wherein the first member of the dimerization pair comprises a ligand-binding domain (LBD) of a nuclear hormone receptor, and the second member of the dimerization pair comprises a co-regulator of the nuclear hormone receptor, or wherein the first member of the dimerization pair is a co-regulator of a nuclear hormone receptor, and the second member of the dimerization pair comprises an LBD of the nuclear hormone receptor, wherein the first chimeric polypeptide and the second chimeric polypeptide are dimerized in the presence of a dimerization agent that induces binding of the LBD to the co-regulator.

[00724] 16. The heterodimeric, conditionally active receptor of aspect 15, wherein the first polypeptide comprises a hinge region interposed between the first member of the specific binding pair and the transmembrane domain.

[00725] 17. The heterodimeric, conditionally active receptor of aspect 15, wherein the first member of the specific binding pair is an antibody or antibody fragment, a ligand, a receptor, or a non-antibody-based recognition scaffold.

[00726] 18. The heterodimeric, conditionally active receptor of aspect 17, wherein the hinge region is an immunoglobulin IgG hinge region or a hinge derived from CD8.

[00727] 19. The heterodimeric, conditionally active receptor of aspect 15, wherein the first and second modulatory domains are selected from 4-1BB (CD137), CD28, ICOS, BTLA, OX-40, CD27, CD30, GITR, HVEM, DAP10, DAP12, and CD28.

[00728] 20. The heterodimeric, conditionally active receptor of aspect 15, wherein the intracellular signaling domain is selected from ZAP70 and CD3-zeta.

[00729] 21. The heterodimeric, conditionally active receptor of aspect 15, wherein the intracellular signaling domain comprises an immunoreceptor tyrosine-based activation motif (ITAM).

[00730] 22. The heterodimeric, conditionally active receptor of any one of aspects 15-21, wherein LBD of the nuclear hormone binding member of the dimerization pair is an LBD of a nuclear hormone receptor selected from estrogen receptor, an ecdysone receptor, a PPARγ receptor, a glucocorticoid receptor, an androgen receptor, a thyroid hormone receptor, a mineralocorticoid receptor, a progesterone receptor, a vitamin D receptor, a PPARβ receptor, a PPARα receptor, a pregnane X receptor, a liver X receptor, a farnesoid X receptor, a retinoid X receptor, a RAR-related orphan receptor, and a retinoic acid receptor.

[00731] 23. The heterodimeric, conditionally active receptor of any one of aspects 15-22, wherein the co-regulator of the nuclear hormone receptor is selected from SRC1, GRIP1, AIB1, PGC1a, PGC1b, PRC,

TRAP220, ASC2, CBP, P300, CIA, ARA70, TIF1, NSD1, SMAP, Tip60, ERAP140, Nix1, LCoR, N-CoR, SMRT, RIP140, and PRIC285.

[00732] 24. The heterodimeric, conditionally active receptor of any one of aspects 15-22, wherein the co-regulator of the nuclear hormone receptor is selected from:

a) SRC1: CPSSHSSLTERHKILHRLLQEGSPS (SEQ ID NO:1);

b) SRC1–2: SLTARHKILHRLLQEGSPSDI (SEQ ID NO:2);

c) SRC3-1: ESKGHKKLLQLLTCSSDDR (SEQ ID NO:3);

d) SRC3: PKKENNALLRYLLDRDDPSDV (SEQ ID NO:4);

e) PGC-1: AEEPSLLKKLLLAPANT (SEQ ID NO:5);

f) PGC1a: QEAEEPSLLKKLLLAPANTQL (SEQ ID NO:6);

g) TRAP220–1: SKVSQNPILTSLLQITGNGGS (SEQ ID NO:7);

h) NCoR (2051–2075): GHSFADPASNLGLEDIIRKALMGSF (SEQ ID NO:8);

i) NR0B1: PRQGSILYSMLTSAKQT (SEQ ID NO:9);

j) NRIP1: AANNSLLLHLLKSQTIP (SEQ ID NO:10);

k) TIF2: PKKKENALLRYLLDKDDTKDI (SEQ ID NO:11);

l) CoRNR Box: DAFQLRQLILRGLQDD (SEQ ID NO:12);

m) αβV: SPGSREWFKDMLS (SEQ ID NO:13);

n) TRAP220-2: GNTKNHPMLMNLLKDNPAQDF (SEQ ID NO:14);

o) EA2: SSKGVLWRMLAEPVSR (SEQ ID NO:15);

p) TA1: SRTLQLDWGTLYWSR (SEQ ID NO:16);

q) EAB1: SSNHQSSRLIELLSR (SEQ ID NO:17);

r) SRC2: LKEKHKILHRLLQDSSSPV (SEQ ID NO:18);

s) SRC1-3: QAQQKSLLQQLLTE (SEQ ID NO:19);

t) SRC1–1: KYSQTSHKLVQLLTTTAEQQL (SEQ ID NO:20);

u) SRC1–2: SLTARHKILHRLLQEGSPSDI (SEQ ID NO:21);

v) SRC1–3: KESKDHQLLRYLLDKDEKDLR (SEQ ID NO:22);

w) SRC1–4a: PQAQQKSLLQQLLTE (SEQ ID NO:23);;

x) SRC1–4b: PQAQQKSLRQQLLTE (SEQ ID NO:24);

y) GRIP1–1: HDSKGQTKLLQLLTTKSDQME (SEQ ID NO:25);

z) GRIP1–2: SLKEKHKILHRLLQDSSSPVD (SEQ ID NO:26);

aa) GRIP1–3: PKKKENALLRYLLDKDDTKDI (SEQ ID NO:27);

bb) AIB1–1: LESKGHKKLLQLLTCSSDDRG (SEQ ID NO:28);

cc) AIB1–2: LLQEKHRILHKLLQNGNSPAE (SEQ ID NO:29);

dd) AIB1–3: KKKENNALLRYLLDRDDPSDA (SEQ ID NO:30);

ee) PGC1a: QEAEEPSLLKKLLLAPANTQL (SEQ ID NO:31);

ff) PGC1b: PEVDELSLLQKLLLATSYPTS (SEQ ID NO:32);

gg) PRC: VSPREGSSLHKLLTLSRTPPE (SEQ ID NO:33);

hh) TRAP220–1: SKVSQNPILTSLLQITGNGGS (SEQ ID NO:34);

ii) TRAP220–2: GNTKNHPMLMNLLKDNPAQDF (SEQ ID NO:35);

jj) ASC2–1: DVTLTSPLLVNLLQSDISAGH (SEQ ID NO:36);

kk) ASC2–2: AMREAPTSLSQLLDNSGAPNV (SEQ ID NO:37);

ll) CBP-1: DAASKHKQLSELLRGGSGSSI (SEQ ID NO:38);

mm) CBP-2: KRKLIQQQLVLLLHAHKCQRR (SEQ ID NO:39);

nn) P300: DAASKHKQLSELLRSGSSPNL (SEQ ID NO:40);

oo) CIA: GHPPAIQSLINLLADNRYLTA (SEQ ID NO:41);

pp) ARA70–1: TLQQQAQQLYSLLGQFNCLTH (SEQ ID NO:42);

qq) ARA70–2: GSRETSEKFKLLFQSYNVNDW (SEQ ID NO:43);

rr) TIF1: NANYPRSILTSLLLNSSQSST (SEQ ID NO:44);

ss) NSD1: IPIEPDYKFSTLLMMLKDMHD (SEQ ID NO:45);

tt) SMAP: ATPPPSPLLSELLKKGSLLPT (SEQ ID NO:46);

uu) Tip60: VDGHERAMLKRLLRIDSKCLH (SEQ ID NO:47);

vv) ERAP140: HEDLDKVKLIEYYLTKNKEGP (SEQ ID NO:48);

ww) Nix1: ESPEFCLGLQTLLSLKCCIDL (SEQ ID NO:49);

xx) LCoR: AATTQNPVLSKLLMADQDSPL (SEQ ID NO:50);

yy) CoRNR1 (N-CoR): MGQVPRTHRLITLADHICQIITQDFARNQV (SEQ ID NO:51);

zz) CoRNR2 (N-CoR): NLGLEDIIRKALMG (SEQ ID NO:52);

aaa) CoRNR1 (SMRT): APGVKGHQRVVTLAQHISEVITQDTYRHHPQQLSAPLPAP (SEQ ID NO:53);

bbb) CoRNR2 (SMRT): NMGLEAIIRKALMG (SEQ ID NO:54);

ccc) RIP140-C: RLTKTNPILYYMLQKGGNSVA (SEQ ID NO:55);

ddd) RIP140-1: QDSIVLTYLEGLLMHQAAGGS (SEQ ID NO:56);

eee) RIP140-2: KGKQDSTLLASLLQSFSSRLQ (SEQ ID NO:57);

fff) RIP140-3: CYGVASSHLKTLLKKSKVKDQ (SEQ ID NO:58);

ggg) RIP140-4: KPSVACSQLALLLSSEAHLQQ (SEQ ID NO:59);

hhh) RIP140-5: KQAANNSLLLHLLKSQTIPKP (SEQ ID NO:60);

iii) RIP140-6: NSHQKVTLLQLLLGHKNEENV (SEQ ID NO:61);

jjj) RIP140-7: NLLERRTVLQLLLGNPTKGRV (SEQ ID NO:62);

kkk) RIP140-8: FSFSKNGLLSRLLRQNQDSYL (SEQ ID NO:63);

lll) RIP140-9: RESKSFNVLKQLLLSENCVRD (SEQ ID NO:64);

mmm) PRIC285-1: ELNADDAILRELLDESQKVMV (SEQ ID NO:65);

nnn) PRIC285-2: YENLPPAALRKLLRAEPERYR (SEQ ID NO:66);

ooo) PRIC285-3: MAFAGDEVLVQLLSGDKAPEG (SEQ ID NO:67);

ppp) PRIC285-4: SCCYLCIRLEGLLAPTASPRP (SEQ ID NO:68); and

qqq) PRIC285-5: PSNKSVDVLAGLLLRRMELKP (SEQ ID NO:69).

[00733] 25. The heterodimeric, conditionally active receptor of aspect 18, wherein: i) the first and second modulatory domains are derived from 4-1BB; ii) the first and second members of the dimerization pair are PPARγ and SRC3; and ii) the signaling domain comprises an ITAM.

[00734] 26. The heterodimeric, conditionally active receptor of aspect 15, wherein the first member of the specific binding pair is a single-chain Fv.

[00735] 27. The heterodimeric, conditionally active receptor of aspect 15, wherein the first member of the specific binding pair binds an epitope present on a cell, on a solid surface, or a lipid bilayer.

[00736] 28. The heterodimeric, conditionally active receptor of aspect 27, wherein the cell is a cancer cell.

[00737] 29. The heterodimeric, conditionally active receptor of aspect 15, wherein the intracellular signaling domain is an intracellular inhibitory domain.

[00738] 30. The heterodimeric, conditionally active receptor of aspect 29, wherein the intracellular inhibitory domain is derived from a protein selected from the group consisting of: PD-1, CTLA4, HPK1, SHP1, SHP2, Sts1, and Csk.

[00739] 31. A heterodimeric, conditionally repressible synthetic immune cell receptor (ICR) comprising: a synthetic stimulatory ICR comprising a first member of a dimerization pair linked to the synthetic stimulatory ICR; and a synthetic ICR repressor comprising a second member of the dimerization pair linked to an intracellular inhibitory domain, wherein the first member of the dimerization pair comprises a ligand-binding domain (LBD) of a nuclear hormone receptor, and the second member of the dimerization pair comprises a co-regulator of the nuclear hormone receptor, or wherein the first member of the dimerization pair is a co-regulator of a nuclear hormone receptor, and the second member of the dimerization pair comprises an LBD of the nuclear hormone receptor, wherein the synthetic stimulatory ICR and the synthetic ICR repressor are dimerized in the presence of a dimerization agent that induces binding of the LBD to the co-regulator.

[00740] 32. The conditionally repressible synthetic ICR of Aspect 31, wherein the synthetic stimulatory ICR comprises an intracellular co-stimulatory domain.

[00741] 33. The conditionally repressible synthetic ICR of Aspect 32, wherein the intracellular co-stimulatory domain is selected from the group consisting of: 4-1BB (CD137), CD28, ICOS, OX-40, BTLA, CD27, CD30, GITR, and HVEM.

[00742] 34. The conditionally repressible synthetic ICR of any one of aspects 31-33, wherein the first member of a dimerization pair is linked intracellularly to the synthetic stimulatory ICR and the second member of the dimerization pair is linked intracellularly to the intracellular inhibitory domain.

[00743] 35. The conditionally repressible synthetic ICR of any one of aspects 31-34, wherein the synthetic ICR repressor further comprises a transmembrane domain.

[00744] 36. The conditionally repressible synthetic ICR of Aspect 35, wherein the second member of the dimerization pair is linked intracellularly to the transmembrane domain.

[00745] 37. The conditionally repressible synthetic ICR of Aspect 35, wherein the second member of the dimerization pair is extracellular and linked to the intracellular inhibitory domain by way of the transmembrane domain.

[00746] 38. The conditionally repressible synthetic ICR of any one of aspects 31-37, wherein the stimulatory ICR binds a soluble antigen.

[00747] 39. The conditionally repressible synthetic ICR of any one of aspects 31-38, wherein the stimulatory ICR binds a cell surface antigen.

[00748] 40. The conditionally repressible synthetic ICR of any one aspects 31-39, wherein the intracellular inhibitory domain is an inhibitory domain derived from a protein selected from the group consisting of: PD-1, CTLA4, HPK1, SHP1, SHP2, Sts1 and Csk.

[00749] 41. The conditionally repressible synthetic ICR of any one of aspects 31-40, wherein the synthetic stimulatory ICR comprises an intracellular signaling domain selected from the group consisting of: a CD3-zeta signaling domain, a ZAP70 signaling domain and an immunoreceptor tyrosine-based activation motif (ITAM).

[00750] 42. The conditionally repressible synthetic ICR of any one of aspects 31-41, wherein LBD of the nuclear hormone binding member of the dimerization pair is an LBD of a nuclear hormone receptor selected from estrogen receptor, an ecdysone receptor, a PPARγ receptor, a glucocorticoid receptor, an androgen receptor, a thyroid hormone receptor, a mineralocorticoid receptor, a progesterone receptor, a vitamin D receptor, a PPARβ receptor, a PPARα receptor, a pregnane X receptor, a liver X receptor, a farnesoid X receptor, a retinoid X receptor, a RAR-related orphan receptor, and a retinoic acid receptor.

[00751] 43. The conditionally repressible synthetic ICR of any one of aspects 41-42, wherein the co-regulator of the nuclear hormone receptor is selected from SRC1, GRIP1, AIB1, PGC1a, PGC1b, PRC, TRAP220, ASC2, CBP, P300, CIA, ARA70, TIF1, NSD1, SMAP, Tip60, ERAP140, Nix1, LCoR, N-CoR, SMRT, RIP140, and PRIC285.

[00752] 44. The conditionally repressible synthetic ICR of any one of aspects 41-42, wherein the co-regulator of the nuclear hormone receptor is selected from:

a) SRC1: CPSSHSSLTERHKILHRLLQEGSPS (SEQ ID NO:1);

b) SRC1–2: SLTARHKILHRLLQEGSPSDI (SEQ ID NO:2);

c) SRC3-1: ESKGHKKLLQLLTCSSDDR (SEQ ID NO:3);

d) SRC3: PKKENNALLRYLLDRDDPSDV (SEQ ID NO:4);

e) PGC-1: AEEPSLLKKLLLAPANT (SEQ ID NO:5);

f) PGC1a: QEAEEPSLLKKLLLAPANTQL (SEQ ID NO:6);

g) TRAP220–1: SKVSQNPILTSLLQITGNGGS (SEQ ID NO:7);

h) NCoR (2051–2075): GHSFADPASNLGLEDIIRKALMGSF (SEQ ID NO:8);

i) NR0B1: PRQGSILYSMLTSAKQT (SEQ ID NO:9);

j) NRIP1: AANNSLLLHLLKSQTIP (SEQ ID NO:10);

k) TIF2: PKKKENALLRYLLDKDDTKDI (SEQ ID NO:11);

l) CoRNR Box: DAFQLRQLILRGLQDD (SEQ ID NO:12);

m) αβV: SPGSREWFKDMLS (SEQ ID NO:13);

n) TRAP220-2: GNTKNHPMLMNLLKDNPAQDF (SEQ ID NO:14);

o) EA2: SSKGVLWRMLAEPVSR (SEQ ID NO:15);

p) TA1: SRTLQLDWGTLYWSR (SEQ ID NO:16);

q) EAB1: SSNHQSSRLIELLSR (SEQ ID NO:17);

r) SRC2: LKEKHKILHRLLQDSSSPV (SEQ ID NO:18);

s) SRC1-3: QAQQKSLLQQLLTE (SEQ ID NO:19);

t) SRC1–1: KYSQTSHKLVQLLTTTAEQQL (SEQ ID NO:20);

u) SRC1–2: SLTARHKILHRLLQEGSPSDI (SEQ ID NO:21);

v) SRC1–3: KESKDHQLLRYLLDKDEKDLR (SEQ ID NO:22);

w) SRC1–4a: PQAQQKSLLQQLLTE (SEQ ID NO:23);;

x) SRC1–4b: PQAQQKSLRQQLLTE (SEQ ID NO:24);

y) GRIP1–1: HDSKGQTKLLQLLTTKSDQME (SEQ ID NO:25);

z) GRIP1–2: SLKEKHKILHRLLQDSSSPVD (SEQ ID NO:26);

aa) GRIP1–3: PKKKENALLRYLLDKDDTKDI (SEQ ID NO:27);

bb) AIB1–1: LESKGHKKLLQLLTCSSDDRG (SEQ ID NO:28);

cc) AIB1–2: LLQEKHRILHKLLQNGNSPAE (SEQ ID NO:29);

dd) AIB1–3: KKKENNALLRYLLDRDDPSDA (SEQ ID NO:30);

ee) PGC1a: QEAEEPSLLKKLLLAPANTQL (SEQ ID NO:31);

ff) PGC1b: PEVDELSLLQKLLLATSYPTS (SEQ ID NO:32);

gg) PRC: VSPREGSSLHKLLTLSRTPPE (SEQ ID NO:33);

hh) TRAP220–1: SKVSQNPILTSLLQITGNGGS (SEQ ID NO:34);

ii) TRAP220–2: GNTKNHPMLMNLLKDNPAQDF (SEQ ID NO:35);

jj) ASC2–1: DVTLTSPLLVNLLQSDISAGH (SEQ ID NO:36);

kk) ASC2–2: AMREAPTSLSQLLDNSGAPNV (SEQ ID NO:37);

ll) CBP-1: DAASKHKQLSELLRGGSGSSI (SEQ ID NO:38);

mm) CBP-2: KRKLIQQQLVLLLHAHKCQRR (SEQ ID NO:39);

nn) P300: DAASKHKQLSELLRSGSSPNL (SEQ ID NO:40);

oo) CIA: GHPPAIQSLINLLADNRYLTA (SEQ ID NO:41);

pp) ARA70–1: TLQQQAQQLYSLLGQFNCLTH (SEQ ID NO:42);

qq) ARA70–2: GSRETSEKFKLLFQSYNVNDW (SEQ ID NO:43);

rr) TIF1: NANYPRSILTSLLLNSSQSST (SEQ ID NO:44);

ss) NSD1: IPIEPDYKFSTLLMMLKDMHD (SEQ ID NO:45);

tt) SMAP: ATPPPSPLLSELLKKGSLLPT (SEQ ID NO:46);

uu) Tip60: VDGHERAMLKRLLRIDSKCLH (SEQ ID NO:47);

vv) ERAP140: HEDLDKVKLIEYYLTKNKEGP (SEQ ID NO:48);

ww) Nix1: ESPEFCLGLQTLLSLKCCIDL (SEQ ID NO:49);

xx) LCoR: AATTQNPVLSKLLMADQDSPL (SEQ ID NO:50);

yy) CoRNR1 (N-CoR): MGQVPRTHRLITLADHICQIITQDFARNQV (SEQ ID NO:51);

zz) CoRNR2 (N-CoR): NLGLEDIIRKALMG (SEQ ID NO:52);

aaa) CoRNR1 (SMRT): APGVKGHQRVVTLAQHISEVITQDTYRHHPQQLSAPLPAP (SEQ ID NO:53);

bbb) CoRNR2 (SMRT): NMGLEAIIRKALMG (SEQ ID NO:54);

ccc) RIP140-C: RLTKTNPILYYMLQKGGNSVA (SEQ ID NO:55);

ddd) RIP140-1: QDSIVLTYLEGLLMHQAAGGS (SEQ ID NO:56);

eee) RIP140-2: KGKQDSTLLASLLQSFSSRLQ (SEQ ID NO:57);

fff) RIP140-3: CYGVASSHLKTLLKKSKVKDQ (SEQ ID NO:58);

ggg) RIP140-4: KPSVACSQLALLLSSEAHLQQ (SEQ ID NO:59);

hhh) RIP140-5: KQAANNSLLLHLLKSQTIPKP (SEQ ID NO:60);

iii) RIP140-6: NSHQKVTLLQLLLGHKNEENV (SEQ ID NO:61);

jjj) RIP140-7: NLLERRTVLQLLLGNPTKGRV (SEQ ID NO:62);

kkk) RIP140-8: FSFSKNGLLSRLLRQNQDSYL (SEQ ID NO:63);

lll) RIP140-9: RESKSFNVLKQLLLSENCVRD (SEQ ID NO:64);

mmm) PRIC285-1: ELNADDAILRELLDESQKVMV (SEQ ID NO:65);

nnn) PRIC285-2: YENLPPAALRKLLRAEPERYR (SEQ ID NO:66);

ooo) PRIC285-3: MAFAGDEVLVQLLSGDKAPEG (SEQ ID NO:67);

ppp) PRIC285-4: SCCYLCIRLEGLLAPTASPRP (SEQ ID NO:68); and

qqq) PRIC285-5: PSNKSVDVLAGLLLRRMELKP (SEQ ID NO:69).

[00753] 45. The conditionally repressible synthetic ICR of any one of aspects 31-44, wherein the synthetic stimulatory ICR is a synthetic chimeric antigen receptor (CAR) or portion thereof.

[00754] 46. The conditionally repressible synthetic ICR of any one of aspects 31-45, wherein the synthetic stimulatory ICR is a synthetic T cell receptor (TCR) or portion thereof.

[00755] 47. A heterodimeric, conditionally repressible synthetic chimeric antigen receptor (CAR) comprising: a) a synthetic stimulatory CAR comprising: i) a extracellular recognition domain; ii) a transmembrane domain linked to the extracellular recognition domain; iii) a first member of a dimerization pair linked to the transmembrane domain; and iv) an intracellular stimulation domain; and b) a synthetic CAR repressor comprising: i) a second member of the dimerization pair; and ii) an intracellular inhibitory domain linked to the second member of the dimerization pair, wherein the first member of the dimerization pair comprises a ligand-binding domain (LBD) of a nuclear hormone receptor, and the second member of the dimerization pair comprises a co-regulator of the nuclear hormone receptor, or wherein the first member of the dimerization pair is a co-regulator of a nuclear hormone receptor, and the second member of the dimerization pair comprises an LBD of the nuclear hormone receptor; and wherein the synthetic stimulatory CAR and the synthetic CAR repressor are dimerized in the presence of a dimerization agent that induces binding of the LBD to the co-regulator.

[00756] 48. The heterodimeric, conditionally repressible synthetic CAR of Aspect 47, wherein the synthetic CAR repressor further comprises a transmembrane domain linked to the second member of the dimerization pair, the intracellular inhibitory domain or both.

[00757] 49. A heterodimeric, conditionally repressible synthetic T cell receptor (TCR) comprising: a) a synthetic stimulatory TCR comprising: i) a transmembrane domain; ii) a first member of a dimerization pair linked to the transmembrane domain; iii) an engineered TCR polypeptide comprising at least one TCR alpha or beta chain, wherein the at least one TCR alpha or beta chain is linked to the transmembrane domain or the first member of a dimerization pair; and b) a synthetic TCR repressor comprising: i) a second member of the dimerization pair; and ii) an intracellular inhibitory domain linked to the second member of the dimerization pair, wherein the first member of the dimerization pair comprises a ligand-binding domain (LBD) of a nuclear hormone receptor, and the second member of the dimerization pair comprises a co-regulator of the nuclear hormone receptor, or wherein the first member of the dimerization pair is a co-regulator of a nuclear hormone receptor, and the second member of the dimerization pair comprises an LBD of the nuclear hormone receptor; and wherein the synthetic stimulatory TCR and the synthetic TCR repressor are dimerized in the presence of a dimerization agent that induces binding of the LBD to the co-regulator.

[00758] 50. The heterodimeric, conditionally repressible synthetic TCR of Aspect 49, wherein the synthetic TCR repressor further comprises a transmembrane domain linked to the second member of the dimerization pair, the intracellular inhibitory domain or both.

[00759] 51. The heterodimeric, conditionally repressible synthetic TCR of Aspects 49 or 50, wherein the engineered TCR polypeptide further comprises a TCR gamma chain.

[00760] 52. A heterodimeric, conditionally active chimeric antigen receptor (CAR) comprising: a) a first polypeptide comprising: i) a first member of a specific binding pair; ii) a first modulatory domain; iii) a first member of a dimerization pair; and iv) a transmembrane domain interposed between the first member of a specific binding pair and the first modulatory domain; and b) a second polypeptide comprising: i) a transmembrane domain; ii) a second modulatory domain; iii) a second member of the dimerization pair; and iv) an intracellular signaling domain; or comprising: a) a first polypeptide comprising: i) a first member of a specific binding pair; ii) a modulatory domain; iii) a first member of a dimerization pair; iv) a transmembrane domain interposed between the first member of a specific binding pair and the modulatory domain; and b) a second polypeptide comprising: i) a second member of the dimerization pair; and ii) an intracellular signaling domain, wherein the first member of the dimerization pair comprises a ligand-binding domain (LBD) of a nuclear hormone receptor, and the second member of the dimerization pair comprises a co-regulator of the nuclear hormone receptor, or wherein the first member of the dimerization pair is a co-regulator of a nuclear hormone receptor, and the second member of the dimerization pair comprises an LBD of the nuclear hormone receptor; and wherein the first polypeptide and the second polypeptide are dimerized in the presence of a dimerization agent that induces binding of the LBD to the co-regulator.

[00761] 53. The heterodimeric, conditionally active CAR of aspect 52, wherein the first polypeptide comprises a hinge region interposed between the first member of the specific binding pair and the transmembrane domain.

[00762] 54. The heterodimeric, conditionally active CAR of aspect 52, wherein the first member of the specific binding pair is an antibody or antibody fragment, a ligand, or a receptor.

[00763] 55. The heterodimeric, conditionally active CAR of aspect 53, wherein the hinge region is an immunoglobulin IgG hinge region or a hinge derived from CD8.

[00764] 56. The heterodimeric, conditionally active CAR of aspect 52, wherein the first and second modulatory domains are selected from 4-1BB (CD137), CD28, ICOS, BTLA, OX-40, CD27, CD30, GITR, HVEM, DAP10, DAP12, and CD28.

[00765] 57. The heterodimeric, conditionally active CAR of aspect 52, wherein the intracellular signaling domain is selected from ZAP70 and CD3-zeta.

[00766] 58. The heterodimeric, conditionally active CAR of aspect 52, wherein the intracellular signaling domain comprises an immunoreceptor tyrosine-based activation motif (ITAM).

[00767] 59. The heterodimeric, conditionally active CAR of any one of aspects 52-58, wherein LBD of the nuclear hormone binding member of the dimerization pair is an LBD of a nuclear hormone receptor selected from estrogen receptor, an ecdysone receptor, a PPARγ receptor, a glucocorticoid receptor, an androgen receptor, a thyroid hormone receptor, a mineralocorticoid receptor, a progesterone receptor, a vitamin D receptor, a PPARβ receptor, a PPARα receptor, a pregnane X receptor, a liver X receptor, a farnesoid X receptor, a retinoid X receptor, a RAR-related orphan receptor, and a retinoic acid receptor.

[00768] 60. The heterodimeric, conditionally active CAR of any one of aspects 52-59, wherein the co-regulator of the nuclear hormone receptor is selected from SRC1, GRIP1, AIB1, PGC1a, PGC1b, PRC, TRAP220, ASC2, CBP, P300, CIA, ARA70, TIF1, NSD1, SMAP, Tip60, ERAP140, Nix1, LCoR, N-CoR, SMRT, RIP140, and PRIC285.

[00769] 61. The heterodimeric, conditionally active CAR of any one of aspects 52-59, wherein the co-regulator of the nuclear hormone receptor is selected from:

a) SRC1: CPSSHSSLTERHKILHRLLQEGSPS (SEQ ID NO:1);

b) SRC1–2: SLTARHKILHRLLQEGSPSDI (SEQ ID NO:2);

c) SRC3-1: ESKGHKKLLQLLTCSSDDR (SEQ ID NO:3);

d) SRC3: PKKENNALLRYLLDRDDPSDV (SEQ ID NO:4);

e) PGC-1: AEEPSLLKKLLLAPANT (SEQ ID NO:5);

f) PGC1a: QEAEEPSLLKKLLLAPANTQL (SEQ ID NO:6);

g) TRAP220–1: SKVSQNPILTSLLQITGNGGS (SEQ ID NO:7);

h) NCoR (2051–2075): GHSFADPASNLGLEDIIRKALMGSF (SEQ ID NO:8);

i) NR0B1: PRQGSILYSMLTSAKQT (SEQ ID NO:9);

j) NRIP1: AANNSLLLHLLKSQTIP (SEQ ID NO:10);

k) TIF2: PKKKENALLRYLLDKDDTKDI (SEQ ID NO:11);

l) CoRNR Box: DAFQLRQLILRGLQDD (SEQ ID NO:12);

m) αβV: SPGSREWFKDMLS (SEQ ID NO:13);

n) TRAP220-2: GNTKNHPMLMNLLKDNPAQDF (SEQ ID NO:14);

o) EA2: SSKGVLWRMLAEPVSR (SEQ ID NO:15);

p) TA1: SRTLQLDWGTLYWSR (SEQ ID NO:16);

q) EAB1: SSNHQSSRLIELLSR (SEQ ID NO:17);

r) SRC2: LKEKHKILHRLLQDSSSPV (SEQ ID NO:18);

s) SRC1-3: QAQQKSLLQQLLTE (SEQ ID NO:19);

t) SRC1–1: KYSQTSHKLVQLLTTTAEQQL (SEQ ID NO:20);

u) SRC1–2: SLTARHKILHRLLQEGSPSDI (SEQ ID NO:21);

v) SRC1–3: KESKDHQLLRYLLDKDEKDLR (SEQ ID NO:22);

w) SRC1–4a: PQAQQKSLLQQLLTE (SEQ ID NO:23);;

x) SRC1–4b: PQAQQKSLRQQLLTE (SEQ ID NO:24);

y) GRIP1–1: HDSKGQTKLLQLLTTKSDQME (SEQ ID NO:25);

z) GRIP1–2: SLKEKHKILHRLLQDSSSPVD (SEQ ID NO:26);

aa) GRIP1–3: PKKKENALLRYLLDKDDTKDI (SEQ ID NO:27);

bb) AIB1–1: LESKGHKKLLQLLTCSSDDRG (SEQ ID NO:28);

cc) AIB1–2: LLQEKHRILHKLLQNGNSPAE (SEQ ID NO:29);

dd) AIB1–3: KKKENNALLRYLLDRDDPSDA (SEQ ID NO:30);

ee) PGC1a: QEAEEPSLLKKLLLAPANTQL (SEQ ID NO:31);

ff) PGC1b: PEVDELSLLQKLLLATSYPTS (SEQ ID NO:32);

gg) PRC: VSPREGSSLHKLLTLSRTPPE (SEQ ID NO:33);

hh) TRAP220–1: SKVSQNPILTSLLQITGNGGS (SEQ ID NO:34);

ii) TRAP220–2: GNTKNHPMLMNLLKDNPAQDF (SEQ ID NO:35);

jj) ASC2–1: DVTLTSPLLVNLLQSDISAGH (SEQ ID NO:36);

kk) ASC2–2: AMREAPTSLSQLLDNSGAPNV (SEQ ID NO:37);

ll) CBP-1: DAASKHKQLSELLRGGSGSSI (SEQ ID NO:38);

mm) CBP-2: KRKLIQQQLVLLLHAHKCQRR (SEQ ID NO:39);

nn) P300: DAASKHKQLSELLRSGSSPNL (SEQ ID NO:40);

oo) CIA: GHPPAIQSLINLLADNRYLTA (SEQ ID NO:41);

pp) ARA70–1: TLQQQAQQLYSLLGQFNCLTH (SEQ ID NO:42);

qq) ARA70–2: GSRETSEKFKLLFQSYNVNDW (SEQ ID NO:43);

rr) TIF1: NANYPRSILTSLLLNSSQSST (SEQ ID NO:44);

ss) NSD1: IPIEPDYKFSTLLMMLKDMHD (SEQ ID NO:45);

tt) SMAP: ATPPPSPLLSELLKKGSLLPT (SEQ ID NO:46);

uu) Tip60: VDGHERAMLKRLLRIDSKCLH (SEQ ID NO:47);

vv) ERAP140: HEDLDKVKLIEYYLTKNKEGP (SEQ ID NO:48);

ww) Nix1: ESPEFCLGLQTLLSLKCCIDL (SEQ ID NO:49);

xx) LCoR: AATTQNPVLSKLLMADQDSPL (SEQ ID NO:50);

yy) CoRNR1 (N-CoR): MGQVPRTHRLITLADHICQIITQDFARNQV (SEQ ID NO:51);

zz) CoRNR2 (N-CoR): NLGLEDIIRKALMG (SEQ ID NO:52);

aaa) CoRNR1 (SMRT): APGVKGHQRVVTLAQHISEVITQDTYRHHPQQLSAPLPAP (SEQ ID NO:53);

bbb) CoRNR2 (SMRT): NMGLEAIIRKALMG (SEQ ID NO:54);

ccc) RIP140-C: RLTKTNPILYYMLQKGGNSVA (SEQ ID NO:55);

ddd) RIP140-1: QDSIVLTYLEGLLMHQAAGGS (SEQ ID NO:56);

eee) RIP140-2: KGKQDSTLLASLLQSFSSRLQ (SEQ ID NO:57);

fff) RIP140-3: CYGVASSHLKTLLKKSKVKDQ (SEQ ID NO:58);

ggg) RIP140-4: KPSVACSQLALLLSSEAHLQQ (SEQ ID NO:59);

hhh) RIP140-5: KQAANNSLLLHLLKSQTIPKP (SEQ ID NO:60);

iii) RIP140-6: NSHQKVTLLQLLLGHKNEENV (SEQ ID NO:61);

jjj) RIP140-7: NLLERRTVLQLLLGNPTKGRV (SEQ ID NO:62);

kkk) RIP140-8: FSFSKNGLLSRLLRQNQDSYL (SEQ ID NO:63);

lll) RIP140-9: RESKSFNVLKQLLLSENCVRD (SEQ ID NO:64);

mmm) PRIC285-1: ELNADDAILRELLDESQKVMV (SEQ ID NO:65);

nnn) PRIC285-2: YENLPPAALRKLLRAEPERYR (SEQ ID NO:66);

ooo) PRIC285-3: MAFAGDEVLVQLLSGDKAPEG (SEQ ID NO:67);

ppp) PRIC285-4: SCCYLCIRLEGLLAPTASPRP (SEQ ID NO:68); and

qqq) PRIC285-5: PSNKSVDVLAGLLLRRMELKP (SEQ ID NO:69).

[00770] 63. The heterodimeric, conditionally active CAR of any one of aspects 52-62, wherein the first member of the specific binding pair is a single-chain Fv.

[00771] 64. The heterodimeric, conditionally active CAR of any one of aspects 52-63, wherein the first member of the specific binding pair binds an epitope present on a cell, on a solid surface, or a lipid bilayer.

[00772] 65. The heterodimeric, conditionally active CAR of aspect 64, wherein the cell is a cancer cell.

[00773] 66. A mammalian cell genetically modified to produce the heterodimeric, conditionally active polypeptide or receptor of any one of aspects 1-65.

[00774] 67. The cell of aspect 66, wherein the cell is a stem cell, a progenitor cell, or a cell derived from a stem cell or a progenitor cell.

[00775] 68. The cell of aspect 66, wherein the cell is a T lymphocyte or an NK cell.

[00776] 69. A nucleic acid comprising nucleotide sequences encoding the heterodimeric, conditionally active receptor or polypeptide of any one of aspects 1-65.

[00777] 70. The nucleic acid of aspect 69, wherein the nucleotide sequences are operably linked to a promoter.

[00778] 71. The nucleic acid of aspect 69, wherein the promoter is an inducible promoter.

[00779] 72. The nucleic acid of aspect 69, wherein the promoter is a cell type-specific or tissue-specific promoter.

[00780] 73. The nucleic acid of aspect 72, wherein the promoter is a T lymphocyte-specific promoter or an NK cell-specific promoter.

[00781] 74. The nucleic acid of any one of aspects 69-73, wherein the nucleic acid is in vitro transcribed RNA.

[00782] 75. A recombinant expression vector comprising the nucleic acid of any one of aspects 69-74.

[00783] 76. A method of modulating an activity of a eukaryotic cell, the method comprising: a) expressing the heterodimeric, conditionally active polypeptide or receptor of any one of aspects 1-65 in the eukaryotic cell; and b) contacting the cell with the ligand.

[00784] 77. A method of modulating an activity of a T lymphocyte, the method comprising contacting the T lymphocyte with a dimerizing agent and a second member of a specific binding pair, wherein the T lymphocyte is genetically modified to produce a heterodimeric, conditionally active receptor of any one of aspects 15-65, and wherein, in the presence of the dimerizing agent and the second member of a specific binding pair, the heterodimeric, conditionally active receptor dimerizes and modulates an activity of the T lymphocyte, thereby producing a modulated T lymphocyte.

[00785] 78. The method of aspect 77, wherein the second member of a specific binding pair is an antigen.

[00786] 79. The method of aspect 77, wherein said contacting occurs in vivo.

[00787] 80. The method of aspect 77, wherein the T lymphocyte is activated, thereby producing an activated T lymphocyte.

[00788] 81. The method of aspect 80, wherein the activated T lymphocyte mediates killing of a target cell.

[00789] 82. The method of aspect 80, wherein the activated T lymphocyte produces IL-2 and/or IFN-γ.

[00790] 83. The method of aspect 81, wherein the target cell is a cancer cell.

[00791] 84. A method of making the cell of any one of aspects 66-68, the method comprising genetically modifying a mammalian cell with an expression vector comprising nucleotide sequences encoding the heterodimeric, conditionally active receptor or polypeptide of any one of aspects 1-65, or genetically modifying a mammalian cell with an RNA comprising nucleotide sequences encoding the heterodimeric, conditionally active receptor or polypeptide of any one of aspects 1-65.

[00792] 85. The method of aspect 84, wherein said genetic modification is carried out ex vivo.

[00793] 86. The method of aspect 84 wherein the cell is a T lymphocyte, a stem cell, an NK cell, a progenitor cell, a cell derived from a stem cell, or a cell derived from a progenitor cell.

[00794] 87. A method of treating a cancer in an individual, the method comprising: i) genetically modifying T lymphocytes obtained from the individual with an expression vector comprising nucleotide sequences encoding the heterodimeric, conditionally active chimeric antigen receptor (CAR) of any one of aspects 49-65, wherein the antigen-binding domain of the heterodimeric, conditionally active CAR is specific for an epitope on a cancer cell in the individual, and wherein said genetic modification is carried out ex vivo; ii) introducing the genetically modified T lymphocytes into the individual; and iii) administering to the individual an effective amount of a dimerizing agent, wherein the dimerizing agent induces dimerization

of the heterodimeric, conditionally active receptor, wherein said dimerization provides for activation of the genetically modified T lymphocytes and killing of the cancer cell, thereby treating the cancer.

[00795] 88. The method of aspect 87, wherein the dimerizing agent is a nuclear hormone that binds the LBD of the nuclear hormone receptor and the co-regulator.

[00796] 89. A method of modulating the activity of a host cell, the method comprising contacting the host cell with a dimerizing agent and a second member of a specific binding pair, wherein the T lymphocyte is genetically modified to produce a heterodimeric, conditionally active receptor of any one of aspects 49-65, and wherein, in the presence of the dimerizing agent and the second member of a specific binding pair, the heterodimeric, conditionally active receptor dimerizes and modulates at least one activity of the host cell.

[00797] 90. The method of aspect 89, wherein the activity is proliferation, cell survival, apoptosis, gene expression, or immune activation.

[00798] 91. The method of aspect 89, wherein the second member of a specific binding pair is an antigen.

EXAMPLES

[00799] The following examples are put forth so as to provide those of ordinary skill in the art with a complete disclosure and description of how to make and use the present invention, and are not intended to limit the scope of what the inventors regard as their invention nor are they intended to represent that the experiments below are all or the only experiments performed. Efforts have been made to ensure accuracy with respect to numbers used (e.g. amounts, temperature, etc.) but some experimental errors and deviations should be accounted for. Unless indicated otherwise, parts are parts by weight, molecular weight is weight average molecular weight, temperature is in degrees Celsius, and pressure is at or near atmospheric. Standard abbreviations may be used, e.g., bp, base pair(s); kb, kilobase(s); pl, picoliter(s); s or sec, second(s); min, minute(s); h or hr, hour(s); aa, amino acid(s); kb, kilobase(s); bp, base pair(s); nt, nucleotide(s); i.m., intramuscular(ly); i.p., intraperitoneal(ly); s.c., subcutaneous(ly); and the like.

MATERIALS AND METHODS

[00800] The following Materials and Methods were used for the experiments described in Examples 1 and 2.

Construction of PPARγ-based ON-switch CARs

[00801] The sequence encoding the anti-human CD19 scFv was cloned into expression vectors. The human 4-1BB co-stimulation and CD3 zeta ITAM signaling chains were cloned from cDNAs supplied by Open Biosystems. PPARgamma LBD and SRC3 co-activator peptide encoding sequences were custom synthesized by IDT DNA. Standard molecular cloning techniques (polymerase chain reaction (PCR), restriction digestion, ligation, homology-based DNA recombination *etc.*) were applied to generate lentiviral expression plasmids for each ON-switch CAR molecule.

Effector and target cell culturing conditions

[00802] A Jurkat cell line expressing Green Fluorescent Protein upon NFAT activation was used. The cell line was maintained in RPMI-1640 medium supplemented with 10% FBS, penicillin and streptomycin. K562 target cells (CD19+/-) from U. Penn were cultured in IMDM supplemented with 10% FBS.

Effector cell engineering with lentivirus

[00803] Pantropic VSV-G pseudotyped lentivirus was produced from Lenti-X 293T cells (Clontech Laboratories #632180) co-transfected with a pHR'SIN:CSW transgene expression vector, viral packaging plasmids pCMVdR8.91 and pMD2.G using Lipofectamine LTX (Life Technologies #15338). Infection medium supernatant was collected 48 hours after transfection and used directly for transduction.

[00804] Jurkat cells were split 1~2 days prior to transduction to ensure that the cell culture would be in log phase at the time of transduction. Transduced cells were cultured for at least 7 days and sorted for abundant CAR expression as needed before experiments were conducted. Expression levels of ON-switch CAR molecules were quantified by flow cytometry. Part 1 of the ON-switch CAR (featuring the scFv) was stained with a fluorophore-conjugated anti-myc antibody, which recognized a myc epitope upstream of the anti-CD19 scFv. Part 2 of the ON-switch CAR (featuring the CD3zeta ITAMs) was quantified using fluorescence of mCherry, which was downstream of the ITAMs.

Quantitation of IL-2 production by ON-switch Jurkat cells

[00805] Jurkat T cells expressing ON-switch CARs were co-cultured with CD19+/- K562 target cells at a 1:2 effector:target ratio. Rosiglitazone (Sigma-Aldrich #R2408) was dissolved in DMSO and added to samples to a final concentration of 10μM. Sample without dimerizer contained the respective vehicle control (1:3000 dilution of dimethyl sulfoxide (DMSO) or 1:1000 dilution of ethanol). After 18 hours of incubation, medium supernatants were collected and analyzed with BD OptEIA Human IL-2 ELISA Set (BD Biosciences #555190).

Construction of Hormone Receptor-based ON-switch CARs

[00806] The sequence encoding the anti-human CD19 scFv was cloned. The human 4-1BB co-stimulation and CD3 zeta ITAM signaling chains were cloned from cDNAs supplied by Open Biosystems. Estrogen receptor LBD and co-activator peptide encoding sequences were custom synthetized by IDT DNA. The sequences of the coactivator peptides were obtained from Heldring et al J Biol Chem. 2007 Apr 6;282(14):10449-55, PMID 17283072. Standard molecular cloning techniques (PCR, restriction digestion, ligation, homology-based DNA recombination *etc.*) were applied to generate lenti-viral expression plasmids for each ON-switch CAR molecule.

Quantitation of CD-69 expression by ON-switch Jurkat cells

[00807] A Jurkat cell line expressing Green Fluorescent Protein upon NFAT activation was used. The cell line was maintained in RPMI-1640 medium supplemented with 10% FBS and glutamine. K562 target cells (CD19+/-) were cultured in DMEM supplemented with 10% FBS. Jurkat cells infected with lentivirus with the CAR constructs were co-cultured with K562 target cells that expressed the target antigen (CD19) or an irrelevant antigen (mesothelin). 4-Hydroxytamoxifen (Sigma-Aldrich #H7904) was dissolved in DMSO and added to samples to a final concentration of 0-10 μM. The Rapalog A/C Heterodimerizer (Clontech Laboratories #635055) was dissolved in ethanol and added to a final concentration of 500 nM. The cells were cultured for 24 hours, stained for CD69 expression, and analyzed on a flow cytomter.

Effector cell engineering with lentivirus

[00808] Pantropic VSV-G pseudotyped lentivirus was produced from Lenti-X 293T cells (Clontech Laboratories #632180) co-transfected with a pHR'SIN:CSW transgene expression vector, viral packaging plasmids pCMVdR8.91 and pMD2.G using Lipofectamine LTX (Life Technologies #15338). Infection medium supernatant was collected 48 hours after transfection and used directly for transduction.

[00809] Jurkat cells were split 1~2 days prior to transduction to ensure that the cell culture would be in log phase at the time of transduction. Transduced cells were cultured for at least 7 days and sorted for abundant CAR expression as needed before experiments were conducted. Expression levels of ON-switch CAR molecules were quantified by flow cytometry. Part 1 of the ON-switch CAR (featuring the scFv) was stained with a fluorophore-conjugated anti-myc antibody, which recognized a myc epitope upstream of the anti-CD19 scFv. Part 2 of the ON-switch CAR (featuring the CD3zeta ITAMs) was quantified using fluorescence of mCherry, which was downstream of the ITAMs.

EXAMPLE 1: PPARγ-BASED ON-SWITCH CAR CONSTRUCTS

[00810] PPARγ-based ON-switch CAR constructs were generated. FIG. 12 presents a schematic diagram of the overall structure of a generalized nuclear hormone ligand binding domain (LBD)/co-activator peptide ON-switch CAR. FIG. 13 presents a schematic diagram of the overall structure of the constructs. Constructs are listed in Table 3. ON-switch constructs (bCW197, bCW206, bCW207), with FKBP and FRB* domains, were used as positive and negative control CARs.

Table 3

construct ID #	encoded CAR molecule
bCW492	Part 1 (antigen binding) with SRC3 co-regulator peptide, short version
bCW493	Part 1 with SRC3 co-regulator peptide, short version, 3 tandem copies
bCW494	Part 1 with SRC3 co-regulator peptide, long version
bCW495	Part 2 with PPARgamma LBD

[00811] Amino acid sequences of the ligand-binding domain (LBD) of PPARγ included in the CAR constructs, and amino acid sequences of the co-regulator peptides used, are set forth below.

[00812] The amino acid sequence of the LBD of PPARγ included in the CAR construct bCW495 is as follows:

ESADLRALAKHLYDSYIKSFPLTKAKARAILTGKTTDKSPFVIYDMNSLMMGEDKIKFKHITPLQ EQSKEVAIRIFQGCQFRSVEAVQEITEYAKSIPGFVNLDLNDQVTLLKYGVHEIIYTMLASLMNK DGVLISEGQGFMTREFLKSLRKPFGDFMEPKFEFAVKFNALELDDSDLAIFIAVIILSGDRPGLLN VKPIEDIQDNLLQALELQLKLNHPESSQLFAKLLQKMTDLRQIVTEHVQLLQVIKKTETDMSLHP LLQEIYKDLY (SEQ ID NO:695).

[00813] The amino acid sequence of human SRC3 co-regulator peptide, short version (P729~A750) in construct bCW492 is as follows: PKKENNALLRYLLDRDDPSDA (SEQ ID NO:696).

[00814] Construct bCW493 contained three tandem copies, with a linker/spacer between the copies, of the shorter version (P729-A750) of human SRC3 co-regulator peptide, such that the amino acid sequence of the co-regulator peptide, with linkers/spacers, in bCW493 is as follows:

PKKENNALLRYLLDRDDPSDAGGGSGGGSPKKENNALLRYLLDRDDPSDAGGGSGGGSPKKE NNALLRYLLDRDDPSDA (SEQ ID NO:697), where the linker/spacer amino acid are underlined.

[00815] Construct bCW494 contained the long version (M673-A750) of human SRC3 co-regulator peptide; the amino acid sequence of the human SRC3 in bCW494 is:

MHGSLLQEKHRILHKLLQNGNSPAEVAKITAEATGKDTSSITSCGDGNVVKQEQLSPKKKENNA LLRYLLDRDDPSDA (SEQ ID NO:698).

[00816] The amino acid sequence of a co-regulator peptide-containing polypeptide chain of a PPARγ CAR construct p51 (p51 bCW 492 myc anti-CD19 ON-switch part 1 with 1x SRC3 short co-regulator peptide and 4-1BB) is as follows:

[00817] MALPVTALLLPLALLLHAARPEQKLISEEDLDIQMTQTTSSLSASLGDRVTISCRASQDISKY LNWYQQKPDGTVKLLIYHTSRLHSGVPSRFSGSGSGTDYSLTISNLEQEDIATYFCQQGNTLPYT FGGGTKLEITGGGGSGGGGSGGGGSEVKLQESGPGLVAPSQSLSVTCTVSGVSLPDYGVSWIRQ PPRKGLEWLGVIWGSETTYYNSALKSRLTIIKDNSKSQVFLKMNSLQTDDTAIYYCAKHYYYGG SYAMDYWGQGTSVTVSSTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYI WAPLAGTCGVLLLSLVITLYCSL*KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELS* RGSGSGSTSPKKENNALLRYLLDRDDPSDAGS* (SEQ ID NO:699), where the anti-CD19 sequence is in bold, the CD8α transmembrane (TM) domain is double underlined, the 4-1BB sequence is in italics and bold text, and the co-regulator peptide is underlined (single underline).

[00818] The amino acid sequence of the PPARγ CAR construct p52 (p52 bCW 494 myc aCD19 ON-switch part 1 with 1x SRC3 long co-regulator peptide and 4-1BB) is as follows:

MALPVTALLLPLALLLHAARPEQKLISEEDL**DIQMTQTTSSLSASLGDRVTISCRASQDISKYL NWYQQKPDGTVKLLIYHTSRLHSGVPSRFSGSGSGTDYSLTISNLEQEDIATYFCQQGNTL PYTFGGGTKLEITGGGGSGGGGSGGGGSEVKLQESGPGLVAPSQSLSVTCTVSGVSLPDY GVSWIRQPPRKGLEWLGVIWGSETTYYNSALKSRLTIIKDNSKSQVFLKMNSLQTDDTAIY YCAKHYYYGGSYAMDYWGQGTSVTVSSTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGG AVHTRGLDFACD**IYIWAPLAGTCGVLLLSLVITLYCSL***KRGRKKLLYIFKQPFMRPVQTTQEED GCSCRFPEEEEGGCEL*SRGSGSGSTSMHGSLLQEKHRILHKLLQNGNSPAEVAKITAEATGKDT SSITSCGDGNVVKQEQLSPKKKENNALLRYLLDRDDPSDAGS* (SEQ ID NO:700), where the anti-CD19 sequence is in bold, the CD8α transmembrane (TM) domain is double underlined, the 4-1BB sequence is in italics and bold text, and the co-regulator peptide is underlined (single underline).

[00819] The amino acid sequence of the PPARγ CAR construct p55 (p55 bCW493 dimeric myc aCD19 CD8a hinge TM 41BB linker 3x short SRC3 peptide in pHR) is as follows:

[00820] MALPVTALLLPLALLLHAARPEQKLISEEDLDIQMTQTTSSLSASLGDRVTISCRASQDISKY LNWYQQKPDGTVKLLIYHTSRLHSGVPSRFSGSGSGTDYSLTISNLEQEDIATYFCQQGNTLPYT FGGGTKLEITGGGGSGGGGSGGGGSEVKLQESGPGLVAPSQSLSVTCTVSGVSLPDYGVSWIRQ PPRKGLEWLGVIWGSETTYYNSALKSRLTIIKDNSKSQVFLKMNSLQTDDTAIYYCAKHYYYGG SYAMDYWGQGTSVTVSSTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYI WAPLAGTCGVLLLSLVITLYCSL*KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCEL*S RGSGSGSTSPKKENNALLRYLLDRDDPSDAGGGSGGGSPKKENNALLRYLLDRDDPSDAGGGS GGGSKKENNALLRYLLDRDDPSDAGS* (SEQ ID NO:701), where the anti-CD19 sequence is in bold, the CD8α transmembrane (TM) domain is double underlined, the 4-1BB sequence is in italics and bold text, and the co-regulator peptide is underlined (single underline).

[00821] The amino acid sequence of the PPARγ CAR construct P56 (p56 bCW495 Kozak dDAP10 CD8a TM-41BB-GSx8-PPARg LBD-GSx4-zeta-GSx4-mCherry in pHR) is as follows:

[00822] MIHLGHILFLLLLPVAAAQTTPGERSSLPAFYPGTSGSCSGCGSLSLPIYIWAPLAGTCGVLLL SLVITLYCSL**KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCEL**GSGSGSGSGS GSGSTSESADLRALAKHLYDSYIKSFPLTKAKARAILTGKTTDKSPFVIYDMNSLMMGEDKIKFK HITPLQEQSKEVAIRIFQGCQFRSVEAVQEITEYAKSIPGFVNLDLNDQVTLLKYGVHEIIYTMLA SLMNKDGVLISEGQGFMTREFLKSLRKPFGDFMEPKFEFAVKFNALELDDSDLAIFIAVIILSGDR PGLLNVKPIEDIQDNLLQALELQLKLNHPESSQLFAKLLQKMTDLRQIVTEHVQLLQVIKKTETD MSLHPLLQEIYKDLYGSGSGSGSSL***RVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRR GRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTY DALHMQALPPR***SRGSGSGSGSMVSKGEEDNMAIIKEFMRFKVHMEGSVNGHEFEIEGEGEGRP YEGTQTAKLKVTKGGPLPFAWDILSPQFMYGSKAYVKHPADIPDYLKLSFPEGFKWERVMNFE DGGVVTVTQDSSLQDGEFIYKVKLRGTNFPSDGPVMQKKTMGWEASSERMYPEDGALKGEIK

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QRLKLKDGGHYDAEVKTTYKAKKPVQLPGAYNVNIKLDITSHNEDYTIVEQYERAEGRHSTGG MDELYKCVTD* (SEQ ID NO:702). The LBD is underlined (single underline); the CD8α TM domain is double underlined; 4-1BB is in bold text; and zeta is in bold and italics.

Results

0823] FIG. 14 depicts IL-2 cytokine production by ON-switch CAR+ Jurkat cells (transduced with the indicated lentiviral constructs) after 18 hours of co-culturing with K562 target cells (+/- CD19 Ag, as indicated), in the presence or absence of rosiglitazone dimerizer (10 micromolar).

EXAMPLE 2: ER-ALPHA-BASED ON-SWITCH CAR CONSTRUCTS

0824] ERα-based ON-switch CAR constructs were generated. Constructs are listed in Table 4. ON-switch constructs (bCW197, bCW206, bCW207), with FKBP and FRB* domains, were used as positive and negative control CARs.

Table 4

construct ID #	encoded CAR molecule
bCW501	Part 1 myc aCD19 ON-switch part 1 with 3x AlphaBetaV peptide and 4-1BB
bCW502	Part 1 myc aCD19 ON-switch part 1 with 3x CoRNR peptide and 4-1BB
bCW503	ON-switch CAR part 2 with human ER alpha LBD
bCW504	ON-switch CAR part 2 with human ER alpha LBD w Y537F
bCW505	ON-switch CAR part 2 with human ER alpha LBD w Y537F G521R

0825] Amino acid sequences of the various components of the ERα-based ON-switch CAR are as follows.

0826] The LBD of human estrogen receptor alpha in construct bCW503:

0827] DRRGGRMLKHKRQRDDGEGRGEVGSAGDMRAANLWPSPLMIKRSKKNSLALSLTADQMV SALLDAEPPILYSEYDPTRPFSEASMMGLLTNLADRELVHMINWAKRVPGFVDLTLHDQVHLLE CAWLEILMIGLVWRSMEHPGKLLFAPNLLLDRNQGKCVEGMVEIFDMLLATSSRFRMMNLQGE EFVCLKSIILLNSGVYTFLSSTLKSLEEKDHIHRVLDKITDTLIHLMAKAGLTLQQQHQRLAQLLLI LSHIRHMSNKGMEHLYSMKCKNVVPLYDLLLEMLDAHRLHAPTS (SEQ ID NO:703);

[00828] b. The LBD of mutated human estrogen receptor alpha in construct bCW504:

[00829] DRRGGRMLKHKRQRDDGEGRGEVGSAGDMRAANLWPSPLMIKRSKKNSLALSLTADQMV SALLDAEPPILYSEYDPTRPFSEASMMGLLTNLADRELVHMINWAKRVPGFVDLTLHDQVHLLE CAWLEILMIGLVWRSMEHPGKLLFAPNLLLDRNQGKCVEGMVEIFDMLLATSSRFRMMNLQGE EFVCLKSIILLNSGVYTFLSSTLKSLEEKDHIHRVLDKITDTLIHLMAKAGLTLQQQHQRLAQLLLI LSHIRHMSNKGMEHLYSMKCKNVVPLFDLLLEMLDAHRLHAPTS (SEQ ID NO:704);

[00830] c. The LBD of mutated human estrogen receptor alpha in construct bCW505:

[00831] DRRGGRMLKHKRQRDDGEGRGEVGSAGDMRAANLWPSPLMIKRSKKNSLALSLTADQMV SALLDAEPPILYSEYDPTRPFSEASMMGLLTNLADRELVHMINWAKRVPGFVDLTLHDQVHLLE CAWLEILMIGLVWRSMEHPGKLLFAPNLLLDRNQGKCVEGMVEIFDMLLATSSRFRMMNLQG

EEFVCLKSIILLNSGVYTFLSSTLKSLEEKDHIHRVLDKITDTLIHLMAKAGLTLQQQHQRLAQLL LILSHIRHMSNKRMEHLYSMKCKNVVPLFDLLLEMLDAHRLHAPTS (SEQ ID NO:705);

[00832] d. The 3x AlphaBetaV co-activator peptide in bCW501:

[00833] SGSGPGSREWFKDMLGGGSGGGSSGSGPGSREWFKDMLGGGSGGGSSGSGPGSREWFKD M (SEQ ID NO:706);

[00834] e. The 3x CoRNR co-activator peptide in bCW502:

[00835] DAFQLRQLILRGLQDDGGGSGGGSDAFQLRQLILRGLQDDGGGSGGGSDAFQLRQLILRGL QDD (SEQ ID NO:707).

[00836] The amino acid sequence of the bCW501 construct (p25 bCW501 myc aCD19 ON-switch part 1 with 3x AlphaBetaV peptide and 4-1BB) is as follows:

[00837] MALPVTALLLPLALLLHAARPEQKLISEEDLDIQMTQTTSSLSASLGDRVTISCRASQDISKY LNWYQQKPDGTVKLLIYHTSRLHSGVPSRFSGSGSGTDYSLTISNLEQEDIATYFCQQGNTLPYT FGGGTKLEITGGGGSGGGGSGGGGSEVKLQESGPGLVAPSQSLSVTCTVSGVSLPDYGVSWIRQ PPRKGLEWLGVIWGSETTYYNSALKSRLTIIKDNSKSQVFLKMNSLQTDDTAIYYCAKHYYYGG SYAMDYWGQGTSVTVSSTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYI WAPLAGTCGVLLLSLVITLYCSLKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCEL SRGSGSGSTSSGSGPGSREWFKDMLGGGSGGGSSGSGPGSREWFKDMLGGGSGGGSSGSGPGS REWFKDMLGS* (SEQ ID NO:708), where the co-regulator peptide αβV is underlined.

[00838] The amino acid sequence of the bCW502 construct (p26 bCW502 myc aCD19 ON-switch part 1 with 3x CoRNR peptide and 4-1BB) is as follows:

[00839] MALPVTALLLPLALLLHAARPEQKLISEEDLDIQMTQTTSSLSASLGDRVTISCRASQDISKY LNWYQQKPDGTVKLLIYHTSRLHSGVPSRFSGSGSGTDYSLTISNLEQEDIATYFCQQGNTLPYT FGGGTKLEITGGGGSGGGGSGGGGSEVKLQESGPGLVAPSQSLSVTCTVSGVSLPDYGVSWIRQ PPRKGLEWLGVIWGSETTYYNSALKSRLTIIKDNSKSQVFLKMNSLQTDDTAIYYCAKHYYYGG SYAMDYWGQGTSVTVSSTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYI WAPLAGTCGVLLLSLVITLYCSLKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCEL SRGSGSGSTSDAFQLRQLILRGLQDDGGGSGGGSDAFQLRQLILRGLQDDGGGSGGGSDAFQLR QLILRGLQDDGS* (SEQ ID NO:709), where the 3x CoRNR co-regulator peptide is underlined.

[00840] The amino acid sequence of the bCW503 construct (p27 bCW503 ON-switch CAR part 2 with human ER alpha LBD) is as follows:

[00841] MIHLGHILFLLLLPVAAAQTTPGERSSLPAFYPGTSGSCSGCGSLSLPIYIWAPLAGTCGVLLL SLVITLYCSLKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELGSGSGSGSGSGSGS TSDRRGGRMLKHKRQRDDGEGRGEVGSAGDMRAANLWPSPLMIKRSKKNSLALSLTADQMV SALLDAEPPILYSEYDPTRPFSEASMMGLLTNLADRELVHMINWAKRVPGFVDLTLHDQVHLLE

CAWLEILMIGLVWRSMEHPGKLLFAPNLLLDRNQGKCVEGMVEIFDMLLATSSRFRMMNLQG
EEFVCLKSIILLNSGVYTFLSSTLKSLEEKDHIHRVLDKITDTLIHLMAKAGLTLQQQHQRLAQLL
LILSHIRHMSNKGMEHLYSMKCKNVVPLYDLLLEMLDAHRLHAPTSGSGSGSGSSLRVKFSRSA
DAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAE
AYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPRSRGSGSGSGSMVSKGEEDN
MAIIKEFMRFKVHMEGSVNGHEFEIEGEGEGRPYEGTQTAKLKVTKGGPLPFAWDILSPQFMYG
SKAYVKHPADIPDYLKLSFPEGFKWERVMNFEDGGVVTVTQDSSLQDGEFIYKVKLRGTNFPSD
GPVMQKKTMGWEASSERMYPEDGALKGEIKQRLKLKDGGHYDAEVKTTYKAKKPVQLPGAY
NVNIKLDITSHNEDYTIVEQYERAEGRHSTGGMDELYKCVTD* (SEQ ID NO:710), where the ER LBD is underlined.

[00842] The amino acid sequence of the bCW504 construct (p28 bCW504 ON-switch CAR part 2 with human ER alpha LBD w Y537F) is as follows:

[00843] MIHLGHILFLLLLPVAAAQTTPGERSSLPAFYPGTSGSCSGCGSLSLPIYIWAPLAGTCGVLLL
SLVITLYCSLKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELGSGSGSGSGSGSGS
TSDRRGGRMLKHKRQRDDGEGRGEVGSAGDMRAANLWPSPLMIKRSKKNSLALSLTADQMV
SALLDAEPPILYSEYDPTRPFSEASMMGLLTNLADRELVHMINWAKRVPGFVDLTLHDQVHLLE
CAWLEILMIGLVWRSMEHPGKLLFAPNLLLDRNQGKCVEGMVEIFDMLLATSSRFRMMNLQG
EEFVCLKSIILLNSGVYTFLSSTLKSLEEKDHIHRVLDKITDTLIHLMAKAGLTLQQQHQRLAQLL
LILSHIRHMSNKGMEHLYSMKCKNVVPL**F**DLLLEMLDAHRLHAPTSGSGSGSGSSLRVKFSRSA
DAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAE
AYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPRSRGSGSGSGSMVSKGEEDN
MAIIKEFMRFKVHMEGSVNGHEFEIEGEGEGRPYEGTQTAKLKVTKGGPLPFAWDILSPQFMYG
SKAYVKHPADIPDYLKLSFPEGFKWERVMNFEDGGVVTVTQDSSLQDGEFIYKVKLRGTNFPSD
GPVMQKKTMGWEASSERMYPEDGALKGEIKQRLKLKDGGHYDAEVKTTYKAKKPVQLPGAY
NVNIKLDITSHNEDYTIVEQYERAEGRHSTGGMDELYKCVTD* (SEQ ID NO:711), where the ERα LBD is underlined and the Y537F substitution is in bold.

[00844] The amino acid sequence of the bCW505 construct (p29 bCW505 ON-switch CAR part 2 with human ER alpha LBD w Y537F G521R) is as follows:

[00845] MIHLGHILFLLLLPVAAAQTTPGERSSLPAFYPGTSGSCSGCGSLSLPIYIWAPLAGTCGVLLL
SLVITLYCSLKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELGSGSGSGSGSGSGS
TSDRRGGRMLKHKRQRDDGEGRGEVGSAGDMRAANLWPSPLMIKRSKKNSLALSLTADQMV
SALLDAEPPILYSEYDPTRPFSEASMMGLLTNLADRELVHMINWAKRVPGFVDLTLHDQVHLLE
CAWLEILMIGLVWRSMEHPGKLLFAPNLLLDRNQGKCVEGMVEIFDMLLATSSRFRMMNLQG
EEFVCLKSIILLNSGVYTFLSSTLKSLEEKDHIHRVLDKITDTLIHLMAKAGLTLQQQHQRLAQLL
LILSHIRHMSNK**R**MEHLYSMKCKNVVPL**F**DLLLEMLDAHRLHAPTSGSGSGSGSSLRVKFSRSA

DAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAE AYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPRSRGSGSGSGSMVSKGEEDN MAIIKEFMRFKVHMEGSVNGHEFEIEGEGEGRPYEGTQTAKLKVTKGGPLPFAWDILSPQFMYG SKAYVKHPADIPDYLKLSFPEGFKWERVMNFEDGGVVTVTQDSSLQDGEFIYKVKLRGTNFPSD GPVMQKKTMGWEASSERMYPEDGALKGEIKQRLKLKDGGHYDAEVKTTYKAKKPVQLPGAY NVNIKLDITSHNEDYTIVEQYERAEGRHSTGGMDELYKCVTD* (SEQ ID NO:712), where the ERα LBD is underlined, and the Y536F and G521R substitutions are in bold.

[00846] The amino acid sequence of the bCW506 construct (p30 bCW506 ON-switch CAR part 2 with human ER alpha LBD w/o helix12) is as follows:

[00847] MIHLGHILFLLLLPVAAAQTTPGERSSLPAFYPGTSGSCSGCGSLSLPIYIWAPLAGTCGVLLL SLVITLYCSLKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELGSGSGSGSGSGSGS TSDRRGGRMLKHKRQRDDGEGRGEVGSAGDMRAANLWPSPLMIKRSKKNSLALSLTADQMV SALLDAEPPILYSEYDPTRPFSEASMMGLLTNLADRELVHMINWAKRVPGFVDLTLHDQVHLLE CAWLEILMIGLVWRSMEHPGKLLFAPNLLLDRNQGKCVEGMVEIFDMLLATSSRFRMMNLQG EEFVCLKSIILLNSGVYTFLSSTLKSLEEKDHIHRVLDKITDTLIHLMAKAGLTLQQQHQRLAQLL LILSHIRHMSNKGMEHLYSMKCKNVAGSGSGSGSSLRVKFSRSADAPAYQQGQNQLYNELNLG RREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDG LYQGLSTATKDTYDALHMQALPPRSRGSGSGSGSMVSKGEEDNMAIIKEFMRFKVHMEGSVNG HEFEIEGEGEGRPYEGTQTAKLKVTKGGPLPFAWDILSPQFMYGSKAYVKHPADIPDYLKLSFPE GFKWERVMNFEDGGVVTVTQDSSLQDGEFIYKVKLRGTNFPSDGPVMQKKTMGWEASSERM YPEDGALKGEIKQRLKLKDGGHYDAEVKTTYKAKKPVQLPGAYNVNIKLDITSHNEDYTIVEQ YERAEGRHSTGGMDELYKCVTD* (SEQ ID NO:713), where the ERα LBD (without helix 12) is underlined.

[00848] The amino acid sequence of the bCW507 construct (p31 bCW507 ON-switch CAR part 2 with human ER alpha LBD w/o helix12 w G521R) is as follows:

[00849] MIHLGHILFLLLLPVAAAQTTPGERSSLPAFYPGTSGSCSGCGSLSLPIYIWAPLAGTCGVLLL SLVITLYCSLKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELGSGSGSGSGSGSGS TSDRRGGRMLKHKRQRDDGEGRGEVGSAGDMRAANLWPSPLMIKRSKKNSLALSLTADQMV SALLDAEPPILYSEYDPTRPFSEASMMGLLTNLADRELVHMINWAKRVPGFVDLTLHDQVHLLE CAWLEILMIGLVWRSMEHPGKLLFAPNLLLDRNQGKCVEGMVEIFDMLLATSSRFRMMNLQG EEFVCLKSIILLNSGVYTFLSSTLKSLEEKDHIHRVLDKITDTLIHLMAKAGLTLQQQHQRLAQLL LILSHIRHMSNK**R**MEHLYSMKCKNVAGSGSGSGSSLRVKFSRSADAPAYQQGQNQLYNELNLG RREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDG LYQGLSTATKDTYDALHMQALPPRSRGSGSGSGSMVSKGEEDNMAIIKEFMRFKVHMEGSVNG HEFEIEGEGEGRPYEGTQTAKLKVTKGGPLPFAWDILSPQFMYGSKAYVKHPADIPDYLKLSFPE

GFKWERVMNFEDGGVVTVTQDSSLQDGEFIYKVKLRGTNFPSDGPVMQKKTMGWEASSERM YPEDGALKGEIKQRLKLKDGGHYDAEVKTTYKAKKPVQLPGAYNVNIKLDITSHNEDYTIVEQ YERAEGRHSTGGMDELYKCVTD* (SEQ ID NO:714), where the ERα LBD (without helix 12) is underlined, and the G521R substitution is in bold.

[00850] The amino acid sequence of the construct referred to as "p40 dimeric myc aCD19 CD8a hinge TM 41BB linker 3x NR0B1 peptide in pHR" is as follows:

[00851] MALPVTALLLPLALLLHAARPEQKLISEEDLDIQMTQTTSSLSASLGDRVTISCRASQDISKY LNWYQQKPDGTVKLLIYHTSRLHSGVPSRFSGSGSGTDYSLTISNLEQEDIATYFCQQGNTLPYT FGGGTKLEITGGGGSGGGGSGGGGSEVKLQESGPGLVAPSQSLSVTCTVSGVSLPDYGVSWIRQ PPRKGLEWLGVIWGSETTYYNSALKSRLTIIKDNSKSQVFLKMNSLQTDDTAIYYCAKHYYYGG SYAMDYWGQGTSVTVSSTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYI WAPLAGTCGVLLLSLVITLYCSLKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCEL SRGSGSGSTS<u>PRQGSILYSMLTSAKQTGGGSGGGSPRQGSILYSMLTSAKQTGGGSGGGSPRQGS ILYSMLTSAKQT</u>GS* (SEQ ID NO:715), where the 3x NR0B1 co-regulator peptide is underlined.

[00852] The amino acid sequence of the construct referred to as "p41 dimeric myc aCD19 CD8a hinge TM 41BB linker 3x NCOA1 peptide in pHR" is as follows:

[00853] MALPVTALLLPLALLLHAARPEQKLISEEDLDIQMTQTTSSLSASLGDRVTISCRASQDISKY LNWYQQKPDGTVKLLIYHTSRLHSGVPSRFSGSGSGTDYSLTISNLEQEDIATYFCQQGNTLPYT FGGGTKLEITGGGGSGGGGSGGGGSEVKLQESGPGLVAPSQSLSVTCTVSGVSLPDYGVSWIRQ PPRKGLEWLGVIWGSETTYYNSALKSRLTIIKDNSKSQVFLKMNSLQTDDTAIYYCAKHYYYGG SYAMDYWGQGTSVTVSSTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYI WAPLAGTCGVLLLSLVITLYCSLKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCEL SRGSGSGSTS<u>LTERHKILHRLLQEGSPSDGGGSGGGSLTERHKILHRLLQEGSPSDGGGSGGGSL TERHKILHRLLQEGSPSD</u>GS (SEQ ID NO:716), where the 3x NCOA1 peptide is underlined.

[00854] The amino acid sequence of the construct referred to as "p42 dimeric myc aCD19 CD8a hinge TM 41BB linker 3x NCOA2 peptide in pHR" is as follows:

[00855] MALPVTALLLPLALLLHAARPEQKLISEEDLDIQMTQTTSSLSASLGDRVTISCRASQDISKY LNWYQQKPDGTVKLLIYHTSRLHSGVPSRFSGSGSGTDYSLTISNLEQEDIATYFCQQGNTLPYT FGGGTKLEITGGGGSGGGGSGGGGSEVKLQESGPGLVAPSQSLSVTCTVSGVSLPDYGVSWIRQ PPRKGLEWLGVIWGSETTYYNSALKSRLTIIKDNSKSQVFLKMNSLQTDDTAIYYCAKHYYYGG SYAMDYWGQGTSVTVSSTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYI WAPLAGTCGVLLLSLVITLYCSLKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCEL SRGSGSGSTS<u>SKGQTKLLQLLTTKSDQGGGSGGGSSKGQTKLLQLLTTKSDQGGGSGGGSSKGQ TKLLQLLTTKSDQ</u>GS* (SEQ ID NO:717), where the 3x NCOA2 peptide is underlined.

[00856] The amino acid sequence of the construct referred to as "p43 dimeric myc aCD19 CD8a hinge TM 41BB linker 3x PGC-1 peptide in pHR" is as follows:

[00857] MALPVTALLLPLALLLHAARPEQKLISEEDLDIQMTQTTSSLSASLGDRVTISCRASQDISKY LNWYQQKPDGTVKLLIYHTSRLHSGVPSRFSGSGSGTDYSLTISNLEQEDIATYFCQQGNTLPYT FGGGTKLEITGGGGSGGGGSGGGGSEVKLQESGPGLVAPSQSLSVTCTVSGVSLPDYGVSWIRQ PPRKGLEWLGVIWGSETTYYNSALKSRLTIIKDNSKSQVFLKMNSLQTDDTAIYYCAKHYYYGG SYAMDYWGQGTSVTVSSTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYI WAPLAGTCGVLLLSLVITLYCSLKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCEL SRGSGSGSTSAEEPSLLKKLLLAPANTGGGSGGGSAEEPSLLKKLLLAPANTGGGSGGGSAEEPS LLKKLLLAPANTGS* (SEQ ID NO:718), where the 3x PGC-1 peptide is underlined.

[00858] The amino acid sequence of the construct referred to as "p44 dimeric myc aCD19 CD8a hinge TM 41BB linker 3x NRIP1 peptide in pHR" is as follows:

[00859] MALPVTALLLPLALLLHAARPEQKLISEEDLDIQMTQTTSSLSASLGDRVTISCRASQDISKY LNWYQQKPDGTVKLLIYHTSRLHSGVPSRFSGSGSGTDYSLTISNLEQEDIATYFCQQGNTLPYT FGGGTKLEITGGGGSGGGGSGGGGSEVKLQESGPGLVAPSQSLSVTCTVSGVSLPDYGVSWIRQ PPRKGLEWLGVIWGSETTYYNSALKSRLTIIKDNSKSQVFLKMNSLQTDDTAIYYCAKHYYYGG SYAMDYWGQGTSVTVSSTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYI WAPLAGTCGVLLLSLVITLYCSLKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCEL SRGSGSGSTSAANNSLLLHLLKSQTIPGGGSGGGSAANNSLLLHLLKSQTIPGGGSGGGSAANNS LLLHLLKSQTIPGS* (SEQ ID NO:719), where the 3x NRIP1 peptide is underlined.

[00860] The amino acid sequence of the construct referred to as "p45 Kozak dDAP10 CD8a TM-41BB-GSx8-ERb LBD-GSx4-zeta-GSx4-mCherry in pHR" is as follows:

[00861] MIHLGHILFLLLLPVAAAQTTPGERSSLPAFYPGTSGSCSGCGSLSLPIYIWAPLAGTCGVLLL SLVITLYCSLKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELGSGSGSGSGSGSGS TSVKCGSRRERCGYRLVRRQRSADEQLHCAGKAKRSGGHAPRVRELLLDALSPEQLVLTLLEA EPPHVLISRPSAPFTEASMMMSLTKLADKELVHMISWAKKIPGFVELSLFDQVRLLESCWMEVL MMGLMWRSIDHPGKLIFAPDLVLDRDEGKCVEGILEIFDMLLATTSRFRELKLQHKEYLCVKA MILLNSSMYPLVTATQDADSSRKLAHLLNAVTDALVWVIAKSGISSQQQSMRLANLLMLLSHV RHASNKGMEHLLNMKCKNVVPVYDLLLEMLNAHVLRGCKSSITGSECSPAEDSKSKEGSQNPQ SQGSGSGSGSSLRVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRR KNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPRS RGSGSGSGSMVSKGEEDNMAIIKEFMRFKVHMEGSVNGHEFEIEGEGEGRPYEGTQTAKLKVT KGGPLPFAWDILSPQFMYGSKAYVKHPADIPDYLKLSFPEGFKWERVMNFEDGGVVTVTQDSS LQDGEFIYKVKLRGTNFPSDGPVMQKKTMGWEASSERMYPEDGALKGEIKQRLKLKDGGHYD

AEVKTTYKAKKPVQLPGAYNVNIKLDITSHNEDYTIVEQYERAEGRHSTGGMDELYKCVTD* (SEQ ID NO:720), where the ERβ LBD is underlined.

[00862] The amino acid sequence of the construct referred to as "p179 dimeric myc aCD19 CD8a hinge TM 41BB linker 3x SRC-1 NRIV peptide in pHR" is as follows:

[00863] MALPVTALLLPLALLLHAARPEQKLISEEDLDIQMTQTTSSLSASLGDRVTISCRASQDISKY LNWYQQKPDGTVKLLIYHTSRLHSGVPSRFSGSGSGTDYSLTISNLEQEDIATYFCQQGNTLPYT FGGGTKLEITGGGGSGGGGSGGGGSEVKLQESGPGLVAPSQSLSVTCTVSGVSLPDYGVSWIRQ PPRKGLEWLGVIWGSETTYYNSALKSRLTIIKDNSKSQVFLKMNSLQTDDTAIYYCAKHYYYGG SYAMDYWGQGTSVTVSSTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYI WAPLAGTCGVLLLSLVITLYCSLKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCEL SRGSGSGSTSQAQQKSLLQQLLTEGGGSGGGSQAQQKSLLQQLLTEGGGSGGGSQAQQKSLLQ QLLTEGS* (SEQ ID NO:721), where the 3x NRIV1 peptide is underlined

Results

[00864] The data are depicted in FIG. 16A and FIG. 16B. Fig. 16A. CD69 upregulation by Jurkat cells expressing ER CAR+ (bCW502 and bCW505) after 24 hours of co-culturing with K562 target cells expressing CD19 or mesothelin, an irrelevant antigen ("meso"), in the presence or absence of a small-molecule dimerizer (4-hydroxytamoxifen or rapalog AP21967). CD69 expression in ER CAR+ Jurkat cells is strongly induced by 4-hydroxytamoxifen (EC50 ~100 nM) only in the presence of K562 cells expressing CD19. Rapamycin CAR and dead rapamycin CAR (with a mutation in ITAM that abolishes signalling) were tested as positive and negative controls, respectively. Fig. 16B. FACS data from the experiment described in Fig. 16A, showing CD69 upregulation in ER CAR+ Jurkat cells in a manner dependent on CD19 antigen and treatment with 4-hydroxytamoxifen.

EXAMPLE 3: DIMERIZER CONTROLED ACTIVATION OF PRIMARY HUMAN T CELLS

[00865] Control of cellular functions by induced heterodimerization of the ligand binding domain of human estrogen receptor beta with small peptides derived from transcriptional co-repressors in the presence of the drug 4-hydroxytamoxifen was evaluated. This method does not involve DNA-binding and/or transcriptional activation or any DNA-binding function or transcription activating function of the human estrogen receptor beta from which polypeptide components are derived.

[00866] A human estrogen receptor beta nuclear receptor-peptide system was expressed in primary human T cells and found to capable of modulating ON-switch CAR activity. A CD19 specific ON-switch CAR was constructed to include human estrogen receptor beta ligand binding domain and co-repressor peptide (CoRNR). A schematic representation of the general construct within the T cell membrane, and the associated CD19 antigen expressed on the surface of the target cell, is provided in FIG. 17. Upon introduction into primary CD8+ T cells, stable expression was observed and transduced cells displaed increased T cell activation upon addition of the drug 4-hyroxytamoxifen.

[00867] Nucleic acid sequences encoding the following constructs were employed: "p26 bCW 502 myc aCD19 ON-switch part 1 with 3x CoRNR peptide and 4-1BB" having the following sequence:

[00868] MALPVTALLLPLALLLHAARPEQKLISEEDLDIQMTQTTSSLSASLGDRVTISCRASQDISKY LNWYQQKPDGTVKLLIYHTSRLHSGVPSRFSGSGSGTDYSLTISNLEQEDIATYFCQQGNTLPYT FGGGTKLEITGGGGSGGGGSGGGGSEVKLQESGPGLVAPSQSLSVTCTVSGVSLPDYGVSWIRQ PPRKGLEWLGVIWGSETTYYNSALKSRLTIIKDNSKSQVFLKMNSLQTDDTAIYYCAKHYYYGG SYAMDYWGQGTSVTVSSTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYI WAPLAGTCGVLLLSLVITLYCSLKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCEL SRGSGSGSTSDAFQLRQLILRGLQDDGGGSGGGSDAFQLRQLILRGLQDDGGGSGGGSDAFQLR QLILRGLQDDGS* (SEQ ID NO:722), where the 3x CoRNR co-regulator peptide is underlined, and "p45 Kozak dDAP10 CD8a TM-41BB-GSx8-ERb LBD-GSx4-zeta-GSx4-mCherry in pHR" having the following sequence:

[00869] MIHLGHILFLLLLPVAAAQTTPGERSSLPAFYPGTSGSCSGCGSLSLPIYIWAPLAGTCGVLLL SLVITLYCSLKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELGSGSGSGSGSGSGS TSVKCGSRRERCGYRLVRRQRSADEQLHCAGKAKRSGGHAPRVRELLLDALSPEQLVLTLLEA EPPHVLISRPSAPFTEASMMMSLTKLADKELVHMISWAKKIPGFVELSLFDQVRLLESCWMEVL MMGLMWRSIDHPGKLIFAPDLVLDRDEGKCVEGILEIFDMLLATTSRFRELKLQHKEYLCVKA MILLNSSMYPLVTATQDADSSRKLAHLLNAVTDALVWVIAKSGISSQQQSMRLANLLMLLSHV RHASNKGMEHLLNMKCKNVVPVYDLLLEMLNAHVLRGCKSSITGSECSPAEDSKSKEGSQNPQ SQGSGSGSGSSLRVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRR KNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPRS RGSGSGSGSMVSKGEEDNMAIIKEFMRFKVHMEGSVNGHEFEIEGEGEGRPYEGTQTAKLKVT KGGPLPFAWDILSPQFMYGSKAYVKHPADIPDYLKLSFPEGFKWERVMNFEDGGVVTVTQDSS LQDGEFIYKVKLRGTNFPSDGPVMQKKTMGWEASSERMYPEDGALKGEIKQRLKLKDGGHYD AEVKTTYKAKKPVQLPGAYNVNIKLDITSHNEDYTIVEQYERAEGRHSTGGMDELYKCVTD* (SEQ ID NO:723), where the ERβ LBD is underlined.

[00870] Specifically, CD69 upregulation by primary human CD8+ T cells expressing a CD19 specific ON-switch CAR constructed to include human estrogen receptor beta ligand binding domain (ER-beta) and co-repressor peptide (CoRNR) was measured after 24 hours of co-culturing with K562 target cells expressing CD19 or mesothelin, an irrelevant antigen ("meso"), in the presence or absence of a small-molecule dimerizer (4-hydroxytamoxifen or rapalog "rapa"). As shown in FIG. 18A, CD19-antigen induced activation of the primary human CD8+ T cells expressing the ER-beta/CoRNR on-switch CAR construct was dependent on the dose of small-molecule dimerizer provided to the culture. Histograms derived from the flow cytometery data, showing the correlation between increasing 4-hydroxytamoxifen dose and increasing numbers of CD69 positive primary human CD8+ T cells, are provided in FIG. 18B.

[00871] Cell killing by primary human CD8+ T cells expressing the CD19 specific ER-beta/CoRNR ON-switch CAR was also assessed. Specifically, the percent of CD19-expressing K562 target cells remaining after 22 hours of co-culture with primary human CD8+ T cells expressing the CD19 specific ER-beta/CoRNR ON-switch CAR (ER-CAR) in the presence of various concentrations of drug (4-hydroxytamoxifen (4HT) or rapalog) was measured (FIG. 52). Cells expressing a CD19 specific single-chain second generation CAR ("2nd gen CAR") and cells expressing a CD19 speicific rapalog on-switch CAR, with administered rapalog dimerizer, were used as positive controls. Negative controls included cells expressing ER-CAR T cells in absence of 4HT (ethanol vehicle only, "ER-CAR + EtOH") and cells expressing only part 2 of the ER-CAR on-switch construct, i.e., without part 1, in the presence of 4HT. These results demonstrate drug (4HT) inducible target cell killing (i.e., inducible cytotoxic activity) by primary T cells expressing an ER-beta/CoRNR dimerizable ON-switch CAR.

[00872] Increased T cell activation was also observed in primary CD8+ T cells expressing a split ON-switch CAR construct in which the heterodimerization modules consisted of a portion of the human Vitamin D receptor ligand binding domain and a SRC2-3 coactivator peptide. In this system, the T cells showed increased activation in the presence of the vitamin D analog calcipotriol.

[00873] While the present invention has been described with reference to the specific embodiments thereof, it should be understood by those skilled in the art that various changes may be made and equivalents may be substituted without departing from the true spirit and scope of the invention. In addition, many modifications may be made to adapt a particular situation, material, composition of matter, process, process step or steps, to the objective, spirit and scope of the present invention. All such modifications are intended to be within the scope of the claims appended hereto.

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CLAIMS

What is claimed is:

1. A heterodimeric, conditionally active polypeptide comprising:

a) a first chimeric polypeptide comprising a first member of a dimerization pair and a first heterologous polypeptide; and

b) a second chimeric polypeptide comprising a second member of a dimerization pair and a second heterologous polypeptide,

wherein the first member of the dimerization pair comprises a ligand-binding domain (LBD) of a nuclear hormone receptor, and the second member of the dimerization pair comprises a co-regulator of the nuclear hormone receptor, or

wherein the first member of the dimerization pair is a co-regulator of a nuclear hormone receptor, and the second member of the dimerization pair comprises an LBD of the nuclear hormone receptor; and

wherein the first chimeric polypeptide and the second chimeric polypeptide are dimerized in the presence of a dimerization agent that induces binding of the LBD to the co-regulator.

2. The heterodimeric, conditionally active polypeptide of claim 1, wherein:

a) the first heterologous polypeptide is an N-terminal portion of a receptor; and

b) the second heterologous polypeptide is a C-terminal portion of the receptor, wherein dimerization of the first chimeric polypeptide and the second chimeric polypeptide mediated by the dimerization agent restores signaling activity of the receptor; or

a) the first heterologous polypeptide is an N-terminal portion of an enzyme; and

b) the second heterologous polypeptide is a C-terminal portion of the enzyme, wherein dimerization of the first chimeric polypeptide and the second chimeric polypeptide restore enzymatic activity of the enzyme.

3. The heterodimeric, conditionally active polypeptide of claim 2, wherein the receptor is a chimeric antigen receptor (CAR) heterodimer and:

a) the first heterologous polypeptide is a first polypeptide of the CAR heterodimer; and

b) the second heterologous polypeptide is a second polypeptide of the CAR heterodimer; or

wherein the receptor is a T-cell receptor (TCR) and:

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a) the first heterologous polypeptide is a TCR alpha chain; and

b) the second heterologous polypeptide is a TCR beta chain.

4. The heterodimeric, conditionally active polypeptide of claim 2, wherein the enzyme is an RNA-guided endonuclease, optionally a class 2 CRISPR/Cas endonuclease, optionally a type II CRISPR/Cas protein, a type V CRISPR/Cas protein, or a type VI CRISPR/Cas protein, and:

a) the first heterologous polypeptide is an N-terminal portion of the RNA-guided endonuclease; and

b) the second heterologous polypeptide is a C-terminal portion of the RNA-guided endonuclease,

wherein dimerization of the first chimeric polypeptide and the second chimeric polypeptide, mediated by the dimerization agent that induces binding of the LBD to the co-regulator, restores enzymatic function of the RNA-guided endonuclease.

5. The heterodimeric, conditionally active polypeptide of any one of claims 1-4, wherein the LBD of the nuclear hormone binding member of the dimerization pair is an LBD of a nuclear hormone receptor selected from: an estrogen receptor, an ecdysone receptor, a PPARγ receptor, a glucocorticoid receptor, an androgen receptor, a thyroid hormone receptor, a mineralocorticoid receptor, a progesterone receptor, a vitamin D receptor, a PPARβ receptor, a PPARα receptor, a pregnane X receptor, a liver X receptor, a farnesoid X receptor, a retinoid X receptor, a RAR-related orphan receptor, and a retinoic acid receptor.

6. The heterodimeric, conditionally active polypeptide of any one of claims 1-5, wherein the co-regulator of the nuclear hormone receptor is selected from SRC1, GRIP1, AIB1, PGC1a, PGC1b, PRC, TRAP220, ASC2, CBP, P300, CIA, ARA70, TIF1, NSD1, SMAP, Tip60, ERAP140, Nix1, LCoR, N-CoR, SMRT, RIP140, and PRIC285.

7. The heterodimeric, conditionally active polypeptide of any one of claims 1-6, wherein the co-regulator of the nuclear hormone receptor is selected from:

a) SRC1: CPSSHSSLTERHKILHRLLQEGSPS (SEQ ID NO:1);

b) SRC1–2: SLTARHKILHRLLQEGSPSDI (SEQ ID NO:2);

c) SRC3-1: ESKGHKKLLQLLTCSSDDR (SEQ ID NO:3);

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d) SRC3: PKKENNALLRYLLDRDDPSDV (SEQ ID NO:4);

e) PGC-1: AEEPSLLKKLLLAPANT (SEQ ID NO:5);

f) PGC1a: QEAEEPSLLKKLLLAPANTQL (SEQ ID NO:6);

g) TRAP220–1: SKVSQNPILTSLLQITGNGGS (SEQ ID NO:7);

h) NCoR (2051–2075): GHSFADPASNLGLEDIIRKALMGSF (SEQ ID NO:8);

i) NR0B1: PRQGSILYSMLTSAKQT (SEQ ID NO:9);

j) NRIP1: AANNSLLLHLLKSQTIP (SEQ ID NO:10);

k) TIF2: PKKKENALLRYLLDKDDTKDI (SEQ ID NO:11);

l) CoRNR Box: DAFQLRQLILRGLQDD (SEQ ID NO:12);

m) αβV: SPGSREWFKDMLS (SEQ ID NO:13);

n) TRAP220-2: GNTKNHPMLMNLLKDNPAQDF (SEQ ID NO:14);

o) EA2: SSKGVLWRMLAEPVSR (SEQ ID NO:15);

p) TA1: SRTLQLDWGTLYWSR (SEQ ID NO:16);

q) EAB1: SSNHQSSRLIELLSR (SEQ ID NO:17);

r) SRC2: LKEKHKILHRLLQDSSSPV (SEQ ID NO:18);

s) SRC1-3: QAQQKSLLQQLLTE (SEQ ID NO:19);

t) SRC1–1: KYSQTSHKLVQLLTTTAEQQL (SEQ ID NO:20);

u) SRC1–2: SLTARHKILHRLLQEGSPSDI (SEQ ID NO:21);

v) SRC1–3: KESKDHQLLRYLLDKDEKDLR (SEQ ID NO:22);

w) SRC1–4a: PQAQQKSLLQQLLTE (SEQ ID NO:23);;

x) SRC1–4b: PQAQQKSLRQQLLTE (SEQ ID NO:24);

y) GRIP1–1: HDSKGQTKLLQLLTTKSDQME (SEQ ID NO:25);

z) GRIP1–2: SLKEKHKILHRLLQDSSSPVD (SEQ ID NO:26);

aa) GRIP1–3: PKKKENALLRYLLDKDDTKDI (SEQ ID NO:27);

bb) AIB1–1: LESKGHKKLLQLLTCSSDDRG (SEQ ID NO:28);

cc) AIB1–2: LLQEKHRILHKLLQNGNSPAE (SEQ ID NO:29);

dd) AIB1–3: KKKENNALLRYLLDRDDPSDA (SEQ ID NO:30);

ee) PGC1a: QEAEEPSLLKKLLLAPANTQL (SEQ ID NO:31);

ff) PGC1b: PEVDELSLLQKLLLATSYPTS (SEQ ID NO:32);

gg) PRC: VSPREGSSLHKLLTLSRTPPE (SEQ ID NO:33);

hh) TRAP220–1: SKVSQNPILTSLLQITGNGGS (SEQ ID NO:34);

ii) TRAP220–2: GNTKNHPMLMNLLKDNPAQDF (SEQ ID NO:35);

jj) ASC2–1: DVTLTSPLLVNLLQSDISAGH (SEQ ID NO:36);

kk) ASC2–2: AMREAPTSLSQLLDNSGAPNV (SEQ ID NO:37);

ll) CBP-1: DAASKHKQLSELLRGGSGSSI (SEQ ID NO:38);

mm) CBP-2: KRKLIQQQLVLLLHAHKCQRR (SEQ ID NO:39);

nn) P300: DAASKHKQLSELLRSGSSPNL (SEQ ID NO:40);

oo) CIA: GHPPAIQSLINLLADNRYLTA (SEQ ID NO:41);

pp) ARA70–1: TLQQQAQQLYSLLGQFNCLTH (SEQ ID NO:42);

qq) ARA70–2: GSRETSEKFKLLFQSYNVNDW (SEQ ID NO:43);

rr) TIF1: NANYPRSILTSLLLNSSQSST (SEQ ID NO:44);

ss) NSD1: IPIEPDYKFSTLLMMLKDMHD (SEQ ID NO:45);

tt) SMAP: ATPPPSPLLSELLKKGSLLPT (SEQ ID NO:46);

uu) Tip60: VDGHERAMLKRLLRIDSKCLH (SEQ ID NO:47);

vv) ERAP140: HEDLDKVKLIEYYLTKNKEGP (SEQ ID NO:48);

ww) Nix1: ESPEFCLGLQTLLSLKCCIDL (SEQ ID NO:49);

xx) LCoR: AATTQNPVLSKLLMADQDSPL (SEQ ID NO:50);

yy) CoRNR1 (N-CoR): MGQVPRTHRLITLADHICQIITQDFARNQV (SEQ ID NO:51);

zz) CoRNR2 (N-CoR): NLGLEDIIRKALMG (SEQ ID NO:52);

aaa) CoRNR1 (SMRT): APGVKGHQRVVTLAQHISEVITQDTYRHHPQQLSAPLPAP (SEQ ID NO:53);

bbb) CoRNR2 (SMRT): NMGLEAIIRKALMG (SEQ ID NO:54);

ccc) RIP140-C: RLTKTNPILYYMLQKGGNSVA (SEQ ID NO:55);

ddd) RIP140-1: QDSIVLTYLEGLLMHQAAGGS (SEQ ID NO:56);

eee) RIP140-2: KGKQDSTLLASLLQSFSSRLQ (SEQ ID NO:57);

fff) RIP140-3: CYGVASSHLKTLLKKSKVKDQ (SEQ ID NO:58);

ggg) RIP140-4: KPSVACSQLALLLSSEAHLQQ (SEQ ID NO:59);

hhh) RIP140-5: KQAANNSLLLHLLKSQTIPKP (SEQ ID NO:60);

iii) RIP140-6: NSHQKVTLLQLLLGHKNEENV (SEQ ID NO:61);

jjj) RIP140-7: NLLERRTVLQLLLGNPTKGRV (SEQ ID NO:62);

kkk) RIP140-8: FSFSKNGLLSRLLRQNQDSYL (SEQ ID NO:63);

lll) RIP140-9: RESKSFNVLKQLLLSENCVRD (SEQ ID NO:64);

mmm) PRIC285-1: ELNADDAILRELLDESQKVMV (SEQ ID NO:65);

nnn) PRIC285-2: YENLPPAALRKLLRAEPERYR (SEQ ID NO:66);

ooo) PRIC285-3: MAFAGDEVLVQLLSGDKAPEG (SEQ ID NO:67);

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ppp) PRIC285-4: SCCYLCIRLEGLLAPTASPRP (SEQ ID NO:68); and

qqq) PRIC285-5: PSNKSVDVLAGLLLRRMELKP (SEQ ID NO:69).

8. The heterodimeric, conditionally active polypeptide of claim 2, wherein the receptor is a CAR heterodimer, wherein either:

a) the first polypeptide of the CAR heterodimer comprises:

i) a first member of a specific binding pair;

ii) a first modulatory domain;

iii) the first member of the dimerization pair; and

iv) a transmembrane domain interposed between the first member of the specific binding pair and the first modulatory domain; and

b) the second polypeptide of the CAR heterodimer comprises:

i) a transmembrane domain;

ii) a second modulatory domain;

iii) the second member of the dimerization pair; and

iv) an intracellular signaling domain;

or:

a) the first polypeptide of the CAR heterodimer comprises:

i) a first member of a specific binding pair;

ii) a modulatory domain;

iii) the first member of the dimerization pair;

iv) a transmembrane domain interposed between the first member of the specific binding pair and the modulatory domain; and

b) the second polypeptide of the CAR heterodimer comprises:

i) a second member of the dimerization pair; and

ii) an intracellular signaling domain.

9. The heterodimeric, conditionally active receptor of claim 8, wherein the first member of the specific binding pair is an antibody or antibody fragment, a ligand, a receptor, or a non-antibody-based recognition scaffold, optionally, that binds an epitope present on a cell, on a solid surface, or a lipid bilayer;

wherein the first and second modulatory domains are selected from 4-1BB (CD137), CD28, ICOS, BTLA, OX-40, CD27, CD30, GITR, HVEM, DAP10, DAP12, and CD28; and/or

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wherein the intracellular signaling domain is selected from ZAP70 and CD3-zeta.

10. A heterodimeric, conditionally repressible synthetic immune cell receptor (ICR) comprising:

a synthetic stimulatory ICR comprising a first member of a dimerization pair linked to the synthetic stimulatory ICR; and

a synthetic ICR repressor comprising a second member of the dimerization pair linked to an intracellular inhibitory domain,

wherein the first member of the dimerization pair comprises a ligand-binding domain (LBD) of a nuclear hormone receptor, and the second member of the dimerization pair comprises a co-regulator of the nuclear hormone receptor, or

wherein the first member of the dimerization pair is a co-regulator of a nuclear hormone receptor, and the second member of the dimerization pair comprises an LBD of the nuclear hormone receptor,

wherein the synthetic stimulatory ICR and the synthetic ICR repressor are dimerized in the presence of a dimerization agent that induces binding of the LBD to the co-regulator.

11. The conditionally repressible synthetic ICR of Claim 10, wherein the synthetic stimulatory ICR comprises an intracellular co-stimulatory domain, optionally selected from the group consisting of: 4-1BB (CD137), CD28, ICOS, OX-40, BTLA, CD27, CD30, GITR, and HVEM;

wherein the intracellular inhibitory domain is an inhibitory domain derived from a protein selected from the group consisting of: PD-1, CTLA4, HPK1, SHP1, SHP2, Sts1 and Csk; and/or

wherein the synthetic stimulatory ICR comprises an intracellular signaling domain selected from the group consisting of: a CD3-zeta signaling domain, a ZAP70 signaling domain and an immunoreceptor tyrosine-based activation motif (ITAM).

12. The conditionally repressible synthetic ICR of claims 10 or 11, wherein LBD of the nuclear hormone binding member of the dimerization pair is an LBD of a nuclear hormone receptor selected from estrogen receptor, an ecdysone receptor, a PPARγ receptor, a glucocorticoid receptor, an androgen receptor, a thyroid hormone receptor, a mineralocorticoid receptor, a progesterone receptor, a vitamin D receptor, a PPARβ receptor, a PPARα receptor, a pregnane X receptor, a liver X receptor, a farnesoid X receptor, a retinoid X receptor, a RAR-

related orphan receptor, and a retinoic acid receptor; optionally wherein the co-regulator of the nuclear hormone receptor is selected from SRC1, GRIP1, AIB1, PGC1a, PGC1b, PRC, TRAP220, ASC2, CBP, P300, CIA, ARA70, TIF1, NSD1, SMAP, Tip60, ERAP140, Nix1, LCoR, N-CoR, SMRT, RIP140, and PRIC285; and optionally wherein the co-regulator of the nuclear hormone receptor is selected from:

a) SRC1: CPSSHSSLTERHKILHRLLQEGSPS (SEQ ID NO:1);

b) SRC1–2: SLTARHKILHRLLQEGSPSDI (SEQ ID NO:2);

c) SRC3-1: ESKGHKKLLQLLTCSSDDR (SEQ ID NO:3);

d) SRC3: PKKENNALLRYLLDRDDPSDV (SEQ ID NO:4);

e) PGC-1: AEEPSLLKKLLLAPANT (SEQ ID NO:5);

f) PGC1a: QEAEEPSLLKKLLLAPANTQL (SEQ ID NO:6);

g) TRAP220–1: SKVSQNPILTSLLQITGNGGS (SEQ ID NO:7);

h) NCoR (2051–2075): GHSFADPASNLGLEDIIRKALMGSF (SEQ ID NO:8);

i) NR0B1: PRQGSILYSMLTSAKQT (SEQ ID NO:9);

j) NRIP1: AANNSLLLHLLKSQTIP (SEQ ID NO:10);

k) TIF2: PKKKENALLRYLLDKDDTKDI (SEQ ID NO:11);

l) CoRNR Box: DAFQLRQLILRGLQDD (SEQ ID NO:12);

m) αβV: SPGSREWFKDMLS (SEQ ID NO:13);

n) TRAP220-2: GNTKNHPMLMNLLKDNPAQDF (SEQ ID NO:14);

o) EA2: SSKGVLWRMLAEPVSR (SEQ ID NO:15);

p) TA1: SRTLQLDWGTLYWSR (SEQ ID NO:16);

q) EAB1: SSNHQSSRLIELLSR (SEQ ID NO:17);

r) SRC2: LKEKHKILHRLLQDSSSPV (SEQ ID NO:18);

s) SRC1-3: QAQQKSLLQQLLTE (SEQ ID NO:19);

t) SRC1–1: KYSQTSHKLVQLLTTTAEQQL (SEQ ID NO:20);

u) SRC1–2: SLTARHKILHRLLQEGSPSDI (SEQ ID NO:21);

v) SRC1–3: KESKDHQLLRYLLDKDEKDLR (SEQ ID NO:22);

w) SRC1–4a: PQAQQKSLLQQLLTE (SEQ ID NO:23);;

x) SRC1–4b: PQAQQKSLRQQLLTE (SEQ ID NO:24);

y) GRIP1–1: HDSKGQTKLLQLLTTKSDQME (SEQ ID NO:25);

z) GRIP1–2: SLKEKHKILHRLLQDSSSPVD (SEQ ID NO:26);

aa) GRIP1–3: PKKKENALLRYLLDKDDTKDI (SEQ ID NO:27);

bb) AIB1–1: LESKGHKKLLQLLTCSSDDRG (SEQ ID NO:28);

cc) AIB1–2: LLQEKHRILHKLLQNGNSPAE (SEQ ID NO:29);

dd) AIB1–3: KKKENNALLRYLLDRDDPSDA (SEQ ID NO:30);

ee) PGC1a: QEAEEPSLLKKLLLAPANTQL (SEQ ID NO:31);

ff) PGC1b: PEVDELSLLQKLLLATSYPTS (SEQ ID NO:32);

gg) PRC: VSPREGSSLHKLLTLSRTPPE (SEQ ID NO:33);

hh) TRAP220–1: SKVSQNPILTSLLQITGNGGS (SEQ ID NO:34);

ii) TRAP220–2: GNTKNHPMLMNLLKDNPAQDF (SEQ ID NO:35);

jj) ASC2–1: DVTLTSPLLVNLLQSDISAGH (SEQ ID NO:36);

kk) ASC2–2: AMREAPTSLSQLLDNSGAPNV (SEQ ID NO:37);

ll) CBP-1: DAASKHKQLSELLRGGSGSSI (SEQ ID NO:38);

mm) CBP-2: KRKLIQQQLVLLLHAHKCQRR (SEQ ID NO:39);

nn) P300: DAASKHKQLSELLRSGSSPNL (SEQ ID NO:40);

oo) CIA: GHPPAIQSLINLLADNRYLTA (SEQ ID NO:41);

pp) ARA70–1: TLQQQAQQLYSLLGQFNCLTH (SEQ ID NO:42);

qq) ARA70–2: GSRETSEKFKLLFQSYNVNDW (SEQ ID NO:43);

rr) TIF1: NANYPRSILTSLLLNSSQSST (SEQ ID NO:44);

ss) NSD1: IPIEPDYKFSTLLMMLKDMHD (SEQ ID NO:45);

tt) SMAP: ATPPPSPLLSELLKKGSLLPT (SEQ ID NO:46);

uu) Tip60: VDGHERAMLKRLLRIDSKCLH (SEQ ID NO:47);

vv) ERAP140: HEDLDKVKLIEYYLTKNKEGP (SEQ ID NO:48);

ww) Nix1: ESPEFCLGLQTLLSLKCCIDL (SEQ ID NO:49);

xx) LCoR: AATTQNPVLSKLLMADQDSPL (SEQ ID NO:50);

yy) CoRNR1 (N-CoR): MGQVPRTHRLITLADHICQIITQDFARNQV (SEQ ID NO:51);

zz) CoRNR2 (N-CoR): NLGLEDIIRKALMG (SEQ ID NO:52);

aaa) CoRNR1 (SMRT): APGVKGHQRVVTLAQHISEVITQDTYRHHPQQLSAPLPAP (SEQ ID NO:53);

bbb) CoRNR2 (SMRT): NMGLEAIIRKALMG (SEQ ID NO:54);

ccc) RIP140-C: RLTKTNPILYYMLQKGGNSVA (SEQ ID NO:55);

ddd) RIP140-1: QDSIVLTYLEGLLMHQAAGGS (SEQ ID NO:56);

eee) RIP140-2: KGKQDSTLLASLLQSFSSRLQ (SEQ ID NO:57);

fff) RIP140-3: CYGVASSHLKTLLKKSKVKDQ (SEQ ID NO:58);

ggg) RIP140-4: KPSVACSQLALLLSSEAHLQQ (SEQ ID NO:59);

hhh) RIP140-5: KQAANNSLLLHLLKSQTIPKP (SEQ ID NO:60);
iii) RIP140-6: NSHQKVTLLQLLLGHKNEENV (SEQ ID NO:61);
jjj) RIP140-7: NLLERRTVLQLLLGNPTKGRV (SEQ ID NO:62);
kkk) RIP140-8: FSFSKNGLLSRLLRQNQDSYL (SEQ ID NO:63);
lll) RIP140-9: RESKSFNVLKQLLLSENCVRD (SEQ ID NO:64);
mmm) PRIC285-1: ELNADDAILRELLDESQKVMV (SEQ ID NO:65);
nnn) PRIC285-2: YENLPPAALRKLLRAEPERYR (SEQ ID NO:66);
ooo) PRIC285-3: MAFAGDEVLVQLLSGDKAPEG (SEQ ID NO:67);
ppp) PRIC285-4: SCCYLCIRLEGLLAPTASPRP (SEQ ID NO:68); and
qqq) PRIC285-5: PSNKSVDVLAGLLLRRMELKP (SEQ ID NO:69).

13. The conditionally repressible synthetic ICR of any one of claims 10-12, wherein the synthetic stimulatory ICR is a synthetic chimeric antigen receptor (CAR) or portion thereof, or the synthetic stimulatory ICR is a synthetic T cell receptor (TCR) or portion thereof.

14. A mammalian cell genetically modified to produce the heterodimeric, conditionally active polypeptide or receptor of any one of claims 1-13, optionally wherein the cell is a stem cell, a progenitor cell, or a cell derived from a stem cell or a progenitor cell, a T lymphocyte or an NK cell.

15. A nucleic acid, or recombinant expression vector comprising a nucleic acid, comprising nucleotide sequences encoding the heterodimeric, conditionally active receptor or polypeptide of any one of claims 1-13.

16. An ex vivo method of modulating an activity of a eukaryotic cell, the method comprising:

a) expressing the heterodimeric, conditionally active polypeptide or receptor of any one of claims 1-13 in the eukaryotic cell; and

b) contacting the cell with the ligand.

17. A method of modulating an activity of a T lymphocyte, the method comprising contacting the T lymphocyte with a dimerizing agent and a second member of a specific binding pair, wherein the T lymphocyte is genetically modified to produce a heterodimeric, conditionally

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active receptor of any one of claims 2 and 8-13, and wherein, in the presence of the dimerizing agent and the second member of a specific binding pair, the heterodimeric, conditionally active receptor dimerizes and modulates an activity of the T lymphocyte, thereby producing a modulated T lymphocyte; optionally wherein the second member of a specific binding pair is an antigen, said contacting occurs *in vivo*, and/or the T lymphocyte is activated, thereby producing an activate T lymphocyte.

18. A method of making the cell of claim 14, the method comprising genetically modifying a mammalian cell with an expression vector comprising nucleotide sequences encoding the heterodimeric, conditionally active receptor or polypeptide of any one of claims 1-13, or genetically modifying a mammalian cell with an RNA comprising nucleotide sequences encoding the heterodimeric, conditionally active receptor or polypeptide of any one of claims 1-13; optionally wherein said genetic modification is carried out *ex vivo*, and /or wherein the cell is a T lymphocyte, a stem cell, an NK cell, a progenitor cell, a cell derived from a stem cell, or a cell derived from a progenitor cell.

19. A method of treating a cancer in an individual, the method comprising:

i) genetically modifying T lymphocytes obtained from the individual with an expression vector comprising nucleotide sequences encoding the heterodimeric, conditionally active chimeric antigen receptor (CAR) of any one of claims 8-9, wherein the antigen-binding domain of the heterodimeric, conditionally active CAR is specific for an epitope on a cancer cell in the individual, and wherein said genetic modification is carried out *ex vivo*;

ii) introducing the genetically modified T lymphocytes into the individual; and

iii) administering to the individual an effective amount of a dimerizing agent, wherein the dimerizing agent induces dimerization of the heterodimeric, conditionally active receptor, wherein said dimerization provides for activation of the genetically modified T lymphocytes and killing of the cancer cell, thereby treating the cancer.

20. Use of an expression vector comprising a nucleotide sequences encoding the heterodimeric, conditionally active chimeric antigen receptor (CAR) of any one of claims 8-9, in the manufacture of a cell preparation for the treatment of cancer in an individual, wherein the treatment comprises;

i) genetically modifying T lymphocytes obtained from the individual with the expression vector wherein the antigen-binding domain of the heterodimeric, conditionally active CAR is specific for an epitope on a cancer cell in the individual, and wherein said genetic modification is carried out *ex vivo*;

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ii) introducing the genetically modified T lymphocytes into the individual; and

iii) administering to the individual an effective amount of a dimerizing agent, wherein the dimerizing agent induces dimerization of the heterodimeric, conditionally active receptor, wherein said dimerization provides for activation of the genetically modified T lymphocytes and killing of the cancer cell, thereby treating the cancer.

FIG. 1A

Mineralocorticoid receptor (*Homo sapiens*)

```
  1 metkgyhslp egldmerrwg qvsqaverss lgptertden nymeivnvsc vsgaipnnst
 61 qgsskekqel lpclqqdnnr pgiltsdikt eleskelsat vaesmglymd svrdadysye
121 qqnqqgsmsp akiyqnveql vkfykgnghr pstlscvntp lrsfmsdsgs svnggvmrav
181 vkspimchek spsvcsplnm tssvcspagi nsvssttasf gsfpvhspit qgtpltcspn
241 venrgsrshs pahasnvgsp lssplssmks sissppshcs vkspvsspnn vtlrssvssp
301 aninnsrcsv sspsntnnrs tlsspaastv gsicspvnna fsytasgtsa gsstlrdvvp
361 spdtqekgaq evpfpkteev esaisngvtg qlnivqyikp epdgafsssc lggnskinsd
421 ssfsvpikqe stkhscsgts fkgnptvnpf pfmdgsyfsf mddkdyysls gilgppvpgf
481 dgncegsgfp vgikqepddg syypeasips saivgvnsgg qsfhyrigaq gtislsrsar
541 dqsfqhlssf ppvntlvesw kshgdlssrr sdgypvleyi penvssstlr svstgssrps
601 kiclvcgdea sgchygvvtc gsckvffkra vegqhnylca grndciidki rrkncpacrl
661 qkclqagmnl garkskklgk lkgiheeqpq qqqpppppppp pqspeegtty iapakepsvn
721 talvpqlsti sraltpspvm vleniepeiv yagydsskpd taenllstln rlagkqmiqv
781 vkwakvlpgf knlpledqit liqyswmcls sfalswrsyk htnsqflyfa pdlvfneekm
841 hqsamyelcq gmhqislqfv rlqltfeeyt imkvllllst ipkdglksqa afeemrtnyi
901 kelrkmvtkc pnnsgqswqr fyqltkllds mhdlvsdlle fcfytfresh alkvefpaml
961 veiisdqlpk vesgnakply fhrk
```

FIG. 1B

Amino acids 686-984 of *Homo sapiens* mineralocorticoid receptor

```
686                              eeqpq qqqpppppppp pqspeegtty iapakepsvn
721 talvpqlsti sraltpspvm vleniepeiv yagydsskpd taenllstln rlagkqmiqv
781 vkwakvlpgf knlpledqit liqyswmcls sfalswrsyk htnsqflyfa pdlvfneekm
841 hqsamyelcq gmhqislqfv rlqltfeeyt imkvllllst ipkdglksqa afeemrtnyi
901 kelrkmvtkc pnnsgqswqr fyqltkllds mhdlvsdlle fcfytfresh alkvefpaml
961 veiisdqlpk vesgnakply fhrk
```

FIG. 1C

Amino acids 737-984 of *Homo sapiens* mineralocorticoid receptor

```
737                        spvm vleniepeiv yagydsskpd taenllstln rlagkqmiqv
781 vkwakvlpgf knlpledqit liqyswmcls sfalswrsyk htnsqflyfa pdlvfneekm
841 hqsamyelcq gmhqislqfv rlqltfeeyt imkvllllst ipkdglksqa afeemrtnyi
901 kelrkmvtkc pnnsgqswqr fyqltkllds mhdlvsdlle fcfytfresh alkvefpaml
961 veiisdqlpk vesgnakply fhrk
```

FIG. 1D

Amino acids 686-984 of *Homo sapiens* mineralocorticoid receptor, with S810L substitution

```
686                              eeqpq qqqpppppppp pqspeegtty iapakepsvn
721 talvpqlsti sraltpspvm vleniepeiv yagydsskpd taenllstln rlagkqmiqv
781 vkwakvlpgf knlpledqit liqyswmcll sfalswrsyk htnsqflyfa pdlvfneekm
841 hqsamyelcq gmhqislqfv rlqltfeeyt imkvllllst ipkdglksqa afeemrtnyi
901 kelrkmvtkc pnnsgqswqr fyqltkllds mhdlvsdlle fcfytfresh alkvefpaml
961 veiisdqlpk vesgnakply fhrk
```

FIG. 1E

Amino acids 737-984 of *Homo sapiens* mineralocorticoid receptor, with S810L substitution

```
737                     spvm vleniepeiv yagydsskpd taenllstln rlagkqmiqv
781 vkwakvlpgf knlpledqit liqyswmcll sfalswrsyk htnsqflyfa pdlvfneekm
841 hqsamyelcq gmhqislqfv rlqltfeeyt imkvllllst ipkdglksqa afeemrtnyi
901 kelrkmvtkc pnnsgqswqr fyqltkllds mhdlvsdlle fcfytfresh alkvefpaml
961 veiisdqlpk vesgnakply fhrk
```

FIG. 1F

Multiple sequence alignment of ligand-binding domain of mineralocorticoid receptors of various species

```
                        10        20        30        40        50        60        70        80
                  ....*....|....*....|....*....|....*....|....*....|....*....|....*....|....*....|
Feature 1                                     ## ##  #                                 #  #    #
2AA6_A         28 SPVMVLENIEPEIVYAGYDSSKPDTAENLLSTLNRLAGKQMIQVVKWAKVLPGFKNLPLEDQITLIQYSWMSLLSFALSW 107
gi 115529242  734 SPVKILESIEPEIVYAGYDSSKPDTAEYLLSTLNRLAGKQMIQVVKWAKILPGFRNLPLEDQITLIQYSWMCLSSFALSW 813
2AA2_A         28 SPVMVLENIEPEIVYAGYDSSKPDTAENLLSTLNRLAGKQMIQVVKWAKVLPGFKNLPLEDQITLIQYSWMSLSSFALSW 107
2A3I_A          6 SPVMVLENIEPEIVYAGYDSSKPDTAENLLSTLNRLAGKQMIQVVKWAKVLPGFKNLPLEDQITLIQYSWMSLSSFALSW  85
2OAX_A          9 SPVMVLENIEPEIVYAGYDSSKPDTAENLLSTLNRLAGKQMIQVVKWAKVLPGFKNLPLEDQITLIQYSWMCLLSFALSW  88
1Y9R_A          8 SPVMVLENIEPEIVYAGYDSSKPDTAENLLSTLNRLAGKQMIQVVKWAKVLPGFKNLPLEDQITLIQYSWMCLLSFALSW  87
2ABI_A          9 SPVMVLENIEPEIVYAGYDSSKPDTAENLLSTLNRLAGKQMIQVVKWAKVLPGFKNLPLEDQITLIQYSWMCLSSFALSW  88
gi 2500914    365 SAAVILENIEPEIVYAGYDNTQPDTAENLLSSLNQLAGKQMVQVVKWAKVIPGFRNLPLEDQITLIQYSWMCLSSFALSW 444
gi 30315969   112 SICSVLELIEPEVVFAGYDNTQPDTTDHLLSSLNQLAGKQMIRVVKWAKVLPGFRGLPIEDQITLIQYSWMCLSSFSLSW 191
gi 47217367   173 SICSILELIEPEEVYSGYDNTQPDTTDHLLSSLNRLAGKQMVRMVKWAKVLPGFRGLPIEDQITLIQYSWMCLSSFCLSW 252
                        90       100       110       120       130       140       150       160
                  ....*....|....*....|....*....|....*....|....*....|....*....|....*....|....*....|
Feature 1         #           #               #       #
2AA6_A        108 RSYKHTNSQFLYFAPDLVFNEEKMHQSAMYELCQGMHQISLQFVRLQLTFEEYTIMKVLLLLSTIPKDGLKS-------- 179
gi 115529242  814 RSYKHTNSQFLYFAPDLIFDEERMRQSAMFELCQGMHQISLQFVRLQLSFEEYTIMKVLLLLSTVPKDGLKS-------- 885
2AA2_A        108 RSYKHTNSQFLYFAPDLVFNEEKMHQSAMYELCQGMHQISLQFVRLQLTFEEYTIMKVLLLLSTIPKDGLKS-------- 179
2A3I_A         86 RSYKHTNSQFLYFAPDLVFNEEKMHQSAMYELCQGMHQISLQFVRLQLTFEEYTIMKVLLLLSTIPKDGLKS-------- 157
2OAX_A         89 RSYKHTNSQFLYFAPDLVFNEEKMHQSAMYELCQGMHQISLQFVRLQLTFEEYTIMKVLLLLSTIPKDGLKS-------- 160
1Y9R_A         88 RSYKHTNSQFLYFAPDLVFNEEKMHQSAMYELCQGMHQISLQFVRLQLTFEEYTIMKVLLLLSTIPKDGLKS-------- 159
2ABI_A         89 RSYKHTNSQFLYFAPDLVFNEEKMHQSAMYELCQGMHQISLQFVRLQLTFEEYTIMKVLLLLSTIPKDGLKS-------- 160
gi 2500914    445 RSYKHASSQFLYFAPDLIFNEERMRQSAMYDLCQGMQQISLEFSRLQLTFEEYTLMKVLLLLSTVPKDGLKC-------- 516
gi 30315969   192 RSYKHTNGQMLYFAPDLVFNEDRMQQSAMYDLCLGMRQVSQEFVRLQLTYQEFLSMKVLLLLSTVPKEGLKN-------- 263
gi 47217367   253 RSYKHTNGQMLYFAPDLIFNEERMRQSAMYDLCLGMRQVSQEFLRLQLSYDEFLSMKVLLLLSTGLGRLTLFgfhcskql 332
```

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FIG. 1F (Cont.)

```
                 170       180       190       200       210       220       230       240
                 ....*....|....*....|....*....|....*....|....*....|....*....|....*....|
Feature 1                                                                    ##  #
2AA6_A           180 ----------------QAAFEEMRTNYIKELRKMVTKCPNNSGQSWQRFYQLTKLLDSMHDLVSDLLEFCFYTFRES-- 240
gi 115529242     886 ----------------QAAFEEMRANYIKELKKMVTKCPSNSGQSWQRFYQLTKLLDSMHDLVSDLLEFCFYTFRES-- 946
2AA2_A           180 ----------------QAAFEEMRTNYIKELRKMVTKCPNNSGQSWQRFYQLTKLLDSMHDLVSDLLEFCFYTFRES-- 240
2A3I_A           158 ----------------QAAFEEMRTNYIKELRKMVTKCPNNSGQSWQRFYQLTKLLDSMHDLVSDLLEFCFYTFRES-- 218
2OAX_A           161 ----------------QAAFEEMRTNYIKELRKMVTKAPNNSGQSWQRFYQLTKLLDSMHDLVSDLLEFCFYTFRES-- 221
1Y9R_A           160 ----------------QAAFEEMRTNYIKELRKMVTKAPNNSGQSWQRFYQLTKLLDSMHDLVSDLLEFCFYTFRES-- 220
2ABI_A           161 ----------------QAAFEEMRTNYIKELRKMVTKAPNNSGQSWQRFYQLTKLLDSMHDLVSDLLEFCFYTFRES-- 221
gi 2500914       517 ----------------QAAFEEMRVNYIKELRKVLLKSPHNSGQSWQRYFQLTKLLDSMQDLVGDLLEFCFYTFRES-- 577
gi 30315969      264 ----------------QAAFEEMRVNYIKELRRSVGKAPTTLDRRGNRSSQLTKLLDAMHDLGGELLDFCFYTFRES-- 324
gi 47217367      333 ppspphmrtvpkeglknQAAFEEMRLNYIKELRRSVGKATNNSGQTWQRFFQLTKLLDAMHDVSTLCLPRHAAPLGRPhd 412
                     250       260       270       280       290       300       310       320
                     ....*....|....*....|....*....|....*....|....*....|....*....|....*....|
Feature 1
2AA6_A           241 ------------------------------------------------HALKVEFPAMLVEIISDQLPKVESGN 266
gi 115529242     947 ------------------------------------------------QALKVEFPAMLVEIISDQLPKVESGN 972
2AA2_A           241 ------------------------------------------------HALKVEFPAMLVEIISDQLPKVESGN 266
2A3I_A           219 ------------------------------------------------HALKVEFPAMLVEIISDQLPKVESGN 244
2OAX_A           222 ------------------------------------------------HALKVEFPAMLVEIISDQLPKVESGN 247
1Y9R_A           221 ------------------------------------------------HALKVEFPAMLVEIISDQLPKVESGN 246
2ABI_A           222 ------------------------------------------------HALKVEFPAMLVEIISDQLPKVESGN 247
gi 2500914       578 ------------------------------------------------QALKVEFPAMLVEIISDQLPKVESGI 603
gi 30315969      325 ------------------------------------------------QALKVEFPEMLVEIISDQIPKVESGN 350
gi 47217367      413 ttqfppsfqesphlhtqskkaaqtpcetaskymceysklvgnlldfcfytfresQVLKVEFPEMLVEIISDQIPKVESGL 492
```

FIG. 1F (Cont.)

```
                    ....*....
Feature 1
2AA6_A          267 AKPLYFHRK 275
gi 115529242    973 AKPLYFHRK 981
2AA2_A          267 AKPLYFHRK 275
2A3I_A          245 AKPLYFHRK 253
2OAX_A          248 AKPLYFHRK 256
1Y9R_A          247 AKPLYFHRK 255
2ABI_A          248 AKPLYFHRK 256
gi 2500914      604 AKPLYFHRK 612
gi 30315969     351 THTLYFHKK 359
gi 47217367     493 THTIYFHKK 501
```

FIG. 2A

Androgen receptor (*Homo sapiens*)

```
  1 mevqlglgrv yprppsktyr gafqnlfqsv reviqnpgpr hpeaasaapp qaslllqqq
 61 qqqqqqqqqq qqqqqqqqet sprqqqqqqg edgspqahrr gptgylvlde eqqpsqpqsa
121 lechpergcv pepgaavaas kglpqqlpap pdeddsaaps tlsllgptfp glsscsadlk
181 dilseastmq llqqqqqeav segsssgrar easgaptssk dnylggtsti sdnakelcka
241 vsvsmglgve alehlspgeq lrgdcmyapl lgvppavrpt pcaplaeckg sllddsagks
301 tedtaeyspf kggytkgleg eslgcsgsaa agssgtlelp stlslyksga ldeaaayqsr
361 dyynfplala gpppppppph phariklenp ldygsawaaa aaqcrygdla slhgagaagp
421 gsgspsaaas sswhtlftae egqlygpcgg gggggggggg gggggggggg ggeagavapy
481 gytrppqgla gqesdftapd vwypggmvsr vpypsptcvk semgpwmdsy sgpygdmrle
541 tardhvlpid yyfppqktcl icgdeasgch ygaltcgsck vffkraaegk qkylcasrnd
601 ctidkfrrkn cpscrlrkcy eagmtlgark lkklgnlklq eegeasstts pteettqklt
661 vshiegyecq piflnvleai epgvvcaghd nnqpdsfaal lsslnelger qlvhvvkwak
721 alpgfrnlhv ddqmaviqys wmglmvfamg wrsftnvnsr mlyfapdlvf neyrmhksrm
781 ysqcvrmrhl sqefgwlqit pqeflcmkal llfsiipvdg lknqkffdel rmnyikeldr
841 iiackrknpt scsrrfyqlt klldsvqpia relhqftfdl likshmvsvd fpemmaeiis
901 vqvpkilsgk vkpiyfhtq
```

FIG. 2B

Amino acids 619-919 of *Homo sapiens* androgen receptor

```
619                     cy eagmtlgark lkklgnlklq eegeasstts pteettqklt
661 vshiegyecq piflnvleai epgvvcaghd nnqpdsfaal lsslnelger qlvhvvkwak
721 alpgfrnlhv ddqmaviqys wmglmvfamg wrsftnvnsr mlyfapdlvf neyrmhksrm
781 ysqcvrmrhl sqefgwlqit pqeflcmkal llfsiipvdg lknqkffdel rmnyikeldr
841 iiackrknpt scsrrfyqlt klldsvqpia relhqftfdl likshmvsvd fpemmaeiis
901 vqvpkilsgk vkpiyfhtq
```

FIG. 2C

Amino acids 690-919 of *Homo sapiens* androgen receptor

```
690                                 d nnqpdsfaal lsslnelger qlvhvvkwak
721 alpgfrnlhv ddqmaviqys wmglmvfamg wrsftnvnsr mlyfapdlvf neyrmhksrm
781 ysqcvrmrhl sqefgwlqit pqeflcmkal llfsiipvdg lknqkffdel rmnyikeldr
841 iiackrknpt scsrrfyqlt klldsvqpia relhqftfdl likshmvsvd fpemmaeiis
901 vqvpkilsgk vkpiyfhtq
```

FIG. 2D

Amino acids 619-919 of *Homo sapiens* androgen receptor, with T877A substitution

```
619                    cy eagmtlgark lkklgnlklq eegeasstts pteettqklt
661 vshiegyecq piflnvleai epgvvcaghd nnqpdsfaal lsslnelger qlvhvvkwak
721 alpgfrnlhv ddqmaviqys wmglmvfamg wrsftnvnsr mlyfapdlvf neyrmhksrm
781 ysqcvrmrhl sqefgwlqit pqeflcmkal llfsiipvdg lknqkffdel rmnyikeldr
841 iiackrknpt scsrrfyqlt klldsvqpia relhqfafdl likshmvsvd fpemmaeiis
901 vqvpkilsgk vkpiyfhtq
```

FIG. 2E

Amino acids 690-919 of *Homo sapiens* androgen receptor with T877A substitution

```
690                                d nnqpdsfaal lsslnelger qlvhvvkwak
721 alpgfrnlhv ddqmaviqys wmglmvfamg wrsftnvnsr mlyfapdlvf neyrmhksrm
781 ysqcvrmrhl sqefgwlqit pqeflcmkal llfsiipvdg lknqkffdel rmnyikeldr
841 iiackrknpt scsrrfyqlt klldsvqpia relhqfafdl likshmvsvd fpemmaeiis
901 vqvpkilsgk vkpiyfhtq
```

FIG. 2F

Amino acids 619-919 of *Homo sapiens* androgen receptor, with F876L substitution

```
619                    cy eagmtlgark lkklgnlklq eegeasstts pteettqklt
661 vshiegyecq piflnvleai epgvvcaghd nnqpdsfaal lsslnelger qlvhvvkwak
721 alpgfrnlhv ddqmaviqys wmglmvfamg wrsftnvnsr mlyfapdlvf neyrmhksrm
781 ysqcvrmrhl sqefgwlqit pqeflcmkal llfsiipvdg lknqkffdel rmnyikeldr
841 iiackrknpt scsrrfyqlt klldsvqpia relhqltfdl likshmvsvd fpemmaeiis
901 vqvpkilsgk vkpiyfhtq
```

FIG. 2G

Amino acids 690-919 of *Homo sapiens* androgen receptor, with F876L substitution

```
690                                 d nnqpdsfaal lsslnelger qlvhvvkwak
721 alpgfrnlhv ddqmaviqys wmglmvfamg wrsftnvnsr mlyfapdlvf neyrmhksrm
781 ysqcvrmrhl sqefgwlqit pqeflcmkal llfsiipvdg lknqkffdel rmnyikeldr
841 iiackrknpt scsrrfyqlt klldsvqpia relhqltfdl likshmvsvd fpemmaeiis
901 vqvpkilsgk vkpiyfhtq
```

FIG. 2H

Amino acids 619-919 of *Homo sapiens* androgen receptor, with F876L/T877A double substitution

```
619                     cy eagmtlgark lkklgnlklq eegeasstts pteettqklt
661 vshiegyecq piflnvleai epgvvcaghd nnqpdsfaal lsslnelger qlvhvvkwak
721 alpgfrnlhv ddqmaviqys wmglmvfamg wrsftnvnsr mlyfapdlvf neyrmhksrm
781 ysqcvrmrhl sqefgwlqit pqeflcmkal llfsiipvdg lknqkffdel rmnyikeldr
841 iiackrknpt scsrrfyqlt klldsvqpia relhqlafdl likshmvsvd fpemmaeiis
901 vqvpkilsgk vkpiyfhtq
```

FIG. 2I

Amino acids 690-919 of *Homo sapiens* androgen receptor, with F876L/T877A double substitution

```
690                                 d nnqpdsfaal lsslnelger qlvhvvkwak
721 alpgfrnlhv ddqmaviqys wmglmvfamg wrsftnvnsr mlyfapdlvf neyrmhksrm
781 ysqcvrmrhl sqefgwlqit pqeflcmkal llfsiipvdg lknqkffdel rmnyikeldr
841 iiackrknpt scsrrfyqlt klldsvqpia relhqlafdl likshmvsvd fpemmaeiis
901 vqvpkilsgk vkpiyfhtq
```

FIG. 3A

Progesterone receptor (*Homo sapiens*)

```
  1 mtelkakgpr aphvaggpps pevgspllcr paagpfpgsq tsdtlpevsa ipisldgllf
 61 prpcqgqdps dektqdqqsl sdvegaysra eatrgaggss ssppekdsgl ldsvldtlla
121 psgpgqsqps ppacevtssw clfgpelped ppaapatqrv lsplmsrsgc kvgdssgtaa
181 ahkvlprgls parqlllpas esphwsgapv kpspqaaave veeedgsese esagpllkgk
241 pralggaaag ggaaavppga aaggvalvpk edsrfsaprv alveqdapma pgrsplattv
301 mdfihvpilp lnhallaart rqlledesyd ggagaasafa pprsspcass tpvavgdfpd
361 cayppdaepk ddayplysdf qppalkikee eegaeasars prsylvagan paafpdfplg
421 pppplpprat psrpgeaavt aapasasvss asssgstlec ilykaegapp qqgpfapppc
481 kapgasgcll prdglpstsa saaaagaapa lypalglngl pqlgyqaavl keglpqvypp
541 ylnylrpdse asqspqysfe slpqkiclic gdeasgchyg vltcgsckvf fkramegqhn
601 ylcagrndci vdkirrkncp acrlrkccqa gmvlggrkfk kfnkvrvvra ldavalpqpv
661 gvpnesqals qrftfspgqd iqlipplinl lmsiepdviy aghdntkpdt sssllltslnq
721 lgerqllsvv kwskslpgfr nlhiddqitl iqyswmslmv fglgwrsykh vsgqmlyfap
781 dlilneqrmk essfyslclt mwqipqefvk lqvsqeeflc mkvlllinti pleglrsqtq
841 feemrssyir elikaiglrq kgvvsssqrf yqltkllдnl hdlvkqlhly clntfiqsra
901 lsvefpemms eviaaqlpki lagmvkpllf hkk
```

FIG. 3B

Amino acids 678-933 of *Homo sapiens* progesterone receptor

```
678                  gqd iqlipplinl lmsiepdviy aghdntkpdt sssllltslnq
721 lgerqllsvv kwskslpgfr nlhiddqitl iqyswmslmv fglgwrsykh vsgqmlyfap
781 dlilneqrmk essfyslclt mwqipqefvk lqvsqeeflc mkvlllinti pleglrsqtq
841 feemrssyir elikaiglrq kgvvsssqrf yqltkllдnl hdlvkqlhly clntfiqsra
901 lsvefpemms eviaaqlpki lagmvkpllf hkk
```

FIG. 3C

Amino acids 686-933 of *Homo sapiens* progesterone receptor

```
686                          plinl lmsiepdviy aghdntkpdt sssllltslnq
721 lgerqllsvv kwskslpgfr nlhiddqitl iqyswmslmv fglgwrsykh vsgqmlyfap
781 dlilneqrmk essfyslclt mwqipqefvk lqvsqeeflc mkvlllinti pleglrsqtq
841 feemrssyir elikaiglrq kgvvsssqrf yqltkllдnl hdlvkqlhly clntfiqsra
901 lsvefpemms eviaaqlpki lagmvkpllf hkk
```

FIG. 3D

Multiple sequence alignment of ligand-binding domain of progesterone receptors of various species

```
                        10        20        30        40        50        60        70        80
                  ....*....|....*....|....*....|....*....|....*....|....*....|....*....|....*....|
Feature 1                                    #  ##  ##  #                                  #  ##
1SR7_A         12 PLINLLMSIEPDVIYAGHDNTKPDTSSSLLTSLNQLGERQLLSVVKWSKSLPGFRNLHIDDQITLIQYSWMSLMVFGLGW 91
gi 130893     539 PMISVLRGIEPEVVYAGYDNTKPETPSSLLTSLNHLCERQLLCVVKWSKLLPGFRNLHIDDQITLIQYSWMSLMVFAMGW 618
gi 82216083   456 ELLQILQSIEPEVVYAGYDNTQPETPSALLSSLNQLCERQLVCVVKWSKSLPGFRNLHIDDQITLLQYSWMSLMVFALGW 535
gi 169146179  306 QMISILENIEPQVVYSGYDNTQPEVPHLLLNSLNRLCERQLLWIVRWSKSLPGFRNLHINDQMTLIQYSWMGLMLFSLGW 385
1SQN_A         14 PLINLLMSIEPDVIYAGHDNTKPDTSSSLLTSLNQLGERQLLSVVKWSKSLPGFRNLHIDDQITLIQYSWMSLMVFGLGW 93
1E3K_A         11 PLINLLMSIEPDVIYAGHDNTKPDTSSSLLTSLNQLGERQLLSVVKWSKSLPGFRNLHIDDQITLIQYSWMSLMVFGLGW 90
1A28_A          9 PLINLLMSIEPDVIYAGHDNTKPDTSSSLLTSLNQLGERQLLSVVKWSKSLPGFRNLHIDDQITLIQYSWMSLMVFGLGW 88

                        90       100       110       120       130       140       150       160
                  ....*....|....*....|....*....|....*....|....*....|....*....|....*....|....*....|
Feature 1         #           #               #  ##  #
1SR7_A         92 RSYKHVSGQMLYFAPDLILNEQRMKESSFYSLCLTMWQIPQEFVKLQVSQEEFLCMKVLLLLNTIPLEGLRSQTQFEEMR 171
gi 130893     619 RSYKHVSGQMLYFAPDLILNEQRMKESSFYSLCLSMWQLPQEFVRLQVSQEEFLCMKALLLLNTIPLEGLRSQSQFDEMR 698
gi 82216083   536 RSYQHVSGQMLYFAPDLILNEQRMKDSSFYTLCLSMWQLPQEFMKLQVTHEEFLCMKALLLLNTIPLEGLKSQTNFDEMR 615
gi 169146179  386 RTFQNVTPDYLYFAPDLVLSNDQLRRSPIYDLCLAMQFVPQEFANLQVTKEEFLCMKALMLLNTVPLEGLKSQTQFDEMR 465
1SQN_A         94 RSYKHVSGQMLYFAPDLILNEQRMKESSFYSLCLTMWQIPQEFVKLQVSQEEFLCMKVLLLLNTIPLEGLRSQTQFEEMR 173
1E3K_A         91 RSYKHVSGQMLYFAPDLILNEQRMKESSFYSLCLTMWQIPQEFVKLQVSQEEFLCMKVLLLLNTIPLEGLRSQTQFEEMR 170
1A28_A         89 RSYKHVSGQMLYFAPDLILNEQRMKESSFYSLCLTMWQIPQEFVKLQVSQEEFLCMKVLLLLNTIPLEGLRSQTQFEEMR 168

                       170       180       190       200       210       220       230       240
                  ....*....|....*....|....*....|....*....|....*....|....*....|....*....|....*....|
Feature 1                                              #  ##  #        # #   #
1SR7_A        172 SSYIRELIKAIGLRQKGVVSsSQRFYQLTKLLDNLHDLVKQLHLYCLNTFIQSRALSVEFPEMMSEVIAAQLPKILAGMV 251
gi 130893     699 TSYIRELVKAIGLRQKGVVAnSQRFYQLTKLMDSMHDLVKQLHLFCLNTFLQSRALSVEFPEMMSEVIAAQLPKILAGMV 778
gi 82216083   616 SNYIRELAKAISLRHKGVIAsSQRFYQLTKLMDSMHELVKQLHLYCLNTFLQSRSLSVEFPEMMSEVISAQLPKILAGMV 695
gi 169146179  466 QNYICELSKAIQLKEKGVVAsSQRFYHLTKLMDNMHEIVKKVNLYCLSTFIQADAMKVEFPEMMTEVIASQLPKVLAGMV 545
1SQN_A        174 SSYIRELIKAIGLRQKGVVSsSQRFYQLTKLLDNLHDLVKQLHLYCLNTFIQSRALSVEFPEMMSEVIAAQLPKILAGMV 253
1E3K_A        171 SSYIRELIKAIGLRQKGVVSsSQRFYQLTKLLDNLHDLVKQLHLYCLNTFIQSRALSVEFPEMMSEVIAAQLPKILAGMV 250
1A28_A        169 SSYIRELIKAIGLRQKGVVSsSQRFYQLTKLLDNLHDLVKQLHLYCLNTFIQSRALSVEFPEMMSEVIAAQLPKILAGMV 248
```

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FIG. 3D (Cont.)

```
                    ....*...
Feature 1
1SR7_A          252 KPLLFHKK 259
gi 130893       779 KPLLFHKK 786
gi 82216083     696 KPLVFHKK 703
gi 169146179    546 KPLMFHHK 553
1SQN_A          254 KPLLFHKK 261
1E3K_A          251 KPLLFHKK 258
1A28_A          249 KPLLFHKK 256
```

FIG. 4A

Thyroid hormone receptor-β (*Homo sapiens*)

```
  1 mtpnsmteng ltawdkpkhc pdrehdwklv gmseaclhrk shserrstlk neqssphliq
 61 ttwtssifhl dhddvndqsv ssaqtfqtee kkckgyipsy ldkdelcvvc gdkatgyhyr
121 citcegckgf frrtiqknlh psysckyegk cvidkvtrnq cqecrfkkci yvgmatdlvl
181 ddskrlakrk lieenrekrr reelqksigh kpeptdeewe liktvteahv atnaqgshwk
241 qkrkflpedi gqapivnape ggkvdleafs hftkiitpai trvvdfakkl pmfcelpced
301 qiillkgccm eimslraavr ydpesetltl ngemavtrgq lkngglgvvs daifdlgmsl
361 ssfnlddtev allqavllms sdrpglacve riekyqdsfl lafehyinyr khhvthfwpk
421 llmkvtdlrm igachasrfl hmkvecptel fpplflevfe d
```

FIG. 4B

Amino acids 202-461 of *Homo sapiens* thyroid hormone receptor-β

```
202                      eelqksigh kpeptdeewe liktvteahv atnaqgshwk
241 qkrkflpedi gqapivnape ggkvdleafs hftkiitpai trvvdfakkl pmfcelpced
301 qiillkgccm eimslraavr ydpesetltl ngemavtrgq lkngglgvvs daifdlgmsl
361 ssfnlddtev allqavllms sdrpglacve riekyqdsfl lafehyinyr khhvthfwpk
421 llmkvtdlrm igachasrfl hmkvecptel fpplflevfe d
```

FIG. 4C

Amino acids 216-461 of *Homo sapiens* thyroid hormone receptor-β

```
181 ddskrlakrk lieenrekrr reelqksigh kpeptdeewe liktvteahv atnaqgshwk
241 qkrkflpedi gqapivnape ggkvdleafs hftkiitpai trvvdfakkl pmfcelpced
301 qiillkgccm eimslraavr ydpesetltl ngemavtrgq lkngglgvvs daifdlgmsl
361 ssfnlddtev allqavllms sdrpglacve riekyqdsfl lafehyinyr khhvthfwpk
421 llmkvtdlrm igachasrfl hmkvecptel fpplflevfe d
```

FIG. 4D

Multiple sequence alignment of ligand-binding domain of thyroid hormone receptor-β of various species

```
                          10        20        30        40        50        60        70        80
                   ....*....|....*....|....*....|....*....|....*....|....*....|....*....|....*....|
Feature 1                                                                    #  ##  ##  #  #
1NAV_A         17 PEEWDLIHIATEAHRSTnaqgshwkqrrkf----------lpddigqspivsmPDGDKVDLEAFSEFTKIITPAITRVVD 86
1N46_A         13 DEEWELIKTVTEAHVATnaqgshwkqkrkf----------lpedigqapivnaPEGGKVDLEAFSHFTKIITPAITRVVD 82
1BSX_A         15 DEEWELIKTVTEAHVATnaqgshwkqkrkf----------lpedigqapivnaPEGGKVDLEAFSHFTKIITPAITRVVD 84
2PIN_A          8 DEEWELIKTVTEAHVATnaqgshwkqkrkf----------lpedigqapivnaPEGGKVDLEAFSHFTKIITPAITRVVD 77
3D57_A         22 DEEWELIKTVTEAHVATnaqgshwkqkrkf----------lpedigqapivnaPEGGKVDLEAFSHFTKIITPAITRVVD 91
gi 151413583  179 TCPKKVNRYYLNGSPKPgmpvpeaprppvv----------qngvvreadssgaMDDDMVDQDIFSHLAEVITPAIIKVVE 248
gi 13431914   159 AEEWELIHVVTEAHRSTnaqgshwkqkrkf----------lpedigqspmasmPDGDKVDLEAFSEFTKIITPAITRVVD 228
gi 6175061    170 SEEWELIRIVTEAHRSTnaqgshwkqrrkf----------lpedigqspmasmPDGDKVDLEAFSEFTKIITPAITRVVD 239
gi 82274155   223 SDPSGLIPDPLLDSRATsstfpqlltcpilrpgfsrpadappdkigqspvaptSDGDKVDLEAFSEFTKIITPAITRVVD 302
gi 115732680  186 DHEEALIRAILVAHKQTshmyrres--------------------ssgeesePDSKKQKLEDEKPLSEIMTPSIVKVVE 244
gi 586092     216 DEEWELIKTVTEAHVATnaqgshwkqkrkf----------lpedigqapivnaPEGGKVDLEAFSHFTKIITPAITRVVD 285
gi 215273960  141 QEEWEMIRVVTEAHMATnaqgnhwkqkrkflsavg-vkeakpedigsapivnaPEGNKVDIEAFSQFTKIITPAITRVVD 219

                          90       100       110       120       130       140       150       160
                   ....*....|....*....|....*....|....*....|....*....|....*....|....*....|....*....|
Feature 1                             #  #   #           ###         #  # #      #
1NAV_A         87 FAKKLPMFsELPCEDQIILLKGCCMEIMSLRAAVRYDPESDTLTLSGEMaVKREQLKNGGLGVVSDAIFELGKSLSaFNL 166
1N46_A         83 FAKKLPMFcELPCEDQIILLKGCCMEIMSLRAAVRYDPESETLTLNGEMaVTRGQLKNGGLGVVSDAIFDLGMSLSsFNL 162
1BSX_A         85 FAKKLPMFcELPCEDQIILLKGCCMEIMSLRAAVRYDPESETLTLNGEMaVTRGQLKNGGLGVVSDAIFDLGMSLSsFNL 164
2PIN_A         78 FAKKLPMFcELPCEDQIILLKGCCMEIMSLRAAVRYDPESETLTLNGEMaVTRGQLKNGGLGVVSDAIFRLGMSLSsFNL 157
3D57_A         92 FAKKLPMFcELPCEDQIILLKGCCMEIMSLRAAVRYDPESETLTLNGEMaVTRGQLKNGGLGVVSDAIFRLGMSLSsFNL 171
gi 151413583  249 FAKQIPGFtKLVPDDQVALLKNCCFEVMCLRAASRFDKQRRTITMFGGLtVTKEQVSQGGLGRLAEPLFEFAEGLSqLHL 328
gi 13431914   229 FAKKLPMFsELPCEDQIILLKGCCMEIMSLRAAVRYDPESETLTLSGEMaVKREQLKNGGLGVVSDAIFDLGKSLSaFNL 308
gi 6175061    240 FAKKLPMFsELTCEDQIILLKGCCMEIMSLRAAVRYDPDSETLTLSGEMaVKREQLKNGGLGVVSDAIFDLGRSLAaFNL 319
gi 82274155   303 FAKKLPMFsELPCEDQIILLKGCCMEIMSLRAAMRYDPESETLTLSGEMaVKREQLKNGGLGVVSDAIFDLGKSLAqFNL 382
gi 115732680  245 FAKRIPGFtGLHHDDQILLLKTCCMEIMCLRVAQKFDPDSQKLILSNGLrVGKSDMDHGVLSELIEPIFDFAVSMSrLQL 324
gi 586092     286 FAKKLPMFcELPCEDQIILLKGCCMEIMSLRAAVRYDPESETLTLNGEMaVTRGQLKNGGLGVVSDAIFDLGMSLSsFNL 365
gi 215273960  220 FAKKLPMFcELPCEDQIILLKGCCMEIMSLRAAVRYDPESDTLTLNGEMaVTRGQLKNGGLGVVSDAIFDLGVSLSsFNL 299
```

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FIG. 4D (Cont.)

```
                    170       180       190       200       210       220       230       240
                    ....*....|....*....|....*....|....*....|....*....|....*....|....*....|....*....|
Feature 1
1NAV_A          167 DDTEVALLQAVLIMSTDRs----------------------------------GLLCVDKIEKSQEAYLLAFEHYVVNhrKHNIPHFW 219
1N46_A          163 DDTEVALLQAVLIMSSDRp----------------------------------GLACVERIEKYQDSFLLAFEHYINyrKHHVTHFW 215
1BSX_A          165 DDTEVALLQAVLIMSSDRp----------------------------------GLACVERIEKYQDSFLLAFEHYINyrKHHVTHFW 217
2PIN_A          158 DDTEVALLQAVLIMSSDRp----------------------------------GLACVERIEKYQDSFLLAFEHYINyrKHHVTHFW 210
3D57_A          172 DDTEVALLQAVLIMSSDRp----------------------------------GLACVERIEKYQDSFLLAFEHYINyrKHHVTHFW 224
gi 151413583    329 DDTEVALLAALLVVADRP----------------------------------GVQDQESIDRLQDIILTAYKNYITrqRPHQPVLW 380
gi 13431914     309 DDTEVALLQAVLIMSSDRt----------------------------------GLICVDKIEKCQETYLLAFEHYINyrKHNIPHFW 361
gi 6175061      320 DDTEVALLQAVLIMSSDRt----------------------------------GLICTDKIEKCQETYLLAFEHYINhrKHNIPHFW 372
gi 82274155     383 DDTEVALLQAVLIMSSGNrrrgrprpspapgstsssssssssdrsGLTCTDKIEKCQETYLLAFEHYINyrKHNIPHFW 462
gi 115732680    325 TETEMALLAAVLLIAGDRp----------------------------------GLKEAKLVETLQDSLLTAFQHFINesRPKTPVHW 377
gi 586092       366 DDTEVALLQAVLIMSSDRp----------------------------------GLACVERIEKYQDSFLIAFEHYINyrKHHVTHFW 418
gi 215273960    300 DDSEVALLQAVILLSSDRp----------------------------------GLTSVERIERCQEEFLLAFEHYINyrKHKVAHFW 352

                    250       260       270       280
                    ....*....|....*....|....*....|....*....|
                         #         #         #
Feature 1
1NAV_A          220 PKLLMKVTDLRMIGACHASRFLHMKVECPTELfPPLFLEV 259
1N46_A          216 PKLLMKVTDLRMIGACHASRFLHMKVECPTELfPPLFLEV 255
1BSX_A          218 PKLLMKVTDLRMIGACHASRFLHMKVECPTELfPPLFLEV 257
2PIN_A          211 PKLLMKVTDLRMIGACHASRFLHMKVECPTELfPPLFLEV 250
3D57_A          225 PKLLMKVTDLRMIGACHASRFLHMKVECPTELfPPLFLEV 264
gi 151413583    381 GKILMKVTDLRALSVAHAEQVKLVKMECTNDI-PPLFLEM 419
gi 13431914     362 PKLLMKVTDLRMIGACHASRFLHMKVECPTELfPPLFLEV 401
gi 6175061      373 PKLLMKVTDLRMIGACHASRFLHMKVECPTELfPPLFLEV 412
gi 82274155     463 PKLLMKVTDLRMIGACHASRFLHMKVECPNELfPPLFLEV 502
gi 115732680    378 AKILMKITDLRTISAREAERIMCIKLDRPNEI-PQIFLEM 416
gi 586092       419 PKLLMKVTDLRMIGACHASRFLHMKVECPTELfPPLFLEV 458
gi 215273960    353 PKLLMKVTDLRMIGACHASRFLHMKVECPTELfPPLFLEV 392
```

FIG. 5A

Estrogen hormone receptor-α (*Homo sapiens*)

```
  1 mtmtlhtkas gmallhqiqg neleplnrpq lkiplerplg evyldsskpa vynypegaay
 61 efnaaaaana qvygqtglpy gpgseaaafg snglggfppl nsvspsplml lhpppqlspf
121 lqphgqqvpy ylenepsgyt vreagppafy rpnsdnrrqg grerlastnd kgsmamesak
181 etrycavcnd yasgyhygvw scegckaffk rsiqghndym cpatnqctid knrrkscqac
241 rlrkcyevgm mkggirkdrr ggrmlkhkrq rddgegrgev gsagdmraan lwpsplmikr
301 skknslalsl tadqmvsall daeppilyse ydptrpfsea smmglltnla drelvhminw
361 akrvpgfvdl tlhdqvhlle cawleilmig lvwrsmehpv kllfapnlll drnqgkcveg
421 mveifdmlla tssrfrmmnl qgeefvclks iillnsgvyt flsstlksle ekdhihrvld
481 kitdtlihlm akagltlqqq hqrlaqllli lshirhmsnk gmehlysmkc knvvplydll
541 lemldahrlh aptsrggasv eetdqshlat agstsshslq kyyitgeaeg fpatv
```

FIG. 5B

Amino acids 305-533 of *Homo sapiens* estrogen hormone receptor-α

```
305     slalsl tadqmvsall daeppilyse ydptrpfsea smmglltnla drelvhminw
361 akrvpgfvdl tlhdqvhlle cawleilmig lvwrsmehpv kllfapnlll drnqgkcveg
421 mveifdmlla tssrfrmmnl qgeefvclks iillnsgvyt flsstlksle ekdhihrvld
481 kitdtlihlm akagltlqqq hqrlaqllli lshirhmsnk gmehlysmkc knv
```

FIG. 5C

Amino acids 282-595 of *Homo sapiens* estrogen hormone receptor-α

```
282                                          sagdmraan lwpsplmikr
301 skknslalsl tadqmvsall daeppilyse ydptrpfsea smmglltnla drelvhminw
361 akrvpgfvdl tlhdqvhlle cawleilmig lvwrsmehpv kllfapnlll drnqgkcveg
421 mveifdmlla tssrfrmmnl qgeefvclks iillnsgvyt flsstlksle ekdhihrvld
481 kitdtlihlm akagltlqqq hqrlaqllli lshirhmsnk gmehlysmkc knvvplydll
541 lemldahrlh aptsrggasv eetdqshlat agstsshslq kyyitgeaeg fpatv
```

FIG. 5D

Amino acids 310-547 of *Homo sapiens* estrogen hormone receptor-α

```
310          1 tadqmvsall daeppilyse ydptrpfsea smmglltnla drelvhminw
361 akrvpgfvdl tlhdqvhlle cawleilmig lvwrsmehpv kllfapnlll drnqgkcveg
421 mveifdmlla tssrfrmmnl qgeefvclks iillnsgvyt flsstlksle ekdhihrvld
481 kitdtlihlm akagltlqqq hqrlaqllli lshirhmsnk gmehlysmkc knvvplydll
541 lemldah
```

FIG. 5E

Amino acids 305-533 of *Homo sapiens* estrogen hormone receptor-α, with D351Y substitution

```
305     slalsl tadqmvsall daeppilyse ydptrpfsea smmglltnla yrelvhminw
361 akrvpgfvdl tlhdqvhlle cawleilmig lvwrsmehpv kllfapnlll drnqgkcveg
421 mveifdmlla tssrfrmmnl qgeefvclks iillnsgvyt flsstlksle ekdhihrvld
481 kitdtlihlm akagltlqqq hqrlaqllli lshirhmsnk gmehlysmkc knv
```

FIG. 5F

Amino acids 282-595 of *Homo sapiens* estrogen hormone receptor-α, with D351Y substitution

```
282                                                 sagdmraan lwpsplmikr
301 skknslalsl tadqmvsall daeppilyse ydptrpfsea smmglltnla yrelvhminw
361 akrvpgfvdl tlhdqvhlle cawleilmig lvwrsmehpv kllfapnlll drnqgkcveg
421 mveifdmlla tssrfrmmnl qgeefvclks iillnsgvyt flsstlksle ekdhihrvld
481 kitdtlihlm akagltlqqq hqrlaqllli lshirhmsnk gmehlysmkc knvvplydll
541 lemldahrlh aptsrggasv eetdqshlat agstsshslq kyyitgeaeg fpatv
```

FIG. 5G

Amino acids 310-547 of *Homo sapiens* estrogen hormone receptor-α, with D351Y substitution

```
310          1 tadqmvsall daeppilyse ydptrpfsea smmglltnla yrelvhminw
361 akrvpgfvdl tlhdqvhlle cawleilmig lvwrsmehpv kllfapnlll drnqgkcveg
421 mveifdmlla tssrfrmmnl qgeefvclks iillnsgvyt flsstlksle ekdhihrvld
481 kitdtlihlm akagltlqqq hqrlaqllli lshirhmsnk gmehlysmkc knvvplydll
541 lemldah
```

FIG. 5H

Multiple sequence alignment of ligand-binding domain of estrogen receptor alpha of various species

```
                    10        20        30        40        50        60        70        80
                    ....*....|....*....|....*....|....*....|....*....|....*....|....*....|
Feature 1                                                   #    # #
1XP9_A        4 LTADQMVSALLDAEPPILYSEYdptr--------pfsEASMMGLLTNLADRELVHMINWAKRVPGFVDLTLHDQVHLLECA 76
1YY4_A        1 LSPEQLVLTLLEAEPPHVLISRpsa---------pfsEASMMMSLTKLADKELVHMISWAKKIPGFVELSLFDQVRLLESC 72
gi 170178459 303 NPTVPLISHLVNIEPNPILTGYnpqc---------tptEGYLMALVTDLANREIEGLVDWAARLPGYGMLPMDDQVNLIRTV 375
gi 82209527  280 LSPEELISRIMEAEPPEIYYLMKdmkk---------pftEANVMMSLTNLADKELVHMISWAKKIPGFVELSLFDQVHLLECC 352
gi 1195597   304 LTAEQMVSALLEAEPPIVYSEYdpnr---------pfnEASMMTLLTNLADRELVHMINWAKRVPGFVDLTLHDQVHLLECA 376
gi 6015120   302 LTAEQLISALMEAEAPIVYSEHdstk---------plsEASMMTLLTNLADRELVHMINWAKRVPGFVDLTLHDQVHLLECA 374
gi 146742358 226 QRLKALIDALDVKEGEHRGEENhptgqqagnwqeisNPELIESVSSLVDRELTGIICWGKKIPGYSKLSLNDQVLLMEST 305
gi 186659995 141 LSSEQFLTCLLNAEPPNMTCHHdvsr---------pftAERLMMLLTNLADRELVHMIGWAKKVPGFVQISLRDQVLLLESS 213
                              90        100       110       120       130       140       150       160
                    ....*....|....*....|....*....|....*....|....*....|....*....|....*....|....*....|
                        #
Feature 1
1XP9_A       77 WLEILMIGLVWRSMEHPG-KLLFAPNLLLDRNQGKc---------VEGMVEIFDMLLATSSRFRMMNLQGEEFVCLKSIIL 147
1YY4_A       73 WMEVLMMGLMWRSIDHPG-KLIFAPDLVLDRDEGKc---------VEGILEIFDMLLATTSRFRELKLQHKEYLCVKAMIL 143
gi 170178459 376 WLDLLMLGLVWRSMEHRGeWLVFAPDLLMDRSLCR---------LSGMEYICTPMLEFARQFADLQVPQEVYVCLKALTL 446
gi 82209527  353 WLEVLMLGLMWRSVNHPG-KLIFSPDLCLSRDESSc---------VQGLVEIFDMLLAATSRFFELKLQREEYVCLKAMIL 423
gi 1195597   377 WLEILMIGLVWRSMEHPG-KLLFAPNLLLDRNQGKc---------VEGMVEIFDMLLATAARFRMMNLQGEEFVCLKSIIL 447
gi 6015120   375 WLEILMVGLIWRSVEHPG-KLSFAPNLLLDRNQGRc---------VEGLVEIFDMLVTATRFRMMRLRGEEFICLKSIIL 445
gi 146742358 306 WLDLLILDLVWCSIRHKGeKLLLSGGVLVNRNTISnrrnnssgdDMEVLEMCDQILSIATKFYEFDLQRREYLCLKAITL 385
gi 186659995 214 WLEVLIMGLIWRSMSQPG-KLVFASNLILDRDDGEc---------VEGIFEIFDILLNIVQHFRELQVWMDEYVCLKAIIL 284
```

FIG. 5H (Cont.)

```
                  170       180       190       200       210       220       230       240
                  ....*....|....*....|....*....|....*....|....*....|....*....|....*....|
Feature 1                                                                  #  #
1XP9_A       148 LNSGVYtflsstlksLEEKDHIHRVLDKITDTLIHLMAKAgltlqQQEQRLAQLLLILSHIRHMSNKGMEHLysMKCKNV 227
1YY4_A       144 LNSSMYpivt-atqdADSSRKLAHLLNAVTDALVWVIAKSgissqQQSMRLANLLMLLSHVRHASNKGMEHLinMKCKNV 222
gi 170178459 447 YTTAVSr-------LQDYRQVQRLQHEINEALAEACSSTf---gFSPGNIARLMMIVSQVRQLSSLGVDHLnrLRGAET 515
gi 82209527  424 LNSNMClgsseggedLQSRSKLLCLLLDSVTDALVWAISKTglsfqQRSTRLAHLLMLLSHIRHVSNKGMDHLhcMKMKKM 503
gi 119597    448 LNSGVYtflsstlksLEERDYIHRVLDKITDTLIHLMAKSglslqQQHRRLAQLLLILSHIRHMSNKGMEHLynMKCKNV 527
gi 6015120   446 LNSGVYtflsstlesLEDTDLIHIILDKIIDTILVHFMAKSglslqQQQRRLAQLLLILSHIRHMSNKGMEHLysMKCKNV 525
gi 146742358 386 VHGSLKg--------LESDTQVRQLQDDLTDALMDVCSERh---aLGSRRPAKMLLLLSHLRQVSARASSHLgaVRNGLK 454
gi 186659995 285 LNASMMvat---sekDGSRAKVQQLVEATTDTILVKCIARRslatpEQFRRLSHLLTILSHIRHISNKGIQHMysMKCKNL 361
                       250
                       ....*....|....
Feature 1
1XP9_A       228 VPLYDLLLEMLDAH 241
1YY4_A       223 VPVYDLLLEMLNAH 236
gi 170178459 516 VSVEGLLREIVDEP 529
gi 82209527  504 VPLYDLLLEMLDAH 517
gi 119597    528 VPLYDLLLEMLDAH 541
gi 6015120   526 VPLYDLLLEMLDAH 539
gi 146742358 455 VPLYDILLDILTDQ 468
gi 186659995 362 VPTYDLLLEMLDAH 375
```

FIG. 6A

Estrogen receptor-β (*Homo sapiens*)

```
  1 mdiknspssl nspssyncsq silplehgsi yipssyvdsh heypamtfys pavmnysips
 61 nvtnleggpg rqttspnvlw ptpghlsplv vhrqlshlya epqkspwcea rslehtlpvn
121 retlkrkvsg nrcaspvtgp gskrdahfca vcsdyasgyh ygvwscegck affkrsiqgh
181 ndyicpatnq ctidknrrks cqacrlrkcy evgmvkcgsr rercgyrlvr rqrsadeqlh
241 cagkakrsgg haprvrelll dalspeqlvl tlleaepphv lisrpsapft easmmmsltk
301 ladkelvhmi swakkipgfv elslfdqvrl lescwmevlm mglmwrsidh pgklifapdl
361 vldrdegkcv egileifdml lattsrfrel klqhkeylcv kamillnssm yplvtatqda
421 dssrklahll navtdalvwv iaksgissqq qsmrlanllm llshvrhasn kgmehllnmk
481 cknvvpvydl llemlnahvl rgckssitgs ecspaedsks kegsqnpqsq
```

FIG. 6B

Amino acids 260-502 of *Homo sapiens* estrogen hormone receptor-β

```
260                   1 dalspeqlvl tlleaepphv lisrpsapft easmmmsltk
301 ladkelvhmi swakkipgfv elslfdqvrl lescwmevlm mglmwrsidh pgklifapdl
361 vldrdegkcv egileifdml lattsrfrel klqhkeylcv kamillnssm yplvtatqda
421 dssrklahll navtdalvwv iaksgissqq qsmrlanllm llshvrhasn kgmehllnmk
481 cknvvpvydl llemlnahvl rg
```

FIG. 6B (Cont.)

```
                                170       180       190       200       210       220       230       240
                                ....*.....|.....*.....|.....*.....|.....*.....|.....*.....|.....*.....|
                                                                                          #   #
Feature 1
1XP9_A              148 LNSGVYtflsstlksLEEKDKITDTLIHLMAKAgltlqQQHQRLAQLLLILSHIRHMSNKGMEHLysMKCKNV 227
1YY4_A              144 LNSSMYplvt-atqdADSSRKLAHLLNAVTDALVWVIAKSgissqQQSMRLANLLMLLSHVRHASNKGMEHLlnMKCKNV 222
gi 170178459        447 YTTAVSr---------LQDYRQVQRLQHEINEALAEACSSTf---gFSPGNIARLMMIVSQVRQLSSLGVDHLnrLRGAET 515
gi 82209527         424 LNSNMClgsseggqedLQSRSKLLCLLDSVTDALVWAISKTglsfqQRSTRLAELLMLLSHIRHVSNKGMDHLhcMKMKKM 503
gi 119597           448 LNSGVYtflsstlksLEERDYIERVLDKITDTLIHLMAKSgislqQQHRRLAQLLLILSHIRHMSNKGMEHLynMKCKNV 527
gi 60115120         446 LNSGVYtflsstlesLEDTDLIHIILDKIIDTLVHFMAKSgislqQQQRRLAQLLLILSHIRHMSNKGMEHLysMKCKNV 525
gi 146742358        386 VHGSLKg---------LESDTQVRQLQDDLTDALMDVCSERh---aLGSRRPAKMLLLLSHLRQVSARASSHLgaVRNGLK 454
gi 186659995        285 LNASMMvat---sekDGSRAKVQQLVEATTDTLVKCIARRslatpEQFRRLSHILLTILSHIRHISNKGIQHMysMKCKNL 361

                                     250
                                     ....*.....|....
Feature 1
1XP9_A              228 VPLYDLLLEMLDAH 241
1YY4_A              223 VPVYDLLLEMLNAH 236
gi 170178459        516 VSVEGLLREIVDEP 529
gi 82209527         504 VPLYDLLLEMLDAH 517
gi 119597           528 VPLYDLLLEMLDAH 541
gi 60115120         526 VPLYDLLLEMLDAH 539
gi 146742358        455 VPLYDILLDILTDQ 468
gi 186659995        362 VPFYDLLLEMLDAH 375
```

FIG. 6C

Multiple sequence alignment of ligand-binding domain of estrogen receptor beta of various species

```
                    10        20        30        40        50        60        70        80
                    ....*.....|.....*.....|.....*.....|.....*.....|.....*.....|.....*.....|
Feature 1                                                    #     # #
1XP9_A         4 LTADQMVSALLDAEPPILYSEYdptr--------pfsEASMMGLLTNLADRELVHMINWAKRVPGFVDLTLHDQVHLLECA  76
1YY4_A         1 LSPEQIVLTLLEAEPPHVLISRpsa--------pftEASMMMSLTKLADKELVHMISWAKKIPGFVELSLFDQVRLLESC  72
gi 170178459 303 NPTVPLISHLVNIEPNPILTGYnpqc--------tptEGYLMALVTDLANREIEGLVDWAARLPGYGMLPMDDQVNLIRTV 375
gi 82209527  280 LSPEELISRIMEAEPPEIYLMKdmkk--------pftEANVMMSLTNLADKELVHMISWAKKIPGFVELSLFDQVHLLECC 352
gi 119597    304 LTAEQMVSALLEAEPPIVYSEYdpnr--------pfnEASMMTLLTNLADRELVHMINWAKRVPGFVDLTLHDQVHLLECA 376
gi 6015120   302 LTAEQLISAIMEAEAPIVYSEHdstk--------plsEASMMTLLTNLADRELVHMINWAKRVPGFVDLTLHDQVHLLECA 374
gi 146742358 226 QPLKALLIDALDVKEGEHRGEENhptgqqaqnwqeisNPELIESVSSLVDRELTGIICWGKKIPGYSKLSLNDQVLLMEST 305
gi 186659995 141 LSSEQFLTCLLNAEPPNMTCHHdvsr--------pftAERLMMLLTNLADRELVHMIGWAKKVPGFVQISLRDQVLLLESS 213

                    90       100       110       120       130       140       150       160
                    ....*.....|.....*.....|.....*.....|.....*.....|.....*.....|.....*.....|
Feature 1              #     #
1XP9_A        77 WLEILMIGLVWRSMEHPG-KLLFAPNLLLDRNQGKc---------VEGMVEIFDMLLATSSRFRMMNLQGEEFVCLKSIIL 147
1YY4_A        73 WMEVLMMGLMWRSIDHPG-KLIFAPDLVLDRDEGKc---------VEGILEIFDMLLATTSRFRELKLQHKEYLCVKAMIL 143
gi 170178459 376 WLDLLMLGLVWRSMEHRGeWLVFAPDLLMDRSLCR----------LSGMEYICTPMLEFARQFADLQVPQEVYVCLKALTL 446
gi 82209527  353 WLEVLMLGLMWRSVNHPG-KLIFSPDLCLSRDESSc---------VQGLVEIFDMLLAATSRFRELKLQREEYVCLKAMIL 423
gi 1195597   377 WLEILMIGLVWRSMEHPG-KLLFAPNLLLDRNQGKc---------VEGMVEIFDMLLATAARFRMMNLQGEEFVCLKSIIL 447
gi 6015120   375 WLEILMVGLIWRSVEHPG-KLSFAPNLLLDRNQGRc---------VEGLVEIFDMLVTTATRFRMMRLRGEEFICLKSIIL 445
gi 146742358 306 WLDLLIILDLVWCSIRHKGeKLLLSGGVLVNRNTISnrrnnssgdDMEVLEMCDQILSIATKFYEFDLQRREYLCLKAITL 385
gi 186659995 214 WLEVLIMGLIWRSMSQPG-KLVFASNLILDRDDGEc---------VEGIFEIFDILLNIVQHFRELQVWMDEYVCLKAIIL 284
```

FIG. 7A

Peroxisome proliferator-activated receptor-gamma (PPAR-γ) (*Homo sapiens*)

```
  1 mvdtempfwp tnfgissvdl svmedhshsf dikpfttvdf ssistphyed ipftrtdpvv
 61 adykydlklq eyqsaikvep asppyysekt qlynkpheep snslmaiecr vcgdkasgfh
121 ygvhacegck gffrrtirlk liydrcdlnc rihkksrnkc qycrfqkcla vgmshnairf
181 grmpqaekek llaeissdid qlnpesadlr alakhlydsy iksfpltkak arailtgktt
241 dkspfviydm nslmmgedki kfkhitplqe qskevairif qgcqfrsvea vqeiteyaks
301 ipgfvnldln dqvtllkygv heiiytmlas lmnkdgvlis egqgfmtref lkslrkpfgd
361 fmepkfefav kfnaleldds dlaifiavii lsgdrpglln vkpiediqdn llqalelqlk
421 lnhpessqlf akllqkmtdl rqivtehvql lqvikktetd mslhpllqei ykdly
```

FIG. 7B

Amino acids 174-475 of *Homo sapiens* PPAR-γ

```
174                                                        shnairf
181 grmpqaekek llaeissdid qlnpesadlr alakhlydsy iksfpltkak arailtgktt
241 dkspfviydm nslmmgedki kfkhitplqe qskevairif qgcqfrsvea vqeiteyaks
301 ipgfvnldln dqvtllkygv heiiytmlas lmnkdgvlis egqgfmtref lkslrkpfgd
361 fmepkfefav kfnaleldds dlaifiavii lsgdrpglln vkpiediqdn llqalelqlk
421 lnhpessqlf akllqkmtdl rqivtehvql lqvikktetd mslhpllqei ykdly
```

FIG. 7C

Amino acids 207-475 of *Homo sapiens* PPAR-γ

```
181 grmpqaekek llaeissdid qlnpesadlr alakhlydsy iksfpltkak arailtgktt
241 dkspfviydm nslmmgedki kfkhitplqe qskevairif qgcqfrsvea vqeiteyaks
301 ipgfvnldln dqvtllkygv heiiytmlas lmnkdgvlis egqgfmtref lkslrkpfgd
361 fmepkfefav kfnaleldds dlaifiavii lsgdrpglln vkpiediqdn llqalelqlk
421 lnhpessqlf akllqkmtdl rqivtehvql lqvikktetd mslhpllqei ykdly
```

FIG. 7D

LBD of human PPARγ
Amino acids 205-475 of *Homo sapiens* PPAR-γ

```
205                          esadlr alakhlydsy iksfpltkak arailtgktt
241 dkspfviydm nslmmgedki kfkhitplqe qskevairif qgcqfrsvea vqeiteyaks
301 ipgfvnldln dqvtllkygv heiiytmlas lmnkdgvlis egqgfmtref lkslrkpfgd
361 fmepkfefav kfnaleldds dlaifiavii lsgdrpglln vkpiediqdn llqalelqlk
421 lnhpessqlf akllqkmtdl rqivtehvql lqvikktetd mslhpllqei ykdly
```

FIG. 7E

Multiple sequence alignment of ligand-binding domain of PPAR-γ of various species

```
                                10        20        30        40        50        60        70        80
                     ....*....|....*....|....*....|....*....|....*....|....*....|....*....|....*....|
Feature 1
1FM6_D          4 ADLRALAKHLYDSYIKsfpltkaKARAILTGKttdkspfviydmnslmmge---------------------------------- 54
2J14_A         17 ADLKAFSKHIYNAYLKnfnmtkkKARSILTGKashtapfvihdietlwqae---------------------------------- 67
gi 47825369   207 ADLRALAKHLYDSYIKsfpltkaKARAILTGKttdkspfviydmnslrmge---------------------------------- 257
gi 82240332   230 ADLRALARHLYEAYLKyfpltkaKARAILSGKtgdnapfvihdiksimegeqfincrqmpiqeqqqas---------------- 297
gi 122049643  176 TKLVSPCDEMLTPDLKarllfasQVFKKNIGKdkptiykn---------------------------------------------- 215
gi 585720     129 SDLDVLSQLIHSSYMNtftmtkkRARDILTGRnsispfvihdmdtlwqaeq---------------------------------- 179
gi 72164991   137 RIHSIYINMWMGQFISmpvgsraTRSKEPNGKtedhksm-------------------------------------------- 175
gi 115899356  219 VDSIAQQFNDIVCAMTqed--leKFWKRCSRPftahmpsgtyyviegm---------------------------------- 263
gi 16565492    95 SDLRSLARLVQEAYLRifplskaKAQAILAGKvqnnavvihdhesiaqaedtilqksgygtihnhgsigvniasvgggcg 174
                                90        100       110       120       130       140       150       160
                     ....*....|....*....|....*....|....*....|....*....|....*....|....*....|....*....|
                                                                                ##    #
Feature 1
1FM6_D         55 ----------------------------------------dkikfkhitplqeqskevaIRIFQGCQFRSVEAVQE 90
2J14_A         68 ----------------------------------------kglvwkqlvnglppykeisVHVFYRCQCTTVETVRE 103
gi 47825369   258 ----------------------------------------dqikckhaspiqeqnkevaIRIFQRCQFRSVEAVQE 293
gi 82240332   298 ----------------------------vltathggltehhmqsdygvwgttsisggepqnaleLRFFQSCQSRSAEAVRE 350
gi 122049643  216 ----------------------------------------vigskivQILYSDFQARVVNGICE 239
gi 585720     180 ----------------------------------------gtvweqlptqnltgteigVHVFYRCQCTSVETVRA 214
gi 72164991   176 ----------------------------------------keltekEALTKFCRGALLAIIES 198
gi 115899356  264 ----------------------------------------qlnkdqppqeitsrAEMAQQCFVSMEVTIEK 294
gi 16565492   175 gargqticdgrggpcdsttrgrvlgtdcvfitansvtdtelaadaegnrssdqevtpprgaaeIRIFNRCHYRLVEAVRE 254
```

FIG. 7E (Cont.)

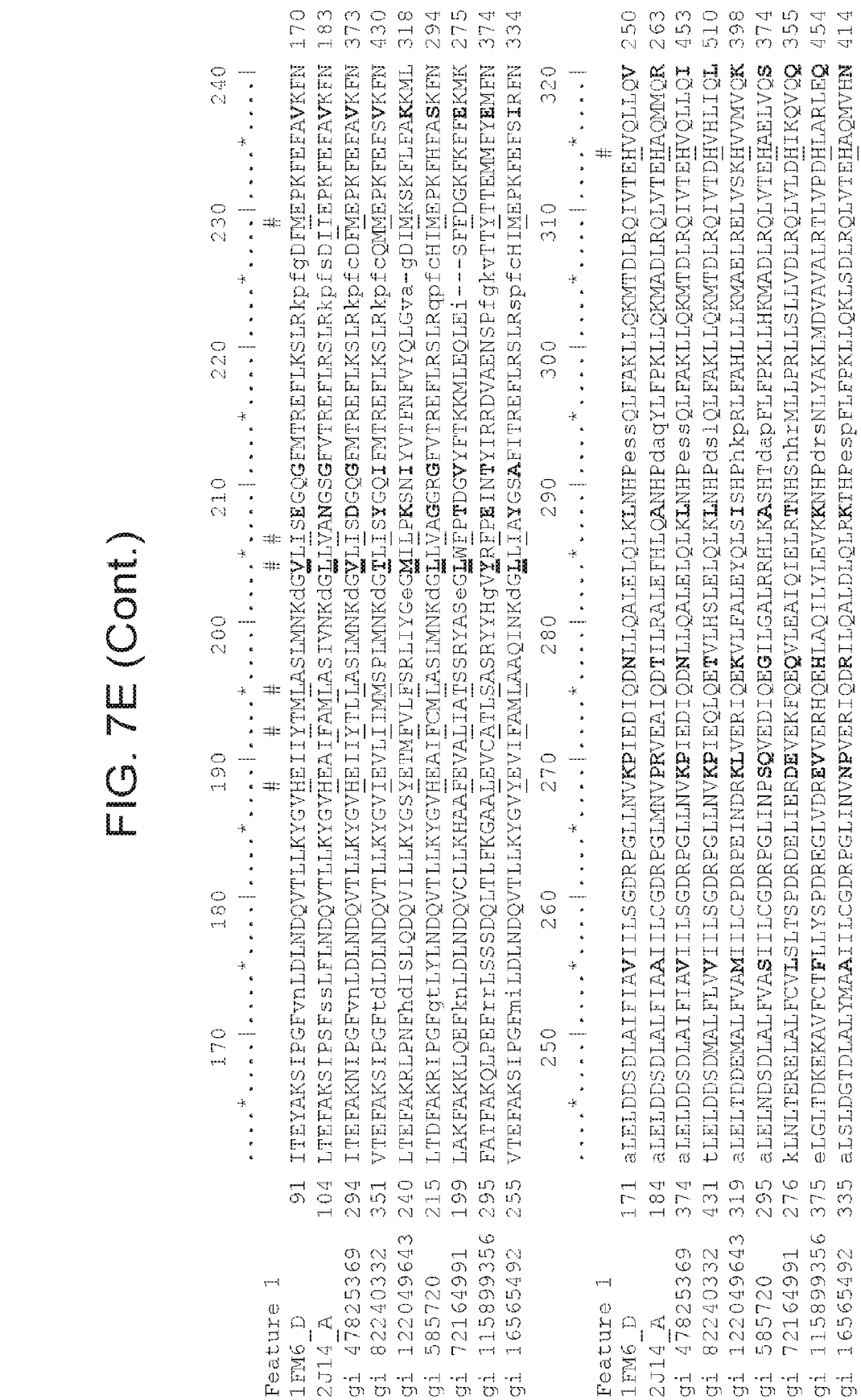
170 180 190 200 210 220 230 240
Feature 1 91 ITEYAKSIPGFVnLDLNDQVTLLKYGVHEIIYTMLASLMNKdGVLISEGQGFMTREFLKSLRkpfgDFMEPKFEEFAVKFN 170
1FM6_D 104 LTEFAKSIPSFssLFLNDQVTLLKYGVHEAIFAMLASIVNKdGLLVANGSGFVTREFLRSLRkpfsDIIEPKFEFFAVKFN 183
2J14_A 294 ITEFAKNIPGFVnLDLNDQVTLLKYGVHEIIYTLLASLMNKdGVLISDGQGFMTREFLKSLRkpfcDFMEPKFEFFAVKFN 373
gi 47825369 351 VTEFAKSIPGFtdLDLNDQVTLLKYGVIEVLIIMMSPLMNKdGTLISYGQIFMTREFLKSLRkpfcQMMEPKFEFFSVKFN 430
gi 82240332 240 LTEFAKRLPNFhdISLQDQVILLKYGSYETMFVLFSRLIYGeGMILPKSNIYVTFNFVYQLGva-gDIMKSKFLFAKKML 318
gi 122049643 215 LTDFAKRIPGFqtLYLNDQVTLLKYGVHEAIFCMLASLMNKdGLLVAGGRGFVTREFLRSLRqpfcHIMEPKFHFASKFN 294
gi 585720 199 LAKFAKKLQEFknLDLNDQVCLLKHAAFEVALIATSSRYASeGLWFPTDGVYFTKKMLEQLEi---SFFDGKFKFFEKMK 275
gi 721649991 295 FATFAKQLPEFrrLSSSDQLTLFKGAALEVCATLSASRYYHgVYRFPEINTYIRRDVAENSPfgkvTTYTTEMMFYEMFN 374
gi 115899356 255 VTEFAKSIPGFmiLDLNDQVTLLKYGVYEVIFAMLAAQINKdGLLIAYGSAFITREFLRSLRspfcHIMEPKFEEFSIRFN 334
250 260 270 280 290 300 310 320
Feature 1 171 aLELDDSDLAIAFIAVIILSGDRPGLLNVKPIEDIQDNLLQALELQLKLNHPessQLFAKLLQKMTDLRQIVTEHVQLLQV 250
1FM6_D 184 aLELDDSDLALFIAAIILCGDRPGLMNVPRVEAIQDTILRALETHLQANHPdaqYLFPKLLQKMADLRQLVTEHAQMMQR 263
2J14_A 374 aLELDDSDLAIAFIAVIILSGDRPGLLNVKPIEDIQDNLLQALELQLKLNHPessQLFAKLLQKMTDLRQIVTEHVQLLQI 453
gi 47825369 431 tLELDDSDMALFLVVIILSGDRPGLLNVKPIEQLQETVLHSLELQLKLNHPdslQLFAKLLQKMTDLRQIVTDHVHLIQL 510
gi 82240332 319 aLELTDDEMALFVAMIILCPDRPEINDRKLVERIQEKVLFALEYQLSISHPhkpRLFAHLLLKMAELRELVSKHVVMVQK 398
gi 122049643 295 aLELNDSDLALFVASIILCGDRPGLINPSQVEDIQEGILGALRRHLKASHTdapFLFPKLLHKMADLRQLVTEHAELVQS 374
gi 585720 276 kLNLTERELALFCVLSLTSPDRDELIERDEVEKFQEQVLEAIQIELRTNHSnhrMLLPRLLSLLVDLRQLVLDHIKQVQQ 355
gi 721649991 375 eLGLTDKEKAVFCTFLLYSPDREGLVDREVVERHQEHLAQILYLEVKKNHPdrsNLYAKLMDVAVALRTLVPDHLARLEQ 454
gi 115899356 335 aLSLDGTDLALYMAAIILCGDRPGLINVNPVERIQDRILQALDLQLPKTHPespFLFPKLLQKLSDLRQLVTEHAQMVHN 414

FIG. 7E (Cont.)

```
                          330       340
                     ....*....|....*....|....
Feature 1
1FM6_D          251 IKKtet---dmsLHPLLQEIYKDL 271
2J14_A          264 IKKtet---etsLHPLLQEIYKDM 284
gi 47825369     454 IKKtet---dmsLHPLLQEIYKDL 474
gi 82240332     511 LKKtev---dmcLHPLLQEIMKDL 531
gi 122049643    399 LADak-----dfVPPLLCEIMQDM 417
gi 585720       375 IKRtes---saaLHPLLQEIYRDM 395
gi 72164991     356 LMLmddp-sysgPPPLIKEIFGLY 378
gi 115899356    455 IKMrcnghlpaePSPLLNEVYGSI 478
gi 16565492     415 IRKtea---dtaLPPLLQEIFKDM 435
```

FIG. 8A

Glucocorticoid receptor (*Homo sapiens*)

```
  1 mdskesltpg reenpssvla qergdvmdfy ktlrggatvk vsasspslav asqsdskqrr
 61 llvdfpkgsv snaqqpdlsk avslsmglym getetkvmgn dlgfpqqgqi slssgetdlk
121 lleesianln rstsvpenpk ssastavsaa ptekefpkth sdvsseqqhl kgqtgtnggn
181 vklyttdqst fdilqdlefs sgspgketne spwrsdllid encllsplag eddsfllegn
241 snedckplil pdtkpkikdn gdlvlsspsn vtlpqvktek edfielctpg vikqeklgtv
301 ycqasfpgan iignkmsais vhgvstsggq myhydmntas lsqqqdqkpi fnvippipvg
361 senwnrcqgs gddnltslgt lnfpgrtvfs ngysspsmrp dvssppssss tattgpppkl
421 clvcsdeasg chygvltcgs ckvffkrave grqhnylcag rndciidkir rkncpacryr
481 kclqagmnle arktkkkikg iqqattgvsq etsenpgnkt ivpatlpqlt ptlvsllevi
541 epevlyagyd ssvpdstwri mttlnmlggr qviaavkwak aipgfrnlhl ddqmtllqys
601 wmflmafalg wrsyrqssan llcfapdlii neqrmtlpcm ydqckhmlyv sselhrlqvs
661 yeeylcmktl lllssvpkdg lksqelfdei rmtyikelgk aivkregnss qnwqrfyqlt
721 klldsmhevv enllnycfqt fldktmsief pemlaeiitn qipkysngni kkllfhqk
```

FIG. 8B

Amino acids 532-778 of *Homo sapiens* glucocorticoid receptor

```
532                                                      tlvsllevi
541 epevlyagyd ssvpdstwri mttlnmlggr qviaavkwak aipgfrnlhl ddqmtllqys
601 wmflmafalg wrsyrqssan llcfapdlii neqrmtlpcm ydqckhmlyv sselhrlqvs
661 yeeylcmktl lllssvpkdg lksqelfdei rmtyikelgk aivkregnss qnwqrfyqlt
721 klldsmhevv enllnycfqt fldktmsief pemlaeiitn qipkysngni kkllfhqk
```

FIG. 8C

Multiple sequence alignment of ligand-binding domain of glucocorticoid receptor of various species

```
                    10        20        30        40        50        60        70        80
                    ....*.....|.....*.....|.....*.....|.....*.....|.....*.....|.....*.....|
Feature 1                                  #  ##  #  ##                          ##  ##  #
1NHZ_A          34  TLVSLLEVIEPEVLYAGYDSSVPDSTWRIMTTLNMLGGRQVIAAVKWAKAIPGFRNLHLDDQMTLLQYSWMSLMAFALGW 113
gi 83721947    526  TLVSLLEVIEPEVLYSGYDSTLPDSSWRIMSTLNMLGGRQVVAAVKWAKAIPGFRNLHLDDQMTLLQYSWMFLMAFALGW 605
gi 1730255     530  TLISLLEVIEPEVLYSGYDSSIPDTTRRIMSSLNMLGGRQVVSAVRWAKAIPGFRNLHLDDQMTLLQYSWMFLMVFALGW 609
gi 82253198    110  TMLSVLKAIEPETIYSGYDSTLPDTSSRLMSTLNRLGGQQVVSAVKWAKSLPGFRNLHLDDQMILLQCSWLFLMSFSLGW 189
3CLD_A          13  TLVSLLEVIEPEVLYAGYDSSVPDSTWRIMTTLNMLGGRQVIAAVKWAKAIPGFRNLHLDDQMTLLQYSWMYLMAFALGW  92
1M2Z_A          11  TLVSLLEVIEPEVLYAGYDSSVPDSTWRIMTTLNMLGGRQVIAAVKWAKAIPGFRNLHLDDQMTLLQYSWMSLMAFALGW  90
3BQD_A           9  TLVSLLEVIEPEVLYAGYDSSVPDSTWRIMTTLNMLGGRQVIAAVKWAKAIPGFRNLHLDDQMTLLQYSWMSLMAFALGW  88

                        90        100       110       120       130       140       150       160
                    ....*.....|.....*.....|.....*.....|.....*.....|.....*.....|.....*.....|.....*.....|
                    #                 #  #
Feature 1
1NHZ_A         114  RSYRQSSANLLCFAPDLIINEQRMTLPDMYDQCKHMLYVSSELHRLQVSYEEYLCMKTLLLLSSVPKDGLKSQELFDEIR 193
gi 83721947    606  RSYKQSNGNLLCFAPDLITNEQRMNLPCMYEQCKHMLMVARELSRLQVSYEEYLCMKTLLLISTIPKEGLKSQTLFEEIR 685
gi 1730255     610  RSYKQTNGSILYFAPDLVITEDRMHLPFMQERCQEMLKIAGEMSSLQISYDEYLCMKVLLLMCTIPKEGLKSHALFEEIR 689
gi 82253198    190  RSYQQCNGSMLCFAPDLVINEERMRLPFMNDQCEKMLRICREFTVRLQLSHEEYLCMKVLLLISTVPKDGLKSQAVFDEIR 269
3CLD_A          93  RSYRQSSANLLCFAPDLIINEQRMTLPGMYDQCKHMLYVSSELHRLQVSYEEYLCMKTLLLLSSVPKDGLKSQELFDEIR 172
1M2Z_A          91  RSYRQSSANLLCFAPDLIINEQRMTLPCMYDQCKHMLYVSSELHRLQVSYEEYLCMKTLLLLSSVPKDGLKSQELFDEIR 170
3BQD_A          89  RSYRQSSANLLCFAPDLIINEQRMTLPCMYDQCKHMLYVSSELHRLQVSYEEYLCMKTLLLLSSVPKDGLKSQELFDEIR 168

                        170       180       190       200       210       220       230       240
                    ....*.....|.....*.....|.....*.....|.....*.....|.....*.....|.....*.....|.....*.....|
                                                      #  #  #
Feature 1
1NHZ_A         194  MTYIKELGKAIVKREGNSSQNWQRFYQLTKLLDSMHEVVENLLNYCFQTFLDKTMSIEFPEMLAEIITNQIPKYSNGNIK 273
gi 83721947    686  MTYIKELGKATVKREGNSSQNWQRFYQLTKLLDSMHDVVENLISFCFQTFLDKSMSIEFPEMLAEIISNQIPKYSNGNIK 765
gi 1730255     690  MTYIKELGKATVKREGNSSQNWQRFYQLTKLLDSMHEVAENLLAFCFLSFLDKSMSIEFPDMLSEIISNQIPKYSSGNLK 769
gi 82253198    270  MTYIKELGKATVKREENPSQNWQRFYQLTKLLDSMQEMVEGLIKFCFYTFTVNKTLSVEFPEMLVEIITNQIPKFQEGGIK 349
3CLD_A         173  MTYIKELGKATVKREGNSSQNWQRFYQLTKLLDSMHEVVENLLNYCFQTFLDKTMSIEFPEMLAEIITNQIPKYSNGNIK 252
1M2Z_A         171  MTYIKELGKATVKREGNSSQNWQRFYQLTKLLDSMHEVVENLLNYCFQTFLDKTMSIEFPEMLAEIITNQIPKYSNGNIK 250
3BQD_A         169  MTYIKELGKATVKREGNSSQNWQRFYQLTKLLDSMHEVVENLLNYCFQTFLDKTMSIEFPEMLAEIITNQIPKYSNGNIK 248
```

FIG. 8C (Cont.)

```
                    ....*..
Feature 1
1NHZ_A       274 KLLFHQK 280
gi 83721947  766 KLLFHQK 772
gi 1730255   770 KLLFHQK 776
gi 82253198  350 ALLFHQK 356
3CLD_A       253 KLLFHQK 259
1M2Z_A       251 KLLFHQK 257
3BQD_A       249 KLLFHQK 255
```

FIG. 9A

Vitamin D receptor (

```
  1 meamaastsl pdpgdfdrnv pricgvcgdr atgfhfnamt cegckgffrr smkrkalftc
 61 pfngdcritk dnrrhcqacr lkrcvdigmm kefiltdeev qrkremilkr keeealkdsl
121 rpklseeqqr iiailldahh ktydptysdf cqfrppvrvn dgggshpsrp nsrhtpsfsg
181 dsssscsdhc itssdmmdss sfsnldlsee dsddpsvtle lsqlsmlphl adlvsysiqk
241 vigfakmipg frdltsedqi vllkssaiev imlrsnesft mddmswtcgn qdykyrvsdv
301 tkaghsleli eplikfqvgl kklnlheeeh vllmaicivs pdrpgvqdaa lieaiqdrls
361 ntlqtyircr hpppgshlly akmiqkladl rslneehskq yrclsfqpec smkltplvle
421 vfgneis
```

FIG. 9B

Amino acids 124-426 of *Homo sapiens* Vitamin D receptor

```
12e    lseeqqr iiailldahh ktydptysdf cqfrppvrvn dgggshpsrp nsrhtpsfsg
181 dsssscsdhc itssdmmdss sfsnldlsee dsddpsvtle lsqlsmlphl adlvsysiqk
241 vigfakmipg frdltsedqi vllkssaiev imlrsnesft mddmswtcgn qdykyrvsdv
301 tkaghsleli eplikfqvgl kklnlheeeh vllmaicivs pdrpgvqdaa lieaiqdrls
361 ntlqtyircr hpppgshlly akmiqkladl rslneehskq yrclsfqpec smkltplvle
421 vfgneis
```

FIG. 9C

Multiple sequence alignment of ligand-binding domain Vitamin D receptors of various species

```
                    10        20        30        40        50        60        70        80
                    ....*....|....*....|....*....|....*....|....*....|....*....|....*....|
Feature 1                     # #
2HBH_A        5 LSDEQMQIINSLVEAHHKTYDdSYSDFVRFRPPVREgpvtrsasraaslhslsdassdsfnhspes----vdtklnfsn  79
1S0Z_A       11 LSEEQQRIIAILLDAHHKTYDpTYSDFCQFRPPVRvndgggs-------------------------------------  52
gi 147903351 125 ISDEQQKMIDILLEAHRKTFDtTYSDFNKFRPPVRenvdpfrritrsssvhtqgspsedsdvfts-------spdssehg 197
gi 3915243   147 LSEEQQKVIDTLLEAHHKTFDtTYSDFNKFRPPVRskfssrmathsssvvsqdfssedsndvfgsdafaafpepmepqmf 226

                              90        100       110       120       130       140       150       160
                    ....*....|....*....|....*....|....*....|....*....|....*....|....*....|....*....|
Feature 1                                 # #  ##  #                                  #  ##  #
2HBH_A       80 llmmyqdsgspdsseedqqsrLSMLPHLADLVSYSIQKVIGFAKMIPGFRDLTAEDQIALLKSSAIEIIMLRSNQSFSLE 159
1S0Z_A       53 ----------------vtlelsqLSMLPHLADLVSYSIQKVIGFAKMIPGFRDLTSEDQIVLLKSSAIEVTMLRSNESFTMD 118
gi 147903351 198 ffsaslfgqfeyssmggksgeLSMLPHIADLVSYSIQKIIGFAKMIPGFRDLIAEDQIALLKSSVIEVIMLRSNQSFSLD 277
gi 3915243   227 snldlseesdespsmnielphLPMLPHLADLVSYSIQKVIGFAKMIPGFRDLTAEDQIALLKSSAIEVTMLRSNQSFTME 306

                              170       180       190       200       210       220       230       240
                    ....*....|....*....|....*....|....*....|....*....|....*....|....*....|....*....|
Feature 1                     # #          #  # #
2HBH_A       160 DMSWSCGGPDFKYcinDVTKAGHTLELLEPLVKFQVGLKKLKLHEEEHVLLMAICLLSPDRPGVQDHVRIEALQDRLCDV 239
1S0Z_A       119 DMSWTCGNQDYKYrvsDVTKAGHSLELIEPLIKFQVGLKKLNLHEEEHVLLMAICIVSPDRPGVQDAALIEAIQDRLSNT 198
gi 147903351 278 DMSWTCGSEDFKYkvdDVTQAGHNMELLEPLVKFQVGLKKLDLHEEEHVLLMAICILSPDRPGLQDKALVESIQDRLSST 357
gi 39915243  307 DMSWTCGSNDFKYkvsDVTQAGHSMDLLEPLVKFQVGLKKLNLHEEEHVLLMAICILSPDRPGVQDTSLVESIQDRLSDI 386

                              250       260       270       280       290       300
                    ....*....|....*....|....*....|....*....|....*....|....*....|....
                                          #  #  #
Feature 1
2HBH_A       240 LQAYIRiq--hPGGRLLYAKMIQKLADLRSLNEEHSKQYRSLSFQPEHSMQLTPLVLEVFGSEV 301
1S0Z_A       199 LQTYIRcrhppPGSHLLYAKMIQKLADLRSLNEEHSKQYRCLSFQPECSMKLTPLVLEVFGNEI 262
gi 147903351 358 LQTYILckhppPGSRLLYAKMIQKLADLRSLNEEHSKQYRSISFLPEHSMKLTPLMLEVFSDEI 421
gi 3915243   387 LQTYIRcrhppPGSRLLYAKMIQKLADLRSLNEEHSKQYRCLSFQPEHSMQLTPLVLEVFGNEI 450
```

FIG. 10A

Thyroid hormone receptor alpha (*Homo sapiens*)

```
  1 meqkpskvec gsdpeensar spdgkrkrkn gqcslktsms gyipsyldkd eqcvvcgdka
 61 tgyhyrcitc egckgffrrt iqknlhptys ckydsccvid kitrnqcqlc rfkkciavgm
121 amdlvlddsk rvakrklieq nrerrrkeem irslqqrpep tpeewdlihi ateahrstna
181 qgshwkqrrk flpddigqsp ivsmpdgdkv dleafseftk iitpaitrvv dfakklptfs
241 elpcedqiil lkgccmeims lraavrydpe sdtltlsgem avkreqlkng glgvvsdaif
301 elgkslsafn lddtevallq avllmstdrs gllcvdkiek sqeayllafe hyvnhrkhni
361 phfwpkqlmk vtdlrmigac hasrflhmkv ecptelfppl flevfedqev
```

FIG. 10B

Amino acids 162-404 of *Homo sapiens* thyroid hormone receptor-alpha

```
162                                                peewdlihi ateahrstna
181 qgshwkqrrk flpddigqsp ivsmpdgdkv dleafseftk iitpaitrvv dfakklptfs
241 elpcedqiil lkgccmeims lraavrydpe sdtltlsgem avkreqlkng glgvvsdaif
301 elgkslsafn lddtevallq avllmstdrs gllcvdkiek sqeayllafe hyvnhrkhni
361 phfwpkqlmk vtdlrmigac hasrflhmkv ecptelfppl flev
```

FIG. 10C

Multiple sequence alignment of ligand-binding domain of thyroid hormone receptor-alpha of various species

```
                    10        20        30        40        50        60        70        80
                    ....*....|....*....|....*....|....*....|....*....|....*....|....*....|....*....|
                                                                  #   ##  ##   #  #
Feature 1
1NAV_A          17  PEEWDLIHIATEAHRSTnaqgshwkqrrkf----------lpddiqgspivsmPDGDKVDLEAFSEFTKIITPAITRVVD  86
1N46_A          13  DEEWELIKTVTEAHVATnaqgshwkqkrkf----------lpediggapivnaPEGGKVDLEAFSHFTKIITPAITRVVD  82
1BSX_A          15  DEEWELIKTVTEAHVATnaqgshwkqkrkf----------lpediggapivnaPEGGKVDLEAFSHFTKIITPAITRVVD  84
2PIN_A           8  DEEWELIKTVTEAHVATnaqgshwkqkrkf----------lpediggapivnaPEGGKVDLEAFSHFTKIITPAITRVVD  77
3D57_A          22  DEEWELIKTVTEAHVATnaqgshwkqkrkf----------lpediggapivnaPEGGKVDLEAFSHFTKIITPAITRVVD  91
gi 15141413583 179  TCPKKVNRYYLNGSPKPgmpvpeaprppvv----------qngvvvreadssgaMDDDMVDQDIFSHLAEVITPAIIKVVE 248
gi 13431914    159  AEEWELIHVVTEAHRSTnaqgshwkqkrkf----------lpediggspmasmPDGDKVDLEAFSEFTKIITPAITRVVD 228
gi 6175061     170  SEEWELIRIVTEAHRSTnaqgshwkqrrkf----------lpediggspmasmPDGDKVDLEAFSEFTKIITPAITRVVD 239
gi 82274155    223  SDFSGLIPDPILLDSRATsstfpqiltcpilrpgfsrpadappdkigqspvaptSDGDKVDLEAFSEFTKIITPAITRVVD 302
gi 115732680   186  DHEEALIRAILVAHKQTshmyrres----------ssgeeesePDSKKQKLEDEKPLSEIMTPSIVKVVE 244
gi 586092      216  DEEWELIKTVTEAHVATnaqgshwkqkrkf----------lpediggapivnaPEGGKVDLEAFSHFTKIITPAITRVVD 285
gi 215273960   141  QEEWEMIRVVTEAHMATnaqgnhwkqkrkflsavg-vkeakpediggsapivnaPEGNKVDIEAFSQFTKIITPAITRVVD 219

                    90        100       110       120       130       140       150       160
                    ....*....|....*....|....*....|....*....|....*....|....*....|....*....|....*....|
                                  #  #   #                ###          #  #  #
Feature 1
1NAV_A          87  FAKKLPMFsELPCEDQIILLKGCCMEIMSLRAAVRYDPESDTLTLSGEMaVKREQLKNGGLGVVSDAIFELGKSLSaFNL 166
1N46_A          83  FAKKLPMFcELPCEDQIILLKGCCMEIMSLRAAVRYDPESETLTLNGEMaVTRGQLKNGGLGVVSDAIFDLGMSLSsFNL 162
1BSX_A          85  FAKKLPMFcELPCEDQIILLKGCCMEIMSLRAAVRYDPESETLTLNGEMaVTRGQLKNGGLGVVSDAIFDLGMSLSsFNL 164
2PIN_A          78  FAKKLPMFcELPCEDQIILLKGCCMEIMSLRAAVRYDPESETLTLNGEMaVTRGQLKNGGLGVVSDAIFRLGMSLSsFNL 157
3D57_A          92  FAKKLPMFcELPCEDQIILLKGCCMEIMSLRAAVRYDPESETLTLNGEMaVTRGQLKNGGLGVVSDAIFRLGMSLSsFNL 171
gi 151413583   249  FAKQIPGFtKLVPDDQVALLKNCCFEVMCLRAASRFDKQRRTITMFGGLtVTKEQVSQGGLGRLAEPLEFEFAEGLSQLHL 328
gi 13431914    229  FAKKLPMFsELPCEDQIILLKGCCMEIMSLRAAVRYDPESETLTLSGEMaVKREQLKNGGLGVVSDAIFDLGKSLSaFNL 308
gi 6175061     240  FAKKLPMFsELTCEDQIILLKGCCMEIMSLRAAVRYDPDSETLTLSGEMaVKREQLKNGGLGVVSDAIFDLGRSLAaFNL 319
gi 82274155    303  FAKKLPMFsELPCEDQIILLKGCCMEIMSLRAAMRYDPESETLTLSGEMaVKREQLKNGGLGVVSDAIFDLGKSLAqFNL 382
gi 115732680   245  FAKRIFGFtGLHHDDQILLLKTCCMEIMCLRVAQKFDPDSQKLILSNGLrVGKSDMDHGVLSELIEPIFDFAVSMSrLQL 324
gi 586092      286  FAKKLPMFcELPCEDQIILLKGCCMEIMSLRAAVRYDPESETLTLNGEMaVTRGQLKNGGLGVVSDAIFDLGMSLSsFNL 365
gi 215273960   220  FAKKLPMFcELPCEDQIILLKGCCMEIMSLRAAVRYDPESDTLTLNGEMaVTRGQLKNGGLGVVSDAIFDLGVSLSsFNL 299
```

FIG. 10C (Cont.)

```
                 170       180       190       200       210       220       230       240
                 ....*.....|.....*.....|.....*.....|.....*.....|.....*.....|.....*.....|
Feature 1
1NAV_A           167 DDTEVALLQAVLLMSTDRs----------------------------GLLCVDKIEKSQEAYLLAFEHYVNhrKHNIPHFW 219
1N46_A           163 DDTEVALLQAVLLMSSDRp----------------------------GLACVERIEKYQDSFLLAFEHYINyrKHHVTHFW 215
1BSX_A           165 DDTEVALLQAVLLMSSDRp----------------------------GLACVERIEKYQDSFLLAFEHYINyrKHHVTHFW 217
2PIN_A           158 DDTEVALLQAVLLMSSDRp----------------------------GLACVERIEKYQDSFLLAFEHYINyrKHHVTHFW 210
3D57_A           172 DDTEVALLQAVLLMSSDRp----------------------------GLACVERIEKYQDSFLLAFEHYINyrKHHVTHFW 224
gi 151413583     329 DDTEVALLAALLVVADRP----------------------------GVQDQESIDRLQDIILTAYKNYITrqRPHQPVLW 380
gi 13431914      309 DDTEVALLQAVLLMSSDRt----------------------------GLICVDKIEKCQETYLLAFEHYINyrKHNIPHFW 361
gi 61750061      320 DDTEVALLQAVLLMSSDRt----------------------------GLICTDKIEKCQETYLLAFEHYINhrKHNIPHFW 372
gi 82274155      383 DDTEVALLQAVLLMSSGNrrrgrprpspapgstsssssssssdrsGLTCTDKIEKCQETYLLAFEHYINyrKHNIPHFW 462
gi 115732680     325 TETEMALLAAVLLIAGDRp----------------------------GLKEAKLVETLQDSLLTAFQHFINesRPKTPVHW 377
gi 586092        366 DDTEVALLQAVLLMSSDRp----------------------------GLACVERIEKYQDSFLLAFEHYINyrKHHVTHFW 418
gi 215273960     300 DDSEVALLQAVILLSSDRp----------------------------GLTSVERIERCQEEFLLAFEHYINyrKHKVAHFW 352

                          250       260       270       280
                          ....*.....|.....*.....|.....*.....|.....*.....|
                                    #         #         #
Feature 1
1NAV_A           220 PKLLMKVTDLRMIGACHASRFLHMKVECPTELFPPLFLEV 259
1N46_A           216 PKLLMKVTDLRMIGACHASRFLHMKVECPTELFPPLFLEV 255
1BSX_A           218 PKLLMKVTDLRMIGACHASRFLHMKVECPTELFPPLFLEV 257
2PIN_A           211 PKLLMKVTDLRMIGACHASRFLHMKVECPTELFPPLFLEV 250
3D57_A           225 PKLLMKVTDLRMIGACHASRFLHMKVECPTELFPPLFLEV 264
gi 151413583     381 GKILMKVTDLRALSVAHAEQVKLVKMECTNDI-PPLFLEM 419
gi 13431914      362 PKLLMKVTDLRMIGACHASRFLHMKVECPTELFPPLFLEV 401
gi 61750061      373 PKLLMKVTDLRMIGACHASRFLHMKVECPTELFPPLFLEV 412
gi 82274155      463 PKLLMKVTDLRMIGACHASRFLHMKVECPNELFPPLFLEV 502
gi 115732680     378 AKILMKITDLRTISARHAERIMCIKLDRPNEI-PQIFLEM 416
gi 586092        419 PKLLMKVTDLRMIGACHASRFLHMKVECPTELFPPLFLEV 458
gi 215273960     353 PKLLMKVTDLRMIGACHASRFLHMKVECPTELFPPLFLEV 392
```

FIG. 11A

Retinoic acid receptor-beta (*Homo sapiens*)

```
  1 mfdcmdvlsv spgqildfyt aspsscmlqe kalkacfsgl tqtewqhrht aqsietqsts
 61 seelvpspps plppprvykp cfvcqdkssg yhygvsaceg ckgffrrsiq knmiytchrd
121 kncvinkvtr nrcqycrlqk cfevgmskes vrndrnkkkk etskqectes yemtaelddl
181 tekirkahqe tfpslcqlgk yttnssadhr vrldlglwdk fselatkcii kivefakrlp
241 gftgltiadq itllkaacld ililrictry tpeqdtmtfs dgltlnrtqm hnagfgpltd
301 lvftfanqll plemddtetg llsaiclicg drqdleeptk vdklqeplle alkiyirkrr
361 pskphmfpki lmkitdlrsi sakgaervit lkmeipgsmp pliqemlens eghepltpss
421 sgntaehsps ispssvensg vsqsplvq
```

FIG. 11B

Amino acids 179-409 of *Homo sapiens* retinoic acid receptor-beta

```
179                                                                dl
181 tekirkahqe tfpslcqlgk yttnssadhr vrldlglwdk fselatkcii kivefakrlp
241 gftgltiadq itllkaacld ililrictry tpeqdtmtfs dgltlnrtqm hnagfgpltd
301 lvftfanqll plemddtetg llsaiclicg drqdleeptk vdklqeplle alkiyirkrr
361 pskphmfpki lmkitdlrsi sakgaervit lkmeipgsmp pliqemlen
```

FIG. 11C

Multiple sequence alignment of ligand-binding domain of retinoic acid receptor-beta of various species

```
                                10        20        30        40        50        60        70        80
                     ....*.....|.....*.....|.....*.....|.....*.....|.....*.....|.....*.....|.....*.....|
Feature 1                                                          #  ##  #
1XAP_A          32 DLTEKIRKAHQETFPslcqLGKYTTNSsadh---rvrLDLGLWDKFSELATKCIIKIVEFAKRLPGFTqLTIADQITLLK 108
gi 122049638   400 ALVTSVHKFHVETFPlsseLKKYQIPSppivkdtsakTDSNLWEKFAELSTKCIVKIVEFAKGIPGFQdFTIADQITLLK 479
gi 3041719     186 DLTEKIRKAHQETFPslcqLGKYTTNSsadh---rvrLDLGLWDKFSELATKCIIKIVEFAKRLPGFTsLTIADQITLLK 262
gi 28558767    209 ELIQKVSKAHQETFPslcqLGKYTTNSsadq---rvqLDLGLWDKFSELSTKCIIKIVEFAKRLPGFTtLTIADQITLLK 285
gi 118572702   176 ELVNKVSKAHQETFPslcqLGKYTTNSssdh---riqLDLGLWDKFSELSTKCIIKIVEFAKRLPGFTtLTIADQITLLK 252
gi 115681476   134 DILQEVLRAHRDTFPqrplHPIHNAVSagn-----idIDMVMFDYYVTDMSSRAIVMVVDFAKKLPGFLsLSTQDQITLLK 208
gi 219413150   179 TIITTVREAHMATLPdmgkLPKYKVKNaaeq---rgpTDIELWQHFSDLCTETIIKIVQFAKKVPGFTtFGTADQITLLK 255
1XDK_B          34 DLTEKIRKAHQETFPslcqLGKYTTNSsadh---rvrLDLGLWDKFSELATKCIIKIVEFAKRLPGFTgLTIADQITLLK 110
1DKF_B           5 ELIEKVRKAHQETFPalcqLGKYTTNNsseq---rvsLDIDLWDKFSELSTKCITKTVEFAKQLPGFTtLTIADQITLLK  81

                                90        100       110       120       130       140       150       160
                     ....*.....|.....*.....|.....*.....|.....*.....|.....*.....|.....*.....|.....*.....|
                        #  ##  #  #       ##                #
Feature 1
1XAP_A         109 AACLDILILRICTRYTPEQDTMTFSdGLTLNRTQMHNAGFGPLTDLVFTFANQLlpLEMDDTETGLLSAICLICGDRqdL 188
gi 122049638   480 CACLEVLFLRICSRFSPEHDTMTFSdGLTLTRKQMRVCGFGPITEQVFSFAQSLhplNADATEIGLLSAICLVSADRvdL 559
gi 3041719     263 AACLDILILRICTRYTPEQDTMTFSdGLTLNRTQMHNAGFGPLTDLVFTFANQLlpLEMDDTETGLLSAICLICGDRqdL 342
gi 28558767    286 SACLDILMLRICTRYTPEQDTMTFSdGLTLNRTQMHNAGFGPLTDLVFSFADQLlpLEMDDTETGLLSAICLICGDRmdL 365
gi 118572702   253 SACLDILMLRICTRYTPEQDTMTFSdGLTLNRTQMHNAGFGPLTDLVFAFAGQLlpLEMDDTETGLLSAICLICGDRmdL 332
gi 115681476   209 ASCLDIMILRICSRFNPQDASVTFTtGLTLTQGQLKAGGFGSLLDVIFTFASSLsrMHIDETEIALLSAICLISEDRtgL 288
gi 219413150   256 AACLDILILRLATRLDKESDTVTFInGMMLSRTQMHNAGFGPLTDGVFTFAEGMqkLLFDETEIGLMCSICLVCGDRqgL 335
1XDK_B         111 AACLDILILRICTRYTPEQDTMTFSdGLTLNRTQMHNAGFGPLTDLVFTFANQLlpLEMDDTETGLLSAICLICGDRqdL 190
1DKF_B          82 AACLDILILRICTRYTPEQDTMTFSdGLTLNRTQMHNAGFGPLTDLVFAFANQLlpLEMDDAETGLLSAICLICGDRqdL 161
```

FIG. 11C (Cont.)

```
                    170       180       190       200       210       220       230
                    ....*.....|.....*.....|.....*.....|.....*.....|.....*.....|....*
Feature 1                                                    ##  #                  #
1XAP_A          189 EEPTKVDKLQEPLLEALKTYIRKRRPskphMFPKILMKITDLRSISAKGAERVITL-KMEIPGSMPPLIQEMLEN 262
gi 122049638    560 EEPDKVELLQESLVEGLKVYARKRRPhtpqVFPKLIIKISDLRSISLKGADRVVTVkTEIPCGAMPPLMSEMLEN 634
gi 3041719      343 EEPMKVDKLQEPLLEALKIYIRKRRPnkphMFPKILMKITDLRSISAKGAERVITL-KMEIPGSMPPLIQEMLEN 416
gi 28558767     366 EEPEKVEKLQEPLLEALKFYARRRRPdkpyMFPRMLMKITDLRGISTKGAERAITL-KLEIPGPMPPLIREMLEN 439
gi 118572702    333 EEPERVDRLQEPLLEALKIYARRRRPnkphMFPRMLMKITDLRGISTKGAERAITL-KMEIPGPMPPLIREMLEN 406
gi 115681476    289 EDAPRIEKMQEPLLEGLRLYVRKRRPkeshFPAKLLMKITDLRCISVKSAEKVFDM-KVEIFVKEMPALISEMIDK 362
gi 219413150    336 EDIQRAENLQEPLLEALKAYSRRRIPddpqRFPKMIMKITDLRSISSKGAERVITL-KMELSSPMPPLIAEIWEK 409
1XDK_B          191 EEPTKVDKLQEPLLEALKIYIRKRRPskphMFPKILMKITDLRSISAKGAERVITL-KMEIPGSMPPLIQEMLEN 264
1DKF_B          162 EQPDRVDMLQEPLLEALKVYVRKRRPsrphMFPKMLMKITDLRSISAKGAERVITL-KMEIPGSMPPLIQEMLEN 235
```

2017205197 15 Mar 2021

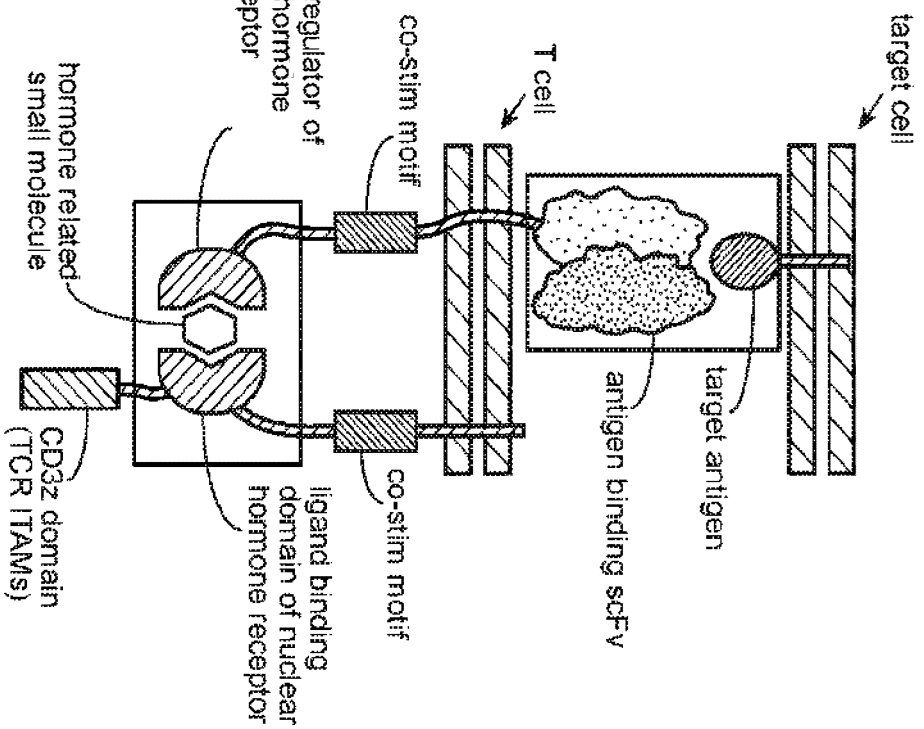

FIG. 12

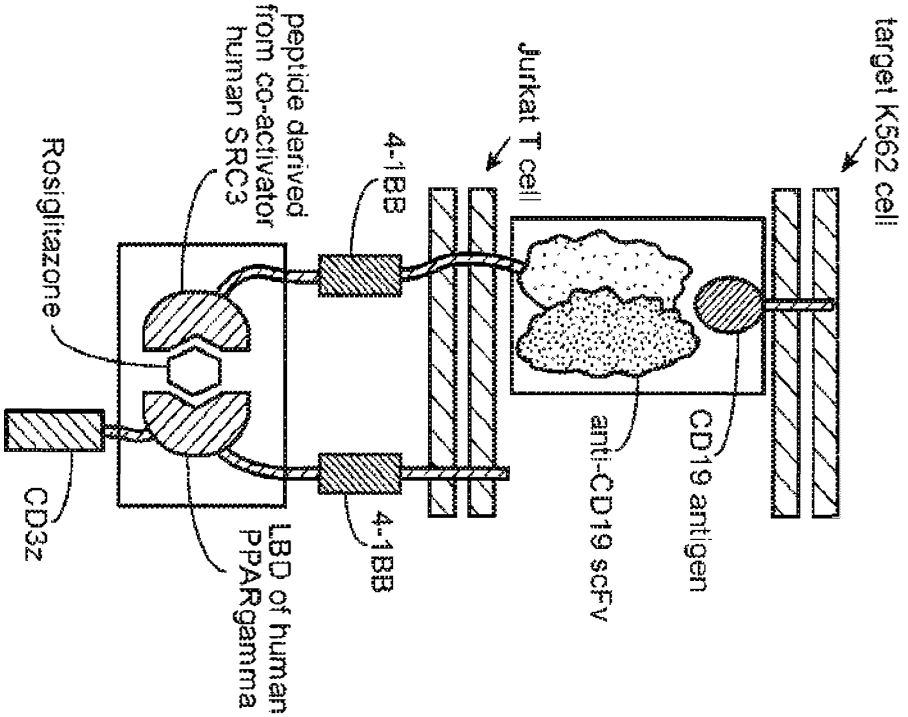

FIG. 13

2017205197 15 Mar 2021

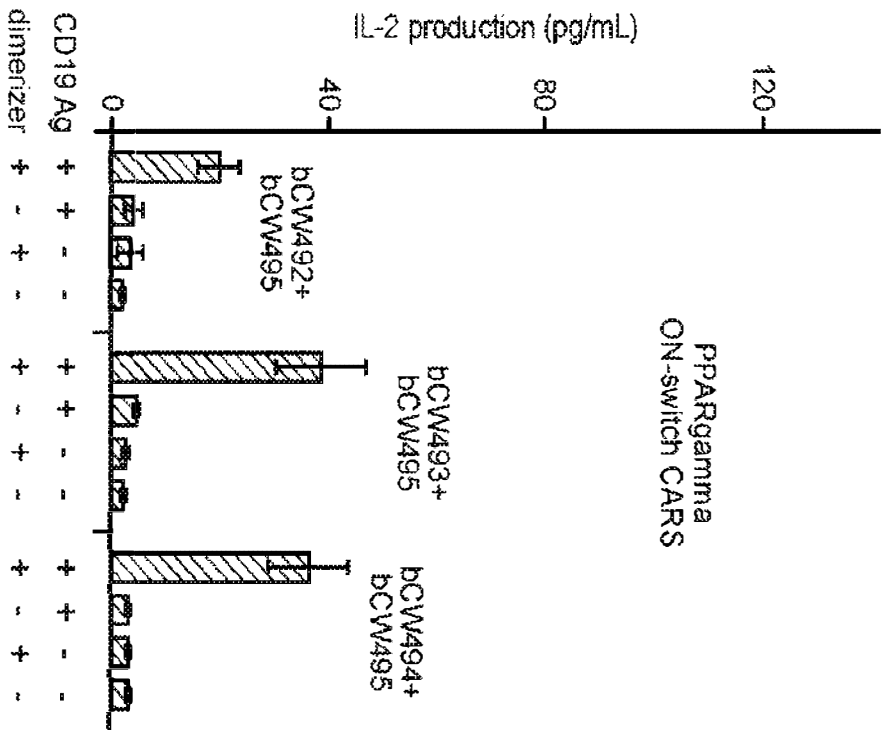

FIG. 14

FIG. 16A

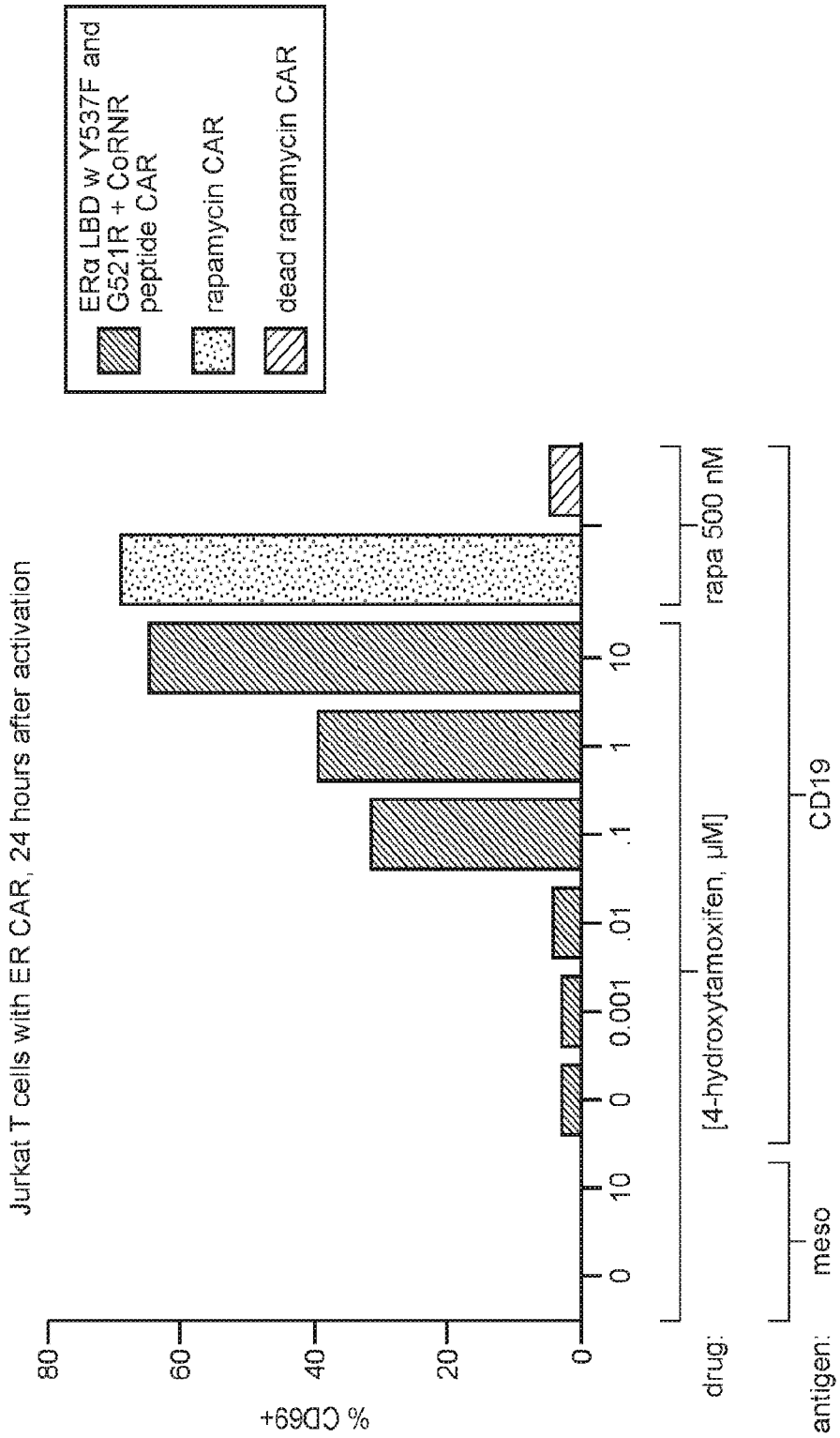
ERα LBD w Y537F and G521R + CoRNR peptide CAR
rapamycin CAR
dead rapamycin CAR
Jurkat T cells with ER CAR, 24 hours after activation
% CD69+
0
20
40
60
80
0
10
0
0.001
.01
.1
1
10
[4-hydroxytamoxifen, µM]
rapa 500 nM
drug:
meso
CD19
antigen:

FIG. 16B

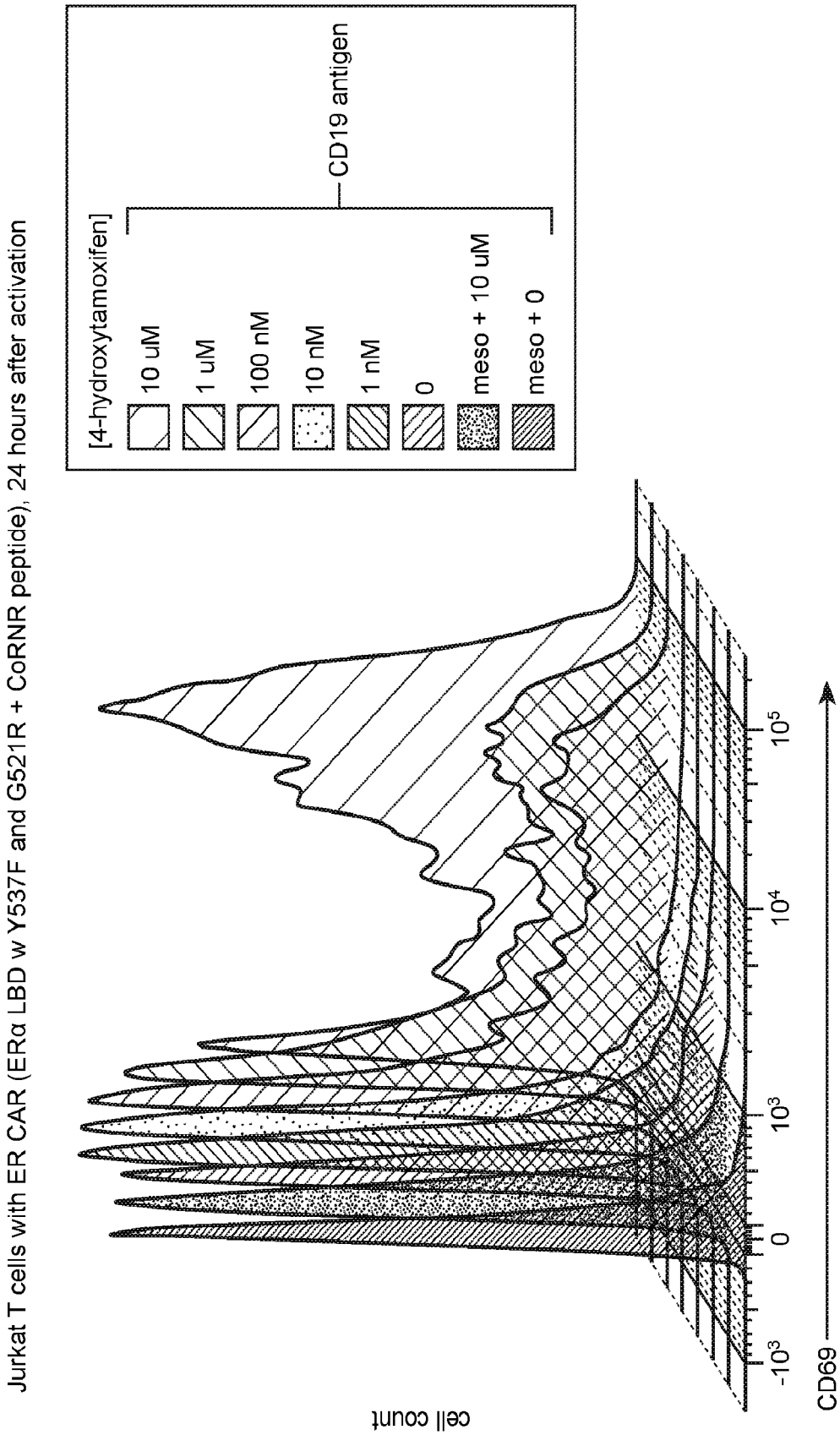
Jurkat T cells with ER CAR (ERα LBD w Y537F and G521R + CoRNR peptide), 24 hours after activation
[4-hydroxytamoxifen]
10 uM
1 uM
100 nM
10 nM
1 nM
0
meso + 10 uM
meso + 0
CD19 antigen
cell count
-10^3
0
10^3
10^4
10^5
CD69

FIG. 17

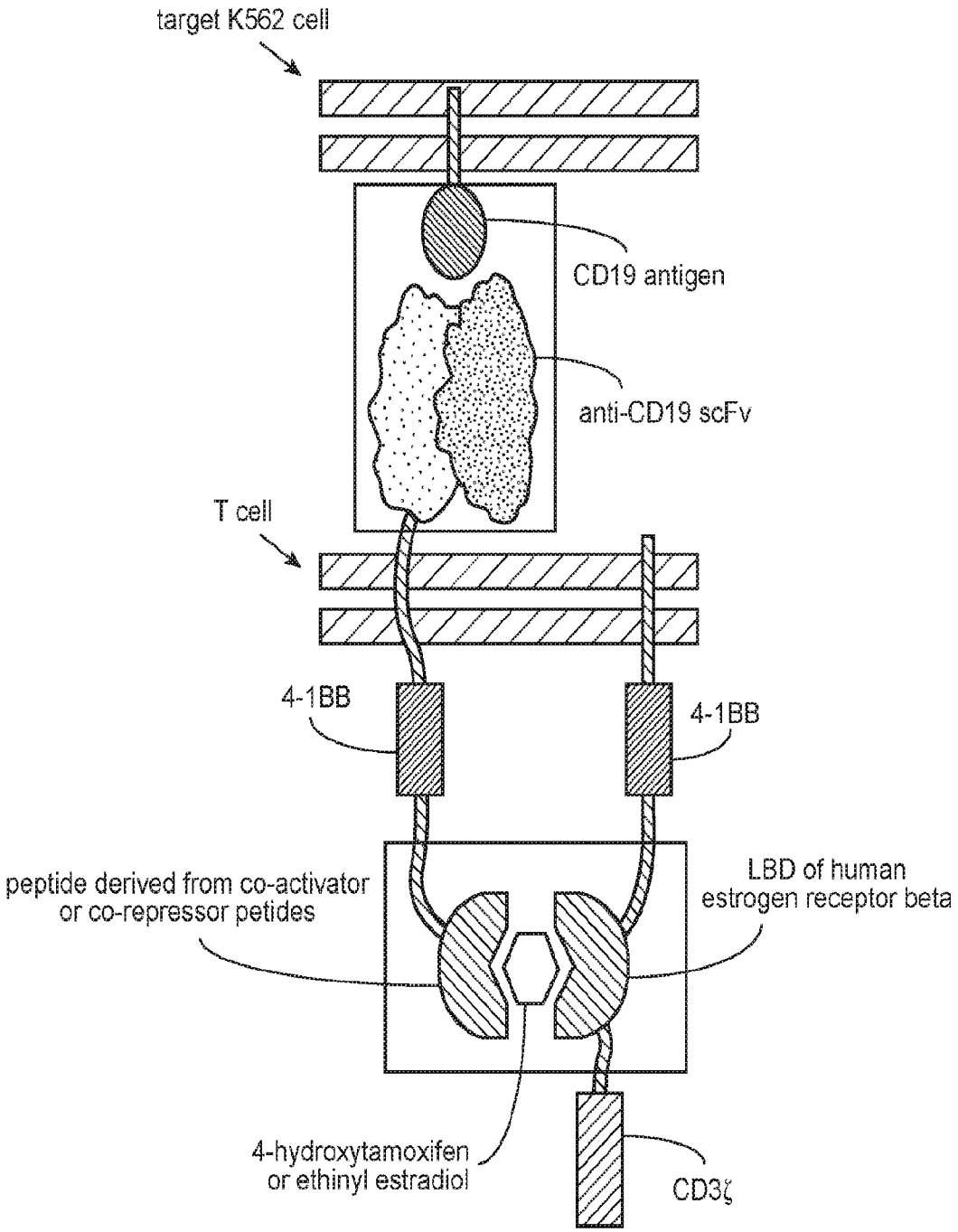
target K562 cell
CD19 antigen
anti-CD19 scFv
T cell
4-1BB
4-1BB
peptide derived from co-activator or co-repressor petides
LBD of human estrogen receptor beta
4-hydroxytamoxifen or ethinyl estradiol
CD3ζ

FIG. 18A

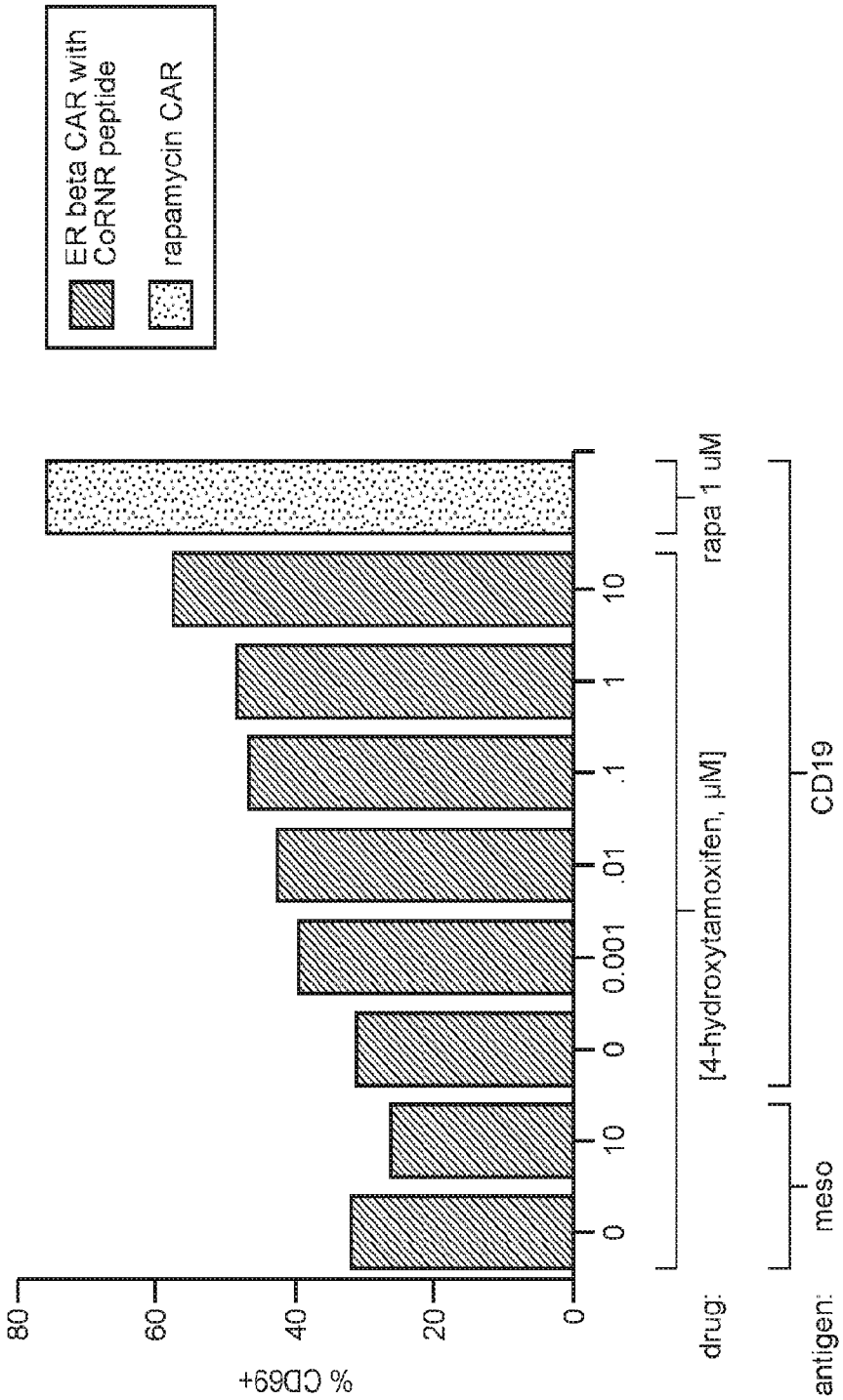
ER beta CAR with CoRNR peptide
rapamycin CAR
% CD69+
80
60
40
20
0
0
10
0
0.001
.01
.1
1
10
rapa 1 uM
[4-hydroxytamoxifen, µM]
drug:
meso
CD19
antigen:

FIG. 18B

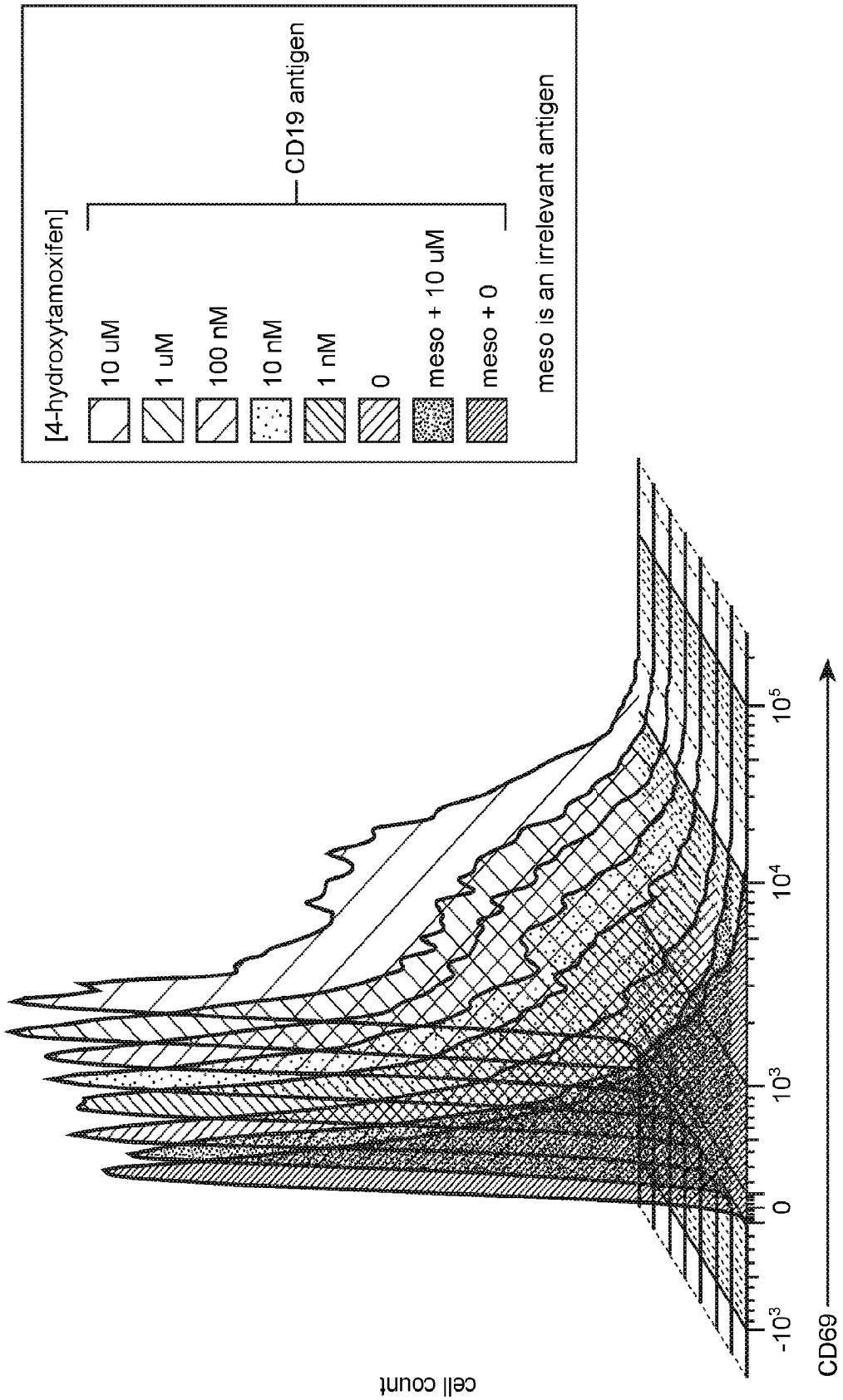
[4-hydroxytamoxifen]
10 uM
1 uM
100 nM
10 nM
1 nM
0
meso + 10 uM
meso + 0
CD19 antigen
meso is an irrelevant antigen
cell count
-10^3
0
10^3
10^4
10^5
CD69

FIG. 19

Drug	NHR LBD	Coactivator
rosiglitazone, pioglitazone, farglitazar, aleglitazar, fenofibric acid	PPARg	SRC1, SRC2, SRC3, TRAP220
tamoxifen, raloxifene, bazedoxifene, lasofoxifene	ERa, ERb (WT and many mutants)	CoRNR, αβV, TA1
eplerenone, spironolactone	MR (WT, S810L)	SRC1, PGC1A, TRAP220
mifepristone, asoprisnil	PR	NCoR
enzalutamide, ARN-509, cyproterone acetate, flutamide	AR (WT, T877A , F876L)	SRC1, SRC2, SRC3, TRAP220
drospirenone	PR	SRC1, SRC2, SRC3, TRAP220, NR0B1, PGC1B, NRIP1, EA2, EAB1
sobetirome	TRb	SRC1, SRC2, SRC3, TRAP220
ethinyl estradiol	ERa, ERb	SRC1, SRC2, SRC3, TRAP220, NR0B1, PGC1B, NRIP1, EA2, EAB1

FIG. 20A

Lyn kinase

```
   1 mgcikskgkd slsddgvdlk tqpvrntert iyvrdptsnk qqrpvpesql lpgqrfqtkd
  61 peeqgdivva lypydgihpd dlsfkkgekm kvleehgeww kakslltkke gfipsnyvak
 121 lntleteewf fkditrkdae rqllapgnsa gaflireset lkgsfslsvr dfdpvhgdvi
 181 khykirsldn ggyyisprit fpcisdmikh yqkqadglcr rlekacispk pqkpwdkdaw
 241 eipresiklv krlgaggfge vwmgyynnst kvavktlkpg tmsvqaflee anlmktlqhd
 301 klvrlyavvt reepiyiite ymakgslldf lksdeggkvl lpklidfsaq iaegmayier
 361 knyihrdlra anvlvseslm ckiadfglar viedneytar egakfpikwt apeainfgcf
 421 tiksdvwsfg illyeivtyg kipypgrtna dvmtalsqgy rmprvencpd elydimkmcw
 481 kekaeerptf dylqsvlddf ytategqyqq qp
```

FIG. 20B

N-terminal portion of Lyn kinase (Y211-E393)

```
211                                 yqkqadglcr rlekacispk pqkpwdkdaw
241 eipresiklv krlgagqfge vwmgyynnst kvavktlkpg tmsvqaflee anlmktlqhd
301 klvrlyavvt reepiyiite ymakgslldf lksdeggkvl lpklidfsaq iaegmayier
361 knyihrdlra anvlvseslm ckiadfglar vie
```

FIG. 20C

C-terminal portion of Lyn kinase (D394-P512)

```
394                                   dneytar egakfpikwt apeainfgcf
421 tiksdvwsfg illyeivtyg kipypgrtna dvmtalsqgy rmprvencpd elydimkmcw
481 kekaeerptf dylqsvlddf ytategqyqq qp
```

FIG. 21

Fak kinase

```
   1 maaayldpnl nhtpssstkt hlgtgtersp gamervlkvf hyfessnept twasiirhgd
  61 atdvrgiiqk ivdshkvkhv acygfrlshl rseevhwlhv dmgvssvrek yelahppeew
 121 kyelrirylp kgflnqfted kptlnffyqq vksdymleia dqvdqdialk lgcleirrsy
 181 wemrgnalek ksnyevlekd vglkrffpks lldsvkaktl rkliqqtfrq fanlnreesi
 241 lkffeilspv yrfdkecfkc algsswiisv elaigpeegi syltdkgcnp thladfnqvq
 301 tiqysnsedk drkgmlqlki agapepltvt apsltiaenm adlidqycrl vngatqsfii
 361 rpqkegeral psipklanne kqgmrthavs vsetddyaei ideedtytmp strdyeiqre
 421 rielgrcige gqfgdvhqgv ylspenpala vaiktcknct sdsvrekflq ealtmrqfdh
 481 phivkligvi tenpvwiime lctlgelrsf lqvrkysldl aslilyayql stalaylesk
 541 rfvhrdiaar nvlvssndcv klgdfglsry medstyykas kgklpikwma pesinfrrft
 601 sasdvwmfgv cmweilmhgv kpfqgvknnd vigrienger lpmppncppt lyslmtkcwa
 661 ydpsrrprft elkaqlstil eeekvqqeer mrmesrrqat vswdsggsde appkpsrpgy
 721 psprssegfy pspqhmvqtn hyqisgypgs hgipamagsi ypgqaslldq telwnhrpqe
 781 msmwqpsved saaldlrgmg qvlpphlmee rlirqqqeme edqrwlekee rflkpdvrls
 841 rgsidredgs fqgptgnqhi yqpvgkpdpa appkkpprpg apghlsnlss isspaesyne
 901 gvkpwrlqpq eisppptanl drsndkvyen vtglvkavie msskiqpapp eeyvpmvkev
 961 glalrtllat vdetipilpa sthreiemaq kllnsdlgel iskmklaqqy vmtslqqeyk
1021 kqmltaahal avdaknlldv idqarlkmlg qtrph
```

FIG. 22A

FXR

```
  1 mgskmnlieh shlpttdefs fsenlfgvlt eqvagplgqn levepysqys nvqfpqvqpq
 61 issssyysnl gfypqqpeew yspgiyelrr mpaetlyqge tevaempvtk kprmgasagr
121 ikgdelcvvc gdrasgyhyn altcegckgf frrsitknav ykcknggncv mdmymrrkcq
181 ecrlrkckem gmlaecllte iqckskrlrk nvkqhadqtv nedsegrdlr qvtsttkscr
241 ekteltpdqq tllhfimdsy nkqrmpqeit nkilkeefsa eenfliltem atnhvqvlve
301 ftkklpgfqt ldhedqiall kgsaveamfl rsaeifnkkl psghsdllee rirnsgisde
361 yitpmfsfyk sigelkmtqe eyalltaivi lspdrqyikd reaveklqep lldvlqklck
421 ihqpenpqhf acllgrltel rtfnhhhaem lmswrvndhk ftpllceiwd vq
```

FIG. 22B

FXR LBD

```
237                                                          kscr
241 ekteltpdqq tllhfimdsy nkqrmpqeit nkilkeefsa eenfliltem atnhvqvlve
301 ftkklpgfqt ldhedqiall kgsaveamfl rsaeifnkkl psghsdllee rirnsgisde
361 yitpmfsfyk sigelkmtqe eyalltaivi lspdrqyikd reaveklqep lldvlqklck
421 ihqpenpqhf acllgrltel rtfnhhhaem lmswrvndhk ftpllceiwd vq
```

FIG. 23A

LXR-alpha

```
  1 mslwlgapvp dippdsavel wkpgaqdass qaqggsscil reearmphsa ggtagvglea
 61 aeptalltra eppsepteir pqkrkkgpap kmlgnelcsv cgdkasgfhy nvlscegckg
121 ffrrsvikga hyichsgghc pmdtymrrkc qecrlrkcrq agmreecvls eeqirlkklk
181 rqeeeqahat slpprasspp qilpqlspeq lgmieklvaa qqqcnrrsfs drlrvtpwpm
241 apdphsrear qqrfahftel aivsvqeivd fakqlpgflq lsredqiall ktsaievmll
301 etsrrynpgs esitflkdfs ynredfakag lqvefinpif efsramnelq lndaefalli
361 aisifsadrp nvqdqlqver lqhtyvealh ayvsihhphd rlmfprmlmk lvslrtlssv
421 hseqvfalrl qdkklpplls eiwdvhe
```

FIG. 23B

LXR-alpha LBD

```
182  qeeeqahat slpprasspp qilpqlspeq lgmieklvaa qqqcnrrsfs drlrvtpwpm
241 apdphsrear qqrfahftel aivsvqeivd fakqlpgflq lsredqiall ktsaievmll
301 etsrrynpgs esitflkdfs ynredfakag lqvefinpif efsramnelq lndaefalli
361 aisifsadrp nvqdqlqver lqhtyvealh ayvsihhphd rlmfprmlmk lvslrtlssv
421 hseqvfalrl qdkklpplls eiwdvhe
```

FIG. 24A

ROR-gamma

```
  1 mrtqievipc kicgdkssgi hygvitcegc kgffrrsqrc naaysctrqq ncpidrtsrn
 61 rcqhcrlqkc lalgmsrdav kfgrmskkqr dslhaevqkq lqqrqqqqqe pvvktppaga
121 qgadtltytl glpdgqlplg sspdlpeasa cppgllkasg sgpsysnnla kaglngasch
181 leyspergka egresfystg sqltpdrcgl rfeehrhpgl gelgqgpdsy gspsfrstpe
241 apyaslteie hlvqsvcksy retcqlrled llrqrsnifs reevtgyqrk smwemwerca
301 hhlteaiqyv vefakrlsgf melcqndqiv llkagamevv lvrmcrayna dnrtvffegk
361 yggmelfral gcselissif dfshslsalh fsedeialyt alvlinahrp glqekrkveq
421 lqynlelafh hhlckthrqs ilaklppkgk lrslcsqhve rlqifqhlhp ivvqaafppl
481 ykelfstete spvglsk
```

FIG. 24B

ROR-gamma LBD

```
237                                                          stpe
241 apyaslteie hlvqsvcksy retcqlrled llrqrsnifs reevtgyqrk smwemwerca
301 hhlteaiqyv vefakrlsgf melcqndqiv llkagamevv lvrmcrayna dnrtvffegk
361 yggmelfral gcselissif dfshslsalh fsedeialyt alvlinahrp glqekrkveq
421 lqynlelafh hhlckthrqs ilaklppkgk lrslcsqhve rlqifqhlhp ivvqaafppl
481 ykelfstete spvglsk
```

FIG. 25A

RXR-alpha

```
  1 mdtkhflpld fstqvnsslt sptgrgsmaa pslhpslgpg igspgqlhsp istlssping
 61 mgppfsviss pmgphsmsvp ttptlgfstg spqlsspmnp vsssedikpp lglngvlkvp
121 ahpsgnmasf tkhicaicgd rssgkhygvy scegckgffk rtvrkdltyt crdnkdclid
181 krqrnrcqyc ryqkclamgm kreavqeerq rgkdrnenev estssanedm pverileael
241 avepktetyv eanmglnpss pndpvtnicq aadkqlftlv ewakriphfs elplddqvil
301 lragwnelli asfshrsiav kdgillatgl hvhrnsahsa gvgaifdrvl telvskmrdm
361 qmdktelgcl raivlfnpds kglsnpaeve alrekvyasl eayckhkype qpgrfaklll
421 rlpalrsigl kclehlfffk ligdtpidtf lmemleaphq mt
```

FIG. 25B

RXR-alpha LBD

```
225                                                 sanedm pverileael
241 avepktetyv eanmglnpss pndpvtnicq aadkqlftlv ewakriphfs elplddqvil
301 lragwnelli asfshrsiav kdgillatgl hvhrnsahsa gvgaifdrvl telvskmrdm
361 qmdktelgcl raivlfnpds kglsnpaeve alrekvyasl eayckhkype qpgrfaklll
421 rlpalrsigl kclehlfffk ligdtpidtf lmemleaphq mt
```

FIG. 26A

PXR

```
  1 mevrpkeswn hadfvhcedt esvpgkpsvn adeevggpqi crvcgdkatg yhfnvmtceg
 61 ckgffrramk rnarlrcpfr kgaceitrkt rrqcqacrlr kclesgmkke mimsdeavee
121 rralikrkks ertgtqplgv qglteeqrmm irelmdaqmk tfdttfshfk nfrlpgvlss
181 gcelpeslqa psreeaakws qvrkdlcslk vslqlrgedg svwnykppad sggkeifsll
241 phmadmstym fkgiisfakv isyfrdlpie dqisllkgaa felcqlrfnt vfnaetgtwe
301 cgrlsycled taggfqqlll epmlkfhyml kklqlheeey vlmqaislfs pdrpgvlqhr
361 vvdqlqeqfa itlksyiecn rpqpahrflf lkimamltel rsinaqhtqr llriqdihpf
421 atplmqelfg itgs
```

FIG. 26B

PXR LBD

```
130          s ertgtqplgv qglteeqrmm irelmdaqmk tfdttfshfk nfrlpgvlss
181 gcelpeslqa psreeaakws qvrkdlcslk vslqlrgedg svwnykppad sggkeifsll
241 phmadmstym fkgiisfakv isyfrdlpie dqisllkgaa felcqlrfnt vfnaetgtwe
301 cgrlsycled taggfqqlll epmlkfhyml kklqlheeey vlmqaislfs pdrpgvlqhr
361 vvdqlqeqfa itlksyiecn rpqpahrflf lkimamltel rsinaqhtqr llriqdihpf
421 atplmqelfg itgs
```

FIG. 27

Receptor	*Protein Sequence*
CD80	RCRERRRNERLRRESVRPV
PD1L	RKGRMMDVKKCGIQDTNSKKQSDTHLEET
TRML2_human (TLT2)	KKRHMASYSMCSDPSTRDPPGRPEPYVEVYLI
ICOS_human	TKKKYSSSVHDPNGEYMFMRAVNTAKKSRLTDVTL
TNF14_human (HVEM)	MEESVVRPSVFVVDGQTDIPFTRLGRSHRRQSCSV
CTLA4_human	SLSKMLKKRSPLTTGVYVKMPPTEPECEKQFQPYFIPIN
CD7_human	ARTQIKKLCSWRDKNSAACVVYEDMSHSRCNTLSSPNQYQ
TNR9_human (CD137, 41BB)	KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCEL
CD28	WVRSKRSRLLHSDYMNMTPRRPGPTRKHYQPYAPPRDFAAYRS
CD27_human	HQRRKYRSNKGESPVEPAEPCHYSCPREEEGSTIPIQEDYRKPEPACSP
LAG3_human	RRQWRPRRFSALEQGIHPPQAQSKIEELEQEPEPEPEPEPEPEPEPEPEQL
TNR18_human (GITR)	HIWQLRSQCMWPRETQLLLEVPPSTEDARSCQFPEEERGERSAEEKGRLGDLWV
CD226_human (DNAM-1)	NRRRRRERRDLFTESWDTQKAPNNYRSPISTSQPTNQSMDDTREDIYVNYPTFSRRPKTRV
TNR5_human (CD40)	KKVAKKPTNKAPHPKQEPQEINFPDDLPGSNTAAPVQETLHGCQPVTQEDGKESRISVQERQ
HAVR(TIM-3)	KWYSHSKEKIQNLSLISLANLPPSGLANAVAEGIRSEENIYTIEENVYEVEEPNEYYCYVSSRQQPSQPL GCRFAMP
TIGIT_human	RKKKALRIHSVEGDLRRKSAGQEEWSPSAPSPPGSCVQAEAAPAGLCGEQRGEDCAELHDYFNVLSY RSLGNCSFFTETG
CRTAM_human	KLRKAHVIWKKENEVSEHTLESYRSRSNNEETSSEEKNGQSSHPMRCMNYITKLYSEAKTKRKENVQ HSKLEEKHIQVPESIV
PDCD1_human (PD-1)	ICSRAARGTIGARRTGQPLKEDPSAVPVFSVDYGELDFQWREKTPEPPVPCVPEQTEYATIVFPSGM GTSSPARRGSADGPRSAQPLRPEDGHCSWPL
LAIR1_human	HRQNQIKQGPPRSKDEEQKPQQRPDLAVDVLERTADKATVNGLPEKDRETDTSALAAGSSQEVTYA QLDHWALTQRTARAVSPQSTKPMAESITYAAVARH
CXAR_human (CAR)	CCRKKRREEKYEKEVHHDIREDVPPPKSRTSTARSYIGSNHSSLGSMSPSNMEGYSKTQYNQVPSEDF ERTPQSPTLPPAKVAAPNLSRMGAIPVMIPAQSKDGSIV
BTLA_human	CCLRRHQGKQNELSDTAGREINLVDAHLKSEQTEASTRQNSQVLLSETGIYDNDPDLCFRMQEGSEV YSNPCLEENKPGIVYASLNHSVIGPNSRLARNVKEAPTEYASICVRS
CD2	TKRKKQRSRRNDEELETRAHRVATEERGRKPHQIPASTPQNPATSQHPPPPPGHRSQAPSHRPPPP GHRVQHQPQKRPPAPSGTQVHQQKGPPLPRPRVQPKPPHGAAENSLSPSSN
CD244_human (2B4)	WRRKRKEKQSETSPKEFLTIYEDVKDLKTRRNHEQEQTFPGGGSTIYSMIQSQSSAPTSQEPAYTLYSL IQPSRKSGSRKRNHSPSFNSTIYEVIGKSQPKAQNPARLSRKELENFDVYS

FIG. 27 (Cont.)

Receptor	*Protein Sequence*
TNR8_human (CD30)	RRACRKRIRQKLHLCYPVQTSQPKLELVDSRPRRSSTQLRSGASVTEPVAEERGLMSQPLMETCHSV GAAYLESLPLQDASPAGGPSSPRDLPEPRVSTEHTNNKIEKIYIMKADTVIVGTVKAELPEGRGLAGPA EPELEEELEADHTPHYPEQETEPPLGSCSDVMLSVEEEGKEDPLPTAASGK
TNR25_HUMAN (DR3)	TYRHCWPHKPLVTADEAGMEALTPPPATHLSPLDSAHTLLAPPDSSEKICTVQLVGNSWTPGYPETQ EALCPQVTWSWDQLPSRALGPAAAPTLSPESPAGSPAMMLQ
OX40	ALYLLRRDQRLPPDAHKPPGGGSFRTPIQEEQADAHSTLAKI
NKG2D	MGWIRGRRSRHSWEMSEFHNYNLDLKKSDFSTRWQKQRCPVVKSKCRENAS
TIM-1	KKYFFKKEVQQLSVSFSSLQIKALQNAVEKEVQAEDNIYIENSLYATD
CD160	SGFLQEKVWVMLVTSLVALQAL
BAFF-R	SWRRRQRRLRGASSAEAPDGDKDAPEPLDKVIILSPGISDATAPAWPPPGEDPGTTPPGHSVPVPAT ELGSTELVTTKTAGPEQQ
TACI	ACFLKKRGDPCSCQPRSRPRQSPAKSSQDHAMEAGSPVSTSPEPVETCSFCFPECRAPTQESAVTPG TPDPTCAGRWGCHTRTTVLQPCPHIPDSGLGIVCVPAQEGGPGA
CD72	MAEAITYADLRFVKAPLKKSISSRLGQDPGADDDGEITYENVQVPAVLGVPSSLASSVLGDKAAVKSE QPTASWRAVTSPAVGRILPCRTTCLRY
CD22	KLQRRWKRTQSQQGLQENSSGQSFFVRNKKVRRAPLSEGPHSLGCYNPMMEDGISYTTLRFPEMN IPRTGDAESSEMQRPPPDCDDTVTYSALHKRQVGDYENVIPDFPEDEGIHYSELIQFGVGERPQAQE NVDYVILKH
CD96	RKWCQYQKEIMERPPPFKPPPPPIKYTCIQEPNESDLPYHEMETL
NTB-A	LRKRRDSLSLSTQRTQGPAESARNLEYVSVSPTNNTVYASVTHSNRETEIWTPRENDTITIYSTINHSKE SKPTFSRATALDNV
CRACC	WFLKRERQEEYIEEKKRVDICRETPNICPHSGENTEYDTIPHTNRTILKEDPANTVYSTVEIPKKMENP HSLLTMPDTPRLFAYENVI
Siglec-3.7.9	KTHRRKAARTAVGRNDTHPTTGSASPKHQKKSKLHGPTETSSCSGAAPTVEMDEELHYASLNFHGM NPSKDTSTEYSEVRTQ
KLRG1	MTDSVIYSMLELPTATQAQNDYGPQQKSSSSRPSCSCL
NKR-P1A	MDQQAIYAELNLPTDSGPESSSPSSLPRDVCQGSPWHQFALKLSC
ILT2	LRHRRQGKHWTSTQRKADFQHPAGAVGPEPTDRGLQWRSSPAADAQEENLYAAVKHTQPEDGV EMDTRSPHDEDPQAVTYAEVKHSRPRREMASPPSPLSGEFLDTKDRQAEEDRQMDTEAAASEAPQ DVTYAQLHSLTLRREATEPPPSQEGPSPAVPSIYATLAIH
KIR2DL1	RWCSNKKNAAVMDQESAGNRTANSEDSDEQDPQEVTYTQLNHCVFTQRKITRPSQRPKTPPTDIIV YTELPNAESRSKVVSCP
KIR3DL1	HLWCSNKKNAAVMDQEPAGNRTANSEDSDEQDPEEVTYAQLDHCVFTQRKITRPSQRPKTPPTDT ILYTELPNAKPRSKVVSCP
CD94-NKG2A	MAVFKTTLWR
CD300b	KGSQRVPEEPGEQPIYMNFSEPLTKDMAT
CD300e	VNRPQWAPPGR

FIG. 27 (Cont.)

Receptor	*Protein Sequence*
TREM1	
TREM2	AAWHGQKPGTHPPSELDCGHDPGYQLQTLPGLRDT
ILT7	QHSQRSPPRCSQEANSRKDNAPFRVVEPWEQI
ILT3	QHWRQGKHRTLAQRQADFQRPPGAAEPEPKDGGLQRRSSPAADVQGENFCAAVKNTQPEDGVE MDTRQSPHDEDPQAVTYAKVKHSRPRREMASPPSPLSGEFLDTKDRQAEEDRQMDTEAAASEAP QDVTYAQLHSFTLRQKATEPPPSQEGASPAEPSVYATLAIH
ILT4	LRHRRQGKHWTSTQRKADFQHPAGAVGPEPTDRGLQWRSSPAADAQEENLYAAVKDTQPEDGV EMDTRAAASEAPQDVTYAQLHSLTLRRKATEPPPSQEREPPAEPSIYATLAIH
TLT-1	MAKRKQGNRLGVCGRFLSSRVSGMNPSSVVHHVSDSGPAAELPLDVPHIRLDSPPSFDNTTYTSLPL DSPSGKPSLPAPSSLPPLPPKVLVCSKPVTYATVIFPGGNKGGGTSCGPAQNPPNNQTPSS
CD200R	KVNGCRKYKLNKTESTPVVEEDEMQPYASYTEKNNPLYDTTNKVKASEALQSEVDTDLHTL
CD300a	RMFQKWIKAGDHSELSQNPKQAATQSELHYANLELLMWPLQEKPAPPREVEVEYESTVASPREELHY ASVVFDSNTNRIAAQRPREEEPDSDYSVIRKT
CD300f	WRMMKYQQKAAGMSPEQVLQPLEGDLCYADLTLQLAGTSPQKATTKLSSAQVDQVEVEYVTMAS LPKEDISYASLTLGAEDQEPTYCNMGHLSSHLPGRGPEEPTEYSTISRP
DC-SIGN	MSDSKEPRLQQLGLLEEEQLRGLGFRQTRGYKSLAGC
B7-2	RKSSGGKGGSYSQAACSDSAQGSDVSLTA
Allergin-1	LPKYKTRKAMRNNVPRDRGDTAMEVGIYANILEKQAKEESVPEVGSRPCVSTAQDEAKHSQELQYA TPVFQEVAPREQEACDSYKSGYVYSELNF
Pir-B	RRRHRGKFRKDVQKEKDLQLSSGAEEPITRKGELQKRPNPAAATQEESLYASVEDMQTEDGVELNS WTPPEEDPQGETYAQVKPSRLRKAGHVSPSVMSREQLNTEYEQAEEGQGANNQAAESGESQDVT YAQLCSRTLRQGAAASPLSQAGEAPEEPSVYATLAAARPEAVPKDMEQ
NC-14xSAG	SAGSAGSAGSAGSAGSAGSAGSAGSAGSAGSAGSAGSAG
TNR9_2	KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCEL
TNR9_3	KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCEL
TNR9_4	KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCEL
CD5	KKLVKKFRQKKQRQWIGPTGMNQNMSFHRNHTATVRSHAENPTASHVDNEYSQPPRNSHLSAYP ALEGALHRSSMQPDNSSDSDYDLHGAQRL
PECAM-1 (CD31)	KCYFLRKAKAKQMPVEMSRPAVPLLNSNNEKMSDPNMEANSHYGHNDDVRNHAMKPINDNKEP LNSDVQYTEVQVSSAESHKDLGKKDTETVYSEVRKAVPDAVESRYSRTEGSLDGT
CEACAM-1 (CD66a)	HFGKTGRASDQRDLTEHKPSVSNHTQDHSNDPPNKMNEVTYSTLNFEAQQPTQPTSASPSLTATEII YSEVKKQ
Gab2	DVVCTGWLRKSPPEKKLRRYAWKKRWFILRSGRMSGDPDVLEYYKNDHSKKPLRIINLNFCEQVDA GLTFNKKELQDSFVFDIKTSERTFYLVAETEEDMNKWVQSICQICG
DOK1	AVMEGPLFLQSQRFGTKRWRKTWAVLYPASPHGVARLEFFDHKGSSSGGGRGSSRRLDCKVIRLAE CVSVAPVTVETPPEPGATAFRLDTAQRSHLLAADAPSSAAWVQTLCRNAF
DOK2	GAVKQGFLYLQQQQTFGKKWRRFGASLYGGSDCALARLELQEGPEKPRRCEAARKVIRLSDCLRVA EAGGEASSPRDTSAFFLETKERLYLLAAPAAERGDWVQAICLLAF

FIG. 28

Streptococcus pyogenes Cas9

```
   1 mdkkysigld igtnsvgwav itddykvpsk kfkvlgntdr hsikknliga llfdsgetae
  61 atrlkrtarr rytrrknric ylqeifsnem akvddsffhr leesflveed kkherhpifg
 121 nivdevayhe kyptiyhlrk klvdstdkad lrliylalah mikfrghfli egdlnpdnsd
 181 vdklfiqlvq tynqlfeenp inasgvdaka ilsarlsksr rlenliaqlp gekknslfgn
 241 lialslgltp nfksnfdlae daklqlskdt ydddldnlla qigdqyadlf laaknlsdai
 301 llsdilrvnt eitkaplsas mikrydehhq dltllkalvr qqlpekykei ffdqskngya
 361 gyidggasqe efykfikpil ekmdgteell vklnredllr kqrtfdngsi phqihlgelh
 421 ailrrqedfy pflkdnreki ekiltfripy yvgplargns rfawmtrkse etitpwnfee
 481 vvdkgasaqs fiermtnfdk nlpnekvlpk hsllyeyftv yneltkvkyv tegmrkpafl
 541 sgeqkkaivd llfktnrkvt vkqlkedyfk kiecfdsvei sgvedrfnas lgtyhdllki
 601 ikdkdfldne enedilediv ltltlfedre mieerlktya hlfddkvmkq lkrrrytgwg
 661 rlsrklingi rdkqsgktil dflksdgfan rnfmqlihdd sltfkediqk aqvsgqgdsl
 721 hehianlags paikkgilqt vkvvdelvkv mgrhkpeniv iemarenqtt qkgqknsrer
 781 mkrieegike lgsqilkehp ventqlqnek lylyylqngr dmyvdqeldi nrlsdydvdh
 841 ivpqsflkdd sidnkvltrs dknrgksdnv pseevvkkmk nywrqllnak litqrkfdnl
 901 tkaergglse ldkagfikrq lvetrqitkh vaqildsrmn tkydendkli revkvitlks
 961 klvsdfrkdf qfykvreinn yhhahdayln avvgtalikk ypklesefvy gdykvydvrk
1021 miakseqeig katakyffys nimnffktei tlangeirkr plietngetg eivwdkgrdf
1081 atvrkvlsmp qvnivkktev qtggfskesi lpkrnsdkli arkkdwdpkk yggfdsptva
1141 ysvlvvakve kgkskklksv kellgitime rssfeknpid fleakgykev kkdliiklpk
1201 yslfelengr krmlasagel qkgnelalps kyvnflylas hyeklkgspe dneqkqlfve
1261 qhkhyldeii eqisefskrv iladanldkv lsaynkhrdk pireqaenii hlftltnlga
1321 paafkyfdtt idrkrytstk evldatlihq sitglyetri dlsqlggd
```

FIG. 29

Nuclear receptor coactivator 1 (NCOA1; SRC1)
Homo sapiens

```
   1 msglgdsssd panpdshkrk gspcdtlass tekrrreqen kyleelaell sanisdidsl
  61 svkpdkckil kktvdqiqlm krmeqekstt dddvqksdis sssqgvieke slgpllleal
 121 dgfffvvnce grivfvsenv tsylgynqee lmntsvysil hvgdhaefvk nllpkslvng
 181 vpwpqeatrr nshtfncrml ihppdepgte nqeacqryev mqcftvsqpk siqedgedfq
 241 scliciarrl prppaitgve sfmtkqdttg kiisidtssl raagrtgwed lvrkciyaff
 301 qpqgrepsya rqlfqevmtr gtasspsyrf ilndgtmlsa htkcklcypq spdmqpfimg
 361 ihiidrehsg lspqddtnsg msiprvnpsv npsispahgv arsstlppsn snmvstrinr
 421 qqssdlhsss hsnssnsqgs fgcspgsqiv anvalnqgqa ssqssnpsln lnnspmegtg
 481 islaqfmspr rqvtsglatr prmpnnsfpp nistlsspvg mtssacnnnn rsysnipvts
 541 lqgmnegpnn svgfsasspv lrqmssqnsp srlniqpaka eskdnkeias ilnemiqsdn
 601 sssdgkplds gllhnndrls dgdskysqts hklvqllttt aeqqlrhadi dtsckdvlsc
 661 tgtsnsasan ssggscpssh sslterhkil hrllqegsps dittlsvepd kkdsastsvs
 721 vtgqvqgnss ikleldaskk keskdhqllr ylldkdekdl rstpnlsldd vkvkvekkeq
 781 mdpcntnptp mtkptpeeik leaqsqftad ldqfdqllpt lekaaqlpgl cetdrmdgav
 841 tsvtikseil paslqsatar ptsrlnrlpe leleaidnqf gqpgtgdqip wtnntvtain
 901 qsksedqcis sqldellcpp ttvegrndek alleqlvsfl sgkdetelae ldralgidkl
 961 vqgggldvls erfppqqatp plimeerpnl ysqpysspsp tanlpspfqg mvrqkpslgt
1021 mpvqvtpprg afspgmgmqp rqtlnrppaa pnqlrlqlqq rlqgqqqlih qnrqailnqf
1081 aatapvginm rsgmqqqitp qpplnaqmla qrqrelysqq hrqrqliqqq ramlmrqqsf
1141 gnnlppssgl pvqmgnprlp qgapqqfpyp pnygtnpgtp pastspfsql aanpeaslan
1201 rnsmvsrgmt gniggqfgtg inpqmqqnvf qypgagmvpq geanfapsls pqssmvpmpi
1261 pppqssllqq tppasgyqsp dmkawqqgai gnnnvfsqav qnqptpaqpg vynnmsitvs
1321 maggntnvqn mnpmmaqmqm sslqmpgmnt vcpeqindpa lrhtglycnq lsstdllkte
1381 adgtqqvqqv qvfadvqctv nlvggdpyln qpgplgtqkp tsgpqtpqaq qksllqqllt
1441 e
```

FIG. 30

GRIP1 (NCOA2; TIF2; SRC2)
Homo sapiens

```
   1 msgmgentsd psraetrkrk ecpdqlgpsp krntekrnre qenkyieela elifanfndi
  61 dnfnfkpdkc ailketvkqi rqikeqekaa aanidevqks dvsstgqgvi dkdalgpmml
 121 ealdgfffvv nlegnvvfvs envtqylryn qeelmnksvy silhvgdhte fvknllpksi
 181 vnggswsqep prrnshtfnc rmlvkplpds eeeghdnqea hqkyetmqcf avsqpksike
 241 egedlqscli cvarrvpmke rpvlpssesf ttrqdlqgki tsldtstmra amkpgwedlv
 301 rrciqkfhaq hegesvsyak rhhhevlrqg lafsqiyrfs lsdgtlvaaq tksklirsqt
 361 tnepqlvisl hmlhreqnvc vmnpdltgqt mgkplnpiss nspahqalcs gnpgqdmtls
 421 sninfpingp keqmgmpmgr fggsggmnhv sgmqattpqg snyalkmnsp sqsspgmnpg
 481 qptsmlsprh rmspgvagsp rippsqfspa gslhspvgvc sstgnshsyt nsslnalqal
 541 seghgvslgs slaspdlkmg nlqnspvnmn ppplskmgsl dskdcfglyg epsegttgqa
 601 esschpgeqk etndpnlppa vsseradgqs rlhdskgqtk llqlltttksd qmepsplass
 661 lsdtnkdstg slpgsgsthg tslkekhkil hrllqdsssp vdlakltaea tgkdlsqess
 721 stapgsevti kqepvspkkk enallrylld kddtkdiglp eitpklerld sktdpasntk
 781 liamktekee msfepgdqpg seldnleeil ddlqnsqlpq lfpdtrpgap agsvdkqaii
 841 ndlmqltaen spvtpvgaqk talrisqstf nnprpgqlgr llpnqnlpld itlqsptgag
 901 pfppirnssp ysvipqpgmm gnqgmignqg nlgnsstgmi gnsasrptmp sgewapqssa
 961 vrvtcaatts amnrpvqggm irnpaasipm rpssqpgqrq tlqsqvmnig pselemnmgg
1021 pqysqqqapp nqtapwpesi lpidqasfas qnrqpfgssp ddllcphpaa espsdegall
1081 dqlylalrnf dgleeidral gipelvsqsq avdpeqfssq dsnimleqka pvfpqqyasq
1141 aqmaqgsysp mqdpnfhtmg qrpsyatlrm qprpglrptg lvqnqpnqlr lqlqhrlqaq
1201 qnrqplmnqi snvsnvnltl rpgvptqapi naqmlaqrqr eilnqhlrqr qmhqqqqvqq
1261 rtlmmrgqgl nmtpsmvaps qmpatmsnpr ipqanaqqfp fppnygisqq pdpgftgatt
1321 pqsplmsprm ahtqspmmqq sqanpayqap sdingwaqgn mggnsmfsqq spphfgqqan
1381 tsmysnnmni nvsmatntgg mssmnqmtgq ismtsvtsvp tsglssmqpe qvndpalrgg
1441 nlfpnqlpqm dmikqegdtt rkyc
```

FIG. 31

AIB1 (NCOA3; SRC3)
Homo sapiens

```
   1 msglgenldp lasdsrkrkl pcdtpgqglt csgekrrreq eskyieelae lisanlsdid
  61 nfnvkpdkca ilketvrqir qikeqgktis ndddvqkadv sstgqgvidk dslgplllqa
 121 ldgflfvvnr dgnivfvsen vtqylqykqe dlvntsvyni lheedrkdfl knlpkstvng
 181 vswtnetqrq kshtfncrml mktphdiled inaspemrqr yetmqcfals qprammeege
 241 dlqscmicva rrittgertf psnpesfitr hdlsgkvvni dtnslrssmr pgfediirrc
 301 iqrffslndg qswsqkrhyq eaylnghaet pvyrfsladg tivtaqtksk lfrnpvtndr
 361 hgfvsthflq reqngyrpnp npvgqgirpp magcnssvgg msmspnqglq mpssraygla
 421 dpsttgqmsg aryggssnia sltpgpgmqs pssyqnnnyg lnmsspphgs pglapnqqni
 481 misprnrgsp kiashqfspv agvhspmass gntgnhsfss sslsalqais egvgtslist
 541 lsspgpkldn spnmnitqps kvsnqdsksp lgfycdqnpv essmcqsnsr dhlsdkeske
 601 ssvegaenqr gpleskghkk llqlltcssd drghssltns pldssckess vsvtspsgvs
 661 sstsggvsst snmhgsllqe khrilhkllq ngnspaevak itaeatgkdt ssitscgdgn
 721 vvkqeqlspk kkennallry lldrddpsda lskelqpqve gvdnkmsqct sstipsssqe
 781 kdpkiktets eegsgdldnl dailgdltss dfynnsissn gshlgtkqqv fqgtnslglk
 841 ssqsvqsirp pynravslds pvsvgssppv knisafpmlp kqpmlggnpr mmdsqenygs
 901 smggpnrnvt vtqtpssgdw glpnskagrm epmnsnsmgr pggdyntslp rpalggsipt
 961 lplrsnsipg arpvlqqqqq mlqmrpgeip mgmganpygq aaasnqlgsw pdgmlsmeqv
1021 shgtqnrpll rnslddlvgp psnlegqsde ralldqlhtl lsntdatgle eidralgipe
1081 lvnqgqalep kqdafqgqea avmmdqkagl ygqtypaqgp pmqggfhlqg qspsfnsmmn
1141 qmnqqgnfpl qgmhpranim rprtntpkql rmqlqqrlqg qqflnqsrqa lelkmenpta
1201 ggaavmrpmm qpqqgflnaq mvaqrsrell shhfrqqrva mmmqqqqqqq qqqqqqqqqq
1261 qqqqqqqqqq qqtqafsppp nvtaspsmdg llaqptmpqa ppqqfpyqpn ygmgqqpdpa
1321 fgrvssppna mmssrmgpsq npmmqhpqaa siyqssemkg wpsgnlarns sfsqqqfahq
1381 gnpavysmvh mngssghmgq mnmmnpmpmsg mpmgpdqkyc
```

FIG. 32

PGC1a (PPARγ coactivator 1α; PPARGC1-α)
Homo sapiens

```
   1 mawdmcnqds esvwsdieca alvgedqplc pdlpeldlse ldvndldtds flgglkwcsd
  61 qseiisnqyn nepsnifeki deeneanlla vltetldslp vdedglpsfd altdgdvttd
 121 neaspssmpd gtpppqeaee psllkkllla pantqlsyne csglstqnha nhnhrirtnp
 181 aivktensws nkaksicqqq kpqrrpcsel lkylttnddp phtkptenrn ssrdkctskk
 241 kshtqsqsqh lqakpttlsl pltpespndp kgspfenkti ertlsvelsg tagltppttp
 301 phkanqdnpf raspklkssc ktvvpppskk prysessgtq gnnstkkgpe qselyaqlsk
 361 ssvltgghee rktkrpslrl fgdhdycqsi nskteilini sqelqdsrql enkdvssdwq
 421 gqicsstdsd qcylretlea skqvspcstr kqlqdqeira elnkhfghps qavfddeadk
 481 tgelrdsdfs neqfsklpmf insglamdgl fddsedesdk lsypwdgtqs yslfnvspsc
 541 ssfnspcrds vsppkslfsq rpqrmrsrsr sfsrhrscsr spysrsrsrs pgsrsssrsc
 601 yyyesshyrh rthrnsplyv rsrsrspysr rprydsyeey qherlkreey rreyekrese
 661 rakqrerqrq kaieerrviy vgkirpdttr telrdrfevf geieectvnl rddqdsygfi
 721 tyrytcdafa alengytlrr snetdfelyf cgrkqffksn yadldsnsdd fdpastksky
 781 dsldfdsllk eaqrslrr
```

FIG. 33

PGC1b (PPARγ coactivator 1β; PERC)
Homo sapiens

```
   1 magndcgall deelssffln yladtqgggs geeqlyadfp eldlsqldas dfdsatcfge
  61 lqwcpenset epnqyspdds elfqidsene allaeltktl ddipeddvgl aafpaldggd
 121 alsctsaspa pssappspap ekpsapapev delsllqkll latsyptsss dtqkegtawr
 181 qaglrsksqr pcvkadstqd kkapmmqsqs rsctelhkhl tsaqcclqdr glqppclqsp
 241 rlpakedkep gedcpspqpa pasprdslal gradpgapvs qedmqamvql irymhtyclp
 301 qrklppqtpe plpkacsnps qqvrsrpwsr hhskaswaef silrellaqd vlcdvskpyr
 361 latpvyaslt prsrprppkd sqaspgrpss veevriaasp kstgprpslr plrlevkrev
 421 rrparlqqqe eedeeeeeee eeeekeeeee wgrkrpgrgl pwtklgrkle ssvcpvrrsr
 481 rlnpelgpwl tfadeplvps epqgalpslc lapkaydver elgsptdeds gqdqqllrgp
 541 qipalespce sgcgdmdedp scpqlpprds prclmlalsq sdptfgkksf eqtltvelcg
 601 tagltppttp pykpteedpf kpdikhslgk eialslpspe glslkatpga ahklpkkhpe
 661 rsellshlrh ataqpasqag qkrpfscsfg dhdycqvlrp egvlqrkvlr swepsgvhle
 721 dwpqqgapwa eaqapgreed rscdagappk dstllrdhei rasltkhfgl letaleeedl
 781 asckspeydt vfedssssss essflpeeee eegeeeeedd eeedsgvspt csdhcpyqsp
 841 pskanrqlcs rsrssssgssp chswspatrr nfrcesrgpc sdrtpsirha rkrrekaige
 901 grvvyiqnls sdmssrelkr rfevfgeiee cevltrnrrg ekygfityrc sehaalsltk
 961 gaalrkrnep sfqlsygglr hfcwprytdy dsnseealpa sgkskyeamd fdsllkeaqq
1021 slh
```

FIG. 34

PRC (peroxisome proliferator-activated receptor gamma coactivator-related protein 1)

```
   1 maarrgrrdq vapppsggpg pdpgggargs gwgsrsqapy gtlgavsgge qvllheeagd
  61 sgfvslsrlg pslrdkdlem eelmlqdetl lgtmqsymda slisliedfg slgesrlsle
 121 dqnevsllta lteildnads enlspfdsip dsellvspre gsslhklltl srtpperdli
 181 tpvdplgpst gssrgsgvem slpdpswdfs ppsfletssp klpswrpprs rprwgqsppp
 241 qqrsdgeeee evasfsgqil ageldncvss ipdfpmhlac peeedkataa emavpaagde
 301 sisslselvr amhpyclpnl thlasledel qeqpddltlp egcvvleivg qaatagddle
 361 ipvvvrqvsp gprpvlldds letssalqll mptlesetea avpkvtlcse keglslnsee
 421 kldsacllkp revvepvvpk epqnppanaa pgsqrarkgr kkkskeqpaa cvegyarrlr
 481 sssrgqstvg tevtsqvdnl qkqpqeelqk esgplqgkgk prawarawaa alensspknl
 541 ersagqsspa kegpldlypk ladtiqtnpi pthlslvdsa qaspmpvdsv eadptavgpv
 601 lagpvpvdpg lvdlastsse lveplpaepv linpvladsa avdpavvpis dnlppvdavp
 661 sgpapvdlal vdpvpndltp vdpvlvksrp tdprrgavss alggsapqll vesesldppk
 721 tiipevkevv dslkiesqts atthearprp lslseyrrrr qqrqaeteer spqpptgkwp
 781 slpetptgla dipclvippa pakktalqrs petpleiclv pvgpspasps peppvskpva
 841 sspteqvpsq empllarpsp pvqsvspavp tppsmsaalp fpagglgmpp slpppplqpp
 901 slplsmgpvl pdpfthyapl pswpcyphvs psgypclppp ptvplvsgtp gayavpptcs
 961 vpwapppapv spysstctyg plgwgpgpqh apfwstvppp plppasigra vpqpkmesrg
1021 tpagppenvl plsmapplsl glpghgapqt eptkvevkpv pasphpkhkv salvqspqmk
1081 alacvsaegv tveepaserl kpetqetrpr ekpplpatka vptprqstvp klpavhparl
1141 rklsflptpr tqgsedvvqa fiseigieas dlsslleqfe kseakkecpp papadslavg
1201 nsggvdipqe krpldrlqap elanvagltp patpphqlwk plaavsllak akspkstaqe
1261 gtlkpegvte akhpaavrlq egvhgpsrvh vgsgdhdycv rsrtppkkmp alvipevgsr
1321 wnvkrhqdit ikpvlslgpa appppciaas repldhrtss eqadpsapcl apssllspea
1381 spcrndmntr tppepsakqr smrcyrkacr saspssqgwq grrgrnsrsv ssgsnrtsea
1441 ssssssssss srsrsrslsp phkrwrrssc sssgrsrrcs ssssssssss sssssssssr
1501 srsrspsprr rsdrrrryss yrshdhyqrq rvlqkeraie errvvfigki pgrmtrselk
1561 qrfsvfgeie ectihfrvqg dnygfvtyry aeeafaaies ghklrqadeq pfdlcfggrr
1621 qfckrsysdl dsnredfdpa pvkskfdsld fdtllkqaqk nlrr
```

FIG. 35

TRAP220 (TRIP-2; PPARGBP; PBP)
Homo sapiens

```
   1 mkaqgetees eklskmssll erlhakfnqn rpwsetiklv rqvmekrvvm ssgghqhlvs
  61 cletlqkalk vtslpamtdr lesiarqngl gshlsasgte cyitsdmfyv evqldpagql
 121 cdvkvahhge npvscpelvq qlreknfdef skhlkglvnl ynlpgdnklk tkmylalqsl
 181 eqdlskmaim ywkatnagpl dkilhgsvgy ltprsgghlm nlkyyvspsd llddktaspi
 241 ilhennvsrs lgmnasvtie gtsavyklpi aplimgshpv dnkwtpsfss itsansvdlp
 301 acfflkfpqp ipvsrafvqk lqnctgiplf etqptyaply elitqfelsk dpdpiplnhn
 361 mrfyaalpgq qhcyflnkda plpdgrslqg tlvskitfqh pgrvplilnl irhqvayntl
 421 igscvkrtil kedspgllqf evcplsesrf svsfqhpvnd slvcvvmdvq dsthvsckly
 481 kglsdalict ddfiakvvqr cmsipvtmra irrkaetiqa dtpalsliae tvedmvkknl
 541 ppasspgygm ttgnnpmsgt ttptntfpgg pittlfnmsm sikdrhesvg hgedfskvsq
 601 npiltsllqi tgnggstigs sptpphhtpp pvssmagntk nhpmlmnllk dnpaqdfstl
 661 ygssplerqn sssgsprmei csgsnktkkk kssrlppekp khqteddfqr elfsmdvdsq
 721 npifdvnmta dtldtphitp apsqcstppt typqpvphpq psiqrmvrls ssdsigpdvt
 781 dilsdiaeea sklpstsddc paigtplrds ssseghsqstl fdsdvfqtnn nenpytdpad
 841 liadaagsps sdsptnhffh dgvdfnpdll nsqsqsgfge eyfdessqsg dnddfkgfas
 901 qalntlgvpm lggdngetkf kgnnqadtvd fsiisvagka lapadlmehh sgsqgplltt
 961 gdlgkektqk rvkegngtsn stlsgpglds kpgkrsrtps ndgkskdkpp krkkadtegk
1021 spshsssnrp ftpptstggs kspgsagrsq tppgvatppi pkitiqipkg tvmvgkpssh
1081 sqytssgsvs ssgskshhsh sssssssast sgkmksskse gsssskslsss myssqgssgs
1141 sqsknssqsg gkpgsspitk hglssgssst kmkpqgkpss lmnpslskpn ispshsrppg
1201 gsdklaspmk pvpgtppssk akspissgsg gshmsgtsss sgmksssglg ssgslsqktp
1261 pssnsctass ssfsssgssm sssqnqhgss kgkspsrnkk psltavidkl khgvvtsgpg
1321 gedpldgqmg vstnsshpm sskhnmsgge fqgkreksdk dkskvstsgs svdsskktse
1381 sknvgstgva kiiiskhdgg spsikakvtl qkpgessgeg lrpqmasskn ygsplisgst
1441 pkhergspsh skspaytpqn ldsesesgss iaeksyqnsp ssddgirplp eystekhkkh
1501 kkekkkvkdk drdrdrdkdr dkkkshsikp eswskspiss dqslsmtsnt ilsadrpsrl
1561 spdfmigeed ddlmdvalig n
```

FIG. 36A

ASC2 (NCOA6; RAP250; PRIP; AIB3; NRC)
Homo sapiens

```
   1 mvlddlpnle diytslcsst medsemdfds gledddtksd siledstifv afkgniddkd
  61 fkwkldailk nvpnllhmes sklkvqkvep wnsvrvtfni preaaerlri laqsnnqqlr
 121 dlgilsvqie gegainlala qnrsqdvrmn gpmgagnsvr meagfpmasg pgiirmnnpa
 181 tvmippggnv sssmmapgpn pelqprtprp asqsdamdpl lsglhiqqqs hpsgslapph
 241 hpmqpvsvnr qmnpanfpql qqqqqqqqqq qqqqqqqqqq qqqqqlqarp pqqhqqqqpq
 301 girpqftapt qvpvppgwnq lpsgalqppp aqgslgtmta nqgwkkaplp gpmqqqlqar
 361 pslatvqtps hppppypfgs qqasqahtnf pqmsnpgqft apqmkslqgg psrvptplqq
 421 phltnkspas spssfqqgsp assptvnqtq qqmgprppqn nplpqgfqqp vsspgrnpmv
 481 qqgnvppnfm vmqqqppnqg pqslhpglgg mpkrlppgfs agqanpnfmq gqvpsttatt
 541 pgnsgapqlq anqnvqhagg qgagppqnqm qvshgppnmm qpslmgihgn mnnqqagtsg
 601 vpqvnlsnmq gqpqqgppsq lmgmhqqivp sqgqmvqqqg tlnpqnpmil sraqlmpqgq
 661 mmvnppsqnl gpspqrmtpp kqmlsqqgpq mmaphnqmmg pqgqvllqqn pmieqimtnq
 721 mqgnkqqfnt qnqsnvmpgp aqimrgptpn mqgnmvqftg qmsgqmlpqq gpvnnspsqv
 781 mgiqgqvlrp pgpsphmaqq hgdpattann dvslsqmmpd vsiqqtnmvp phvqamqgns
 841 asgnhfsghg msfnapfsga pngnqmscgq npgfpvnkdv tltspllvnl lqsdisaghf
 901 gvnnkqnntn ankpkkkkpp rkkknsqqdl ntpdtrpagl eeadqpplpg eqginldnsg
 961 pklpefsnrp pgypsqpveq rplqqmppql mqhvapppqp pqqqpqpqlp qqqqppppsq
1021 pqsqqqqqqq qqmmmmlmmq qdpksvrlpv sqnvhpprgp lnpdsqrmpm qqsgsvpvmv
1081 slqgpasvpp spdkqrmpmp vntplgsnsr kmvyqespqn psssplaema slpeasgsea
1141 psvpggpnnm pshvvlpqnq lmmtgpkpgp splsatqgat pqqppvnslp sshghhfpnv
1201 aaptqtsrpk tpnrasprpy ypqtpnnrpp stepseisls perlnasiag lfppqinipl
1261 pprpnlnrgf dqqglnpttl kaigqapsnl tmnpsnfatp qthkldsvvv nsgkqsnsga
1321 tkraspsnsr rsspgssrkt tpspgrqnsk apkltlasqt naallqnvel prnvlvsptp
1381 lanppvpgsf pnnsglnpqn stvsvaavgg vvednkesln vpqdsdcqns qsrkeqvnie
1441 lkavpaqevk mvvpedqskk dgqpsdpnkl psveenknlv spamreapts lsqlldnsga
1501 pnvtikppgl tdlevtppvv sgedlkkasv iptlqdlsss kepsnslnlp hsnelcsslv
1561 hpelsevssn vapsippvms rpvssssist plppnqitvf vtsnpittsa ntsaalpthl
1621 qsalmstvvt mpnagskvmv segqsaaqsn arpqfitpvf insssiiqvm kgsqpstipa
1681 aplttnsglm ppsvavvgpl hipqnikfss apvppnalss spapniqtgr plvlssratp
```

FIG. 36B

```
1741 vqlpsppcts spvvpshppv qqvkelnpde aspqvntsad qntlpssqst tmvsplltns
1801 pgssgnrrsp vssskgkgkv dkigqilltk ackkvtgsle kgeeqygadg etegqgldtt
1861 apglmgteql steldsktpt ppaptllkmt sspvgpgtas agpslpggal ptsvrsivtt
1921 lvpselisav pttksnhggi aseslagglv eekvgshpel lpsiapsqnl vsketsttal
1981 qasvarpele vnaaivsgqs sepkeiveks kipgrrnsrt eeptvasesv enghrkrssr
2041 pasassstkd itsavqskrr ksk
```

FIG. 37A

CBP (RSTS; KAT3A)
Homo sapiens

```
   1 maenlldgpp npkraklssp gfsandstdf gslfdlendl pdelipngge lgllnsgnlv
  61 pdaaskhkql sellrggsgs sinpgignvs asspvqqglg gqaqgqpnsa nmaslsamgk
 121 splsqgdssa pslpkqaast sgptpaasqa lnpqaqkqvg latsspatsq tgpgicmnan
 181 fnqthpglln snsghslinq asqgqaqvmn gslgaagrgr gagmpyptpa mqgasssvla
 241 etltqvspqm tghaglntaq aggmakmgit gntspfgqpf sqaggqpmga tgvnpqlask
 301 qsmvnslptf ptdikntsvt nvpnmsqmqt svgivptqai atgptadpek rkliqqqlvl
 361 llhahkcqrr eqangevrac slphcrtmkn vlnhmthcqa gkacqvahca ssrqiishwk
 421 nctrhdcpvc lplknasdkr nqqtilgspa sgiqntigsv gtgqqnatsl snpnpidpss
 481 mqrayaalgl pymnqpqtql qpqvpgqqpa qpqthqqmrt lnplgnnpmn ipaggittdq
 541 qppnlisesa lptslgatnp lmndgsnsgn igtlstipta appsstgvrk gwhehvtqdl
 601 rshlvhklvq aifptpdpaa lkdrrmenlv ayakkvegdm yesansrdey yhllaekiyk
 661 iqkeleekrr srlhkqgilg nqpalpapga qppvipqaqp vrppngplsl pvnrmqvsqg
 721 mnsfnpmslg nvqlpqapmg praaspmnhs vqmnsmgsvp gmaispsrmp qppnmmgaht
 781 nnmmaqapaq sqflpqnqfp sssgamsvgm gqppaqtgvs qgqvpgaalp nplnmlgpqa
 841 sqlpcppvtq splhptpppa staagmpslq httppgmtpp qpaaptqpst pvsssgqtpt
 901 ptpgsvpsat qtqstptvqa aaqaqvtpqp qtpvqppsva tpqssqqqpt pvhaqppgtp
 961 lsqaaasidn rvptpssvas aetnsqqpgp dvpvlemkte tqaedtepdp geskgeprse
1021 mmeedlqgas qvkeetdiae qksepmevde kkpevkvevk eeeesssngt asqstspsqp
1081 rkkifkpeel rqalmptlea lyrqdpeslp frqpvdpqll gipdyfdivk npmdlstikr
1141 kldtgqyqep wqyvddvwlm fnnawlynrk tsrvykfcsk laevfeqeid pvmqslgycc
1201 grkyefspqt lccygkqlct iprdaayysy qnryhfcekc fteiqgenvt lgddpsqpqt
1261 tiskdqfekk kndtldpepf vdckecgrkm hqicvlhydi iwpsgfvcdn clkktgrprk
1321 enkfsakrlq ttrlgnhled rvnkflrrqn hpeagevfvr vvassdktve vkpgmksrfv
1381 dsgemsesfp yrtkalfafe eidgvdvcff gmhvqeygsd cpppntrrvy isyldsihff
1441 rprclrtavy heiligyley vkklgyvtgh iwacppsegd dyifhchppd qkipkpkrlq
1501 ewykkmldka faeriihdyk difkqatedr ltsakelpyf egdfwpnvle esikeleqee
1561 eerkkeesta asettegsqg dsknakkknn kktnknkssi srankkkpsm pnvsndlsqk
1621 lyatmekhke vffvihlhag pvintlppiv dpdpllscdl mdgrdafltl ardkhwefss
1681 lrrskwstlc mlvelhtqgq drfvytcnec khhvetrwhc tvcedydlci ncyntkshah
1741 kmvkwglgld degssqgepq skspqesrrl siqrciqslv hacqcrnanc slpscqkmkr
```

FIG. 37B

```
1801 vvqhtkgckr ktnggcpvck qlialccyha khcqenkcpv pfclnikhkl rqqqiqhrlq
1861 qaqlmrrrma tmntrnvpqq slpsptsapp gtptqqpstp qtpqppaqpq pspvsmspag
1921 fpsvartqpp ttvstgkpts qvpappppaq pppaaveaar qiereaqqqq hlyrvninns
1981 mppgrtgmgt pgsqmapvsl nvprpnqvsg pvmpsmppgq wqqaplpqqq pmpglprpvi
2041 smqaqaavag prmpsvqppr sispsalqdl lrtlkspssp qqqqqvlnil ksnpqlmaaf
2101 ikqrtakyva nqpgmqpqpg lqsqpgmqpq pgmhqqpslq nlnamqagvp rpgvppqqqa
2161 mgglnpqgqa lnimnpghnp nmasmnpqyr emlrrqllqq qqqqqqqqqq qqqqqqgsag
2221 maggmaghgq fqqpqgpggy ppamqqqqrm qqhlplqgss mgqmaaqmgq lgqmgqpglg
2281 adstpniqqa lqqrilqqqq mkqqiqspgq pnpmspqqhm lsgqpqashl pgqqiatsls
2341 nqvrspapvq sprpqsqpph sspspriqpq psphhvspqt gsphpglavt massidqghl
2401 gnpeqsamlp qlntpsrsal sselslvgdt tgdtlekfve gl
```

FIG. 38A

P300 (KAT3B; RSTS2)
Homo sapiens

```
   1 maenvvepgp psakrpklss palsasasdg tdfgslfdle hdlpdelins telgltnggd
  61 inqlqtslgm vqdaaskhkq lsellrsgss pnlnmgvggp gqvmasqaqq sspglglins
 121 mvkspmtqag ltspnmgmgt sgpnqgptqs tgmmnspvnq pamgmntgmn agmnpgmlaa
 181 gngqgimpnq vmngsigagr grqnmqypnp gmgsagnllt eplqqgspqm ggqtglrgpq
 241 plkmgmmnnp npygspytqn pgqqigasgl glqiqtktvl snnlspfamd kkavpgggmp
 301 nmgqqpapqv qqpglvtpva qgmgsgahta dpekrkliqq qlvlllhahk cqrreqange
 361 vrqcnlphcr tmknvlnhmt hcqsgkscqv ahcassrqii shwknctrhd cpvclplkna
 421 gdkrnqqpil tgapvglgnp sslgvgqqsa pnlstvsqid pssierayaa lglpyqvnqm
 481 ptqpqvqakn qqnqqpgqsp qgmrpmsnms aspmgvnggv gvqtpsllsd smlhsainsq
 541 npmmsenasv pslgpmptaa qpsttgirkq wheditqdlr nhlvhklvqa ifptpdpaal
 601 kdrrmenlva yarkvegdmy esannraeyy hllaekiyki qkeleekrrt rlqkqnmlpn
 661 aagmvpvsmn pgpnmgqpqp gmtsngplpd psmirgsvpn qmmpritpqs glnqfgqmsm
 721 aqppivprqt pplqhhgqla qpgalnppmg ygprmqqpsn qgqflpqtqf psqgmnvtni
 781 plapssgqap vsqaqmssss cpvnspimpp gsqgshihcp qlpqpalhqn spspvpsrtp
 841 tphhtppsig aqqppattip apvptppamp pgpqsqalhp pprqtptppt tqlpqqvqps
 901 lpaapsadqp qqqprsqqst aasvptptap llppqpatpl sqpavsiegq vsnppstsst
 961 evnsqaiaek qpsqevkmea kmevdqpepa dtqpedises kvedckmest eteerstelk
1021 teikeeedqp stsatqsspa pgqskkkifk peelrqalmp tlealyrqdp eslpfrqpvd
1081 pqilgipdyf divkspmdls tikrkldtgq yqepwqyvdd iwlmfnnawl ynrktsrvyk
1141 ycsklsevfe qeidpvmqsl gyccgrklef spqtlccygk qlctiprdat yysyqnryhf
1201 cekcfneiqg esvslgddps qpqttinkeq fskrkndtld pelfvectec grkmhqicvl
1261 hheiiwpagf vcdgclkksa rtrkenkfsa krlpstrlgt flenrvndfl rrqnhpesge
1321 vtvrvvhasd ktvevkpgmk arfvdsgema esfpyrtkal fafeeidgvd lcffgmhvqe
1381 ygsdcpppnq rrvyisylds vhffrpkclr tavyheilig yleyvkklgy ttghiwacpp
1441 segddyifhc hppdqkipkp krlqewykkm ldkavseriv hdykdifkqa tedrltsake
1501 lpyfegdfwp nvleesikel eqeeeerkre entsnestdv tkgdsknakk knnkktsknk
1561 sslsrgnkkk pgmpnvsndl sqklyatmek hkevffvirl iagpaanslp pivdpdplip
1621 cdlmdgrdaf ltlardkhle fsslrraqws tmcmlvelht qsqdrfvytc neckhhvetr
1681 whctvcedyd lcitcyntkn hdhkmeklgl glddesnnqq aaatqspgds rrlsiqrciq
```

FIG. 38B

```
1741 slvhacqcrn ancslpscqk mkrvvqhtkg ckrktnggcp ickqlialcc yhakhcqenk
1801 cpvpfclnik qklrqqqlqh rlqqaqmlrr rmasmqrtgv vgqqqglpsp tpatpttptg
1861 qqpttpqtpq ptsqpqptpp nsmppylprt qaagpvsqgk aagqvtpptp pqtaqpplpg
1921 pppaavemam qiqraaetqr qmahvqifqr piqhqmppmt pmapmgmnpp pmtrgpsghl
1981 epgmgptgmq qqppwsqggl pqpqqlqsgm prpammsvaq hgqplnmapq pglgqvgisp
2041 lkpgtvsqqa lqnllrtlrs pssplqqqqv lsilhanpql laafikqraa kyansnpqpi
2101 pgqpgmpqgq pglqpptmpg qqgvhsnpam qnmnpmqagv qraglpqqqp qqqlqppmgg
2161 mspqaqqmnm nhntmpsqfr dilrrqqmmq qqqqqgagpg igpgmanhnq fqqpqgvgyp
2221 pqqqqrmqhh mqqmqqgnmg qigqlpqalg aeagaslqay qqrllqqqmg spvqpnpmsp
2281 qqhmlpnqaq sphlqgqqip nslsnqvrsp qpvpsprpqs qpphsspspr mqpqpsphhv
2341 spqtssphpg lvaaqanpme qghfaspdqn smlsqlasnp qmanlhgasa tdlglstdns
2401 dlnsnlsqst ldih
```

FIG. 39

CIA (NCOA5;
Homo sapiens

```
  1 mntapsrpsp trrdpygfgd srdsrrdrsp irgsprrepr dgrngrdard srdirdprdl
 61 rdhrhsrdlr dhrdsrsvrd vrdvrdlrdf rdlrdsrdfr dqrdpmydry rdmrdsrdpm
121 yrregsydry lrmddycrrk ddsyfdryrd sfdgrgppgp esqsrakerl kreerrreel
181 yrqyfeeiqr rfdaerpvdc svivvnkqtk dyaesvgrkv rdlgmvvdli flntevslsq
241 aledvsrggs pfaivitqqh qihrsctvni mfgtpqehrn mpqadamvlv arnyerykne
301 crekereeia rqaakmadea ilqererggp eegvrgghpp aiqslinlla dnryltaeet
361 dkiinylrer kerlmrsstd slpgpisrqp lgatsgaslk tqpssqplqs gqvlpsatpt
421 psapptsqqe lqakilslfn sgtvtansss aspsvaagnt pnqnfstaan sqpqqrsqas
481 gnqppsilgq ggsaqnmgpr pgapsqglfg qpssrlapas nmtsqrpvss tginfdnpsv
541 qkaldtliqs gpalshlvsq ttaqmgqpqa pmgsyqrhy
```

FIG. 40

ARA70 (NCOA4; PTC3; RFG; ELE1)
Homo sapiens

```
  1 mntfqdqsgs ssnrepllrc sdarrdlela iggvlraeqq ikdnlrevka qihscisrhl
 61 eclrsrevwl yeqvdliyql keetlqqqaq qlysllgqfn clthqlectq nkdlanqvsv
121 clerlgsltl kpedstvllf eadtitlrqt ittfgslkti qipehlmaha ssanigpfle
181 krgcismpeq ksasgivavp fsewllgskp asgyqapyip stdpqdwltq kqtlensqts
241 sracnffnnv ggnlkglenw llksekssyq kcnshsttss fsiemekvgd qelpdqdemd
301 lsdwlvtpqe shklrkpeng sretsekfkl lfqsynvndw lvktdsctnc qgnqpkgvei
361 enlgnlkcln dhleakkpls tpsmvtedwl vqnhqdpckv eevcranepc tsfaecvcde
421 ncekealykw llkkegkdkn gmpvepkpep ekhkdslnmw lcprkevieq tkapkamtps
481 riadsfqvik nsplsewlir ppykegspke vpgtedragk qkfkspmnts wcsfntadwv
541 lpgkkmgnls qlssgedkwl lrkkaqevll nsplqeehnf ppdhyglpav cdlfacmqlk
601 vdkekwlyrt plqm
```

FIG. 41

TIF1 (RNF82; PTC6; HTIF1)
Homo sapiens

```
   1 mevavekava aaaaasaaas ggpsaapsge neaesrqgpd serggeaarl nlldtcavch
  61 qniqsrapkl lpclhsfcqr clpapqrylm lpapmlgsae tpppvpapgs pvsgsspfat
 121 qvgvircpvc sqecaerhii dnffvkdtte vpsstveksn qvctscedna eangfcvecv
 181 ewlcktcira hqrvkftkdh tvrqkeevsp eavgvtsqrp vfcpfhkkeq lklycetcdk
 241 ltcrdcqlle hkehryqfie eafqnqkvii dtlitklmek tkyikftgnq iqnriievnq
 301 nqkqveqdik vaiftlmvei nkkgkallhq leslakdhrm klmqqqqeva glskqlehvm
 361 hfskwavssg sstallyskr lityrlrhll rarcdaspvt nntiqfhcdp sfwaqniinl
 421 gslviedkes qpqmpkqnpv veqnsqppsg lssnqlskfp tqislaqlrl qhmqqqqppp
 481 rlinfqnhsp kpngpvlpph pqqlryppnq niprqaikpn plqmaflaqq aikqwqissg
 541 qgtpsttnst sstpssptit saagydgkaf gspmidlssp vggsynlpsl pdidcsstim
 601 ldnivrkdtn idhgqprpps nrtvqspnss vpspglagpv tmtsvhppir spsassvgsr
 661 gssgssskpa gadsthkvpv vmlepirikq ensgppenyd fpvvivkqes deesrpqnan
 721 yprsiltsil lnssqsstse etvlrsdapd stgdqpglhq dnssngksew ldpsqksplh
 781 vgetrkeddp nedwcavcqn ggellccekc pkvfhlschv ptltnfpsge wictfcrdls
 841 kpeveydcda pshnsekkkt eglvkltpid krkcerlllf lychemslaf qdpvpltvpd
 901 yykiiknpmd lstikkrlqe dysmyskped fvadfrlifq ncaefnepds evanagikle
 961 nyfeellknl ypekrfpkpe frnesednkf sddsdddfvq prkkrlksie erqllk
```

FIG. 42A

NSD1 (ARA267; SOTOS1; KMT3B)
Homo sapiens

```
   1 mdqtcelprr ncllpfsnpv nldapedkds pfgngqsnfs eplngctmql stvsgtsqna
  61 ygqdspscyi plrrlqdlas minveylngs adgsesfqdp eksdsraqtp ivctslspgg
 121 ptalamkqep scnnspelqv kvtktikngf lhfenftcvd dadvdsemdp eqpvtedesi
 181 eeifeetqtn atcnyetkse ngvkvamgse qdstpesrhg avkspflpla pqtetqknkq
 241 rnevdgsnek aallpapfsl qdtnitieeq lnsinlsfqd dpdssststlg nmlelpgtss
 301 sstsqelpfc qpkkkstplk yevgdliwak fkrrpwwpcr icsdplinth skmkvsnrrp
 361 yrqyyveafg dpserawvag kaivmfegrh qfeelpvlrr rgkqkekgyr hkvpqkilsk
 421 weasvglaeq ydvpkgsknr kcipgsikld seedmpfedc tndpesehdl llngclksla
 481 fdsehsadek ekpcaksrar kssdnpkrts vkkghiqfea hkderrgkip enlglnfisg
 541 disdtqasne lsriansltg sntapgsflf sscgkntakk efetsngdsl lglpegalis
 601 kcsreknkpq rslvcgskvk lcyigagdee krsdsisict tsddgssdld piehssesdn
 661 svleipdafd rtenmlsmqk nekikysrfa atntrvkakq kplisnshtd hlmgctksae
 721 pgtetsqvnl sdlkastlvh kpqsdftnda lspkfnlsss issenslikg gaanqallhs
 781 kskqpkfrsi kckhkenpvm aeppvineec slkccssdtk gsplasisks gkvdglklln
 841 nmhektrdss dietavvkhv lselkelsyr slgedvsdsg tskpskpllf ssassqnhip
 901 iepdykfstl lmmlkdmhds ktkeqrlmta qnlvsyrspg rgdcstnspv gvskvlvsgg
 961 sthnsekkgd gtqnsanpsp sggdsalsge lsaslpglls dkrdlpasgk srsdcvtrrn
1021 cgrskpsskl rdafsaqmvk ntvnrkalkt erkrklnqlp svtldavlqg drerggslrg
1081 gaedpskedp lqimghltse dgdhfsdvhf dskvkqsdpg kisekglsfe ngkgpeldsv
1141 mnsendelng vnqvvpkkrw qrlnqrrtkp rkrmnrfkek ensecafrvl lpsdpvqegr
1201 defpehrtps asileeplte qnhadcldsa gprlnvcdks sasigdmeke pgipsltpqa
1261 elpepavrse kkrlrkpskw lleyteeydq ifapkkkqkk vqeqvhkvss rceeesllar
1321 grssaqnkqv denslistke eppvlereap flegplaqse lggghaelpq ltlsvpvape
1381 vsprpalese ellvktpgny eskrqrkptk kllesndldp gfmpkkgdlg lskkcyeagh
1441 lengitesca tsyskdfggg ttkifdkprk rkrqrhaaak mqckkvkndd sskeipgseg
1501 elmphrtats pketveegve hdpgmpaskk mqgergggaa lkenvcqnce klgelllcea
1561 qccgafhlec lgltemprgk ficnecrtgi htcfvckqsg edvkrcllpl cgkfyheecv
1621 qkypptvmqn kgfrcslhic itchaanpan vsaskgrlmr cvrcpvayha ndfclaagsk
1681 ilasnsiicp nhftprrgcr nhehvnvswc fvcseggsll ccdscpaafh reclnidipe
```

FIG. 42B

```
1741 gnwycndcka gkkphyreiv wvkvgryrww paeichprav psnidkmrhd vgefpvlffg
1801 sndylwthqa rvfpymegdv sskdkmgkgv dqtykkalqe aaarfeelka qkelrqlqed
1861 rkndkkpppy khikvnrpig rvqiftadls eiprcnckat denpcgidse cinrmllyec
1921 hptvcpaggr cqnqcfskrq ypeveifrtl qrgwglrtkt dikkgefvne yvgelideee
1981 crariryaqe hditnfymlt ldkdriidag pkgnyarfmn hccqpncetq kwsvngdtrv
2041 glfalsdika gteltfnynl eclgngktvc kcgapncsgf lgvrpknqpi ateekskkfk
2101 kkqqgkrrtq geitkerede cfscgdagql vsckkpgcpk vyhadclnlt krpagkwecp
2161 whqcdicgke aasfcemcps sfckqhregm lfiskldgrl sctehdpcgp nplepgeire
2221 yvpppvplpp gpsthlaeqs tgmaaqapkm sdkppadtnq mlslskkala gtcqrpllpe
2281 rplertdsrp qpldkvrdla gsgtksqslv ssqrpldrpp avagprpqls dkpspvtsps
2341 sspsvrsqpl erplgtadpr ldksigaasp rpqslektsv ptglrlpppd rllitsspkp
2401 qtsdrptdkp haslsqrlpp pekvlsavvq tlvakekalr pvdqntqskn raalvmdlid
2461 ltprqkeraa sphqvtpqad ekmpvlesss wpaskglghm pravekgcvs dplqtsgkaa
2521 apsedpwqav ksltqarlls qppakaflye pttqasgras agaeqtpgpl sqspglvkqa
2581 kqmvggqqlp alaaksgqsf rslgkapasl pteekklvtt eqspwalgka ssraglwpiv
2641 agqtlaqscw sagstqtlaq tcwslgrgqd pkpeqntlpa lnqapsshkc aeseqk
```

FIG. 43

SMAP

Homo sapiens

```
   1 matgtgkhkl lstgptepws irekiclass vmrsgdqnwv svsraikpfa epgrppdwfs
  61 qkhcasqyse llettetpkr krgekgevve tvedvivrkl taerveelkk viketqeryr
 121 rlkrdaeliq aghmdsrlde lcndiatkkk leeeeaevkr katdaayqar qavktpprrl
 181 ptvmvrspid saspggdypl gdltpttmee atsgvtpgtl pstpvtsfpg ipdtlppgsa
 241 pleapmtpvt ddspqkkmlg qkatpppspl lsellkkgsl lptsprlvne semavasghl
 301 nstgvllevg gvlpmihgge iqqtpntvaa spaasgaptl srlleagptq fttplasftt
 361 vaseppvklv pppvesvsqa tivmmpalpa pssapavstt esvapvsqpd ncvpmeavgd
 421 phtvtvsmds seismiinsi keecfrsgva eapvgskaps idgkeeldla ekmdiavsyt
 481 geeldfetvg diiaiiedkv ddhpevldva aveaalsfce enddpqslpg pwehpiqqer
 541 dkpvplpape mtvkqerldf eetenkgihe lvdirepsae ikvepaepep visgaeivag
 601 vvpatsmepp elrsqdldee lgstaageiv eadvaigkgd etpltnvkte aspesmlsps
 661 hgsnpiedpl eaetqhkfem sdslkeesgt ifgsqikdap gedeeedgvs eaasleepke
 721 edqgegylse mdneppvses ddgfsihnat lqshtladsi psspassqfs vcsedqeaiq
 781 aqkiwkkaim lvwraaanhr yanvflqpvt ddiapgyhsi vqrpmdlsti kknienglir
 841 staefqrdim lmfqnavmyn ssdhdvyhma vemqrdvleq iqqflatqli mqtsesgisa
 901 kslrgrdstr kqdasekdsv pmgspaflls lfdggtrgrr caieadmkmk k
```

FIG. 44

Tip60 (HTATIP; ESA1; PLIP; Tat ineracting protein; CPLA2)
Homo sapiens

```
  1 maevgeiieg crlpvlrrnq dnedewplae ilsvkdisgr klfyvhyidf nkrldewvth
 61 erldlkkiqf pkkeaktptk nglpgsrpgs perevpasaq asgktlpipv qitlrfnlpk
121 ereaipggep dqplsssscl qpnhrstkrk vevvspatpv psetapasvf pqngaarrav
181 aaqpgrkrks nclgtdedsq dssdgipsap rmtgslvsdr shddivtrmk niecielgrh
241 rlkpwyfspy pqelttlpvl ylcefclkyg rslkclqrhl tkcdlrhppg neiyrkgtis
301 ffeidgrknk sysqnlclla kcfldhktly ydtdpflfyv mteydckgfh ivgyfskeke
361 stedynvaci ltlppyqrrg ygklliefsy elskvegktg tpekplsdlg llsyrsywsq
421 tileilmglk sesgerpqit ineiseitsi kkedvistlq ylnlinyykg qyiltlsedi
481 vdgheramlk rllridskcl hftpkdwskr gkw
```

FIG. 45

ERAP140 (NCOA7)
Homo sapiens

```
  1 mdtkeekker kqsyfarlkk kkqakqnaet asavatrtht gkednntvvl epdkcniave
 61 eeymtdekkk rksnqlkeir rtelkryysi ddnqnkthdk kekkmvvqkp hgtmeytagn
121 qdtlnsialk fnitpnklve lnklfthtiv pgqvlfvpda nspsstlrls ssspgatvsp
181 sssdaeydkl pdadlarkal kpiervlsst seedepgvvk flkmncryft dgkgvvggvm
241 ivtpnnimfd phksdplvie ngceeyglic pmeevvsial yndishmkik dalpsdlpqd
301 lcplyrpgew edlasekdin pfskfksink ekrqqngeki mtsdsrpivp lekstghtpt
361 kpsgssvsek lkkldssret shgsptvtkl skepsdtssa festakenfl gedddfvdle
421 elssqtgggm hkkdtlkecl sldpeerkka esqinnsave mqvqsalafl gtendvelkg
481 aldletcekq dimpevdkqs gspesrvent lnihedldkv klieyyltkn kegpqvsenl
541 qktelsdgks iepggiditl ssslsqagdp itegnkepdk twvkkgeplp vklnsstean
601 vikealdssl estldnscqg aqmdnksevq lwllkriqvp iedilpskee ksktppmflc
661 ikvgkpmrks fathtaamvq qygkrrkqpe ywfavprerv dhlytffvqw spdvygkdak
721 eqgfvvveke elnmidnffs epttksweii tveeakrrks tcsyyededе evlpvlrphs
781 allenmhieq larrlparvq gypwrlayst lehgtslktl yrksasldsp vllvikdmdn
841 qifgayathp fkfsdhyygt getflytfsp hfkvfkwsge nsyfingdis slelgggggr
901 fglwldadly hgrsnscstf nndilskked fivqdlevwa fd
```

FIG. 46

Nix1 (NIP3L; BNIP3H; BNIP3a)
Homo sapiens

```
  1 mlfifplslp wrpscwkesc stgqrqagrs redsvtppps spwptppaga mstkqearrd
 61 egeartrgqe aqlrdrahls qqrrlkqatq flhkdsadll pldslkrlgt skdlqprsvi
121 qrrlvegnpn wlqgepprmq dlihgqesrr ktsrteipal lvnckcqdql lrvavdtgtq
181 ynrisagcls rlglekrvlk asagdlapgp ptqveqlelq lgqetvvcsa qvvdaespef
241 clglqtllsl kccidlehgv lrlkapfsel pflplyqepg q
```

FIG. 47

LCoR (MLR2)
Homo sapiens

```
  1 mqrmiqqfaa eytsknsstq dpsqpnstkn qslpkaspvt tsptaattqn pvlskllmad
 61 qdspldltvr ksqsepseqd gvldlstkks pcagstslsh spgcsstqgn grpgrpsqyr
121 pdglrsgdgv pprslqdgtr egfghstslk vplarslqis eellsrnqls taaslgpsgl
181 qnhgqhllls reaswakphy efnlsrmkfr gngalsnisd lpflaensaf pkmalqakqd
241 gkkdvshssp vdlkipqvrg mdlswesrtg dqysysslvm gsqtesalsk klrailpkqs
301 rksmldagpd swgsdaeqst sgqpyptsdq egdpgskqpr kkrgryrqyn seileeaisv
361 vmsgkmsvsk aqsiygiphs tleykvkerl gtlknppkkk mklmrsegpd vsvkieldpq
421 geaaqsanes kne
```

FIG. 48A

N-CoR (TRAC1; NCOR1)
Homo sapiens

```
   1 msssgyppnq gafsteqsry pphsvqytfp ntrhqqefav pdyrsshlev sqasqllqqq
  61 qqqqlrrrps llsefhpgsd rpqerrtsye pfhpgpspvd hdsleskrpr leqvsdshfq
 121 rvsaavlplv hplpeglras adakkdpafg gkheapsspi sgqpcgddqn aspsklskee
 181 liqsmdrvdr eiakveqqil klkkkqqqle eeaakppepe kpvspppveq khrsivqiiy
 241 denrkkaeea hkifeglgpk velplynqps dtkvyhenik tnqvmrkkli lffkrrnhar
 301 kqreqkicqr ydqlmeawek kvdriennpr rkakesktre yyekqfpeir kqreqqerfq
 361 rvgqrgagls atiarsehei seiidglseq ennekqmrql svippmmfda eqrrvkfinm
 421 nglmedpmkv ykdrqfmnvw tdhekeifkd kfiqhpknfg liasylerks vpdcvlyyyl
 481 tkknenykal vrrnygkrrg rnqqiarpsq eekveekeed kaektekkee ekkdeeekde
 541 kedskentke kdkidgtaee teereqatpr grktansqgr rkgritrsmt neaaaasaaa
 601 aaateepppp lppppepist epvetsrwte eemevakkgl vehgrnwaai akmvgtksea
 661 qcknfyfnyk rrhnldnllq qhkqktsrkp reerdvsqce svastvsaqe dedieasnee
 721 enpedsevea vkpsedspen atsrgntepa velepttеta pstspslavp stkpaedesv
 781 etqvndsisa etaeqmdvdq qehsaeegsv cdpppatkad svdvevrvpe nhaskvegdn
 841 tkerdldras ekveprdedl vvaqqinaqr pepqsdndss atcsadedvd geperqrmfp
 901 mdskpsllnp tgsilvsspl kpnpldlpql qhraavippm vsctpcnipi gtpvsgyaly
 961 qrhikamhes alleeqrqrq eqidlecrss tspcgtsksp nrewevlqpa phqvitnlpe
1021 gvrlpttrpt rpppplipss kttvasekps fimggsisqg tpgtyltshn qasytqetpk
1081 psvgsislgl prqqesaksa tlpyikqeef sprsqnsqpe gllvraqheg vvrgtagaiq
1141 egsitrgtpt skisvesips lrgsitqgtp alpqtgipte alvkgsisrm piedsspekg
1201 reeaaskghv iyegksghil sydniknare gtrsprtahe islkrsyesv egnikqgmsm
1261 respvsaple glicralprg sphsdlkert vlsgsimqgt prattesfed glkypkqikr
1321 esppirafeg aitkgkpydg ittikemgrs iheiprqdil tqesrktpev vqstrpiieq
1381 sisqgtpikf dnnsgqsaik hnvkslitgp sklsrqmppl eivpenikvv ergkyedvka
1441 getvrsrhts vvssgpsvlr stlheapkaq lspgiyddts arrtpvsyqn tmsrgspmmn
1501 rtsdvtissn kstnherkst ltptqresip akspvpgvdp vvshspfdph hrgstagevy
1561 rshlpthldp ampfhraldp aaaaylfqrq lsptpgypsq yqlyamentr qtilndyits
1621 qqmqvnlrpd varglspreq plglpypatr giidltnmpp tilvphpggt stppmdrity
1681 ipgtqitfpp rpynsasmsp ghpthlaaaa saerererer ekerereria aassdlylrp
```

FIG. 48B

```
1741 gseqpgrpgs hgyvrspsps vrtqetmlqq rpsvfqgtng tsvitpldpt aqlrimplpa
1801 ggpsisqglp asryntaada laalvdaaas apqmdvsktk eskheaarle enlrsrsaav
1861 seqqqleqkt levekrsvqc lytssafpsg kpqphssvvy seagkdkgpp pksryeeelr
1921 trgkttitaa nfidviitrq iasdkdarer gsqssdssss lsshryetps daievispas
1981 spappqeklq tyqpevvkan qaendptrqy egplhhyrpq qespspqqql ppssqaegmg
2041 qvprthrlit ladhicqiit qdfarnqvss qtpqqpptst fqnspsalvs tpvrtktsnr
2101 yspesqaqsv hhqrpgsrvs penlvdksrq srpgkspers hvssepyepi sppqvpvvhe
2161 kqdsllllsq rgaepaeqrn darspgsisy lpsfftklen tspmvkskkq eifrklnssg
2221 ggdsdmaaaq pgteifnlpa vttsgsvssr ghsfadpasn lglediirka lmgsfddkve
2281 dhgvvmsqpm gvvpgtants vvtsgetrre egdpsphsgg vckpklisks nsrkskspip
2341 gqgylgterp ssvssvhseg dyhrqtpgwa wedrpsstgs tqfpynpltm rmlsstpptp
2401 iacapsavnq aaphqqnriw erepapllsa qyetlsdsdd
```

FIG. 49A

SMRT (NCOR2; SMAP270; TRAC)
Homo sapiens

```
   1 msgstqpvaq twratepryp phslsypvqi arthtdvgll eyqhhsrdya shlspgsiiq
  61 pqrrrpslls efqpgnersq elhlrpeshs ylpelgksem efieskrprl ellpdpllrp
 121 spllatgqpa gsedltkdrs ltgklepvsp pspphtdpel elvpprlske eliqnmdrvd
 181 reitmveqqi sklkkkqqql eeeaakppep ekpvspppie skhrslvqii ydenrkkaea
 241 ahrileglgp qvelplynqp sdtrqyheni kinqamrkkl ilyfkrrnha rkqweqkfcq
 301 rydqlmeawe kkveriennp rrrakeskvr eyyekqfpei rkqrelqerm qsrvgqrgsg
 361 lsmsaarseh evseiidqls eqenlekqmr qlavippmly dadqqrikfi nmnglmadpm
 421 kvykdrqvmn mwseqeketf rekfmqhpkn fgliasfler ktvaecvlyy yltkknenyk
 481 slvrrsyrrr gksqqqqqqq qqqqqqqqqq pmprssqeek dekekekeae keeekpeven
 541 dkedllkekt ddtsgednde keavaskgrk tansqgrrkg ritrsmanea nseeaitpqq
 601 saelasmeln essrwteeem etakkglleh grnwsaiarm vgsktvsqck nfyfnykkrq
 661 nldeilqqhk lkmekernar rkkkkapaaa seeaafppvv edeemeasgv sgneeemvee
 721 aealhasgne vprgecsgpa tvnnssdtes ipsphteaak dtgqngpkpp atlgadgppp
 781 gpptpppedi papteptpas eatgaptppp appspsappp vvpkeekeee taaappveeg
 841 eeqkppaaee lavdtgkaee pvksecteea eegpakgkda eaaeataega lkaekkeggs
 901 grattakssg apqdsdssat csadevdeae ggdknrllsp rpslltptgd pranaspqkp
 961 ldlkqlkqra aaippiqvtk vheppredaa ptkpappapp ppqnlqpesd apqqpgsspr
1021 gksrspappa dkeafaaeaq klpgdppcwt sglpfpvppr evikasphap dpsafsyapp
1081 ghplplglhd tarpvlprpp tisnppplis sakhpsvler qigaisqgms vqlhvpyseh
1141 akapvgpvtm glplpmdpkk lapfsgvkqe qlsprgqagp peslgvptaq easvlrgtal
1201 gsvpggsitk gipstrvpsd saityrgsit hgtpadvlyk gtitriiged spsrldrgre
1261 dslpkghviy egkkghvlsy eggmsvtqcs kedgrssspp phetaapkrt ydmmegrvgr
1321 aissasiegl mgraipperh sphhlkeqhh irgsitqgip rsyveaqedy lrreakllkr
1381 egtpppppps rdlteayktq algplklkpa heglvatvke agrsiheipr eelrhtpelp
1441 laprplkegs itqgtplkyd tgasttgskk hdvrsligsp grtfppvhpl dvmadarale
1501 racyeeslks rpgtasssgg siargapviv pelgkprqsp ltyedhgapf aghlprgspv
1561 ttreptprlq egslsssskas qdrkltstpr eiaksphstv pehhphpisp yehllrgvsg
1621 vdlyrshipl afdptsiprg ipldaaaayy lprhlapnpt yphlyppyli rgypdtaale
1681 nrqtiindyi tsqqmhhnaa tamaqradml rglspressl alnyaagprg iidlsqvphl
```

FIG. 49B

```
1741 pvlvpptpgt patamdrlay lptapqpfss rhssplspg gpthltkptt tsssererdr
1801 drerdrdrer eksiltsttt vehapiwrpg teqssgssgg gggsssrpas hshahqhspi
1861 sprtqdalqq rpsvlhntgm kgiitaveps tptvlrstst sspvrpaatf ppathcplgg
1921 tldgvyptlm epvllpkeap rvarperpra dtghaflakp parsglepas spskgseprp
1981 lvppvsghat iartpaknla phhaspdppa ppasasdphr ektqskpfsi qelelrslgy
2041 hgssyspegv epvspvssps lthdkglpkh leeldkshle gelrpkqpgp vklggeaahl
2101 phlrplpesq psssplqta pgvkghqrvv tlaqhisevi tqdytrhhpq qlsaplpapl
2161 ysfpgascpv ldlrrppsdl ylpppdhgap argsphsegg krspepnkts vlgggedgie
2221 pvsppegmte pghsrsavyp llyrdgeqte psrmgskspg ntsqppaffs kltesnsamv
2281 kskkqeinkk lnthnrnepe ynisqpgtei fnmpaitgtg lmtyrsqavq ehastnmgle
2341 aiirkalmgk ydqweesppl sanafnplna saslpaampi taadgrsdht ltspggggka
2401 kvsgrpssrk akspapglas gdrppsvssv hsegdcnrrt pltnrvwedr pssagstpfp
2461 ynplimrlqa gvmasppppg lpagsgplaq phhawdeepk pllcsqyetl sdse
```

FIG. 50

RIP140 (NRIP1)
Homo sapiens

```
   1 mthgeelgsd vhqdsivlty legllmhqaa ggsgtavdkk saghneedqn fnisgsafpt
  61 cqsngpvlnt htyqgsgmlh lkkarllqss edwnaakrkr lsdsimnlnv kkeallagmv
 121 dsvpkgkqds tllasllqsf ssrlqtvals qqirqslkeq gyalshdslk vekdlrcygv
 181 asshlktllk kskvkdqkpd tnlpdvtknl irdrfaesph hvgqsgtkvm seplscaarl
 241 qavasmvekr aspatspkps vacsqlalll sseahlqqys rehalktqna nqaaserlaa
 301 marlqengqk dvgsyqlpkg msshlngqar tsssklmask ssatvfqnpm giipsspkna
 361 gyknslernn ikqaannsll lhllksqtip kpmnghshse rgsifeesst pttideysdn
 421 npsftddssg dessysncvp idlsckhrte ksesdqpvsl dnftqsllnt wdpkvpdvdi
 481 kedqdtskns klnshqkvtl lqlllghkne enveknspq gvhndvskfn tqnyartsvi
 541 espstnrttp vstppltss kagspinlsq hslvikwnsp pyvcstqsek ltntasnhsm
 601 dltkskdppg ekpaqnegaq nsatfsaskl lqnlaqcgmq ssmsveeqrp skqlltgntd
 661 kpigmidrln spllsnktna veenkafssq ptgpepglsg seienllerr tvlqlllgnp
 721 nkgksekkek tplrdestqe hseralseqi lmvkiksepc ddlqipntnv hlshdaksap
 781 flgmapavqr sapalpvsed fksepvspqd fsfsknglls rllrqnqdsy laddsdrshr
 841 nnemallesk nlcmvpkkrk lyteplenpf kkmknnivda annhsapevl ygsllnqeel
 901 kfsrndlefk ypaghgsase sehrswares ksfnvlkqll lsencvrdls phrsnsvads
 961 kkkghknnvt nskpefsiss lnglmysstq psscmdnrtf sypgvvktpv sptfpehlgc
1021 agsrpesgll ngcsmpsekg pikwvitdae kneyekdspr ltktnpilyy mlqkggnsvt
1081 sretqdkdiw reassaesvs qvtakeellp taetkasffn lrspynshmg nnasrphsan
1141 gevygllgsv ltikkese
```

FIG. 51A

PRIC285 (PDIP-1)
Homo sapiens

```
   1 mssspsrsaa diyireyfhs hvsgghpeat plrvmytdrp lsqtdpvtlq yccltddrqa
  61 frpptraela rhrvvvttts qarelrvpvq ffshilidea aqmlecealt playashgtr
 121 lvlagdhmqv tprlfsvara raaehtllhr lflcyqqeth evarqsrlvf henyrctdai
 181 vsfisrhfyv akgnpiharg kvpphprhyp lmfchvagsp drdmsmaswl nlaeiaqvve
 241 kvqeayntwp scwggreqrc icvvshgaqv salrqelrrr dlgqvsvgsf eilpgrqfrv
 301 vvlstvhtcq sllspgalap efftdarvln tvltraqsql vvvgdavalc sfgacgklwe
 361 sfirecverh svcpeglsme qveqgvaqrr rwpprgtqag aagnweaape pvgdlaeeqa
 421 avvtamvkae pgdealspas rditattaqt eaaaapagda vkedvvpgac aagaaaaagv
 481 esteaedaea dfwpwdgeln addailrell desqkvmvtv gedglldtva rpeslqqarl
 541 yenlppaalr kllhaepery rhcsfvpetf erasaipldd assgpiqvrg rldcgmafag
 601 devlvqllsg dkapegrlrg rvlgvlkrkr helafvcrmd twdprimvpi ngsvtkifva
 661 elkdpsqvpi yslrkgrlqr vglerltaea rhsrlfwvqi vlwrqgfyyp lgivrevlpe
 721 astweqglri lgleyslrvp psdqatitkv lqkyhtelgr vagrredcra fltftvdpqg
 781 acnlddalsv rdlgprceva vhitdvasfv prdgvldvea rrqgaafyap grepvpmlpa
 841 slcqdvlsll pgrdrlaisl fltmekasgq lkslrfapsv vqsdrqlsye eaeevirqhp
 901 gagrelparl dsvdacvvaa cyfsrllrrh rlrsdcfyeq pdedgtlgfr aahimvkeym
 961 iqfnrlvaef lvgsectrtv tplrwqpapr sqqlkalcek hgdrvplslh lghhlhgggg
1021 sppdtrlhll aslwkqvqfa artqdyeqmv dlvttddmhp flapagrdlr kalersafgr
1081 carghqqqgg hyslqvdwyt watspirryl dvvlqrqill alghggsays ardidglcqa
1141 fslqhalaqs yqrrarslhl avqlkaqpld klgfvvdvea gsrcfrllfp snretlpdpc
1201 pvpygslqla ehphalagrp glrllwrrrv ysaqgssppl plpgtvpdph tlavetalwk
1261 qllelvelqr wpeaaaliqe kgeasqrrel vqvqrshcgh flevarelgs gdtlqvqlgt
1321 slqhgflvps pqlwtvapgf slclehverp gdcfsgrvyr aprdryrdvd eyacvwepfc
1381 alesatgava endsvtlqhl svsweasrtp qgqlqgafrl eaafleenca dinfsccylc
1441 irleglpapt asprpgpssl gpglnvdpgt ytwvahgqtq dwdqerradr qeaprrvhlf
1501 vhhmgmekvp eevlrpgtlf tvellpkqlp dlrkeeavrg leeasplvts ialgrpvpqp
1561 lcrvipsrfl erqtynipgg rhklnpsqnv avrealekpf tviqgppgtg ktivglhivf
1621 wfhksnqeqv qpggpprgek rlggpcilyc gpsnksvdvl aglllrrmel kplrvyseqa
```

FIG. 51B

```
1681 easefpvprv gsrkllrksp regrpnqslr sitlhhrirq apnpysseik afdtrlqrge
1741 lfsredlvwy kkvlwearkf eldrhevilc tcscaasasl kildvrqilv deagmatepe
1801 tliplvqfpq aekvvllgdh kqlrpvvkne rlqnlgldrs lferyhedah mldtqyrmhe
1861 gicafpsvaf yksklktwqg lrrppsvlgh agkescpvif ghvqghersl lvstdegnen
1921 skanleevae vvritkqltl grtvepqdia vltpynaqas eiskalrreg iagvavssit
1981 ksqgsewryv lvstvrtcak sdldqrptks wlkkflgfvv dpnqvnvavt raqeglclig
2041 dhlllrccpl wrslldfcea qqtlvpagqv rvcrrptmps
```

FIG. 52

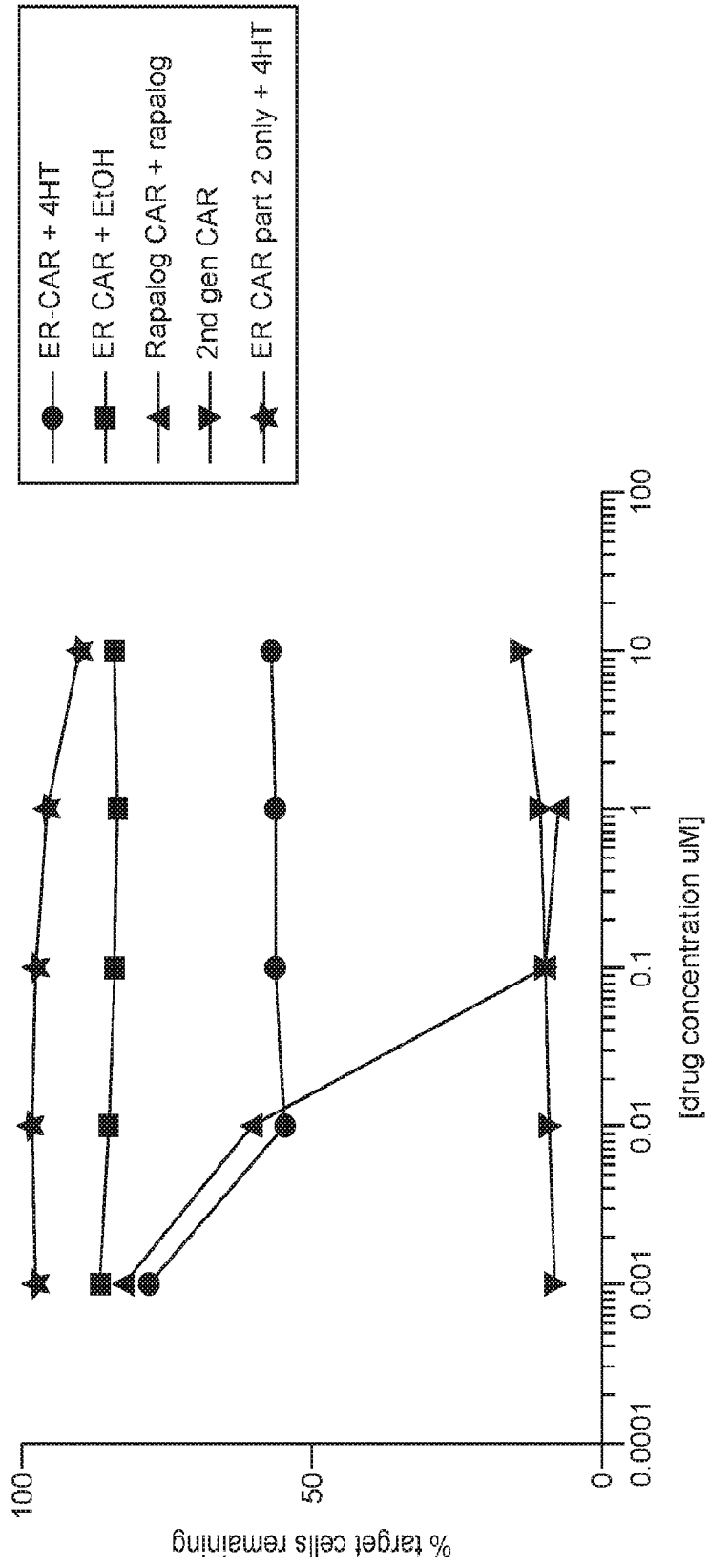
ER-CAR + 4HT
ER CAR + EtOH
Rapalog CAR + rapalog
2nd gen CAR
ER CAR part 2 only + 4HT
% target cells remaining
100
50
0
0.0001
0.001
0.01
0.1
1
10
100
[drug concentration uM]

FIG. 53

IL-2 receptor family member	UniProt ID	RefSeq Accession	Amino Acid Sequence
Interleukin 13 receptor, α2	Q14627	NP_000631.1	MAFVCLAIGCLYTFLISTTFGCTSSDTEIKVNPPQDFEIVDPGYLGYLYLQWQPPLSLDHFKECTVEYELKYRNIGSETWKTIITKNLHYKDGFDLNKGIEAKIHTLLPWQCTNG SEVQSSWAETTYWISPQGIPETKVQDMDCVYYNWQYLLCSWKPGIGVLLDTNYNLFYWYEGLDHALQCVDYIKADGQNIGCRFPYLEASDYKDFYICVNGSSENKPIRSSYF TFQLQNIVKPLPPVYLTFTRESSCEIKLKWSIPLGPIPARCFDYEIEIREDDTTLVTATVENETYTLKTTNETRQLCFVVRSKVNIYCSDDGIWSEWSDKQCWEGEDLSKKTLLRF WLPFGFILILVIFVTGLLLRKPNTYPKMIPEFFCDT
Interleukin-2 receptor subunit α	P01589	NP_000408.1	MDSYLLMWGLLTFIMVPGCQAELCDDDPPEIPHATFKAMAYKEGTMLNCECKRGFRRIKSGSLYMLCTGNSSHSSWDNQCQCTSSATRNTTKQVTPQPEEQKERKTTEM QSPMQPVDQASLPGHCREPPPWENEATERIYHFVVGQMVYYQCVQGYRALHRGPAESVCKMTHGKTRWTQPQLICTGEMETSQFPGEEKPQASPEGRPESETSCLVTT TDFQIQTEMAATMETSIFTTEYQVAVAGCVFLLISVLLLSGLTWQRRQRKSRRTI
Interleukin-2 receptor subunit β	P14784	NP_000869.1	MAAPALSWRLPLLILLLPLATSWASAAVNGTSQFTCFYNSRANISCVWSQDGALQDTSCQVHAWPDRRRWNQTCELLPVSQASWACNLILGAPDSQKLTTVDIVTLRVLC REGVRWRVMAIQDFKPFENLRLMAPISLQVVHVETHRCNISWEISQASHYFERHLEFEARTLSPGHTWEEAPLLTLKQKQEWICLETLTPDTQYEFQVRVKPLQGEFTTWSP WSQPLAFRTKPAALGKDTIPWLGHLLVGLSGAFGFIILVYLLINCRNTGPWLKKVLKCNTPDPSKFFSQLSSEHGGDVQKWLSSPFPSSSFSPGGLAPEISPLEVLERDKVTQLL LQQDKVPEPASLSSNHSLTSCFTNQGYFFFHLPDALEIEACQVYFTYDPYSEEDPDEGVAGAPTGSSPQPLQPLSGEDDAYCTFPSRDDLLLFSPSLLGGPSPPSTAPGGSGAG EERMPPSLQERVPRDWDPQPLGPPTPGVPDLVDFQPPPELVLREAGEEVPDAGPREGVSFPWSRPPGQGEFRALNARLPLNTDAYLSLQELQGQDPTHLV
Interleukin-2 receptor subunit γ	P31785	NP_000197.1	MLKPSLPFTSLLFLQLPLLGVGLNTTILTPNGNEDTTADFFLTTMPTDSLSVSTLPLPEVQCFVFNVEYMNCTWNSSSEPQPTNLTLHYWYKNSDNDKVQKCSHYLFSEEITSG CQLQKEIHLYQTFVVQLQDPREPRRQATQMLKLQNLVIPWAPENLTLHKLSESQLELNWNNRFLNHCLEHLVQYRTDWDHSWTEQSVDYRHKFSLPSVDGQKRYTFRV RSRFNPLCGSAQHWSEWSHPIHWGSNTSKENPFLFALEAVVISVGSMGLIISLLCVYFWLERTMPRIPTLKNLEDLVTEYHGNFSAWSGVSKGLAESLQPDYSERLCLVSEIPP KGGALGEGPGASPCNQHSPYWAPPCYTLKPET
Interleukin-4 receptor subunit α	P24394	NP_000409.1	MGWLCSGLLFPVSCLVLLQVASSGNMKVLQEPTCVSDYMSISTCEWKMNGPTNCSTELRLLYQLVFLLSEAHTCIPENNGGAGCVCHLLMDDVVSADNYTLDLWAGQQL LWKGSFKPSEHVKPRAPGNLTVHTNVSDTLLLTWSNPYPPDNYLYNHLTYAVNIWSENDPADFRIYNVTYLEPSLRIAASTLKSGISYRARVRAWAQCYNTTWSEWSPSTK WHNSYREPFEQHLLLGVSVSCIVILAVCLLCYVSITKIKKEWWDQIPNPARSRLVAIIIQDAQGSQWEKRSRGQEPAKCPHWKNCLTKLLPCFLEHNMKRDEDPHKAAKEMP FQGSGKSAWCPVEISKTVLWPESISVVRCVELFEAPVECEEEEEVEEEKGSFCASPESSRDDFQEGREGIVARLTESLFLDLLGEENGGFCQQDMGESCLLPPSGSTSAHMPW DEFPSAGPKEAPPWGKEQPLHLEPSPPASPTQSPDNLTCTETPLVIAGNPAYRSFSNSLSQSPCPRELGPDPLLARHLEEVEPEMPCVPQLSEPTTVPQPEPETWEQILRRNVL QHGAAAAPVSAPTSGYQEFVHAVEQGGTQASAVVGLGPPGEAGYKAFSSLLASSAVSPEKCGFGASSGEEGYKPFQDLIPGCPGDPAPVPVPLFTFGLDREPPRSPQSSHLP SSSPEHLGLEPGEKVEDMPKPPLPQEQATDPLVDSLGSGIVYSALTCHLCGHLKQCHGQEDGGQTPVMASPCCGCCCGDRSSPPTTPLRAPDPSPGGVPLEASLCPASLAPS GISERSKSSSSFHPAPGNAQSSSQTPKIVNFVSVGPTYMRVS

FIG. 53 (Cont.)

Interleukin-7 receptor subunit α	P16871	NP_002176.2	MTILGTTFGMVFSLLQVVSGESGYAQNGDLEDAELDDYSFSCYSQLEVNGSQHSLTCAFEDPDVNITNLEFEICGALVEVKCLNFRKLQEIYFIETKKFLLIGKSNICVKVGEKSL TCKKIDLTTIVKPEAPFDLSVVYREGANDFVVTFNTSHLQKKYVKVLMHDVAYRQEKDENKWTHVNLSSTKLTLLQRKLQPAAMYEIKVRSIPDHYFKGFWSEWSPSYYFRT PEINNSSGEMDPILLTISILSFFSVALLVILACVLWKKRIKPIVWPSLPDHKKTLEHLCKKPRKNLNVSFNPESFLDCQIHRVDDIQARDEVEGFLQDTFPQQLEESEKQRLGGDV QSPNCPSEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRSLDCRESGKNGPHVYQDLLLSLGTTNSTLPPFSLQSGILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ
Interleukin 9 receptor	Q01113	NP_002177.2	MGLGRCIWEGWTLESEALRRDMGTWLLACICTCVCLGVSVTGEGQGPRSRTFTCLTNNILRIDCHWSAPELGQGSSPWLLFTSNQAPGGTHKCILRGSECTVVLPPEAVL VPSDNFTITFHHCMSGREQVSLVDPEYLPRRHVKLDPPSDLQSNISSGHCLTWSISPALEPMTTLLSYELAFKKQEEAWEQAQHRDHIVGVTWLLLEAFELDPGFIHEARLRV QMATLEDDVVEEERYTGQWSEWSQPVCFQAPQRQGPLIPPWGWPGNTLVAVSIFLLLTGPTYLLFKLSPRVKRIFYQNVPSPAMFFQPLYSVHNGNFQTWMGAHGAGV LLSQDCAGTPQGALEPCVQEATALLTCGPARPWKSVALEEEQEGPGTRLPGNLSSEDVLPAGCTEWRVQTLAYLPQEDWAPTSLTRPAPPDSEGSRSSSSSSSNNNNYCA LGCYGGWHLSALPGNTCSSGPIPALACGLSCDHQGLETQQGVAWVLAGHEQRPGLHEDLQGMLLPSVLSKARSWTF
Interleukin-13 receptor subunit α1	P78552	NP_001551.1	MEWPARLCGLWALLLCAGGGGGGGGAAPTETQPPVTNLSVSVENLCTVIWTWNPPEGASSNCSLWYFSHFGDKQDKKIAPETRRSIEVPLNERICLQVGSQCSTNESEKP SILVEKCISPPEGDPESAVTELQCIWHNLSYMKCSWLPGRNTSPDTNYTLYYWHRSLEKIHQCENIFREGQYFGCSFDLTKVKDSSFEQHSVQIMVKDNAGKIKPSFNIVPLTS RVKPDPPHIKNLSFHNDDLYVQWENPQNFISRCLFYEVEVNNSQTETHNVFYVQEAKCENPEFERNVENTSCFMVPGVLPDTLNTVRIRVKTNKLCYEDDKLWSNWSQEM SIGKKRNSTLYITMLLIVPVIVAGAIIVLLYLKRLKIIIFPPIPDPGKIFKEMFGDQNDDTLHWKKYDIYEKQTKEETDSVVLIENLKKASQ
Interleukin-15 receptor subunit α	Q13261	NP_00123046 8.1	MSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIRDPALVHQRPAPPSTVTTAGVTPQPESLSPSGKEPAASSPSSNNTAATTAAIVPGS QLMPSKSPSTGTTEISSHESSHGTPSQTTAKNWELTASASHQPPGVYPQGHSDTTVAISTSTVLLCGLSAVSLLACYLKSRQTPPLASVEMEAMEALPVTWGTSSRDEDLENC SHHL
Interleukin 21 receptor	Q9HBE5	NP_068570.1	MPRGWAAPLLLLLLQGWGCPDLVCYTDYLQTVICILEMWNLHPSTLTLTWQDQYEELKDEATSCSLHRSAHNATHATYTCHMDVFHFMADDIFSVNITDQSGNYSQEC GSFLLAESIKPAPPFNVTVTFSGQYNISWRSDYEDPAFYMLKGKLQYELQYRNRGDPWAVSPRRKLISVDSRSVSLLPLEFRKDSSYELQVRAGPMPGSSYQGTWSEWSDPV IFQTQSEELKEGWNPHLLLLLLLVIVFIPAFWSLKTHPLWRLWKKIWAVPSPERFFMPLYKGCSGDFKKWVGAPFTGSSLELGPWSPEVPSTLEVYSCHPPRSPAKRLQLTEL QEPAELVESDGVPKPSFWPTAQNSGGSAYSEERDRPYGLVSIDTVTVLDAEGPCTWPCSCEDDGYPALDLDAGLEPSPGLEDPLLDAGTTVLSCGCVSAGSPGLGGPLGSLL DRLKPPLADGEDWAGGLPWGGRSPGGVSESEAGSPLAGLDMDTFDSGFVGSDCSSPVECDFTSPGDEGPPRSYLRQWVVIPPPLSSPGPQAS
Cytokine receptor-like factor 2	Q9HC73	NP_00101228 8.2	MVYYLKPSSPKHVRFSWHQDAVTVTCSDLSYGDLLYEVQYRSPFDTEWQSKQENTCNVTIEGLDAEKCYSFWVRVKAMEDVYGPDTYPSDWSEVTCWQRGEIRDACAET PTPPKPKLSKFILISSLAILLMVSLLLLSLWKLWRVKKFLIPSVPDPKSIFPGLFEIHQGNFQEWITDTQNVAHLHKMAGAEQESGPEEPLVVQLAKTEAESPRMLDPQTEEKEA SGGSLQLPHQPLQGGDVVTIGGFTFVMNDRSYVAL

FIG. 54

IL-3 receptor family	UniProt ID	RefSeq Accession	Amino Acid Sequence
Interleukin 3 receptor, α subunit	P26951	NP_00125464 2.1	MVLLWLTLLIALPCLLQTKEGGKPWAGAENLTCWIHDVDFLSCSWAVGPGAPADVQYDLYLNVANRRQQYECLHYKTDAQGTRIGCRFDDISRLSSGSQSSHILVRGRSA AEGIPCTDKFVVFSQIFILTPPNMTAKCNKTHSFMHWKMRSHFNRKFRYELQIQKRMQPVITEQVRDRTSFQLLNPGTYTVQIRARERVYEFLSAWSTPQRFECDQEEGAN TRAWRTSLLIALGTLLALVCVFVICRRYLVMQRLFPRIPHMKDPIGDSFQNDKLVVWEAGKAGLEECLVTEVQVVQKT
Interleukin 5 receptor, α subunit	Q01344	NP_000555.2	MIIVAHVLLIILGATEILQADLLPDEKISLLPPVNFTIKVTGLAQVLLQWKPNPDQEQRNVNLEYQVKINAPKEDDVETRITESKCVTILHKGFSASVRTILQNDHSLLASSWASA ELHAPPGSPGTSIVNLTCTTNTTEDNYSRLRSYQVSLHCTWLVGTDAPEDTQYFLVYRYGSWTEECQEYSKDTLGRNIACWFPRTFILSKGRDWLAVLVNGSSKHSAIRPFDQ LFALHAIDQINPPLNVTAEIEGTRLSIQWEKPVSAFPIHCFDYEVKIHNTRNGYLQIEKLMTNAFISIIDDLSKYDVQVRAAVSSMCREAGLWSEWSQPIYVGNDEHKPLREWF VIVIMATICFILLILSLICKICHLWIKLFPPIPAPKSNIKDLFVTTNYEKAGSSETEIEVICYIEKPGVETLEDSVF
GM-CSF receptor, α subunit	P15509	NP_00115500 1.1	MLLLVTSLLLCELPHPAFLLIPEKSDLRTVAPASSLNVRFDSRTMNLSWDCQENTTFSKCFLTDKKNRVVEPRLSNNECSCTFREICLHEGVTFEVHVNTSQRGFQQKLLYPNS GREGTAAQNFSCFIYNADLMNCTWARGPTAPRDVQYFLYIRNSKRREIRCPYYIQDSGTHVGCHLDNLSGLTSRNYFLVNGTSREIGIQFFDSLLDTKKIERFNPPSNVTVRC NTTHCLVRWKQPRTYQKLSYLDFQYQLDVHRKNTQPGTENLLINVSGDLENRYNPFSSEPRAKHSVKIRAADVRILNWSSWSEAIEFGSDDGNLGSVYIYVLLIVGTLVCGIV LGFLFKRFLRIQRLFPPVPQIKDKLNDNHEVEDEIIWEEFTPEEGKGYREEVLTVKEIT
Cytokine receptor common β subunit	P32927	NP_000386.1	MVLAQGLLSMALLALCWERSLAGAEETIPLQTLRCYNDYTSHITCRWADTQDAQRLVNVTLIRRVNEDLLEPVSCDLSDDMPWSACPHPRCVPRRCVIPCQSFVVTDVDYF SFQPDRPLGTRLTVTLTQHVQPPEPRDLQISTDQDHFLLTWSVALGSPQSHWLSPGDLEFEVVYKRLQDSWEDAAILLSNTSQATLGPEHLMPSSTYVARVRTRLAPGSRLS GRPSKWSPEVCWDSQPGDEAQPQNLECFFDGAAVLSCSWEVRKEVASSVSFGLFYKPSPDAGEEECSPVLREGLGSLHTRHHCQIPVPDPATHGQYIVSVQPRRAEKHIKS SVNIQMAPPSLNVTKDGDSYSLRWETMKMRYEHIDHTFEIQYRKDTATWKDSKTETLQNAHSMALPALEPSTRYWARVRVRTSRTGYNGIWSEWSEARSWDTESVLPM WVLALIVIFLTIAVLLALRFCGIYGYRLRRKWEEKIPNPSKSHLFQNGSAELWPPGSMSAFTSGSPPHQGPWGSRFPELEGVFPVGFGDSEVSPLTIEDPKHVCDPPSGPDTTP AASDLPTEQPPSPQPGPPAASHTPEKQASSFDFNGPYLGPPHSRSLPDILGQPEPPQEGGSQKSPPPGSLEYLCLPAGGQVQLVPLAQAMGPGQAVEVERRPSQGAAGSPS LESGGGPAPPALGPRVGGQDQKDSPVAIPMSSGDTEDPGVASGYVSSADLVFTPNSGASSVSLVPSLGLPSDQTPSLCPGLASGPPGAPGPVKSGFEEGYVELPPIEGRSPRSP RNNPVPPEAKSPVLNPGERPADVSPTSPQPEGLLVLQQVGDYCFLPGLGPGPLSLRSKPSSPGPGPEIKNLDQAFQVKKPPGQAVPQVPVIQLFKALKQQDYLSLPPWEVNK PGEVC

FIG. 55

IL-6 receptor family	UniProt ID	RefSeq Accession	Amino Acid Sequence
Leptin receptor	P48357	NP_001003679.1	MICQKFCVVLLHWEFIYVITAFNLSYPITPWRFKLSCMPPNSTYDYFLLPAGLSKNTSNSNGHYETAVEPKFNSSGTHFSNLSKTTFHCCFRSEQDRNCSLCADNIEGKTFVSTV NSLVFQQIDANWNIQCWLKGDLKLFICYVESLFKNLFRNYNYKVHLLYVLPEVLEDSPLVPQKGSFQMVHCNCSVHECCECLVPVPTAKLNDTLLMCLKITSGGVIFQSPLMS VQPINMVKPDPPLGLHMEITDDGNLKISWSSPPLVPFPLQYQVKYSENSTTVIREADKIVSATSLLVDSILPGSSYEVQVRGKRLDGPGIWSDWSTPRVFTTQDVIYFPPKILTS VGSNVSFHCIYKKENKIVPSKEIVWWMNLAEKIPQSQYDVVSDHVSKVTFFNLNETKPRGKFTYDAVYCCNEHECHHRYAELYVIDVNINISCETDGYLTKMTCRWSTSTIQS LAESTLQLRYHRSSLYCSDIPSIHPISEPKDCYLQSDGFYECIFQPIFLLSGYTMWIRINHSLGSLDSPPTCVLPDSVVKPLPPSSVKAEITINIGLLKISWEKPVFPENNLQFQIRYGL SGKEVQWKMYEVYDAKSKSVSLPVPDLCAVYAVQVRCKRLDGLGYWSNWSNPAYTVVMDIKVPMRGPEFWRIINGDTMKKEKNVTLLWKPLMKNDSLCSVQRYVINH HTSCNGTWSEDVGNHTKFTFLWTEQAHTVTVLAINSIGASVANFNLTFSWPMSKVNIVQSLSAYPLNSSCVIVSWILSPSDYKLMYFIIEWKNLNEDGEIKWLRISSSVKKYYI HDHFIPIEKYQFSLYPHFMEGVGKPKIINSFTQDDIEKHQSDAGLYVNVPVIISSILLLGTLLISHQRMKKLFWEDVPNPKNCSWAQGLNFQKRTDIL
IL6R (Interleukin-6 receptor, α subunit / interleukin 6 receptor)	P08887	NP_000556.1	MLAVGCALLAALLAAPGAALAPRRCPAQEVARGVLTSLPGDSVTLTCPGVEPEDNATVHWVLRKPAAGSHPSRWAGMGRRLLLRSVQLHDSGNYSCYRAGRPAGTVHLL VDVPPEEPQLSCFRKSPLSNVVCEWGPRSTPSLTTKAVLLVRKFQNSPAEDFQEPCQYSQESQKFSCQLAVPEGDSSFYIVSMCVASSVGSKFSKTQTFQGCGILQPDPPANI TVTAVARNPRWLSVTWQDPHSWNSSFYRLRFELRYRAERSKTFTTWMVKDLQHHCVIHDAWSGLRHVVQLRAQEEFGQGEWSEWSPEAMGTPWTESRSPPAENEVS TPMQALTTNKDDDNILFRDSANATSLPVQDSSSVPLPTFLVAGGSIAFGTLLCIAIVLRFKKTWKLRALKEGKTSMHPPYSLGQLVPERPRPTPVLVPLISPPVSPSSLGSDNTS SHNRPDARDPRSPYDISNTDYFFPR
IL6ST (Interleukin-6 receptor, β subunit / interleukin 6 signal transducer)	P40189	NP_001117791.1	MLTLQTWLVQALFIFLTTESTGELLDPCGYISPESPVVQLHSNFTAVCVLKEKCMDYFHVNANYIVWKTNHFTIPKEQYTIINRTASSVTFTDIASLNIQLTCNILTFGQLEQNVY GITIISGLPPEKPKNLSCIVNEGKKMRCEWDGGRETHLETNFTLKSEWATHKFADCKAKRDTPTSCTVDYSTVYFVNIEVWVEAENALGKVTSDHINFDPVYKVKPNPPHNLS VINSEELSSILKLTWTNPSIKSVIILKYNIQYRTKDASTWSQIPPEDTASTRSSFTVQDLKPFTEYVFRIRCMKEDGKGYWSDWSEEASGITYEDRPSKAPSFWYKIDPSHTQGYR TVQLVWKTLPPFEANGKILDYEVTLTRWKSHLQNYTVNATKLTVNLTNDRYLATLTVRNLVGKSDAAVLTIPACDFQATHPVMDLKAFPKDNMLWVEWTTPRESVKKYILEWCVLSDKAPCITDWQQEDGTVHRTYLRGNLAESKCYLITVTPVYADGPGSPESIKAYLKQAPPS KGPTVRTKKVGKNEAVLEWDQLPVDVQNGFIRNYTIFYRTIIGNETAVNVDSSHTEYTLSSLTSDTLYMVRMAAYTDEGGKDGPEFTFTTPKFAQGEIEAIVVPVCLAFLLTTL LGVLFCFNKRDLIKKHIWPNVPDPSKSHIAQWSPHTPPRHNFNSKDQMYSDGNFTDVSVVEIEANDKKPFPEDLKSLDLFKKEKINTEGHSSGIGGSSCMSSSRPSISSSDENE SSQNTSSTVQYSTVVHSGYRHQVPSVQVFSRSESTQPLLDSEERPEDLQLVDHVDGGDGILPRQQYFKQNCSQHESSPDISHFERSKQVSSVNEEDFVRLKQQISDHISQSCG SGQMKMFQEVSAADAFGPGTEGQVERFETVGMEAATDEGMPKSYLPQTVRQGGYMPQ

FIG. 55 (Cont.)

Interleukin-11 receptor, α subunit	Q14626	NP_001136256.1	MSSSCSGLSRVLVAVATALVSASSPCPQAWGPPGVQYGQPGRSVKLCCPGVTAGDPVSWFRDGEPKLLQGPDSGLGHELVLAQADSTDEGTYICQTLDGALGGTVTLQLG YPPARPVVSCQAADYENFSCTWSPSQISGLPTRYLTSYRKKTVLGADSQRRSPSTGPWPCPQDPLGAARCVVHGAEFWSQYRINVTEVNPLGASTRLLDVSLQSILRPDPPQ GLRVESVPGYPRRLRASWTYPASWPCQPHFLLKFRLQYRPAQHPAWSTVEPAGLEEVITDAVAGLPHAVRVSARDFLDAGTWSTWSPEAWGTPSTGTIPKEIPAWGQLH TQPEVEPQVDSPAPPRPSLQPHPRLLDHRDSVEQVAVLASLGILSFLGLVAGALALGLWLRLRRGGKDGSPKPGFLASVIPVDRRPGAPNL
Interleukin 27 receptor, alpha 1	Q6UWB1	NP_004834.1	MRGGRGAPFWLWPLPKLALLPLLWVLFQRTRPQGSAGPLQCYGVGPLGDLNCSWEPLGDLGAPSELHLQSQKYRSNKTQTVAVAAGRSWVAIPREQLTMSDKLLVWGT KAGQPLWPPVFVNLETQMKPNAPRLGPDVDFSEDDPLEATVHWAPPTWPSHKVLICQFHYRRCQEAAWTLLEPELKTIPLTPVEIQDLELATGYKVYGRCRMEKEEDLWG EWSPILSFQTPPSAPKDVWVSGNLCGTPGGEEPLLLWKAPGPCVQVSYKVWFWVGGRELSPEGITCCSLIPSGAEWARVSAVNATSWEPLTNLSLVCLDSASAPRSVAVS SIAGSTELLVTWQPGPGEPLEHVVDWARDGDPLEKLNWVRLPPGNLSALLPGNFTVGVPYRITVTAVSASGLASASSVWGFREELAPLVGPTLWRLQDAPPGTPAIAWGE VPRHQLRGHLTHYTLCAQSGTSPSVCMNVSGNTQSVTLPDLPWGPCELWVTASTIAGQGPPGPILRLHLPDNTLRWKVLPGILFLWGLFLLGCGLSLATSGRCYHLRHKVLP RWVWEKVPDPANSSSGQPHMEQVPEAQPLGDLPILEVEEMEPPPVMESSQPAQATAPLDSGYEKHFLPTPEELGLLGPPRPQVLA
Interleukin-31 receptor, α subunit	Q8NI17	NP_001229565.1	MKLSPQPSCVNLGMMWTWALWMLPSLCKFSLAALPAKPENISCVYYYRKNLTCTWSPGKETSYTQYTVKRTYAFGEKHDNCTTNSSTSENRASCSFFLPRITIPDNYTIEVE AENGDGVIKSHMTPWRLENIAKTEPPKIFRVKPVLGIKRMIQIEWIKPELAPVSSDLKYTLRFRTVNSTSWMEVNFAKNRKDKNQTYNLTGLQPFTEYVIALRCAVKESKFWS DWSQEKMGMTEEEAPCGLELWRVLKPAEADGRRPVRLLWKKARGAPVLEKTLGYNIWYYPESNTNLTETMNTTNQQLELHLGGESFWVSMISVNSLGKSPVATLRIPAIQ EKSFQCIEVMQACVAEDQLVVKWQSSALDVNTWMIEWFPDVDSEPTTLSWEVSQATNWTIQQDKLKPFWCYNISVYPMLHDKVGEPYSIQAYAKEGVPSEGPETKVE NIGVKTVTITWKEIPKSERKGIICNYTIFYQAEGGKGFSKTVNSSILQYGLESLKRKTSYIVQVMASTSAGGTNGTSINFKTLSFSVFEIILITSLIGGGLLILILLTVAYGLKKPNKLTHL CWPTVPNPAESSIATWHGDDFKDKLNIKESDDSVNTEDRILKPCSTPSDKLVIDKLVVNFGNVLQEIFTDEARTGQENNLGGEKNGYVTCPFRPDCPLGKSFEELPVSPEIPP RKSQYLPSRMPEGTRPEAKEQLLFSGQSLVPDHLCEEGAPNPYLKNSVTAREFLVSEKLPEHTKGEV
Ciliary neurotrophic factor receptor α subunit	P26992	NP_000109394.1	MAAPVPWACCAVLAAAAAVVYAQRHSPQEAPHVQYERLGSDVTLPCGTANWDAAVTWRVNGTDLAPDLLNGSQLVLHGLELGHSGLYACHRDSWHLRHQVLLHVG LPPREPVLSCRSNTYPKGFYCSWHLPTPTYIPNTFNVTVLHGSKIMVCEKDPALKNRCHIRYMHLFSTIKYKVSISVSNALGHNATAITFDEFTIVKPDPPENVVARPVPSNPRR LEVTWQTPSTWPDPESFPLKFFLRYRPLILDQWQHVELSDGTAHTITDAYAGKEYIIQVAAKDNEIGTWSDWSVAAHATPWTEEPRHLTTEAQAAETTTSTTSSLAPPPTTKI CDPGELGSGGGPSAPFLVSVPITLALAAAAATASSLLI

FIG. 55 (Cont.)

Leukemia inhibitory factor receptor	P42702	NP_00112114 3.1	MMDIYVCLKRPSWMVDNKRMRTASNFQWLLSTFILLYLMNQVNSQKKGAPHDLKCVTNNLQVWNCSWKAPSGTGRGTDYEVCIENRSRSCYQLEKTSIKIPALSHGDYE ITINSLHDFGSSTSKFTLNEQNVSLIPDTPEILNLSADFSTSTLYLKWNDRGSVFPHRSNVIWEIKVLRKESMELVKLVTHNTTLNGKDTLHHWSWASDMPLECAIHFVEIRCYI DNLHFSGLEEWSDWSPVKNISWIPDSQTKVFPQDKVILVGSDITFCCVSQEKVLSALIGHTNCPLIHLDGENVAIKIRNISVSASSGTNVVFTTEDNIFGTVIFAGYPPDTPQQL NCETHDLKEIICSWNPGRVTALVGPRATSYTLVESFSGKYVRLKRAEAPTNESYQLLFQMLPNQEIYNFTLNAHNPLGRSQSTILVNITEKVYPHTPTSFKVKDINSTAVKLSW HLPGNFAKINFLCEIEIKKSNSVQEQRNVTIKGVENSSYLVALDKLNPYTLYTFRIRCSTETFWKWSKWSNKKQHLTTEASPSKGPDTWREWSSDGKNLIIYWKPLPINEANG KILSYNVSCSSDEETQSLSEIPDPQHKAEIRLDKNDYIISVVAKNSVGSSPPSKIASMEIPNDDLKIEQVVGMGKGILLTWHYDPNMTCDYVIKWCNSSRSEPCLMDWRKVPS NSTETVIESDEFRPGIRYNFFLYGCRNQGYQLLRSMIGYIEELAPIVAPNFTVEDTSADSILVKWEDIPVEELRGFLRGYLFYFGKGERDTSKMRVLESGRSDIKVKNITDISQKTL RIADLQGKTSYHLVLRAYTDGGVGPEKSMYVVTKENSVGLIIAILIPVAVAVIVGVVTSILCYRKREWIKETFYPDIPNPENCKALQFQKSVCEGSSALKTLEMNPCTPNNVEVL ETRSAFPKIEDTEIISPVAERPEDRSDAEPENHVVVSYCPPIIEEEIPNPAADEAGGTAQVIYIDVQSMYQPQAKPEEEQENDPVGGAGVKPQMHLPINSTVEDIAAEEDLDKT AGYRPQANVNTWNLVSPDSPRSIDSNSEIVSFGSPCSINSRQFLIPPKDEDSPKSNGGGWSFTNFFQNKPND

Oncostatin M-specific receptor, β subunit	Q99650	NP_00116182 7.1	MALFAVFQITTFFITLLSLRTYQSEVLAERLPLTPVSLKVSTNSTRQSLHLQWTVHNLPYHQELKMVFQIQISRIETSNVIVWVGNYSTTVKWNQVLHWSWESELPLECATHFV RIKSLVDDAKFPEPNFWSNWSSWEEVSVQDSTGQDILFVFPKDKLVEEGTNVTICYVSRNIQNNVSCYLEGKQIHGEQLDPHVTAFNLNSVPFIRNKGTNIYCEASQSNVSE GMKGIVLFVSKVLEEPKDFSCETEDFKTLHCTWDPGTDTALGWSKQPSQSYTLFESFSGEKKLCTHKNWCNWQITQDSQETYNFTLIAENYLRKRSVNILFNLTHRGETRVV TAHRGH

FIG. 56

IL-12 receptor family	UniProt ID	RefSeq Accession	Amino Acid Sequence
Interleukin-12 receptor, β1 subunit	P42701	NP_001276952.1	MEPLVTWVVPLLFLLSLRQGAACRTSECCFQDPPYPDADSGSASGPRDLRCYRISSDRYECSWQYEGPTAGVSHFLRCCLSSGRCCYFAAGSATRLQFSDQAGVSVLYTVTL WVESWARNQTEKSPEVTLQLYNSVKYEPPLGDIKVSKLAGQLRMEWETPDNQVGAEVQFRHRTPSPWKLGDCGPQDDDTESCLCPLEMNVAQEFQLRRRQLGSQGSS WSKWSSPVCVPPENPPQPQVRFSVEQLGQDGRRRLTLKEQPTQLELPEGCQGLAPGTEVTYRLQLHMLSCPCKAKATRTLHLGKMPYLSGAAYNVAVISSNQFGPGLNQT WHIPADTHTEPVALNISVGTNGTTMYWPARAQSMTYCIEWQPVGQDGGLATCSLTAPQDPDPAGMATYSWSRESGAMGQEKCYYTIFASAHPEKLTLWSTVLSTYHF GGNASAAGTPHHVSVKNHSLDSVSVDWAPSLLSTCPGVLKEYVVRCRDEDSKQVSEHPVQPTETQVTLSGLRAGVAYTVQVRADTAWLRGVWSQPQRFSIEVQVSDWLI FFASLGSFLSILLVGVLGYLGLNRAARHLCPPLPTPCASSAIEFPGGKETWQWINPVDFQEEASLQEALVVEMSWDKGERTEPLEKTELPEGAPELALDTELSLEDGDRCDR
Interleukin-12 receptor, β2 subunit	Q99665	NP_001244514.1	MAHTFRGCSLAFMFIITWLLIKAKIDACKRGDVTVKPSHVILLGSTVNITCSLKPRQGCFHYSRRNKLILYKFDRRINFHHGHSLNSQVTGLPLGTTLFVCKLACINSDEIQICGA EIFVGVAPEQPQNLSCIQKGEQGTVACTWERGRDTHLYTEYTLQLSGPKNLTWQKQCKDIYCDYLDFGINLTPESPESNFTAKVTAVNSLGSSSSLPSTFTFLDIVRPLPPWDI RIKFQKASVSRCTLYWRDEGLVLLNRLRYRPSNSRLWNMVNVTKAKGRHDLLDLKPFTEYEFQISSKLHLYKGSWSDWSESLRAQTPEEEPTGMLDVWYVMKRHIDYSRQQI SLFWKNLSVSEARGKILHYQVTLQELTGGKAMTQNITGHTSWTTVIPRTGNWAVAVSAANSKGSSLPTRINIMNLCEAGLLAPRQVSANSEGMDNILVTWQPPRKDPSAV QEYVVEWRELHPGGDTQVPLNWLRSRPYNVSALISENIKSYICEIRVYALSGDQGGCSSILGNSKHKAPLSGPHINAITEEKGSILISWNSIPVQEQMGCLLHYRIYWKERDS NSQPQLCEIPYRVSQNSHPINSLQPRVTYVLWMTALTAAGESSHGNEREFCLQGKANWMAFVAPSICIAIIMVGIFSTHYFQQKRRHSCPWTGS
Interleukin 23 receptor	Q5VWK5	NP_653302.2	MNQVTICWDAVIALYILFSWCHGGITNINCSGHIWVEPATIFKMGMNISIYCQAAIKNCQPRKLHFYKNGIKERFQITRINKTTARLWYKNFLEPHASMYCTAECPKHFQET LICGKDISSGYPPDIPDEVTCVIYEYSGNMTCTWNAGKLTYIDTKYVVHVKSLETFEFQQYITSSYINISTDSLQGGKKYLVWVQAANALGMEESKQLQIHLDDIVIPSAAVISR AETINATVPKTIIYWDSQTTIEKVSCEMRYKATTNQTWNVKEFDTNFTYVQQSEFYLEPNIKYVFQVRCQETGKRYWQPWSSLFFHKTPETVPQVTSKAFQHDTWNSGLTV ASISTGHLTSDNRGDIGILLGMIVFAVMLSILSLIGIFNRSFRTGIKRRILLLIPKWLYEDIPNMKNSNVVKMLQENSELMNNNSSEQVLYVDPMITEIKEIFIPEHKPTDYKKENT GPLETRDVPQNSLFDNTTVVYIPDLNTGYKPQISNFLPEGSHLSNNNEITSLTLKPPVDSLDSGNNPRLQKHPNFAFSVSSVNSLSNTIFLGELSLILNQGECSSPDIQNSVEEET TMLLENDSPSETIPEQTLLPDEFVSCLGIVNEELPSINTYFPQNILESHFNRISLLEK

FIG. 57

Prolactin receptor family	UniProt ID	RefSeq Accession	Amino Acid Sequence
Erythropoietin receptor	P19235	NP_000112.1	MDHLGASLWPQVGSLCLLAGAAWAPPPNLPDPKFESKAALLAARGPEELICFTERLEDLVCFWEEAASAGVGPGNYSFSYQLEDEPWKLCRLHQAPTARGAVRFWCSLP TADTSSFVPLELRVTAASGAPRYHRVIHINEVVLLDAPVGLVARLADESGHVVLRWLPPPETPMTSHIRYEVDVSAGNGAGSVQRVEILEGRTECVLSNLRGRTRYTFAVRAR MAEPSFGGFWSAWSEPVSLLTPSDLDPLILTLSLILVVILVLLTVLALLSHRRALKQKIWPGIPSPESEFGLFTTHKGNFQLWLYQNDGCLWWSPCTPFTEDPPASLEVLSERC WGTMQAVEPGTDDEGPLLEPVGSEHAQDTYLVLDKWLLPRNPPSEDLPGPGGSVDIVAMDEGSEASSCSSALASKPSPEGASAASFEYTILDPSSQLLRPWTLCPELPPTPP HLKYLYLVVSDSGISTDYSSGDSQGAQGGLSDGPYSNPYENSLIPAAEPLPPSYVACS
Granulocyte colony-stimulating factor receptor	Q99062	NP_000751.1	MARLGNCSLTWAALIILLPGSLEECGHISVSAPIVHLGDPITASCIKQNCSHLDPEPQILWRLGAELQPGGRQQRLSDGTQESIITLPHLNHTQAFLSCCLNWGNSLQILDQV ELRAGYPPAIPHNLSCLMNLTTSSLICQWEPGPETHLPTSFTLKSFKSRGNCQTQGDSILDCVPKDGQSHCCIPRKHLLLYQNMGIWVQAENALGTSMSPQLCLDPMDVVK LEPPMLRTMDPSPEAAPPQAGCLQLCWEPWQPGLHINQKCELRHKPQRGEASWALVGPLPLEALQYELCGLLPATAYTLQIRCIRWPLPGHWSDWSPSLELRTTERAPTV RLDTWWRQRQLDPRTVQLFWKPVPLEEDSGRIQGYVVSWRPSGQAGAILPLCNTTELSCTFHLPSEAQEVALVAYNSAGTSRPTPVVFSESRGPALTRLHAMARDPHSLW VGWEPPNPWPQGYVIEWGLGPPSASNSNKTWRMEQNGRATGFLLKENIRPFQLYEINVTPLYQDTMGPSQHVYAYSQEMAPSHAPELHLKHIGKTWAQLEWVPEPPEL GKSPLTHYTIFWTNAQNQSFSAILNASSRGFVLHGLEPASLYHIHLMAASQAGATNSTVLTLMTLTPEGSELHIILGLFGLLLLLTCLCGTAWLCCSPNRKNPLWPSVPDPAHS SLGSWVPTIMEEDAFQLPGLGTPPITKLTVLEEDEKKPVPWESHNSSETCGLPTLVQTYVLQGDPRAVSTQPQSQSGTSDQVLYGQILGSPTSPGPGHYLRCDSTQPLAGL TPSPKSYENLWFQASPLGTLVTPAPSQEDDCVFGPLLNFPLLQGIRVHGMEALGSF
Growth hormone receptor	P10912	NP_000154.1	MDLWQLLLTLALAGSSDAFSGSEATAAILSRAPWSLQSVNPGLKTNSSKEPKFTKCRSPERETFSCHWTDEVHHGTKNLGPIQLFYTRRNTQEWTQEWKECPDYVSAGENS CYFNSSFTSIWIPYCIKLTSNGGTVDEKCFSVDEIVQPDPPIALNWTLLNVSLTGIHADIQVRWEAPRNADIQKGWMVLEYELQYKEVNETKWKMMDPILTTSVPVYSLKVD KEYEVRVRSKQRNSGNYGEFSEVLYVTLPQMSQFTCEEDFYFPWLLIIIFGIFGLTVMLFVFLFSKQQRIKMLILPPVPVPKIKGIDPDLLKEGKLEEVNTILAIHDSYKPEFHSDD SWVEFIELDIDEPDEKTEESDTDRLLSSDHEKSHSNLGVKDGDSGRTSCCEPDILETDFNANDIHEGTSEVAQPQRLKGEADLLCLDQKNQNNSPYHDACPATQQPSVIQAE KNKPQPLPTEGAESTHQAAHIQLSNPSSLSNIDFYAQVSDITPAGSVVLSPGQKNKAGMSQCDMHPEMVSLCQENFLMDNAYFCEADAKKCIPVAPHIKVESHIQPSLNQE DIYITTESLITAAGRPGTGEHVPGSEMPVPDYTSIHIVQSPQGLILNATALPLPDKEFLSSCGYVSTDQLNKIMP

FIG. 57 (Cont.)

Prolactin receptor	P16471	NP_000940.1	MKENVASATVFTLLFLNTCLLNGQLPPGKPEIFKCRSPNKETFTCWWRPGTDGGLPTNYSLTYHREGETLMHECPDYITGGPNSCHFGKQYTSMWRTYIMMVNATNQM GSSFSDELYVDVTYIVQPDPPLELAVEVKQPEDRKPYLWIKWSPPTLIDLKTGWFTLLYEIRLKPEKAAEWEIHFAGQQTEFKILSLHPGQKYLVQVRCKPDHGYWSAWSPAT FIQIPSDFTMNDTTVWISVAVLSAVICLIVWAVALKGYSMVTCIPPVPGPKIKGFDAHLLEKGKSEELLSALGCQDFPPTSDYEDLLVEYLEVDDSEDQHLMSVHSKEHPSQ GMKPTYLDPDTDSGRGSCDSPSLLSEKCEEPQANPSTFYDPEVIEKPENPETTHTWDPQCISMEGKIPYFHAGGSKCSTWPLPQPSQHNPRSSYHNITDVCELAVGPAGAPA TLLNEAGKDALKSSQTIKSREEGKATQQREVESFHSETDQDTPWILPQEKTPFGSAKPLDYVEIHKVNKDGALSLLPKQRENSGKPKKPGTPENNKEYAKVSGVMDNNILVL VPDPHAKNVACFEESAKEAPPSLEQNQAEKALANFTATSSKCRLQLGGLDYLDPACFTHSFH
Thrombopoietin receptor	P40238	NP_005364.1	MPSWALFMVTSCLLLAPQNLAQVSSQDVSLLASDSEPLKCFSRTFEDLTCFWDEEEAAPSGTYQLLYAYPREKPRACPLSSQSMPHFGTRYVCQFPDQEEVRLFFPLHLWVK NVFLNQTRTQRVLFVDSVGLPAPPSIIKAMGGSQPGELQISWEEPAPEISDFLRYELRYGPRDPKNSTGPTVIQLIATETCCPALQRPHSASALDQSPCAQPTMPWQDGPKQ TSPSREASALTAEGGSCLISGLQPGNSYWLQLRSEPDGISLGGSWGSWSLPVTVDLPGDAVALGLQCFTLDLKNVTCQWQQQDHASSQGFFYHSRARCCPRDRYPIWENC EEEEKTNPGLQTPQFSRCHFKSRNDSIIHILVEVTTAPGTVHSYLGSPFWIHQAVRLPTPNLHWREISSGHLELEWQHPSSWAAQETCYQLRYTGEGHQDWKVLEPPLGAR GGTLELRPRSRYRLQLRARLNGPTYQGPWSSWSDPTRVETATETAWISLVTALHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVS DTCEEVEPSLLEILPKSSERTPLPLCSSQAQMDYRRLQPSCLGTMPLSVCPPMAESGSCCTTHIANHSYLPLSYWQQP

FIG. 58

Interferon receptor family	UniProt ID	RefSeq Accession	Amino Acid Sequence
interferon α/β receptor 1	P17181	NP_000620.2	MMVVLLGATTLVLVAVAPWVLSAAAGGKNLKSPQKVEVDIIDDNFILRWNRSDESVGNVTFSFDYQKTGMDNWIKLSGCQNITSTKCNFSSLKLNVYEEIKLRIRAEKENTS SWYEVDSFTPFRKAQIGPPEVHLEAEDKAIVIHISPGTKDSVMWALDGLSFTYSLVIWKNSSGVEERIENIYSRHKIYKLSPETTYCLKVKAALLTSWKIGVYSPVHCIKTTVENEL PPPENIEVSVQNQNYVLKWDYTYANMTFQVQWLHAFLKRNPGNHLYKWKQIPDCENVKTTQCVFPQNVFQKGIYLLRVQASDGNNTSFWSEEIKFDTEIQAFLLPPVFNI RSLSDSFHIYIGAPKQSGNTPVIQDYPLIYEIIFWENTSNAERKIIEKKTDVTVPNLKPLTVYCVKARAHTMDEKLNKSSVFSDAVCEKTKPGNTSKIWLIVGICIALFLVIVAA KVFLRCINYVFFPSLKPSSSIDEYFSEQPLKNLLLSTSEEQIEKCFIIENISTIATVEETNQTDEDHKKYSSQTSQDSGNYSNEDESESKTSEELQQDFV
Interferon α/β receptor 2	P48551	NP_000865.2	MILSQNAFIFRSLNLVLMVYISLVFGISYDSPDYTDESCTFKISLRNFRSILSWELKNHSIVPTHYTLLYTIMSKPEDLKVVKNCANTTRSFCDLTDEWRSTHEAYVTVLEGFSGN TTLFSCSHNFWLAIDMSFEPPEFEIVGFTNHINVMVKFPSIVEEELQFDLSLVIEEQSEGIVKKHKPEIKGNMSGNFTYIIDKLIPNTNYCVSVYLEHSDEQAVIKSPLKCTLLPPG QESESAESAKIGGIITVFLIALVLTSTIVTLKWIGYICLRNSLPKVLRQGLAKGWNAVAIHRCSHNALQSETPELKQSSCLSFPSSWDYKRASLCPSD
Interferon γ receptor 1	P15260	NP_000407.1	MALLFLPLVMQGVSRAEMGTADLGPSSVPTPTNVTIESYNMNPIVYWEYQIMPQVPVFTVEVKNYGVKNSEWIDACINISHHYCNISDHVGDPSNSLWVRVKARVGQK ESAYAKSEEFAVCRDGKIGPPKLDIRKEEKQIMIDIFHPSVFVNGDEQEVDYDPETTCYIRVVNVYVRMNGSEIQYKILTQKEDDCDEIQCQLAIPVSSLNSQYCVSAEGVLHV WGVTTEKSKEVCITIFNSSIKGSLWIPVVAALLFLVLSLVFICFYIKKINPLKEKSIILPKSLISVVRSATLETKPESKYVSLITSYQPFSLEKEVVCEEPLSPATVPGMHTEDNPGKVE HTEELSSITEVVTTEENIPDVVPGSHLTPIERESSSPLSSNQSEPGSIALNSVHSRNCSESDHSRNGFDTDSSCLESHSSLSDSEFPPNNKGEIKTEGQELITVIKAPTSFGYDKPHV LVDLLVDDSGKESLIGYRPTEDSKEFS
Interferon γ receptor 2	P38484	NP_005525.2	MRPTLLWSLLLLLGVFAAAAAPPDPLSQLPAPQHPKIRLYNAEQVLSWEPVALSNSTRPVVYQVQFKYTDSKWFTADIMSIGVNCTQITATECDFTAASPSAGFPMDFNV TLRLRAELGALHSAWVTMPWFQHYRNVTVGPPENIEVTPGEGSLIIRFSSPFDIADTSTAFFCYYVHYWEKGGIQQVKGPFRSNSISLDNLKPSRVYCLQVQAQLLWNKSNIF RVGHLSNISCYETMADASTELQQVILISVGTFSLLSVLAGACFFLVLKYRGLIKYWFHTPPSIPLQIEEYLKDPTQPILEALDKDSSPKDDVWDSVSIISFPEKEQEDVLQTL

FIG. 59

IL-10 receptor family	UniProt ID	RefSeq Accession	Amino Acid Sequence
Interleukin-22 receptor α2	Q969J5	NP_443194.1	MMPKHCFLGFLISFELTGVAGTQSTHESLKPQRVQFQSRNFHNILQWQPGRALTGNSSVFVQYKIMFSCSMKSSHQKPSGCWQHISCNFPGCRTLAKYGQRQWKNKED CWGTQELSCDLTSETSDIQEPYYGRVRAASAGSYSEWSMTPRFTPWWETKIDPPVMNITQVNGSLLVILHAPNLPYRYQKEKNVSIEDYYELLYRVFIINNSLEKEQKVYEGA HRAVEIEALTPHSSYCVVAEIYQPMLDRRSQRSEERCVEIP
Interleukin 10 receptor, α subunit	Q13651	NP_001549.2	MLPCLVVLLAALLSLRLGSDAHGTELPSPPSVWFEAEFFHHILHWTPIPNQSESTCYEVALLRYGIESWNSISNCSQTLSYDLTAVTLDLYHSNGYRARVRAVDGSRHSNWTV TNTRFSVDEVTLTVGSVNLEIHNGFILGKIQLPRPKMAPANDTYESIFSHFREYEIAIRKVPGNFTFTHKKVKHENFSLLTSGEVGEFCVQVKPSVASRSNKGMWSKEECISLTR QYFTVTNVIIFFAFVLLLSGALAYCLALQLYVRRRKKLPSVLLFKKPSPFIFISQRPSPETQDTIHPLDEEAFLKVSPELKNLDLHGSTDSGFGSTKPSLQTEEPQFLLPDPHPQADR TLGNREPPVLGDSCSSGSSNSTDSGICLQEPSLSPSTGPTWEQQVGSNSRGQDDSGIDLVQNSEGRAGDTQGGSALGHHSPPEPEVPGEEDPAAVAFQGYLRQTRCAEEK ATKTGCLEEESPLTDGLGPKFGRCLVDEAGLHPPALAKGYLKQDPLEMTLASSGAPTGQWNQPTEEWSLLALSSCSDLGISDWSFAHDLAPLGCVAAPGGLLGSFNSDLVTL PLISSLQSSE
Interleukin 10 receptor, β subunit	Q08334	NP_000619.3	MAWSLGSWLGGCLLVSALGMVPPPENVRMNSVNFKNILQWESPAFAKGNLTFTAQYLSYRIFQDKCMNTTLTECDFSSLSKYGDHTLRVRAEFADEHSDWVNITFCPVD DTIIGPPGMQVEVLADSLHMRFLAPKIENEYETWTMKNVYNSWTYNVQYWKNGTDEKFQITPQYDFEVLRNLEPWTTYCVQVRGFLPDRNKAGEWSEPVCEQTTHDET VPSWMVAVILMASVFMVCLALGCFALLWCVYKKTKYAFSPRNSLPQHLKEFLGHPHHNTLLFFSFPLSDENDVFDKLSVIAEDSESGKQNPGDSCSLGTPPGQGPQS
Interleukin 20 receptor, α subunit	Q9UHF4	NP_00126565 1.1	MKNVLQWTPPEGLQGVKVTYTVQYFIYGQKKWLNKSECRNINRTYCDLSAETSDYEHQYYAKVKAIWGTKCSKWAESGRFYPFLETQIGPPEVALTTDEKSISVVLTAPEK WKRNPEDLPVSMQQIYSNLKYNVSVLNTKSNRTWSQCVTNHTLVLTWLEPNTLYCVHVESFVPGPPRRAQPSEKQCARTLKDQSSEFKAKIIFWYVLPISITVFLFSVMGYSI YRYIHVGKEKHPANLILIYGNEFDKRFFVPAEKIVINFITLNISDDSKISHQDMSLLGKSSDVSSLNDPQPSGNLRPPQEEEEVKHLGYASHLMEIFCDSEENTEGTSLTQQESLSR TIPPDKTVIEYEYDVRTTDICAGPEEQELSLQEEVSTQGTLLESQAALAVIGPQTLQYSYTPQLQDLDPLAQEHTDSEEGPEEEPSTTLVDWDPQTGRLCIPSLSSFDQDSEGCE PSEGDGLGEEGLLSRLYEEPAPDRPPGENETYLMQFMEEWGLYVQMEN

FIG. 59 (Cont.)

Interleukin 20 receptor, β subunit	Q6UXL0	NP_653318.2	MQTFTMVLEEIWTSLFMWFFYALIPCLLTDEVAILPAPQNLSVLSTNMKHLLMWSPVIAPGETVYYSVEYQGEYESLYTSHIWIPSSWCSLTEGPECDVTDDITATVPYNLRV RATLGSQTSAWSILKHPFNRNSTILTRPGMEITKDGFHLVIELEDLGPQFEFLVAYWRREPGAEEHVKMVRSGGIPVHLETMEPGAAYCVKAQTFVKAIGRYSAFSQTECVEV QGEAIPLVLALFAFVGFMLILVVVPLFVWKMGRLLQYSCCPVVVLPDTLKITNSPQKLISCRREEVDACATAVMSPEELLRAWIS
Interleukin 22 receptor, α1 subunit	Q8N6P7	NP_067081.2	MRTLLTILTVGSLAAHAPEDPSDLLQHVKFQSSNFENILTWDSGPEGTPDTVYSIEYKTYGERDWVAKKGCQRITRKSCNLTVETGNLTELYYARVTAVSAGGRSATKMTDRF SSLQHTTLKPPDVTCISKVRSIQMIVHPTPTPIRAGDGHRLTLEDIFHKDLFYHLELQVNRTYQMHLGGKQREYEFFGLTPDTEFLGTIMICVPTWAKESAPYMCRVKTLPDRT WTYSFSGAFLFSMGFLVAVLCYLSYRYVTKPPAPPNSLNVQRVLTFQPLRFIQEHVLIPVFDLSGPSSLAQPVQYSQIRVSGPREPAGAPQRHSLSEITYLGQPDISILQPSNVPP PQILSPLSYAPNAAPEVGPPSYAPQVTPEAQFPFYAPQAISKVGPSSYAPQATPDSWPPSYGVCMEGSGKDSPTGTLSSPKHLRPKGQLQKEPPAGSCMLGGLSLQEVTSLA MEESQEAKSLHQPLGICTDRTSDPNVLHSGEEGTPQYLKGQLPLLSSVQIEGHPMSLPLQPPSRPCSPSDQGPSPWGLLESLVCPKDEAKSPAPETSDLEQPTELDSLFRGLAL TVQWES
Interferon-λ receptor subunit 1	Q8IU57	NP_734464.1	MAGPERWGPLLLCLLQAAPGRPRLAPPQNVTLLSQNFSVYLTWLPGLGNPQDVTYFVAYQSSPTRRWREVEECAGTKELLCSMIMCLKKQDLYNKFKGRVRTVSPSSKSP WVESEYLDYLFEVEPAPPVLVLTQTEEILSANATYQLPPCMPPLDLKYEVAFWKEGAGNKTLFPVTPHGQPVQITLQPAASEHHCLSARTIYTFSVPKYSKFSKPTCFLLEVPEA NWAFLVLPSLLILLVIAAGGVIWKTLMGNPWFQRAKMPRALDFSGHTHPVATFQPSRPESVNDLFLCPQKELTRGVRPTPRVRAPATQQTRWKKDLAEDEEEEDEEDTE DGVSFQPYIEPPSFLGQEHQAPGHSEAGGVDSGRPRAPLVPSEGSSAWDSSDRSWASTVDSSWDRAGSSGYLAEKGPGQGPGGDGHQESLPPPEFSKDSGFLEELPEDNL SSWATWGTLPPEPNLVPGGPPVSLQTLTFCWESSPEEEEEARESEIEDSDAGSWGAESTQRTEDRGRTLGHYMAR

FIG. 60

IL-17 receptor family	UniProt ID	RefSeq Accession	Amino Acid Sequence
Interleukin 17 receptor A	Q96F46	NP_00127683 4.1	MGAARSPPSAVPGPLGLLLLLLGVLAPGGASLRLLDHRALVCSQPGLNCTVKNSTCLDDSWIHPRNLTPSSPKDLQIQLHFAHTQQGDLFPVAHIEWTLQTDASILYLEGAE LSVLQLNTNERLCVRFEFLSKLRHHHRRWRFTFSHFVVDPDQEYEVTVHHLPKPIPDGDPNHQSKNFLVPDCEHARMKVTTPCMSSGSLWDPNITVETLEAHQLRVSFTLW NESTHYQILLTSFPHMENHSCFEHMHHIPAPRPEEFHQRSNVTLTLRNLKGCDHQVQIQPFFSSCLNDCLRHSATVSCPEMPDTPEPIPGPGSEKYSDDTKYTDGLPAADLI PPPLKPRKVWIIYSADHPLYVDVVLKFAQFLLTACGTEVALDLLEEQAISEAGVMTWVGRQKQEMVESNSKIHVLCSRGTRAKWQALLGRGAPVRLRCDHGKPVGDLFTAA MNMILPDFKRPACFGTYVVCYFSEVSCDGDVPDLFGAAPRYPLMDRFEEVYFRIQDLEMFQPGRMHRVGELSGDNYLRSPGGRQLRAALDRFRDWQVRCPDWFECENL YSADDQDAPSLDEEVFEEPLLPPGTGIVKRAPLVREPGSQACLAIDPLVGEEGGAAVAKLEPHLQPRGQPAPQPLHTLVLAAEEGALVAAVEPGPLADGAAVRLALAGEGEA CPLLGSPGAGRNSVLFLPVDPEDSPLGSSTPMASPDLLPEDVREHLEGLMLSLFEQSLSCQAQGGCSRPAMVLTDPHTPYEEEQRQSVQSDQGYISRSSPQPPEGLTEMEEE EEEEQDPGKPALPLSPEDLESLRSLGRQLLFRQLQKNSGWDTMGSESEGPSA
Interleukin 17 receptor B	Q9NRM6	NP_061195.2	MSLVLLSLAALCRSAVPREPTVQCGSETGPSPEWMLQHDLIPGDLRDLRVEPVTTSVATGDYSILMNVSWVLRADASIRLLKATKICVTGKSNFQSYSCVRCNYTEAFQTQTR PSGGKWTFSYIGFPVELNTVYFIGAHNIPNANMNEDGPSMSVNFTSPGCLDHIMKYKKKCVKAGSLWDPNITACKKNEETVEVNFTTTPLGNRYMALIQHSTIIGFSQVFEP HQKKQTRASVIPVTGDSEGATVQLTPYFPTCGSDCIRHKGTVVLCPQTGVPFPLDNNKSKPGGWILPLLLLSLVATWVLVAGIYLMWRHERIKKTSFSTTTLLPPIKVLVVYP SEICFHHTICYFTEFLQNHCRSEVILEKWQKKIAEMGPVQWLATQKAADKVVFLLSNDVNSVCDGTCGKSEGSPSENSQDLFPLAFNLFCSDLRSQIHLHKYVVVYFREIDT KDDYNALSVCPKYHLMKDATAFCAELLHVKQQVSAGKRSQACHDGCCSL
Interleukin 17 receptor C	Q8NAC3	NP_00119019 2.1	MPVPWFLLSLALGRSPVVLSLERLVGPQDATHCSPGLSCRLWDSDILCLPGDIVPAPGPVLAPTHLQTELVIRCQKETDCDLCLRVAVHLAVHGHWEEPEDEEKFGGAADS GVEEPRNASLQAQVVLSFQAYPTARCVLLEVQVPAALVQFGQSVGSVVYDCFEAALGSEVRIWSYTQPRYEKELNHTCQLPDCRGLEVWNSIPSCWALPWLNVSADGDN VHLVLNVSEEQHFGLSLYWNQVQGPPKPRWHKNLTGPQITLNHTDLVPCLCIQVWPLEPDSVRTNICPFREDPRAHQNLWQAARLRLLTLQSWLLDAPCSLPAEAALCW RAPGGDPCQPLVPPLSWENVTVDKVLEFPLLKGHPNLCVQVNSSEKLQLQECLWADSLGPLKDDVLLLETRGPQDNRSLCALEPSGCTSLPSKASTRAARLGEYLLQDLQSG QCLQLWDDDLGALWACPMDKYIHKRWALVWLACLLFAAALSLILLLKKDHAKAAARGRAALLYSADDSGFERLVGALASALCQLPLRVAVDLWSRRELSAQGPVAWFH AQRRQTLQEGGVVVLLFSPGAVALCSEWLQDGVSGPGAHGPHDAFRASLSCVLPDFLQGRAPGSYVGACFDRLLHPDAVPALFRTVPVFTLPSQLPDFLGALQQPRAPRS GRLQERAEQVSRALQPALDSYFHPPGTPAPGRGVGPGAGPGAGDGT

FIG. 60 (Cont.)

Interleukin-17 receptor D	Q8NFM7	NP_00130579 3.1	MESQPFLNMKFETDYFVKVVPFPSIKNESNYHPFFFRTRACDLLLQPDNLACKPFWKPRNLNISQHGSDMQVSFDHAPHNFGFRFFYLHYKLKHEGPFKRKTCKQEQTTET TSCLLQNVSPGDYHELVDDTNTTRKVMHYALKPVHSPWAGPIRAVAITVPLVVISAFATLFTVMCRKKQQENIYSHLDEESSESSTYTAALPRERLRPRPKVFLCYSSKDGQN HMNVVQCFAYFLQDFCGCEVALDLWEDFSLCREGQREWVIQKIHESQFIIVVCSKGMKYFVDKKNYKHKGGRGSGKGELFLVAVSAIIAEKLRQAKQSSSAALSKFIAVYFD YSCEGDVPGILDLSTKYRLMDNLPQLCSHLHSRDHGLQEPGQHTRQGSRRNYFRSKSGRSLYVAICNMHQFIDEEPDWFEKQFVPFHPPPLRYREPVLEKFDSGLVLNDVM CKPGPESDFCLKVEAAVLGATGPADSQHESQHGGLDQDGEARPALDGSAALQPLLHTVKAGSPSDMPRDSGIYDSSVPSSELSLPLMEGLSTDQTETSSLTESVSSSSGLGEE EPPALPSKLLSSGSCKADLGCRSYTDELHAVAPL
Interleukin 17 receptor E	Q8NFR9	NP_00118030 9.1	MGSSRLAALLLPLLLVIDLSDSAGIGFRHLPHWNTRCPLASHTDDSFTGSSAVIPCRTWWALFSTKPWCVRVWHCSRCLCQHLLSGGSGLQRGLFHLLVQKSKKSSTFKFYR RHKMPAPAQRKLLPRRHLSEKSHHISIPSPDISHKGLRSKRTQPSDPETWESLPRLDSQRHGGPEFSFDLLPEARAIRVTISSGPEVSVRLCHQWALECEELSSPYDVQKIVSGG HTVELPYEFLLPCLCIEASYLQEDTVRRKKCPFQSWPEAYGSDFWKSVHFTDYSQHTQMVMALTLRCPLKLEAALCQRHDWHTLCKDLPNATARESDGWYVLEKVDLHPQ LCFKFSFGNSSHVECPHQTGSLTSWNVSMDTQAQQILHFSSRMHATFSAAWSLPGLGQDTLVPPVYTVSQARGSSPVSLDLIIPFLRPGCCVLLHASLSSPGGEDAWLIGV GGSVPSGVAVRCPVCLEAPLVSGCLLQTPGALDPGTAGPPHPTGCCSGPHLPAPTVRPGPSAASAPPARGGLGGAAAPGGSAG

FIG. 61

Immunoglobulin superfamily	UniProt ID	RefSeq Accession	Amino Acid Sequence
Interleukin 1 receptor, type I	P14778	NP_000868.1	MKVLLRLICFALLISSLEADKCKEREEKIILVSSANEIDVRPCPLNPNEHKGTITWYKDDSKTPVSTEQASRIHQHKEKLWFVPAKVEDSGHYYCVVRNSSYCLRIKISAKFVENE PNLCYNAQAIFKQKLPVAGDGGLVCPYMEFFKNENNELPKLQWYKDCKPLLLDNIHFSGVKDRLIVMNVAEKHRGNYTCHASYTYLGKQYPITRVIEFITLEENKPTRPVIVSP ANETMEVDLGSQIQLICNVTGQLSDIAYWKWNGSVIDEDDPVLGEDYYSVENPANKRRSTLITVLNISEIESRFYKHPFTCFAKNTHGIDAAYIQLIYPVTNFQKHMIGICVTLT VIIVCSVFIYKIFKIDIVLWYRDSCYDFLPIKASDGKTYDAYILYPKTVGEGSTSDCDIFVFKVLPEVLEKQCGYKLFIYGRDDYVGEDIVEVINENVKKSRRLIIILVRETSGFSWLGG SSEEQIAMYNALVQDGIKVVLLELEKIQDYEKMPESIKFIKQKHGAIRWSGDFTQGPQSAKTRFWKNVRYHMPVQRRSPSSKHQLLSPATKEKLQREAHVPLG
Interleukin 1 receptor, type II	P27930 8.1	NP_00124834	MLRLYVLVMGVSAFTLQPAAHTGAARSCRFRGRHYKREFRLEGEPVALRCPQVPYWLWASVSPRINLTWHKNDSARTVPGEEETRMWAQDGALWLLPALQEDSGTYVC TTRNASYCDKMSIELRVFENTDAFLPFISYPQILTLSTSGVLVCPDLSEFTRDKTDVKIQWYKDSLLLDKDNEKFLSVRGTTHLLVHDVALEDAGYYRCVLTFAHEGQQYNITRSI ELRIKKKKEETIPVISPLKTISASLGSRLTIPCKVFLGTGTPLTTMLWWTANDTHIESAYPGGRVTEGPRQ
Interleukin-1 receptor-like 1	Q01638 7.1	NP_00126933	MYSTVSGSEKNSKIYCPTIDLYNWTAPLEWFKNCQALQGSRYRAHKSFLVIDNVMTEDAGDYTCKFIHNENGANYSVTATRSFTVKDEQGFSLFPVIGAPAQNEIKEVEIGK NANLTCSACFGKGTQFLAAVLWQLNGTKITDFGEPRIQQEEGQNQSFSNGLACLDMVLRIADVKEEDLLLQYDCLALNLHGLRRHTVRLSRKNPSKECF
Interleukin-1 receptor-like 2	Q9HB29	NP_003845.2	MWSLLLCGLSIALPLSVTADGCKDIFMKNEILSASQPFAFNCTFPPITSGEVSVTWYKNSSKIPVSKIIQSRIHQDETWILFLPMEWGDSGVYQCVIKGRDSCHRIHVNLTVFEK HWCDTSIGGLPNLSDEYKQILHLGKDDSLTCHLHFPKSCVLGPIKWYKDGNEIKGERFTVLETRILVSNVSAEDRGNYACQAILTHSGKQYEVLNGITVSITERAGYGGSVPKII YPKMHSIEVQLGTTLIVDCNVTDTKDNTNLRCWRVNNTLVDDYYDESKRIREGVETHVSFREHNLYTVNITFLEVKMEDYGLPFMCHAGVSTAYIILQLPAPDFRAYLGGLIA LVAVAVSVVYIYNIFKIDIVLWYRSAFHSTETIVDGKLYDAYVLYPKPHKESQRHAVDALVLNILPEVLEROCGYKLFIFGRDEFPGQAYANVIDENVKLCRRLIIVVVPESLGFGL LKNLSEEQIAVYSALIQDGMKVILIELEKIEDYTVMPESIQYIKQKHGAIRWHGDFTEQSQCMKTKFWKTVRYHMPPRRCRPFPPVCQLLQHTPCYRTAGPELGSRRKKCTLTT G
Interleukin-18 1	Q13478 8.1	NP_00126932	MNCKKLLLENNKNPTIKKNAEFEDQGYYSCVHFLHHNGKLFNITKTFNITIVEDRSNIVPVLLGPKLNHVAVELGKNVRLNCSALLNEEDVIYWMFGEENGSDPNIHEEKEMRK IMTPEGKWHASKVLRIENIGESNLNVLYNCTVASTGGTDTKSFHLVRKDMADIPGHYVFTRGMIIAVLILVAVVCLVTVCVIYRVDLVLFYRHLTRRDETLTDGKTYDAFVSYLKE CRPENGEEHTFAVEILPRVLEKHFGYKLCIFERDVVPGGAVVDEIHSLIEKSRRLIIVLSKSYMSNEVRYELESGLHEALVERKIKIILIEFTPVTDFTFLPQSLKLLKSHRVLKWKAD KSLSYNSRFWKNLLYLMPAKTVKPGRDEPEVLPVLSES

FIG. 61 (Cont.)

IL-1 receptor accessory protein	Q9NPH3	NP_00116140 0.1	MTLLWCVVSLYFYGILQSDASERCDDWGLDTMRQIQVFEDEPARIKCPLFEHFLKFNYSTAHSAGLTLIWYWTRQDRDLEEPINFRLPENRISKEKDVLWFRPTLLNDTGNY TCMLRNTTYCSKVAFPLEVVQKDSCFNSPMKLPVHKLYIEYGIQRITCPNVDGYFPSSVKPTITWYMGCYKIQNFNNVIPEGMNLSFLIALISNNGNYTCVTYPENGRTFHLT RTLTVKVVGSPKNAVPPVIHSPNDHVVYEKEPGEELLIPCTVYSFLMDSRNEVWWTIDGKKPDDITIDVTINESISHSRTEDETRTQILSIKKVTSEDLKRSYVCHARSAKGEVA KAAKVKQKVPAPRYTVELACGFGATVILLVVILIVVYHVYWLEMVLFYRAHFGTDETILDGKEYDIYVSYARNAEEEFVLLTLRGVLENEFGYKLCIFDRDSLPGGIVTDETLSFI QKSRRLLVVLSPNYVLQGTQALLELKAGLENMASRGNINVILVQYKAVKETKVKELKRAKTVLTVIKWKGEKSKYPQGRFWKQLQVAMPVKKSPRRSSSDEQGLSYSSLKNV
IL-18 receptor accessory protein	O95256	NP_003844.1	MLCLGWIFLWLVAGERIKGFNISGCSTKKLLWTYSTRSEEEFVLFCDLPEPQKSHFCHRNRLSPKQVPEHLPFMGSNDLSDVQWYQQPSNGDPLEDIRKSYPHIIQDKCTLHF LTPGVNNSGSYKCRPKMIKSPYDVACCVKMILEVKPQTNASCEYSASHKQDLLLGSTGSISCPSLSCQSDAQSPAVTWYKNGKLLSVERSNRIVVDEVYDYHQGTYVCDYTQS DTVSSWTVRAVVQVRTIVGDTKLKPDILDPVEDTLEVELGKPLTISCKARFGFERVFNPVIKWYIKDSDLEWEVSVPEAKSIKSTLKDEIIERNIILEKVTQRDLRRKFVCFVQNSI GNTTQSVQLKEKRGVVLLYILLGTIGTLVAVLAASALLYRHWIEIVLLYRTYQSKDQTLGDKKDFDAFVSYAKWSSFPSEATSSLSEEHLALSLFPDVLENKYGYSLCLLERDVAP GGVYAEDIVSIIKRSRRGIFILSPNYVNGPSIFELQAAVNLALDDQTLKLILIKFCYFQEPESLPHLVKKALRVLPTVTWRGLKSVPPNSRFWAKMRYHMPVKNSQGFTWNQLR ITSRIFQWKGLSRTETTGRSSQPKEW
PDGFRα (platelet derived growth factor receptor alpha)	P16234	NP_006197.1	MGTSHPAFLVLGCLLTGLSLILCQLSLPSILPNENEKVVQLNSSFSLRCFGESEVSWQYPMSEEESSDVEIRNEENNSGLFVTVLEVSSASAAHTGLYTCYYNHTQTEENELEGR HIYIYVPDPDVAFVPLGMTDYLVIVEDDDSAIIPCRTTDPETPVTLHNSEGVVPASYDSRQGFNGTFTVGPYICEATVKGKKFQTIPFNVYALKATSELDLEMEALKTVYKSGETI VVTCAVFNNEVVDLQWTYPGEVKGKGITMLEEIKVPSIKLVYTLTVPEATVKDSGDYECAARQATREVKEMKKVTISVHEKGFIEIKPTFSQLEAVNLHEVKHFVVEVRAYPPP RISWLKNNLTLIENLTEITTDVEKIQEIRYRSKLKLIRAKEEDSGHYTIVAQNEDAVKSYTFELLTQVPSSILDLVDDHHGSTGGQTVRCTAEGTPLPDIEWMICKDIKKCNNETS WTILANNVSNIITEIHSRDRSTVEGRVTFAKVEETIAVRCLAKNLLGAENRELKLVAPTLRSELTVAAAVLVLLVIVIISLIVLVVIWKQKPRYEIRWRVIESISPDGHEYIYVDPMQ LPYDSRWEFPRDGLVLGRVLGSGAFGKVVEGTAYGLSRSQPVMKVAVKMLKPTARSSEKQALMSELKIMTHLGPHLNIVNLLGACTKSGPIYIITEYCFYGDLVNYLHKNRDS FLSHHPEKPKKELDIFGLNPADESTRSYVILSFENNGDYMDMKQADTTQYVPMLERKEVSKYSDIQRSLYDRPASYKKKSMLDSEVKNLLSDDNSEGLTLLDLLSFTYQVARG MEFLASKNCVHRDLAARNVLLAQGKIVKICDFGLARDIMHDSNYVSKGSTFLPVKWMAPESIFDNLYTTLSDVWSYGILLWEIFSLGGTPYPGMMVDSTFYNKIKSGYRMA KPDHATSEVYEIMVKCWNSEPEKRPSFYHLSEIVENLLPGQYKKSYEKIHLDFLKSDHPAVARMRVDSDNAYIGVTYKNEEDKLKDWEGGLDEQRLSADSGYIIPLPDIDPVPE EEDLGKRNRHSSQTSEESAIETGSSSSTFIKREDETIEDIDMMDDIGIDSSDLVEDSFL

FIG. 61 (Cont.)

PDGFRβ (platelet derived growth factor receptor beta)	P09619	NP_002600.1	MRLPGAMPALALKGELLLLSLLLLLEPQISQGLVVTPPGPELVLNVSSTFVLTCSGSAPVVWERMSQEPPQEMAKAQDGTFSSVLTLTNLTGLDTGEYFCTHNDSRGLETDER KRLYIFVPDPTVGFLPNDAEELFIFLTEITEITIPCRVTDPQLVVTLHEKKGDVALPVPYDHQRGFSGIFEDRSYICKTTIGDREVDSDAYYVYRLQVSSINVSVNAVQTVVRQGE NITLMCIVIGNEVVNFEWTYPRKESGRLVEPVTDFLLDMPYHIRSILHIPSAELEDSGTYTCNVTESVNDHQDEKAINITVVESGYVRLLGEVGTLQFAELHRSRTLQVVFEAYP PPTVLWFKDNRTLGDSSAGEIALSTRNVSETRYVSELTLVRVKVAEAGHYTMRAFHEDAEVQLSFQLQINVPVRVLELSESHPDSGEQTVRCRGRGMPQPNIIWSACRDLKR CPRELPPTLLGNSSEEESQLETNVTYWEEEQEFEVVSTLRLQHVDRPLSVRCTLRNAVGQDTQEVIVVPHSLPFKVVVISAILALVVLTIISLIILIMLWQKKPRYEIRWKVIESVSS DGHEYIYVDPMQLPYDSTWELPRDQLVLGRTLGSGAFGQVVEATAHGLSHSQATMKVAVKMLKSTARSSEKQALMSELKIMSHLGPHLNVVNLLGACTKGGPIYIITEYCR YGDLVDYLHRNKHTFLQHHSDKRRPPSAELYSNALPVGLPLPSHVSLTGESDGGYMDMSKDESVDYVPMLDMKGDVKYADIESSNYMAPYDNYVPSAPERTCRATLINES PVLSYMDLVGFSYQVANGMEFLASKNCVHRDLAARNVLICEGKLVKICDFGLARDIMRDSNYISKGSTFLPLKWMAPESIFNSLYTTLSDVWSFGILLWEIFTLGGTPYPELP MNEQFYNAIKRGYRMAQPAHASDEIYEIMQKCWEEKFEIRPPFSQLVLLLERLLGEGYKKKYQQVDEEFLRSDHPAILRSQARLPGFHGLRSPLDTSSVLYTAVQPNEGDND YIIPLPDPKPEVADEGPLEGSPSLASSTLNEVNTSSTISCDSPLEPQDEPEPEPQLELQVEPEPELEQLPDSGCPAPRAEAEDSFL
KIT proto-oncogene receptor tyrosine kinase	P10721	NP_000213.1	MRGARGAWDFLCVLLLLRVQTGSSQPSVSPGEPSPPSIHPGKSDLIVRVGDEIRLLCTDPGFVKWTFEILDETNENKQNEWITEKAEATNTGKYTCTNKHGLSNSIYVFVRD PAKLFLVDRSLYGKEDNDTLVRCPLTDPEVTNYSLKGCQGKPLPKDLRFIPDPKAGIMIKSVKRAYHRLCLHCSVDQEGKSVLSEKFILKVRPAFKAVPVVSVSKASYLLREGEEF TVTCTIKDVSSSVYSTWKRENSQTKLQEKYNSWHHGDFNYERQATLTISSARVNDSGVFMCYANNTFGSANVTTTLEVVDKGFINIFPMINTTVFVNDGENVDLIVEYEAFP KPEHQQWIYMNRTFTDKWEDYPKSENESNIRYVSELHLTRLKGTEGGTYTFLVSNSDVNAAIAFNVYVNTKPEILTYDRLVNGMLQCVAAGFPEPTIDWYFCPGTEQRCSA SVLPVDVQTLNSSGPPFGKLVVQSSIDSSAFKHNGTVECKAYNDVGKTSAYFNFAFKGNNKEQIHPHTLFTPLLIGFVIVAGMMCIIVMILTYKYLQKPMYEVQWKVVEEING NNYVYIDPTQLPYDHKWEFPRNRLSFGKTLGAGAFGKVVEATAYGLIKSDAAMTVAVKMLKPSAHLTEREALMSELKVLSYLGNHMNIVNLLGACTIGGPTLVITEYCCYGD LLNFLRRKRDSFICSKQEDHAEAALYKNLLHSKESSCSDSTNEYMDMKPGVSYVVPTKADKRRSVRIGSYIERDVTPAIMEDDELALDLEDLLSFSYQVAKGMAFLASKNCIHR DLAARNILLTHGRITKICDFGLARDIKNDSNYVVKGNARLPVKWMAPESIFNCVYTFESDVWSYGIFLWELFSLGSSPYPGMPVDSKFYKMIKEGFRMLSPEHAPAEMYDIM KTCWDADPLKRPTFKQIVQLIEKQISESTNHIYSNLANCSPNRQKPVVDHSVRINSVGSTASSSQPLLVHDDV

FIG. 61 (Cont.)

CSFR (colony stimulating factor 1 receptor)	P07333	NP_00127563 4.1	MGPGVLLLLLVATAWHGQGIPVIEPSVPELVVKPGATVTLRCVGNGSVEWDGPPSPHWTLYSDGSSILSTNNATFQNTGTYRCTEPGDPLGGSAAIHLYVKDPARPWNVL AQEVVVFEDQDALLPCLLTDPVLEAGVSLVRVRGRPLMRHTNYSFSPWHGFTIHRAKFIQSQDYQCSALMGGRKVMSISIRLKVQKVIPGPPALTLVPAELVRIRGEAAQIVC SASSVDVNFDVFLQHNNTKLAIPQQSDFHNNRYQKVLTLNLDQVDFQHAGNYSCVASNVQGKHSTSMFFRVVESAYLNLSSEQNLIQEVTVGEGLNLKVMVEAYPGLQG FNWTYLGPFSDHQPEPKLANATTKDTYRHTFTLSLPRLKPSEAGRYSFLARNPGGWRALTFELTLRYPPEVSVIWTFINGSGTLLCAASGYPQPNVTWLQCSGHTDRCDEAQ VLQVWDDPYPEVLSQEPFHKVTVQSLLTVETLEHNQTYECRAHNSVGSGSWAFIPISAGAHTHPPDEFLFTPVVVACMSIMALLLLLLLLYKYKQKPKYQVRWKIIESYEG NSYTFIDPTQLPYNEKWEFPRNNLQFGKTLGAGAFGKVVEATAFGLGKEDAVLKVAVKMLKSTAHADEKEALMSELKIMSHLGQHENIVNLLGACTHGGPVLVITEYCCYG DLLNFLRRKAEAMLGPSLSPGQDPEGGVDYKNIHLEKKYVRRDSGFSSQGVDTYVEMRPVSTSSNDSFSEQDLDKEDGRPLELRDLLHFSSQVAQGMAFLASKNCIHRDVA ARNVLLTNGHVAKIGDFGLARDIMNDSNYIVKGNARLPVKWMAPESIFDCVYTVQSDVWSYGILLWEIFSLGLNPYPGILVNSKFYKLVKDGYQMAQPAFAPKNIYSIMQA CWALEPTHRPTFQQICSFLQEQAQEDRRERDYTNLPSSSRSGGSGSSSSELEEESSSEHLTCCEQGDIAQPLLQPNNYQFC

FIG. 62

Tumor necrosis factor receptor family	UniProt ID	RefSeq Accession	Amino Acid Sequence
TNFR1 (tumor necrosis factor receptor 1 / TNFRSF1A)	P19438	NP_001056.1	MGLSTVPDLLLPLVLLELLVGIYPSGVIGLVPHLGDREKRDSVCPQGKYIHPQNNSICCTKCHKGTYLYNDCPGPGQDTDCRECESGSFTASENHLRHCLSCSKCRKEMGQVEI SSCTVDRDTVCGCRKNQYRHYWSENLFQCFNCSLCLNGTVHLSCQEKQNTVCTCHAGFFLRENECVSCSNCKKSLECTKLCLPQIENVKGTEDSGTTVLLPLVIFFGLCLLSLL FIGLMYRYQRWKSKLYSIVCGKSTPEKEGELEGTTTKPLAPNPSFSPTPGFTPTLGFSPVPSSTFTSSSTYTPGDCPNFAAPRREVAPPYQGADPILATALASDPIPNPLQKWED SAHKPQSLDTDDPATLYAVVENVPPLRWKEFVRRLGLSDHEIDRLELQNGRCLREAQYSMLATWRRRTPRREATLELLGRVLRDMDLLGCLEDIEEALCGPAALPPAPSLLR
TNFR2 (tumor necrosis factor receptor 2 / TNFRSF1B)	P20333	NP_001057.1	MAPVAVWAALAVGLELWAAAHALPAQVAFTPYAPEPGSTCRLREYYDQTAQMCCSKCSPGQHAKVFCTKTSDTVCDSCEDSTYTQLWNWVPECLSCGSRCSSDQVETQ ACTREQNRICTCRPGWYCALSKQEGCRLCAPLRKCRPGFGVARPGTETSDVVCKPCAPGTFSNTTSSTDICRPHQICNVVAIPGNASMDAVCTSTSPTRSMAPGAVHLPQP VSTRSQHTQPTPEPSTAPSTSFLLPMGPSPPAEGSTGDFALPVGLIVGVTALGLLIIGVVNCVIMTQVKKKPLCLQREAKVPHLPADKARGTQGPEQQHLLITAPSSSSSSLESS ASALDRRAPTRNQPQAPGVEASGAGEARASTGSSDSSPGGHGTQVNVTCIVNVCSSSDHSSQCSSQASSTMGDTDSSPSESPKDEQVPFSKEECAFRSQLETPETLLGSTEE KPLPLGVPDAGMKPS
lymphotoxin β receptor / TNFRSF3	P36941	NP_00125791 6.1	MEATGSLASQLKVPPYASENQTCRDQEKEYYEPQHRICCSRCPPGTYVSAKCSRIRDTVCATCAENSYNEHWNYLTICQLCRPCDPVMGLEEIAPCTSKRKTQCRCQPGMF CAAWALECTHCELLSDCPPGTEAELKDEVCKGNNHCVPCKAGHFQNTSSPSARCQPHTRCENQGLVEAAPGTAQSDTTCKNPLEPLPPEMSGTMLMLAVLLPLAFFLLLA TVF5CIWKSHPSLCRKLGSLLKRRPQGEGPNPVAGSWEPPKAHPYFPDLVQPLLPISGDVSPVSTGLPAAPVLEAGVPQQQSPLDLTREPQLEPGEQSQVAHGTNGIHVTG GSMTITGNIYIYNGPVLGGPPGPGDLPATPEPPYPIPEEGDPGPPGLSTPHQEDGKAWHLAETEHCGATPSNRGPRNQFITHD
OX40 / TNFRSF4	P43489	NP_003318.1	MCVGARRLGRGPCAALLLLGLGLSTVTGLHCVGDTYPSNDRCCHECRPGNGMVSRCSRSQNTVCRPCGPGFYNDVVSSKPCKPCTWCNLRSGSERKQLCTATQDTVCRC RAGTQPLDSYKPGVDCAPCPPGHFSPGDNQACKPWTNCTLAGKHTLQPASNSSDAICEDRDPPATQPQETQGPPARPITVQPTEAWPRTSQGPSTRPVEVPGGRAVAAI LGLGLVLGLLGPLAILLALYLLRRDQRLPPDAHKPPGGGSFRTPIQEEQADAHSTLAKI
CD40 / TNFRSF5	P25942	NP_001241.1	MVRLPLQCVLWGCLLTAVHPEPPTACREKQYLINSQCCSLCQPGQKLVSDCTEFTETECLPCGESEFLDTWNRETHCHQHKYCDPNLGLRVQQKGTSETDTICTCEEGWHC TSEACESCVLHRSCSPGFGVKQIATGVSDTICEPCPVGFFSNVSSAFEKCHPWTSCETKDLVVQQAGTNKTDVVCGPQDRLRALVVIPIIFGILFAILLVLVFIKKVAKKPTNKAP HPKQEPQEINFPDDLPGSNTAAPVQETLHGCQPVTQEDGKESRISVQERQ

FIG. 62 (Cont.)

Fas / TNFRSF6	P25445	NP_000034.1	MLGIWTLLPLVLTSVARLSSKSVNAQVTDINSKGLELRKTVTTVETQNLEGLHHDGQFCHKPCPPGERKARDCTVNGDEPDCVPCQEGKEYTDKAHFSSKCRRCRLCDEGH GLEVEINCTRTQNTKCRCKPNFFCNSTVCEHCDPCTKCEHGIIKECTLTSNTKCKEEGSRSNLGWLCLLLLPIPLIVWVKRKEVQKTCRKHRKENQGSHESPTLNPETVAINLSD VDLSKYITTIAGVMTLSQVKGFVRKNGVNEAKIDEIKNDNVQDTAEQKVQLLRNWHQLHGKKEAYDTLIKDLKKANLCTLAEKIQTIILKDITSDSENSNFRNEIQSLV	
decoy receptor 3 / TNFRSF6B	O95407	NP_003814.1	MRALEGPGLSLLCLVLALPALLPVPAVRGVAETPTYPWRDAETGERLVCAQCPPGTFVQRPCRRDSPTTCGPCPPRHYTQFWNYLERCRYCNVLCGEREEEARACHATHNR ACRCRTGFFAHAGFCLEHASCPPGAGVIAPGTPSQNTQCQPCPPGTFSASSSSEQCQPHRNCTALGLALNVPGSSSHDTLCTSCTGFPLSTRVPGAEECRAVIDFVAFQDI SIKRLQRLLQALEAPEGWGPTPRAGRAALQLKLRRRLTELLGAQDGALLVRLLQALRVARMPGLERSVRERFLPVH	
CD27 / TNFRSF7	P26842	NP_001233.1	MARPHPWWLCVLGTLVGLSATPAPKSCPERHYWAQGKLCCQMCEPGTFLVKDCDQHRKAAQCDPCIPGVSFSPDHHTRPHCESCRHCNSGLLVRNCTITANAECACRN GWQCRDKECTECDPLPNPSLTARSSQALSPHPQPTHLPYVSEMLEARTAGHMQTLADFRQLPARTLSTHWPPQRSLCSSDFIRILVIFSGMFLVFTLAGALFLHQRRKYRSN KGESPVEPAEPCRYSCPREEEGSTIPIQEDYRKPEPACSP	
CD30 / TNFRSF8	P28908	NP_001234.3	MRVLLAALGLLFLGALRAFPQDRPFEDTCHGNPSHYYDKAVRRCCYRCPMGLFPTQQCPQRPTDCRKQCEPDYYLDEADRCTACVTCSRDDLVEKTPCAWNSSRVCECRP GMFCSTSAVNSCARCFFHSVCPAGMIVKFPGTAQKNTVCEPASPGVSPACASPENCKEPSSGTIPQAKPTPVSPATSSASTMPVRGGTRLAQEAASKLTRAPDSPSSVGRPS SDPGLSPTQPCPEGSGDCRKQCEPDYYLDEAGRCTACVSCSRDDLVEKTPCAWNSSRTCECRPGMICATSATNSCARCVPYPICAAETVTKPQDMAEKDTTFEAPPLGTQP DCNPTPENGEAPASTSPTQSLLVDSQASKTLPIPTSAPVALSSTGKPVLDAGPVLFWVILVLVVVVGSSAFLLCHRRACRKRIRQKLHLCYPVQTSQPKLELVDSRPRASSTQLR SGASVTEPVAEERGLMSQPLMETCHSVGAAYLESLPLQDASPAGGPSSPRDLPEPRVSTEHTNNKIEKIYIMKADTVIVGTVKAELPEGRGLAGPAEPELEEELEADHTPHYPE QETEPPLGSCSDVMLSVEEEGKEDPLPTAASGK	
4-1BB / TNFRSF9	Q07011	NP_001552.2	MGNSCYNIVATLLLVLNFERTRSLQDPCSNCPAGTFCDNNRNQICSPCPPNSFSSAGGQRTCDICRQCKGVFRTRKECSSTSNAECDCTPGFHCLGAGCSMCEQDCKQGQ ELTKKGCKDCCFGTFNDQKRGICRPWTNCSLDGKSVLVNGTKERDVVCGPSPADLSPGASSVTPPAPAREPGHSPQIISFFLALTSTALLFLLFFLTLRFSVVKRGRKKLLYIFKQ PFMRPVQTTQEEDGCSCRFPEEEEGGCEL	
DR4 (death receptor 4 / TNFRSF10A)	O00220	NP_003835.3	MAPPPARVHLGAFLAVTPNPGSAASGTEAAAATPSKVWGSSAGRIEPRGGGRGALPTSMGQHGPSARARAGRAPGPRPAREASPRLRVHKTFKFVVVGVLLQAVPSSAA TIKLHDQSIGTQQWEHSPLGELCPPGSHRSEHPGACNRCTEGVGYTNASNNLFACLPCTACKSDEEERSPCTTTRNTACQCKPGTFRNDNSAEMCRKCSRGCPRGMVKVK DCTPWSDIECVHKESGNGHNIWVILVVTLVVPLLLVAVLIVCCIGSGCGGDPKCMDRVCFWRLGLLRGPGAEDNAHNEILSNADSLSTFVSEQQMESQEPADLTGVTVQS PGEAQCLLGPAEAEGSQRRRLLVPANGADPTETLMLFFDKFANIVPFDSWDQLMRQLDLTKNEIDVVRAGTAGPGDALYAMLMKWVNKTGRNASIHTLLDALERMEER HAREKIQDLLVDSGKFIYLEDGTGSAVSLE	

FIG. 62 (Cont.)

DR5 (death receptor 5 / TNFRSF10B)	O14763	NP_003833.4	MEQRGQNAPAASGARKRHGPGPREARGARPGPRVPKTLVLVVAAVLLLVSAESALITQQDLAPQQRAAPQQKRSSPSEGLCPPGHHISEDGRDCISCKYGQDYSTHWND LLFCLRCTRCDSGEVELSPCTTTRNTVCQCEEGTFREEDSPEMCRKCRTGCPRGMVKVGDCTPWSDIECVHKESGTKHSGEVPAVEETVTSSPGTPASPCSLSGIIIGVTVAAV VLIVAVFVCKSLLWKKVLPYLKGICSGGGGDPERVDRSSQRPGAEDNVLNEIVSILQPTQVPEQEMEVQEPAEPTGVNMLSPGESEHLLEPAEAERSQRRRLLVPANEGDPT ETLRQCFDDFADLVPFDSWEPLMRKLGLMDNEIKVAKAEAAGHRDTLYTMLIKWVNKTGRDASVHTLLDALETLGERLAKQKIEDHLLSSGKFMYLEGNADSAMS
decoy receptor 1 / TNFRSF10C	O14798	NP_003832.2	MARIPKTLKFVVVIVAVLLPVLAYSATTARQEEVPQQTVAPQQQRHSFKGEECPAGSHRSEHTGACNPCTEGVDYTNASNNEPSCFPCTVCKSDQKHKSSCTMTRDTVCQ CKEGTFRNENSPEMCRKCSRCPSGEVQVSNCTSWDDIQCVEEFGANATVETPAAEETMNTSPGTPAPAAEETMTTSPGT PAPAAEETMTTSPGTPASSHYLSCTIVGIIVLVLLIVFV
decoy receptor 2 / TNFRSF10D	Q9UBN6	NP_003831.2	MGLWGQSVPTASSARAGRYPGARTASGTRPWLLDPKILKFVVFIVAVLLPVRVDSATIPRQDEVPQQTVAPQQQRRSLKEEECPAGSHRSEYTGACNPCTEGVDYTIASNN LPSCLLCTVCKSGQTNKSSCTTTRDTVCQCEKGSFQDKNSPEMCRTCRTGCPRGMVKVSNCTPRSDIKCKNESAASSTGKTPAAEETVTTILGMLASPYHYLIIIVVLVIILAVV VVGFSCRKKFISYLKGICSGGGGGPERVHRVLFRRRSCPSRVPGAEDNARNETLSNRYLQPTQVSEQEIQGQELAELTGVTVELPEEPQRLLEQAEAEGCQRRLLVPVNDAD SADISTLLDASATLEEGHAKETIQDQLVGSEKLPYEEDEAGSATSCL
RANK (receptor activator of NF-kappa B / TNFRSF11A)	Q9Y6Q6	NP_00125787 8.1	MAPRARRRRPLFALLLLCALLARLQVALQIAPPCTSEKHYEHLGRCCNKCEPGKYMSSKCTTTSDSVCLPCGPDEYLDSWNEEDKCLLHKVCDTGKALVAVVAGNSTTPRRC ACTAGYHWSQDCECCRRNTECAPGLGAQHPLQLNKDTVCKPCLAGYFSDAFSSTDKCRPWTNCTFLGKRVEHHGTEKSDAVCSSSLPARKPPNEPHVYLPGLIIILLFASVA LVAAIIFGVCYRKKGKALTANLWHWINEACGRLSGDKEM
OPG (osteoprotegerin / TNFRSF11B)	O00300	NP_002537.3	MNNLLCCALVFLDISIKWTTQETFPPKYLHYDEETSHQLLCDKCPPGTYLKQHCTAKWKTVCAPCPDHYYTDSWHTSDECLYCSPVCKELQYVKQECNRTHNRVCECKEGR YLEIEFCLKHRSCPPGFGVVQAGTPERNTVCKRCPDGFFSNETSSKAPCRKHTNCSVFGLLLTQKGNATHDNICSGNSESTQKCGIDVTLCEEAFFRFAVPTKFTPNWLSVLVD NLPGTKVNAESVERIKRQHSSQEQTFQLLKLWKHQNKDQDIVKKIIQDIDLCENSVQRHIGHANLTFEQLRSLMESLPGKKVGAEDIEKTIKACKPSDQILKLLSLWRIKNGDQ DTLKGLMHALKHSKTYHFPKTVTQSLKKTIRFLHSFTMYKLYQKLFLEMIGNQVQSVKISCL
DR3 (death receptor 3 / TNFRSF25)	Q93038	NP_00103475 3.1	MEQRPRGCAAVAAALLLVLLGARAQGGTRSPRCDCAGDFHKKIGLFCCRGCPAGHYLKAPCTEPCGNSTCLVCPQDTFLAWENHHNSECARCQACDEQASQVALENCSA VADTRCGCKPGWFVECQVSQCVSSSPFYCQPCLDCGALHRHTRLLCSRRDTDCGTCLPGFYEHGDGCVSCPT
TWEAK receptor / TNFRSF12A	Q9NP84	NP_057723.1	MARGSLRRLLRLVLGLWLALLRSVAGEQAPGTAPCSRGSSWSADLDKCMDCASCRARPHSDFCLGCAAAPPAPFRLLWPILGGALSLTFVLGLLSGFLVWRRCRRREKFTT PIEETGGEGCPAVALIQ
TACI / TNFRSF13B	O14836	NP_036584.1	MSGLGRSRRGGRSRVDQEERFPQGLWTGVAMRSCPEEQYWDPLLGTCMSCKTICNHQSQRTCAAFCRSLSCRKEQGKFYDHLLRDCISCASICGQHPKQCAYFCENKLRS PVNLPPELRRQRSGEVENNSDNSGRYQGLEHRGSEASPALPGLKLSADQVALVYSTLGLCLCAVLCCFLVAVACFLKKRGDPCSCQPRSRPRQSPAKSSQDHAMEAGSPVST SPEPVETCSFCFPECRAPTQESAVTPGTPDPTCAGRWGCHTRTTVLQPCPHIPDSGLGIVCVPAQEGGPGA

FIG. 62 (Cont.)

BAFF-R (BAFF receptor / TNFRSF13C)	Q96RJ3	NP_443177.1	MRRGPRSLRGRDAPAPTPCVPAECFDLLVRHCVACGLLRTPRPKPAGASSPAPRTALQPQESVGAGAGEAALPLPGLLFGAPALLGLALVLALVLVSVWRRRQRRLRGA SSAEAPDGDKDAPEPLDKVIILSPGISDATAPAWPPPGEDPGTTPPGHSVPVPATELGSTELVTTKTAGPEQQ
HVEM (herpes virus entry mediator / TNFRSF14)	Q92956	NP_003811.2	MEPPGDWGPPPWRSTPKTDVLRLVLYLTFLGAPCYAPALPSCKEDEYPVGSECCPKCSPGYRVKEACGELTGTVCEPCPPGTYIAHLNGLSKCLQCQMCDPAMGLRASRNC SRTENAVCGCSPGHFCIVQDGDHCAACRAYATSSPGQRVQKGGTESQDTLCQNCPPGTFSPNGTLEECQHQTKCSWLVTKAGAGTSSSHWVWWFLSGSLVIVIVCSTVG LIICVKRRKPRGDVVKVIVSVQRKRQEAEGEATVIEALQAPPDVTTVAVEETIPSFTGRSPNH
nerve growth factor receptor / TNFRSF16	P08138	NP_002498.1	MGAGATGRAMDGPRLLLLLLLGVSLGGAKEACPTGLYTHSGECCKACNLGEGVAQPCGANQTVCEPCLDSVTFSDVVSATEPCKPCTECVGLQSMSAPCVEADDAVCRC AYGYYQDETTGRCEACRVCEAGSGLVFSCQDKQNTVCEECPDGTYSDEANHVDPCLPCTVCEDTERQLRECTRWADAECEEIPGRWITRSTPPEGSDSTAPSTQEPEAPPE QDLIASTVAGVVTTVMGSSQPVVTRGTTDNLIPVYCSILAAVVVGLVAYIAFKRWNSCKQNKQGANSRPVNQTPPPEGEKLHSDSGISVDSQSLHDQQPHTQTASGQALK GDGGLYSSLPPAKREEVEKLLNGSAGDTWRHLAGELGYQPEHIDSFTHEACPVRALLASWATQDSATLDALLAALRRIQRADLVESLCSESTATSPV
BCMA (B cell maturation antigen / TNFRSF17)	Q02223	NP_001183.2	MLQMAGQCSQNEYFDSLLHACIPCQLRCSSNTPPLTCQRYCNASVTNSVKGTNAILWTCLGLSLIISLAVFVLMFLLRKINSEPLKDEFKNTGSGLLGMANIDLEKSRTGDEIIL PRGLEYTVEECTCEDCIKSKPKVDSDHCFPLPAMEEGATILVTTKTNDYCKSLPAALSATEIEKSISAR
GITR (glucocorticoid-induced TNF receptor / TNFRSF18)	Q9Y5U5	NP_004186.1	MAQHGAMGAFRALCGLALLCALSLGQRPTGGPGCGPGRLLLGTGTDARCCRVHTTRCCRDYPGEECCSEWDCMCVQPEFHCGDPCCTTCRHHPCPPGQGVQSQGKFS FGFQCIDCASGTFSGGHEGHCKPWTDCTQFGFLTVFPGNKTHNAVCVPGSPPAEPLGWLTVVLLAVAACVLLLTSAQLGLHIWQLRSQCMWPRETQLLLEVPPSTEDARS CQFPEEERGERSAEEKGRLGDLWV
BCMA (B cell maturation antigen / TNFRSF17)	Q02223	NP_001183.2	MLQMAGQCSQNEYFDSLLHACIPCQLRCSSNTPPLTCQRYCNASVTNSVKGTNAILWTCLGLSLIISLAVFVLMFLLRKINSEPLKDEFKNTGSGLLGMANIDLEKSRTGDEIIL PRGLEYTVEECTCEDCIKSKPKVDSDHCFPLPAMEEGATILVTTKTNDYCKSLPAALSATEIEKSISAR

FIG. 62 (Cont.)

GITR (glucocorticoid-induced TNF receptor / TNFRSF18)	Q9Y5U5	NP_004186.1	MAQHGAMGAFRALCGLALLCALSLGQRPTGGPGCGPGRLLLGTGTDARCCRVHTTRCCRDYPGEECSEWDCMCVQPEFHCGDPCCTTCRHHPCPPGQGVQSQGKFS FGFQCIDCASGTFSGGHEGHCKPWTDCTQFGFLTVFPGNKTHNAVCVPGSPPAEPLGWLTVVLLAVAACVLLLTSAQLGLHIWQLRSQCMWPRETQLLEVPPSTEDARS CQFPEEERGERSAEEKGRLGDLWV
TAJ (toxicity and JNK inducer / TNFRSF19)	Q9NS68	NP_001119138 7.1	MALKVLLEQEKTFFTLVLLGYLSCKVTCESGDCRQQEFRDRSGNCVPCNQCGPGMELSKECGFGYGEDAQCVTCRLHRFKEDWGFQKCKPCLDCAVVNRFQKANCSATS DAICGDCLPGFYRKTKLVGFQDMECVPCGDPPPPVEPHCASKVNLVKIASTASSPRDTALAAVICSALATVLLALLILCVIYCKRQFMEKKPSWSLRSQDIQYNGSELSCFDRP QLHEYAHRACCQCRRDSVQTCGPVRLLPSMCCEEACSPNPATLGCGVHSAASLQARNAGPAGEMVPTFFGSLTQSICGEFSDAWPLMQNPAMGGDNISFCDSYPELTGED IHSLNPELESSTSLDSNSSQDLVGGAVPVQSHSENFTAATDLSRYNNTLVESASTQDALTMRSQLDQESGAVIHPATQTSLQEA
RELT / TNFRSF19L	Q969Z4	NP_116260.2	MKPSLLCRPLSCFLMILLPWPLATLTSTTLWQCPPGEEPDLDPGQGTLCRPCPPGTFSAAWGSSPCQPHARCSLWRRLEAQVGMATRDTLCGDCWPGWFGPWGVPRVP CQPCSWAPLGTHGCDFWGRRARRGVEVAAGASSCGFTRQPGNGTRAGGPEETAAQYAVIAIVPVFCLMGLLGILVCNLLKRKGYHCTAHKEVGPGPGGGGSGIMPAYRT EDANEDTIGVLVRLITEKKENAAALEELKEYHSKQLVQTSHRPVSKLPPAPPNVPHICPHRHHLHTVQGLASLSGPCCSRCSQKKWPEVLLSPEAVAATTPVPSLLPNPTRVP KAGAKAGRQGEITLSVGRFRVARIPEQRTSSMVSEVKTITEAGPSWGDLPDSPQPGLPPEQQALLGSGGSRTKWLKPPAENKAEENRYVVRLSESNLVI
DR6 (death receptor 6 / TNFRSF21)	O75509	NP_055267.1	MGTSPSSSTALASCSRIARRATATMIAGSLLLLGFLSTTTAQPEQKASNLIGTYRHVDRATGQVLTCDKCPAGTYVSEHCTNTSLRVCSSCPVGTFTRHENGIEKCHDCSQPCP WPMIEKLPCAALTDRECTCPPGMFQSNATCAPHTVCPVGWGVRKKGTETEDVRCKQCARGTFSDVPSSVMKCKAYTDCLSQNLVVIKPGTKETDNVCGTLPSFSSSTSPSP GTAIFPRPEHMETHEVPSSTYVPKGMNSTESNSSASVRPKVLSSIQEGTVPDNTSSARGKEDVNKTLPNLQVVNHQQGPHHRHILKLLPSMEATGGEKSSTPIKGPKRGHPR QNLHKHFDINEHLPWMIVIFLLLVLVVVVCSIRKSSRTLKKGPRQDPSAIVEKAGLKKSMTPTQNREKWIYYCNGHGIDILKLVAAQVGSQWKDIYQFLCNASEREVAAFSN GYTADHERAYAALQHWTIRGPEASLAQLISALRQHRRNDVVEKIRGLMEDTTQLETDKLALPMSPSPLSPSPIPSPNAKLENSALLTVEPSPQDKNKGFFVDESEPLLRCDSTS SGSSALSRNGSFITKEKKDTVLRQVRLDPCDLQPIEDDMLHFLNPEELRVIEEIPQAEDKLDRLFEIIGVKSQEASQTLLDSVYSHLPDLL
TNFRSF22	Q9ER62	NP_001129807 4.1	MFGFFCSLVSSLSRWFLWRRLLLLLLLLLNLPLQVKFAMLELHSFKCPAGEYWSKDVCCKNCSAGTFVKAPCEIPHTQGQCEKCHPGTFTEKDNYLDACILCSTCDKDQEMV ADCSATSDRKCQCRTGLYYYDPKFPESCRPCTKCPQGIPVLQECNSTANTVCSSSVSNPRNRLFLLSPLSVLIVSVVVFRIIRR

FIG. 62 (Cont.)

TNFRSF23	Q9ER63	NP_077252.2	MVTFSHVSSLSHWFLLLLLLNLFLPVIFAMPESYSFNCPDGEYQSNDVCCKTCPSGTFVKAPCKIPHTQGQCEKCHPGTFTGKDNGLHDCELCSTCDKDQNMVADCSATSD RKCECQIGLYYYDPKFPESCRPCTKCPQGIPVLQECNSTANTVCSSSVSNPRNWLFLLMILVFCI
ectodysplasin A2 isoform receptor / TNFRS27	Q9HAV5	NP_00118861 6.1	MDCQENEYWDQWGRCVTCQRCGPGQELSKDCGYGEGGDAYCTACPPRRYKSSWGHHRCQSCITCAVINRVQKVNCTATSNAVCGDCLPRFYRKTRIGGLQDQECIPCT KQTPTSEVQCAFQLSLVEADAPTVPPQEATLVALVSSLLVVFTLAFLGLFFLYCKQFFNRHCQRGGLLQFEADKTAKEESLFPVPPSKETSAESQVSENIFQTQPLNPILEDDCSS TSGFPTQESFTMASCTSESHSHWVHSPIECTELDLQKFSSSASYTGAETLGGNTVESTGDRLELNVPFEVPSP
ectodysplasin 1, anhidrotic receptor	Q9UNE0	NP_071731.1	MAHVGDCTQTPWLPVLVVSLMCSARAEYSNCGENEYYNQTTGLCQECPPCGPGEEPYLSCGYGTKDEDYGCVPCPAEKFSKGGYQICRRHKDCEGFFRATVLTPGDMEN DAECGPCLPGYYMLENRPRNIYGMVCYSCLLAPPNTKECVGATSGASANFPGTSGSSTILSPFQHAHKELSGQGHLATALLIIAMSTIFIMAIAVLIIMFYILKTKPSAPACCTSH PGKSVEAQVSKDEEKKEAPDNVVMFSEKDEFEKLTATPAKPTKSENDASSENEQLLSRSVDSDEEPAPDKQGSPELCLSLVHLAREKSATSNKSAGIQSRRKKILDVYANVCG VVEGLSPTELPFDCLEKTSRMLSSTYNSEKAVVKTWRHLAESFGLKRDEIGGMTDGMQLFDRISTAGYSIPELLTKLVQIERLDAVESLCADILEWAGVVPPASQPHAAS

FIG. 63

Chemokine receptors	UniProt ID	RefSeq Accession	Amino Acid Sequence
CCR1	P32246	NP_001286.1	METPNTTEDYDTTTEFDYGDATPCQKVNERAFGAQLLPPLYSLVFVIGLVGNILVVLVLVQYKRLKNMTSIYLLNLAISDLLFLFTLPFWIDYKLKDDWVFGDAMCKILSGFYYT GLYSEIFFIILLTIDRYLAIVHAVFALRARTVTFGVITSIIIWALAILASMPGLYFSKTQWEFTHHTCSLHFPHESLREWKLFQALKLNLFGLVLPLLVMIICYTGIIKILLRRPNEKKSK AVRLIFVIMIIFFLFWTPYNLTILISVFQDFLFTHECEQSRHLDLAVQVTEVIAYTHCCVNPVIYAFVGERFRKYLRQLFHRRVAVHLVKWLPFLSVDRLERVSSTSPSTGEHELSA GF
CCR2	P41597	NP_00111651 3.2	MLSTSRSRFIRNTNESGEEVTTFFDYDYGAPCHKFDVKQIGAQLLPPLYSLVFIFGFVGNMLVVLILINCKKLKCLTDIYLLNLAISDLLFLITLPLWAHSAANEWVFGNAMCKLF TGLYHIGYFGGIFFIILLTIDRYLAIVHAVFALKARTVTFGVVTSVITWLVAVFASVPGIIFTKCQKEDSVYVCGPYFPRGWNNFHTIMRNILGLVLPLLIMVICYSGILKTLLRCRN EKKRHRAVRVIFTIMIVYFLFWTPYNIVILLNTFQEFFGLSNCESTSQLDQATQVTETLGMTHCCINPIIYAFVGEKFRSLFHIALGCRIAPLQKPVCGGPGVRPGKNVKVTTQG LLDGRGKGKSIGRAPEASLQDKEGA
CCR3	P51677	NP_001828.1	MTTSLDTVETFGTTSYYDDVGLLCEKADTRALMAQFVPPLYSLVFTVGLLGNVVVVMILIKYRRLRIMTNIYLLNLAISDLLFLVTLPFWIHYVRGHNWVFGHGMCKLLSGFY HTGLYSEIFFIILLTIDRYLAIVHAVFALRARTVTFGVITSIVTWGLAVLAALPEFIFYETEELFEETLCSALYPEDTVYSWRHFHTLRMTIFCLVLPLLVMAICYTGIIKTLLRCPSKKK YKAIRLIFVIMAVFFIFWTPYNVAILLSSYQSILFGNDCERSKHLDLVMLVTEVIAYSHCCMNPVIYAFVGERFRKYLRHFFHRHLLMHLGRYIPFLPSEKLERTSSVSPSTAEPELS IVF
CCR4	P51679	NP_005499.1	MNPTDIADTTLDESIYSNYYLYESIPKPCTKEGIKAFGELFLPPLYSLVFVFGLLGNSVVVLVLFKYKRLRSMTDVYLLNLAISDLLFVFSLPFWGYYAADQWVFGLGLCKMISW MYLVGFYSGIFFVMLMSIDRYLAIVHAVFSLRARTLTYGVITSLATWSVAVFASLPGFLFSTCYTERNHTYCKTKYSLNSTTWKVLSSLEINILGLVIPLGIMLFCYSMIIRTLQHCK NEKKNKAVKMIFAVVVLFLGFWTPYNIVLFLETLVELEVLQDCTFERYLDYAIQATETLAFVHCCLNPIIYFFLGEKFRKYILQLFKTCRGLFVLCQYCGLLQIYSADTPSSYTQST MDHDLHDAL
CCR5	P51681	NP_000570.1	MDYQVSSPIYDINYYTSEPCQKINVKQIAARLLPPLYSLVFIFGFVGNMLVILILINCKRLKSMTDIYLLNLAISDLFFLLTVPFWAHYAAAQWDFGNTMCQLLTGLYFIGFFSGIF FIILLTIDRYLAVVHAVFALKARTVTFGVVTSVITWVVAVFASLPGIIFTRSQKEGLHYTCSSHFPYSQYQFWKNFQTLKIVILGLVLPLLVMVICYSGILKTLLRCRNEKKRHRAVR LIFTIMIVYFLFWAPYNIVLLLNTFQEFFGLNNCSSNRLDQAMQVTETLGMTHCCINPIIYAFVGEKFRNYLLVFFQKHIAKRFCKCCSIFQQEAPERASSVYTRSTGEQEISVG L
CCR6	P51684	NP_004358.2	MSGESMNFSDVFDSSEDYFVSVNTSYYSVDSEMLLCSLQEVRQFSRLFVPIAYSLICVFGLLGNILVVITFAFYKKARSMTDVYLLNLAIADILFVLTLPFWAVSHATGAWVFS NATCKLLKGIYAINFNCGMLLLTCISMDRYIAIVQATKSFRLRSRTLPRSKIICLVVWGLSVIISSSTFVFNQKYNTQGSDVCEPKYQTVSEPIRWKLLMLGLELLFGFFIPLMFMI FCYTFIVKTLVQAQNSKRHKAIRVIIAVVIVFLACQIPHNMVLLVTAANLGKMNRSCQSEKLIGYTKTVTEVLAFLHCCLNPVLYAFIGQKFRNYFLILKDLWCVRRKYKSSGF SCAGRYSENISRQTSETADNDNASSFTM

FIG. 63 (Cont.)

CCR7	P32248	NP_001288643.1	MYSIICFVGLLGNGLVVLTYIYFKRLKTMTDTYLLNLAVADILFLLTLPFWAYSAAKSWVFGVHFCKLIFAIYKMSFFSGMLLLLCISIDRYVAIVQAVSAHRHRARVLLISKLSCV GIWILATVLSIPELLYSDLQRSSSEQAMRCSLITEHVEAFITIQVAQMVIGFLVPLLAMSFCYLVIIRTLLQARNFERNKAIKVIIAVVVVFIVFQLPYNGVVLAQTVANFNITSSTC ELSKQLNIAYDVTYSLACVRCCVNPFLYAFIGVKFRNDLFKLFKDLGCLSQEQLRQWSSCRHIRRSSMSVEAETTTFSP
CCR8	P51685	NP_005192.1	MDYTLDLSVTTVTDYYYPDIFSSPCDAELIQTNGKLLLAVFYCLLFVFSLLGNSLVILVLVCKKLRSITDVYLLNLALSDLLFVFSFPFQTYYLLDQWVFGTVMCKVVSGFYYIGFY SSMFFITLMSVDRYLAVVHAVYALKVRTIRMGTTLCLAVWLTAIMATIPLLVFYQVASEDGVLQCYSFYNQQTLKWKIFTNFKMNILGLLIPFTIFMFCYIKILHQLKRCQNHN KTKAIRLVLIVVIASLLFWVPFNVVLFLTSLHSMHILDGCSISQQLTYATHVTEIISFTHCCVNPVIYAFVGEKFKKHLSEIFQKSCSQIFNYLGRQMPRESCEKSSSCQQHSSRSS VDYIL
CCR9	P51686	NP_001243298.1	MADDYGSESTSSMEDYVNFNFTDFYCEKNNVRQFASHFLPPLYWLVFIVGALGNSLVILVLYWYCTRVKTMTDMFLLNLAIADLLFLVTLPFWAIAAADQWKFQTFMCKVV NSMYKMNFYSCVLLIMCISVDRYIAIAQAMRAHTWREKRLLYSKMVCFTIWVLAAALCIPEILYSQIKEESGIAICTMVYPSDESTKLKSAVLTLKVILGFFIPFVVMACCYFIIIH TLIQAKKSSKHKALKVTITVLTVFVLSQFPYNCILLVQTIDAYAMFISNCAVSTNIDICFQVTQTIAFFHSCLNPVLYVFVGERFRRDLVKTLKNLGCISQAQWVSFTRREGSLKLS SMILETTSGALSL
CCR10	P46092	NP_057686.2	MGTEATEQVSWGHYSGDEEDAYSAEPLPELCYKADVQAFSRAFQPSVSLTVAALGLAGNGLVLATHLAARRAARSPTSAHLLQLALADLLLALTLPFAAAGALQGWSLGSA TCRTISGLYSASFHAGFLFLACISADRYVAIARALPAGPRPSTPGRAHLVSVIVWLISLLLALPALLFSQDGQREGQRRCRLIFPEGLTQTVKGASAVAQVALGFALPLGVMVAC YALLGRTILAARGPERRRALRVVVALVAAFVVLQLPYSLALLLDTADLLAARERSCPASKRKDVALLVTSGLALARCGLNPVLYAFLGLRFRQDLRRLLRGGSCPSGPQPRRGC PRRPRLSSCSAPTETHSLSWDN
CXCR1 (IL8Ra)	P25024	NP_000625.1	MSNITDPQMWDFDDLNFTGMPPADEDYSPCMLETETLNKYVVIIAYALVFLLSLLGNSLVMLVILYSRVGRSVTDVYLLNLALADLLFALTLPIWAASKVNGWIFGTFLCKVV SLLKEVNFYSGILLLACISVDRYLAIVHATRTLTQKRHLVKFVCLGCWGLSMNLSLPFFLFRQAYHPNNSSPVCYEVLGNDTAKWRMVLRILPHTFGFIVPLFVMILFCYGFTLRT LFKAHMGQKHRAMRVIFAVVLIFLLCWLPYNLVLLADTLMRTQVIQESCERRNNIGRALDATEILGFLHSCLNPIIYAFIGQNFRHGFLKILAMHGLVSKEFLARHRVTSYTSSS VNVSSNL
CXCR2 (IL8Rb)	P25025	NP_001116177.1	MEDFNMESDSFEDFWKGEDLSNYSYSSTLPPFLLDAAPCEPESLEINKYFVVIIYALVFLLSLLGNSLVMLVILYSRVGRSVTDVYLLNLALADLLFALTLPIWAASKVNGWIFGT FLCKVVSLLKEVNFYSGILLLACISVDRYLAIVHATRTLTQKRYLVKFICLSIWGLSLLLALPVLLFRRTVYSSNVSPACYEDMGNNTANWRMLLRILPQSFGFIVPLLIMLFCYGFT LRTLFKAHMGQKHRAMRVIFAVVLIFLLCWLPYNLVLLADTLMRTQVIQETCERRNHIDRALDATEILGILHSCLNPLIYAFIGQKFRHGLLKILAIHGLISKDSLPKDSRPSFVGS SSGHTSTTL

FIG. 63 (Cont.)

CXCR3	P49682	NP_001136269.1	MELRKYGPGRLAGTVIGGAAQSKSQTKSDSITKEFLPGLYTAPSSPPPPSQVSDHQVLNDAEVAALLENFSSSYDYGENESDSCCTSPPCPQDFSLNFDRAFLPALYSLLFLLGL LGNGAVAAVLLSRRTALSSTDTFLLHLAVADTLLVLTLPLWAVDAAVQWVFGSGLCKVAGALFNINFYAGALLLACISFDRYLNIVHATQLYRRGPPARVTLTCLAVWGLCLLF ALPDFIFLSAHHDERLNATHCQYNFPQVGRTALRVLQLVAGFLLPLLVMAYCYAHILAVLLVSRGQRRLRAMRLVVVVVVAFALCWTPYHLVVLVDILMDLGALARNCGRES RVDVAKSVTSGLGYMHCCLNPLLYAFVGVKFRERMWMLLLRLGCPNQRGLQRQPSSSRRDSSWSETSEASYSGL
CXCR4	P61073	NP_001008540.1	MSIPLPLLQIYTSDNYTEEMGSGDYDSMKEPCFREENANFNKIFLPTIYSIIFLTGIVGNGLVILVMGYQKKLRSMTDKYRLHLSVADLLFVITLPFWAVDAVANWYFGNFLCK AVHVIYTVNLYSSVLILAFISLDRYLAIVHATNSQRPRKLLAEKVVYVGVWIPALLLTIPDFIFANVSEADDRYICDRFYPNDLWVVVFQFQHIMVGLILPGIVILSCYCIIISKLSHS KGHQKRKALKTTVILAFFACWLPYYIGISIDSFILLEIIKQGCEFENTVHKWISITEALAFFHCCLNPILYAFLGAKFKTSAQHALTSVSRGSSLKILSKGKRGGHSSVSTESESSSF HSS
CXCR5	P32302	NP_001707.1	MNYPLTLEMDLENLEDLFWELDRLDNYNDTSLVENHLCPATEGPLMASFKAVFVPVAYSLIFLLGVIGNVLVILVILERHRQTRSSTETFLFHLAVADLLLVFILPFAVAEGSVG WVLGTFLCKTVIALHKVNFYCSSLLLACIAVDRYLAIVHAVHAYRHRRLLSIHITCGTIWLVGFLLALPEILFAKVSQGHHNNSLPRCTFSQENQAETHAWFTSRFLYHVAGFLL PMLVMGWCYVGVVHRLRQAQRRPQRQKAVRVAILVTSIFFLCWSPYHIVIFLDTLARLKAVDNTCKLNGSLPVAITMCEFLGLAHCCLNPMLYTFAGVKFRSDLSRLLTKLG CTGPASLCQLFPSWRRSSLSESENATSLTTF
CXCR6	O00574	NP_006555.1	MAEHDYHEDYGFSSFNDSSQEEHQDFLQFSKVFLPCMYLVVFVCGLVGNSLVLVISIFYHKLQSLTDVFLVNLPLADLVFVCTLPFWAYAGIHEWVFGQVMCKSLLGIYTINF VTSMLILTCITVDRFIVVVKATKAYNQQAKRMTWGKVTSLLIWVISLLVSLPQIIYGNVFNLDKLICGYHDEAISTVVLATQMTLGFFLPLLTMIVCYSVIIKTLLHAGGFQKHRSL KIIFLVMAVFLLTQMPFNLMKFIRSTHWEYYAMTSFHYTIMVTEAIAYLRACLNPVLYAFVSLKFRKNFWKLVKDIGCLPYLGVSHQWKSSEDNSKTFSASHNVEATSMFQL
CX3CR1	P49238	NP_001164642.1	MDQFPESVTENFEYDDLAEACYIGDIVVFGTVFLSIFYSVIFAIGLVGNLLVVFALTNSKKPKSVTDIYLLNLALSDLLFVATLPFWTHYLINEKGLHNAMCKFTTAFFFIGFFGSIF FITVISIDRYLAIVLAANSMNNRTVQHGVTISLGVWAAAILVAAPQFMFTKQKENECLGDYPEVLQEIWPVLRNVETNFLGFLLPLLIMSYCYFRIIQTLFSCKNHKKAKAIKLIL LVVIVFFLFWTPYNVMIFLETLKLYDFFPSCDMRKDLRLALSVTETVAFSHCCLNPLIYAFAGEKFRRYLYHLYGKCLAVLCGRSVHVDFSSSESQRSRHGSVLSSNFTYHTSDG DALLLL

FIG. 64

TGF beta receptors	UniProt ID	RefSeq Accession	Amino Acid Sequence
transforming growth factor beta, receptor type I (TGFBR1 (ALK5)	P36897	NP_004603.1	MEAAVAAPRPRLLLLVLAAAAAAAALLPGATALQCFCHLCTKDNFTCVTDGLCFVSVTETTDKVIHNSMCIAEIDLIPRDRPFVCAPSSKTGSVTTTYCCNQDHCNKIELPTT VKSSPGLGPVELAAVIAGPVCFVCISLMLMVYICHNRTVIHHRVPNEEDPSLDRPFISEGTTLKDLIYDMTTSGSGSGLPLLVQRTIARTIVLQESIGKGRFGEVWRGKWRGEE VAVKIFSSREERSWFREAEIYQTVMLRHENILGFIAADNKDNGTWTQLWLVSDYHEHGSLFDYLNRYTVTVEGMIKLALSTASGLAHLHMEIVGTQGKPAIAHRDLKSKNIL VKKNGTCCIADLGLAVRHDSATDTIDIAPNHRVGTKRYMAPEVLDDSINMKHFESFKRADIYAMGLVFWEIARRCSIGGIHEDYQLPYYDLVPSDPSVEEMRKVVCEQKLRP NIPNRWQSCEALRVMAKIMRECWYANGAARLTALRIKKTLSQLSQQEGIKM
transforming growth factor beta, receptor type II (TGFBR2 (MFS2))	P37173	NP_003233.4	MGRGLLRGLWPLHIVLWTRIASTIPPHVQKSVNNDMIVTDNNGAVKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCVAVWRKNDENITLETVCHDPKLPYHDF ILEDAASPKCIMKEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPDLLLVIFQVTGISLLPPLGVAISVIIIFYCYRVNRQQKLSSTWETGKTRKLMEFSEHCAIILEDDRSDISST CANNINHNTELLPIELDTLVGKGRFAEVYKAKLKQNTSEQFETVAVKIFPYEEYASWKTEKDIFSDINLKHENILQFITAEERKTELGKQYWLITAFHAKGNLQEYLTRHVISWE DLRKLGSSLARGIAHLHSDHTPCGRPKMPIVHRDLKSSNILVKNDLTCCLCDFGLSLRLDPTLSVDDLANSGQVGTARYMAPEVLESRMNLENVESFKQTDVYSMALVLWE MTSRCNAVGEVKDYEPPFGSKVREHPCVESMKDNVLRDRGRPEIPSFWLNHQGIQMVCETLTECWDHDPEARLTAQCVAERFSELEHLDRLSGRSCSEEKIPEDGSLNTTK
transforming growth factor beta, receptor type III (TGFBR3 (β-Glycan))	Q03167	NP_003234.2	MTSHYVIAIFALMSSCLATAGPEPGALCELSPVSASHPVQALMESFTVLSGCASRGTTGLPQEVHVLNLRTAGQGPGQLQREVTLHLNPISSVHIHHKSVVFLLNSPHPLVW HLKTERLATGVSRLFLVSEGSVVQFSSANFSLTAETEERNFPHGNEHLLNWARKEYGAVTSFTELKIARNIYIKVGEDQVFPPKCNIGKNFLSLNYLAEYLQPKAAEGCVMSSQ PQNEEVHIIELITPNSNPYSAFQVDITIDIRPSQEDLEVVKNLLILILKCKKSVNWVIKSFDVKGSLKIIAPNSIGFGKESERSMTMTKSIRDDIPSTQGNLVKWALDNGYSPITSYT MAPVANRFHLRLENNAEEMGDEEVHTIPPELRILLDPGALPALQNPPIRGGEGQNGGLPFPPPDISRRVWNEEGEDGLPRPKDPVIPSIQLFPGLREPEEVQGSVDIALSVKC DNEKMIVAVEKDSFQASGYSGMDVTLLDPTCKAKMNGTHFVIESPLNGCGTRPPWSALDGVVYYNSIVIQVPALGDSSGWPDGYEDLESGDNGFPGDMDEGDASLFTR PEIVVFNCSLQQVRNPSSFQEQPHGNITFNMELVNTDLFLVPSQGVFSVPENGHVYVEVSVTKAEQELGFAIQTCFISPYSNPDRMSHYTIIENICPKDESVKFYSPKRVHFPIP QADMDKKRFSFVFKPVFNTSLLFLQCELTLCTKMEKHPQKLPKCVPPDEACTSLDASIIWAMMQNKKTFTKPLAVIHHEAESKEKGPSMKEPNPISPPIFHGLDTLTVMGIAF AAFVIGALLTGALWYIYSHTGETAGRQQVPTSPPASENSSAAHSIGSTQSTPCSSSSTA

FIG. 65

Protein	RefSeq	UniProt	Amino Acid Sequence
MERTK	NP_006334	Q12866	MGPAPLPLLLGLFLPALWRAITEAREEAKPYPLFPGPFPGSLQTDHTPLLSLPHASGYQPALMFSPTQPGRPHTGNVAIPQVTSVESKPLPPLAFKHTVGHIILSEHKGVKFNCSISV
			PNIYQDTTISWWKDGKELLGAHHAITQFYPDDEVTAIIASFSITSVQRSDNGSYICKMKINNEEIVSDPIYIEVQGLPHFTKQPESMNVTRNTAFNLTCQAVGPPEPVNIFWVQNSS
			RVNEQPEKSPSVLTVPGLTEMAVFSCEAHNDKGLTVSKGVQINIKAIPSPPTEVSIRNSTAHSILISWVPGFDGYSPFRNCSIQVKEADPLSNGSVMIFNTSALPHLYQIKQLQALANY
			SIGVSCMNEIGWSAVSPWILASTTEGAPSVAPLNVTVFLNESSDNVDIRWMKPPTKQQDGELVGYRISHVWQSAGISKELLEEVGQNGSRARISVQVHNATCTVRIAAVTRGGV
			GPFSDPVKIFIPAHGWVDYAPSSTPAPGNADPVLIIFGCFCGFILILGLILYISLAIRKRVQETKFGNAFTEEDSELVVNYIAKKSFCRRAIELTLHSLGVSEELQNKLEDVVIDRNLLILGKIL
			GEGEFGSVMEGNLKQEDGTSLKVAVKTMKLDNSSQREIEEFLSEAACMKDFSHPNVIRLLGVCIEMSSQGIPKPMVILPFMKYGDLHTYLLYSRLETGPKHIPLQTLLKFMVDIALG
			MEYLSNRNFLHRDLAARNCMLRDDMTVCVADFGLSKKIYSGDYYRQGRIAKMPVKWIAIESLADRVYTSKSDVWAFGVTMWEIATRGMTPYPGVQNHEMYDYLLHGHRLKQ
			PEDCLDELYEIMYSCWRTDPLDRPTFSVLRLQLEKLLESLPDVRNQADVIYVNTQLLESSEGLAQGSTLAPLDLNIDPDSIIASCTPRAAISVVTAEVHDSKPHEGRYILNGGSEEWED
			LTSAPSAAVTAEKNSVLPGERLVRNGVSWSHSSMLPLGSSLPDELLFADDSSEGSEVLM
LMTK3	NP_001073903	A0A0A0MQW5	MRQVLWLCNVCVTARETRHHLHLPAILDKMPAPGALILLAAVSASGCLASPAHPDGFALGRAPLAPPYAVVLISCSGLLAFILLITCLCCKRGDVGFKEFEENPEGEDCSGEYTPPAE
			ETSSSQSLPDVYILPLAEVSLPMPAPQPSHSDMTTPLGLSRQHLSYLQEIGSGWFGKVILGEIFSDYTPAQVVVKELRASAGPLEQRKFISEAQPYRSLQHPNVLQCLGLCVETLPFLLI
			MEFCQLGDLKRYLRAQRPPEGLSPELPRDLRTLQRMGLEIARGLAHLHSHNYVHSDLALRNCLLTSDLTVRIGDYGLAHSNYKEDYYLTPERLWIPLRWAAPELLGELHGTFMVV
			DQSRESNIWSLGVTLWELFEFGAQPYRHLSDEEVLAFVVRQQHVKLARPRLKLPYADYWVDILQSCWRPPAQRPSASDLQLQLTYLLSERPPRPPPPPPPPRDGPFPWVPPAH
			SAPRPGTLSSPFPLLDGFPGADPDDVLVTESSRGLNLECLWEKARRGAGRGGGAPAWQPASAPPAPHANFSNPFYEALSTPSVLPVISARSPSVSSEYYIRLEEHGSPPEPLFPND
			WDPLDPGVPAPQAPQAPSEVPQLVSETWASPLFPAPRPFPAQSSASGSFLLSGWDPEGRGAGETLAGDPAEVLGERGTAPWVEEEEEEEEGSSPGEDSSSLGGGPSRRGPIPCP
			LCSREGACSCLPLERGDAVAGWGGHPALGCPHPPEDDSSLRAERGSLADLPMAPPASAPPEFLDPLMGAAAPQYPGRGPPPAPPPPPPPPRAPADPAASPDPPSAVASPGSGLS
			SPGPKPGDSGYETETPFSPEGAFPGGGAAEEEGVPRPRAPPEPPDPGAPRPPPDPGPLPLPGPREKPTFVVQVSTEQLLMSLREDVTRNLLGEKGATARETGPRKAGRGPGNREK
			VPGLNRDPTVLGNGKQAPSLSLPVNGVTVLENGDQRAPGIEEKAAENGALGSPERFEEKVLENGELTPPRNEEKALENGELRSPEAGEKVLVNGGLTPPKSEDKVSENGGLRFPRNT
			ERPPETGPWRAPGPWEKTPESWGPAPTIGEPAPETSLERAPAPSAVVSSRNGGETAPGPLGPAPKNGTLEPGTERRAPETGGAPRAPGAGRLDLGSGGRAPVGTGTAPGGGPG
			SGVDAKAGWVDNTRPQPPPPPLPPPPEAQPRRLEPAPPRARPEVAPEGEPGAPDSRAGGDTALSGDGDPPKPERKGPEPMPRLFLDLGPPQGNSEQIKARLSRLSLAIPPLTLTPF
			PGPGPRRPPWEGADAGAAGGEAGGAGAPGPAEEDGEDEDEDEEEDEEAAAPGAAAGPRGPGRARAAPVPVVVSSADADAARPLRGLLKSPRGADEPEDSELERKRKMVSFH
			GDVTVYLFDQETPTNELSVQAPPEGDTDPSTPPAPPTPPHPATPGDGFPSNDSGFGGSFEWAEDFPLLPPPGPPLCFSRFSVSPALETPGPPARAPDARPPAGPVEN

FIG. 65 (Cont.)

CSF1R	NP_001275634	P07333	MGPGVLLLLLVATAWHGQGIPVIEPSVPELVVKPGATVTLRCVGNGSVEWDGPPSPHWTLYSDGSSILSTNNATFQNTGTYRCTEPGDPLGGSAAIHLYVKDPARPWNVLAQE VVVFEDQDALLPCLLTDPVLEAGVSLVRVRGRPLMRHTNYSFSPWHGFTIHRAKFIQSQDYQCSALMGGRKVMSISIRLKVQKVIPGPPALTLVPAELVRIRGEAAQIVCSASSVDV NFDVFLQHNNTKLAIPQQSDFHNNRYQKVLTLNLDQVDFQHAGNYSCVASNVQGKHSTSMFFRVVESAYLNLSSEQNLIQEVTVGEGLNLKVMVEAYPGLQGFNWTYLGPFSD HQPEPKLANATTKDTYRHTFTLSLPRLKPSEAGRYSFLARNPGGWRALTFELTLRYPPEVSVIWTFINGSGTLLCAASGYPQPNVTWLQCSGHTDRCDEAQVLQVWDDPYPEVLS QEPFHKVTVQSLLTVETLEHNQTYECRAHNSVGSGSWAFIPISAGAHTHPPDEFLFTPVVVACMSIMALLLLLLLLYKYKQKPKYQVRWKIIESYEGNSYTFIDPTQLPYNEKWEF PRNNLQFGKTLGAGAFGKVVEATAFGLGKEDAVLKVAVKMLKSTAHADEKEALMSELKIMSHLGQHENIVNLLGACTHGGPVLVITEYCCYGDLLNFLRRKAEAMLGPSLSPGQ DPEGGVDYKNIHLEKKYVRRDSGFSSQGVDTYVEMRPVSTSSNDSFSEQDLDKEDGRPLELRDLLHFSSQVAQGMAFLASKNCIHRDVAARNVLLTNGHVAKIGDFGLARDIMN DSNYIVKGNARLPVKWMAPESIFDCVYTVQSDVWSYGILLWEIFSLGLNPYPGILVNSKFYKLVKDGYQMAQPAFAPKNIYSIMQACWALEPTHRPTFQQICSFLQEQAQEDRRE RDYTNLPSSSRSGGSGSSSSELEEESSSEHLTCCEQGDIAQPLLQPNNYQFC
EGFR	NP_005219	P00533	MRPSGTAGAALLALLAALCPASRALEEKKVCQGTSNKLTQLGTFEDHFLSLQRMFNNCEVVLGNLEITYVQRNYDLSFLKTIQEVAGYVLIALNTVERIPLENLQIIRGNMYYENSYA LAVLSNYDANKTGLKELPMRNLQEILHGAVRFSNNPALCNVESIQWRDIVSSDFLSNMSMDFQNHLGSCQKCDPSCPNGSCWGAGEENCQKLTKIICAQQCSGRCRGKSPSDC CHNQCAAGCTGPRESDCLVCRKFRDEATCKDTCPPLMLYNPTTYQMDVNPEGKYSFGATCVKKCPRNYVVTDHGSCVRACGADSYEMEEDGVRKCKKCEGPCRKVCNGIGIGE FKDSLSINATNIKHFKNCTSISGDLHILPVAFRGDSFTHTPPLDPQELDILKTVKEITGFLLIQAWPENRTDLHAFENLEIIRGRTKQHGQFSLAVVSLNITSLGLRSLKEISDGDVIISGNK NLCYANTINWKKLFGTSGQKTKIISNRGENSCKATGQVCHALCSPEGCWGPEPRDCVSCRNVSRGRECVDKCNLLEGEPREFVENSECIQCHPECLPQAMNITCTGRGPDNCIQC AHYIDGPHCVKTCPAGVMGENNTLVWKYADAGHVCHLCHPNCTYGCTGPGLEGCPTNGPKIPSIATGMVGALLLLLVVALGIGLFMRRRHIVRKRTLRRLLQERELVEPLTPSGE APNQALLRILKETEFKKIKVLGSGAFGTVYKGLWIPEGEKVKIPVAIKELREATSPKANKEILDEAYVMASVDNPHVCRLLGICLTSTVQLITQLMPFGCLLDYVREHKDNIGSQYLLN WCVQIAKGMNYLEDRRLVHRDLAARNVLVKTPQHVKITDFGLAKLLGAEEKEYHAEGGKVPIKWMALESILHRIYTHQSDVWSYGVTVWELMTFGSKPYDGIPASEISSILEKGER LPQPPICTIDVYMIMVKCWMIDADSRPKFRELIIEFSKMARDPQRYLVIQGDERMHLPSPTDSNFYRALMDEEDMDDVVDADEYLIPQQGFFSSPSTSRTPLLSSLSATSNNSTVA CIDRNGLQSCPIKEDSFLQRYSSDPTGALTEDSIDDTFLPVPEYINQSVPKRPAGSVQNPVYHNQPLNPAPSRDPHYQDPHSTAVGNPEYLNTVQPTCVNSTFDSPAHWAQKGSH QISLDNPDYQQDFFPKEAKPNGIFKGSTAENAEYLRVAPQSSEFIGA

FIG. 65 (Cont.)

EPHA2	NP_004422	P29317	MELQAARACFALLWGCALAAAAAAQGKEVVLLDFAAAGGELGWLTHPYGKGWDLMQNIMNDMPIYMYSVCNVMSGDQDNWLRTNWVYRGEAERIFIELKFTVRDCNSFP
			GGASSCKETFNLYYAESDLDYGTNFQKRLFTKIDTIAPDEITVSSDFEARHVKLNVEERSVGPLTRKGFYLAFQDIGACVALLSVRVYYKKCPELLQGLAHFPETIAGSDAPSLATVAGT
			CVDHAVVPPGGEEPRMHCAVDGEWLVPIGQCLCQAGYEKVEDACQACSPGFFKFEASESPCLECPEHTLPSPEGATSCECEEGFFRAPQDPASMPCTRPPSAPHYLTAVGMGA
			KVELRWTPPQDSGGREDIVYSVTCEQCWPESGECGPCEASVRYSEPPHGLTRTSVTVSDLEPHMNYTFTVEARNGVSGLVTSRSFRTASVSINQTEPPKVRLEGRSTTSLSVSWSIP
			PPQQSRVWKYEVTYRKKGDSNSYNVRRTEGFSVTLDDLAPDTTYLVQVQALTQEGQGAGSKVHEFQTLSPEGSGNLAVIGGVAVGVVLLVLAGVGFFIHRRRKNQRARQSPED
			VYFSKSEQLKPLKTYVDPHTYEDPNQAVLKFTTEIHPSCVTRQKVIGAGEFGEVYKGMLKTSSGKKEVPVAIKTLKAGYTEKQRVDFLGEAGIMGQFSHHNIIRLEGVISKYKPMMII
			TEYMENGALDKFLREKDGEFSVLQLVGMLRGIAAGMKYLANMNYVHRDLAARNILVNSNLVCKVSDFGLSRVLEDDPEATYTTSGGKIPIRWTAPEAISYRKFTSASDVWSFGIV
			MWEVMTYGERPYWELSNHEVMKAINDGFRLPTPMDCPSAIYQLMMQCWQQERARRPKFADIVSILDKLIRAPDSLKTLADFDPRVSIRLPSTSGSEGVPFRTVSEWLESIKMQQ
			YTEHFMAAGYTAIEKVVQMTNDDIKRIGVRLPGHQKRIAYSLLGLKDQVNTVGIPI
EPHA1	NP_005223	P21709	MERRWPLGLGLVLLLCAPLPPGARAKEVTLMDTSKAQGELGWLLDPPKDGWSEQQQILNGTPLYMVQDCPMQGRRDTDHWLRSNWIYRGEEASRVHVELQFTVRDCKSFPG
			GAGPLGCKETFNLLYMESDQDVGIQLRRPLFQKVTTVAADQSFTIRDLVSGSVKLNVERCSLGRLTRRGLYLAFHNPGACVALVSVRVFYQRCPETLNGLAQFPDTLPGPAGLVEV
			AGTCLPHARASPRPSGAPRMHCSPDGEWLVPVGRCHCEPGYEEGGSGEACVACPSGSYRMDMDTPHCLTCPQQSTAESEGATICTCESGHYRAPGEGPQVACTGPPSAPRNL
			SFSASGTQLSLRWEPPADTGGRQDVRYSVRCSQCQGTAQDGGPCQPCGVGVHFSPGARGLTTPAVHVNGLEPYANYTFNVEAQNGVSGLGSSGHASTSVSISMGHAESLSGLS
			LRLVKKEPRQLELTWAGSRPRSPGANLTYELHVLNQDEERYQMVLEPRVLLTELQPDTTYIVRVRMLTPLGPGPFSPDHEFRTSPPVSRGLTGGEIVAVIFGLLLGAALLIGILVFRSR
			RAQRQRQQRQRDRATDVDREDKLWLKPYVDLQAVEDPAQGALDFTRELDPAWELMVDTVIGEGEFGEVYRGTLRLPSQDCKTVAIKTLKDTSPGGQWWNFLREATIMGQFSH
			PHILHLEGVVTKRKPIMIITEFMENGALDAFLRERDQLVPGQLVAMLQGIASGMNYLSNHNYVHRDLAARNILVNQNLCCKVSDFGLTRLLDDFDGTYETQGGKIPIRWTAPEAI
			AHRIFTTASDVWSFGIVMWEVLSFGDKPYGEMSNQEVMKSIEDGYRLPPPVDCPAPLYELMKNCWAYDRARRPHFQKLQAHLEQLLANPHSLRTIANFDPRMTLRLPSLSGSD
			GIPYRTVSEWLESIRMKRYILHFHSAGLDTMECVLELTAEDLTQMGITLPGHQKRILCSIQGFKD
EPHA3	NP_005224	P29320	MDCQLSILLLSCSVLDSFGELIPQPSNEVNLLDSKTIQGELGWISYPSHGWEEISGVDEHYTPIRTYQVCNVMDHSQNNWLRTNWVPRNSAQKIYVELKFTLRDCNSIPLVLGTCK
			ETFNLYYMESDDDHGVKFREHQFTKIDTIAADESFTQMDLGDRILKLNTEIREVGPVNKKGFYLAFQDVGACVALVSVRVYFKKCPFTVKNLAMFPDTVPMDSQSLVEVRGSCVN
			NSKEEDPPRMYCSTEGEWLVPIGKCSCNAGYEERGFMCQACRPGFYKALDGNMKCAKCPPHSSTQEDGSMNCRCENNYFRADKDPPSMACTRPPSSPRNVISNINETSVILDW
			SWPLDTGGRKDVTFNIICKKCGWNIKQCEPCSPNVRFLPRQFGLTNTTVTVTDLLAHTNYTFEIDAVNGVSELSSPPRQFAAVSITTNQAAPSPVLTIKKDRTSRNSISLSWQEPEHP	
			NGIILDYEVKYYEKQEQETSYTILRARGTNVTISSLKPDTIYVFQIRARTAAGYGTNSRKFEFETSPDSFSISGESSQVVMIAISAAVAIILLTVVIYVLIGRFCGYKSKHGADEKRLHFGNG	
			HLKLPGLRTYVDPHTYEDPTQAVHEFAKELDATNISIDKVVGAGEFGEVCSGRLKLPSKKEISVAIKTLKVGYTEKQRRDFLGEASIMGQFDHPNIIRLEGVVTKSKPVMIVTEYMEN	
			GSLDSFLRKHDAQFTVIQLVGMLRGIASGMKYLSDMGYVHRDLAARNILINSNLVCKVSDFGLSRVLEDDPEAAYTTRGGKIPIRWTSPEAIAYRKFTSASDVWSYGIVLWEVMSY	
			GERPYWEMSNQDVIKAVDEGYRLPPPMDCPAALYQLMLDCWQKDRNNRPKFEQIVSILDKLIRNPGSLKITSAAARPSNLLLDQSNVDITTFRTTGDWLNGVWTAHCKEIFTGV	
			EYSSCDTIAKISTDDMKKVGVTVVGPQKKIISSIKALETQSKNGPVPV	

FIG. 65 (Cont.)

EPHA4	NP_001291465	P54764	MAGIFVFALFSCLFGICDAVTGSRVYPANEVTLLDSRSVQGELGWIASPLEGGWEEVSIMDEKNTPIRTYQVCNVMEPSQNNWLRTDWITREGAQRVYIEIKFTLRDCNSLPGVM
			GTCKETFNLYYYESDNDKERFIRENQFVKIDTIAADESFTQVDIGDRIMKLNTEIRDVGPLSKKGFYLAFQDVGACIALVSVRVFYKKCPLTVRNLAQFPDTITGADTSSLVEVRGSCV
			NNSEEKDVPKMYCGADGEWLVPIGNCLCNAGHEERSGECQACKIGYYKALSTDATCAKCPPHSYSVWEGATSCTCDRGFFRADNDAASMPCTRPPSAPLNLISNVNETSVNLE
			WSSPQNTGGRQDISYNVVCKKCGAGDPSKCRPCGSGVHYTPQQNGLKTTKVSITDLLAHTNYTFEIWAVNGVSKYNPNPDQSVSVTVTTNQAAPSSIALVQAKEVTRYSVALAVW
			LEPDRPNGVILEYEVKYYEKDQNERSYRIVRTAARNTDIKGLNPLTSYVFHVRARTAAGYGDFSEPLEVTTNTVPSRIIGDGANSTVLLVSVSGSVVLVVILIAAFVISRRRSKYSKAKQE
			ADEEKHLNQGVRTYVDPFTYEDPNQAVREFAKEIDASCIKIEKVIGVGEFGEVCSGRLKVPGKREICVAIKTLKAGYTDKQRRDFLSEASIMGQFDHPNIIHLEGVVTKCKPVMIITEY
			MENGSLDAFLRKNDGRFTVIQLVGMLRGIGSGMKYLSDMSYVHRDLAARNILVNSNLVCKVSDFGMSRVLEDDPEAAYTTRGGKIPIRWTAPEAIAYRKFTSASDVWSYGIVM
			WEVMSYGERPYWDMSNQDVIKAIEEGYRLPPPMDCPIALHQLMLDCWQKERSDRPKFGQIVNMLDKLIRNPNSLKRTGTESSRPNTALLDPSSPEFSAVVSVGDWLQAIKMDR
			YKDNFTAAGYTTLEAVVHVNQEDLARIGITAITHQNKILSSVQAMRTQMQQMHGRMVPV
EPHA5	NP_004430	P54756	MRGSGPRGAGRRRPPSGGGDTPITPASLAGCYSAPRRAPLWTCLLLCAALRTLLASPSNEVNLLDSRTVMGDLGWIAFPKNGWEEIGEVDENYAPIHTYQVCKVMEQNQNNW
			LLTSWISNEGASRIFIELKFTLRDCNSLPGGLGTCKETFNMYYFESDDQNGRNIKENQYIKIDTIAADESFTELDLGDRVMKLNTEVRDVGPLSKKGFYLAFQDVGACIALVSVRVYYK
			KCPSVVRHLAVFPDTITGADSSQLLEVSGSCVNHSVTDEPPKMHCSAEGEWLVPIGKCMCKAGYEEKNGTCQVCRPGFFKASPHIQSCGKCPPHSYTHEEASTSCVCEKDYFRRES
			DPPTMACTRPPSAPRNAISNVNETSVFLEWIPPADTGGRKDVSYYIACKKCNSHAGVCEECGGHVRYLPRQSGLKNTSVMMVDLLAHTNYTFEIEAVNGVSDLSPGARQYVSVN
			VTTNQAAPSPVTNVKKGKIAKNSISLSWQEPDRPNGIILEYEIKYFEKDQETSYTIIKSKETTITAEGLKPASVYVFQIRARTAAGYGVFSRRFEFETTPVFAASSDQSQIPVIAVSVTVG
			VILLAVVIGVLLSGSCCECGCGRASSLCAVAHPSLIWRCGYSKAKQDPEEEKMHFHNGHIKLPGVRTYIDPHTYEDPNQAVHEFAKEIEASCITIERVIGAGEFGEVCSGRLKLPGKRE
			LPVAIKTLKVGYTEKQRRDFLGEASIMGQFDHPNIIHLEGVVTKSKPVMIVTEYMENGSLDTFLKKNDGQFTVIQLVGMLRGISAGMKYLSDMGYVHRDLAARNILINSNLVCKVS
			DFGLSRVLEDDPEAAYTTRGGKIPIRWTAPEAIAFRKFTSASDVWSYGIVMWEVVSYGERPYWEMTNQDVIKAVEEGYRLPSPMDCPAALYQLMLDCWQKERNSRPKFDEIVN
			MLDKLIRNPSSLKTLVNASCRVSNLLAEHSPLGSGAYRSVGEWLEAIKMGRYTEIFMENGYSSMDAVAQVTLEDLRRLGVTLVGHQKKIMNSLQEMKVQLVNGMVPL

FIG. 65 (Cont.)

EPHA7	NP_004431	Q15375	MVFQTRYPSWIILCYIWLLRFAHTGEAQAAKEVLLLDSKAQQTELEWISSPPNGWEEISGLDENYTPIRTYQVCQVMEPNQNNWLRTNWISKGNAQRIFVELKFTLRDCNSLPGV LGTCKETFNLYYYETDYDTGRNIRENLYVKIDTIAADESFTQGDLGERKMKLNTEVREIGPLSKKGFYLAFQDVGACIALVSVKVYYKKCWSIIENLAIFPDTVTGSEFSSLVEVRGTCV SSAEEEAENAPRMHCSAEGEWLVPIGKCICKAGYQQKGDTCEPCGRGFYKSSSQDLQCSRCPTHSFSDKEGSSRCECEDGYYRAPSDPPVVACTRPPSAPQNLIFNINQTTVSLEW SPPADNGGRNDVTYRILCKRCSWEQGECVPCGSNIGYMPQQTGLEDNVVTVMDLLAHANYTFEVEAVNGVSDLSRSQRLFAAVSITGQAAPSQVSGVMKERVLQRSVELSW QEPEHPNGVITEYEIKYYEKDQRERTYSTVKTKSTSASINNLKPGTVYVFQIRAFTAAGYGNYSPRLDVATLEEATGKMFEATAVSSEQNPVIIIAVVAVAGTIILVFMVFGFIIGRRHC GYSKADQEGDEELYFHFKPGTKTYIDPETYEDPNRAVHQFAKELDASCIKIERVIGAGEFGEVCSGRLKLPGKRDVAVAIKTLKVGYTEKQRRDFLCEASIMGQFDHPNVVHLEGV VTRGKPVMIVIEFMENGALDAFLRKHDGQFTVIQLVGMLRGIAAGMRYLADMGYVHRDLAARNILVNSNLVCKVSDFGLSRVIEDDPEAVYTTTGGKIPVRWTAPEAIQYRKFTS ASDVWSYGIVMWEVMSYGERPYWDMSNQDVIKAIEEGYRLPAPMDCPAGLHQLMLDCWQKERAERPKFEQIVGILDKMIRNPNSLKTPLGTCSRPISPLLDQNTPDFTTFCSV
EPHA8	NP_065387	P29322	MAPARGRLPPALWVVTAAAAAATCVSAARGEVNLLDTSTIHGDWGWLTYPAHGWDSINEVDESFQPIHTYQVCNVMSPNQNNWLRTSWVPRDGARRVYAEIKFTLRDCNS MPGVLGTCKETFNLYYLESDRDLGASTQESQFLKIDTIAADESFTGADLGVRRLKLNTEVRSVGPLSKRGFYLAFQDIGACLAILSLRIYYKKCPAMVRNLAAFSEAVTGADSSSLVEV RGQCVRHSEERDTPKMYCSAEGEWLVPIGKCVCSAGYEERRDACVACELGFYKSAPGDQLCARCPPHSHSAAPAAQACHCDLSYYRAALDPPSSACTRPPSAPVNLISSVNGTSV TLEWAPPLDPGGRSDITYNAVCRRCPWALSRCEACGSGTRFVPQQTSLVQASLLVANLLAHMNYSFWIEAVNGVSDLSPEPRRAAVVNITTNQAAPSQVVVIRQERAGQTSVSL LWQEPEQPNGIILEYEIKYYEKDKEMQSYSTLKAVTTRATVSGLKPGTRYVFQVRARTSAGCGRFSQAMEVETGKPRPRYDTRTIVWICLTLITGLVVLLLLLICKKRHCGYSKAFQDS DEEKMHYQNGQAPPPVFLPLHHPPGKLPEPQFYAEPHTYEEPGRAGRSITREIEASRIHIEKIIGSGDSGEVCYGRLRVPGQRDVPVAIKALKAGYTERQRRDFLSEASIMGQFDHP NIIRLEGVVTRGRLAMIVTEYMENGSLDTFLRTHDGQFTIMQLVGMLRGVGAGMRYLSDLGYVHRDLAARNVLVDSNLVCKVSDFGLSRVLEDDPDAAYTTTGGKIPIRWTAPE AIAFRTFSSASDVWSFGVVMWEVLAYGERPYWNMTNRDVISSVEEGYRLPAPMGCPHALHQLMLDCWHKDRAQRPRFSQIVSVLDALIRSPESLRATATVSRCPPPAFVRSCFD LRGGSGGGGGLTVGDWLDSIRMGRYRDHFAAGGYSSLGMVLRMNAQDVRALGITLMGHQKKILGSIQTMRAQLTSTQGPRRHL
EPHB1	NP_004432	P54762	MALDYLLLLLASAVAAMEETLMDTRTATAELGWTANPASGWEEVSGYDENLNTIRTYQVCNVFEPNQNNWLLTTFINRRGAHRIYTEMRFTVRDCSSLPNVPGSCKETFNLYYY ETDSVIATKKSAFWSEAPYLKVDTIAADESFSQVDFGGRLMKVNTEVRSFGPLTRNGFYLAFQDYGACMSLLSVRVFFKKCPSIVQNFAVFPETMTGAESTSLVIARGTCIPNAEEV DVPIKLYCNGDGEWMVPIGRCTCKPGYEPENSVACKACPAGTFKASQEAEGCSHCPSNSRSPAEASPICTCRTGYYRADFDPPEVACTSVPSGPRNVISVNETSIILEWHPPRETG GRDDVTYNIICKKCRADRRSCSRCDDNVEFVPRQLGLTECRVSISSLWAHTPYTFDIQAINGVSSKSPFPPQHVSVNITTNQAAPSTVPIMHQVSATMRSITLSWPQPEQPNGIILD YEIRYYEKEHNESMARSQTNTARIDGLRPGMVYVVQVRARTVAGYGKFSGKMCFQTLTDDDYKSELREQLPLIAGSAAAGVVFVVSLVAISIVCSRKRAYSKEAVYSDKLQHYS TGRGSPGMKIYIDPFTYEDPNEAVREFAKEIDVSFVKIEEVIGAGEFGEVYKGRLKLPGKREIYVAIKTLKAGYSEKQRRDFLSEASIMGQFDHPNIIRLEGVVTKSRPVMIITEFMENG ALDSFLRQNDGQFTVIQLVGMLRGIAAGMKYLAEMNYVHRDLAARNILVNSNLVCKVSDFGLSRYLQDDTSDPTYTSSLGGKIPVRWTAPEAIAYRKFTSASDVWSYGIVMWEV MSFGERPYWDMSNQDVINAIEQDYRLPPPMDCPAALHQLMLDCWCKDRNSRPRFAEIVNTLDKMIRNPASLKTVATITAVPSQPLLDRSIPDFTAFTTVDDWLSAIKMVQYRD SFLTAGFTSLQLVTQMTSEDLLRIGITLAGHQKKILNSIHSMRVQISQSPTAAMA

FIG. 65 (Cont.)

EPHB2	NP_001296122	P29323	MALRRLGAALLLLPLLAAVEETLMDSTTATAELGWMVHPPSGWEEVSGYDENMNTIRTYQVCNVFESSQNNWLRTKFIRRRGAHRIHVEMKFSVRDCSSIPSVPGSCKETFNLYY YEADFDSATKTFPNWMENPWVKVDTIAADESFSQVDLGGRVMKINTEVRSFGPVSRSGFYLAFQDYGGCMSLIAVRVFYRKCPRIIQNGAIFQETLSGAESTSLVAARGSCIANAE EVDVPIKLYCNGDGEWLVPIGRCMCKAGFEAVENGTVCRGCPSGTFKANQGDEACTHCPINSRTTSEGATNCVCRNGYYRADLDPLDMPCTTIPSAPQAVISSVNETSLMLEWT PPRDSGGREDLVYNIICKSCGSGRGACTRCGDNVQYAPRQLGLTEPRIYSDLLAHTQYTFEIQAVNGVTDQSPFSPQFASVNITTNQAAPSAVSIMHQVSRTVDSITLSWSQPDQ PNGVILDYELQYYEKELSEYNATAIKSPTNTVTVQGLKAGAIYVFQVRARTVAGYGRYSGKMYFQTMTEAEYQTSIQEKLPLIIGSSAAGLVFLIAVVVIAIVCNRRGFERADSEYTDK LQHYTSGHMTPGMKIYIDPFTYEDPNEAVREFAKEIDISCVKIEQVIGAGEFGEVCSGHLKLPGKREIFVAIKTLKSGYTEKQRRDFLSEASIMGQFDHPNVIHLEGVVTKSTPVMIITE FMENGSLDSFLRQNDGQFTVIQLVGMLRGIAAGMKYLADMNYVHRDLAARNILVNSNLVCKVSDFGLSRFLEDDTSDPTYTSALGGKIPIRWTAPEAIQYRKFTSASDVWSYGIV MWEVMSYGERPYWDMTNQDVINAIEQDYRLPPPMDCPSALHQLMLDCWQKDRNHRPKFGQIVNTLDKMIRNPNSLKAMAPLSSGINLPLLDRTIPDYTSFNTVDEWLEAIK MGQYKESFANAGFTSFDVVSQMMMEDILRVGVTLAGHQKKILNSIQVMRAQMNQIQSVEGQPLARRPRATGRTKRCQPRDVTKKTCNSNDGKKKGMGIKKKTDPGRGREIQ GIFFKEDSHKESNDCSCGG
EPHB3	NP_004434	P54753	MARARPPPPPSPPPGLLPLLPPLLLLPLLLPAGCRALEETLMDTKWVTSELAWTSHPESGWEEVSGYDEAMNPIRTYQVCNVRESSQNNWLRTGFIWRRDVQRVYVELKFTVRD CNSIPNIPGSCKETFNLFYYEADSDVASASSPFWMENPYVKVDTIAPDESFSRLDAGRVNTKVRSFGPLSKAGFYLAFQDQGACMSLISVRAFYKKCASTTAGFALFPETLTGAEPTS LVIAPGTCIPNAVEVSVPLKLYCNGDGEWMVPVGACTCATGHEPAAKESQCRPCPPGSYKAKQGEGPCLPCPPNSRTTSPAASICTCHNNFYRADSDSADSACTTVPSPPRGVIS NVVNETSLILEWSEPRDLGGRDDLLYNVICKKCHGAGGASACSRCDDNVEFVPRQLGLTERRVHISHLLAHTRYTFEVQAVNGVSGKSPLPPRYAAVNITTNQAAPSEVPTLRLHSSS IGSSLTLSWAPPERPNGVILDYEMKYFEKSEGIASTVTSQMNSVQLDGLRPDARYVVQVRARTVAGYGQYSRPAEFETTSERGSGAQQLQEQLPLIVGSATAGLVFVVAVVVIAIVC LRKQRHGSDSEYTEKLQQYIAPGMKVYIDPFTYEDPNEAVREFAKEIDVSCVKIEEVIGAGEFGEVCRGRLKQPGRREVFVAIKTLKVGYTERQRRDFLSEASIMGQFDHPNIIRLEG VVTKSRPVMILTEFMENCALDSFLRLNDGQFTVIQLVGMLRGIAAGMKYLSEMNYVHRDLAARNILVNSNLVCKVSDFGLSRFLEDDPSDPTYTSSLGGKIPIRWTAPEAIAYRKFT SASDVWSYGIVMWEVMSYGERPYWDMSNQDVINAVEQDYRLPPPMDCPTALHQLMLDCWVRDRNLRPKFSQIVNTLDKLIRNAASLKVIASAQSGMSQPLLDRTVPDYTTFT TVGDWLDAIKMGRYKESFVSAGFASFDLVAQMTAEDLLRIGVTLAGHQKKILSSIQDMRLQMNQTLPVQV
EPHB4	NP_004435	P54760	MELRVLLCWASLAAALEETLNTKLETADLKWVTFPQVDGQWEELSGLDEEQHSVRTYEVCDVQRAPGQAHWLRTGWVPRRGAVHVYATLRFTMLECLSLPRAGRSCKETFTV PYYESDADTATALTPAWMENPYIKVDTVAAEHLTRKRPGAEATGKVNVKTLRLGPLSKAGFYLAFQDQGACMALLSLHLFYKKCAQLTVNLTRFPETVPRELVVPVAGSCVVDAV PAPGPSPSLYCREDGQWAEQPVTGCSCAPGFEAAEGNTKCRACAQGTFKPLSGEGSCQPCPANSHSNTIGSAVCQCRVGYFRARTDPRGAPCTTPPSAPRSVVSRLNGSSLHLE WSAPLESGGREDLTYALRCRECRPGGSCAPCGGDLTFDPGPRDLVEPWVVVVRGLRPDFTYTFEVTALNGVSSLATGPVPFEPVNVTTDREVPPAVSDIRVTRSSPSSLSLAWAVPR APSGAVLDYEVKYHEKGAEGPSSVRFLKTSENRAELRGLKRGASYLVQVRARSEAGYGPFGQEHHSQTQLDESEGWREQLALIAGTAVVGVVLVLVIVVAVLCLRKQSNGREAE YSDKHGQYLIGHGTKVYIDPFTYEDPNEAVREFAKEIDVSYVKIEEVIGAGEFGEVCRGRLKAPGKKESCVAIKTLKSGYTERQRREFLSEASIMGQFEHPNIIRLEGVVTNSMPVMIL TEFMENGALDSFLRLNDGQFTVIQLVGMLRGIASGMRYLAEMSYVHRDLAARNILVNSNLVCKVSDFGLSRFLEENSSDPTYTSSLGGKIPIRWTAPEAIAFRKFTSASDAWSYGIV MWEVMSFGERPYWDMSNQDVINAIEQDYRLPPPPDCPTSLHQLMLDCWQKDRNARPRFPQVVSALDKMIRNPASLKIVARENGGASHPLLDQRQPHYSAFGSVGEWLRAIK MGRYEESFAAAGFGSFELVSQISAEDLLRIGVTLAGHQKKILASVQHMKSQAKPGTPGGTGGPAPQY

FIG. 65 (Cont.)

EPHB6	NP_004436	O15197	MATEGAAQLGNRVAGMVCSLWVLLLVSSVLALEEVLLDTTGETSEIGWLTYPPGGWDEVSVLDDQGRRLTRTFEACHVAGAPPGTGQDNWLQTHFVERRGAQRAHIRLHFSVR ACSSLGVSGGTCRETFTLYYRQAEEPDSPDSVSSWHLKRWTKVDTIAADESFPSSSSSSSSSSSSSSSAAWAVGPHGAGQRAGLQLNVKERSFGPLTQRGFYVAFQDTGACLALVAVRLL FSYTCPAVLRSFASFPETQASGAGGASLVAAVGTCVAHAEPEEDGVGGQAGGSPRLHCNGEGKWMVAVGGCRCQPGYQPARGDKACQACPRGLYKASAGNAPCSPCPARS HAPNPAAPVCPCLEGFYRASSDPPEAPCTGPPSAPQELWFEVQGSALMLHWRLPRELGGRGDLLFNVVCKECEGRQEPASGGGGTCHRCRDEVHFDPRQRGLTESRVLVGGLR AHVPYILEVQAVNGVSELSPDPPQAAAINVSTSHEVPSAVPVVHQVSRASNSITVSWPQPDQTNGNILDYQLRYYDQAEDESHSFTLTSETNTATVTQLSPGHIYGFQVRARTAAG HGPYGGKVYFQTLPQGELSSQLPERLSLVIGSILGALAFLLLAAITVLAVVFQRKRRGTGYTEQLQQYSSPGLGVKYYIDPSTYEDPCQAIRELAREVDPAYIKIEEVIGTGSFGEVRQG RLQPRGRREQTVAIQALWAGGAESLQMTFLGRAAVLGQFQHPNILRLEGVVTKSRPLMVLTEFMELGPLDSFLRQREGQFSSLQLVAMQRGVAAAMQYLSSFAFVHRSLSAHS VLVNSHLVCKVARLGHSPQGPSCLLRWAAPEVIAHGKHTTSSDVWSFGILMWEVMSYGERPYWDMSEQEVLNAIEQEFRLPPPPGCPPGLHLLMLDTWQKDRARRPHFDQLV AAFDKMIRKPDTLQAGGDPGERPSQALLTPVALDFPCLDSPQAWLSAIGLECYQDNFSKFGLCTFSDVAQLSLEDLPALGITLAGHQKKLLHHIQLLQQHLRQQGSVEV
ERBB2	NP_004439	P04626	MELAALCRWGLLLALLPPGAASTQVCTGTDMKLRLPASPETHLDMLRHLYQGCQVVQGNLELTYLPTNASLSFLQDIQEVQGYVLIAHNQVRQVPLQRLRIVRGTQLFEDNYALA VLDNGDPLNNTTPVTGASPGGLRELQLRSLTEILKGGVLIQRNPQLCYQDTILWKDIFHKNNQLALTLIDTNRSRACHPCSPMCKGSRCWGESSEDCQSLTRTVCAGGCARCKGPL PTDCCHEQCAAGCTGPKHSDCLACLHFNHSGICELHCPALVTYNTDTFESMPNPEGRYTFGASCVTACPYNYLSTDVGSCTLVCPLHNQEVTAEDGTQRCEKCSKPCARVCYGLG MEHLREVRAVTSANIQEFAGCKKIFGSLAFLPESFDGDPASNTAPLQPEQLQVFETLEEITGYLYISAWPDSLPDLSVFQNLQVIRGRILHNGAYSLTLQGLGISWLGLRSLRELGSGL ALIHHNTHLCFVHTVPWDQLFRNPHQALLHTANRPEDECVGEGLACHQLCARGHCWGPGPTQCVNCSQFLRGQECVEECRVLQGLPREYVNARHCLPCHPECQPQNGSVTCF GPEADQCVACAHYKDPPFCVARCPSGVKPDLSYMPIWKFPDEEGACQPCPINCTHSCVDLDDKGCPAEQRASPLTSIISAVVGILLVVVLGVVFGILIKRRQQKIRKYTMRRLLQET ELVEPLTPSGAMPNQAQMRILKETELRKVKVLGSGAFGTVYKGIWIPDGENVKIPVAIKVLRENTSPKANKEILDEAYVMAGVGSPYVSRLLGICLTSTVQLVTQLMPYGCLLDHVR ENRGRLGSQDLLNWCMQIAKGMSYLEDVRLVHRDLAARNVLVKSPNHVKITDFGLARLLDIDETEYHADGGKVPIKWMALESILRRRFTHQSDVWSYGVTVWELMTFGAKPYD GIPAREIPDLLEKGERLPQPPICTIDVYMIMVKCWMIDSECRPRFRELVSEFSRMARDPQRFVVIQNEDLGPASPLDSTFYRSLLEDDDMGDLVDAEEYLVPQQGFFCPDPAPGAG GMVHHRHRSSSTRSGGGDLTLGLEPSEEEAPRSPLAPSEGAGSDVFDGDLGMGAAKGLQSLPTHDPSPLQRYSEDPTVPLPSETDGYVAPLTCSPQPEYVNQPDVRPQPPSPREG PLPAARPAGATLERPKTLSPGKNGVVKDVFAFGGAVENPEYLTPQGGAAPQPHPPPAFSPAFDNLYYWDQDPPERGAPPSTFKGTPTAENPEYLGLDVPV

FIG. 65 (Cont.)

ERBB3	NP_001973	P21860	MRANDALQVLGLLFSLARGSEVGNSQAVCPGTLNGLSVTGDAENQYQTLYKLYERCEVVMGNLEIVLTGHNADLSFLQWIREVTGYVLVAMNEFSTLPLPNLRVVRGTQVYDGK
			FAIFVMLNYNTNSSHALRQLRLTQLTEILSGGVYIEKNDKLCHMDTIDWRDIVRDRDAEIVVKDNGRSCPPCHEVCKGRRCWGPGSEDCQTLTKTICAPQCNGHCFGPNPNQCCH
			DECAGGCSGPQDTDCFACRHFNDSGACVPRCPQPLVYNKLTFQLEPNPHTKYQYGGVCVASCPHNFVVDQTSCVRACPPDKMEVDKNGLKMCEPCGGLCPKACEGTGSGSRF
			QTVDSSNIDGFVNCTKILGNLDFLITGLNGDPWHKIPALDPEKLNVFRTVREITGYLNIQSWPPHMHNFSVFSNLTTIGGRSLYNRGFSLLIMKNLNVTSLGFRSLKEISAGRIYISAN
			RQLCYHHSLNWTKVLRGPTEERLDIKHNRPRRDCVAEGKVCDPLCSSGGCWGPGPGQCLSCRNYSRGGVCVTHCNFLNGEPREFAHEAECFSCHPECQPMEGTATCNGSGSDT
			CAQCAHFRDGPHCVSSCPHGVLGAKGPIYKYPDVQNECRPCHENCTQGCKGPELQDCLGQTLVLIGKTHLTMALTVIAGLVVIFMMLGGTFLYWRGRRIQNKRAMRRYLERGE
			SIEPLDPSEKANKVLARIFKETELRKLKVLGSGVFGTVHKGVWIPEGESIKIPVCIKVIEDKSGRQSFQAVTDHMLAIGSLDHAHIVRLLGLCPGSSLQLVTQYLPLGSLLDHVRQHRGA
			LGPQLLLNWGVQIAKGMYYLEEHGMVHRNLAARNVLLKSPSQVQVADFGVADLLPPDDKQLLYSEAKTPIKWMALESIHFGKYTHQSDVWSYGVTVWELMTFGAEPYAGLRL
			AEVPDLLEKGERLAQPQICTIDVYMVMVKCWMIDENIRPTFKELANEFTRMARDPPRYLVIKRESGPGIAPGPEPHGLTNKKLEEVELEPELDLDLDLEAEEDNLATTTLGSALSLPV
			GTLNRPRGSQSLLSPSSGYMPMNQGNLGESCQESAVSGSSERCPRPVSLHPMPRGCLASESSEGHVTGSEAELQEKVSMCRSRSRSPRPRGDSAYHSQRHSLLTPVTPLSPPG
			LEEEDVNGYVMPDTHLKGTPSSREGTLSSVGLSSVLGTEEEDEDEEYEYMNRRRHSPPHPPRPSSLEELGYEYMDVGSDLSASLGSTQSCPLHPVPIMPTAGTTPDEDYEYMNRQ
			RDGGGPGGDYAAMGACPASEQGYEEMRAFQGPGHQAPHVHYARLKTLRSLEATDSAFDNPDYWHSRLFPKANAQRT
ERBB4	NP_005226	Q15303	MKPATGLWVWVSLLVAAGTVQPSDSQSVCAGTENKLSSLSDLEQQYRALRKYYENCEVVMGNLEITSIEHNRDLSFLRSVREVTGYVLVALNQFRYLPLENLRIIRGTKLYEDRYAL
			AIFLNYRKDGNFGLQELGLKNLTEILNGGVYVDQNKFLCYADTIHWQDIVRNPWPSNLTLVSTNGSSGCGRCHKSCTGRCWGPTENHCQTLTRTVCAEQCDGRCYGPYVSDCCH
			RECAGGCSGPKDTDCFACMNFNDSGACVTQCPQTFVYNPTTFQLEHNFNAKYTYGAFCVKKCPHNFVVDSSSCVRACPSSKMEVEENGIKMCKPCTDICPKACDGIGTGSLMS
			AQTVDSSNIDKFINCTKINGNLIFLVTGIHGDPYNAIEAIDPEKLNVFRTVREITGFLNIQSWPPNMTDFSVFSNLVTIGGRVLYSGLSLLILKQQGITSLQFQSLKEISAGNIYITDNSNL
			CYYHTINWTTLFSTINQRIVIRDNRKAENCTAEGMVCNHLCSSDGCWGPGPDQCLSCRRFSRGRICIESCNLYDGEFREFENGSICVECDPQCEKMEDGLLTCHGPGPDNCTKCS
			HFKDGPNCVEKCPDGLQGANSFIFKYADPDRECHPCHPNCTQGCNGPTSHDCIYYPWTGHSTLPQHARTPLIAAGVIGGLFILVIVGLTFAVYVRRKSIKKKRALRRFLETELVEPLT
			PSGTAPNQAQLRILKETELKRVKVLGSGAFGTVYKGIWVPEGETVKIPVAIKILNETTGPKANVEFMDEALIMASMDHPHLVRLLGVCLSPTIQLVTQLMPHGCLLEYVHEHKDNIG
			SQLLLNWCVQIAKGMMYLEERRLVHRDLAARNVLVKSPNHVKITDFGLARLLEGDEKEYNADGGKMPIKWMALECIHYRKFTHQSDVWSYGVTIWELMTFGGKPYDGIPTREIP
			DLLEKGERLPQPPICTIDVYMVMVKCWMIDADSRPKFKELAAEFSRMARDPQRYLVIQGDDRMKLPSPNDSKFFQNLLDEEDLEDMMDAEEYLVPQAFNIPPPIYTSRARIDSNR
			SEIGHSPPPAYTPMSGNQFVYRDGGFAAEQGVSVPYRAPTSTIPEAPVAQGATAEIFDDSCCNGTLRKPVAPHVQEDSSTQRYSADPTVFAPERSPRGELDEEGYMTPMRDKPK
			QEYLNPVEENPFVSRRKNGDLQALDNPEYHNASNGPPKAEDEYVNEPLYLNTFAANTLGKAEYLKNNILSMPEKAKKAFDNPDYWNHSLPPRSTLQHPDYLQEYSTKYFYKQNGRI
			RPIVAENPEYLSEFSLKPGTVLPPPPYRHRNTVV

FIG. 65 (Cont.)

FGFR1	NP_075598	P11362	MWSWKCLLFWAVLVTATLCTARPSPTLPEQAQPWGAPVEVESFLVHPGDLLQLRCRLRDDVQSINWLRDGVQLAESNRTRITGEEVEVQDSVPADSGLYACVTSSPSGSDTTYF SVNVSDALPSSEDDDDDDDSSSEEKETDNTKPNRMPVAPYWTSPEKMEKKLHAVPAAKTVKFKCPSSGTPNPTLRWLKNGKEFKPDHRIGGYKVRYATWSIIMDSVVPSDKGNY TCVVENEYGSINHTYQLDVVERSPHRPILQAGLPANKTVALGSNVEFMCKVYSDPQPHIQWIKHIEVNGSKIGPDNLPYVQILKTAGVNTTDKEMEVLHLRNVSFEDAGEYTCLAG NSIGLSHHSAWLTVLEALEERPAVMTSPLYLEIIIYCTGAFLISCMVGSVIVYKMKSGTKKSDFHSQMAVHKLAKSIPLRRQVTVSADSSASMNSGVLLVRPSRLSSSGTPMLAGVSE YELPEDPRWELPRDRLVLGKPLGEGCFGQVVLAEAIGLDKDKPNRVTKVAVKMLKSDATEKDLSDLISEMEMMKMIGKHKNIINLLGACTQDGPLYVIVEYASKGNLREYLQARR PPGLEYCYNPSHNPEEQLSSKDLVSCAYQVARGMEYLASKKCIHRDLAARNVLVTEDNVMKIADFGLARDIHHIDYYKKTTNGRLPVKWMAPEALFDRIYTHQSDVWSFGVLLW EIFTLGGSPYPGVPVEELFKLLKEGHRMDKPSNCTNELYMMMRDCWHAVPSQRPTFKQLVEDLDRIVALTSNQEYLDLSMPLDQYSPSFPDTRSSTCSSGEDSVFSHEPLPEEPCL PRHPAQLANGGLKRR
FGFR3	NP_000133	P22607	MGAPACALALCVAVAIVAGASSESLGTEQRVVGRAAEVPGPEPGQQEQLVFGSGDAVELSCPPPGGGPMGPTVWVKDGTGLVPSERVLVGPQRLQVLNASHEDSGAYSCRQR LTQRVLCHFSVRVTDAPSSGDDEDGEDEAEDTGVDTGAPYWTRPERMDKKLLAVPAANTVRFRCPAAGNPTPSISWLKNGREFRGEHRIGGIKLRHQQWSLVMESVVPSDRG NYTCVVENKFGSIRQTYTLDVLERSPHRPILQAGLPANQTAVLGSDVEFHCKVYSDAQPHIQWLKHVEVNGSKVGPDGTPYVTVLKTAGANTTDKEIEVLSLHNVTFEDAGEYTCL AGNSIGFSHHSAWLVVLPAEEELVEADEAGSVYAGILSYGVGFFLFILVVAAVTLCRLRSPPKKGLGSPTVHKISRFPLKRQVSLESNASMSSNTPLVRIARLSSGEGPTLANVSELELP ADPKWELSRARLTLGKPLGEGCFGQVVMAEAIGIDKDRAAKPVTVAVKMLKDDATDKDLSDLVSEMEMMKMIGKHKNIINLLGACTQGGPLYVLVEYAAKGNLREFLRARRPP GLDYSFDTCKPPEEQLTFKDLVSCAYQVARGMEYLASQKCIHRDLAARNVLVTEDNVMKIADFGLARDVHNLDYYKKTTNGRLPVKWMAPEALFDRVYTHQSDVWSFGVLLWE IFTLGGSPYPGIPVEELFKLLKEGHRMDKPANCTHDLYMIMRECWHAAPSQRPTFKQLVEDLDRVLTVTSTDEYLDLSAPFEQYSPGGQDTPSSSSGDDSVFAHDLLPPAPPSSG GSRT
FGFR2	NP_000132	P21802	MVSWGRFICLVVVTMATLSLARPSFSLVEDTTLEPEEPPTKYQISQPEVYVAAPGESLEVRCLLKDAAVISWTKDGVHLGPNNRTVLIGEYLQIKGATPRDSGLYACTASRTVDSET WYFMVNVTDAISSGDDEDDTDGAEDFVSENSNNKRAPYWTNTEKMEKRLHAVPAANTVKFRCPAGGNPMPTMRWLKNGKEFKQEHRIGGYKVRNQHWSLIMESVVPSDK GNYTCVVENEYGSINHTYHLDVVERSPHRPILQAGLPANASTVVGGDVEFVCKVYSDAQPHIQWIKHVEKNGSKYGPDGLPYLKVLKAAGVNTTDKEIEVLYIRNVTFEDAGEYTC LAGNSIGISFHSAWLTVLPAPGREKEITASPDYLEIAIYCIGVFLIACMVVTVILCRMKNTTKKPDFSSQPAVHKLTKRIPLRRQVTVSAESSSSMNSNTPLVRITTRLSSTADTPMLAG VSEYELPEDPKWEFPRDKLTLGKPLGEGCFGQVVMAEAVGIDKDKPKEAVTVAVKMLKDDATEKDLSDLVSEMEMMKMIGKHKNIINLLGACTQDGPLYVIVEYASKGNLREYL RARRPPGMEYSYDINRVPEEQMTFKDLVSCTYQLARGMEYLASQKCIHRDLAARNVLVTENNVMKIADFGLARDINNIDYYKKTTNGRLPVKWMAPEALFDRVYTHQSDVWSF GVLMWEIFTLGGSPYPGIPVEELFKLLKEGHRMDKPANCTNELYMMMRDCWHAVPSQRPTFKQLVEDLDRILTLTTNEEYLDLSQPLEQYSPSYPDTRSSCSSGDDSVFSPDPMP YEPCLPQYPHINGSVKT

FIG. 65 (Cont.)

FGFR4	NP_002002	P22455	MRLLLALLGVLLSVPGPPVLSLEASEEVELEPCLAPSLEQQEQELTVALGQPVRLCCGRAERGGHWYKEGSRLAPAGRVRGWRGRLEIASFLPEDAGRYLCLARGSMIVLQNLTLIT GDSLTSSNDDEDPKSHRDPSNRHSYPQQAPYWTHPQRMEKKLHAVPAGNTVKFRCPAAGNPTPTIRWLKDGQAFHGENRIGGIRLRHQHWSLVMESVVPSDRGTYTCLVENA VGSIRYNYLLDVLERSPHRPILQAGLPANTTAVVGSDVELLCKVYSDAQPHIQWLKHIVINGSSFGADGFPYVQVLKTADINSSEVEVLYLRNVSAEDAGEYTCLAGNSIGLSYQSAW LTVLPEEDPTWTAAAPEARYTDILYASGSLALAVLLLAGLYRGQALHGRHPRPPATVQKLSRFPLARQFSLESGSSGKSSSSLVRGVRLSSSGPALLAGLVSLDLPDPLWEFPRDRL VLGKPLGEGCFGQVVRAEAFGMDPARPDQASTVAVKMLKDNASDKDLADLVSEMEVMKLIGRHKNIINLLGVCTQEGPLYVIVECAAKGNLREFLRARRPPGPDLSPDGPRSSE GPLSFPVLVSCAYQVARGMQYLESRKCIHRDLAARNVLVTEDNVMKIADFGLARGVHHIDYYKKTSNGRLPVKWMAPEALFDRVYTHQSDVWSFGILLWEIFTLGGSPYPGIPVE ELFSLLREGHRMDRPPHCPPELYGLMRECWHAAPSQRPTFKQLVEALDKVLLAVSEEYLDLRLTFGPYSPSGGDASSTCSSSDSVFSHDPLPLGSSSFPFGSGVQT
LMTK2	NP_055731	Q8IWU2	MPGPPALRRRLLLLLLVLLIAGSAGAAPLPQTGAGEAPPAAEVSSSFVILCVCSLIILVLIAANCVSCCKDPEIDFTPPAEDTPSVQSPAEVFTLSVPNISLPAPSQFQ PSVEGLKSQVARHSLNVIQEIGNGWFGKVLLGEIYTGTSVARVIVKELKASANPKEQDTFLKNGEPYYILQHPNILQCVGQCVEAIPYLLVFEFCDLGDLKAYLRSEQEHMRGDSQT MLLQRMACEVAAGLAAMHKLHFLHSDLALRNCFLTSDLNVKVGDYGIGFSRYKEDYIETDDKKVFPLRWTAPELVTSFQDRLLTADQTKYSNIWSLGVTLWELFDNAAQPYSNLS NLDVLNQVIRERDTKLPKPQLEQPYSDRWYEVLQFCWLSPEKRPAAEDVHRLLTYLRLQSQRDSEVDFEQQWNALKPNTNSRDSSNNAAFPILDHFARDRLGREMEEVLTVTETS CGLSFEYVWEAAKHDHFDERSRGHLDEGLSTSIFYPVEVFESLSDPGPGKQDDSGQDVPLRVPGVVPVFDAHNLSVGSDYYIQLEEKSGSNLELDYPPALLTTDMDNPERTGPE LSQLTALRSVELEESSTDEDFFQSSTIDPKDSSLPGDLHVTSGPESPFNNIFNDVDKSEDLPSHQKIFDLMELNGVQADFKPATLSSSLDNPKESVITGHFEKEKPRKIFDSEPLCLSDNL MHQDNFDPLNVQELSENFLFLQEKNLLKGSLSSKEHINDLQTELKNAGFTEAMLETSCRNSLDTELQFAENKPGLSLLQENVSTKGDDTDVMLTGDTLSTSLQSSPEVQVPPTSFET EETPRRVPPDSLPTQGETQPTCLDVIVPEDCLHQDISPDAVTVPVEILSTDARTHSLDNRSQDSPGESEETLRLTESDSVLADDILASRVSVGSSLPELGQELHNKPFSEDHKSHRRLE KNLEAVETLNQLNSKDAAKEAGLVSALSSDSTSQDSLLEDSLSAPEPASEPSLETPDSLESVDVHEALLDSLGSHTPQKLVPPDKPADSGYETENLESPEWTLHPAPEGTADSEPATT GDGGHSGLPPNPVIVISDAGDGHRGTEVTPETFTAGSQGSYRDSAYFSDNDSEPEKRSEEVPGTSPSALVLVQEQPLPEPVLPEQSPAAQDSCLEARKSQPDESCLSALHNSSDLEL RATPEPAQTGVPQQVHPTEDEASSPWSVLNAELSSGDDFETQDDRPCTLASTGTNTNELLAVTNSALDKSLSSHSEGPKLKEPDIEGKYLGKLGVSGMLDLSEDGMDADEEDENS DDSDEDIRAFNIHSLSSESEDETEHPVPIILSNEDGRHLRSLLKPTAANAPDLPEDWKKEKKAVTFFDDVTVILFDQETPTKELGPCGGEACGPDLSGPAPASGSPYLSRCINSESST DEEGGGFEWDDDFSPDPFMSKTTSNLLSSKPSLQTSKYFSPPPPARSTEQSWPHSAPYSRFSISPANIASFSLTHLTDSDIEQGGSSEDGEKD

FIG. 65 (Cont.)

FLT1	NP_002010	P17948	MVSYWDTGVLLCALLSCLLLTGSSSGSKLKDPELSLKGTQHIMQAGQTLHLQCRGEAAHKWSLPEMVSKESERLSITKSACGRNGKQFCSTLTLNTAQANHTGFYSCKYLAVPTSK KKETESAIYIFISDTGRPFVEMYSEIPEIIHMTEGRELVIPCRVTSPNITVTLKKFPLDTLIPDGKRIIWDSRKGFIISNATYKEIGLLTCEATVNGHLYKTNYLTHRQTNTIIDVQISTPRPVK LLRGHTLVLNCTATTPLNTRVQMTWSYPDEKNKRASVRRRIDQSNSHANIFYSVLTIDKMQNKDKGLYTCRVRSGPSFKSVNTSVHIYDKAFITVKHRKQQVLETVAGKRSYRLSM KVKAFPSPEVVWLKDGLPATEKSARYLTRGYSLIIKDVTEEDAGNYTILLSIKQSNVFKNLTATLIVNVKPQIYEKAVSSFPDPALYPLGSRQILTCTAYGIPQPTIKWFWHPCNHNHSE ARCDFCSNNEESFILDADSNMGNRIESITQRMAIIEGKNKMASTLVVADSRISGIYICIASNKVGTVGRNISFYITDVPNGFHVNLEKMPTEGEDLKLSCTVNKFLYRDVTWILLRTVN NRTMHYSISKQKMAITKEHSITLNLTIMNVSLQDSGTYACRARNVYTGEEILQKKEITIRDQEAPYLLRNLSDHTVAISSSTTLDCHANGVPEPQITWFKNNHKIQQEPGIILGPGSST LFIERVTEEDEGVYHCKATNQKGSVESSAYLTVQGTSDKSNLELITLTCTCVAATLFWLLLTLFIRKMKRSSSEIKTDYLSIIMDPDEVPLDEQCERLPYDASKWEFARERLKLGKSLGR GAFGKVVQASAFGIKKSPTCRTVAVKMLKEGATASEYKALMTELKILTHIGHHLNVVNLLGACTKQGGPLMVIVEYCKYGNLSNYLKSKRDLFFLNKDAALHMEPKKEKMEPGLE QGKKPRLDSVTSSESFASSGFQEDKSLSDVEEEEDSDGFYKEPITMEDLISYSFQVARGMEFLSSRKCIHRDLAARNILLSENNVVKICDFGLARDIYKNPDYVRKGDTRLPLKWMAP ESIFDKIYSTKSDVWSYGVLLWEIFSLGGSPYPGVQMDEDFCSRLREGMRMRAPEYSTPEIYQIMLDCWHRDPKERPRFAELVEKLGDLLQANVQQDGKDYIPINAILTGNSGFTY STPAFSEDFFKESISAPKFNSGSSDDVRYVNAFKFMSLERIKTFEELLPNATSMFDDYQGDSSTLLASPMLKRFTWTDSKPKASLKIDLRVTSKSKESGLSDVSRPSFCHSSCGHVSEG KRRFTYDHAELERKIACCSPPPDYNSVVLYSTPPI
FLT3	NP_004110	P36888	MPALARDGGQLPLLVVFSAMIFGTITNQDLPVIKCVLINHKNNDSSVGKSSSYPMVSESPEDLGCALRPQSSGTVYEAAAVEVDVSASITLQVLVDAPGNISCLWVFKHSSLNCQP HFDLQNRGVVSMVILKMTETQAGEYLLFIQSEATNYTILFTVSIRNTLLYTLRRPYFRKMENQDALVCISESVPEPIVEWVLCDSQGESCKEESPAVVKKEEKVILHELFGTDIRCCARN ELGRECTRLFTIDLNQTPQTTLPQLFLKVGEPLWIRCKAVHVNHGFGLTWELENKALEEGNYFEMSTYSTNRTMIRILFAFVSSVARNDTGYYTCSSSKHPSQSALVTIVEKGFINAT NSSEDYEIDQYEEFCFSVRFKAYPQIRCTWTFSRKSFPCEQKGLDNGYSISKFCNHKHQPGEYIFHAENDDAQFTKMFTLNIRRKPQVLAEASASQASCFSDGYPLPSWTWKKCSD KSPNCTEEITEGVWNRKANRKVFGQWVSSSTLNMSEAIKGFLVKCCAYNSLGTSCETILLNSPGPFPFIQDNISFYATIGVCLLFIVVLTLLICHKYKKQFRYESQLQMVQVTGSSDNE YFYVDFREYEYDLKWEFPRENLEFGKVLGSGAFGKVMNATAYGISKTGVSIQVAVKMLKEKADSSEREALMSELKMMTQLGSHENIVNLLGACTLSGPIYLIFEYCCYGDLLNYLRS KREKFHRTWTEIFKEHNFSFYPTFQSHPNSSMPGSREVQIHPDSDQISGLHGNSFHSEDEIEYENQKRLEEEEDLNVLTFEDLLCFAYQVAKGMEFLEFKSCVHRDLAARNVLVTHG KVVKICDFGLARDIMSDSNYVVRGNARLPVKWMAPESLFEGIYTIKSDVWSYGILLWEIFSLGVNPYPGIPVDANFYKLIQNGFKMDQPFYATEEIYIIMQSCWAFDSRKRPSFPNL TSFLGCQLADAEEAMYQNVDGRVSECPHTYQNRRPFSREMDLGLLSPQAQVEDS

FIG. 65 (Cont.)

FLT4	NP_891555	P35916	MQRGAALCLRLWLCLGLLDGLVSGYSMTPPTLNITEESHVIDTGDSLSISCRGQHPLEWAWPGAQEAPATGDKDSEDTGVVRDCEGTDARPYCKVLLHEVHANDTGSYVCYYK
			YIKARIEGTTAASSYVFVRDFEQPFINKPDTLLVNRKDAMWVPCLVSIPGLNVTLRSQSSVLWPDGQEVVWDDRRGMLVSTPLLHDALYLQCETTWGDQDFLSNPFLVHITGNEL
			YDIQLLPRKSLELLVGEKLVLNCTVWAEFNSGVTFDWDYPGKQAERGKWVPERRSQQTHTELSSILTIHNVSQHDLGSYVCKANNGIQRFRESTEVIVHENPFISVEWLKGPILEAT
			AGDELVKLPVKLAAYPPPEFQWYKDGKALSGRHSPHALVLKEVTEASTGTYTLALWNSAAGLRRNISLELVVNVPPQIHEKEASSPSIYSRHSRQALTCTAYGVPLPLSIQWHWRP
			WTPCKMFAQRSLRRRQQQDLMPQCRDWRAVTTQDAVNPIESLDTWTEFVEGKNKTVSKLVIQNANVSAMYKCVVSNKVGQDERLIYFYVTTIPDGFTIESKPSEELLEGQPVLL
			SCQADSYKYEHLRWYRLNLSTLHDAHGNPLLLDCKNVHLFATPLAASLEEVAPGARHATLSLSIPRVAPEHEGHYVCEVQDRRSHDKHCHKKYLSVQALEAPRLTQNLTDLLVNVS
			DSLEMQCLVAGAHAPSIVWYKDERLLEEKSGVDLADSNQKLSIQRVREEDAGRYLCSVCNAKGCVNSSASVAVEGSEDKGSMEIVILVGTGVIAVFFWVLLLLFCNMRRPAHADI
			KTGYLSIIMDPGEVPLEEQCEYLSYDASQWEFPRERLHLGRVLGYGAFGKVVEASAFGIHKGSSCDTVAVKMLKEGATASEHRALMSELKILIHIGNHLNVVNLLGACTKPQGPLM
			VIVEFCKYGNLSNFLRAKRDAFSPCAEKSPEQRGRFRAMVELARLDRRRPGSSDRVLFARFSKTEGGARRASPDQEAEDLWLSPLTMEDLVCYSFQVARGMEFLASRKCIHRDLAA
			RNILLSESDVVKICDFGLARDIYKDPDYVRKGSARLPLKWMAPESIFDKVYTTQSDVWSFGVLLWEIFSLGASPYPGVQINEEFCQRLRDGTRMRAPELATPAIRRIMLNCWSGDP
			KARPAFSELVEILGDLLQGRGLQEEEEVCMAPRSSQSSEEGSFSQVSTMALHIAQADAEDSPPSLQRHSLAARYYNWVSFPGCLARGAETRGSSRMKTFEEFPMTPTTYKGSVDN
			QTDSGMVLASEEFEQIESRHRQESGFSCKGPGQNVAVTRAHPDSQGRRRRPERGARGGQVFYNSEYGELSEPSEEDHCSPSARVTFFTDNSY
ALK	NP_004295	Q9UM73	MGAIGLLWLLPLLLSTAAVGSGMGTGQRAGSPAAGPPLQPREPLSYSRLQRKSLAVDFVVPSLFRVYARDLLLPPSSSELKAGRPEARGSLALDCAPLHRLLGPAPGVSWTAGSPAP
			AEARTLSRVLKGGSVRKLRRAKQLVLELGEEAIEGCVGPPGEAAVGLLQFNLSELFSWWIRQGEGRLRIRLMPEKKASEVGREGRLSAAIRASQPRLLFQIFGTGHSSLESPTNMPS
			PSPDYFTWNLTWIMKDSFPFLSHRSRYGLECSFDFPCELEYSPPLHDLRNQSWSWRRIPSEEASQMDLLDGPGAERSKEMPRGSFLLNTSADSKHTILSPWMRSSSEHCTLAVSV
			HRHLQPSGRYIAQLLPHNEAAREILLMPTPGKHGWTVLQGRIGRPDNPFRVALEYISSGNRSLSAVDFFALKNCSEGTSPGSKMALQSSFTCWNGTVLQLGQACDFHQDCAQGE
			DESQMCRKLPVGFYCNFEDGFCGWTQGTLSPHTPQWQVRTLKDARFQDHQDHALLLSTTDVPASESATVTSATFPAPIKSSPCELRMSWLIRGVLRGNVSLVLVENKTGKEQGR
			MVWHVAAYEGLSLWQWMVLPLLDVSDRFWLQMVAWWGQGSRAIVAFDNISISLDCYLTISGEDKILQNTAPKSRNLFERNPNKELKPGENSPRQTPIFDPTVHWLFTTCGAS
			GPHGPTQAQCNNAYQNSNLSVEVGSEGPLKGIQIWKVPATDTYSISGYGAAGGKGGKNTMMRSHGVSVLGIFNLEKDDMLYILVGQQGEDACPSTNQLIQKVCIGENNVIEEEI
			RVNRSVHEWAGGGGGGGGATYVFKMKDGVPVPLIIAAGGGGRAYGAKTDTFHPERLENNSSVLGLNGNSGAAGGGGGWNDNTSLLWAGKSLQEGATGGHSCPQAMKKW
			GWETRGGFGGGGGGCSSGGGGGGGYIGGNAASNNDPEMDGEDGVSFISPLGILYTPALKVMEGHGFEVNIKHYLNCSHCEVDECHMDPESHKVICFCDHGTVLAEDGVSCIVSPT
			PEPHLPLSLILSVVTSALVAALVLAFSGIMIVYRRKHQELQAMQMELQSPEYKLSKLRTSTIMTDYNPNYCFAGKTSSISDLKEVPRKNITLIRGLGHGAFGEVYEGQVSGMPNDPSP	
			LQVAVKTLPEVCSEQDELDFLMEALIISKFNHQNIVRCIGVSLQSLPRFILLELMAGGDLKSFLRETRPRPSQPSSLAMLDLLHVARDIACGCQYLEENHFIHRDIAARNCLLTCPGPG	
			RVAKIGDFGMARDIYRASYYRKGGCAMLPVKWMPPEAFMEGIFTSKTDTWSFGVLLWEIFSLGYMPYPSKSNQEVLEFVTSGGRMDPPKNCPGPVYRIMTQCWQHQPEDRP	
			NFAIILERIEYCTQDPDVINTALPIEYGPLVEEEEKVPVRPKDPEGVPPLLVSQQAKREEERSPAAPPPLPTTSSGKAAKKPTAAEISVRVPRGPAVEGGHVNMAFSQSNPPSELHKV	
			HGSRNKPTSLWNPTYGSWFTEKPTKKNNPIAKKEPHDRGNLGLEGSCTVPPNVATGRLPGASLLLEPSSLTAHNMKEVPLFRLRHFPCGNVNYGYQQQGLPLEAATAPGAGHYED	
			TILKSKNSMNQPGP	

FIG. 65 (Cont.)

EPHA10	NP_001092909	Q5JZY3	METCAGPHPLRLFLCRMQLCLALLGPWRPGTAEEVILLDSKASQAELGWTALPSNGWEEISGVDEHDRPIRTYQVCNVLEPNQDNWLQTGWISRGRGQRIFVELQFTLRDCSSI
			PGAAGTCKETFNVYYLETEADLGRGRPRLGGSRPRKIDTIAADESFTQGDLGERKMKLNTEVREIGPLSRRGFHLAFQDVGACVALVSVRVYYKQCRATVRGLATFPATAAESAFST
			LVEVAGTCVAHSEGEPGSPPRMHCGADGEWLVPVGRCSCSAGFQERGDFCEACPPGFYKVSPRRPLCSPCPEHSRALENASTFCVCQDSYARSPTDPPSASCTRPPSAPRDLQYS
			LSRSPLVLRLRWLPPADSGGRSDVTYSLLCLRCGREGPAGACEPCGPRVAFLPRQAGLRERAATLLHLRPGARYTVRVAALNGVSGPAAAAGTTYAQVTVSTGPGAPWEEDEIRR
			DRVEPQSVSLSWREPIPAGAPGANDTEYEIRYYEKGQSEQTYSMVKTGAPTVTVTNLKPATRYVFQIRAASPGPSWEAQSFNPSIEVQTLGEAASGSRDQSPAIVVTVVTISALLVL
			GSVMSVLAIWRRPCSYGKGGGDAHDEEELYFHFKVPTRRTFLDPQSCGDLLQAVHLFAKELDAKSVTLERSLGGGRFGELCCGCLQLPGRQELLVAVHMLRDSASDSQRLGFLAE
			ALTLGQFDHSHIVRLEGVVTRGSTLMIVTEYMSHGALDGFLRRHEGQLVAGQLMGLLPGLASAMKYLSEMGYVHRGLAARHVLVSSDLVCKISGFGRGPRDRSEAVYTTMSGRS
			PALWAAPETLQEGHFSSASDVWSFGIIMWEVMAFGERPYWDMSGQDVIKAVEDGFRLPPPRNCPNILLHRLMLDCWQKDPGERPRFSQIHSILSKMVQDPEPPKCALTTCPRP
			PTPLADRAFSTFPSFGSVGAWLEALDLCRYKDSFAAAGYGSLEAVAEMTAQDLVSLGISLAEHREALLSGISALQARVLQLQGQGVQV
EPHA5	NP_001265229	Q9UF33	MKDSPFQVTKLYWLNEKWDFIASASDMAAEQGQILVIATAAVGGFTLLVILTLFFLITGRCQWYIKAKMKSEEKRRNHLQNGHLRFPGIKTYIDPDTYEDPSLAVHEFAKEIDPSRIR
			IERVIGAGEFGEVCSGRLKTPGKREIPVAIKTLKGGHMDRQRRDFLREASIMGQFDHPNIIRLEGVVTKRSFPAIGVEAFCPSFLRAGFLNSIQAPHPVPGGGSLPPRIPAGRPVMIV
			VEYMENGSLDSFLRKHDGHFTVIQLVGMLRGIASGMKYLSDMGYVHRDLAARNILVNSNLVCKVSDFGLSRVLEDDPEAAYTTRTPTNHNKEQSELVKEDGLESLCEQCESSSGY
			GTGLVLMVWKRNRRAMGASGQTRKQCDKRDNPPTDLFQTLTLNLCVSA
IGF1R	NP_000866	P08069	MKSGSGGGSPTSLWGLLFLSAALSLWPTSGEICGPGIDIRNDYQQLKRLENCTVIEGYLHILLISKAEDYRSYRFPKLTVITEYLLLFRVAGLESLGDLFPNLTVIRGWKLFYNYALVIFE
			MTNLKDIGLYNLRNITRGAIRIEKNADLCYLSTVDWSLILDAVSNNYIVGNKPPKECGDLCPGTMEEKPMCEKTTINNEYNYRCWTTNRCQKMCPSTCGKRACTENNECCHPECL
			GSCSAPDNDTACVACRHYYYAGVCVPACPPNTYRFEGWRCVDRDFCANILSAESSDSEGFVIHDGECMQECPSGFIRNGSQSMYCIPCEGPCPKVCEEEKKTKTIDSVTSAQMLQ
			GCTIFKGNLLINIRRGNNIASELENFMGLIEVVTGYVKIRHSHALVSLSFLKNLRLILGEEQLEGNYSFYVLDNQNLQQLWDWDHRNLTIKAGKMYFAFNPKLCVSEIYRMEEVTGTK
			GRQSKGDINTRNNGERASCESDVLHFTSTTTSKNRIIITWHRYRPPDYRDLISFTVYYKEAPFKNVTEYDGQDACGSNSWNMVDVDLPPNKDVEPGILLHGLKPWTQYAVYVKAV
			TLTMVENDHIRGAKSEILYIRTNASVPSIPLDVLSASNSSSQLIVKWNPPSLPNGNLSYYIVRWQRQPQDGYLYRHNYCSKDKIPIRKYADGTIDIEEVTENPKTEVCGGEKGPCCACP
			KTEAEKQAEKEEAEYRKVFENFLHNSIFVPRPERKRRDVMQVANTTMSSRSRNTTAADTYNITDPEELETEYPFFESRVDNKERTVISNLRPFTLYRIDIHSCNHEAEKLGCSASNFVF
			ARTMPAEGADDIPGPVTWEPRPENSIFLKWPEPENPNGLILMYEIKYGSQVEDQRECVSRQEYRKYGGAKLNRLNPGNYTARIQATSLSGNGSWTDPVFFYVQAKTGYENFIHLII
			ALPVAVLLVGGLVIMLYVFHRKRNNSRLGNGVLYASVNPEYFSAADVYVPDEWEVAREKITMSRELGQGSFGMVYEGVAKGVVKDEPETRVAIKTVNEAASMRERIEFLNEASV
			MKEFNCHHVVRLLGVVSQGQPTLVIMELMTRGDLKSYLRSLRPEMENNPVLAPPSLSKMIQMAGEIADGMAYLNANKFVHRDLAARNCMVAEDFTVKIGDFGMTRDIYETDY
			YRKGGKGLLPVRWMSPESLKDGVFTTYSDVWSFGVVLWEIATLAEQPYQGLSNEQVLRFVMEGGLLDKPDNCPDMLFELMRMCWQYNPKMRPSFLEIISSIKEEMEPGFREVS
			FYYSEENKLPEPEELDLEPENMESVPLDPSASSSSLPLPDRHSGHKAENGPGPGVLVLRASFDERQPYAHMNGGRKNERALPLPQSSTC

FIG. 65 (Cont.)

INSR	NP_000199	P06213	MATGGRRGAAAAPLLVAVAALLLGAAGHLYPGEVCPGMDIRNNLTRLHELENCSVIEGHLQILLMFKTRPEDFRDLSFPKLIMITDYLLLFRVYGLESLKDLFPNLTVIRGSRLFFNYA
			LVIFEMVHLKELGLYNLMNITRGSVRIEKNNELCYLATIDWSRILDSVEDNYVVLNKDDNEECGDICPGTAKGKTNCPATVINGQFVERCWTHSHCQKVCPTICKSHGCTAEGLCCH
			SECLGNCSQPDDPTKCVACRNFYLDGRCVETCPPPYYHFQDWRCVNFSFCQDLHHKCKNSRRQGCHQYVIHNNKCIPECPSGYTMNSSNLLCTPCLGPCPKVCHLLEGEKTIDSV
			TSAQELRGCTVINGSLIINIRGGNNLAAELEANLGLIEEISGYLKIRRSYALVSLSFFRKLRLIRGETLEIGNYSFYALDNQNLRQLWDWSKHNLTITQGKLFFHYNPKLCLSEIHKMEEVS
			GTKGRQERNDIALKTNGDQASCENELLKFSYIRTSFDKILLRWEPYWPPDFRDLLGFMLFYKEAPYQNVTEFDGQDACGSNSWTVVDIDPPLRSNDPKSQNHPGWLMRGLKPW
			TQYAIFVKTLVTFSDERRTYGAKSDIIYVQTDATNPSVPLDPISVSNSSSQIILKWKPPSDPNGNITHYLVFWERQAEDSELFELDYCLKGLKLPSRTWSPPFESEDSQKHNQSEYEDS
			AGECCSCPKTDSQILKELEESSFRKTFEDYLHNVVFVPRKTSSGTGAEDPRPSRKRRSLGDVGNVTVAVPTVAAFPNTSSTSVPTSPEEHRPFEKVVNKESLVISGLRHFTGYRIELQA
			CNQDTPEERCSVAAYVSARTMPEAKADDIVGPVTHEIFENNVVHLMWQEPKEPNGLIVLYEVSYRRYGDEELHLCVSRKHFALERGCRLRGLSPGNYSVRIRATSLAGNGSWTEP
			TYFYVTDYLDVPSNIAKIIIIGPLIFVFLFSVVIGSIYLFLRKRQPDGPLGPLYASSNPEYLSASDVFPCSVYVPDEWEVSREKITLLRELGQGSFGMVYEGNARDIIKGEAETRVAVKTVNE
			SASLRERIEFLNEASVMKGFTCHHVVRLLGVVSKGQPTLVVMELMAHGDLKSYLRSLRPEAENNPGRPPPTLQEMIQMAAEIADGMAYLNAKKFVHRDLAARNCMVAHDFTVK
			IGDFGMTRDIYETDYYRKGGKGLLPVRWMAPESLKDGVFTTSSDMWSFGVVLWEITSLAEQPYQGLSNEQVLKFVMDGGYLDQPDNCPERVTDLMRMCWQFNPKMRPTFLE
			IVNLLKDDLHPSFPEVSFFHSEENKAPESEELEMEFEDMENVPLDRSSHCQREEAGGRDGGSSLGFKRSYEEHIPYTHMNGGKKNGRILTLPRSNPS
INSRR	NP_055030	P14616	MAVPSLWPWGACLPVIFSLGFGLDTVEVCPSLDIRSEVAELRQLENCSVVEGHLQILLMFTATGEDFRGLSFPRLTQVTDYLLLFRVYGLESLRDLFPNLAVIRGTRLFLGYALVIFE
			MPHLRDVALPALGAVLRGAVRVEKNQELCHLSTIDWGLLQPAPGANHIVGNKLGEECADVCPGVLGAAGEPCAKTTFSGHTDYRCWTSSHCQRVCPCPHGMACTARGECCHT
			ECLGGCSQPEDPRACVACRHLYFQGACLWACPPGTYQYESWRCVTAERCASLHSVPGRASTFGIHQGSCLAQCPSGFTRNSSSIFCHKCEGLCPKECKVGTKTIDSIQAAQDLVGC
			THVEGSLILNLRQGYNLEPQLQHSLGLVETITGFLKIKHSFALVSLGFFKNLKLIRGDAMVDGNYTLYVLDNQNLQQLGSWVAAGLTIPVGKIYFAFNPRLCLEHIYRLEEVTGTRGR
			QNKAEINPRTTNGDRAACQTRTLRFVSNVTEADRILLRWERYEPLEARDLLSFHVYYKESPFQNATEHVGPDACGTQSWNLLDVELPLSRTQEPGVTLASLKPWTQYAVFVRAITLTT
			EEDSPHQGAQSPIVYLRTLPAAPTVPQDVISTSNSSSHLLVRWKPPTQRNGNLTYYLVLWQRLAEDGDLYLNDYCHRGLRLPTSNMDPRFDGEDGDPEAEMESDCCPCQHPPPG
			QVLPPLEAQEASFQKKFENFLHNAITIPSPWKVTSINKSPQRDSGRHHRAAGPLRLGGNSSDFEIQEDKVPRERAVLSGLRHFTEYRIDIHACNHAAHTVGCSAATFVFARTIMPHR
			EADGIPGKVAWEASSKNSVLLRWLEPPDPNGLILKYEIKYRRLGEEATVLCVSRLRYAKFGGVHLALLPPGNYSARVRATSLAGNGSWTDSVAFYILGPEEEDAGGLHVLLTATPVG
			LTLLIVLAALGFFYGKKRNRTLYASVNPEYFSASDMYVPDEWEVPREQISIIRELGQGSFGMVYEGLARGLEAGEESTPVALKTVNELASPRECIEFLKEASVMKAFKCHHVVRLLGV
			VSQGQPTLVIMELMTRGDLKSHLRSLRPEAENNPGLPQPALGEMIQMAGEIADGMAYLAANKFVHRDLAARNCMVSQDFTVKIGDFGMTRDVYETDYYRKGGKGLLPVRWM
			APESLKDGIFTTHSDVWSFGVVLWEIVTLAEQPYQGLSNEQVLKFVMDGGVLEELEGCPLQLQELMSRCWQPNPRLRPSFTHILDSIQEELRPSFRLLSFYSPECRGARGSLPTTD
			AEPDSSPTPRDCSPQNGGPGH

FIG. 65 (Cont.)

KDR	NP_002244	P35968	MQSKVLLAVALWLCVETRAASVGLPSVSLDLPRLSIQKDILTIKANTTLQITCRGQRDLDWLWPNNQSGSEQRVEVTECSDGLFCKTLTIPKVIGNDTGAYKCFYRETDLASVIYVYV
			QDYRSPFIASVSDQHGVVYITENKNKTVVIPCLGSISNLNVSLCARYPEKRFVPDGNRISWDSKKGFTIPSYMISYAGMVFCEAKINDESYQSIMYIVVVVGYRIYDVVLSPSHGIELSV
			GEKLVLNCTARTELNVGIDFNWEYPSSKHQHKKLVNRDLKTQSGSEMKKFLSTLTIDGVTRSDQGLYTCAASSGLMTKKNSTFVRVHEKPFVAFGSGMESLVEATVGERVRIPAKY
			LGYPPPEIKWYKNGIPLESNHTIKAGHVLTIMEVSERDTGNYTVILTNPISKEKQSHVVSLVVYVPPQIGEKSLISPVDSYQYGTTQTLTCTVYAIPPPHHIHWYWQLEEECANEPSQA
			VSVTNPYPCEEWRSVEDFQGGNKIEVNKNQFALIEGKNKTVSTLVIQAANVSALYKCEAVNKVGRGERVISFHVTRGPEITLQPDMQPTEQESVSLWCTADRSTFENLTWYKLGP
			QPLPIHVGELPTPVCKNLDTLWKLNATMFSNSTNDILIMELKNASLQDQGDYVCLAQDRKTKKRHCVVRQLTVLERVAPTITGNLENQTTSIGESIEVSCTASGNPPPQIMWFKDN
			ETLVEDSGIVLKDGNRNLTIRRVRKEDEGLYTCQACSVLGCAKVEAFFIIEGAQEKTNLEIIILVGTAVIAMFFWLLLVIILRTVKRANGGELKTGYLSIVMDPDELPLDEHCERLPYDAS
			KWEFPRDRLKLGKPLGRGAFGQVIEADAFGIDKTATCRTVAVKMLKEGATHSEHRALMSELKILIHIGHHLNVVNLLGACTKPGGPLMVIVEFCKFGNLSTYLRSKRNEFVPYKTKG
			ARFRQGKDYVGAIPVDLKRRLDSITSSQSSASGFVEEKSLSDVEEEEAPEDLYKDFLTLEHLICYSFQVAKGMEFLASRKCIHRDLAARNILLSEKNVVKICDFGLARDIYKDPDYVRK
			GDARLPLKWMAPETIFDRVYTIQSDVWSFGVLLWEIFSLGASPYPGVKIDEEFCRRLKEGTRMRAPDYTTPEMYQTMLDCWHGEPSQRPTFSELVEHLGNLLQANAQQDGKDYI
			VLPISETLSMEEDSGLSLPTSPVSCMEEEEVCDPKFHYDNTAGISQYLQNSKRKSRPVSVKTFEDIPLEEPEVKVIPDDNQTDSGMVLASEELKTLEDRTKLSPSFGGMVPSKSRESVA
			SEGSNQTSGYQSGYHSDDTDTTVYSSEEAELLKLIEIGVQTGSTAQILQPDSGTTLSSPPV
KIT	NP_000213	P10721	MRGARGAWDFLCVLLLLRVQTGSSQPSVSPGEPSPPSIHPGKSDLIVRVGDEIRLLCTDPGFVKWTFEILDETNENKQNEWITEKAEATNTGKYTCTNKHGLSNSIYVFVRDPAKL
			FLVDRSLYGKEDNDTLVRCPLTDPEVTNYSLKGCQGKPLPKDLRFIPDPKAGIMIKSVKRAYHRLCLHCSVDQEGKSVLSEKFILKVRPAFKAVPVVSVSKASYLLREGEEFTVTCTIKD
			VSSSVYSTWKRENSQTKLQEKYNSWHHGDFNYERQATLTISSARVNDSGVFMCYANNTFGSANVTTTLEVVDKGFINIFPMINTTVFVNDGENVDLIVEYEAFPKPEHQQWIYM
			NRTFTDKWEDYPKSENESNIRYVSELHLTRLKGTEGGTYTFLVSNSDVNAAIAFNVYVNTKPEILTYDRLVNGMLQCVAAGFPEPTIDWYFCPGTEQRCSASVLPVDVQTLNSSGP
			PFGKLVVQSSIDSSAFKHNGTVECKAYNDVGKTSAYFNFAFKGNNKEQIHPHTLFTPLLIGFVIVAGMMCIIVMILTYKYLQKPMYEVQWKVVEEINGNNYVYIDPTQLPYDHKWE
			FPRNRLSFGKTLGAGAFGKVVEATAYGLIKSDAAMTVAVKMLKPSAHLTEREALMSELKVLSYLGNHMNIVNLLGACTIGGPTLVITEYCCYGDLLNFLRRKRDSFICSKQEDHAEA
			ALYKNLLHSKESCSDSTNEYMDMKPGVSYVVPTKADKRRSVRIGSYIERDVTPAIMEDDELALDLEDLLSFSYQVAKGMAFLASKNCIHRDLAARNILLTHGRITKICDFGLARDIK
			NDSNYVVKGNARLPVKWMAPESIFNCVYTFESDVWSYGIFLWELFSLGSSPYPGMPVDSKFYKMIKEGFRMLSPEHAPAEMYDIMKTCWDADPLKRPTFKQIVQLIEKQISESTN
			HYSNLANCSPNRQKPVVDHSVRINSVGSTASSSQPLLVHDDV

FIG. 65 (Cont.)

LTK	NP_002335	P29376	MGCWGQLLVWFGAAGAILCSPGSQETLRSSPLPLASPSPRDPKVSAPPSILEPASPLNSPGTEGSWLFSTCGASGRHGPTQTQCDGAYAGTSVVVTVGAAGQLRGVQLWRVP GPGQYLISAYGAAGGKGAKNHLSRAHGVFVSAIFSLGLGESLYILVGQQGEDACPGGSPESQLVCLGESRAVEEHAAMDGSEGVPGSRRWAGGGGGGGGATYVFRVRAGELEP LLVAAGGGGRAYLRPRDRGRTQASPEKLENRSEAPGSGGRGGAAGGGGGWTSRAPSPQAGRSLQEGAEGGQGCSEAWATLGWAAAGGFGGGGGGGYRGGD ASETDNLWADGEDGVSFIHPSSELFLQPLAVTENHGEVEIRRHLNCSHCPLRDCQWQAELQLAECLCPEGMELAVDNVTCMDLHKPPGPLVLMVAVVATSTSLLMVCGVLILV KQKKWQGLQEMRLPSPELELSKLRTSAIRTAPNPVYCQVGLGPAQSWPLPPGVTEVSPANVTLLRALGHGAFGEVYEGLVIGLPGDSSPLQVAIKTLPELCSPQDELDFLMEALIISK FRHQNIVRCVGLSLRATPRLILLELMSGGDMKSFLRHSRPHLGQPSPLVMRDLLQLAQDIAQGCHYLEENHFIHRDIAARNCLLSCAGPSRVAKIGDFGMARDIYRASYYRKGDRA LLPVKWMPPEAFLEGIFTSKTDSWSFGVLLWEIFSLGYMPYPGRTNQEVLDFVVGGGRMDPPRGCPGPVYRIMTQCWQHEPELRPSFASILERLQYCTQDPDVLNSLLPMELGP TPEEEGTSGLGNRSLECLRPPQPQELSPEKLKSWGGSPLGPWLSSGLKPLKSRGLQPQNLWNPTYRS
MET	NP_000236	P08581	MKAPAVLAPGILVLLFTLVQRSNGECKEALAKSEMNVNMKYQLPNFTAETPIQNVILHEHHIFLGATNYIYVLNEEDLQKVAEYKTGPVLEHPDCFPCQDCSSKANLSGGVWKDNI NMALVVDTYYDDQLISCGSVNRGTCQRHVFPHNHTADIQSEVHCIFSPQIEEPSQCPDCVVSALGAKVLSSVKDRFINFFVGNTINSSYFPDHPLHSISVRRLKETKDGFMFLTDQS YIDVLPEFRDSYPIKYVHAFESNNFIYFLTVQRETLDAQTFHTRIIRFCSINSGLHSYMEMPLECILTEKRKKRSTKKEVFNILQAAYVSKPGAQLARQIGASLNDDILFGVFAQSKPDSA EPMDRSAMCAFPIKYVNDFFNKIVNKNNVRCLQHFYGPNHEHCFNRTLLRNSSGCEARRDEYRTEFTTALQRVDLFMGQFSEVLLTSISTFIKGDLTIANLGTSEGRFMQVVVSRS GPSTPHVNFLLDSHPVSPEVIVEHTLNQNGYTLVITGKKITKIPLNGLGCRHFQSCSQCLSAPPFVQCGWCHDKCVRSEECLSGTWTQQICLPAIYKVFPNSAPLEGGTRLTICGWD FGFRRNNKFDLKKTRVLLGNESCTLTLSESTMNTLKCTVGPAMNKHFNMSIIISNGHGTTQYSTFSYVDPVITSISPKYGPMAGGTLLTLTGNYLNSGNSRHISIGGKTCTLKSVSNSI LECYTPAQTISTEFAVKLKIDLANRETSIFSYREDPIVYEIHPTKSFISGGSTITGVGKNLNSVSVPRMVINVHEAGRNFTVACQHRSNSEIICCTTPSLQQLNLQLPLKTKAFFMLDGILS KYFDLIYVHNPVFKPFEKPVMISMGNENVLEIKGNDIDPEAVKGEVLKVGNKSCENIHLHSEAVLCTVPNDLLKLNSELNIEWKQAISSTVLGKVIVQPDQNFTGLIAGVVSISTALLL LLGFFLWLKKRKQIKDLGSELVRYDARVHTPHLDRLVSARSVSPTTEMVSNESVDYRATFPEDQFPNSSQNGSCRQVQYPLTDMSPILTSGDSDISSPLLQNTVHIDLSALNPELVQ AVQHVVIGPSSLIVHFNEVIGRGHFGCVYHGTLLDNDGKKIHCAVKSLNRITDIGEVSQFLTEGIIMKDFSHPNVLSLLGICLRSEGSPLVVLPYMKHGDLRNFIRNETHNPTVKDLIG FGLQVAKGMKYLASKKFVHRDLAARNCMLDEKFTVKVADFGLARDMYDKEYYSVHNKTGAKLPVKWMALESLQTQKFTTKSDVWSFGVLLWELMTRGAPPYPDVNTFDITVY LLQGRRLLQPEYCPDPLYEVMLKCWHPKAEMRPSFSELVSRISAIFSTFIGEHYVHVNATYVNVKCVAPYPSLLSSEDNADDEVDTRPASFWETS

FIG. 65 (Cont.)

MST1R	NP_002438	Q4912	MELLPPLPQSFLLLLLLPAKPAAGEDWQCPRTPYAASRDFDVKYVVPSFSAGGLVQAMVTYEGDRNESAVFVAIRNRLHVLGPDLKSVQSLATGPAGDPGCQTCAACGPGPHGP PGDTDTKVLVLDPALPALVSCGSSLQGRCFLHDLEPQGTAVHLAAPACLFSAHHNRPDDCPDCVASPLGTRVTVVEQGCASYFYVASSLDAAVAASFSPRSVSIRRLKADASGFAP GFVALSVLPKHLVSYSIEYVHSFHTGAFWYFLTVQPASVTDDPSALHTRLARLSATEPELGDYRELVLDCRFAPKRRRRGAPEGGQPYPVLRVAHSAPVGAQLATELSIAEGQEVLFG VFVTGKDGGPGVGPNSVVCAFPIDLLDTLIDEGVERCCESPVHPGLRRGLDFFQSPSFCPNPPGLEALSPNTSCRHFPLLVSSSFSRVDLFNGLLGPVQVTALYVTRLDNVTVAHMG TMDGRILQVELVRSLNYLLYVSNFSLGDSGQPVQRDVSRLGDHLLFASGDQVFQVPIQGPGCRHFLTCGRCLRAWHFMGCGWCGNMCGQQKECPGSWQQDHCPPKLTEFH PHSGPLRGSTRLTLCGSNFYLHPSGLVPEGTHQVTVGQSPCRPLPKDSSKLRPVPRKDFVEEFECELEPLGTQAVGPTNVSLTVTNMPPGKHFRVDGTSVLRGFSFMEPVLIAVQPL FGPRAGGTCLTLEGQSLSVGTSRAVLVNGTECLLARVSEGQLLCATPPGATVASVPLSLQVGGAQVPGSWTFQYREDPVVLSISPNCGYINSHITHCGQHLTSAWHLVLSFHDGLR AVESRCERQLPEQQLCRLPEYVVVRDPQGWVAGNLSARGDGAAGFTLPGFRFLPPPHPPSANLVPLKPEEHAIKFEYIGLGAVADCVGINVTVGGESCQHEFRGDMVVCPLPPSLQ LGQDGAPLQVCVDGECHLGRVVRPGPDGVPQSTLLGILPLLLLVAALATALVFSWVWRRKQLVLPPNLNDLASLDQTAGATPLPILYSGSDYRSGLALPAIDGLDSTTCVHGASF SDSEDESCVPLLRKESIQLRDLDSALLAEVKDVLIPHERVVTHSDRVIGKGHFGVVYHGEYIDQAQNRIQCAIKSLSRITEMQQVEAFLREGLLMRGLNHPNVLALIGIMLPPEGLPH VLLPYMCHGDLLQFIRSPQRNPTVKDLISFGLQVARGMEYLAEQKFVHRDLAARNCMLDESFTVKVADFGLARDILDREYYSVQQHRHARLPVKWMALESLQTYRFTTKSDVWS FGVLLWELLTRGAPPYRHIDPFDLTHFLAQGRRLPQPEYCPDSLYQVMQQCWEADPAVRPTFRVLVGEVEQIVSALLGDHYVQLPATYMNLGPSTSHEMNVRPEQPQFSPMPG NVRRPRPLSEPPRPT
MUSK	NP_005583	O15146	MRELVNIPLVHILTLVAFSGTEKLPKAPVITTPLETVDALVEEVATFMCAVESYPQPEISWTRNKILKLFDTRYSIRENGQLLTILSVEDSDDGIYCCTANNGVGGAVESCGALQVKM KPKITRPPINVKIIEGLKAVLPCTTMGNPKPSVSWIKGDSPLRENSRIAVLESGSLRIHNVQKEDAGQYRCVAKNSLGTAYSKVVKLEVEVFARILRAPESHNVTFGSFVTLHCTATGIP VPTITWIENGNAVSSGSIQESVKDRVIDSRLQLFITKPGLYTCIATNKHGEKFSTAKAAATISIAEWSKPQKDNKGYCAQYRGEVCNAVLAKDALVFLNTSYADPEEAQELLVHTAW NELKVVSPVCRPAAEALLCNHIFQECSPGVVPTPIPICREYCLAVKELFCAKEWLVMEEKTHRGLYRSEMHLLSVPECSKLPSMHWDPTACARLPHLDYNKENIKTFPPMTSSKPSV DIPNLPSSSSSSFSVSPTYSMTVIISIMSSFAIFVLLTITTLYCCRRRKQWKNKKRESAAVTLTTLPSELLDRLHPNPMYQRMPLLLNPKLLSLEYPRNNIEYVRDIGEGAFGRVFQARA PGLLPYEPFTMVAVKMLKEEASADMQADFQREAALMAEFDNPNIVKLLGVCAVGKPMCLLFEYMAYGDLNEFLRSMSPHTVCSLSHSDLSMRAQVSSPGPPPLSCAEQLCIAR QVAAGMAYLSERKFVHRDLATRNCLVGENMVVKIADFGLSRNIYSADYYKANENDAIPIRWMPPESIFYNRYTTESDVWAYGVVLWEIFSYGLQPYYGMAHEEVIYYVRDGNILS CPENCPVELYNLMRLCWSKLPADRPSFTSIHRILERMCERAEGTVSV
NTRK1	NP_002520	P04629	MLRGGRRGQLGWHSWAAGPGSLLAWLILASAGAAPCPDACCPHGSSGLRCTRDGALDSLHHLPGAENLTELYIENQQHLQHLELRDLRGLGELRNLTIVKSGLRFVAPDAFHFT PRLSRLNLSFNALESLSWKTVQGLSLQELVLSGNPLHCSCALRWLQRWEEEGLGGVPEQKLQCHGQGPLAHMPNASCGVPTLKVQVPNASVDVGDDVLLRCQVEGRGLEQAG WILTELEQSATVMKSGGLPSLGLTLANVTSDLNRKNVTCWAENDVGRAEVSVQVNVSFPASVQLHTAVEMHHWCIPFSVDGQPAPSLRWLFNGSVLNETSFIFTEFLEPAANET VRHGCLRLNQPTHVNNGNYTLLAANPFGQASASIMAAFMDNPFEFNPEDPIPVSFSPVDTNSTSGDPVEKKDETPFGVSVAVGLAVFACLFLSTLLVLNKCGRRNKFGINRPAVL APEDGLAMSLHFMTLGGSSLSPTEGKGSGLQGHIIENPQYFSDACVHHIKRRDIVLKWELGEGAFGKVFLAECHNLLPEQDKMLVAVKALKEASESARQDFQREAELLTMLQHQ HIVRFFGVCTEGRPLLMVFEYMRHGDLNRFLRSHGPDAKLLAGGEDVAPGPLGLGQLLAVASQVAAGMVYLAGLHFVHRDLATRNCLVGQGLVVKIGDFGMSRDIYSTDYYRV GGRTMLPIRWMPPESILYRKFTTESDVWSFGVVLWEIFTYGKQPWYQLSNTEAIDCITQGRELERPRACPPEVYAIMRGCWQREPQQRHSIKDVHARLQALAQAPPVYLDVLG

FIG. 65 (Cont.)

NTRK2	NP_001018074	Q16620	MSSWIRWHGPAMARLWGFCWLVVGFWRAAFACPTSCKCSASRIWCSDPSPGIVAFPRLEPNSVDPENITEIFIANQKRLEIINEDDVEAYVGLRNLTIVDSGLKFVAHKAFLKNS
			NLQHINFTRNKLTSLSRKHFRHLDLSELILVGNPFTCSCDIMWIKTLQEAKSSPDTQDLYCLNESSKNIPLANLQIPNCGLPSANLAAPNLTVEEGKSITLSCSVAGDPVPNMYWDVG
			NLVSKHMNETSHTQGSLRITNISSDDSGKQISCVAENLVGEDQDSVNLTVHFAPTITFLESPTSDHHWCIPFTVKGNPKPALQWFYNGAILNESKYICTKIHVTNHTEYHGCLQLDN
			PTHMNNGDYTLIAKNEYGKDEKQISAHFMGWPGIDDGANPNYPDVIYEDYGTAANDIGDTTNRSNEIPSTDVTDKTGREHLSVYAVVVIASVVGFCLLVMLFLLKLARHSKFGMK
			KGPASVISNDDDSASPLHHISNGSNTPSSSEGGPDAVIIGMTKIPVIENPQYFGITNSQLKPDTFVQHIKRHNIVLKRELGEGAFGKVFLAECYNLCPEQDKILVAVKTLKDASDNARK
			DFHREAELLTNLQHEHIVKFYGVCVEGDPLIMVFEYMKHGDLNKFLRAHGPDAVLMAEGNPPTELTQSQMLHIAQQIAAGMVYLASQHFVHRDLATRNCLVGENLLVKIGDFG
			MSRDVYSTDYYRVGGHTMLPIRWMPPESIMYRKFTTESDVWSLGVVLWEIFTYGKQPWYQLSNNEVIECITQGRVLQRPRTCPQEVYELMLGCWQREPHMRKNIKGIHTLLQN
			LAKASPVYLDILG
NTRK3	NP_001012338	Q16288	MDVSLCPAKCSFWRIFLLGSVWLDYVGSVLACPANCVCSKTEINCRRPDDGNLFPLLEGQDSGNSNGNASINITDISRNITSIHIENWRSLHTLNAVDMELVTGLQKLTIKNSGLRSI
			QPRAFAKNPHLRYINLSSNRLTTLSWQLFQTLSLRELQLEQNFFNCSCDIRWMQLWQEQGEAKLNSQNLYCINADGSQLPLFRMNISQCDLPEISVSHVNLTVREGDNAVITCNG
			SGSPLPDVDWIVTGLQSINTHQTNLNWTNVHAINLTLVNVTSEDNGFTLTCIAENVVGMSNASVALTVYYPPRVVSLEEPELRLEHCIEFVVRGNPPPTLHWLHNGQPLRESKIIH
			VEYYQEGEISEGCLLFNKPTHYNNGNYTLIAKNPLGTANQTINGHFLKEPFPESTDNFILFDEVSPTPPITVTHKPEEDTFGVSIAVGLAAFACVLLVVLFVMINKYGRRSKFGMKGPV
			AVISGEEDSASPLHHINHGITTPSSLDAGPDTVVIGMTRIPVIENPQYFRQGHNCHKPDTYVQHIKRRDIVLKRELGEGAFGKVFLAECYNLSPTKDKMLVAVKALKDPTLAARKDF
			QREAELLTNLQHEHIVKFYGVCGDGDPLIMVFEYMKHGDLNKFLRAHGPDAMILVDGQPRQAKGELGLSQMLHIASQIASGMVYLASQHFVHRDLATRNCLVGANLLVKIGDF
			GMSRDVYSTDYYRLFNPSGMDFCIWCEVGGHTMLPIRWMPPESIMYRKFTTESDVWSFGVILWEIFTYGKQPWFQLSNTEVIECITQGRVLERPRVCPKEVYDVMLGCWQREP
			QQRLNIKEIYKILHALGKATPIYLDILG
ROR1	NP_005003	Q01973	MHRPRRRGTRPPLLALLAALLLAARGAAAQETELSVSAELVPTSSWNISSELNKDSYLTLDEPMNNITTSLGQTAELHCKVSGNPPPTIRWFKNDAPVVQEPRRLSFRSTVGSRLRI
			RNLDTTDTGYFQCVATNGKEVVSSTGVLFVKFGPPPTASPGYSDEYEEDGFCQPYRGIACARFIGNRTVYMESLHMQGEIENQITAAFTMIGTSSHLSDKCSQFAIPSLCHYAFPYC
			DETSSVPKPRDLCRDECEILENVLCQTEYIFARSNPAMILMRLKLPNCEDLPQPESPEAANCIRIGIPMADPINKNHKCYNSTGVDYRGTVSVTKSGRQCQPWNSQYPHTHTFTALRF
			PELNGGHSYCRNPGNQKEAPWCFTLDENFKSDLCDIPACDSKDSKEKNKMEILYILVPSVAIPLAIALLFFFCVCRNNQKSSSAPVQRQPKHVRGQNVEMSMLNAYKPKSKAKEL
			PLSAVRFMEELGECAFGKIYKGHLYLPGMDHAQLVAIKTLKDYNNPQQWTEFQQEASLMAELHHPNIVCLLGAVTQEQPVCMLFEYINQGDLHEFLIMRSPHSDVGCSSDEDGT
			VKSSLDHGDFLHIAIQIAAGMEYLSSHFFVHKDLAARNILIGEQLHVKISDLGLSREIYSADYYRVQSKSLLPIRWMPPEAIMYGKFSSDSDIWSFGVVLWEIFSFGLQPYYGFSNQEVI
			EMVRKRQLLPCSEDCPPRMYSLMTECWNEIPSRRPRFKDIHVRLRSWEGLSSHTSSTTPSGGNATTQTTSLSASPVSNLSNPRYPNYMFPSQGITPQGQIAGFIGPPIPQNQRFIPI
			NGYPIPPGYAAFPAAHYQPTGPPRVIQHCPPPKSRSPSSASGSTSTGHVTSLPSSGSNQEANIPLLPHMSIPNHPGGMGITVFGNKSQKPYKIDSKQASLLGDANIHGHTESMISAE

FIG. 65 (Cont.)

ROR2	NP_004551	Q01974	MARGSALPRRPLLCIPAVWAAAALLSVSRTSGEVEVLDPNDPLGPLDGQDGPIPTLKGYFLNFLEPVNNITIVQGQTAILHCKVAGNPPPNVRWLKNDAPVVQEPRHIIRKTEYG SRLRIQDLDTTDTGYYQCVATNGMKTITATGVLFVRLGPTHSPNHNFQDDYHEDGFCQPYRGIACARFIGNRTIYVDSLQMQGEIENRITAAFTMIGTSTHLSDQCSQFAIPSFCHF VFPLCDARSRTPKPRELCRDECEVLESDLCRQEYTIARSNPLLIMRLQLPKCEALPMPESPDAANCMRIGIPAERLGRYHQCYNGSGMDYRGTASTTKSGHQCQPWALQHPHSH HLSSTDFPELGGGHAYCRNPGGQMEGPWCFTQNKNVRMELCDVPSCSPRDSSKMGILYILVPSIAIPLVIACLFFLVCMCRNKQKASASTPQRRQLMASPSQDMEMPLINQHK QAKLKEISLSAVRFMEELGEDRFGKVYKGHLFGPAPGEQTQAVAIKTLKDKAEGPLREEFRHEAMLRARLQHPNVVCLLGVVTKDQPLSMIFSYCSHGDLHEFLVMRSPHSDVGS TDDDRTVKSALEPPDFVHLVAQIAAGMEYLSSHHVVHKDLATRNVLVYDKLNVKISDLGLFREVYAADYYKLLGNSLLPIRWMAPEAIMYGKFSIDSDIWSYGVVLWEVFSYGLQP YCGYSNQDVVEMIRNRQVLPCPDDCPAWVYALMIECWNEFPSRRPRFKDIHSRLRAWGNLSNYNSSAQTSGASNTTQTSSLSTSPVSNVSNARYVGPKQKAPPFPQPQFIPMK GQIRPMVPPPQLVVPVNGYQPVPAYGAYLPNFYPVQIPMQMAPQQVPPQMVPKPSSHHSGSGSTSTGYVTTAPSNTSMADRAALLSEGADDTQNAPEDGAQSTVQEAEEEE EGSVPETELLGDCDTLQVDEAQVQLEA
DDR2	NP_001014796	Q16832	MILIPRMLLVLFLLLPILSSAKAQVNPAICRYPLGMSGGQIPDEDITASSQWSESTAAKYGRLDSEEGDGAWCPEIPVEPDDLKEFLQIDLHTLHFITLVGTQGRHAGGHGIELFAPMY KINYSRDGTRWISWRNRHGKQVLDGNSNPYDIFLKDLEPPIVARFVRFIPVTDHSMNVCMRVELYGCVWLDGLVSYNAPAGQQFVLPGGSIIYLNDSVYDGAVGYSMTEGLGQL TDGVSGLDDFTQTHEYHVWPGYDYVGWRNESATNGYIEIMFEFDRIRNFTTMKVHCNNMFAKGVKIFKEVQCYFRSEASEWEPNAISFPLVLDDVNPSARFVTVPLHHRMASAI KCQYHFADTWMMFSEITFQSDAAMYNNSEALPTSPMAPTTYDPMLKVDDSNTRILIGCLVAIIFILLAIIVILWRQFWQKMLEKASRRMLDDEMTVSLSLPSDSSMFNNNRSSSP SEQGSNSTYDRIFPLRPDYQEPSRLIRKLPEFAPGEEESGCSGVVKPVQPSGPEGVPHYAEADIVNLQGVTGGNTYSVPAVTMDLLSGKDVAVEEFPRKLLTFKEKLGEGQFGEVHL CEVEGMEKFKDKDFALDVSANQPVLVAVKMLRADANKNARNDFLKEIKIMSRLKDPNIIHLLAVCITDDPLCMITEYMENGDLNQFLSRHEPPNSSSSDVRTVSYTNLKFMATQIA SGMKYLSSLNFVHRDLATRNCLVGKNYTIKIADFGMSRNLYSGDYYRIQGRAVLPIRWMSWESILLGKFTTASDVWAFGVTLWETFTFCQEQPYSQLSDEQVIENTGEFFRDQGR QTYLPQPAICPDSVYKLMLSCWRRDTKNRPSFQEIHLLLQQGDE
PDGFRA	NP_006197	P16234	MGTSHPAFLVLGCLLTGLSLILCQLSLPSILPNENEKVVQLNSSFSLRCFGESEVSWQYPMSEEESSDVEIRNEENNSGLFVTVLEVSSASAAHTGLYTCYYNHTQTEENELEGRHIYIY VPDPDVAFVPLGMTDYLVIVEDDDSAIIPCRTTDPETPVTLHNSEGVVPASYDSRQGFNGTFTVGPYICEATVKGKKFQTIPFNVYALKATSELDLEMEALKTVYKSGETIVVTCAVF NNEVVDLQWTYPGEVKGKGITMLEEIKVPSIKLVYTLTVPEATVKDSGDYECAARQATREVKEMKKVTISVHEKGFIEIKPTFSQLEAVNLHEVKHFVVEVRAYPPPRISWLKNNLTL IENLTEITTDVEKIQEIRYRSKLKLIRAKEEDSGHYTIVAQNEDAVKSYTFELLTQVPSSILDLVDDHHGSTGGQTVRCTAEGTPLPDIEWMICKDIKKCNNETSWTILANNVSNIITEIH SRDRSTVEGRVTFAKVEETIAVRCLAKNLLGAENRELKLVAPTLRSELTVAAAVLVLLVIVIISLIVLVVIWKQKPRYEIRWRVIESISPDGHEYIYVDPMQLPYDSRWEFPRDGLVLGR VLGSGAFGKVVEGTAYGLSRSQPVMKVAVKMLKPTARSSEKQALMSELKIMTHLGPHLNIVNLLGACTKSGPIYIITEYCFYGDLVNYLHKNRDSFLSHHPEKPKKELDIFGLNPADE STRSYVILSFENNGDYMDMKQADTTQYVPMLERKEVSKYSDIQRSLYDRPASYKKKSMLDSEVKNLLSDDNSEGLTLLDLLSFTYQVARGMEFLASKNCVHRDLAARNVLLAQGKI VKICDFGLARDIMHDSNYVSKGSTFLPVKWMAPESIFDNLYTTLSDVWSYGILLWEIFSLGGTPYPGMMVDSTFYNKIKSGYRMAKPDHATSEVYEIMVKCWNSEPEKRPSFYHL SEIVENLLPGQYKKSYEKIHLDFLKSDHPAVARMRVDSDNAYIGVTYKNEEDKLKDWEGGLDEQRLSADSGYIIPLPDIDPVPEEEDLGKRNRHSSQTSEESAIETGSSSTFIKREDET IEDIDMMDDIGIDSSDLVEDSFL

FIG. 65 (Cont.)

PDGFRB	NP_002600	P09619	MRLPGAMPALALKGELLLLSLLLLLEPQISQGLVVTPPGPELVLNVSSTFVLTCSGSAPVVWERMSQEPPQEMAKAQDGTFSSVLTLTNLTGLDTGEYFCTHNDSRGLETDERKRLY IFVPDPTVGFLPNDAEELFIFLTEITEITIPCRVTDPQLVVTLHEKKGDVALPVPYDHQRGFSGIFEDRSYICKTTIGDREVDSDAYYVYRLQVSSINVSVNAVQTVVRQGENITLMCIVI GNEVVNFEWTYPRKESGRLVEPVTDFLLDMPYHIRSILHIPSAELEDSGTYTCNVTESVNDHQDEKAINITVVESGYVRLLGEVGTLQFAELHRSRTLQVVFEAYPPPTVLWFKDNR TLGDSSAGEIALSTRNVSETRYVSELTLVRVKVAEAGHYTMRAFHEDAEVQLSFQLQINVPVRVLELSESHPDSGEQTVRCRGRGMPQPNIIWSACRDLKRCPRELPPTLLGNSSEE ESQLETNVTYWEEEQEFEVVSTLRLQHVDRPLSVRCTLRNAVGQDTQEVIVVPHSLPFKVVVISAILALVVLTIISLIILIMLWQKKPRYEIRWKVIESVSSDGHEYIYVDPMQLPYDST WELPRDQLVLGRTLGSGAFGQVVEATAHGLSHSQATMKVAVKMLKSTARSSEKQALMSELKIMSHLGPHLNVVNLLGACTKGGPIYIITEYCRYGDLVDYLHRNKHTFLQHHSD KRRPPSAELYSNALPVGLPLPSHVSLTGESDGGYMDMSKDESVDYVPMLDMKGDVKYADIESSNYMAPYDNYVPSAPERTCRATLINESPVLSYMDLVGFSYQVANGMEFLASK NCVHRDLAARNVLICEGKLVKICDFGLARDIMRDSNYISKGSTFLPLKWMAPESIFNSLYTTLSDVWSFGILLWEIFTLGGTPYPELPMNEQFYNAIKRGYRMAQPAHASDEIYEIM QKCWEEKFEIRPPFSQLVLLLERLLGEGYKKKYQQVDEEFLRSDHPAILRSQARLPGFHGLRSPLDTSSVLYTAVQPNEGDNDYIIPLPDPKPEVADEGPLEGSPSLASSTLNEVNTSST ISCDSPLEPQDEPEPEPQLELQVEPEPELEQLPDSGCPAPRAEAEDSFL
AXL	NP_068713	P30530	MAWRCPRMGRVPLAWCLALCGWACMAPRGTQAEESPFVGNPGNITGARGLTGTLRCQLQVQGEPPEVHWLRDGQILELADSTQTQVPLGEDEQDDWIVVSQLRITSLQLSD TGQYQCLVFLGHQTFVSQPGYVGLEGLPYFLEEPEDRTVAANTPFNLSCQAQGPPEPVDLLWLQDAVPLATAPGHGPQRSLHVPGLNKTSSFSCEAHNAKGVTTSRTATITVLPQ QPRNLHLVSRQPTELEVAWTPGLSGIYPLTHCTLQAVLSDDGMGIQAGEPDPPEEPLTSQASVPPHQLRLGSLHPHTPYHIRVACTSSQGPSSWTHWLPVETPEGVPLGPPENISA TRNGSQAFVHWQEPRAPLQGTLLGYRLAYQGQDTPEVLMDIGLRQEVTLELQGDGSVSNLTVCVAAYTAAGDGPWSLPVPLEAWRPGQAQPVHQLVKEPSTPAFSWPWWY VLLGAVVAAACVLILALFLVHRRKKETRYGEVFEPTVERGELVVRYRVRVSYSRITEATLNSLIGISEELKERLRDVMVDRHKVALGKTLGEGEFGAVMEGQLNQDDSILKVAVKTM KIAICTRSELEDFLSEAVCMKEFDHPNVMRLIGVCFQGSERESFPAPVVILPFMKHGDLHSFLLYSRLGDQPVYLPTQMLVKFMADIASGMEYLSTKRFIHRDLAARNCMLNENMS VCVADFGLSKKIYNGDYYRQGRIAKMPVKWIAIESLADRVYTSKSDVWSFGVTMWEIATRGQTPYPGVENSEIYDYLRQGNRLKQPADCLDGLYALMSRCWELNPQDRPSFTEL REDLENTLKALPPAQEPDEILYVNMDEGGGYEPPPGAAGGADPPTQPDPKDSCSCLTAAEVHPAGRYVLCPSTTPSPAQPADRGSPAAPGQEDGA
PTK7	NP_002812	Q13308	MGAARGSPARPRRLPLLSVLLLPLLGGTQTAIVFIKQPSSQDALQGRRALLRCEVEAPGPVHVYWLLDGAPVQDTERRFAQGSSLSFAAVDRLQDSGTFQCVARDDVTGEEARSA NASFNIKWIEAGPVVLKHPASEAEIQPQTQVTLRCHIDGHPRPTYQWFRDGTPLSDGQSNHTVSSKERNLTLRPAGPEHSGLYSCCAHSAFGQACSSQNFTLSIADESFARVVLAP QDVVVARYEEAMFHCQFSAQPPPSLQWLFEDETPITNRSRPPHLRRATVFANGSLLLTQVRPRNAGIYRCIGQGQRGPPIILEATLHLAEIEDMPLFEPRVFTAGSEERVTCLPPKG LPEPSVWWEHAGVRLPTHGRVYQKGHELVLANIAESDAGVYTCHAANLAGQRRQDVNITVATVPSWLKKPQDSQLEEGKPGYLDCLTQATPKPTVVWYRNQMLISEDSRFEVF KNGTLRINSVEVYDGTWYRCMSSTPAGSIEAQARVQVLEKLKFTPPPQPQQCMEFDKEATVPCSATGREKPTIKWERADGSSLPEWVTDNAGTLHFARVTRDDAGNYTCIASNG PQGQIRAHVQLTVAVFITFKVEPERTTVYQGHTALLQCEAQGDPKPLIQWKGKDRILDPTKLGPRMHIFQNGSLVIHDVAPEDSGRYTCIAGNSCNIKHTEAPLYVVDKPVPEESE GPGSPPPYKMIQTIGLSVGAAVAYIIAVLGLMFYCKKRCKAKRLQKQPEGEEPEMECLNGGPLQNGQPSAEIQEEVALTSLGSGPAATNKRHSTSDKMHFPRSSLQPITTLGKSEF GEVFLAKAQGLEEGVAETLVLVKSLQSKDEQQQLDFRRELEMFGKLNHANVVRLLGLCREAEPHYMVLEYVDLGDLKQFLRISKSKDEKLKSQPLSTKQKVALCTQVALGMEHLSN NRFVHKDLAARNCLVSAQRQVKVSALGLSKDVYNSEYYHFRQAWVPLRWMSPEAILEGDFSTKSDVWAFGVLMWEVFTHGEMPHGGQADDEVLADLQAGKARLPQPEGCP SKLYRLMQRCWALSPKDRPSFSEIASALGDSTVDSKP

FIG. 65 (Cont.)

RET	NP_066124	P07949	MAKATSGAAGLRLLLLLLPLLGKVALGLYFSRDAYWEKLYVDQAAGTPLLYVHALRDAPEEVPSFRLGQHLYGTYRTRLHENNWICIQEDTGLLYLNRSLDHSSWEKLSVRNRGFP
			LLTVYLKVFLSPTSLREGECQWPGCARVYFSFFNTSFPACSSLKPRELCFPETRPSFRIRENRPPGTFHQFRLLPVQFLCPNISVAYRLLEGEGLPFRCAPDSLEVSTRWALDREQREKY
			ELVAVCTVHAGAREEVVMVPFPVTVYDEDDSAPTFPAGVDTASAVVEFKRKEDTVVATLRVFDADVVPASGELVRRYTSTLLPGDTWAQQTFRVEHWPNETSVQANGSFVRAT
			VHDYRLVLNRNLSISENRTMQLAVLVNDSDFQGPGAGVLLLHFNVSVLPVSLHLPSTYSLSVSRRARRFAQIGKVCVENCQAFSGINVQYKLHSSGANCSTLGVVTSAEDTSGILFV
			NDTKALRRPKCAELHYMVVATDQQTSRQAQAQLLVTVEGSYVAEEAGCPLSCAVSKRRLECEECGGLGSPTGRCEWRQGDGKGITRNFSTCSPSTKTCPDGHCDVVETQDINIC
			PQDCLRGSIVGGHEPGEPRGIKAGYGTCNCFPEEEKCFCEPEDIQDPLCDELCRTVIAAAVLFSFIVSVLLSAFCIHCYHKFAHKPPISSAEMTFRRPAQAFPVSYSSSGARRPSLDSM
			ENQVSVDAFKILEDPKWEFPRKNLVLGKTLGEGEFGKVVKATAFHLKGRAGYTTVAVKMLKENASPSELRDLLSEFNVLKQVNHPHVIKLYGACSQDGPLLLIVEYAKYGSLRGFLR
			ESRKVGPGYLGSGGSRNSSSLDHPDERALTMGDLISFAWQISQGMQYLAEMKLVHRDLAARNILVAEGRKMKISDFGLSRDVYEEDSYVKRSQGRIPVKWMAIESLFDHIYTTQS
			DVWSFGVLLWEIVTLGGNPYPGIPPERLFNLLKTGHRMERPDNCSEEMYRLMLQCWKQEPDKRPVFADISKDLEKMMVKRRDYLDLAASTPSDSLIYDDGLSEEETPLVDCNNA
			PLPRALPSTWIENKLYGMSDPNWPGESPVPLTRADGTNTGFPRYPNDSVYANWMLSPSAAKLMDTFDS

FIG. 65 (Cont.)

ROS1	NP_002935	P08922	MKNIYCLIPKLVNFATLGCLWISVVQCTVLNSCLKSCVTNLGQQLDLGTPHNLSEPCIQGCHFWNSVDQKNCALKCRESCEVGCSSAEGAYEEEVLENADLPTAPFASSIGSHNMT LRWKSANFSGVKYIIQWKYAQLLGSWTYTKTVSRPSYVVKPLHPFTEYIFRVVVWIFTAQLQLYSPPSPSYRTHPHGVPETAPLIRNIESSSPDTVEVSWDPPQFPGGPILGYNLRLISK NQKLDAGTQRTSFQFYSTLPNTIYRFSIAAVNEVGEGPEAESSITTSSSAVQQEEQWLFLSRKTSLRKRSLKHLVDEAHCLRLDAIYHNITGISVDVHQQNVYFSEGTLIWAKKAANM SDVSDLRIFYRGSGLISSISIDWLYQRMYFIMDELVCVCDLENCSNIEEITPPSISAPQKIVADSYNGYVFYLLRDGIYRADLPVPSGRCAEAVRIVESCTLKDFAIKPQAKRIIYFNDTAQ VFMSTFLDGSASHLILPRIPFADVKSFACENNDFLVTDGKVIFQQDALSFNEFIVGCDLSHIEEFGFGNLVIFGSSSQLHPLPGRPQELSVLFGSHQALVQWKPPALAIGANVILISDIIE LFELGPSAWQNWTYEVKVSTQDPPEVTHIFLNISGTMLNVPELQSAMKYKVSVRASSPKRPGPWSEPSVGTTLVPASEPPFIMAVKEDGLWSKPLNSFGPGEFLSSDIGNVSDMD WYNNSLYYSDTKGDVFVWLLNGTDISENYHLPSIAGAGALAFEWLGHFLYWAGKTYVIQRQSVLTGHTDIVTHVKLLVNDMVVDSVGGYLYWTTLYSVESTRLNGESSLVLQTQ PWFSGKKVIALTLDLSDGLLYWLVQDSQCHLYTAVLRGQSTGDTTITEFAAWSTSEISQNALMVYSGRLFWINGFRIITTQEIGQKTSVSVLEPARFNQFTHQTSLKPLPGNFSFTPK VIPDSVQESSFRIEGNASSFQILWNGPPAVDWGVVFVSVEFSAHSKFLASEQHSLPVFTVEGLEPYALFNLSVTPVTYWGKGPKTSLSLRAPETVPSAPENPRIFILPSGKCCNKNEVV VEFRWNKPKHENGVLTKFEIFYNISNQSITNKTCEDWIAVNVTPSVMSFQLEGMSPRCFIIAFQVRAFTSKGPGPYADVVKSTTSEINPFPHLITLLGNKIVFLDMDQNQVVWTFSA ERVISAVCYTADNEMGYYAEGDSLFLLHLHNRSSSELFQDSLVFDITVITIDWISRHLYFAIKESQNGMQVFDVDLEHKVKYPREVKIHNRNSTIISFSVYPLLSRLYWTEVSNFGYQ MFYYSIISHTLHRILQPTATNQQNKRNQCSCNVTEFELSGAMAIDTSNLEKPLIYFAKAQEIWAMDLEGCQCWRVITVPAMLAGKTLVSLTVDGDLIYWIITAKDSTQIYQAKKGN GAIVSQVKALRSRHILAYSSVMQPFPDKAFLSLASDTVEPTILNATNTSLTIRLPLAKTNLTWYGITSPTPTYLVYYAEVNDRKNSSDLKYRILEFQDSIALIEDLQPFSTYMIQIAVKNYY SDPLEHLPPGKEIWGKTKNGVPEAVQLINTTVRSDTSLIISWRESHKPNGPKESVRYQLAISHLALIPETPLRQSEFPNGRLTLLVTRLSGGNIYVLKVLACHSEEMWCTESHPVTVE MFNVTPEKPYSLVPENTSLQFNWKAPLNVNLIRFWVELQKWKYNEFYHVKTSCSQGPAYVCNITNLQPYTSYNVRVVVYYKTGENSTSLPESFKTKAGVPNKPGIPKLLEGSKNSIQ WEKAEDNGCRITYYILEIRKSTSNNLQNQNLRWKMTFNGSCSSVCTWKSKNLKGIFQFRVVAANNLGFGEYSGISENIILVGDDFWIPETSFILTIIVGIFLVVTIPLTFVWHRRLKNQ KSAKEGVTVLINEDKELAELRGLAAGVGLANACYAIHTLPTQEEIENLPAFPREKLTLRLLLGSGAFGEVYEGTAVDILGVGSGEIKVAVKTLKKGSTDQEKIEFLKEAHLMSKFNHPNI LKQLGVCLLNEPQYIILELMEGGDLLTYLRKARMATFYGPLLTLVDLVDLCVDISKGCVYLERMHFIHRDLAARNCLVSVKDYTSPRIVKIGDFGLARDIYKNDYYRKRGEGLLPVRW MAPESLMDGIFTTQSDVWSFGILIWEILTLGHQPYPAHSNLDVLNYVQTGGRLEPPRNCPDDLWNLMTQCWAQEPDQRPTFHRIQDQLQLFRNFFLNSIYKSRDEAMNSGVIN ESFEGEDGDVICLNSDDIMPVALMETKNREGLNYMVLATECGQGEEKSEGPLGSQESESCGLRKEEKEPHADKDFCQEKQVAYCPSGKPEGLNYACLTHSGYGDGSD
RYK	NP_002949	P34925	MRGAARLGRPGRSCLPGARGLRAPPPPPLLLLALLPLLPAPGAAAAPAPRPPELQSASAGPSVSLYLSEDEVRRLIGLDAELYYVRNDLISHYALSFSLVPSETNFLHFTWHAKSKV EYKLGFQVDNVLAMDMIPQVNISVQGEVPRTLSVFRVELSCTGKVDSEVMILMQLNLTVNSSKNFTVLNFKRKRKMCYKKLEEVKTSALDKNTSRTIYDPVHAAPTTSTRVFYISVGV CCAVIFLVAIILALVLHLHSMKRIELDDSISASSSSQGLSQPSTQTTQYLRADTPNMATPITSYPTLRIEKMDLRSVTLLEAKGKVKDIAISRERITLKDVLQEGTFGRIFHGILIDEKDPNKE KQAFVKTVKDQASEIQVTMMLTESCKLRGLHHRNLLPITHVCIEEGEKPMVILPYMNWGNLKLFLRQCKLVEANNPQAISQQDLVHMAIQIACGMSYLARREVIHKDLAARNCVI DDTLQVKITDNALSRDLFPMDYHCLGDNENRPVRWMALESLVNNEFSSASDVWAFGVTLWELMTLGQTPYVDIDPFEMAAYLKDGYRIAQPINCPDELFAVMACCWALDPEE RPKFQQLVQCLTEFHAALGAYV

FIG. 65 (Cont.)

TEK	NP_000450	Q02763	MDSLASLVLCGVSLLLSGTVEGAMDLILINSLPLVSDAETSLTCIASGWRPHEPITIGRDFEALMNQHQDPLEVTQDVTREWAKKVVWKREKASKINGAYFCEGRVRGEAIRIRTM KMRQQASFLPATLTMTVDKGDNVNISFKKVLIKEEDAVIYKNGSFIHSVPRHEVPDILEVHLPHAQPQDAGVYSARYIGGNLFTSAFTRLIVRRCEAQKWGPECNHLCTACMNNG VCHEDTGECICPPGFMGRTCEKACELHTFGRTCKERCSGQEGCKSYVFCLPDPYGCSCATGWKGLQCNEACHPGFYGPDCKLRCSCNNGEMCDRFQGCLCSPGWQGLQCERE GIPRMTPKIVDLPDHIEVNSGKFNPICKASGWPLPTNEEMTLVKPDGTVLHPKDFNHTDHFSVAIFTIHRILPPDSGVWVCSVNTVAGMVEKPFNISVKVLPKPLNAPNVIDTGHN FAVINISEPYFGDGPIKSKKLLYKPVNHYEAWQHIQVTNEIVTLNYLEPRTEYELCVQLVRRGEGGEGHPGPVRRFTTASIGLPPPRGLNLLPKSQTTLNLTWQPIFPSSEDDFYVEV ERRSVQKSDQQNIKVPGNLTSVLLNNLHPREQYVVRARVNTKAQGEWSEDLTAWTLSDILPPQPENIKISNITHSSAVISWTILDGYSISSITIRYKVQGKNEDQHVDVKIKNATITQ YQLKGLEPETAYQVDIFAENNIGSSNPAFSHELVTLPESQAPADLGGGKMLLIAILGSAGMTCLTVLLAFLIILQLKRANVQRRMAQAFQNVREEPAVQFNSGTLALNRKVKNNPD PTIYPVLDWNDIKFQDVIGEGNFGQVLKARIKKDGLRMDAAIKRMKEYASKDDHRDFAGELEVLCKLGHHPNIINLLGACEHRGYLYLAIEYAPHGNLLDFLRKSRVLETDPAFAIA NSTASTLSSQQLLHFAADVARGMDYLSQKQFIHRDLAARNILVGENYVAKIADFGLSRGQEVYVKKTMGRLPVRWMAIESLNYSVYTTNSDVWSYGVLLWEIVSLGGTPYCGMT CAELYEKLPQGYRLEKPLNCDDEVYDLMRQCWREKPYERPSFAQILVSLNRMLEERKTYVNTTLYEKFTYAGIDCSAEEAA
TIE1	NP_005415	P35590	MVWRVPPFLLPILFLASHVGAAVDLTLLANLRLTDPQRFFLTCVSGFEAGAGRGSDAWGPPLLLEKDDRIVRTPFGPPLRLARNGSHQVTLRGFSKPSDLVGVFSCVGGAGARRTR VIYVHNSPGAHLLPDKVTHTVNKGDTAVLSARVHKEKQTDVIWKSNGSYFYTLDWHEAQDGRFLLQLPNVQPPSSGIYSATYLEASPLGSAFFRLIVRGCGAGRWGPGCTKECPG CLHGGVCHDHDGECVCPPGFTGTRCEQACREGRFGQSCQEQCPGISGCRGLTFCLPDPYGCSCGSGWRGSQCQEACAPGHFGADCRLQCQCQNGGTCDRFSGCVCPSGWH GVHCEKSDRIPQILNMASELEFNLETMPRINCAAAGNPFPVRGSIELRKPDGTVLLSTKAIVEPEKTTAEFEVPRLVLADSGFWECRVSTSGGQDSRRFKVNVKVPPVPIAAPRLLTK QSRQLVVSPLVSFSGDGPISTVRLHYRPQDSTMDWSTIVVDPSENVTLMNLRPKTGYSVRVQLSRPGEGGEGAWGPPTLMTTDCPEPLLQPWILEGWHVEGTDRLRVSWSLPLV PGPLVGDGFLLRLWDGTRGQERRENVSSPQARTALLTGLTPGTHYQLDVQLYHCTLLGPASPPAHVLLPPSGPPAPRHLHAQALSDSEIQLTWKHPEALPGPISKYVVEVQVAGG AGDPLWIDVDRPEETSTIIRGLNASTRYLFRMRASIQGLGDWSNTVEESTLGNGLQAEGPVQESRAAEEGLDQQLILAVVGSVSATCLTILAALLTLVCIRRSCLHRRRTFTYQSGSG EETILQFSSGTLTLTRRPKLQPEPLSYPVLEWEDITFEDLIGEGNFGQVIRAMIKKDGLKMNAAIKMLKEYASENDHRDFAGELEVLCKLGHHPNIINLLGACKNRGYLYIAIEYAPYG NLLDFLRKSRVLETDPAFAREHGTASTLSSRQLLRFASDAANGMQYLSEKQFIHRDLAARNVLVGENLASKIADFGLSRGEEVYVKKTMGRLPVRWMAIESLNYSVYTTKSDVWSF GVLLWEIVSLGGTPYCGMTCAELYEKLPQGYRMEQPRNCDDEVYELMRQCWRDRPYERPPFAQIALQLGRMLEARKAYVNMSLFENFTYAGIDATAEEA
TYRO3	NP_006284	Q06418	MALRRSMGRPGLPPLPLPPPPRLGLLLAALASLLLPESAAAGLKLMGAPVKLTVSQGQPVKLNCSVEGMEEPDIQWVKDGAVVQNLDQLYIPVSEQHWIGFLSLKSVERSDAGRY WCQVEDGGETEISQPVWLTVEGVPFFTVEPKDLAVPPNAPFQLSCEAVGPPEPVTIVWWRGTTKIGGPAPSPSVLNVTGVTQSTMFSCEAHNLKGLASSRTATVHLQALPAAPF NITVTKLSSSNASVAWMPGADGRALLQSCTVQVTQAPGGWEVLAVVVPVPPFTCLLRDLVPATNYSLRVRCANALGPSPYADWVPFQTKGLAPASAPQNLHAIRTDSGLILEWE EVIPEAPLEGPLGPYKLSWVQDNGTQDELTVEGTRANLTGWDPQKDLIVRVCVSNAVGCGPWSQPLVVSSHDRAGQQGPPHSRTSWVPVVLGVLTALVTAAALALILLRKRRKE TRFGQAFDSVMARGEPAVHFRAARSFNRERPERIEATLDSLGISDELKEKLEDVLIPEQQFTLGRMLGKGEFGSVREAQLKQEDGSFVKVAVKMLKADIIASSDIEEFLREAACMKE FDHPHVAKLVGVSLRSRAKGRLPIPMVILPFMKHGDLHAFLLASRIGENPFNLPLQTLIRFMVDIACGMEYLSSRNFIHRDLAARNCMLAEDMTVCVADFGLSRKIYSGDYYRQGC ASKLPVKWLALESLADNLYTVQSDVWAFGVTMWEIMTRGQTPYAGIENAEIYNYLIGGNRLKQPPECMEDVYDLMYQCWSADPKQRPSFTCLRMELENILGQLSVLSASQDPL YINIERAEEPTAGGSLELPGRDQPYSGAGDGSGMGAVGGTPSDCRYILTPGGLAEQPGQAEHQPESPLNETQRLLLLQQGLLPHSSC

FIG. 65 (Cont.)

DDR1	NP_001284583	Q08345	MGPEALSLLLLLLVASGDADMKGHFDPAKCRYALGMQDRTIPDSDISASSSWSDSTAARHSRLESSDGDGAWCPAGSVFPKEEEYLQVDLQRLHLVALVGTQGRHAGGLGKEF
			SRSYRLRYSRDGRRWMGWKDRWGQEVISGNEDPEGVVLKDLGPPMVARLVRFYPRADRVMSVCLRVELYGCLWRDGLLSYTAPVGQTMYLSEAVTLNDSTYDGHTVGGLQY
			GGLGQLADGVVGLDDFRKSQELRVWPGYDYVGWSNHSFSSGYYEMEFEFDRLRAFQAMQVHCNNMHTLGARLPGGVECRFRGPAMAWEGEPMRHNLGGNLGDPRARA
			VSVPLGGRVARFLQCRFLFAGPWLLFSEISFISDVVNNSSPALGGTFPPAPWWPPGPPPTNFSSLELEPRGQQPVAKAEGSPTAILIGCLVAIIILLLLIIALMLWRLIHWRRLLSKAER
			RVLEEELTVHLSVPGDTILIINNRPGPREPPPYQEPRPRGNPPHSAPCVPNGSALLSNPAYRLLLATYARPPRGPGPPTPAWAKPTNTQAYSGDYMEPEKPGAPLLPPPPQNSVPH
			YAEADVTLQGVTGGNTYAVPALPPGAVGDGPPRVDFPRSRLRFKEKLGEGQFGEVHLCEVDSPQDLVSLDFPLNVRKGHPLLVAVKILRPDATKNARNDFLKEVKIMSRLKDPNII
			RLLGVCVQDDPLCMITDYMENGDLNQFLSAHQLEDKAAEGAPGDGQAAQGPTISYPMLLHVAAQIASGMRYLATLNFVHRDLATRNCLVGENFTIKIADFGMSRNLYAGDYYR
			VQGRAVLPIRWMAWECILMGKFTTASDVWAFGVTLWEVLMLCRAQPFGQLTDEQVIENAGEFFRDQGRQVYLSRPPACPQGLYELMLRCWSRESEQRPPFSQLHRFLAEDAL
			NTV
AATK	NP_001073864	Q67MQ8	MSSSFFNPSFAFSSHFDPDGAPLSELSWPSSLAVVAVSFSGLFAVIVLMLACLCCKKGGIGFKEFENAEGDEYAADLAQGSPATAAQNGPDVYVLPLTEVSLPMAKQPGRSVQLLK
			STDVGRHSLLYLKEIGRGWFGKVFLGEVNSGISSAQVVVKELQASASVQEQMQFLEEVQPYRALKHSNLLQCLAQCAEVTPYLLVMEFCPLGDLKGYLRSCRVAESMAPDPRTLQ
			RMACEVACGVLHLHRNNFVHSDLALRNCLLTADLTVKIGDYGLAHCKYREDYFVTADQLWVPLRWIAPELVDEVHSNLLVVDQTKSGNVWSLGVTIWELFELGTQPYPQHSDQ
			QVLAYTVREQQLKLPKPQLQLTLSDRWYEVMQFCWLQPEQRPTAEEVHLLLSYLCAKGATEAEEFERWRSLRPGGGGVGPGPGAAGPMLGGVVELAAASSFPLEQFAGDG
			FHADGGDDVLTVTETSRGINFEYKWEAGRGAEAFPATLSPGRTARLQELCAPDGAPPGVVPVLSAHSPSLGSEYFIRLEEAAPAAGHDPDCAGCAPSPPATADQDDDSDGSTAASL
			AMEPLLGHGPPVDVPWGRGDHYPRRSLARDPLCPSRSPSPSAGPLSLAEGGAEDADWGVAAFCPAFFEDPLGTSPLGSSGAPPLPLTGEDELEEVGARRAAQRGHWRSNVSAN
			NNSGSRCPESWDPVSAGGHAEGCPSPKQTPRASPEPGYPGFPLLGLQAASAQEPGCCPGLPHLCSAQGLAPAPCLVTPSWTETASSGGDHPQAEPKLATEAEGTTGPRLPLPSV
			PSPSQEGAPLPSEEASAPDAPDALPDSPTPATGGFVSAIKLASALNGSSSSPEVEAPSSEDEDTAEATSGIFTDTSSDGLQARRPDVVPAFRSLQKQVGTPDSLDSLDIPSSASDGGYE
			VFSPSATGPSGGQPRALDSGYDTENYESPEFVLKEAQEGECPQAFAELASEGEGPGPETRLSTSLSGLNEKNPYRDSAYFSDLEAEAEATSGPEKKCGGDRAPGPELGLPSTGQPSE
			QVCLRPGVSGEAQGSGPGEVLPPLLQLEGSSPEPSTCPSGLVPEPPEPQGPAKVRPGPSPSCSQFFLLTPVPLRSEGNSSEFQGPPGLLSGPAPQKRMGGPGTPRAPLRLALPGLPA
			ALEGRPEEEEEDSEDSDESDEELRCYSVQEPSEDSEEEAPAVPVVVAESQSARNLRSLEKMPSLLSETFCEDLERKKKAVSFFDDVTVYLEDQESPTRELGEPPPGAKESPPTFLRGSP
			GSPSAPNRPQQADGSPNGSTAEEGGGFAWDDDFPLMTAKAAFAMALDPAAPAPAAPTPTPAPFSRFTVSPAPTSRFSITHVSDSDAESKRGPEAGAGGESKEA

SEQUENCE LISTING

<110> The Regents of the University of California
Taunton, John W.
Lim, Wendell A.
Wu, Chia-Yung

<120> CONDITIONALLY ACTIVE HETERODIMERIC POLYPEPTIDES AND METHODS OF USE THEREOF

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<151> 2016-01-08

<160> 723

<170> PatentIn version 3.5

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Arg Leu Leu Gln Glu Gly Ser Pro Ser
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Ser Pro Ser Asp Ile
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<400> 3

Glu Ser Lys Gly His Lys Lys Leu Leu Gln Leu Leu Thr Cys Ser Ser
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Asp Asp Arg

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Pro Lys Lys Glu Asn Asn Ala Leu Leu Arg Tyr Leu Leu Asp Arg Asp
1 5 10 15

Asp Pro Ser Asp Val
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Ala Glu Glu Pro Ser Leu Leu Lys Lys Leu Leu Leu Ala Pro Ala Asn
1 5 10 15

Thr

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<400> 6

Gln Glu Ala Glu Glu Pro Ser Leu Leu Lys Lys Leu Leu Leu Ala Pro
1 5 10 15

Ala Asn Thr Gln Leu
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<400> 7

Ser Lys Val Ser Gln Asn Pro Ile Leu Thr Ser Leu Leu Gln Ile Thr
1 5 10 15

Gly Asn Gly Gly Ser
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<400> 8

Gly His Ser Phe Ala Asp Pro Ala Ser Asn Leu Gly Leu Glu Asp Ile
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Ile Arg Lys Ala Leu Met Gly Ser Phe
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<400> 9

Pro Arg Gln Gly Ser Ile Leu Tyr Ser Met Leu Thr Ser Ala Lys Gln
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Thr

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Ala Ala Asn Asn Ser Leu Leu Leu His Leu Leu Lys Ser Gln Thr Ile
1 5 10 15

Pro

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<400> 11

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1 5 10 15

Asp Thr Lys Asp Ile
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<400> 12

Asp Ala Phe Gln Leu Arg Gln Leu Ile Leu Arg Gly Leu Gln Asp Asp
1 5 10 15

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<400> 13

Ser Pro Gly Ser Arg Glu Trp Phe Lys Asp Met Leu Ser
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Gly Asn Thr Lys Asn His Pro Met Leu Met Asn Leu Leu Lys Asp Asn
1 5 10 15

Pro Ala Gln Asp Phe
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Ser Ser Lys Gly Val Leu Trp Arg Met Leu Ala Glu Pro Val Ser Arg
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Ser Arg Thr Leu Gln Leu Asp Trp Gly Thr Leu Tyr Trp Ser Arg
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<400> 17

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<400> 18

Leu Lys Glu Lys His Lys Ile Leu His Arg Leu Leu Gln Asp Ser Ser
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Ser Pro Val

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<400> 19

Gln Ala Gln Gln Lys Ser Leu Leu Gln Gln Leu Leu Thr Glu
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Lys Tyr Ser Gln Thr Ser His Lys Leu Val Gln Leu Leu Thr Thr Thr
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Ala Glu Gln Gln Leu
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<400> 21

Ser Leu Thr Ala Arg His Lys Ile Leu His Arg Leu Leu Gln Glu Gly
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Ser Pro Ser Asp Ile
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<400> 22

Lys Glu Ser Lys Asp His Gln Leu Leu Arg Tyr Leu Leu Asp Lys Asp
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Glu Lys Asp Leu Arg
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Pro Gln Ala Gln Gln Lys Ser Leu Leu Gln Gln Leu Leu Thr Glu
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<400> 24

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1 5 10 15

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<400> 25

His Asp Ser Lys Gly Gln Thr Lys Leu Leu Gln Leu Leu Thr Thr Lys
1 5 10 15

Ser Asp Gln Met Glu
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<400> 26

Ser Leu Lys Glu Lys His Lys Ile Leu His Arg Leu Leu Gln Asp Ser
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Ser Ser Pro Val Asp
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<400> 27

Pro Lys Lys Lys Glu Asn Ala Leu Leu Arg Tyr Leu Leu Asp Lys Asp
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Asp Thr Lys Asp Ile
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<400> 28

Leu Glu Ser Lys Gly His Lys Lys Leu Leu Gln Leu Leu Thr Cys Ser
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Ser Asp Asp Arg Gly
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<400> 29

Leu Leu Gln Glu Lys His Arg Ile Leu His Lys Leu Leu Gln Asn Gly
1 5 10 15

Asn Ser Pro Ala Glu
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<400> 30

Lys Lys Lys Glu Asn Asn Ala Leu Leu Arg Tyr Leu Leu Asp Arg Asp
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Asp Pro Ser Asp Ala
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<400> 31

Gln Glu Ala Glu Glu Pro Ser Leu Leu Lys Lys Leu Leu Leu Ala Pro
1 5 10 15

Ala Asn Thr Gln Leu
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Pro Glu Val Asp Glu Leu Ser Leu Leu Gln Lys Leu Leu Leu Ala Thr
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Ser Tyr Pro Thr Ser
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<400> 33

Val Ser Pro Arg Glu Gly Ser Ser Leu His Lys Leu Leu Thr Leu Ser
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Arg Thr Pro Pro Glu
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<400> 34

Ser Lys Val Ser Gln Asn Pro Ile Leu Thr Ser Leu Leu Gln Ile Thr
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Gly Asn Gly Gly Ser
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Gly Asn Thr Lys Asn His Pro Met Leu Met Asn Leu Leu Lys Asp Asn
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Pro Ala Gln Asp Phe
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Asp Val Thr Leu Thr Ser Pro Leu Leu Val Asn Leu Leu Gln Ser Asp
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Ile Ser Ala Gly His
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<400> 37

Ala Met Arg Glu Ala Pro Thr Ser Leu Ser Gln Leu Leu Asp Asn Ser
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Gly Ala Pro Asn Val
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<400> 38

Asp Ala Ala Ser Lys His Lys Gln Leu Ser Glu Leu Leu Arg Gly Gly
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Ser Gly Ser Ser Ile
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<400> 39

Lys Arg Lys Leu Ile Gln Gln Gln Leu Val Leu Leu Leu His Ala His
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Lys Cys Gln Arg Arg
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Asp Ala Ala Ser Lys His Lys Gln Leu Ser Glu Leu Leu Arg Ser Gly
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Ser Ser Pro Asn Leu
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Gly His Pro Pro Ala Ile Gln Ser Leu Ile Asn Leu Leu Ala Asp Asn
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Arg Tyr Leu Thr Ala
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Thr Leu Gln Gln Gln Ala Gln Gln Leu Tyr Ser Leu Leu Gly Gln Phe
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Asn Cys Leu Thr His
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Gly Ser Arg Glu Thr Ser Glu Lys Phe Lys Leu Leu Phe Gln Ser Tyr
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Asn Val Asn Asp Trp
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Asn Ala Asn Tyr Pro Arg Ser Ile Leu Thr Ser Leu Leu Leu Asn Ser
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Ser Gln Ser Ser Thr
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Ile Pro Ile Glu Pro Asp Tyr Lys Phe Ser Thr Leu Leu Met Met Leu
1 5 10 15

Lys Asp Met His Asp
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<400> 46

Ala Thr Pro Pro Pro Ser Pro Leu Leu Ser Glu Leu Leu Lys Lys Gly
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Ser Leu Leu Pro Thr
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<400> 47

Val Asp Gly His Glu Arg Ala Met Leu Lys Arg Leu Leu Arg Ile Asp
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Ser Lys Cys Leu His
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<400> 48

His Glu Asp Leu Asp Lys Val Lys Leu Ile Glu Tyr Tyr Leu Thr Lys
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Asn Lys Glu Gly Pro
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Glu Ser Pro Glu Phe Cys Leu Gly Leu Gln Thr Leu Leu Ser Leu Lys
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Cys Cys Ile Asp Leu
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Ala Ala Thr Thr Gln Asn Pro Val Leu Ser Lys Leu Leu Met Ala Asp
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Gln Asp Ser Pro Leu

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<400> 51

Met Gly Gln Val Pro Arg Thr His Arg Leu Ile Thr Leu Ala Asp His
1 5 10 15

Ile Cys Gln Ile Ile Thr Gln Asp Phe Ala Arg Asn Gln Val
20 25 30

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<400> 52

Asn Leu Gly Leu Glu Asp Ile Ile Arg Lys Ala Leu Met Gly
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<400> 53

Ala Pro Gly Val Lys Gly His Gln Arg Val Val Thr Leu Ala Gln His
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Ile Ser Glu Val Ile Thr Gln Asp Thr Tyr Arg His His Pro Gln Gln
20 25 30

Leu Ser Ala Pro Leu Pro Ala Pro
35 40

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<400> 54

Asn Met Gly Leu Glu Ala Ile Ile Arg Lys Ala Leu Met Gly

1 5 10

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<400> 55

Arg Leu Thr Lys Thr Asn Pro Ile Leu Tyr Tyr Met Leu Gln Lys Gly
1 5 10 15

Gly Asn Ser Val Ala
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<400> 56

Gln Asp Ser Ile Val Leu Thr Tyr Leu Glu Gly Leu Leu Met His Gln
1 5 10 15

Ala Ala Gly Gly Ser
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<400> 57

Lys Gly Lys Gln Asp Ser Thr Leu Leu Ala Ser Leu Leu Gln Ser Phe
1 5 10 15

Ser Ser Arg Leu Gln
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<400> 58

Cys Tyr Gly Val Ala Ser Ser His Leu Lys Thr Leu Leu Lys Lys Ser

1 5 10 15

Lys Val Lys Asp Gln
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<210> 59
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<400> 59

Lys Pro Ser Val Ala Cys Ser Gln Leu Ala Leu Leu Leu Ser Ser Glu
1 5 10 15

Ala His Leu Gln Gln
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<210> 60
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<400> 60

Lys Gln Ala Ala Asn Asn Ser Leu Leu Leu His Leu Leu Lys Ser Gln
1 5 10 15

Thr Ile Pro Lys Pro
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<400> 61

Asn Ser His Gln Lys Val Thr Leu Leu Gln Leu Leu Leu Gly His Lys
1 5 10 15

Asn Glu Glu Asn Val
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<400> 62

Asn Leu Leu Glu Arg Arg Thr Val Leu Gln Leu Leu Leu Gly Asn Pro
1 5 10 15

Thr Lys Gly Arg Val
20

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<400> 63

Phe Ser Phe Ser Lys Asn Gly Leu Leu Ser Arg Leu Leu Arg Gln Asn
1 5 10 15

Gln Asp Ser Tyr Leu
20

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<400> 64

Arg Glu Ser Lys Ser Phe Asn Val Leu Lys Gln Leu Leu Leu Ser Glu
1 5 10 15

Asn Cys Val Arg Asp
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<400> 65

Glu Leu Asn Ala Asp Asp Ala Ile Leu Arg Glu Leu Leu Asp Glu Ser
1 5 10 15

Gln Lys Val Met Val
20

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<400> 66

Tyr Glu Asn Leu Pro Pro Ala Ala Leu Arg Lys Leu Leu Arg Ala Glu
1 5 10 15

Pro Glu Arg Tyr Arg
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Met Ala Phe Ala Gly Asp Glu Val Leu Val Gln Leu Leu Ser Gly Asp
1 5 10 15

Lys Ala Pro Glu Gly
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<400> 68

Ser Cys Cys Tyr Leu Cys Ile Arg Leu Glu Gly Leu Leu Ala Pro Thr
1 5 10 15

Ala Ser Pro Arg Pro
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<210> 69
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<400> 69

Pro Ser Asn Lys Ser Val Asp Val Leu Ala Gly Leu Leu Leu Arg Arg
1 5 10 15

Met Glu Leu Lys Pro
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<210> 70
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<213> Homo sapiens

<400> 70

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

Pro Thr Glu Arg Thr Asp Glu Asn Asn Tyr Met Glu Ile Val Asn Val
35 40 45

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

Lys Glu Lys Gln Glu Leu Leu Pro Cys Leu Gln Gln Asp Asn Asn Arg
65 70 75 80

Pro Gly Ile Leu Thr Ser Asp Ile Lys Thr Glu Leu Glu Ser Lys Glu
85 90 95

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

Arg Asp Ala Asp Tyr Ser Tyr Glu Gln Gln Asn Gln Gln Gly Ser Met
115 120 125

Ser Pro Ala Lys Ile Tyr Gln Asn Val Glu Gln Leu Val Lys Phe Tyr
130 135 140

Lys Gly Asn Gly His Arg Pro Ser Thr Leu Ser Cys Val Asn Thr Pro
145 150 155 160

Leu Arg Ser Phe Met Ser Asp Ser Gly Ser Ser Val Asn Gly Gly Val
165 170 175

Met Arg Ala Val Val Lys Ser Pro Ile Met Cys His Glu Lys Ser Pro
180 185 190

Ser Val Cys Ser Pro Leu Asn Met Thr Ser Ser Val Cys Ser Pro Ala
195 200 205

Gly Ile Asn Ser Val Ser Ser Thr Thr Ala Ser Phe Gly Ser Phe Pro
210 215 220

Val His Ser Pro Ile Thr Gln Gly Thr Pro Leu Thr Cys Ser Pro Asn
225 230 235 240

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Val Glu Asn Arg Gly Ser Arg Ser His Ser Pro Ala His Ala Ser Asn
                245                 250                 255

Val Gly Ser Pro Leu Ser Ser Pro Leu Ser Ser Met Lys Ser Ser Ile
            260                 265                 270

Ser Ser Pro Pro Ser His Cys Ser Val Lys Ser Pro Val Ser Ser Pro
        275                 280                 285

Asn Asn Val Thr Leu Arg Ser Ser Val Ser Ser Pro Ala Asn Ile Asn
    290                 295                 300

Asn Ser Arg Cys Ser Val Ser Ser Pro Ser Asn Thr Asn Asn Arg Ser
305                 310                 315                 320

Thr Leu Ser Ser Pro Ala Ala Ser Thr Val Gly Ser Ile Cys Ser Pro
                325                 330                 335

Val Asn Asn Ala Phe Ser Tyr Thr Ala Ser Gly Thr Ser Ala Gly Ser
            340                 345                 350

Ser Thr Leu Arg Asp Val Val Pro Ser Pro Asp Thr Gln Glu Lys Gly
        355                 360                 365

Ala Gln Glu Val Pro Phe Pro Lys Thr Glu Glu Val Glu Ser Ala Ile
    370                 375                 380

Ser Asn Gly Val Thr Gly Gln Leu Asn Ile Val Gln Tyr Ile Lys Pro
385                 390                 395                 400

Glu Pro Asp Gly Ala Phe Ser Ser Ser Cys Leu Gly Gly Asn Ser Lys
                405                 410                 415

Ile Asn Ser Asp Ser Ser Phe Ser Val Pro Ile Lys Gln Glu Ser Thr
            420                 425                 430

Lys His Ser Cys Ser Gly Thr Ser Phe Lys Gly Asn Pro Thr Val Asn
        435                 440                 445

Pro Phe Pro Phe Met Asp Gly Ser Tyr Phe Ser Phe Met Asp Asp Lys
    450                 455                 460

Asp Tyr Tyr Ser Leu Ser Gly Ile Leu Gly Pro Pro Val Pro Gly Phe
465                 470                 475                 480

Asp Gly Asn Cys Glu Gly Ser Gly Phe Pro Val Gly Ile Lys Gln Glu
                485                 490                 495

Pro Asp Asp Gly Ser Tyr Tyr Pro Glu Ala Ser Ile Pro Ser Ser Ala
            500                 505                 510
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Ile Val Gly Val Asn Ser Gly Gly Gln Ser Phe His Tyr Arg Ile Gly
        515                 520                 525

Ala Gln Gly Thr Ile Ser Leu Ser Arg Ser Ala Arg Asp Gln Ser Phe
    530                 535                 540

Gln His Leu Ser Ser Phe Pro Pro Val Asn Thr Leu Val Glu Ser Trp
545                 550                 555                 560

Lys Ser His Gly Asp Leu Ser Ser Arg Arg Ser Asp Gly Tyr Pro Val
                565                 570                 575

Leu Glu Tyr Ile Pro Glu Asn Val Ser Ser Ser Thr Leu Arg Ser Val
            580                 585                 590

Ser Thr Gly Ser Ser Arg Pro Ser Lys Ile Cys Leu Val Cys Gly Asp
        595                 600                 605

Glu Ala Ser Gly Cys His Tyr Gly Val Val Thr Cys Gly Ser Cys Lys
    610                 615                 620

Val Phe Phe Lys Arg Ala Val Glu Gly Gln His Asn Tyr Leu Cys Ala
625                 630                 635                 640

Gly Arg Asn Asp Cys Ile Ile Asp Lys Ile Arg Arg Lys Asn Cys Pro
                645                 650                 655

Ala Cys Arg Leu Gln Lys Cys Leu Gln Ala Gly Met Asn Leu Gly Ala
            660                 665                 670

Arg Lys Ser Lys Lys Leu Gly Lys Leu Lys Gly Ile His Glu Glu Gln
        675                 680                 685

Pro Gln Gln Gln Gln Pro Pro Pro Pro Pro Pro Pro Pro Gln Ser Pro
    690                 695                 700

Glu Glu Gly Thr Thr Tyr Ile Ala Pro Ala Lys Glu Pro Ser Val Asn
705                 710                 715                 720

Thr Ala Leu Val Pro Gln Leu Ser Thr Ile Ser Arg Ala Leu Thr Pro
                725                 730                 735

Ser Pro Val Met Val Leu Glu Asn Ile Glu Pro Glu Ile Val Tyr Ala
            740                 745                 750

Gly Tyr Asp Ser Ser Lys Pro Asp Thr Ala Glu Asn Leu Leu Ser Thr
        755                 760                 765

Leu Asn Arg Leu Ala Gly Lys Gln Met Ile Gln Val Val Lys Trp Ala
    770                 775                 780
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Lys Val Leu Pro Gly Phe Lys Asn Leu Pro Leu Glu Asp Gln Ile Thr
785                 790                 795                 800

Leu Ile Gln Tyr Ser Trp Met Cys Leu Ser Ser Phe Ala Leu Ser Trp
                805                 810                 815

Arg Ser Tyr Lys His Thr Asn Ser Gln Phe Leu Tyr Phe Ala Pro Asp
            820                 825                 830

Leu Val Phe Asn Glu Glu Lys Met His Gln Ser Ala Met Tyr Glu Leu
        835                 840                 845

Cys Gln Gly Met His Gln Ile Ser Leu Gln Phe Val Arg Leu Gln Leu
    850                 855                 860

Thr Phe Glu Glu Tyr Thr Ile Met Lys Val Leu Leu Leu Leu Ser Thr
865                 870                 875                 880

Ile Pro Lys Asp Gly Leu Lys Ser Gln Ala Ala Phe Glu Glu Met Arg
                885                 890                 895

Thr Asn Tyr Ile Lys Glu Leu Arg Lys Met Val Thr Lys Cys Pro Asn
            900                 905                 910

Asn Ser Gly Gln Ser Trp Gln Arg Phe Tyr Gln Leu Thr Lys Leu Leu
        915                 920                 925

Asp Ser Met His Asp Leu Val Ser Asp Leu Leu Glu Phe Cys Phe Tyr
    930                 935                 940

Thr Phe Arg Glu Ser His Ala Leu Lys Val Glu Phe Pro Ala Met Leu
945                 950                 955                 960

Val Glu Ile Ile Ser Asp Gln Leu Pro Lys Val Glu Ser Gly Asn Ala
                965                 970                 975

Lys Pro Leu Tyr Phe His Arg Lys
            980
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<213> Homo sapiens

<400> 71

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Glu Glu Gln Pro Gln Gln Gln Gln Pro Pro Pro Pro Pro Pro Pro Pro
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Gln Ser Pro Glu Glu Gly Thr Thr Tyr Ile Ala Pro Ala Lys Glu Pro
            20                  25                  30

Ser Val Asn Thr Ala Leu Val Pro Gln Leu Ser Thr Ile Ser Arg Ala
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35 40 45

Leu Thr Pro Ser Pro Val Met Val Leu Glu Asn Ile Glu Pro Glu Ile
50 55 60

Val Tyr Ala Gly Tyr Asp Ser Ser Lys Pro Asp Thr Ala Glu Asn Leu
65 70 75 80

Leu Ser Thr Leu Asn Arg Leu Ala Gly Lys Gln Met Ile Gln Val Val
85 90 95

Lys Trp Ala Lys Val Leu Pro Gly Phe Lys Asn Leu Pro Leu Glu Asp
100 105 110

Gln Ile Thr Leu Ile Gln Tyr Ser Trp Met Cys Leu Ser Ser Phe Ala
115 120 125

Leu Ser Trp Arg Ser Tyr Lys His Thr Asn Ser Gln Phe Leu Tyr Phe
130 135 140

Ala Pro Asp Leu Val Phe Asn Glu Glu Lys Met His Gln Ser Ala Met
145 150 155 160

Tyr Glu Leu Cys Gln Gly Met His Gln Ile Ser Leu Gln Phe Val Arg
165 170 175

Leu Gln Leu Thr Phe Glu Glu Tyr Thr Ile Met Lys Val Leu Leu Leu
180 185 190

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

Glu Met Arg Thr Asn Tyr Ile Lys Glu Leu Arg Lys Met Val Thr Lys
210 215 220

Cys Pro Asn Asn Ser Gly Gln Ser Trp Gln Arg Phe Tyr Gln Leu Thr
225 230 235 240

Lys Leu Leu Asp Ser Met His Asp Leu Val Ser Asp Leu Leu Glu Phe
245 250 255

Cys Phe Tyr Thr Phe Arg Glu Ser His Ala Leu Lys Val Glu Phe Pro
260 265 270

Ala Met Leu Val Glu Ile Ile Ser Asp Gln Leu Pro Lys Val Glu Ser
275 280 285

Gly Asn Ala Lys Pro Leu Tyr Phe His Arg Lys
290 295

<210> 72

<211> 248
<212> PRT
<213> Homo sapiens

<400> 72

```
Ser Pro Val Met Val Leu Glu Asn Ile Glu Pro Glu Ile Val Tyr Ala
1               5                  10                  15

Gly Tyr Asp Ser Ser Lys Pro Asp Thr Ala Glu Asn Leu Leu Ser Thr
            20                  25                  30

Leu Asn Arg Leu Ala Gly Lys Gln Met Ile Gln Val Val Lys Trp Ala
        35                  40                  45

Lys Val Leu Pro Gly Phe Lys Asn Leu Pro Leu Glu Asp Gln Ile Thr
    50                  55                  60

Leu Ile Gln Tyr Ser Trp Met Cys Leu Ser Ser Phe Ala Leu Ser Trp
65                  70                  75                  80

Arg Ser Tyr Lys His Thr Asn Ser Gln Phe Leu Tyr Phe Ala Pro Asp
                85                  90                  95

Leu Val Phe Asn Glu Glu Lys Met His Gln Ser Ala Met Tyr Glu Leu
            100                 105                 110

Cys Gln Gly Met His Gln Ile Ser Leu Gln Phe Val Arg Leu Gln Leu
        115                 120                 125

Thr Phe Glu Glu Tyr Thr Ile Met Lys Val Leu Leu Leu Leu Ser Thr
    130                 135                 140

Ile Pro Lys Asp Gly Leu Lys Ser Gln Ala Ala Phe Glu Glu Met Arg
145                 150                 155                 160

Thr Asn Tyr Ile Lys Glu Leu Arg Lys Met Val Thr Lys Cys Pro Asn
                165                 170                 175

Asn Ser Gly Gln Ser Trp Gln Arg Phe Tyr Gln Leu Thr Lys Leu Leu
            180                 185                 190

Asp Ser Met His Asp Leu Val Ser Asp Leu Leu Glu Phe Cys Phe Tyr
        195                 200                 205

Thr Phe Arg Glu Ser His Ala Leu Lys Val Glu Phe Pro Ala Met Leu
    210                 215                 220

Val Glu Ile Ile Ser Asp Gln Leu Pro Lys Val Glu Ser Gly Asn Ala
225                 230                 235                 240

Lys Pro Leu Tyr Phe His Arg Lys
                245
```

<210> 73
<211> 299
<212> PRT
<213> Homo sapiens

<400> 73

```
Glu Glu Gln Pro Gln Gln Gln Gln Pro Pro Pro Pro Pro Pro Pro Pro
1               5                  10                  15

Gln Ser Pro Glu Glu Gly Thr Thr Tyr Ile Ala Pro Ala Lys Glu Pro
            20                  25                  30

Ser Val Asn Thr Ala Leu Val Pro Gln Leu Ser Thr Ile Ser Arg Ala
        35                  40                  45

Leu Thr Pro Ser Pro Val Met Val Leu Glu Asn Ile Glu Pro Glu Ile
    50                  55                  60

Val Tyr Ala Gly Tyr Asp Ser Ser Lys Pro Asp Thr Ala Glu Asn Leu
65                  70                  75                  80

Leu Ser Thr Leu Asn Arg Leu Ala Gly Lys Gln Met Ile Gln Val Val
                85                  90                  95

Lys Trp Ala Lys Val Leu Pro Gly Phe Lys Asn Leu Pro Leu Glu Asp
            100                 105                 110

Gln Ile Thr Leu Ile Gln Tyr Ser Trp Met Cys Leu Leu Ser Phe Ala
        115                 120                 125

Leu Ser Trp Arg Ser Tyr Lys His Thr Asn Ser Gln Phe Leu Tyr Phe
    130                 135                 140

Ala Pro Asp Leu Val Phe Asn Glu Glu Lys Met His Gln Ser Ala Met
145                 150                 155                 160

Tyr Glu Leu Cys Gln Gly Met His Gln Ile Ser Leu Gln Phe Val Arg
                165                 170                 175

Leu Gln Leu Thr Phe Glu Glu Tyr Thr Ile Met Lys Val Leu Leu Leu
            180                 185                 190

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

Glu Met Arg Thr Asn Tyr Ile Lys Glu Leu Arg Lys Met Val Thr Lys
    210                 215                 220

Cys Pro Asn Asn Ser Gly Gln Ser Trp Gln Arg Phe Tyr Gln Leu Thr
225                 230                 235                 240
```

Lys Leu Leu Asp Ser Met His Asp Leu Val Ser Asp Leu Leu Glu Phe
245 250 255

Cys Phe Tyr Thr Phe Arg Glu Ser His Ala Leu Lys Val Glu Phe Pro
260 265 270

Ala Met Leu Val Glu Ile Ile Ser Asp Gln Leu Pro Lys Val Glu Ser
275 280 285

Gly Asn Ala Lys Pro Leu Tyr Phe His Arg Lys
290 295

<210> 74
<211> 248
<212> PRT
<213> Homo sapiens

<400> 74

Ser Pro Val Met Val Leu Glu Asn Ile Glu Pro Glu Ile Val Tyr Ala
1 5 10 15

Gly Tyr Asp Ser Ser Lys Pro Asp Thr Ala Glu Asn Leu Leu Ser Thr
20 25 30

Leu Asn Arg Leu Ala Gly Lys Gln Met Ile Gln Val Val Lys Trp Ala
35 40 45

Lys Val Leu Pro Gly Phe Lys Asn Leu Pro Leu Glu Asp Gln Ile Thr
50 55 60

Leu Ile Gln Tyr Ser Trp Met Cys Leu Leu Ser Phe Ala Leu Ser Trp
65 70 75 80

Arg Ser Tyr Lys His Thr Asn Ser Gln Phe Leu Tyr Phe Ala Pro Asp
85 90 95

Leu Val Phe Asn Glu Glu Lys Met His Gln Ser Ala Met Tyr Glu Leu
100 105 110

Cys Gln Gly Met His Gln Ile Ser Leu Gln Phe Val Arg Leu Gln Leu
115 120 125

Thr Phe Glu Glu Tyr Thr Ile Met Lys Val Leu Leu Leu Leu Ser Thr
130 135 140

Ile Pro Lys Asp Gly Leu Lys Ser Gln Ala Ala Phe Glu Glu Met Arg
145 150 155 160

Thr Asn Tyr Ile Lys Glu Leu Arg Lys Met Val Thr Lys Cys Pro Asn
165 170 175

Asn Ser Gly Gln Ser Trp Gln Arg Phe Tyr Gln Leu Thr Lys Leu Leu
180 185 190

Asp Ser Met His Asp Leu Val Ser Asp Leu Leu Glu Phe Cys Phe Tyr
195 200 205

Thr Phe Arg Glu Ser His Ala Leu Lys Val Glu Phe Pro Ala Met Leu
210 215 220

Val Glu Ile Ile Ser Asp Gln Leu Pro Lys Val Glu Ser Gly Asn Ala
225 230 235 240

Lys Pro Leu Tyr Phe His Arg Lys
245

<210> 75
<211> 248
<212> PRT
<213> Homo sapiens

<400> 75

Ser Pro Val Met Val Leu Glu Asn Ile Glu Pro Glu Ile Val Tyr Ala
1 5 10 15

Gly Tyr Asp Ser Ser Lys Pro Asp Thr Ala Glu Asn Leu Leu Ser Thr
20 25 30

Leu Asn Arg Leu Ala Gly Lys Gln Met Ile Gln Val Val Lys Trp Ala
35 40 45

Lys Val Leu Pro Gly Phe Lys Asn Leu Pro Leu Glu Asp Gln Ile Thr
50 55 60

Leu Ile Gln Tyr Ser Trp Met Ser Leu Leu Ser Phe Ala Leu Ser Trp
65 70 75 80

Arg Ser Tyr Lys His Thr Asn Ser Gln Phe Leu Tyr Phe Ala Pro Asp
85 90 95

Leu Val Phe Asn Glu Glu Lys Met His Gln Ser Ala Met Tyr Glu Leu
100 105 110

Cys Gln Gly Met His Gln Ile Ser Leu Gln Phe Val Arg Leu Gln Leu
115 120 125

Thr Phe Glu Glu Tyr Thr Ile Met Lys Val Leu Leu Leu Leu Ser Thr
130 135 140

Ile Pro Lys Asp Gly Leu Lys Ser Gln Ala Ala Phe Glu Glu Met Arg
145 150 155 160

Thr Asn Tyr Ile Lys Glu Leu Arg Lys Met Val Thr Lys Cys Pro Asn

165 170 175

Asn Ser Gly Gln Ser Trp Gln Arg Phe Tyr Gln Leu Thr Lys Leu Leu
180 185 190

Asp Ser Met His Asp Leu Val Ser Asp Leu Leu Glu Phe Cys Phe Tyr
195 200 205

Thr Phe Arg Glu Ser His Ala Leu Lys Val Glu Phe Pro Ala Met Leu
210 215 220

Val Glu Ile Ile Ser Asp Gln Leu Pro Lys Val Glu Ser Gly Asn Ala
225 230 235 240

Lys Pro Leu Tyr Phe His Arg Lys
245

<210> 76
<211> 248
<212> PRT
<213> Homo sapiens

<400> 76

Ser Pro Val Lys Ile Leu Glu Ser Ile Glu Pro Glu Ile Val Tyr Ala
1 5 10 15

Gly Tyr Asp Ser Ser Lys Pro Asp Thr Ala Glu Tyr Leu Leu Ser Thr
20 25 30

Leu Asn Arg Leu Ala Gly Lys Gln Met Ile Gln Val Val Lys Trp Ala
35 40 45

Lys Ile Leu Pro Gly Phe Arg Asn Leu Pro Leu Glu Asp Gln Ile Thr
50 55 60

Leu Ile Gln Tyr Ser Trp Met Cys Leu Ser Ser Phe Ala Leu Ser Trp
65 70 75 80

Arg Ser Tyr Lys His Thr Asn Ser Gln Phe Leu Tyr Phe Ala Pro Asp
85 90 95

Leu Ile Phe Asp Glu Glu Arg Met Arg Gln Ser Ala Met Phe Glu Leu
100 105 110

Cys Gln Gly Met His Gln Ile Ser Leu Gln Phe Val Arg Leu Gln Leu
115 120 125

Ser Phe Glu Glu Tyr Thr Ile Met Lys Val Leu Leu Leu Leu Ser Thr
130 135 140

Val Pro Lys Asp Gly Leu Lys Ser Gln Ala Ala Phe Glu Glu Met Arg
145 150 155 160

```
Ala Asn Tyr Ile Lys Glu Leu Lys Lys Met Val Thr Lys Cys Pro Ser
                165                 170                 175

Asn Ser Gly Gln Ser Trp Gln Arg Phe Tyr Gln Leu Thr Lys Leu Leu
            180                 185                 190

Asp Ser Met His Asp Leu Val Ser Asp Leu Leu Glu Phe Cys Phe Tyr
        195                 200                 205

Thr Phe Arg Glu Ser Gln Ala Leu Lys Val Glu Phe Pro Ala Met Leu
    210                 215                 220

Val Glu Ile Ile Ser Asp Gln Leu Pro Lys Val Glu Ser Gly Asn Ala
225                 230                 235                 240

Lys Pro Leu Tyr Phe His Arg Lys
                245
```

<210> 77
<211> 248
<212> PRT
<213> Homo sapiens

<400> 77

```
Ser Pro Val Met Val Leu Glu Asn Ile Glu Pro Glu Ile Val Tyr Ala
1               5                   10                  15

Gly Tyr Asp Ser Ser Lys Pro Asp Thr Ala Glu Asn Leu Leu Ser Thr
            20                  25                  30

Leu Asn Arg Leu Ala Gly Lys Gln Met Ile Gln Val Val Lys Trp Ala
        35                  40                  45

Lys Val Leu Pro Gly Phe Lys Asn Leu Pro Leu Glu Asp Gln Ile Thr
    50                  55                  60

Leu Ile Gln Tyr Ser Trp Met Ser Leu Ser Ser Phe Ala Leu Ser Trp
65                  70                  75                  80

Arg Ser Tyr Lys His Thr Asn Ser Gln Phe Leu Tyr Phe Ala Pro Asp
                85                  90                  95

Leu Val Phe Asn Glu Glu Lys Met His Gln Ser Ala Met Tyr Glu Leu
            100                 105                 110

Cys Gln Gly Met His Gln Ile Ser Leu Gln Phe Val Arg Leu Gln Leu
        115                 120                 125

Thr Phe Glu Glu Tyr Thr Ile Met Lys Val Leu Leu Leu Leu Ser Thr
    130                 135                 140
```

```
Ile Pro Lys Asp Gly Leu Lys Ser Gln Ala Ala Phe Glu Glu Met Arg
145                 150                 155                 160

Thr Asn Tyr Ile Lys Glu Leu Arg Lys Met Val Thr Lys Cys Pro Asn
                165                 170                 175

Asn Ser Gly Gln Ser Trp Gln Arg Phe Tyr Gln Leu Thr Lys Leu Leu
            180                 185                 190

Asp Ser Met His Asp Leu Val Ser Asp Leu Leu Glu Phe Cys Phe Tyr
        195                 200                 205

Thr Phe Arg Glu Ser His Ala Leu Lys Val Glu Phe Pro Ala Met Leu
    210                 215                 220

Val Glu Ile Ile Ser Asp Gln Leu Pro Lys Val Glu Ser Gly Asn Ala
225                 230                 235                 240

Lys Pro Leu Tyr Phe His Arg Lys
                245
```

<210> 78
<211> 248
<212> PRT
<213> Homo sapiens

<400> 78

```
Ser Pro Val Met Val Leu Glu Asn Ile Glu Pro Glu Ile Val Tyr Ala
1               5                   10                  15

Gly Tyr Asp Ser Ser Lys Pro Asp Thr Ala Glu Asn Leu Leu Ser Thr
            20                  25                  30

Leu Asn Arg Leu Ala Gly Lys Gln Met Ile Gln Val Val Lys Trp Ala
        35                  40                  45

Lys Val Leu Pro Gly Phe Lys Asn Leu Pro Leu Glu Asp Gln Ile Thr
    50                  55                  60

Leu Ile Gln Tyr Ser Trp Met Ser Leu Ser Ser Phe Ala Leu Ser Trp
65                  70                  75                  80

Arg Ser Tyr Lys His Thr Asn Ser Gln Phe Leu Tyr Phe Ala Pro Asp
                85                  90                  95

Leu Val Phe Asn Glu Glu Lys Met His Gln Ser Ala Met Tyr Glu Leu
            100                 105                 110

Cys Gln Gly Met His Gln Ile Ser Leu Gln Phe Val Arg Leu Gln Leu
        115                 120                 125
```

Thr Phe Glu Glu Tyr Thr Ile Met Lys Val Leu Leu Leu Ser Thr
130 135 140

Ile Pro Lys Asp Gly Leu Lys Ser Gln Ala Ala Phe Glu Glu Met Arg
145 150 155 160

Thr Asn Tyr Ile Lys Glu Leu Arg Lys Met Val Thr Lys Cys Pro Asn
165 170 175

Asn Ser Gly Gln Ser Trp Gln Arg Phe Tyr Gln Leu Thr Lys Leu Leu
180 185 190

Asp Ser Met His Asp Leu Val Ser Asp Leu Leu Glu Phe Cys Phe Tyr
195 200 205

Thr Phe Arg Glu Ser His Ala Leu Lys Val Glu Phe Pro Ala Met Leu
210 215 220

Val Glu Ile Ile Ser Asp Gln Leu Pro Lys Val Glu Ser Gly Asn Ala
225 230 235 240

Lys Pro Leu Tyr Phe His Arg Lys
245

<210> 79
<211> 248
<212> PRT
<213> Homo sapiens

<400> 79

Ser Pro Val Met Val Leu Glu Asn Ile Glu Pro Glu Ile Val Tyr Ala
1 5 10 15

Gly Tyr Asp Ser Ser Lys Pro Asp Thr Ala Glu Asn Leu Leu Ser Thr
20 25 30

Leu Asn Arg Leu Ala Gly Lys Gln Met Ile Gln Val Val Lys Trp Ala
35 40 45

Lys Val Leu Pro Gly Phe Lys Asn Leu Pro Leu Glu Asp Gln Ile Thr
50 55 60

Leu Ile Gln Tyr Ser Trp Met Cys Leu Leu Ser Phe Ala Leu Ser Trp
65 70 75 80

Arg Ser Tyr Lys His Thr Asn Ser Gln Phe Leu Tyr Phe Ala Pro Asp
85 90 95

Leu Val Phe Asn Glu Glu Lys Met His Gln Ser Ala Met Tyr Glu Leu
100 105 110

Cys Gln Gly Met His Gln Ile Ser Leu Gln Phe Val Arg Leu Gln Leu

115 120 125

Thr Phe Glu Glu Tyr Thr Ile Met Lys Val Leu Leu Leu Ser Thr
130 135 140

Ile Pro Lys Asp Gly Leu Lys Ser Gln Ala Ala Phe Glu Glu Met Arg
145 150 155 160

Thr Asn Tyr Ile Lys Glu Leu Arg Lys Met Val Thr Lys Ala Pro Asn
165 170 175

Asn Ser Gly Gln Ser Trp Gln Arg Phe Tyr Gln Leu Thr Lys Leu Leu
180 185 190

Asp Ser Met His Asp Leu Val Ser Asp Leu Leu Glu Phe Cys Phe Tyr
195 200 205

Thr Phe Arg Glu Ser His Ala Leu Lys Val Glu Phe Pro Ala Met Leu
210 215 220

Val Glu Ile Ile Ser Asp Gln Leu Pro Lys Val Glu Ser Gly Asn Ala
225 230 235 240

Lys Pro Leu Tyr Phe His Arg Lys
245

<210> 80
<211> 248
<212> PRT
<213> Homo sapiens

<400> 80

Ser Pro Val Met Val Leu Glu Asn Ile Glu Pro Glu Ile Val Tyr Ala
1 5 10 15

Gly Tyr Asp Ser Ser Lys Pro Asp Thr Ala Glu Asn Leu Leu Ser Thr
20 25 30

Leu Asn Arg Leu Ala Gly Lys Gln Met Ile Gln Val Val Lys Trp Ala
35 40 45

Lys Val Leu Pro Gly Phe Lys Asn Leu Pro Leu Glu Asp Gln Ile Thr
50 55 60

Leu Ile Gln Tyr Ser Trp Met Cys Leu Leu Ser Phe Ala Leu Ser Trp
65 70 75 80

Arg Ser Tyr Lys His Thr Asn Ser Gln Phe Leu Tyr Phe Ala Pro Asp
85 90 95

Leu Val Phe Asn Glu Glu Lys Met His Gln Ser Ala Met Tyr Glu Leu
100 105 110

```
Cys Gln Gly Met His Gln Ile Ser Leu Gln Phe Val Arg Leu Gln Leu
        115                 120                 125

Thr Phe Glu Glu Tyr Thr Ile Met Lys Val Leu Leu Leu Leu Ser Thr
    130                 135                 140

Ile Pro Lys Asp Gly Leu Lys Ser Gln Ala Ala Phe Glu Glu Met Arg
145                 150                 155                 160

Thr Asn Tyr Ile Lys Glu Leu Arg Lys Met Val Thr Lys Ala Pro Asn
                165                 170                 175

Asn Ser Gly Gln Ser Trp Gln Arg Phe Tyr Gln Leu Thr Lys Leu Leu
            180                 185                 190

Asp Ser Met His Asp Leu Val Ser Asp Leu Leu Glu Phe Cys Phe Tyr
        195                 200                 205

Thr Phe Arg Glu Ser His Ala Leu Lys Val Glu Phe Pro Ala Met Leu
    210                 215                 220

Val Glu Ile Ile Ser Asp Gln Leu Pro Lys Val Glu Ser Gly Asn Ala
225                 230                 235                 240

Lys Pro Leu Tyr Phe His Arg Lys
                245
```

<210> 81
<211> 248
<212> PRT
<213> Homo sapiens

<400> 81

```
Ser Pro Val Met Val Leu Glu Asn Ile Glu Pro Glu Ile Val Tyr Ala
1               5                   10                  15

Gly Tyr Asp Ser Ser Lys Pro Asp Thr Ala Glu Asn Leu Leu Ser Thr
            20                  25                  30

Leu Asn Arg Leu Ala Gly Lys Gln Met Ile Gln Val Val Lys Trp Ala
        35                  40                  45

Lys Val Leu Pro Gly Phe Lys Asn Leu Pro Leu Glu Asp Gln Ile Thr
    50                  55                  60

Leu Ile Gln Tyr Ser Trp Met Cys Leu Ser Ser Phe Ala Leu Ser Trp
65                  70                  75                  80

Arg Ser Tyr Lys His Thr Asn Ser Gln Phe Leu Tyr Phe Ala Pro Asp
                85                  90                  95
```

Leu Val Phe Asn Glu Glu Lys Met His Gln Ser Ala Met Tyr Glu Leu
100 105 110

Cys Gln Gly Met His Gln Ile Ser Leu Gln Phe Val Arg Leu Gln Leu
115 120 125

Thr Phe Glu Glu Tyr Thr Ile Met Lys Val Leu Leu Leu Leu Ser Thr
130 135 140

Ile Pro Lys Asp Gly Leu Lys Ser Gln Ala Ala Phe Glu Glu Met Arg
145 150 155 160

Thr Asn Tyr Ile Lys Glu Leu Arg Lys Met Val Thr Lys Ala Pro Asn
165 170 175

Asn Ser Gly Gln Ser Trp Gln Arg Phe Tyr Gln Leu Thr Lys Leu Leu
180 185 190

Asp Ser Met His Asp Leu Val Ser Asp Leu Leu Glu Phe Cys Phe Tyr
195 200 205

Thr Phe Arg Glu Ser His Ala Leu Lys Val Glu Phe Pro Ala Met Leu
210 215 220

Val Glu Ile Ile Ser Asp Gln Leu Pro Lys Val Glu Ser Gly Asn Ala
225 230 235 240

Lys Pro Leu Tyr Phe His Arg Lys
245

<210> 82
<211> 248
<212> PRT
<213> Homo sapiens

<400> 82

Ser Ala Ala Val Ile Leu Glu Asn Ile Glu Pro Glu Ile Val Tyr Ala
1 5 10 15

Gly Tyr Asp Asn Thr Gln Pro Asp Thr Ala Glu Asn Leu Leu Ser Ser
20 25 30

Leu Asn Gln Leu Ala Gly Lys Gln Met Val Gln Val Val Lys Trp Ala
35 40 45

Lys Val Ile Pro Gly Phe Arg Asn Leu Pro Leu Glu Asp Gln Ile Thr
50 55 60

Leu Ile Gln Tyr Ser Trp Met Cys Leu Ser Ser Phe Ala Leu Ser Trp
65 70 75 80

```
Arg Ser Tyr Lys His Ala Ser Ser Gln Phe Leu Tyr Phe Ala Pro Asp
                85                  90                  95

Leu Ile Phe Asn Glu Glu Arg Met Arg Gln Ser Ala Met Tyr Asp Leu
            100                 105                 110

Cys Gln Gly Met Gln Gln Ile Ser Leu Glu Phe Ser Arg Leu Gln Leu
        115                 120                 125

Thr Phe Glu Glu Tyr Thr Leu Met Lys Val Leu Leu Leu Leu Ser Thr
    130                 135                 140

Val Pro Lys Asp Gly Leu Lys Cys Gln Ala Ala Phe Glu Glu Met Arg
145                 150                 155                 160

Val Asn Tyr Ile Lys Glu Leu Arg Lys Val Leu Leu Lys Ser Pro His
                165                 170                 175

Asn Ser Gly Gln Ser Trp Gln Arg Tyr Phe Gln Leu Thr Lys Leu Leu
            180                 185                 190

Asp Ser Met Gln Asp Leu Val Gly Asp Leu Leu Glu Phe Cys Phe Tyr
        195                 200                 205

Thr Phe Arg Glu Ser Gln Ala Leu Lys Val Glu Phe Pro Ala Met Leu
    210                 215                 220

Val Glu Ile Ile Ser Asp Gln Leu Pro Lys Val Glu Ser Gly Ile Ala
225                 230                 235                 240

Lys Pro Leu Tyr Phe His Arg Lys
                245
```

<210> 83
<211> 248
<212> PRT
<213> Homo sapiens

<400> 83

```
Ser Ile Cys Ser Val Leu Glu Leu Ile Glu Pro Glu Val Val Phe Ala
1               5                   10                  15

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

Leu Asn Gln Leu Ala Gly Lys Gln Met Ile Arg Val Val Lys Trp Ala
        35                  40                  45

Lys Val Leu Pro Gly Phe Arg Gly Leu Pro Ile Glu Asp Gln Ile Thr
    50                  55                  60

Leu Ile Gln Tyr Ser Trp Met Cys Leu Ser Ser Phe Ser Leu Ser Trp
```

65 70 75 80

Arg Ser Tyr Lys His Thr Asn Gly Gln Met Leu Tyr Phe Ala Pro Asp
85 90 95

Leu Val Phe Asn Glu Asp Arg Met Gln Gln Ser Ala Met Tyr Asp Leu
100 105 110

Cys Leu Gly Met Arg Gln Val Ser Gln Glu Phe Val Arg Leu Gln Leu
115 120 125

Thr Tyr Gln Glu Phe Leu Ser Met Lys Val Leu Leu Leu Leu Ser Thr
130 135 140

Val Pro Lys Glu Gly Leu Lys Asn Gln Ala Ala Phe Glu Glu Met Arg
145 150 155 160

Val Asn Tyr Ile Lys Glu Leu Arg Arg Ser Val Gly Lys Ala Pro Thr
165 170 175

Thr Leu Asp Arg Arg Gly Asn Arg Ser Ser Gln Leu Thr Lys Leu Leu
180 185 190

Asp Ala Met His Asp Leu Gly Gly Glu Leu Leu Asp Phe Cys Phe Tyr
195 200 205

Thr Phe Arg Glu Ser Gln Ala Leu Lys Val Glu Phe Pro Glu Met Leu
210 215 220

Val Glu Ile Ile Ser Asp Gln Ile Pro Lys Val Glu Ser Gly Asn Thr
225 230 235 240

His Thr Leu Tyr Phe His Lys Lys
245

<210> 84
<211> 329
<212> PRT
<213> Homo sapiens

<400> 84

Ser Ile Cys Ser Ile Leu Glu Leu Ile Glu Pro Glu Glu Val Tyr Ser
1 5 10 15

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

Leu Asn Arg Leu Ala Gly Lys Gln Met Val Arg Met Val Lys Trp Ala
35 40 45

Lys Val Leu Pro Gly Phe Arg Gly Leu Pro Ile Glu Asp Gln Ile Thr
50 55 60

```
Leu Ile Gln Tyr Ser Trp Met Cys Leu Ser Ser Phe Cys Leu Ser Trp
65                  70                  75                  80

Arg Ser Tyr Lys His Thr Asn Gly Gln Met Leu Tyr Phe Ala Pro Asp
                85                  90                  95

Leu Ile Phe Asn Glu Glu Arg Met Arg Gln Ser Ala Met Tyr Asp Leu
            100                 105                 110

Cys Leu Gly Met Arg Gln Val Ser Gln Glu Phe Leu Arg Leu Gln Leu
        115                 120                 125

Ser Tyr Asp Glu Phe Leu Ser Met Lys Val Leu Leu Leu Leu Ser Thr
    130                 135                 140

Gly Leu Gly Arg Leu Thr Leu Phe Gly Phe His Cys Ser Lys Gln Leu
145                 150                 155                 160

Pro Pro Ser Pro Pro His Met Arg Thr Val Pro Lys Glu Gly Leu Lys
                165                 170                 175

Asn Gln Ala Ala Phe Glu Glu Met Arg Leu Asn Tyr Ile Lys Glu Leu
            180                 185                 190

Arg Arg Ser Val Gly Lys Ala Thr Asn Asn Ser Gly Gln Thr Trp Gln
        195                 200                 205

Arg Phe Phe Gln Leu Thr Lys Leu Leu Asp Ala Met His Asp Val Ser
    210                 215                 220

Thr Leu Cys Leu Pro Arg His Ala Ala Pro Leu Gly Arg Pro His Asp
225                 230                 235                 240

Thr Thr Gly Phe Pro Pro Ser Phe Gln Glu Ser Pro His Leu His Thr
                245                 250                 255

Gln Ser Lys Lys Ala Ala Gln Thr Pro Cys Glu Thr Ala Ser Lys Tyr
            260                 265                 270

Met Cys Glu Tyr Ser Lys Leu Val Gly Asn Leu Leu Asp Phe Cys Phe
        275                 280                 285

Tyr Thr Phe Arg Glu Ser Gln Val Leu Lys Val Glu Phe Pro Glu Met
    290                 295                 300

Leu Val Glu Ile Ile Ser Asp Gln Ile Pro Lys Val Glu Ser Gly Leu
305                 310                 315                 320

Thr His Thr Ile Tyr Phe His Lys Lys
                325
```

<210> 85
<211> 919
<212> PRT
<213> Homo sapiens

<400> 85

```
Met Glu Val Gln Leu Gly Leu Gly Arg Val Tyr Pro Arg Pro Pro Ser
1               5                   10                  15

Lys Thr Tyr Arg Gly Ala Phe Gln Asn Leu Phe Gln Ser Val Arg Glu
            20                  25                  30

Val Ile Gln Asn Pro Gly Pro Arg His Pro Glu Ala Ala Ser Ala Ala
        35                  40                  45

Pro Pro Gly Ala Ser Leu Leu Leu Leu Gln Gln Gln Gln Gln Gln Gln
    50                  55                  60

Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln Glu Thr
65                  70                  75                  80

Ser Pro Arg Gln Gln Gln Gln Gln Gln Gly Glu Asp Gly Ser Pro Gln
                85                  90                  95

Ala His Arg Arg Gly Pro Thr Gly Tyr Leu Val Leu Asp Glu Glu Gln
            100                 105                 110

Gln Pro Ser Gln Pro Gln Ser Ala Leu Glu Cys His Pro Glu Arg Gly
        115                 120                 125

Cys Val Pro Glu Pro Gly Ala Ala Val Ala Ala Ser Lys Gly Leu Pro
    130                 135                 140

Gln Gln Leu Pro Ala Pro Pro Asp Glu Asp Asp Ser Ala Ala Pro Ser
145                 150                 155                 160

Thr Leu Ser Leu Leu Gly Pro Thr Phe Pro Gly Leu Ser Ser Cys Ser
                165                 170                 175

Ala Asp Leu Lys Asp Ile Leu Ser Glu Ala Ser Thr Met Gln Leu Leu
            180                 185                 190

Gln Gln Gln Gln Gln Glu Ala Val Ser Glu Gly Ser Ser Ser Gly Arg
        195                 200                 205

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

Gly Gly Thr Ser Thr Ile Ser Asp Asn Ala Lys Glu Leu Cys Lys Ala
225                 230                 235                 240
```

```
Val Ser Val Ser Met Gly Leu Gly Val Glu Ala Leu Glu His Leu Ser
                245                 250                 255

Pro Gly Glu Gln Leu Arg Gly Asp Cys Met Tyr Ala Pro Leu Leu Gly
            260                 265                 270

Val Pro Pro Ala Val Arg Pro Thr Pro Cys Ala Pro Leu Ala Glu Cys
        275                 280                 285

Lys Gly Ser Leu Leu Asp Asp Ser Ala Gly Lys Ser Thr Glu Asp Thr
    290                 295                 300

Ala Glu Tyr Ser Pro Phe Lys Gly Gly Tyr Thr Lys Gly Leu Glu Gly
305                 310                 315                 320

Glu Ser Leu Gly Cys Ser Gly Ser Ala Ala Ala Gly Ser Ser Gly Thr
                325                 330                 335

Leu Glu Leu Pro Ser Thr Leu Ser Leu Tyr Lys Ser Gly Ala Leu Asp
            340                 345                 350

Glu Ala Ala Ala Tyr Gln Ser Arg Asp Tyr Tyr Asn Phe Pro Leu Ala
        355                 360                 365

Leu Ala Gly Pro Pro Pro Pro Pro Pro Pro Pro His Pro His Ala Arg
    370                 375                 380

Ile Lys Leu Glu Asn Pro Leu Asp Tyr Gly Ser Ala Trp Ala Ala Ala
385                 390                 395                 400

Ala Ala Gln Cys Arg Tyr Gly Asp Leu Ala Ser Leu His Gly Ala Gly
                405                 410                 415

Ala Ala Gly Pro Gly Ser Gly Ser Pro Ser Ala Ala Ala Ser Ser Ser
            420                 425                 430

Trp His Thr Leu Phe Thr Ala Glu Glu Gly Gln Leu Tyr Gly Pro Cys
        435                 440                 445

Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly
    450                 455                 460

Gly Gly Gly Gly Gly Gly Gly Gly Glu Ala Gly Ala Val Ala Pro Tyr
465                 470                 475                 480

Gly Tyr Thr Arg Pro Pro Gln Gly Leu Ala Gly Gln Glu Ser Asp Phe
                485                 490                 495

Thr Ala Pro Asp Val Trp Tyr Pro Gly Gly Met Val Ser Arg Val Pro
            500                 505                 510
```

```
Tyr Pro Ser Pro Thr Cys Val Lys Ser Glu Met Gly Pro Trp Met Asp
        515                 520                 525

Ser Tyr Ser Gly Pro Tyr Gly Asp Met Arg Leu Glu Thr Ala Arg Asp
    530                 535                 540

His Val Leu Pro Ile Asp Tyr Tyr Phe Pro Pro Gln Lys Thr Cys Leu
545                 550                 555                 560

Ile Cys Gly Asp Glu Ala Ser Gly Cys His Tyr Gly Ala Leu Thr Cys
                565                 570                 575

Gly Ser Cys Lys Val Phe Phe Lys Arg Ala Ala Glu Gly Lys Gln Lys
            580                 585                 590

Tyr Leu Cys Ala Ser Arg Asn Asp Cys Thr Ile Asp Lys Phe Arg Arg
        595                 600                 605

Lys Asn Cys Pro Ser Cys Arg Leu Arg Lys Cys Tyr Glu Ala Gly Met
    610                 615                 620

Thr Leu Gly Ala Arg Lys Leu Lys Lys Leu Gly Asn Leu Lys Leu Gln
625                 630                 635                 640

Glu Glu Gly Glu Ala Ser Ser Thr Thr Ser Pro Thr Glu Glu Thr Thr
                645                 650                 655

Gln Lys Leu Thr Val Ser His Ile Glu Gly Tyr Glu Cys Gln Pro Ile
            660                 665                 670

Phe Leu Asn Val Leu Glu Ala Ile Glu Pro Gly Val Val Cys Ala Gly
        675                 680                 685

His Asp Asn Asn Gln Pro Asp Ser Phe Ala Ala Leu Leu Ser Ser Leu
    690                 695                 700

Asn Glu Leu Gly Glu Arg Gln Leu Val His Val Val Lys Trp Ala Lys
705                 710                 715                 720

Ala Leu Pro Gly Phe Arg Asn Leu His Val Asp Asp Gln Met Ala Val
                725                 730                 735

Ile Gln Tyr Ser Trp Met Gly Leu Met Val Phe Ala Met Gly Trp Arg
            740                 745                 750

Ser Phe Thr Asn Val Asn Ser Arg Met Leu Tyr Phe Ala Pro Asp Leu
        755                 760                 765

Val Phe Asn Glu Tyr Arg Met His Lys Ser Arg Met Tyr Ser Gln Cys
    770                 775                 780
```

Val Arg Met Arg His Leu Ser Gln Glu Phe Gly Trp Leu Gln Ile Thr
785 790 795 800

Pro Gln Glu Phe Leu Cys Met Lys Ala Leu Leu Leu Phe Ser Ile Ile
805 810 815

Pro Val Asp Gly Leu Lys Asn Gln Lys Phe Phe Asp Glu Leu Arg Met
820 825 830

Asn Tyr Ile Lys Glu Leu Asp Arg Ile Ile Ala Cys Lys Arg Lys Asn
835 840 845

Pro Thr Ser Cys Ser Arg Arg Phe Tyr Gln Leu Thr Lys Leu Leu Asp
850 855 860

Ser Val Gln Pro Ile Ala Arg Glu Leu His Gln Phe Thr Phe Asp Leu
865 870 875 880

Leu Ile Lys Ser His Met Val Ser Val Asp Phe Pro Glu Met Met Ala
885 890 895

Glu Ile Ile Ser Val Gln Val Pro Lys Ile Leu Ser Gly Lys Val Lys
900 905 910

Pro Ile Tyr Phe His Thr Gln
915

<210> 86
<211> 301
<212> PRT
<213> Homo sapiens

<400> 86

Cys Tyr Glu Ala Gly Met Thr Leu Gly Ala Arg Lys Leu Lys Lys Leu
1 5 10 15

Gly Asn Leu Lys Leu Gln Glu Glu Gly Glu Ala Ser Ser Thr Thr Ser
20 25 30

Pro Thr Glu Glu Thr Thr Gln Lys Leu Thr Val Ser His Ile Glu Gly
35 40 45

Tyr Glu Cys Gln Pro Ile Phe Leu Asn Val Leu Glu Ala Ile Glu Pro
50 55 60

Gly Val Val Cys Ala Gly His Asp Asn Asn Gln Pro Asp Ser Phe Ala
65 70 75 80

Ala Leu Leu Ser Ser Leu Asn Glu Leu Gly Glu Arg Gln Leu Val His
85 90 95

Val Val Lys Trp Ala Lys Ala Leu Pro Gly Phe Arg Asn Leu His Val
100 105 110

Asp Asp Gln Met Ala Val Ile Gln Tyr Ser Trp Met Gly Leu Met Val
115 120 125

Phe Ala Met Gly Trp Arg Ser Phe Thr Asn Val Asn Ser Arg Met Leu
130 135 140

Tyr Phe Ala Pro Asp Leu Val Phe Asn Glu Tyr Arg Met His Lys Ser
145 150 155 160

Arg Met Tyr Ser Gln Cys Val Arg Met Arg His Leu Ser Gln Glu Phe
165 170 175

Gly Trp Leu Gln Ile Thr Pro Gln Glu Phe Leu Cys Met Lys Ala Leu
180 185 190

Leu Leu Phe Ser Ile Ile Pro Val Asp Gly Leu Lys Asn Gln Lys Phe
195 200 205

Phe Asp Glu Leu Arg Met Asn Tyr Ile Lys Glu Leu Asp Arg Ile Ile
210 215 220

Ala Cys Lys Arg Lys Asn Pro Thr Ser Cys Ser Arg Arg Phe Tyr Gln
225 230 235 240

Leu Thr Lys Leu Leu Asp Ser Val Gln Pro Ile Ala Arg Glu Leu His
245 250 255

Gln Phe Thr Phe Asp Leu Leu Ile Lys Ser His Met Val Ser Val Asp
260 265 270

Phe Pro Glu Met Met Ala Glu Ile Ile Ser Val Gln Val Pro Lys Ile
275 280 285

Leu Ser Gly Lys Val Lys Pro Ile Tyr Phe His Thr Gln
290 295 300

<210> 87
<211> 230
<212> PRT
<213> Homo sapiens

<400> 87

Asp Asn Asn Gln Pro Asp Ser Phe Ala Ala Leu Leu Ser Ser Leu Asn
1 5 10 15

Glu Leu Gly Glu Arg Gln Leu Val His Val Val Lys Trp Ala Lys Ala
20 25 30

Leu Pro Gly Phe Arg Asn Leu His Val Asp Asp Gln Met Ala Val Ile

35 40 45

Gln Tyr Ser Trp Met Gly Leu Met Val Phe Ala Met Gly Trp Arg Ser
50 55 60

Phe Thr Asn Val Asn Ser Arg Met Leu Tyr Phe Ala Pro Asp Leu Val
65 70 75 80

Phe Asn Glu Tyr Arg Met His Lys Ser Arg Met Tyr Ser Gln Cys Val
85 90 95

Arg Met Arg His Leu Ser Gln Glu Phe Gly Trp Leu Gln Ile Thr Pro
100 105 110

Gln Glu Phe Leu Cys Met Lys Ala Leu Leu Leu Phe Ser Ile Ile Pro
115 120 125

Val Asp Gly Leu Lys Asn Gln Lys Phe Phe Asp Glu Leu Arg Met Asn
130 135 140

Tyr Ile Lys Glu Leu Asp Arg Ile Ile Ala Cys Lys Arg Lys Asn Pro
145 150 155 160

Thr Ser Cys Ser Arg Arg Phe Tyr Gln Leu Thr Lys Leu Leu Asp Ser
165 170 175

Val Gln Pro Ile Ala Arg Glu Leu His Gln Phe Thr Phe Asp Leu Leu
180 185 190

Ile Lys Ser His Met Val Ser Val Asp Phe Pro Glu Met Met Ala Glu
195 200 205

Ile Ile Ser Val Gln Val Pro Lys Ile Leu Ser Gly Lys Val Lys Pro
210 215 220

Ile Tyr Phe His Thr Gln
225 230

<210> 88
<211> 301
<212> PRT
<213> Homo sapiens

<400> 88

Cys Tyr Glu Ala Gly Met Thr Leu Gly Ala Arg Lys Leu Lys Lys Leu
1 5 10 15

Gly Asn Leu Lys Leu Gln Glu Glu Gly Glu Ala Ser Ser Thr Thr Ser
20 25 30

Pro Thr Glu Glu Thr Thr Gln Lys Leu Thr Val Ser His Ile Glu Gly
35 40 45

```
Tyr Glu Cys Gln Pro Ile Phe Leu Asn Val Leu Glu Ala Ile Glu Pro
    50                  55                  60

Gly Val Val Cys Ala Gly His Asp Asn Asn Gln Pro Asp Ser Phe Ala
65                  70                  75                  80

Ala Leu Leu Ser Ser Leu Asn Glu Leu Gly Glu Arg Gln Leu Val His
                85                  90                  95

Val Val Lys Trp Ala Lys Ala Leu Pro Gly Phe Arg Asn Leu His Val
            100                 105                 110

Asp Asp Gln Met Ala Val Ile Gln Tyr Ser Trp Met Gly Leu Met Val
        115                 120                 125

Phe Ala Met Gly Trp Arg Ser Phe Thr Asn Val Asn Ser Arg Met Leu
    130                 135                 140

Tyr Phe Ala Pro Asp Leu Val Phe Asn Glu Tyr Arg Met His Lys Ser
145                 150                 155                 160

Arg Met Tyr Ser Gln Cys Val Arg Met Arg His Leu Ser Gln Glu Phe
                165                 170                 175

Gly Trp Leu Gln Ile Thr Pro Gln Glu Phe Leu Cys Met Lys Ala Leu
            180                 185                 190

Leu Leu Phe Ser Ile Ile Pro Val Asp Gly Leu Lys Asn Gln Lys Phe
        195                 200                 205

Phe Asp Glu Leu Arg Met Asn Tyr Ile Lys Glu Leu Asp Arg Ile Ile
    210                 215                 220

Ala Cys Lys Arg Lys Asn Pro Thr Ser Cys Ser Arg Arg Phe Tyr Gln
225                 230                 235                 240

Leu Thr Lys Leu Leu Asp Ser Val Gln Pro Ile Ala Arg Glu Leu His
                245                 250                 255

Gln Phe Ala Phe Asp Leu Leu Ile Lys Ser His Met Val Ser Val Asp
            260                 265                 270

Phe Pro Glu Met Met Ala Glu Ile Ile Ser Val Gln Val Pro Lys Ile
        275                 280                 285

Leu Ser Gly Lys Val Lys Pro Ile Tyr Phe His Thr Gln
    290                 295                 300
```

<210> 89
<211> 230

<212> PRT
<213> Homo sapiens

<400> 89

```
Asp Asn Asn Gln Pro Asp Ser Phe Ala Ala Leu Leu Ser Ser Leu Asn
1               5                  10                  15

Glu Leu Gly Glu Arg Gln Leu Val His Val Val Lys Trp Ala Lys Ala
            20                  25                  30

Leu Pro Gly Phe Arg Asn Leu His Val Asp Asp Gln Met Ala Val Ile
        35                  40                  45

Gln Tyr Ser Trp Met Gly Leu Met Val Phe Ala Met Gly Trp Arg Ser
    50                  55                  60

Phe Thr Asn Val Asn Ser Arg Met Leu Tyr Phe Ala Pro Asp Leu Val
65                  70                  75                  80

Phe Asn Glu Tyr Arg Met His Lys Ser Arg Met Tyr Ser Gln Cys Val
                85                  90                  95

Arg Met Arg His Leu Ser Gln Glu Phe Gly Trp Leu Gln Ile Thr Pro
            100                 105                 110

Gln Glu Phe Leu Cys Met Lys Ala Leu Leu Leu Phe Ser Ile Ile Pro
        115                 120                 125

Val Asp Gly Leu Lys Asn Gln Lys Phe Phe Asp Glu Leu Arg Met Asn
    130                 135                 140

Tyr Ile Lys Glu Leu Asp Arg Ile Ile Ala Cys Lys Arg Lys Asn Pro
145                 150                 155                 160

Thr Ser Cys Ser Arg Arg Phe Tyr Gln Leu Thr Lys Leu Leu Asp Ser
                165                 170                 175

Val Gln Pro Ile Ala Arg Glu Leu His Gln Phe Ala Phe Asp Leu Leu
            180                 185                 190

Ile Lys Ser His Met Val Ser Val Asp Phe Pro Glu Met Met Ala Glu
        195                 200                 205

Ile Ile Ser Val Gln Val Pro Lys Ile Leu Ser Gly Lys Val Lys Pro
    210                 215                 220

Ile Tyr Phe His Thr Gln
225                 230
```

<210> 90
<211> 301
<212> PRT

<213> Homo sapiens

<400> 90

```
Cys Tyr Glu Ala Gly Met Thr Leu Gly Ala Arg Lys Leu Lys Lys Leu
1               5                  10                  15

Gly Asn Leu Lys Leu Gln Glu Glu Gly Glu Ala Ser Ser Thr Thr Ser
            20                  25                  30

Pro Thr Glu Glu Thr Thr Gln Lys Leu Thr Val Ser His Ile Glu Gly
        35                  40                  45

Tyr Glu Cys Gln Pro Ile Phe Leu Asn Val Leu Glu Ala Ile Glu Pro
    50                  55                  60

Gly Val Val Cys Ala Gly His Asp Asn Asn Gln Pro Asp Ser Phe Ala
65                  70                  75                  80

Ala Leu Leu Ser Ser Leu Asn Glu Leu Gly Glu Arg Gln Leu Val His
                85                  90                  95

Val Val Lys Trp Ala Lys Ala Leu Pro Gly Phe Arg Asn Leu His Val
            100                 105                 110

Asp Asp Gln Met Ala Val Ile Gln Tyr Ser Trp Met Gly Leu Met Val
        115                 120                 125

Phe Ala Met Gly Trp Arg Ser Phe Thr Asn Val Asn Ser Arg Met Leu
    130                 135                 140

Tyr Phe Ala Pro Asp Leu Val Phe Asn Glu Tyr Arg Met His Lys Ser
145                 150                 155                 160

Arg Met Tyr Ser Gln Cys Val Arg Met Arg His Leu Ser Gln Glu Phe
                165                 170                 175

Gly Trp Leu Gln Ile Thr Pro Gln Glu Phe Leu Cys Met Lys Ala Leu
            180                 185                 190

Leu Leu Phe Ser Ile Ile Pro Val Asp Gly Leu Lys Asn Gln Lys Phe
        195                 200                 205

Phe Asp Glu Leu Arg Met Asn Tyr Ile Lys Glu Leu Asp Arg Ile Ile
    210                 215                 220

Ala Cys Lys Arg Lys Asn Pro Thr Ser Cys Ser Arg Arg Phe Tyr Gln
225                 230                 235                 240

Leu Thr Lys Leu Leu Asp Ser Val Gln Pro Ile Ala Arg Glu Leu His
                245                 250                 255
```

```
Gln Leu Thr Phe Asp Leu Leu Ile Lys Ser His Met Val Ser Val Asp
            260                 265                 270

Phe Pro Glu Met Met Ala Glu Ile Ile Ser Val Gln Val Pro Lys Ile
        275                 280                 285

Leu Ser Gly Lys Val Lys Pro Ile Tyr Phe His Thr Gln
    290                 295                 300
```

<210> 91
<211> 230
<212> PRT
<213> Homo sapiens

<400> 91

```
Asp Asn Asn Gln Pro Asp Ser Phe Ala Ala Leu Leu Ser Ser Leu Asn
1               5                   10                  15

Glu Leu Gly Glu Arg Gln Leu Val His Val Val Lys Trp Ala Lys Ala
            20                  25                  30

Leu Pro Gly Phe Arg Asn Leu His Val Asp Asp Gln Met Ala Val Ile
        35                  40                  45

Gln Tyr Ser Trp Met Gly Leu Met Val Phe Ala Met Gly Trp Arg Ser
    50                  55                  60

Phe Thr Asn Val Asn Ser Arg Met Leu Tyr Phe Ala Pro Asp Leu Val
65                  70                  75                  80

Phe Asn Glu Tyr Arg Met His Lys Ser Arg Met Tyr Ser Gln Cys Val
                85                  90                  95

Arg Met Arg His Leu Ser Gln Glu Phe Gly Trp Leu Gln Ile Thr Pro
            100                 105                 110

Gln Glu Phe Leu Cys Met Lys Ala Leu Leu Leu Phe Ser Ile Ile Pro
        115                 120                 125

Val Asp Gly Leu Lys Asn Gln Lys Phe Phe Asp Glu Leu Arg Met Asn
    130                 135                 140

Tyr Ile Lys Glu Leu Asp Arg Ile Ile Ala Cys Lys Arg Lys Asn Pro
145                 150                 155                 160

Thr Ser Cys Ser Arg Arg Phe Tyr Gln Leu Thr Lys Leu Leu Asp Ser
                165                 170                 175

Val Gln Pro Ile Ala Arg Glu Leu His Gln Leu Thr Phe Asp Leu Leu
            180                 185                 190

Ile Lys Ser His Met Val Ser Val Asp Phe Pro Glu Met Met Ala Glu
```

195 200 205

Ile Ile Ser Val Gln Val Pro Lys Ile Leu Ser Gly Lys Val Lys Pro
210 215 220

Ile Tyr Phe His Thr Gln
225 230

<210> 92
<211> 301
<212> PRT
<213> Homo sapiens

<400> 92

Cys Tyr Glu Ala Gly Met Thr Leu Gly Ala Arg Lys Leu Lys Lys Leu
1 5 10 15

Gly Asn Leu Lys Leu Gln Glu Glu Gly Glu Ala Ser Ser Thr Thr Ser
20 25 30

Pro Thr Glu Glu Thr Thr Gln Lys Leu Thr Val Ser His Ile Glu Gly
35 40 45

Tyr Glu Cys Gln Pro Ile Phe Leu Asn Val Leu Glu Ala Ile Glu Pro
50 55 60

Gly Val Val Cys Ala Gly His Asp Asn Asn Gln Pro Asp Ser Phe Ala
65 70 75 80

Ala Leu Leu Ser Ser Leu Asn Glu Leu Gly Glu Arg Gln Leu Val His
85 90 95

Val Val Lys Trp Ala Lys Ala Leu Pro Gly Phe Arg Asn Leu His Val
100 105 110

Asp Asp Gln Met Ala Val Ile Gln Tyr Ser Trp Met Gly Leu Met Val
115 120 125

Phe Ala Met Gly Trp Arg Ser Phe Thr Asn Val Asn Ser Arg Met Leu
130 135 140

Tyr Phe Ala Pro Asp Leu Val Phe Asn Glu Tyr Arg Met His Lys Ser
145 150 155 160

Arg Met Tyr Ser Gln Cys Val Arg Met Arg His Leu Ser Gln Glu Phe
165 170 175

Gly Trp Leu Gln Ile Thr Pro Gln Glu Phe Leu Cys Met Lys Ala Leu
180 185 190

Leu Leu Phe Ser Ile Ile Pro Val Asp Gly Leu Lys Asn Gln Lys Phe
195 200 205

```
Phe Asp Glu Leu Arg Met Asn Tyr Ile Lys Glu Leu Asp Arg Ile Ile
    210                 215                 220

Ala Cys Lys Arg Lys Asn Pro Thr Ser Cys Ser Arg Arg Phe Tyr Gln
225                 230                 235                 240

Leu Thr Lys Leu Leu Asp Ser Val Gln Pro Ile Ala Arg Glu Leu His
                245                 250                 255

Gln Leu Ala Phe Asp Leu Leu Ile Lys Ser His Met Val Ser Val Asp
            260                 265                 270

Phe Pro Glu Met Met Ala Glu Ile Ile Ser Val Gln Val Pro Lys Ile
        275                 280                 285

Leu Ser Gly Lys Val Lys Pro Ile Tyr Phe His Thr Gln
    290                 295                 300


<210>  93
<211>  230
<212>  PRT
<213>  Homo sapiens

<400>  93

Asp Asn Asn Gln Pro Asp Ser Phe Ala Ala Leu Leu Ser Ser Leu Asn
1               5                   10                  15

Glu Leu Gly Glu Arg Gln Leu Val His Val Val Lys Trp Ala Lys Ala
            20                  25                  30

Leu Pro Gly Phe Arg Asn Leu His Val Asp Asp Gln Met Ala Val Ile
        35                  40                  45

Gln Tyr Ser Trp Met Gly Leu Met Val Phe Ala Met Gly Trp Arg Ser
    50                  55                  60

Phe Thr Asn Val Asn Ser Arg Met Leu Tyr Phe Ala Pro Asp Leu Val
65                  70                  75                  80

Phe Asn Glu Tyr Arg Met His Lys Ser Arg Met Tyr Ser Gln Cys Val
                85                  90                  95

Arg Met Arg His Leu Ser Gln Glu Phe Gly Trp Leu Gln Ile Thr Pro
            100                 105                 110

Gln Glu Phe Leu Cys Met Lys Ala Leu Leu Leu Phe Ser Ile Ile Pro
        115                 120                 125

Val Asp Gly Leu Lys Asn Gln Lys Phe Phe Asp Glu Leu Arg Met Asn
    130                 135                 140
```

```
Tyr Ile Lys Glu Leu Asp Arg Ile Ile Ala Cys Lys Arg Lys Asn Pro
145                 150                 155                 160

Thr Ser Cys Ser Arg Arg Phe Tyr Gln Leu Thr Lys Leu Leu Asp Ser
                165                 170                 175

Val Gln Pro Ile Ala Arg Glu Leu His Gln Leu Ala Phe Asp Leu Leu
            180                 185                 190

Ile Lys Ser His Met Val Ser Val Asp Phe Pro Glu Met Met Ala Glu
        195                 200                 205

Ile Ile Ser Val Gln Val Pro Lys Ile Leu Ser Gly Lys Val Lys Pro
    210                 215                 220

Ile Tyr Phe His Thr Gln
225                 230
```

<210> 94
<211> 933
<212> PRT
<213> Homo sapiens

<400> 94

```
Met Thr Glu Leu Lys Ala Lys Gly Pro Arg Ala Pro His Val Ala Gly
1               5                   10                  15

Gly Pro Pro Ser Pro Glu Val Gly Ser Pro Leu Leu Cys Arg Pro Ala
            20                  25                  30

Ala Gly Pro Phe Pro Gly Ser Gln Thr Ser Asp Thr Leu Pro Glu Val
        35                  40                  45

Ser Ala Ile Pro Ile Ser Leu Asp Gly Leu Leu Phe Pro Arg Pro Cys
    50                  55                  60

Gln Gly Gln Asp Pro Ser Asp Glu Lys Thr Gln Asp Gln Gln Ser Leu
65                  70                  75                  80

Ser Asp Val Glu Gly Ala Tyr Ser Arg Ala Glu Ala Thr Arg Gly Ala
                85                  90                  95

Gly Gly Ser Ser Ser Ser Pro Pro Glu Lys Asp Ser Gly Leu Leu Asp
            100                 105                 110

Ser Val Leu Asp Thr Leu Leu Ala Pro Ser Gly Pro Gly Gln Ser Gln
        115                 120                 125

Pro Ser Pro Pro Ala Cys Glu Val Thr Ser Ser Trp Cys Leu Phe Gly
    130                 135                 140
```

```
Pro Glu Leu Pro Glu Asp Pro Pro Ala Ala Pro Ala Thr Gln Arg Val
145                 150                 155                 160

Leu Ser Pro Leu Met Ser Arg Ser Gly Cys Lys Val Gly Asp Ser Ser
                165                 170                 175

Gly Thr Ala Ala Ala His Lys Val Leu Pro Arg Gly Leu Ser Pro Ala
            180                 185                 190

Arg Gln Leu Leu Leu Pro Ala Ser Glu Ser Pro His Trp Ser Gly Ala
        195                 200                 205

Pro Val Lys Pro Ser Pro Gln Ala Ala Ala Val Glu Val Glu Glu Glu
    210                 215                 220

Asp Gly Ser Glu Ser Glu Glu Ser Ala Gly Pro Leu Leu Lys Gly Lys
225                 230                 235                 240

Pro Arg Ala Leu Gly Gly Ala Ala Ala Gly Gly Gly Ala Ala Ala Val
                245                 250                 255

Pro Pro Gly Ala Ala Ala Gly Gly Val Ala Leu Val Pro Lys Glu Asp
            260                 265                 270

Ser Arg Phe Ser Ala Pro Arg Val Ala Leu Val Glu Gln Asp Ala Pro
        275                 280                 285

Met Ala Pro Gly Arg Ser Pro Leu Ala Thr Thr Val Met Asp Phe Ile
    290                 295                 300

His Val Pro Ile Leu Pro Leu Asn His Ala Leu Leu Ala Ala Arg Thr
305                 310                 315                 320

Arg Gln Leu Leu Glu Asp Glu Ser Tyr Asp Gly Gly Ala Gly Ala Ala
                325                 330                 335

Ser Ala Phe Ala Pro Pro Arg Ser Ser Pro Cys Ala Ser Ser Thr Pro
            340                 345                 350

Val Ala Val Gly Asp Phe Pro Asp Cys Ala Tyr Pro Pro Asp Ala Glu
        355                 360                 365

Pro Lys Asp Asp Ala Tyr Pro Leu Tyr Ser Asp Phe Gln Pro Pro Ala
    370                 375                 380

Leu Lys Ile Lys Glu Glu Glu Glu Gly Ala Glu Ala Ser Ala Arg Ser
385                 390                 395                 400

Pro Arg Ser Tyr Leu Val Ala Gly Ala Asn Pro Ala Ala Phe Pro Asp
                405                 410                 415
```

```
Phe Pro Leu Gly Pro Pro Pro Pro Leu Pro Pro Arg Ala Thr Pro Ser
            420                 425                 430

Arg Pro Gly Glu Ala Ala Val Thr Ala Ala Pro Ala Ser Ala Ser Val
        435                 440                 445

Ser Ser Ala Ser Ser Ser Gly Ser Thr Leu Glu Cys Ile Leu Tyr Lys
    450                 455                 460

Ala Glu Gly Ala Pro Pro Gln Gln Gly Pro Phe Ala Pro Pro Pro Cys
465                 470                 475                 480

Lys Ala Pro Gly Ala Ser Gly Cys Leu Leu Pro Arg Asp Gly Leu Pro
                485                 490                 495

Ser Thr Ser Ala Ser Ala Ala Ala Ala Gly Ala Ala Pro Ala Leu Tyr
            500                 505                 510

Pro Ala Leu Gly Leu Asn Gly Leu Pro Gln Leu Gly Tyr Gln Ala Ala
        515                 520                 525

Val Leu Lys Glu Gly Leu Pro Gln Val Tyr Pro Pro Tyr Leu Asn Tyr
    530                 535                 540

Leu Arg Pro Asp Ser Glu Ala Ser Gln Ser Pro Gln Tyr Ser Phe Glu
545                 550                 555                 560

Ser Leu Pro Gln Lys Ile Cys Leu Ile Cys Gly Asp Glu Ala Ser Gly
                565                 570                 575

Cys His Tyr Gly Val Leu Thr Cys Gly Ser Cys Lys Val Phe Phe Lys
            580                 585                 590

Arg Ala Met Glu Gly Gln His Asn Tyr Leu Cys Ala Gly Arg Asn Asp
        595                 600                 605

Cys Ile Val Asp Lys Ile Arg Arg Lys Asn Cys Pro Ala Cys Arg Leu
    610                 615                 620

Arg Lys Cys Cys Gln Ala Gly Met Val Leu Gly Gly Arg Lys Phe Lys
625                 630                 635                 640

Lys Phe Asn Lys Val Arg Val Val Arg Ala Leu Asp Ala Val Ala Leu
                645                 650                 655

Pro Gln Pro Val Gly Val Pro Asn Glu Ser Gln Ala Leu Ser Gln Arg
            660                 665                 670

Phe Thr Phe Ser Pro Gly Gln Asp Ile Gln Leu Ile Pro Pro Leu Ile
        675                 680                 685
```

```
Asn Leu Leu Met Ser Ile Glu Pro Asp Val Ile Tyr Ala Gly His Asp
    690                 695                 700

Asn Thr Lys Pro Asp Thr Ser Ser Ser Leu Leu Thr Ser Leu Asn Gln
705                 710                 715                 720

Leu Gly Glu Arg Gln Leu Leu Ser Val Val Lys Trp Ser Lys Ser Leu
                725                 730                 735

Pro Gly Phe Arg Asn Leu His Ile Asp Asp Gln Ile Thr Leu Ile Gln
            740                 745                 750

Tyr Ser Trp Met Ser Leu Met Val Phe Gly Leu Gly Trp Arg Ser Tyr
        755                 760                 765

Lys His Val Ser Gly Gln Met Leu Tyr Phe Ala Pro Asp Leu Ile Leu
    770                 775                 780

Asn Glu Gln Arg Met Lys Glu Ser Ser Phe Tyr Ser Leu Cys Leu Thr
785                 790                 795                 800

Met Trp Gln Ile Pro Gln Glu Phe Val Lys Leu Gln Val Ser Gln Glu
                805                 810                 815

Glu Phe Leu Cys Met Lys Val Leu Leu Leu Leu Asn Thr Ile Pro Leu
            820                 825                 830

Glu Gly Leu Arg Ser Gln Thr Gln Phe Glu Glu Met Arg Ser Ser Tyr
        835                 840                 845

Ile Arg Glu Leu Ile Lys Ala Ile Gly Leu Arg Gln Lys Gly Val Val
    850                 855                 860

Ser Ser Ser Gln Arg Phe Tyr Gln Leu Thr Lys Leu Leu Asp Asn Leu
865                 870                 875                 880

His Asp Leu Val Lys Gln Leu His Leu Tyr Cys Leu Asn Thr Phe Ile
                885                 890                 895

Gln Ser Arg Ala Leu Ser Val Glu Phe Pro Glu Met Met Ser Glu Val
            900                 905                 910

Ile Ala Ala Gln Leu Pro Lys Ile Leu Ala Gly Met Val Lys Pro Leu
        915                 920                 925

Leu Phe His Lys Lys
    930
```

<210> 95
<211> 256
<212> PRT
<213> Homo sapiens

<400> 95

```
Gly Gln Asp Ile Gln Leu Ile Pro Pro Leu Ile Asn Leu Leu Met Ser
1               5                  10                  15

Ile Glu Pro Asp Val Ile Tyr Ala Gly His Asp Asn Thr Lys Pro Asp
            20                  25                  30

Thr Ser Ser Ser Leu Leu Thr Ser Leu Asn Gln Leu Gly Glu Arg Gln
        35                  40                  45

Leu Leu Ser Val Val Lys Trp Ser Lys Ser Leu Pro Gly Phe Arg Asn
    50                  55                  60

Leu His Ile Asp Asp Gln Ile Thr Leu Ile Gln Tyr Ser Trp Met Ser
65                  70                  75                  80

Leu Met Val Phe Gly Leu Gly Trp Arg Ser Tyr Lys His Val Ser Gly
                85                  90                  95

Gln Met Leu Tyr Phe Ala Pro Asp Leu Ile Leu Asn Glu Gln Arg Met
            100                 105                 110

Lys Glu Ser Ser Phe Tyr Ser Leu Cys Leu Thr Met Trp Gln Ile Pro
        115                 120                 125

Gln Glu Phe Val Lys Leu Gln Val Ser Gln Glu Glu Phe Leu Cys Met
    130                 135                 140

Lys Val Leu Leu Leu Leu Asn Thr Ile Pro Leu Glu Gly Leu Arg Ser
145                 150                 155                 160

Gln Thr Gln Phe Glu Glu Met Arg Ser Ser Tyr Ile Arg Glu Leu Ile
                165                 170                 175

Lys Ala Ile Gly Leu Arg Gln Lys Gly Val Val Ser Ser Ser Gln Arg
            180                 185                 190

Phe Tyr Gln Leu Thr Lys Leu Leu Asp Asn Leu His Asp Leu Val Lys
        195                 200                 205

Gln Leu His Leu Tyr Cys Leu Asn Thr Phe Ile Gln Ser Arg Ala Leu
    210                 215                 220

Ser Val Glu Phe Pro Glu Met Met Ser Glu Val Ile Ala Ala Gln Leu
225                 230                 235                 240

Pro Lys Ile Leu Ala Gly Met Val Lys Pro Leu Leu Phe His Lys Lys
                245                 250                 255
```

<210> 96

<211> 248
<212> PRT
<213> Homo sapiens

<400> 96

```
Pro Leu Ile Asn Leu Leu Met Ser Ile Glu Pro Asp Val Ile Tyr Ala
1               5                  10                  15

Gly His Asp Asn Thr Lys Pro Asp Thr Ser Ser Ser Leu Leu Thr Ser
            20                  25                  30

Leu Asn Gln Leu Gly Glu Arg Gln Leu Leu Ser Val Val Lys Trp Ser
        35                  40                  45

Lys Ser Leu Pro Gly Phe Arg Asn Leu His Ile Asp Asp Gln Ile Thr
    50                  55                  60

Leu Ile Gln Tyr Ser Trp Met Ser Leu Met Val Phe Gly Leu Gly Trp
65                  70                  75                  80

Arg Ser Tyr Lys His Val Ser Gly Gln Met Leu Tyr Phe Ala Pro Asp
                85                  90                  95

Leu Ile Leu Asn Glu Gln Arg Met Lys Glu Ser Ser Phe Tyr Ser Leu
            100                 105                 110

Cys Leu Thr Met Trp Gln Ile Pro Gln Glu Phe Val Lys Leu Gln Val
        115                 120                 125

Ser Gln Glu Glu Phe Leu Cys Met Lys Val Leu Leu Leu Leu Asn Thr
    130                 135                 140

Ile Pro Leu Glu Gly Leu Arg Ser Gln Thr Gln Phe Glu Glu Met Arg
145                 150                 155                 160

Ser Ser Tyr Ile Arg Glu Leu Ile Lys Ala Ile Gly Leu Arg Gln Lys
                165                 170                 175

Gly Val Val Ser Ser Ser Gln Arg Phe Tyr Gln Leu Thr Lys Leu Leu
            180                 185                 190

Asp Asn Leu His Asp Leu Val Lys Gln Leu His Leu Tyr Cys Leu Asn
        195                 200                 205

Thr Phe Ile Gln Ser Arg Ala Leu Ser Val Glu Phe Pro Glu Met Met
    210                 215                 220

Ser Glu Val Ile Ala Ala Gln Leu Pro Lys Ile Leu Ala Gly Met Val
225                 230                 235                 240

Lys Pro Leu Leu Phe His Lys Lys
                245
```

<210> 97
<211> 248
<212> PRT
<213> Homo sapiens

<400> 97

```
Pro Leu Ile Asn Leu Leu Met Ser Ile Glu Pro Asp Val Ile Tyr Ala
1               5                  10                  15

Gly His Asp Asn Thr Lys Pro Asp Thr Ser Ser Ser Leu Leu Thr Ser
            20                  25                  30

Leu Asn Gln Leu Gly Glu Arg Gln Leu Leu Ser Val Val Lys Trp Ser
        35                  40                  45

Lys Ser Leu Pro Gly Phe Arg Asn Leu His Ile Asp Asp Gln Ile Thr
    50                  55                  60

Leu Ile Gln Tyr Ser Trp Met Ser Leu Met Val Phe Gly Leu Gly Trp
65                  70                  75                  80

Arg Ser Tyr Lys His Val Ser Gly Gln Met Leu Tyr Phe Ala Pro Asp
                85                  90                  95

Leu Ile Leu Asn Glu Gln Arg Met Lys Glu Ser Ser Phe Tyr Ser Leu
            100                 105                 110

Cys Leu Thr Met Trp Gln Ile Pro Gln Glu Phe Val Lys Leu Gln Val
        115                 120                 125

Ser Gln Glu Glu Phe Leu Cys Met Lys Val Leu Leu Leu Leu Asn Thr
    130                 135                 140

Ile Pro Leu Glu Gly Leu Arg Ser Gln Thr Gln Phe Glu Glu Met Arg
145                 150                 155                 160

Ser Ser Tyr Ile Arg Glu Leu Ile Lys Ala Ile Gly Leu Arg Gln Lys
                165                 170                 175

Gly Val Val Ser Ser Ser Gln Arg Phe Tyr Gln Leu Thr Lys Leu Leu
            180                 185                 190

Asp Asn Leu His Asp Leu Val Lys Gln Leu His Leu Tyr Cys Leu Asn
        195                 200                 205

Thr Phe Ile Gln Ser Arg Ala Leu Ser Val Glu Phe Pro Glu Met Met
    210                 215                 220

Ser Glu Val Ile Ala Ala Gln Leu Pro Lys Ile Leu Ala Gly Met Val
225                 230                 235                 240
```

Lys Pro Leu Leu Phe His Lys Lys
245

<210> 98
<211> 248
<212> PRT
<213> Homo sapiens

<400> 98

Pro Met Ile Ser Val Leu Arg Gly Ile Glu Pro Glu Val Val Tyr Ala
1 5 10 15

Gly Tyr Asp Asn Thr Lys Pro Glu Thr Pro Ser Ser Leu Leu Thr Ser
20 25 30

Leu Asn His Leu Cys Glu Arg Gln Leu Leu Cys Val Val Lys Trp Ser
35 40 45

Lys Leu Leu Pro Gly Phe Arg Asn Leu His Ile Asp Asp Gln Ile Thr
50 55 60

Leu Ile Gln Tyr Ser Trp Met Ser Leu Met Val Phe Ala Met Gly Trp
65 70 75 80

Arg Ser Tyr Lys His Val Ser Gly Gln Met Leu Tyr Phe Ala Pro Asp
85 90 95

Leu Ile Leu Asn Glu Gln Arg Met Lys Glu Ser Ser Phe Tyr Ser Leu
100 105 110

Cys Leu Ser Met Trp Gln Leu Pro Gln Glu Phe Val Arg Leu Gln Val
115 120 125

Ser Gln Glu Glu Phe Leu Cys Met Lys Ala Leu Leu Leu Leu Asn Thr
130 135 140

Ile Pro Leu Glu Gly Leu Arg Ser Gln Ser Gln Phe Asp Glu Met Arg
145 150 155 160

Thr Ser Tyr Ile Arg Glu Leu Val Lys Ala Ile Gly Leu Arg Gln Lys
165 170 175

Gly Val Val Ala Asn Ser Gln Arg Phe Tyr Gln Leu Thr Lys Leu Met
180 185 190

Asp Ser Met His Asp Leu Val Lys Gln Leu His Leu Phe Cys Leu Asn
195 200 205

Thr Phe Leu Gln Ser Arg Ala Leu Ser Val Glu Phe Pro Glu Met Met
210 215 220

Ser Glu Val Ile Ala Ala Gln Leu Pro Lys Ile Leu Ala Gly Met Val
225 230 235 240

Lys Pro Leu Leu Phe His Lys Lys
245

<210> 99
<211> 248
<212> PRT
<213> Homo sapiens

<400> 99

Glu Leu Leu Gln Ile Leu Gln Ser Ile Glu Pro Glu Val Val Tyr Ala
1 5 10 15

Gly Tyr Asp Asn Thr Gln Pro Glu Thr Pro Ser Ala Leu Leu Ser Ser
20 25 30

Leu Asn Gln Leu Cys Glu Arg Gln Leu Val Cys Val Val Lys Trp Ser
35 40 45

Lys Ser Leu Pro Gly Phe Arg Asn Leu His Ile Asp Asp Gln Ile Thr
50 55 60

Leu Leu Gln Tyr Ser Trp Met Ser Leu Met Val Phe Ala Leu Gly Trp
65 70 75 80

Arg Ser Tyr Gln His Val Ser Gly Gln Met Leu Tyr Phe Ala Pro Asp
85 90 95

Leu Ile Leu Asn Glu Gln Arg Met Lys Asp Ser Ser Phe Tyr Thr Leu
100 105 110

Cys Leu Ser Met Trp Gln Leu Pro Gln Glu Phe Met Lys Leu Gln Val
115 120 125

Thr His Glu Glu Phe Leu Cys Met Lys Ala Leu Leu Leu Leu Asn Thr
130 135 140

Ile Pro Leu Glu Gly Leu Lys Ser Gln Thr Asn Phe Asp Glu Met Arg
145 150 155 160

Ser Asn Tyr Ile Arg Glu Leu Ala Lys Ala Ile Ser Leu Arg His Lys
165 170 175

Gly Val Ile Ala Ser Ser Gln Arg Phe Tyr Gln Leu Thr Lys Leu Met
180 185 190

Asp Ser Met His Glu Leu Val Lys Gln Leu His Leu Tyr Cys Leu Asn
195 200 205

Thr Phe Leu Gln Ser Arg Ser Leu Ser Val Glu Phe Pro Glu Met Met

210 215 220

Ser Glu Val Ile Ser Ala Gln Leu Pro Lys Ile Leu Ala Gly Met Val
225 230 235 240

Lys Pro Leu Val Phe His Lys Lys
245

<210> 100
<211> 248
<212> PRT
<213> Homo sapiens

<400> 100

Gln Met Ile Ser Ile Leu Glu Asn Ile Glu Pro Gln Val Val Tyr Ser
1 5 10 15

Gly Tyr Asp Asn Thr Gln Pro Glu Val Pro His Leu Leu Leu Asn Ser
20 25 30

Leu Asn Arg Leu Cys Glu Arg Gln Leu Leu Trp Ile Val Arg Trp Ser
35 40 45

Lys Ser Leu Pro Gly Phe Arg Asn Leu His Ile Asn Asp Gln Met Thr
50 55 60

Leu Ile Gln Tyr Ser Trp Met Gly Leu Met Leu Phe Ser Leu Gly Trp
65 70 75 80

Arg Thr Phe Gln Asn Val Thr Pro Asp Tyr Leu Tyr Phe Ala Pro Asp
85 90 95

Leu Val Leu Ser Asn Asp Gln Leu Arg Arg Ser Pro Ile Tyr Asp Leu
100 105 110

Cys Leu Ala Met Gln Phe Val Pro Gln Glu Phe Ala Asn Leu Gln Val
115 120 125

Thr Lys Glu Glu Phe Leu Cys Met Lys Ala Leu Met Leu Leu Asn Thr
130 135 140

Val Pro Leu Glu Gly Leu Lys Ser Gln Thr Gln Phe Asp Glu Met Arg
145 150 155 160

Gln Asn Tyr Ile Cys Glu Leu Ser Lys Ala Ile Gln Leu Lys Glu Lys
165 170 175

Gly Val Val Ala Ser Ser Gln Arg Phe Tyr His Leu Thr Lys Leu Met
180 185 190

Asp Asn Met His Glu Ile Val Lys Lys Val Asn Leu Tyr Cys Leu Ser
195 200 205

```
Thr Phe Ile Gln Ala Asp Ala Met Lys Val Glu Phe Pro Glu Met Met
    210                 215                 220

Thr Glu Val Ile Ala Ser Gln Leu Pro Lys Val Leu Ala Gly Met Val
225                 230                 235                 240

Lys Pro Leu Met Phe His His Lys
                245
```

<210> 101
<211> 248
<212> PRT
<213> Homo sapiens

<400> 101

```
Pro Leu Ile Asn Leu Leu Met Ser Ile Glu Pro Asp Val Ile Tyr Ala
1               5                   10                  15

Gly His Asp Asn Thr Lys Pro Asp Thr Ser Ser Ser Leu Leu Thr Ser
            20                  25                  30

Leu Asn Gln Leu Gly Glu Arg Gln Leu Leu Ser Val Val Lys Trp Ser
        35                  40                  45

Lys Ser Leu Pro Gly Phe Arg Asn Leu His Ile Asp Asp Gln Ile Thr
    50                  55                  60

Leu Ile Gln Tyr Ser Trp Met Ser Leu Met Val Phe Gly Leu Gly Trp
65                  70                  75                  80

Arg Ser Tyr Lys His Val Ser Gly Gln Met Leu Tyr Phe Ala Pro Asp
                85                  90                  95

Leu Ile Leu Asn Glu Gln Arg Met Lys Glu Ser Ser Phe Tyr Ser Leu
            100                 105                 110

Cys Leu Thr Met Trp Gln Ile Pro Gln Glu Phe Val Lys Leu Gln Val
        115                 120                 125

Ser Gln Glu Glu Phe Leu Cys Met Lys Val Leu Leu Leu Leu Asn Thr
    130                 135                 140

Ile Pro Leu Glu Gly Leu Arg Ser Gln Thr Gln Phe Glu Glu Met Arg
145                 150                 155                 160

Ser Ser Tyr Ile Arg Glu Leu Ile Lys Ala Ile Gly Leu Arg Gln Lys
                165                 170                 175

Gly Val Val Ser Ser Ser Gln Arg Phe Tyr Gln Leu Thr Lys Leu Leu
            180                 185                 190
```

```
Asp Asn Leu His Asp Leu Val Lys Gln Leu His Leu Tyr Cys Leu Asn
        195                 200                 205

Thr Phe Ile Gln Ser Arg Ala Leu Ser Val Glu Phe Pro Glu Met Met
    210                 215                 220

Ser Glu Val Ile Ala Ala Gln Leu Pro Lys Ile Leu Ala Gly Met Val
225                 230                 235                 240

Lys Pro Leu Leu Phe His Lys Lys
                245
```

<210> 102
<211> 248
<212> PRT
<213> Homo sapiens

<400> 102

```
Pro Leu Ile Asn Leu Leu Met Ser Ile Glu Pro Asp Val Ile Tyr Ala
1               5                   10                  15

Gly His Asp Asn Thr Lys Pro Asp Thr Ser Ser Ser Leu Leu Thr Ser
            20                  25                  30

Leu Asn Gln Leu Gly Glu Arg Gln Leu Leu Ser Val Val Lys Trp Ser
        35                  40                  45

Lys Ser Leu Pro Gly Phe Arg Asn Leu His Ile Asp Asp Gln Ile Thr
    50                  55                  60

Leu Ile Gln Tyr Ser Trp Met Ser Leu Met Val Phe Gly Leu Gly Trp
65                  70                  75                  80

Arg Ser Tyr Lys His Val Ser Gly Gln Met Leu Tyr Phe Ala Pro Asp
                85                  90                  95

Leu Ile Leu Asn Glu Gln Arg Met Lys Glu Ser Ser Phe Tyr Ser Leu
            100                 105                 110

Cys Leu Thr Met Trp Gln Ile Pro Gln Glu Phe Val Lys Leu Gln Val
        115                 120                 125

Ser Gln Glu Glu Phe Leu Cys Met Lys Val Leu Leu Leu Leu Asn Thr
    130                 135                 140

Ile Pro Leu Glu Gly Leu Arg Ser Gln Thr Gln Phe Glu Glu Met Arg
145                 150                 155                 160

Ser Ser Tyr Ile Arg Glu Leu Ile Lys Ala Ile Gly Leu Arg Gln Lys
                165                 170                 175
```

Gly Val Val Ser Ser Ser Gln Arg Phe Tyr Gln Leu Thr Lys Leu Leu
180 185 190

Asp Asn Leu His Asp Leu Val Lys Gln Leu His Leu Tyr Cys Leu Asn
195 200 205

Thr Phe Ile Gln Ser Arg Ala Leu Ser Val Glu Phe Pro Glu Met Met
210 215 220

Ser Glu Val Ile Ala Ala Gln Leu Pro Lys Ile Leu Ala Gly Met Val
225 230 235 240

Lys Pro Leu Leu Phe His Lys Lys
245

<210> 103
<211> 248
<212> PRT
<213> Homo sapiens

<400> 103

Pro Leu Ile Asn Leu Leu Met Ser Ile Glu Pro Asp Val Ile Tyr Ala
1 5 10 15

Gly His Asp Asn Thr Lys Pro Asp Thr Ser Ser Ser Leu Leu Thr Ser
20 25 30

Leu Asn Gln Leu Gly Glu Arg Gln Leu Leu Ser Val Val Lys Trp Ser
35 40 45

Lys Ser Leu Pro Gly Phe Arg Asn Leu His Ile Asp Asp Gln Ile Thr
50 55 60

Leu Ile Gln Tyr Ser Trp Met Ser Leu Met Val Phe Gly Leu Gly Trp
65 70 75 80

Arg Ser Tyr Lys His Val Ser Gly Gln Met Leu Tyr Phe Ala Pro Asp
85 90 95

Leu Ile Leu Asn Glu Gln Arg Met Lys Glu Ser Ser Phe Tyr Ser Leu
100 105 110

Cys Leu Thr Met Trp Gln Ile Pro Gln Glu Phe Val Lys Leu Gln Val
115 120 125

Ser Gln Glu Glu Phe Leu Cys Met Lys Val Leu Leu Leu Leu Asn Thr
130 135 140

Ile Pro Leu Glu Gly Leu Arg Ser Gln Thr Gln Phe Glu Glu Met Arg
145 150 155 160

Ser Ser Tyr Ile Arg Glu Leu Ile Lys Ala Ile Gly Leu Arg Gln Lys

165 170 175

Gly Val Val Ser Ser Ser Gln Arg Phe Tyr Gln Leu Thr Lys Leu Leu
180 185 190

Asp Asn Leu His Asp Leu Val Lys Gln Leu His Leu Tyr Cys Leu Asn
195 200 205

Thr Phe Ile Gln Ser Arg Ala Leu Ser Val Glu Phe Pro Glu Met Met
210 215 220

Ser Glu Val Ile Ala Ala Gln Leu Pro Lys Ile Leu Ala Gly Met Val
225 230 235 240

Lys Pro Leu Leu Phe His Lys Lys
245

<210> 104
<211> 461
<212> PRT
<213> Homo sapiens

<400> 104

Met Thr Pro Asn Ser Met Thr Glu Asn Gly Leu Thr Ala Trp Asp Lys
1 5 10 15

Pro Lys His Cys Pro Asp Arg Glu His Asp Trp Lys Leu Val Gly Met
20 25 30

Ser Glu Ala Cys Leu His Arg Lys Ser His Ser Glu Arg Arg Ser Thr
35 40 45

Leu Lys Asn Glu Gln Ser Ser Pro His Leu Ile Gln Thr Thr Trp Thr
50 55 60

Ser Ser Ile Phe His Leu Asp His Asp Asp Val Asn Asp Gln Ser Val
65 70 75 80

Ser Ser Ala Gln Thr Phe Gln Thr Glu Glu Lys Lys Cys Lys Gly Tyr
85 90 95

Ile Pro Ser Tyr Leu Asp Lys Asp Glu Leu Cys Val Val Cys Gly Asp
100 105 110

Lys Ala Thr Gly Tyr His Tyr Arg Cys Ile Thr Cys Glu Gly Cys Lys
115 120 125

Gly Phe Phe Arg Arg Thr Ile Gln Lys Asn Leu His Pro Ser Tyr Ser
130 135 140

Cys Lys Tyr Glu Gly Lys Cys Val Ile Asp Lys Val Thr Arg Asn Gln
145 150 155 160

```
Cys Gln Glu Cys Arg Phe Lys Lys Cys Ile Tyr Val Gly Met Ala Thr
                165                 170                 175

Asp Leu Val Leu Asp Asp Ser Lys Arg Leu Ala Lys Arg Lys Leu Ile
            180                 185                 190

Glu Glu Asn Arg Glu Lys Arg Arg Arg Glu Glu Leu Gln Lys Ser Ile
        195                 200                 205

Gly His Lys Pro Glu Pro Thr Asp Glu Glu Trp Glu Leu Ile Lys Thr
    210                 215                 220

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

Gln Lys Arg Lys Phe Leu Pro Glu Asp Ile Gly Gln Ala Pro Ile Val
                245                 250                 255

Asn Ala Pro Glu Gly Gly Lys Val Asp Leu Glu Ala Phe Ser His Phe
            260                 265                 270

Thr Lys Ile Ile Thr Pro Ala Ile Thr Arg Val Val Asp Phe Ala Lys
        275                 280                 285

Lys Leu Pro Met Phe Cys Glu Leu Pro Cys Glu Asp Gln Ile Ile Leu
    290                 295                 300

Leu Lys Gly Cys Cys Met Glu Ile Met Ser Leu Arg Ala Ala Val Arg
305                 310                 315                 320

Tyr Asp Pro Glu Ser Glu Thr Leu Thr Leu Asn Gly Glu Met Ala Val
                325                 330                 335

Thr Arg Gly Gln Leu Lys Asn Gly Gly Leu Gly Val Val Ser Asp Ala
            340                 345                 350

Ile Phe Asp Leu Gly Met Ser Leu Ser Ser Phe Asn Leu Asp Asp Thr
        355                 360                 365

Glu Val Ala Leu Leu Gln Ala Val Leu Leu Met Ser Ser Asp Arg Pro
    370                 375                 380

Gly Leu Ala Cys Val Glu Arg Ile Glu Lys Tyr Gln Asp Ser Phe Leu
385                 390                 395                 400

Leu Ala Phe Glu His Tyr Ile Asn Tyr Arg Lys His His Val Thr His
                405                 410                 415

Phe Trp Pro Lys Leu Leu Met Lys Val Thr Asp Leu Arg Met Ile Gly
            420                 425                 430
```

```
Ala Cys His Ala Ser Arg Phe Leu His Met Lys Val Glu Cys Pro Thr
        435                 440                 445


Glu Leu Phe Pro Pro Leu Phe Leu Glu Val Phe Glu Asp
    450                 455                 460


<210>  105
<211>  260
<212>  PRT
<213>  Homo sapiens

<400>  105

Glu Glu Leu Gln Lys Ser Ile Gly His Lys Pro Glu Pro Thr Asp Glu
1               5                   10                  15


Glu Trp Glu Leu Ile Lys Thr Val Thr Glu Ala His Val Ala Thr Asn
            20                  25                  30


Ala Gln Gly Ser His Trp Lys Gln Lys Arg Lys Phe Leu Pro Glu Asp
        35                  40                  45


Ile Gly Gln Ala Pro Ile Val Asn Ala Pro Glu Gly Gly Lys Val Asp
    50                  55                  60


Leu Glu Ala Phe Ser His Phe Thr Lys Ile Ile Thr Pro Ala Ile Thr
65                  70                  75                  80


Arg Val Val Asp Phe Ala Lys Lys Leu Pro Met Phe Cys Glu Leu Pro
                85                  90                  95


Cys Glu Asp Gln Ile Ile Leu Leu Lys Gly Cys Cys Met Glu Ile Met
            100                 105                 110


Ser Leu Arg Ala Ala Val Arg Tyr Asp Pro Glu Ser Glu Thr Leu Thr
        115                 120                 125


Leu Asn Gly Glu Met Ala Val Thr Arg Gly Gln Leu Lys Asn Gly Gly
    130                 135                 140


Leu Gly Val Val Ser Asp Ala Ile Phe Asp Leu Gly Met Ser Leu Ser
145                 150                 155                 160


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


Leu Met Ser Ser Asp Arg Pro Gly Leu Ala Cys Val Glu Arg Ile Glu
            180                 185                 190


Lys Tyr Gln Asp Ser Phe Leu Leu Ala Phe Glu His Tyr Ile Asn Tyr
        195                 200                 205
```

```
Arg Lys His His Val Thr His Phe Trp Pro Lys Leu Leu Met Lys Val
    210                 215                 220

Thr Asp Leu Arg Met Ile Gly Ala Cys His Ala Ser Arg Phe Leu His
225                 230                 235                 240

Met Lys Val Glu Cys Pro Thr Glu Leu Phe Pro Pro Leu Phe Leu Glu
                245                 250                 255

Val Phe Glu Asp
            260
```

<210> 106
<211> 281
<212> PRT
<213> Homo sapiens

<400> 106

```
Asp Asp Ser Lys Arg Leu Ala Lys Arg Lys Leu Ile Glu Glu Asn Arg
1               5                   10                  15

Glu Lys Arg Arg Arg Glu Glu Leu Gln Lys Ser Ile Gly His Lys Pro
            20                  25                  30

Glu Pro Thr Asp Glu Glu Trp Glu Leu Ile Lys Thr Val Thr Glu Ala
        35                  40                  45

His Val Ala Thr Asn Ala Gln Gly Ser His Trp Lys Gln Lys Arg Lys
    50                  55                  60

Phe Leu Pro Glu Asp Ile Gly Gln Ala Pro Ile Val Asn Ala Pro Glu
65                  70                  75                  80

Gly Gly Lys Val Asp Leu Glu Ala Phe Ser His Phe Thr Lys Ile Ile
                85                  90                  95

Thr Pro Ala Ile Thr Arg Val Val Asp Phe Ala Lys Lys Leu Pro Met
            100                 105                 110

Phe Cys Glu Leu Pro Cys Glu Asp Gln Ile Ile Leu Leu Lys Gly Cys
        115                 120                 125

Cys Met Glu Ile Met Ser Leu Arg Ala Ala Val Arg Tyr Asp Pro Glu
    130                 135                 140

Ser Glu Thr Leu Thr Leu Asn Gly Glu Met Ala Val Thr Arg Gly Gln
145                 150                 155                 160

Leu Lys Asn Gly Gly Leu Gly Val Val Ser Asp Ala Ile Phe Asp Leu
                165                 170                 175
```

```
Gly Met Ser Leu Ser Ser Phe Asn Leu Asp Asp Thr Glu Val Ala Leu
            180                 185                 190

Leu Gln Ala Val Leu Leu Met Ser Ser Asp Arg Pro Gly Leu Ala Cys
        195                 200                 205

Val Glu Arg Ile Glu Lys Tyr Gln Asp Ser Phe Leu Leu Ala Phe Glu
    210                 215                 220

His Tyr Ile Asn Tyr Arg Lys His His Val Thr His Phe Trp Pro Lys
225                 230                 235                 240

Leu Leu Met Lys Val Thr Asp Leu Arg Met Ile Gly Ala Cys His Ala
                245                 250                 255

Ser Arg Phe Leu His Met Lys Val Glu Cys Pro Thr Glu Leu Phe Pro
            260                 265                 270

Pro Leu Phe Leu Glu Val Phe Glu Asp
        275                 280


<210>  107
<211>  243
<212>  PRT
<213>  Homo sapiens

<400>  107

Pro Glu Glu Trp Asp Leu Ile His Ile Ala Thr Glu Ala His Arg Ser
1               5                   10                  15

Thr Asn Ala Gln Gly Ser His Trp Lys Gln Arg Arg Lys Phe Leu Pro
            20                  25                  30

Asp Asp Ile Gly Gln Ser Pro Ile Val Ser Met Pro Asp Gly Asp Lys
        35                  40                  45

Val Asp Leu Glu Ala Phe Ser Glu Phe Thr Lys Ile Ile Thr Pro Ala
    50                  55                  60

Ile Thr Arg Val Val Asp Phe Ala Lys Lys Leu Pro Met Phe Ser Glu
65                  70                  75                  80

Leu Pro Cys Glu Asp Gln Ile Ile Leu Leu Lys Gly Cys Cys Met Glu
                85                  90                  95

Ile Met Ser Leu Arg Ala Ala Val Arg Tyr Asp Pro Glu Ser Asp Thr
            100                 105                 110

Leu Thr Leu Ser Gly Glu Met Ala Val Lys Arg Glu Gln Leu Lys Asn
        115                 120                 125

Gly Gly Leu Gly Val Val Ser Asp Ala Ile Phe Glu Leu Gly Lys Ser
```

130 135 140

Leu Ser Ala Phe Asn Leu Asp Asp Thr Glu Val Ala Leu Leu Gln Ala
145 150 155 160

Val Leu Leu Met Ser Thr Asp Arg Ser Gly Leu Leu Cys Val Asp Lys
165 170 175

Ile Glu Lys Ser Gln Glu Ala Tyr Leu Leu Ala Phe Glu His Tyr Val
180 185 190

Asn His Arg Lys His Asn Ile Pro His Phe Trp Pro Lys Leu Leu Met
195 200 205

Lys Val Thr Asp Leu Arg Met Ile Gly Ala Cys His Ala Ser Arg Phe
210 215 220

Leu His Met Lys Val Glu Cys Pro Thr Glu Leu Phe Pro Pro Leu Phe
225 230 235 240

Leu Glu Val

<210> 108
<211> 243
<212> PRT
<213> Homo sapiens

<400> 108

Asp Glu Glu Trp Glu Leu Ile Lys Thr Val Thr Glu Ala His Val Ala
1 5 10 15

Thr Asn Ala Gln Gly Ser His Trp Lys Gln Lys Arg Lys Phe Leu Pro
20 25 30

Glu Asp Ile Gly Gln Ala Pro Ile Val Asn Ala Pro Glu Gly Gly Lys
35 40 45

Val Asp Leu Glu Ala Phe Ser His Phe Thr Lys Ile Ile Thr Pro Ala
50 55 60

Ile Thr Arg Val Val Asp Phe Ala Lys Lys Leu Pro Met Phe Cys Glu
65 70 75 80

Leu Pro Cys Glu Asp Gln Ile Ile Leu Leu Lys Gly Cys Cys Met Glu
85 90 95

Ile Met Ser Leu Arg Ala Ala Val Arg Tyr Asp Pro Glu Ser Glu Thr
100 105 110

Leu Thr Leu Asn Gly Glu Met Ala Val Thr Arg Gly Gln Leu Lys Asn
115 120 125

Gly Gly Leu Gly Val Val Ser Asp Ala Ile Phe Asp Leu Gly Met Ser
130 135 140

Leu Ser Ser Phe Asn Leu Asp Asp Thr Glu Val Ala Leu Leu Gln Ala
145 150 155 160

Val Leu Leu Met Ser Ser Asp Arg Pro Gly Leu Ala Cys Val Glu Arg
165 170 175

Ile Glu Lys Tyr Gln Asp Ser Phe Leu Leu Ala Phe Glu His Tyr Ile
180 185 190

Asn Tyr Arg Lys His His Val Thr His Phe Trp Pro Lys Leu Leu Met
195 200 205

Lys Val Thr Asp Leu Arg Met Ile Gly Ala Cys His Ala Ser Arg Phe
210 215 220

Leu His Met Lys Val Glu Cys Pro Thr Glu Leu Phe Pro Pro Leu Phe
225 230 235 240

Leu Glu Val

<210> 109
<211> 243
<212> PRT
<213> Homo sapiens

<400> 109

Asp Glu Glu Trp Glu Leu Ile Lys Thr Val Thr Glu Ala His Val Ala
1 5 10 15

Thr Asn Ala Gln Gly Ser His Trp Lys Gln Lys Arg Lys Phe Leu Pro
20 25 30

Glu Asp Ile Gly Gln Ala Pro Ile Val Asn Ala Pro Glu Gly Gly Lys
35 40 45

Val Asp Leu Glu Ala Phe Ser His Phe Thr Lys Ile Ile Thr Pro Ala
50 55 60

Ile Thr Arg Val Val Asp Phe Ala Lys Lys Leu Pro Met Phe Cys Glu
65 70 75 80

Leu Pro Cys Glu Asp Gln Ile Ile Leu Leu Lys Gly Cys Cys Met Glu
85 90 95

Ile Met Ser Leu Arg Ala Ala Val Arg Tyr Asp Pro Glu Ser Glu Thr
100 105 110

Leu Thr Leu Asn Gly Glu Met Ala Val Thr Arg Gly Gln Leu Lys Asn
115 120 125

Gly Gly Leu Gly Val Val Ser Asp Ala Ile Phe Asp Leu Gly Met Ser
130 135 140

Leu Ser Ser Phe Asn Leu Asp Asp Thr Glu Val Ala Leu Leu Gln Ala
145 150 155 160

Val Leu Leu Met Ser Ser Asp Arg Pro Gly Leu Ala Cys Val Glu Arg
165 170 175

Ile Glu Lys Tyr Gln Asp Ser Phe Leu Leu Ala Phe Glu His Tyr Ile
180 185 190

Asn Tyr Arg Lys His His Val Thr His Phe Trp Pro Lys Leu Leu Met
195 200 205

Lys Val Thr Asp Leu Arg Met Ile Gly Ala Cys His Ala Ser Arg Phe
210 215 220

Leu His Met Lys Val Glu Cys Pro Thr Glu Leu Phe Pro Pro Leu Phe
225 230 235 240

Leu Glu Val

<210> 110
<211> 243
<212> PRT
<213> Homo sapiens

<400> 110

Asp Glu Glu Trp Glu Leu Ile Lys Thr Val Thr Glu Ala His Val Ala
1 5 10 15

Thr Asn Ala Gln Gly Ser His Trp Lys Gln Lys Arg Lys Phe Leu Pro
20 25 30

Glu Asp Ile Gly Gln Ala Pro Ile Val Asn Ala Pro Glu Gly Gly Lys
35 40 45

Val Asp Leu Glu Ala Phe Ser His Phe Thr Lys Ile Ile Thr Pro Ala
50 55 60

Ile Thr Arg Val Val Asp Phe Ala Lys Lys Leu Pro Met Phe Cys Glu
65 70 75 80

Leu Pro Cys Glu Asp Gln Ile Ile Leu Leu Lys Gly Cys Cys Met Glu
85 90 95

Ile Met Ser Leu Arg Ala Ala Val Arg Tyr Asp Pro Glu Ser Glu Thr
100 105 110

Leu Thr Leu Asn Gly Glu Met Ala Val Thr Arg Gly Gln Leu Lys Asn
115 120 125

Gly Gly Leu Gly Val Val Ser Asp Ala Ile Phe Arg Leu Gly Met Ser
130 135 140

Leu Ser Ser Phe Asn Leu Asp Asp Thr Glu Val Ala Leu Leu Gln Ala
145 150 155 160

Val Leu Leu Met Ser Ser Asp Arg Pro Gly Leu Ala Cys Val Glu Arg
165 170 175

Ile Glu Lys Tyr Gln Asp Ser Phe Leu Leu Ala Phe Glu His Tyr Ile
180 185 190

Asn Tyr Arg Lys His His Val Thr His Phe Trp Pro Lys Leu Leu Met
195 200 205

Lys Val Thr Asp Leu Arg Met Ile Gly Ala Cys His Ala Ser Arg Phe
210 215 220

Leu His Met Lys Val Glu Cys Pro Thr Glu Leu Phe Pro Pro Leu Phe
225 230 235 240

Leu Glu Val

<210> 111
<211> 243
<212> PRT
<213> Homo sapiens

<400> 111

Asp Glu Glu Trp Glu Leu Ile Lys Thr Val Thr Glu Ala His Val Ala
1 5 10 15

Thr Asn Ala Gln Gly Ser His Trp Lys Gln Lys Arg Lys Phe Leu Pro
20 25 30

Glu Asp Ile Gly Gln Ala Pro Ile Val Asn Ala Pro Glu Gly Gly Lys
35 40 45

Val Asp Leu Glu Ala Phe Ser His Phe Thr Lys Ile Ile Thr Pro Ala
50 55 60

Ile Thr Arg Val Val Asp Phe Ala Lys Lys Leu Pro Met Phe Cys Glu
65 70 75 80

Leu Pro Cys Glu Asp Gln Ile Ile Leu Leu Lys Gly Cys Cys Met Glu

85 90 95

Ile Met Ser Leu Arg Ala Ala Val Arg Tyr Asp Pro Glu Ser Glu Thr
100 105 110

Leu Thr Leu Asn Gly Glu Met Ala Val Thr Arg Gly Gln Leu Lys Asn
115 120 125

Gly Gly Leu Gly Val Val Ser Asp Ala Ile Phe Arg Leu Gly Met Ser
130 135 140

Leu Ser Ser Phe Asn Leu Asp Asp Thr Glu Val Ala Leu Leu Gln Ala
145 150 155 160

Val Leu Leu Met Ser Ser Asp Arg Pro Gly Leu Ala Cys Val Glu Arg
165 170 175

Ile Glu Lys Tyr Gln Asp Ser Phe Leu Leu Ala Phe Glu His Tyr Ile
180 185 190

Asn Tyr Arg Lys His His Val Thr His Phe Trp Pro Lys Leu Leu Met
195 200 205

Lys Val Thr Asp Leu Arg Met Ile Gly Ala Cys His Ala Ser Arg Phe
210 215 220

Leu His Met Lys Val Glu Cys Pro Thr Glu Leu Phe Pro Pro Leu Phe
225 230 235 240

Leu Glu Val

<210> 112
<211> 241
<212> PRT
<213> Homo sapiens

<400> 112

Thr Cys Pro Lys Lys Val Asn Arg Tyr Tyr Leu Asn Gly Ser Pro Lys
1 5 10 15

Pro Gly Met Pro Val Pro Glu Ala Pro Arg Pro Pro Val Val Gln Asn
20 25 30

Gly Val Val Arg Glu Ala Asp Ser Ser Gly Ala Met Asp Asp Asp Met
35 40 45

Val Asp Gln Asp Ile Phe Ser His Leu Ala Glu Val Ile Thr Pro Ala
50 55 60

Ile Ile Lys Val Val Glu Phe Ala Lys Gln Ile Pro Gly Phe Thr Lys
65 70 75 80

```
Leu Val Pro Asp Asp Gln Val Ala Leu Leu Lys Asn Cys Cys Phe Glu
                85                  90                  95

Val Met Cys Leu Arg Ala Ala Ser Arg Phe Asp Lys Gln Arg Arg Thr
            100                 105                 110

Ile Thr Met Phe Gly Gly Leu Thr Val Thr Lys Glu Gln Val Ser Gln
        115                 120                 125

Gly Gly Leu Gly Arg Leu Ala Glu Pro Leu Phe Glu Phe Ala Glu Gly
    130                 135                 140

Leu Ser Gln Leu His Leu Asp Asp Thr Glu Val Ala Leu Leu Ala Ala
145                 150                 155                 160

Leu Leu Val Val Ala Asp Arg Pro Gly Val Gln Asp Gln Glu Ser Ile
                165                 170                 175

Asp Arg Leu Gln Asp Ile Ile Leu Thr Ala Tyr Lys Asn Tyr Ile Thr
            180                 185                 190

Arg Gln Arg Pro His Gln Pro Val Leu Trp Gly Lys Ile Leu Met Lys
        195                 200                 205

Val Thr Asp Leu Arg Ala Leu Ser Val Ala His Ala Glu Gln Val Lys
    210                 215                 220

Leu Val Lys Met Glu Cys Thr Asn Asp Ile Pro Pro Leu Phe Leu Glu
225                 230                 235                 240

Met
```

<210> 113
<211> 243
<212> PRT
<213> Homo sapiens

<400> 113

```
Ala Glu Glu Trp Glu Leu Ile His Val Val Thr Glu Ala His Arg Ser
1               5                   10                  15

Thr Asn Ala Gln Gly Ser His Trp Lys Gln Lys Arg Lys Phe Leu Pro
            20                  25                  30

Glu Asp Ile Gly Gln Ser Pro Met Ala Ser Met Pro Asp Gly Asp Lys
        35                  40                  45

Val Asp Leu Glu Ala Phe Ser Glu Phe Thr Lys Ile Ile Thr Pro Ala
    50                  55                  60
```

```
Ile Thr Arg Val Val Asp Phe Ala Lys Lys Leu Pro Met Phe Ser Glu
65                  70                  75                  80

Leu Pro Cys Glu Asp Gln Ile Ile Leu Leu Lys Gly Cys Cys Met Glu
                85                  90                  95

Ile Met Ser Leu Arg Ala Ala Val Arg Tyr Asp Pro Glu Ser Glu Thr
            100                 105                 110

Leu Thr Leu Ser Gly Glu Met Ala Val Lys Arg Glu Gln Leu Lys Asn
        115                 120                 125

Gly Gly Leu Gly Val Val Ser Asp Ala Ile Phe Asp Leu Gly Lys Ser
    130                 135                 140

Leu Ser Ala Phe Asn Leu Asp Asp Thr Glu Val Ala Leu Leu Gln Ala
145                 150                 155                 160

Val Leu Leu Met Ser Ser Asp Arg Thr Gly Leu Ile Cys Val Asp Lys
                165                 170                 175

Ile Glu Lys Cys Gln Glu Thr Tyr Leu Leu Ala Phe Glu His Tyr Ile
            180                 185                 190

Asn Tyr Arg Lys His Asn Ile Pro His Phe Trp Pro Lys Leu Leu Met
        195                 200                 205

Lys Val Thr Asp Leu Arg Met Ile Gly Ala Cys His Ala Ser Arg Phe
    210                 215                 220

Leu His Met Lys Val Glu Cys Pro Thr Glu Leu Phe Pro Pro Leu Phe
225                 230                 235                 240

Leu Glu Val
```

<210> 114
<211> 243
<212> PRT
<213> Homo sapiens

<400> 114

```
Ser Glu Glu Trp Glu Leu Ile Arg Ile Val Thr Glu Ala His Arg Ser
1               5                   10                  15

Thr Asn Ala Gln Gly Ser His Trp Lys Gln Arg Arg Lys Phe Leu Pro
            20                  25                  30

Glu Asp Ile Gly Gln Ser Pro Met Ala Ser Met Pro Asp Gly Asp Lys
        35                  40                  45
```

```
Val Asp Leu Glu Ala Phe Ser Glu Phe Thr Lys Ile Ile Thr Pro Ala
    50                  55                  60

Ile Thr Arg Val Val Asp Phe Ala Lys Lys Leu Pro Met Phe Ser Glu
65                  70                  75                  80

Leu Thr Cys Glu Asp Gln Ile Ile Leu Leu Lys Gly Cys Cys Met Glu
                85                  90                  95

Ile Met Ser Leu Arg Ala Ala Val Arg Tyr Asp Pro Asp Ser Glu Thr
            100                 105                 110

Leu Thr Leu Ser Gly Glu Met Ala Val Lys Arg Glu Gln Leu Lys Asn
        115                 120                 125

Gly Gly Leu Gly Val Val Ser Asp Ala Ile Phe Asp Leu Gly Arg Ser
    130                 135                 140

Leu Ala Ala Phe Asn Leu Asp Asp Thr Glu Val Ala Leu Leu Gln Ala
145                 150                 155                 160

Val Leu Leu Met Ser Ser Asp Arg Thr Gly Leu Ile Cys Thr Asp Lys
                165                 170                 175

Ile Glu Lys Cys Gln Glu Thr Tyr Leu Leu Ala Phe Glu His Tyr Ile
            180                 185                 190

Asn His Arg Lys His Asn Ile Pro His Phe Trp Pro Lys Leu Leu Met
        195                 200                 205

Lys Val Thr Asp Leu Arg Met Ile Gly Ala Cys His Ala Ser Arg Phe
    210                 215                 220

Leu His Met Lys Val Glu Cys Pro Thr Glu Leu Phe Pro Pro Leu Phe
225                 230                 235                 240

Leu Glu Val
```

<210> 115
<211> 280
<212> PRT
<213> Homo sapiens

<400> 115

```
Ser Asp Pro Ser Gly Leu Ile Pro Asp Pro Leu Leu Asp Ser Arg Ala
1               5                   10                  15

Thr Ser Ser Thr Phe Pro Gln Leu Leu Thr Cys Pro Ile Leu Arg Pro
            20                  25                  30

Gly Phe Ser Arg Pro Ala Asp Ala Pro Pro Asp Lys Ile Gly Gln Ser
```

35 40 45

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

Ser Glu Phe Thr Lys Ile Ile Thr Pro Ala Ile Thr Arg Val Val Asp
65 70 75 80

Phe Ala Lys Lys Leu Pro Met Phe Ser Glu Leu Pro Cys Glu Asp Gln
85 90 95

Ile Ile Leu Leu Lys Gly Cys Cys Met Glu Ile Met Ser Leu Arg Ala
100 105 110

Ala Met Arg Tyr Asp Pro Glu Ser Glu Thr Leu Thr Leu Ser Gly Glu
115 120 125

Met Ala Val Lys Arg Glu Gln Leu Lys Asn Gly Gly Leu Gly Val Val
130 135 140

Ser Asp Ala Ile Phe Asp Leu Gly Lys Ser Leu Ala Gln Phe Asn Leu
145 150 155 160

Asp Asp Thr Glu Val Ala Leu Leu Gln Ala Val Leu Leu Met Ser Ser
165 170 175

Gly Asn Arg Arg Arg Gly Arg Pro Arg Pro Ser Pro Ala Pro Gly Ser
180 185 190

Thr Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Asp Arg Ser Gly Leu
195 200 205

Thr Cys Thr Asp Lys Ile Glu Lys Cys Gln Glu Thr Tyr Leu Leu Ala
210 215 220

Phe Glu His Tyr Ile Asn Tyr Arg Lys His Asn Ile Pro His Phe Trp
225 230 235 240

Pro Lys Leu Leu Met Lys Val Thr Asp Leu Arg Met Ile Gly Ala Cys
245 250 255

His Ala Ser Arg Phe Leu His Met Lys Val Glu Cys Pro Asn Glu Leu
260 265 270

Phe Pro Pro Leu Phe Leu Glu Val
275 280

<210> 116
<211> 231
<212> PRT
<213> Homo sapiens

<400> 116

Asp His Glu Glu Ala Leu Ile Arg Ala Ile Leu Val Ala His Lys Gln
1 5 10 15

Thr Ser His Met Tyr Arg Arg Glu Ser Ser Ser Gly Glu Glu Ser Glu
20 25 30

Pro Asp Ser Lys Lys Gln Lys Leu Glu Asp Glu Lys Pro Leu Ser Glu
35 40 45

Ile Met Thr Pro Ser Ile Val Lys Val Val Glu Phe Ala Lys Arg Ile
50 55 60

Pro Gly Phe Thr Gly Leu His His Asp Asp Gln Ile Leu Leu Leu Lys
65 70 75 80

Thr Cys Cys Met Glu Ile Met Cys Leu Arg Val Ala Gln Lys Phe Asp
85 90 95

Pro Asp Ser Gln Lys Leu Ile Leu Ser Asn Gly Leu Arg Val Gly Lys
100 105 110

Ser Asp Met Asp His Gly Val Leu Ser Glu Leu Ile Glu Pro Ile Phe
115 120 125

Asp Phe Ala Val Ser Met Ser Arg Leu Gln Leu Thr Glu Thr Glu Met
130 135 140

Ala Leu Leu Ala Ala Val Leu Leu Ile Ala Gly Asp Arg Pro Gly Leu
145 150 155 160

Lys Glu Ala Lys Leu Val Glu Thr Leu Gln Asp Ser Leu Leu Thr Ala
165 170 175

Phe Gln His Phe Ile Asn Glu Ser Arg Pro Lys Thr Pro Val His Trp
180 185 190

Ala Lys Ile Leu Met Lys Ile Thr Asp Leu Arg Thr Ile Ser Ala Arg
195 200 205

His Ala Glu Arg Ile Met Cys Ile Lys Leu Asp Arg Pro Asn Glu Ile
210 215 220

Pro Gln Ile Phe Leu Glu Met
225 230

<210> 117
<211> 243
<212> PRT
<213> Homo sapiens

<400> 117

```
Asp Glu Glu Trp Glu Leu Ile Lys Thr Val Thr Glu Ala His Val Ala
1               5                  10                  15

Thr Asn Ala Gln Gly Ser His Trp Lys Gln Lys Arg Lys Phe Leu Pro
            20                  25                  30

Glu Asp Ile Gly Gln Ala Pro Ile Val Asn Ala Pro Glu Gly Gly Lys
        35                  40                  45

Val Asp Leu Glu Ala Phe Ser His Phe Thr Lys Ile Ile Thr Pro Ala
    50                  55                  60

Ile Thr Arg Val Val Asp Phe Ala Lys Lys Leu Pro Met Phe Cys Glu
65                  70                  75                  80

Leu Pro Cys Glu Asp Gln Ile Ile Leu Leu Lys Gly Cys Cys Met Glu
                85                  90                  95

Ile Met Ser Leu Arg Ala Ala Val Arg Tyr Asp Pro Glu Ser Glu Thr
            100                 105                 110

Leu Thr Leu Asn Gly Glu Met Ala Val Thr Arg Gly Gln Leu Lys Asn
        115                 120                 125

Gly Gly Leu Gly Val Val Ser Asp Ala Ile Phe Asp Leu Gly Met Ser
    130                 135                 140

Leu Ser Ser Phe Asn Leu Asp Asp Thr Glu Val Ala Leu Leu Gln Ala
145                 150                 155                 160

Val Leu Leu Met Ser Ser Asp Arg Pro Gly Leu Ala Cys Val Glu Arg
                165                 170                 175

Ile Glu Lys Tyr Gln Asp Ser Phe Leu Leu Ala Phe Glu His Tyr Ile
            180                 185                 190

Asn Tyr Arg Lys His His Val Thr His Phe Trp Pro Lys Leu Leu Met
        195                 200                 205

Lys Val Thr Asp Leu Arg Met Ile Gly Ala Cys His Ala Ser Arg Phe
    210                 215                 220

Leu His Met Lys Val Glu Cys Pro Thr Glu Leu Phe Pro Pro Leu Phe
225                 230                 235                 240

Leu Glu Val
```

<210> 118
<211> 252
<212> PRT

<213> Homo sapiens

<400> 118

```
Gln Glu Glu Trp Glu Met Ile Arg Val Val Thr Glu Ala His Met Ala
1               5                  10                  15

Thr Asn Ala Gln Gly Asn His Trp Lys Gln Lys Arg Lys Phe Leu Ser
            20                  25                  30

Ala Val Gly Val Lys Glu Ala Lys Pro Glu Asp Ile Gly Ser Ala Pro
        35                  40                  45

Ile Val Asn Ala Pro Glu Gly Asn Lys Val Asp Ile Glu Ala Phe Ser
    50                  55                  60

Gln Phe Thr Lys Ile Ile Thr Pro Ala Ile Thr Arg Val Val Asp Phe
65                  70                  75                  80

Ala Lys Lys Leu Pro Met Phe Cys Glu Leu Pro Cys Glu Asp Gln Ile
                85                  90                  95

Ile Leu Leu Lys Gly Cys Cys Met Glu Ile Met Ser Leu Arg Ala Ala
            100                 105                 110

Val Arg Tyr Asp Pro Glu Ser Asp Thr Leu Thr Leu Asn Gly Glu Met
        115                 120                 125

Ala Val Thr Arg Gly Gln Leu Lys Asn Gly Gly Leu Gly Val Val Ser
    130                 135                 140

Asp Ala Ile Phe Asp Leu Gly Val Ser Leu Ser Ser Phe Asn Leu Asp
145                 150                 155                 160

Asp Ser Glu Val Ala Leu Leu Gln Ala Val Ile Leu Leu Ser Ser Asp
                165                 170                 175

Arg Pro Gly Leu Thr Ser Val Glu Arg Ile Glu Arg Cys Gln Glu Glu
            180                 185                 190

Phe Leu Leu Ala Phe Glu His Tyr Ile Asn Tyr Arg Lys His Lys Val
        195                 200                 205

Ala His Phe Trp Pro Lys Leu Leu Met Lys Val Thr Asp Leu Arg Met
    210                 215                 220

Ile Gly Ala Cys His Ala Ser Arg Phe Leu His Met Lys Val Glu Cys
225                 230                 235                 240

Pro Thr Glu Leu Phe Pro Pro Leu Phe Leu Glu Val
                245                 250
```

<210> 119
<211> 595
<212> PRT
<213> Homo sapiens

<400> 119

Met Thr Met Thr Leu His Thr Lys Ala Ser Gly Met Ala Leu Leu His
1 5 10 15

Gln Ile Gln Gly Asn Glu Leu Glu Pro Leu Asn Arg Pro Gln Leu Lys
20 25 30

Ile Pro Leu Glu Arg Pro Leu Gly Glu Val Tyr Leu Asp Ser Ser Lys
35 40 45

Pro Ala Val Tyr Asn Tyr Pro Glu Gly Ala Ala Tyr Glu Phe Asn Ala
50 55 60

Ala Ala Ala Ala Asn Ala Gln Val Tyr Gly Gln Thr Gly Leu Pro Tyr
65 70 75 80

Gly Pro Gly Ser Glu Ala Ala Ala Phe Gly Ser Asn Gly Leu Gly Gly
85 90 95

Phe Pro Pro Leu Asn Ser Val Ser Pro Ser Pro Leu Met Leu Leu His
100 105 110

Pro Pro Pro Gln Leu Ser Pro Phe Leu Gln Pro His Gly Gln Gln Val
115 120 125

Pro Tyr Tyr Leu Glu Asn Glu Pro Ser Gly Tyr Thr Val Arg Glu Ala
130 135 140

Gly Pro Pro Ala Phe Tyr Arg Pro Asn Ser Asp Asn Arg Arg Gln Gly
145 150 155 160

Gly Arg Glu Arg Leu Ala Ser Thr Asn Asp Lys Gly Ser Met Ala Met
165 170 175

Glu Ser Ala Lys Glu Thr Arg Tyr Cys Ala Val Cys Asn Asp Tyr Ala
180 185 190

Ser Gly Tyr His Tyr Gly Val Trp Ser Cys Glu Gly Cys Lys Ala Phe
195 200 205

Phe Lys Arg Ser Ile Gln Gly His Asn Asp Tyr Met Cys Pro Ala Thr
210 215 220

Asn Gln Cys Thr Ile Asp Lys Asn Arg Arg Lys Ser Cys Gln Ala Cys
225 230 235 240

Arg Leu Arg Lys Cys Tyr Glu Val Gly Met Met Lys Gly Gly Ile Arg

245 250 255

Lys Asp Arg Arg Gly Gly Arg Met Leu Lys His Lys Arg Gln Arg Asp
260 265 270

Asp Gly Glu Gly Arg Gly Glu Val Gly Ser Ala Gly Asp Met Arg Ala
275 280 285

Ala Asn Leu Trp Pro Ser Pro Leu Met Ile Lys Arg Ser Lys Lys Asn
290 295 300

Ser Leu Ala Leu Ser Leu Thr Ala Asp Gln Met Val Ser Ala Leu Leu
305 310 315 320

Asp Ala Glu Pro Pro Ile Leu Tyr Ser Glu Tyr Asp Pro Thr Arg Pro
325 330 335

Phe Ser Glu Ala Ser Met Met Gly Leu Leu Thr Asn Leu Ala Asp Arg
340 345 350

Glu Leu Val His Met Ile Asn Trp Ala Lys Arg Val Pro Gly Phe Val
355 360 365

Asp Leu Thr Leu His Asp Gln Val His Leu Leu Glu Cys Ala Trp Leu
370 375 380

Glu Ile Leu Met Ile Gly Leu Val Trp Arg Ser Met Glu His Pro Val
385 390 395 400

Lys Leu Leu Phe Ala Pro Asn Leu Leu Leu Asp Arg Asn Gln Gly Lys
405 410 415

Cys Val Glu Gly Met Val Glu Ile Phe Asp Met Leu Leu Ala Thr Ser
420 425 430

Ser Arg Phe Arg Met Met Asn Leu Gln Gly Glu Glu Phe Val Cys Leu
435 440 445

Lys Ser Ile Ile Leu Leu Asn Ser Gly Val Tyr Thr Phe Leu Ser Ser
450 455 460

Thr Leu Lys Ser Leu Glu Glu Lys Asp His Ile His Arg Val Leu Asp
465 470 475 480

Lys Ile Thr Asp Thr Leu Ile His Leu Met Ala Lys Ala Gly Leu Thr
485 490 495

Leu Gln Gln Gln His Gln Arg Leu Ala Gln Leu Leu Leu Ile Leu Ser
500 505 510

His Ile Arg His Met Ser Asn Lys Gly Met Glu His Leu Tyr Ser Met

515 520 525

Lys Cys Lys Asn Val Val Pro Leu Tyr Asp Leu Leu Leu Glu Met Leu
530 535 540

Asp Ala His Arg Leu His Ala Pro Thr Ser Arg Gly Gly Ala Ser Val
545 550 555 560

Glu Glu Thr Asp Gln Ser His Leu Ala Thr Ala Gly Ser Thr Ser Ser
565 570 575

His Ser Leu Gln Lys Tyr Tyr Ile Thr Gly Glu Ala Glu Gly Phe Pro
580 585 590

Ala Thr Val
595

<210> 120
<211> 229
<212> PRT
<213> Homo sapiens

<400> 120

Ser Leu Ala Leu Ser Leu Thr Ala Asp Gln Met Val Ser Ala Leu Leu
1 5 10 15

Asp Ala Glu Pro Pro Ile Leu Tyr Ser Glu Tyr Asp Pro Thr Arg Pro
20 25 30

Phe Ser Glu Ala Ser Met Met Gly Leu Leu Thr Asn Leu Ala Asp Arg
35 40 45

Glu Leu Val His Met Ile Asn Trp Ala Lys Arg Val Pro Gly Phe Val
50 55 60

Asp Leu Thr Leu His Asp Gln Val His Leu Leu Glu Cys Ala Trp Leu
65 70 75 80

Glu Ile Leu Met Ile Gly Leu Val Trp Arg Ser Met Glu His Pro Val
85 90 95

Lys Leu Leu Phe Ala Pro Asn Leu Leu Leu Asp Arg Asn Gln Gly Lys
100 105 110

Cys Val Glu Gly Met Val Glu Ile Phe Asp Met Leu Leu Ala Thr Ser
115 120 125

Ser Arg Phe Arg Met Met Asn Leu Gln Gly Glu Glu Phe Val Cys Leu
130 135 140

Lys Ser Ile Ile Leu Leu Asn Ser Gly Val Tyr Thr Phe Leu Ser Ser
145 150 155 160

Thr Leu Lys Ser Leu Glu Glu Lys Asp His Ile His Arg Val Leu Asp
165 170 175

Lys Ile Thr Asp Thr Leu Ile His Leu Met Ala Lys Ala Gly Leu Thr
180 185 190

Leu Gln Gln Gln His Gln Arg Leu Ala Gln Leu Leu Leu Ile Leu Ser
195 200 205

His Ile Arg His Met Ser Asn Lys Gly Met Glu His Leu Tyr Ser Met
210 215 220

Lys Cys Lys Asn Val
225

<210> 121
<211> 314
<212> PRT
<213> Homo sapiens

<400> 121

Ser Ala Gly Asp Met Arg Ala Ala Asn Leu Trp Pro Ser Pro Leu Met
1 5 10 15

Ile Lys Arg Ser Lys Lys Asn Ser Leu Ala Leu Ser Leu Thr Ala Asp
20 25 30

Gln Met Val Ser Ala Leu Leu Asp Ala Glu Pro Pro Ile Leu Tyr Ser
35 40 45

Glu Tyr Asp Pro Thr Arg Pro Phe Ser Glu Ala Ser Met Met Gly Leu
50 55 60

Leu Thr Asn Leu Ala Asp Arg Glu Leu Val His Met Ile Asn Trp Ala
65 70 75 80

Lys Arg Val Pro Gly Phe Val Asp Leu Thr Leu His Asp Gln Val His
85 90 95

Leu Leu Glu Cys Ala Trp Leu Glu Ile Leu Met Ile Gly Leu Val Trp
100 105 110

Arg Ser Met Glu His Pro Val Lys Leu Leu Phe Ala Pro Asn Leu Leu
115 120 125

Leu Asp Arg Asn Gln Gly Lys Cys Val Glu Gly Met Val Glu Ile Phe
130 135 140

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

```
Gly Glu Glu Phe Val Cys Leu Lys Ser Ile Ile Leu Leu Asn Ser Gly
                165                 170                 175

Val Tyr Thr Phe Leu Ser Ser Thr Leu Lys Ser Leu Glu Glu Lys Asp
            180                 185                 190

His Ile His Arg Val Leu Asp Lys Ile Thr Asp Thr Leu Ile His Leu
        195                 200                 205

Met Ala Lys Ala Gly Leu Thr Leu Gln Gln Gln His Gln Arg Leu Ala
    210                 215                 220

Gln Leu Leu Leu Ile Leu Ser His Ile Arg His Met Ser Asn Lys Gly
225                 230                 235                 240

Met Glu His Leu Tyr Ser Met Lys Cys Lys Asn Val Val Pro Leu Tyr
                245                 250                 255

Asp Leu Leu Leu Glu Met Leu Asp Ala His Arg Leu His Ala Pro Thr
            260                 265                 270

Ser Arg Gly Gly Ala Ser Val Glu Glu Thr Asp Gln Ser His Leu Ala
        275                 280                 285

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

Gly Glu Ala Glu Gly Phe Pro Ala Thr Val
305                 310
```

<210> 122
<211> 238
<212> PRT
<213> Homo sapiens

<400> 122

```
Leu Thr Ala Asp Gln Met Val Ser Ala Leu Leu Asp Ala Glu Pro Pro
1               5                   10                  15

Ile Leu Tyr Ser Glu Tyr Asp Pro Thr Arg Pro Phe Ser Glu Ala Ser
            20                  25                  30

Met Met Gly Leu Leu Thr Asn Leu Ala Asp Arg Glu Leu Val His Met
        35                  40                  45

Ile Asn Trp Ala Lys Arg Val Pro Gly Phe Val Asp Leu Thr Leu His
    50                  55                  60

Asp Gln Val His Leu Leu Glu Cys Ala Trp Leu Glu Ile Leu Met Ile
65                  70                  75                  80
```

Gly Leu Val Trp Arg Ser Met Glu His Pro Val Lys Leu Leu Phe Ala
85 90 95

Pro Asn Leu Leu Leu Asp Arg Asn Gln Gly Lys Cys Val Glu Gly Met
100 105 110

Val Glu Ile Phe Asp Met Leu Leu Ala Thr Ser Ser Arg Phe Arg Met
115 120 125

Met Asn Leu Gln Gly Glu Glu Phe Val Cys Leu Lys Ser Ile Ile Leu
130 135 140

Leu Asn Ser Gly Val Tyr Thr Phe Leu Ser Ser Thr Leu Lys Ser Leu
145 150 155 160

Glu Glu Lys Asp His Ile His Arg Val Leu Asp Lys Ile Thr Asp Thr
165 170 175

Leu Ile His Leu Met Ala Lys Ala Gly Leu Thr Leu Gln Gln Gln His
180 185 190

Gln Arg Leu Ala Gln Leu Leu Leu Ile Leu Ser His Ile Arg His Met
195 200 205

Ser Asn Lys Gly Met Glu His Leu Tyr Ser Met Lys Cys Lys Asn Val
210 215 220

Val Pro Leu Tyr Asp Leu Leu Leu Glu Met Leu Asp Ala His
225 230 235

<210> 123
<211> 229
<212> PRT
<213> Homo sapiens

<400> 123

Ser Leu Ala Leu Ser Leu Thr Ala Asp Gln Met Val Ser Ala Leu Leu
1 5 10 15

Asp Ala Glu Pro Pro Ile Leu Tyr Ser Glu Tyr Asp Pro Thr Arg Pro
20 25 30

Phe Ser Glu Ala Ser Met Met Gly Leu Leu Thr Asn Leu Ala Tyr Arg
35 40 45

Glu Leu Val His Met Ile Asn Trp Ala Lys Arg Val Pro Gly Phe Val
50 55 60

Asp Leu Thr Leu His Asp Gln Val His Leu Leu Glu Cys Ala Trp Leu
65 70 75 80

Glu Ile Leu Met Ile Gly Leu Val Trp Arg Ser Met Glu His Pro Val

85 90 95

Lys Leu Leu Phe Ala Pro Asn Leu Leu Leu Asp Arg Asn Gln Gly Lys
100 105 110

Cys Val Glu Gly Met Val Glu Ile Phe Asp Met Leu Leu Ala Thr Ser
115 120 125

Ser Arg Phe Arg Met Met Asn Leu Gln Gly Glu Glu Phe Val Cys Leu
130 135 140

Lys Ser Ile Ile Leu Leu Asn Ser Gly Val Tyr Thr Phe Leu Ser Ser
145 150 155 160

Thr Leu Lys Ser Leu Glu Glu Lys Asp His Ile His Arg Val Leu Asp
165 170 175

Lys Ile Thr Asp Thr Leu Ile His Leu Met Ala Lys Ala Gly Leu Thr
180 185 190

Leu Gln Gln Gln His Gln Arg Leu Ala Gln Leu Leu Leu Ile Leu Ser
195 200 205

His Ile Arg His Met Ser Asn Lys Gly Met Glu His Leu Tyr Ser Met
210 215 220

Lys Cys Lys Asn Val
225

<210> 124
<211> 314
<212> PRT
<213> Homo sapiens

<400> 124

Ser Ala Gly Asp Met Arg Ala Ala Asn Leu Trp Pro Ser Pro Leu Met
1 5 10 15

Ile Lys Arg Ser Lys Lys Asn Ser Leu Ala Leu Ser Leu Thr Ala Asp
20 25 30

Gln Met Val Ser Ala Leu Leu Asp Ala Glu Pro Pro Ile Leu Tyr Ser
35 40 45

Glu Tyr Asp Pro Thr Arg Pro Phe Ser Glu Ala Ser Met Met Gly Leu
50 55 60

Leu Thr Asn Leu Ala Tyr Arg Glu Leu Val His Met Ile Asn Trp Ala
65 70 75 80

Lys Arg Val Pro Gly Phe Val Asp Leu Thr Leu His Asp Gln Val His
85 90 95

```
Leu Leu Glu Cys Ala Trp Leu Glu Ile Leu Met Ile Gly Leu Val Trp
            100                 105                 110

Arg Ser Met Glu His Pro Val Lys Leu Leu Phe Ala Pro Asn Leu Leu
        115                 120                 125

Leu Asp Arg Asn Gln Gly Lys Cys Val Glu Gly Met Val Glu Ile Phe
    130                 135                 140

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

Gly Glu Glu Phe Val Cys Leu Lys Ser Ile Ile Leu Leu Asn Ser Gly
                165                 170                 175

Val Tyr Thr Phe Leu Ser Ser Thr Leu Lys Ser Leu Glu Glu Lys Asp
            180                 185                 190

His Ile His Arg Val Leu Asp Lys Ile Thr Asp Thr Leu Ile His Leu
        195                 200                 205

Met Ala Lys Ala Gly Leu Thr Leu Gln Gln Gln His Gln Arg Leu Ala
    210                 215                 220

Gln Leu Leu Leu Ile Leu Ser His Ile Arg His Met Ser Asn Lys Gly
225                 230                 235                 240

Met Glu His Leu Tyr Ser Met Lys Cys Lys Asn Val Val Pro Leu Tyr
                245                 250                 255

Asp Leu Leu Leu Glu Met Leu Asp Ala His Arg Leu His Ala Pro Thr
            260                 265                 270

Ser Arg Gly Gly Ala Ser Val Glu Glu Thr Asp Gln Ser His Leu Ala
        275                 280                 285

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

Gly Glu Ala Glu Gly Phe Pro Ala Thr Val
305                 310


<210>  125
<211>  238
<212>  PRT
<213>  Homo sapiens

<400>  125

Leu Thr Ala Asp Gln Met Val Ser Ala Leu Leu Asp Ala Glu Pro Pro
1               5                   10                  15
```

Ile Leu Tyr Ser Glu Tyr Asp Pro Thr Arg Pro Phe Ser Glu Ala Ser
            20   25   30

Met Met Gly Leu Leu Thr Asn Leu Ala Tyr Arg Glu Leu Val His Met
        35   40   45

Ile Asn Trp Ala Lys Arg Val Pro Gly Phe Val Asp Leu Thr Leu His
    50   55   60

Asp Gln Val His Leu Leu Glu Cys Ala Trp Leu Glu Ile Leu Met Ile
65   70   75   80

Gly Leu Val Trp Arg Ser Met Glu His Pro Val Lys Leu Leu Phe Ala
                85   90   95

Pro Asn Leu Leu Leu Asp Arg Asn Gln Gly Lys Cys Val Glu Gly Met
            100   105   110

Val Glu Ile Phe Asp Met Leu Leu Ala Thr Ser Ser Arg Phe Arg Met
        115   120   125

Met Asn Leu Gln Gly Glu Glu Phe Val Cys Leu Lys Ser Ile Ile Leu
    130   135   140

Leu Asn Ser Gly Val Tyr Thr Phe Leu Ser Ser Thr Leu Lys Ser Leu
145   150   155   160

Glu Glu Lys Asp His Ile His Arg Val Leu Asp Lys Ile Thr Asp Thr
                165   170   175

Leu Ile His Leu Met Ala Lys Ala Gly Leu Thr Leu Gln Gln Gln His
            180   185   190

Gln Arg Leu Ala Gln Leu Leu Leu Ile Leu Ser His Ile Arg His Met
        195   200   205

Ser Asn Lys Gly Met Glu His Leu Tyr Ser Met Lys Cys Lys Asn Val
    210   215   220

Val Pro Leu Tyr Asp Leu Leu Leu Glu Met Leu Asp Ala His
225   230   235

<210> 126
<211> 238
<212> PRT
<213> Homo sapiens

<400> 126

Leu Thr Ala Asp Gln Met Val Ser Ala Leu Leu Asp Ala Glu Pro Pro
1   5   10   15

```
Ile Leu Tyr Ser Glu Tyr Asp Pro Thr Arg Pro Phe Ser Glu Ala Ser
            20                  25                  30

Met Met Gly Leu Leu Thr Asn Leu Ala Asp Arg Glu Leu Val His Met
        35                  40                  45

Ile Asn Trp Ala Lys Arg Val Pro Gly Phe Val Asp Leu Thr Leu His
    50                  55                  60

Asp Gln Val His Leu Leu Glu Cys Ala Trp Leu Glu Ile Leu Met Ile
65                  70                  75                  80

Gly Leu Val Trp Arg Ser Met Glu His Pro Gly Lys Leu Leu Phe Ala
                85                  90                  95

Pro Asn Leu Leu Leu Asp Arg Asn Gln Gly Lys Cys Val Glu Gly Met
            100                 105                 110

Val Glu Ile Phe Asp Met Leu Leu Ala Thr Ser Ser Arg Phe Arg Met
        115                 120                 125

Met Asn Leu Gln Gly Glu Glu Phe Val Cys Leu Lys Ser Ile Ile Leu
    130                 135                 140

Leu Asn Ser Gly Val Tyr Thr Phe Leu Ser Ser Thr Leu Lys Ser Leu
145                 150                 155                 160

Glu Glu Lys Asp His Ile His Arg Val Leu Asp Lys Ile Thr Asp Thr
                165                 170                 175

Leu Ile His Leu Met Ala Lys Ala Gly Leu Thr Leu Gln Gln Gln His
            180                 185                 190

Gln Arg Leu Ala Gln Leu Leu Leu Ile Leu Ser His Ile Arg His Met
        195                 200                 205

Ser Asn Lys Gly Met Glu His Leu Tyr Ser Met Lys Cys Lys Asn Val
    210                 215                 220

Val Pro Leu Tyr Asp Leu Leu Leu Glu Met Leu Asp Ala His
225                 230                 235


<210>  127
<211>  236
<212>  PRT
<213>  Homo sapiens

<400>  127

Leu Ser Pro Glu Gln Leu Val Leu Thr Leu Leu Glu Ala Glu Pro Pro
1               5                   10                  15

His Val Leu Ile Ser Arg Pro Ser Ala Pro Phe Thr Glu Ala Ser Met
```

20 25 30

Met Met Ser Leu Thr Lys Leu Ala Asp Lys Glu Leu Val His Met Ile
35 40 45

Ser Trp Ala Lys Lys Ile Pro Gly Phe Val Glu Leu Ser Leu Phe Asp
50 55 60

Gln Val Arg Leu Leu Glu Ser Cys Trp Met Glu Val Leu Met Met Gly
65 70 75 80

Leu Met Trp Arg Ser Ile Asp His Pro Gly Lys Leu Ile Phe Ala Pro
85 90 95

Asp Leu Val Leu Asp Arg Asp Glu Gly Lys Cys Val Glu Gly Ile Leu
100 105 110

Glu Ile Phe Asp Met Leu Leu Ala Thr Thr Ser Arg Phe Arg Glu Leu
115 120 125

Lys Leu Gln His Lys Glu Tyr Leu Cys Val Lys Ala Met Ile Leu Leu
130 135 140

Asn Ser Ser Met Tyr Pro Leu Val Thr Ala Thr Gln Asp Ala Asp Ser
145 150 155 160

Ser Arg Lys Leu Ala His Leu Leu Asn Ala Val Thr Asp Ala Leu Val
165 170 175

Trp Val Ile Ala Lys Ser Gly Ile Ser Ser Gln Gln Gln Ser Met Arg
180 185 190

Leu Ala Asn Leu Leu Met Leu Leu Ser His Val Arg His Ala Ser Asn
195 200 205

Lys Gly Met Glu His Leu Leu Asn Met Lys Cys Lys Asn Val Val Pro
210 215 220

Val Tyr Asp Leu Leu Leu Glu Met Leu Asn Ala His
225 230 235

<210> 128
<211> 227
<212> PRT
<213> Homo sapiens

<400> 128

Asn Pro Thr Val Pro Leu Ile Ser His Leu Val Asn Ile Glu Pro Asn
1 5 10 15

Pro Ile Leu Thr Gly Tyr Asn Pro Gln Cys Thr Pro Thr Glu Gly Tyr
20 25 30

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

Val Asp Trp Ala Ala Arg Leu Pro Gly Tyr Gly Met Leu Pro Met Asp
50 55 60

Asp Gln Val Asn Leu Ile Arg Thr Val Trp Leu Asp Leu Leu Met Leu
65 70 75 80

Gly Leu Val Trp Arg Ser Met Glu His Arg Gly Glu Trp Leu Val Phe
85 90 95

Ala Pro Asp Leu Leu Met Asp Arg Ser Leu Cys Arg Leu Ser Gly Met
100 105 110

Glu Tyr Ile Cys Thr Pro Met Leu Glu Phe Ala Arg Gln Phe Ala Asp
115 120 125

Leu Gln Val Pro Gln Glu Val Tyr Val Cys Leu Lys Ala Leu Thr Leu
130 135 140

Tyr Thr Thr Ala Val Ser Arg Leu Gln Asp Tyr Arg Gln Val Gln Arg
145 150 155 160

Leu Gln His Glu Ile Asn Glu Ala Leu Ala Glu Ala Cys Ser Ser Thr
165 170 175

Phe Gly Phe Ser Pro Gly Asn Ile Ala Arg Leu Met Met Ile Val Ser
180 185 190

Gln Val Arg Gln Leu Ser Ser Leu Gly Val Asp His Leu Asn Arg Leu
195 200 205

Arg Gly Ala Glu Thr Val Ser Val Glu Gly Leu Leu Arg Glu Ile Val
210 215 220

Asp Glu Pro
225

<210> 129
<211> 238
<212> PRT
<213> Homo sapiens

<400> 129

Leu Ser Pro Glu Glu Leu Ile Ser Arg Ile Met Glu Ala Glu Pro Pro
1 5 10 15

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

```
Val Met Met Ser Leu Thr Asn Leu Ala Asp Lys Glu Leu Val His Met
        35                  40                  45

Ile Ser Trp Ala Lys Lys Ile Pro Gly Phe Val Glu Leu Ser Leu Phe
    50                  55                  60

Asp Gln Val His Leu Leu Glu Cys Cys Trp Leu Glu Val Leu Met Leu
65                  70                  75                  80

Gly Leu Met Trp Arg Ser Val Asn His Pro Gly Lys Leu Ile Phe Ser
                85                  90                  95

Pro Asp Leu Cys Leu Ser Arg Asp Glu Ser Ser Cys Val Gln Gly Leu
            100                 105                 110

Val Glu Ile Phe Asp Met Leu Leu Ala Ala Thr Ser Arg Phe Arg Glu
        115                 120                 125

Leu Lys Leu Gln Arg Glu Glu Tyr Val Cys Leu Lys Ala Met Ile Leu
    130                 135                 140

Leu Asn Ser Asn Met Cys Leu Gly Ser Ser Glu Gly Gly Glu Asp Leu
145                 150                 155                 160

Gln Ser Arg Ser Lys Leu Leu Cys Leu Leu Asp Ser Val Thr Asp Ala
                165                 170                 175

Leu Val Trp Ala Ile Ser Lys Thr Gly Leu Ser Phe Gln Gln Arg Ser
            180                 185                 190

Thr Arg Leu Ala His Leu Leu Met Leu Leu Ser His Ile Arg His Val
        195                 200                 205

Ser Asn Lys Gly Met Asp His Leu His Cys Met Lys Met Lys Lys Met
    210                 215                 220

Val Pro Leu Tyr Asp Leu Leu Leu Glu Met Leu Asp Ala His
225                 230                 235


<210>  130
<211>  238
<212>  PRT
<213>  Homo sapiens

<400>  130

Leu Thr Ala Glu Gln Met Val Ser Ala Leu Leu Glu Ala Glu Pro Pro
1               5                   10                  15

Ile Val Tyr Ser Glu Tyr Asp Pro Asn Arg Pro Phe Asn Glu Ala Ser
            20                  25                  30
```

```
Met Met Thr Leu Leu Thr Asn Leu Ala Asp Arg Glu Leu Val His Met
        35                  40                  45

Ile Asn Trp Ala Lys Arg Val Pro Gly Phe Val Asp Leu Thr Leu His
    50                  55                  60

Asp Gln Val His Leu Leu Glu Cys Ala Trp Leu Glu Ile Leu Met Ile
65                  70                  75                  80

Gly Leu Val Trp Arg Ser Met Glu His Pro Gly Lys Leu Leu Phe Ala
                85                  90                  95

Pro Asn Leu Leu Leu Asp Arg Asn Gln Gly Lys Cys Val Glu Gly Met
            100                 105                 110

Val Glu Ile Phe Asp Met Leu Leu Ala Thr Ala Ala Arg Phe Arg Met
        115                 120                 125

Met Asn Leu Gln Gly Glu Glu Phe Val Cys Leu Lys Ser Ile Ile Leu
    130                 135                 140

Leu Asn Ser Gly Val Tyr Thr Phe Leu Ser Ser Thr Leu Lys Ser Leu
145                 150                 155                 160

Glu Glu Arg Asp Tyr Ile His Arg Val Leu Asp Lys Ile Thr Asp Thr
                165                 170                 175

Leu Ile His Leu Met Ala Lys Ser Gly Leu Ser Leu Gln Gln Gln His
            180                 185                 190

Arg Arg Leu Ala Gln Leu Leu Leu Ile Leu Ser His Ile Arg His Met
        195                 200                 205

Ser Asn Lys Gly Met Glu His Leu Tyr Asn Met Lys Cys Lys Asn Val
    210                 215                 220

Val Pro Leu Tyr Asp Leu Leu Leu Glu Met Leu Asp Ala His
225                 230                 235


<210>  131
<211>  238
<212>  PRT
<213>  Homo sapiens

<400>  131

Leu Thr Ala Glu Gln Leu Ile Ser Ala Leu Met Glu Ala Glu Ala Pro
1               5                   10                  15

Ile Val Tyr Ser Glu His Asp Ser Thr Lys Pro Leu Ser Glu Ala Ser
            20                  25                  30

Met Met Thr Leu Leu Thr Asn Leu Ala Asp Arg Glu Leu Val His Met
```

35 40 45

Ile Asn Trp Ala Lys Arg Val Pro Gly Phe Val Asp Leu Thr Leu His
50 55 60

Asp Gln Val His Leu Leu Glu Cys Ala Trp Leu Glu Ile Leu Met Val
65 70 75 80

Gly Leu Ile Trp Arg Ser Val Glu His Pro Gly Lys Leu Ser Phe Ala
85 90 95

Pro Asn Leu Leu Leu Asp Arg Asn Gln Gly Arg Cys Val Glu Gly Leu
100 105 110

Val Glu Ile Phe Asp Met Leu Val Thr Thr Ala Thr Arg Phe Arg Met
115 120 125

Met Arg Leu Arg Gly Glu Glu Phe Ile Cys Leu Lys Ser Ile Ile Leu
130 135 140

Leu Asn Ser Gly Val Tyr Thr Phe Leu Ser Ser Thr Leu Glu Ser Leu
145 150 155 160

Glu Asp Thr Asp Leu Ile His Ile Ile Leu Asp Lys Ile Ile Asp Thr
165 170 175

Leu Val His Phe Met Ala Lys Ser Gly Leu Ser Leu Gln Gln Gln Gln
180 185 190

Arg Arg Leu Ala Gln Leu Leu Leu Ile Leu Ser His Ile Arg His Met
195 200 205

Ser Asn Lys Gly Met Glu His Leu Tyr Ser Met Lys Cys Lys Asn Val
210 215 220

Val Pro Leu Tyr Asp Leu Leu Leu Glu Met Leu Asp Ala His
225 230 235

<210> 132
<211> 243
<212> PRT
<213> Homo sapiens

<400> 132

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

His Arg Gly Glu Glu Asn His Pro Thr Gly Gln Gln Ala Gly Asn Trp
20 25 30

Gln Glu Ile Ser Asn Pro Glu Leu Ile Glu Ser Val Ser Ser Leu Val
35 40 45

```
Asp Arg Glu Leu Thr Gly Ile Ile Cys Trp Gly Lys Lys Ile Pro Gly
    50                  55                  60

Tyr Ser Lys Leu Ser Leu Asn Asp Gln Val Leu Leu Met Glu Ser Thr
65                  70                  75                  80

Trp Leu Asp Leu Leu Ile Leu Asp Leu Val Trp Cys Ser Ile Arg His
                85                  90                  95

Lys Gly Glu Lys Leu Leu Leu Ser Gly Gly Val Leu Val Asn Arg Asn
            100                 105                 110

Thr Ile Ser Asn Arg Arg Asn Asn Ser Ser Gly Asp Asp Met Glu Val
        115                 120                 125

Leu Glu Met Cys Asp Gln Ile Leu Ser Ile Ala Thr Lys Phe Tyr Glu
    130                 135                 140

Phe Asp Leu Gln Arg Arg Glu Tyr Leu Cys Leu Lys Ala Ile Thr Leu
145                 150                 155                 160

Val His Gly Ser Leu Lys Gly Leu Glu Ser Asp Thr Gln Val Arg Gln
                165                 170                 175

Leu Gln Asp Asp Leu Thr Asp Ala Leu Met Asp Val Cys Ser Glu Arg
            180                 185                 190

His Ala Leu Gly Ser Arg Arg Pro Ala Lys Met Leu Leu Leu Leu Ser
        195                 200                 205

His Leu Arg Gln Val Ser Ala Arg Ala Ser Ser His Leu Gly Ala Val
    210                 215                 220

Arg Asn Gly Leu Lys Val Pro Leu Tyr Asp Ile Leu Leu Asp Ile Leu
225                 230                 235                 240

Thr Asp Gln
```

<210> 133
<211> 235
<212> PRT
<213> Homo sapiens

<400> 133

```
Leu Ser Ser Glu Gln Phe Leu Thr Cys Leu Leu Asn Ala Glu Pro Pro
1               5                   10                  15

Asn Met Thr Cys His His Asp Val Ser Arg Pro Phe Thr Ala Glu Arg
            20                  25                  30
```

```
Leu Met Met Leu Leu Thr Asn Leu Ala Asp Arg Glu Leu Val His Met
        35                  40                  45

Ile Gly Trp Ala Lys Lys Val Pro Gly Phe Val Gln Ile Ser Leu Arg
    50                  55                  60

Asp Gln Val Leu Leu Leu Glu Ser Ser Trp Leu Glu Val Leu Ile Met
65                  70                  75                  80

Gly Leu Ile Trp Arg Ser Met Ser Gln Pro Gly Lys Leu Val Phe Ala
                85                  90                  95

Ser Asn Leu Ile Leu Asp Arg Asp Asp Gly Glu Cys Val Glu Gly Ile
            100                 105                 110

Phe Glu Ile Phe Asp Ile Leu Leu Asn Ile Val Gln His Phe Arg Glu
        115                 120                 125

Leu Gln Val Trp Met Asp Glu Tyr Val Cys Leu Lys Ala Ile Ile Leu
    130                 135                 140

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

Ala Lys Val Gln Gln Leu Val Glu Ala Thr Thr Asp Thr Leu Val Lys
                165                 170                 175

Cys Ile Ala Arg Arg Ser Leu Ala Thr Pro Glu Gln Phe Arg Arg Leu
            180                 185                 190

Ser His Leu Leu Thr Ile Leu Ser His Ile Arg His Ile Ser Asn Lys
        195                 200                 205

Gly Ile Gln His Met Tyr Ser Met Lys Cys Lys Asn Leu Val Pro Phe
    210                 215                 220

Tyr Asp Leu Leu Leu Glu Met Leu Asp Ala His
225                 230                 235


<210>  134
<211>  530
<212>  PRT
<213>  Homo sapiens

<400>  134

Met Asp Ile Lys Asn Ser Pro Ser Ser Leu Asn Ser Pro Ser Ser Tyr
1               5                   10                  15

Asn Cys Ser Gln Ser Ile Leu Pro Leu Glu His Gly Ser Ile Tyr Ile
            20                  25                  30
```

```
Pro Ser Ser Tyr Val Asp Ser His His Glu Tyr Pro Ala Met Thr Phe
        35                  40                  45

Tyr Ser Pro Ala Val Met Asn Tyr Ser Ile Pro Ser Asn Val Thr Asn
    50                  55                  60

Leu Glu Gly Gly Pro Gly Arg Gln Thr Thr Ser Pro Asn Val Leu Trp
65                  70                  75                  80

Pro Thr Pro Gly His Leu Ser Pro Leu Val Val His Arg Gln Leu Ser
                85                  90                  95

His Leu Tyr Ala Glu Pro Gln Lys Ser Pro Trp Cys Glu Ala Arg Ser
            100                 105                 110

Leu Glu His Thr Leu Pro Val Asn Arg Glu Thr Leu Lys Arg Lys Val
        115                 120                 125

Ser Gly Asn Arg Cys Ala Ser Pro Val Thr Gly Pro Gly Ser Lys Arg
    130                 135                 140

Asp Ala His Phe Cys Ala Val Cys Ser Asp Tyr Ala Ser Gly Tyr His
145                 150                 155                 160

Tyr Gly Val Trp Ser Cys Glu Gly Cys Lys Ala Phe Phe Lys Arg Ser
                165                 170                 175

Ile Gln Gly His Asn Asp Tyr Ile Cys Pro Ala Thr Asn Gln Cys Thr
            180                 185                 190

Ile Asp Lys Asn Arg Arg Lys Ser Cys Gln Ala Cys Arg Leu Arg Lys
        195                 200                 205

Cys Tyr Glu Val Gly Met Val Lys Cys Gly Ser Arg Arg Glu Arg Cys
    210                 215                 220

Gly Tyr Arg Leu Val Arg Arg Gln Arg Ser Ala Asp Glu Gln Leu His
225                 230                 235                 240

Cys Ala Gly Lys Ala Lys Arg Ser Gly Gly His Ala Pro Arg Val Arg
                245                 250                 255

Glu Leu Leu Leu Asp Ala Leu Ser Pro Glu Gln Leu Val Leu Thr Leu
            260                 265                 270

Leu Glu Ala Glu Pro Pro His Val Leu Ile Ser Arg Pro Ser Ala Pro
        275                 280                 285

Phe Thr Glu Ala Ser Met Met Met Ser Leu Thr Lys Leu Ala Asp Lys
    290                 295                 300
```

```
Glu Leu Val His Met Ile Ser Trp Ala Lys Lys Ile Pro Gly Phe Val
305                 310                 315                 320

Glu Leu Ser Leu Phe Asp Gln Val Arg Leu Leu Glu Ser Cys Trp Met
                325                 330                 335

Glu Val Leu Met Met Gly Leu Met Trp Arg Ser Ile Asp His Pro Gly
            340                 345                 350

Lys Leu Ile Phe Ala Pro Asp Leu Val Leu Asp Arg Asp Glu Gly Lys
        355                 360                 365

Cys Val Glu Gly Ile Leu Glu Ile Phe Asp Met Leu Leu Ala Thr Thr
    370                 375                 380

Ser Arg Phe Arg Glu Leu Lys Leu Gln His Lys Glu Tyr Leu Cys Val
385                 390                 395                 400

Lys Ala Met Ile Leu Leu Asn Ser Ser Met Tyr Pro Leu Val Thr Ala
                405                 410                 415

Thr Gln Asp Ala Asp Ser Ser Arg Lys Leu Ala His Leu Leu Asn Ala
            420                 425                 430

Val Thr Asp Ala Leu Val Trp Val Ile Ala Lys Ser Gly Ile Ser Ser
        435                 440                 445

Gln Gln Gln Ser Met Arg Leu Ala Asn Leu Leu Met Leu Leu Ser His
    450                 455                 460

Val Arg His Ala Ser Asn Lys Gly Met Glu His Leu Leu Asn Met Lys
465                 470                 475                 480

Cys Lys Asn Val Val Pro Val Tyr Asp Leu Leu Leu Glu Met Leu Asn
                485                 490                 495

Ala His Val Leu Arg Gly Cys Lys Ser Ser Ile Thr Gly Ser Glu Cys
            500                 505                 510

Ser Pro Ala Glu Asp Ser Lys Ser Lys Glu Gly Ser Gln Asn Pro Gln
        515                 520                 525

Ser Gln
    530
```

<210> 135
<211> 243
<212> PRT
<213> Homo sapiens

<400> 135

```
Leu Asp Ala Leu Ser Pro Glu Gln Leu Val Leu Thr Leu Leu Glu Ala
```

1 5 10 15

Glu Pro Pro His Val Leu Ile Ser Arg Pro Ser Ala Pro Phe Thr Glu
20 25 30

Ala Ser Met Met Met Ser Leu Thr Lys Leu Ala Asp Lys Glu Leu Val
35 40 45

His Met Ile Ser Trp Ala Lys Lys Ile Pro Gly Phe Val Glu Leu Ser
50 55 60

Leu Phe Asp Gln Val Arg Leu Leu Glu Ser Cys Trp Met Glu Val Leu
65 70 75 80

Met Met Gly Leu Met Trp Arg Ser Ile Asp His Pro Gly Lys Leu Ile
85 90 95

Phe Ala Pro Asp Leu Val Leu Asp Arg Asp Glu Gly Lys Cys Val Glu
100 105 110

Gly Ile Leu Glu Ile Phe Asp Met Leu Leu Ala Thr Thr Ser Arg Phe
115 120 125

Arg Glu Leu Lys Leu Gln His Lys Glu Tyr Leu Cys Val Lys Ala Met
130 135 140

Ile Leu Leu Asn Ser Ser Met Tyr Pro Leu Val Thr Ala Thr Gln Asp
145 150 155 160

Ala Asp Ser Ser Arg Lys Leu Ala His Leu Leu Asn Ala Val Thr Asp
165 170 175

Ala Leu Val Trp Val Ile Ala Lys Ser Gly Ile Ser Ser Gln Gln Gln
180 185 190

Ser Met Arg Leu Ala Asn Leu Leu Met Leu Leu Ser His Val Arg His
195 200 205

Ala Ser Asn Lys Gly Met Glu His Leu Leu Asn Met Lys Cys Lys Asn
210 215 220

Val Val Pro Val Tyr Asp Leu Leu Leu Glu Met Leu Asn Ala His Val
225 230 235 240

Leu Arg Gly

<210> 136
<211> 238
<212> PRT
<213> Homo sapiens

<400> 136

Leu Thr Ala Asp Gln Met Val Ser Ala Leu Leu Asp Ala Glu Pro Pro
1 5 10 15

Ile Leu Tyr Ser Glu Tyr Asp Pro Thr Arg Pro Phe Ser Glu Ala Ser
20 25 30

Met Met Gly Leu Leu Thr Asn Leu Ala Asp Arg Glu Leu Val His Met
35 40 45

Ile Asn Trp Ala Lys Arg Val Pro Gly Phe Val Asp Leu Thr Leu His
50 55 60

Asp Gln Val His Leu Leu Glu Cys Ala Trp Leu Glu Ile Leu Met Ile
65 70 75 80

Gly Leu Val Trp Arg Ser Met Glu His Pro Gly Lys Leu Leu Phe Ala
85 90 95

Pro Asn Leu Leu Leu Asp Arg Asn Gln Gly Lys Cys Val Glu Gly Met
100 105 110

Val Glu Ile Phe Asp Met Leu Leu Ala Thr Ser Ser Arg Phe Arg Met
115 120 125

Met Asn Leu Gln Gly Glu Glu Phe Val Cys Leu Lys Ser Ile Ile Leu
130 135 140

Leu Asn Ser Gly Val Tyr Thr Phe Leu Ser Ser Thr Leu Lys Ser Leu
145 150 155 160

Glu Glu Lys Asp His Ile His Arg Val Leu Asp Lys Ile Thr Asp Thr
165 170 175

Leu Ile His Leu Met Ala Lys Ala Gly Leu Thr Leu Gln Gln Gln His
180 185 190

Gln Arg Leu Ala Gln Leu Leu Leu Ile Leu Ser His Ile Arg His Met
195 200 205

Ser Asn Lys Gly Met Glu His Leu Tyr Ser Met Lys Cys Lys Asn Val
210 215 220

Val Pro Leu Tyr Asp Leu Leu Leu Glu Met Leu Asp Ala His
225 230 235

<210> 137
<211> 236
<212> PRT
<213> Homo sapiens

<400> 137

```
Leu Ser Pro Glu Gln Leu Val Leu Thr Leu Leu Glu Ala Glu Pro Pro
1               5                  10                  15

His Val Leu Ile Ser Arg Pro Ser Ala Pro Phe Thr Glu Ala Ser Met
            20                  25                  30

Met Met Ser Leu Thr Lys Leu Ala Asp Lys Glu Leu Val His Met Ile
        35                  40                  45

Ser Trp Ala Lys Lys Ile Pro Gly Phe Val Glu Leu Ser Leu Phe Asp
    50                  55                  60

Gln Val Arg Leu Leu Glu Ser Cys Trp Met Glu Val Leu Met Met Gly
65                  70                  75                  80

Leu Met Trp Arg Ser Ile Asp His Pro Gly Lys Leu Ile Phe Ala Pro
                85                  90                  95

Asp Leu Val Leu Asp Arg Asp Glu Gly Lys Cys Val Glu Gly Ile Leu
            100                 105                 110

Glu Ile Phe Asp Met Leu Leu Ala Thr Thr Ser Arg Phe Arg Glu Leu
        115                 120                 125

Lys Leu Gln His Lys Glu Tyr Leu Cys Val Lys Ala Met Ile Leu Leu
    130                 135                 140

Asn Ser Ser Met Tyr Pro Leu Val Thr Ala Thr Gln Asp Ala Asp Ser
145                 150                 155                 160

Ser Arg Lys Leu Ala His Leu Leu Asn Ala Val Thr Asp Ala Leu Val
                165                 170                 175

Trp Val Ile Ala Lys Ser Gly Ile Ser Ser Gln Gln Gln Ser Met Arg
            180                 185                 190

Leu Ala Asn Leu Leu Met Leu Leu Ser His Val Arg His Ala Ser Asn
        195                 200                 205

Lys Gly Met Glu His Leu Leu Asn Met Lys Cys Lys Asn Val Val Pro
    210                 215                 220

Val Tyr Asp Leu Leu Leu Glu Met Leu Asn Ala His
225                 230                 235
```

<210> 138
<211> 227
<212> PRT
<213> Homo sapiens

<400> 138

```
Asn Pro Thr Val Pro Leu Ile Ser His Leu Val Asn Ile Glu Pro Asn
1               5                  10                  15

Pro Ile Leu Thr Gly Tyr Asn Pro Gln Cys Thr Pro Thr Glu Gly Tyr
            20                  25                  30

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

Val Asp Trp Ala Ala Arg Leu Pro Gly Tyr Gly Met Leu Pro Met Asp
    50                  55                  60

Asp Gln Val Asn Leu Ile Arg Thr Val Trp Leu Asp Leu Leu Met Leu
65                  70                  75                  80

Gly Leu Val Trp Arg Ser Met Glu His Arg Gly Glu Trp Leu Val Phe
                85                  90                  95

Ala Pro Asp Leu Leu Met Asp Arg Ser Leu Cys Arg Leu Ser Gly Met
            100                 105                 110

Glu Tyr Ile Cys Thr Pro Met Leu Glu Phe Ala Arg Gln Phe Ala Asp
        115                 120                 125

Leu Gln Val Pro Gln Glu Val Tyr Val Cys Leu Lys Ala Leu Thr Leu
    130                 135                 140

Tyr Thr Thr Ala Val Ser Arg Leu Gln Asp Tyr Arg Gln Val Gln Arg
145                 150                 155                 160

Leu Gln His Glu Ile Asn Glu Ala Leu Ala Glu Ala Cys Ser Ser Thr
                165                 170                 175

Phe Gly Phe Ser Pro Gly Asn Ile Ala Arg Leu Met Met Ile Val Ser
            180                 185                 190

Gln Val Arg Gln Leu Ser Ser Leu Gly Val Asp His Leu Asn Arg Leu
        195                 200                 205

Arg Gly Ala Glu Thr Val Ser Val Glu Gly Leu Leu Arg Glu Ile Val
    210                 215                 220

Asp Glu Pro
225
```

<210> 139
<211> 238
<212> PRT
<213> Homo sapiens

<400> 139

```
Leu Ser Pro Glu Glu Leu Ile Ser Arg Ile Met Glu Ala Glu Pro Pro
```

1 5 10 15

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

Val Met Met Ser Leu Thr Asn Leu Ala Asp Lys Glu Leu Val His Met
35 40 45

Ile Ser Trp Ala Lys Lys Ile Pro Gly Phe Val Glu Leu Ser Leu Phe
50 55 60

Asp Gln Val His Leu Leu Glu Cys Cys Trp Leu Glu Val Leu Met Leu
65 70 75 80

Gly Leu Met Trp Arg Ser Val Asn His Pro Gly Lys Leu Ile Phe Ser
85 90 95

Pro Asp Leu Cys Leu Ser Arg Asp Glu Ser Ser Cys Val Gln Gly Leu
100 105 110

Val Glu Ile Phe Asp Met Leu Leu Ala Ala Thr Ser Arg Phe Arg Glu
115 120 125

Leu Lys Leu Gln Arg Glu Glu Tyr Val Cys Leu Lys Ala Met Ile Leu
130 135 140

Leu Asn Ser Asn Met Cys Leu Gly Ser Ser Glu Gly Gly Glu Asp Leu
145 150 155 160

Gln Ser Arg Ser Lys Leu Leu Cys Leu Leu Asp Ser Val Thr Asp Ala
165 170 175

Leu Val Trp Ala Ile Ser Lys Thr Gly Leu Ser Phe Gln Gln Arg Ser
180 185 190

Thr Arg Leu Ala His Leu Leu Met Leu Leu Ser His Ile Arg His Val
195 200 205

Ser Asn Lys Gly Met Asp His Leu His Cys Met Lys Met Lys Lys Met
210 215 220

Val Pro Leu Tyr Asp Leu Leu Leu Glu Met Leu Asp Ala His
225 230 235

<210> 140
<211> 238
<212> PRT
<213> Homo sapiens

<400> 140

Leu Thr Ala Glu Gln Met Val Ser Ala Leu Leu Glu Ala Glu Pro Pro
1 5 10 15

Ile Val Tyr Ser Glu Tyr Asp Pro Asn Arg Pro Phe Asn Glu Ala Ser
            20   25   30

Met Met Thr Leu Leu Thr Asn Leu Ala Asp Arg Glu Leu Val His Met
        35   40   45

Ile Asn Trp Ala Lys Arg Val Pro Gly Phe Val Asp Leu Thr Leu His
    50   55   60

Asp Gln Val His Leu Leu Glu Cys Ala Trp Leu Glu Ile Leu Met Ile
65   70   75   80

Gly Leu Val Trp Arg Ser Met Glu His Pro Gly Lys Leu Leu Phe Ala
                85   90   95

Pro Asn Leu Leu Leu Asp Arg Asn Gln Gly Lys Cys Val Glu Gly Met
            100   105   110

Val Glu Ile Phe Asp Met Leu Leu Ala Thr Ala Ala Arg Phe Arg Met
        115   120   125

Met Asn Leu Gln Gly Glu Glu Phe Val Cys Leu Lys Ser Ile Ile Leu
    130   135   140

Leu Asn Ser Gly Val Tyr Thr Phe Leu Ser Ser Thr Leu Lys Ser Leu
145   150   155   160

Glu Glu Arg Asp Tyr Ile His Arg Val Leu Asp Lys Ile Thr Asp Thr
                165   170   175

Leu Ile His Leu Met Ala Lys Ser Gly Leu Ser Leu Gln Gln Gln His
            180   185   190

Arg Arg Leu Ala Gln Leu Leu Leu Ile Leu Ser His Ile Arg His Met
        195   200   205

Ser Asn Lys Gly Met Glu His Leu Tyr Asn Met Lys Cys Lys Asn Val
    210   215   220

Val Pro Leu Tyr Asp Leu Leu Leu Glu Met Leu Asp Ala His
225   230   235

<210> 141
<211> 238
<212> PRT
<213> Homo sapiens

<400> 141

Leu Thr Ala Glu Gln Leu Ile Ser Ala Leu Met Glu Ala Glu Ala Pro
1   5   10   15

```
Ile Val Tyr Ser Glu His Asp Ser Thr Lys Pro Leu Ser Glu Ala Ser
            20                  25                  30

Met Met Thr Leu Leu Thr Asn Leu Ala Asp Arg Glu Leu Val His Met
        35                  40                  45

Ile Asn Trp Ala Lys Arg Val Pro Gly Phe Val Asp Leu Thr Leu His
    50                  55                  60

Asp Gln Val His Leu Leu Glu Cys Ala Trp Leu Glu Ile Leu Met Val
65                  70                  75                  80

Gly Leu Ile Trp Arg Ser Val Glu His Pro Gly Lys Leu Ser Phe Ala
                85                  90                  95

Pro Asn Leu Leu Leu Asp Arg Asn Gln Gly Arg Cys Val Glu Gly Leu
            100                 105                 110

Val Glu Ile Phe Asp Met Leu Val Thr Thr Ala Thr Arg Phe Arg Met
        115                 120                 125

Met Arg Leu Arg Gly Glu Glu Phe Ile Cys Leu Lys Ser Ile Ile Leu
    130                 135                 140

Leu Asn Ser Gly Val Tyr Thr Phe Leu Ser Ser Thr Leu Glu Ser Leu
145                 150                 155                 160

Glu Asp Thr Asp Leu Ile His Ile Ile Leu Asp Lys Ile Ile Asp Thr
                165                 170                 175

Leu Val His Phe Met Ala Lys Ser Gly Leu Ser Leu Gln Gln Gln Gln
            180                 185                 190

Arg Arg Leu Ala Gln Leu Leu Leu Ile Leu Ser His Ile Arg His Met
        195                 200                 205

Ser Asn Lys Gly Met Glu His Leu Tyr Ser Met Lys Cys Lys Asn Val
    210                 215                 220

Val Pro Leu Tyr Asp Leu Leu Leu Glu Met Leu Asp Ala His
225                 230                 235


<210>  142
<211>  243
<212>  PRT
<213>  Homo sapiens

<400>  142

Gln Arg Leu Lys Ala Leu Ile Asp Ala Leu Asp Val Lys Glu Gly Glu
1               5                   10                  15
```

His Arg Gly Glu Glu Asn His Pro Thr Gly Gln Gln Ala Gly Asn Trp
20 25 30

Gln Glu Ile Ser Asn Pro Glu Leu Ile Glu Ser Val Ser Ser Leu Val
35 40 45

Asp Arg Glu Leu Thr Gly Ile Ile Cys Trp Gly Lys Lys Ile Pro Gly
50 55 60

Tyr Ser Lys Leu Ser Leu Asn Asp Gln Val Leu Leu Met Glu Ser Thr
65 70 75 80

Trp Leu Asp Leu Leu Ile Leu Asp Leu Val Trp Cys Ser Ile Arg His
85 90 95

Lys Gly Glu Lys Leu Leu Leu Ser Gly Gly Val Leu Val Asn Arg Asn
100 105 110

Thr Ile Ser Asn Arg Arg Asn Asn Ser Ser Gly Asp Asp Met Glu Val
115 120 125

Leu Glu Met Cys Asp Gln Ile Leu Ser Ile Ala Thr Lys Phe Tyr Glu
130 135 140

Phe Asp Leu Gln Arg Arg Glu Tyr Leu Cys Leu Lys Ala Ile Thr Leu
145 150 155 160

Val His Gly Ser Leu Lys Gly Leu Glu Ser Asp Thr Gln Val Arg Gln
165 170 175

Leu Gln Asp Asp Leu Thr Asp Ala Leu Met Asp Val Cys Ser Glu Arg
180 185 190

His Ala Leu Gly Ser Arg Arg Pro Ala Lys Met Leu Leu Leu Leu Ser
195 200 205

His Leu Arg Gln Val Ser Ala Arg Ala Ser Ser His Leu Gly Ala Val
210 215 220

Arg Asn Gly Leu Lys Val Pro Leu Tyr Asp Ile Leu Leu Asp Ile Leu
225 230 235 240

Thr Asp Gln

<210> 143
<211> 235
<212> PRT
<213> Homo sapiens

<400> 143

Leu Ser Ser Glu Gln Phe Leu Thr Cys Leu Leu Asn Ala Glu Pro Pro

1 5 10 15

Asn Met Thr Cys His His Asp Val Ser Arg Pro Phe Thr Ala Glu Arg
20 25 30

Leu Met Met Leu Leu Thr Asn Leu Ala Asp Arg Glu Leu Val His Met
35 40 45

Ile Gly Trp Ala Lys Lys Val Pro Gly Phe Val Gln Ile Ser Leu Arg
50 55 60

Asp Gln Val Leu Leu Leu Glu Ser Ser Trp Leu Glu Val Leu Ile Met
65 70 75 80

Gly Leu Ile Trp Arg Ser Met Ser Gln Pro Gly Lys Leu Val Phe Ala
85 90 95

Ser Asn Leu Ile Leu Asp Arg Asp Asp Gly Glu Cys Val Glu Gly Ile
100 105 110

Phe Glu Ile Phe Asp Ile Leu Leu Asn Ile Val Gln His Phe Arg Glu
115 120 125

Leu Gln Val Trp Met Asp Glu Tyr Val Cys Leu Lys Ala Ile Ile Leu
130 135 140

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

Ala Lys Val Gln Gln Leu Val Glu Ala Thr Thr Asp Thr Leu Val Lys
165 170 175

Cys Ile Ala Arg Arg Ser Leu Ala Thr Pro Glu Gln Phe Arg Arg Leu
180 185 190

Ser His Leu Leu Thr Ile Leu Ser His Ile Arg His Ile Ser Asn Lys
195 200 205

Gly Ile Gln His Met Tyr Ser Met Lys Cys Lys Asn Leu Val Pro Phe
210 215 220

Tyr Asp Leu Leu Leu Glu Met Leu Asp Ala His
225 230 235

<210> 144
<211> 475
<212> PRT
<213> Homo sapiens

<400> 144

Met Val Asp Thr Glu Met Pro Phe Trp Pro Thr Asn Phe Gly Ile Ser
1 5 10 15

```
Ser Val Asp Leu Ser Val Met Glu Asp His Ser His Ser Phe Asp Ile
            20                  25                  30

Lys Pro Phe Thr Thr Val Asp Phe Ser Ser Ile Ser Thr Pro His Tyr
        35                  40                  45

Glu Asp Ile Pro Phe Thr Arg Thr Asp Pro Val Val Ala Asp Tyr Lys
    50                  55                  60

Tyr Asp Leu Lys Leu Gln Glu Tyr Gln Ser Ala Ile Lys Val Glu Pro
65                  70                  75                  80

Ala Ser Pro Pro Tyr Tyr Ser Glu Lys Thr Gln Leu Tyr Asn Lys Pro
                85                  90                  95

His Glu Glu Pro Ser Asn Ser Leu Met Ala Ile Glu Cys Arg Val Cys
            100                 105                 110

Gly Asp Lys Ala Ser Gly Phe His Tyr Gly Val His Ala Cys Glu Gly
        115                 120                 125

Cys Lys Gly Phe Phe Arg Arg Thr Ile Arg Leu Lys Leu Ile Tyr Asp
    130                 135                 140

Arg Cys Asp Leu Asn Cys Arg Ile His Lys Lys Ser Arg Asn Lys Cys
145                 150                 155                 160

Gln Tyr Cys Arg Phe Gln Lys Cys Leu Ala Val Gly Met Ser His Asn
                165                 170                 175

Ala Ile Arg Phe Gly Arg Met Pro Gln Ala Glu Lys Glu Lys Leu Leu
            180                 185                 190

Ala Glu Ile Ser Ser Asp Ile Asp Gln Leu Asn Pro Glu Ser Ala Asp
        195                 200                 205

Leu Arg Ala Leu Ala Lys His Leu Tyr Asp Ser Tyr Ile Lys Ser Phe
    210                 215                 220

Pro Leu Thr Lys Ala Lys Ala Arg Ala Ile Leu Thr Gly Lys Thr Thr
225                 230                 235                 240

Asp Lys Ser Pro Phe Val Ile Tyr Asp Met Asn Ser Leu Met Met Gly
                245                 250                 255

Glu Asp Lys Ile Lys Phe Lys His Ile Thr Pro Leu Gln Glu Gln Ser
            260                 265                 270

Lys Glu Val Ala Ile Arg Ile Phe Gln Gly Cys Gln Phe Arg Ser Val
        275                 280                 285
```

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

Val Asn Leu Asp Leu Asn Asp Gln Val Thr Leu Leu Lys Tyr Gly Val
305 310 315 320

His Glu Ile Ile Tyr Thr Met Leu Ala Ser Leu Met Asn Lys Asp Gly
325 330 335

Val Leu Ile Ser Glu Gly Gln Gly Phe Met Thr Arg Glu Phe Leu Lys
340 345 350

Ser Leu Arg Lys Pro Phe Gly Asp Phe Met Glu Pro Lys Phe Glu Phe
355 360 365

Ala Val Lys Phe Asn Ala Leu Glu Leu Asp Asp Ser Asp Leu Ala Ile
370 375 380

Phe Ile Ala Val Ile Ile Leu Ser Gly Asp Arg Pro Gly Leu Leu Asn
385 390 395 400

Val Lys Pro Ile Glu Asp Ile Gln Asp Asn Leu Leu Gln Ala Leu Glu
405 410 415

Leu Gln Leu Lys Leu Asn His Pro Glu Ser Ser Gln Leu Phe Ala Lys
420 425 430

Leu Leu Gln Lys Met Thr Asp Leu Arg Gln Ile Val Thr Glu His Val
435 440 445

Gln Leu Leu Gln Val Ile Lys Lys Thr Glu Thr Asp Met Ser Leu His
450 455 460

Pro Leu Leu Gln Glu Ile Tyr Lys Asp Leu Tyr
465 470 475

<210> 145
<211> 302
<212> PRT
<213> Homo sapiens

<400> 145

Ser His Asn Ala Ile Arg Phe Gly Arg Met Pro Gln Ala Glu Lys Glu
1 5 10 15

Lys Leu Leu Ala Glu Ile Ser Ser Asp Ile Asp Gln Leu Asn Pro Glu
20 25 30

Ser Ala Asp Leu Arg Ala Leu Ala Lys His Leu Tyr Asp Ser Tyr Ile
35 40 45

```
Lys Ser Phe Pro Leu Thr Lys Ala Lys Ala Arg Ala Ile Leu Thr Gly
    50                  55                  60

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

Met Met Gly Glu Asp Lys Ile Lys Phe Lys His Ile Thr Pro Leu Gln
                85                  90                  95

Glu Gln Ser Lys Glu Val Ala Ile Arg Ile Phe Gln Gly Cys Gln Phe
            100                 105                 110

Arg Ser Val Glu Ala Val Gln Glu Ile Thr Glu Tyr Ala Lys Ser Ile
        115                 120                 125

Pro Gly Phe Val Asn Leu Asp Leu Asn Asp Gln Val Thr Leu Leu Lys
    130                 135                 140

Tyr Gly Val His Glu Ile Ile Tyr Thr Met Leu Ala Ser Leu Met Asn
145                 150                 155                 160

Lys Asp Gly Val Leu Ile Ser Glu Gly Gln Gly Phe Met Thr Arg Glu
                165                 170                 175

Phe Leu Lys Ser Leu Arg Lys Pro Phe Gly Asp Phe Met Glu Pro Lys
            180                 185                 190

Phe Glu Phe Ala Val Lys Phe Asn Ala Leu Glu Leu Asp Asp Ser Asp
        195                 200                 205

Leu Ala Ile Phe Ile Ala Val Ile Ile Leu Ser Gly Asp Arg Pro Gly
    210                 215                 220

Leu Leu Asn Val Lys Pro Ile Glu Asp Ile Gln Asp Asn Leu Leu Gln
225                 230                 235                 240

Ala Leu Glu Leu Gln Leu Lys Leu Asn His Pro Glu Ser Ser Gln Leu
                245                 250                 255

Phe Ala Lys Leu Leu Gln Lys Met Thr Asp Leu Arg Gln Ile Val Thr
            260                 265                 270

Glu His Val Gln Leu Leu Gln Val Ile Lys Lys Thr Glu Thr Asp Met
        275                 280                 285

Ser Leu His Pro Leu Leu Gln Glu Ile Tyr Lys Asp Leu Tyr
    290                 295                 300
```

<210> 146
<211> 295
<212> PRT

<213> Homo sapiens

<400> 146

```
Gly Arg Met Pro Gln Ala Glu Lys Glu Lys Leu Leu Ala Glu Ile Ser
1               5                  10                  15

Ser Asp Ile Asp Gln Leu Asn Pro Glu Ser Ala Asp Leu Arg Ala Leu
            20                  25                  30

Ala Lys His Leu Tyr Asp Ser Tyr Ile Lys Ser Phe Pro Leu Thr Lys
        35                  40                  45

Ala Lys Ala Arg Ala Ile Leu Thr Gly Lys Thr Thr Asp Lys Ser Pro
    50                  55                  60

Phe Val Ile Tyr Asp Met Asn Ser Leu Met Met Gly Glu Asp Lys Ile
65                  70                  75                  80

Lys Phe Lys His Ile Thr Pro Leu Gln Glu Gln Ser Lys Glu Val Ala
                85                  90                  95

Ile Arg Ile Phe Gln Gly Cys Gln Phe Arg Ser Val Glu Ala Val Gln
            100                 105                 110

Glu Ile Thr Glu Tyr Ala Lys Ser Ile Pro Gly Phe Val Asn Leu Asp
        115                 120                 125

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

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

Glu Gly Gln Gly Phe Met Thr Arg Glu Phe Leu Lys Ser Leu Arg Lys
                165                 170                 175

Pro Phe Gly Asp Phe Met Glu Pro Lys Phe Glu Phe Ala Val Lys Phe
            180                 185                 190

Asn Ala Leu Glu Leu Asp Asp Ser Asp Leu Ala Ile Phe Ile Ala Val
        195                 200                 205

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

Glu Asp Ile Gln Asp Asn Leu Leu Gln Ala Leu Glu Leu Gln Leu Lys
225                 230                 235                 240

Leu Asn His Pro Glu Ser Ser Gln Leu Phe Ala Lys Leu Leu Gln Lys
                245                 250                 255
```

Met Thr Asp Leu Arg Gln Ile Val Thr Glu His Val Gln Leu Leu Gln
260 265 270

Val Ile Lys Lys Thr Glu Thr Asp Met Ser Leu His Pro Leu Leu Gln
275 280 285

Glu Ile Tyr Lys Asp Leu Tyr
290 295

<210> 147
<211> 271
<212> PRT
<213> Homo sapiens

<400> 147

Glu Ser Ala Asp Leu Arg Ala Leu Ala Lys His Leu Tyr Asp Ser Tyr
1 5 10 15

Ile Lys Ser Phe Pro Leu Thr Lys Ala Lys Ala Arg Ala Ile Leu Thr
20 25 30

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

Leu Met Met Gly Glu Asp Lys Ile Lys Phe Lys His Ile Thr Pro Leu
50 55 60

Gln Glu Gln Ser Lys Glu Val Ala Ile Arg Ile Phe Gln Gly Cys Gln
65 70 75 80

Phe Arg Ser Val Glu Ala Val Gln Glu Ile Thr Glu Tyr Ala Lys Ser
85 90 95

Ile Pro Gly Phe Val Asn Leu Asp Leu Asn Asp Gln Val Thr Leu Leu
100 105 110

Lys Tyr Gly Val His Glu Ile Ile Tyr Thr Met Leu Ala Ser Leu Met
115 120 125

Asn Lys Asp Gly Val Leu Ile Ser Glu Gly Gln Gly Phe Met Thr Arg
130 135 140

Glu Phe Leu Lys Ser Leu Arg Lys Pro Phe Gly Asp Phe Met Glu Pro
145 150 155 160

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

Asp Leu Ala Ile Phe Ile Ala Val Ile Ile Leu Ser Gly Asp Arg Pro
180 185 190

Gly Leu Leu Asn Val Lys Pro Ile Glu Asp Ile Gln Asp Asn Leu Leu

195 200 205

Gln Ala Leu Glu Leu Gln Leu Lys Leu Asn His Pro Glu Ser Ser Gln
210 215 220

Leu Phe Ala Lys Leu Leu Gln Lys Met Thr Asp Leu Arg Gln Ile Val
225 230 235 240

Thr Glu His Val Gln Leu Leu Gln Val Ile Lys Lys Thr Glu Thr Asp
245 250 255

Met Ser Leu His Pro Leu Leu Gln Glu Ile Tyr Lys Asp Leu Tyr
260 265 270

<210> 148
<211> 247
<212> PRT
<213> Homo sapiens

<400> 148

Ala Asp Leu Arg Ala Leu Ala Lys His Leu Tyr Asp Ser Tyr Ile Lys
1 5 10 15

Ser Phe Pro Leu Thr Lys Ala Lys Ala Arg Ala Ile Leu Thr Gly Lys
20 25 30

Thr Thr Asp Lys Ser Pro Phe Val Ile Tyr Asp Met Asn Ser Leu Met
35 40 45

Met Gly Glu Asp Lys Ile Lys Phe Lys His Ile Thr Pro Leu Gln Glu
50 55 60

Gln Ser Lys Glu Val Ala Ile Arg Ile Phe Gln Gly Cys Gln Phe Arg
65 70 75 80

Ser Val Glu Ala Val Gln Glu Ile Thr Glu Tyr Ala Lys Ser Ile Pro
85 90 95

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

Gly Val His Glu Ile Ile Tyr Thr Met Leu Ala Ser Leu Met Asn Lys
115 120 125

Asp Gly Val Leu Ile Ser Glu Gly Gln Gly Phe Met Thr Arg Glu Phe
130 135 140

Leu Lys Ser Leu Arg Lys Pro Phe Gly Asp Phe Met Glu Pro Lys Phe
145 150 155 160

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

```
Ala Ile Phe Ile Ala Val Ile Ile Leu Ser Gly Asp Arg Pro Gly Leu
            180                 185                 190

Leu Asn Val Lys Pro Ile Glu Asp Ile Gln Asp Asn Leu Leu Gln Ala
        195                 200                 205

Leu Glu Leu Gln Leu Lys Leu Asn His Pro Glu Ser Ser Gln Leu Phe
    210                 215                 220

Ala Lys Leu Leu Gln Lys Met Thr Asp Leu Arg Gln Ile Val Thr Glu
225                 230                 235                 240

His Val Gln Leu Leu Gln Val
                245
```

<210> 149
<211> 268
<212> PRT
<213> Homo sapiens

<400> 149

```
Ala Asp Leu Arg Ala Leu Ala Lys His Leu Tyr Asp Ser Tyr Ile Lys
1               5                   10                  15

Ser Phe Pro Leu Thr Lys Ala Lys Ala Arg Ala Ile Leu Thr Gly Lys
            20                  25                  30

Thr Thr Asp Lys Ser Pro Phe Val Ile Tyr Asp Met Asn Ser Leu Met
        35                  40                  45

Met Gly Glu Asp Lys Ile Lys Phe Lys His Ile Thr Pro Leu Gln Glu
    50                  55                  60

Gln Ser Lys Glu Val Ala Ile Arg Ile Phe Gln Gly Cys Gln Phe Arg
65                  70                  75                  80

Ser Val Glu Ala Val Gln Glu Ile Thr Glu Tyr Ala Lys Ser Ile Pro
                85                  90                  95

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

Gly Val His Glu Ile Ile Tyr Thr Met Leu Ala Ser Leu Met Asn Lys
        115                 120                 125

Asp Gly Val Leu Ile Ser Glu Gly Gln Gly Phe Met Thr Arg Glu Phe
    130                 135                 140

Leu Lys Ser Leu Arg Lys Pro Phe Gly Asp Phe Met Glu Pro Lys Phe
145                 150                 155                 160
```

```
Glu Phe Ala Val Lys Phe Asn Ala Leu Glu Leu Asp Asp Ser Asp Leu
                165                 170                 175

Ala Ile Phe Ile Ala Val Ile Ile Leu Ser Gly Asp Arg Pro Gly Leu
            180                 185                 190

Leu Asn Val Lys Pro Ile Glu Asp Ile Gln Asp Asn Leu Leu Gln Ala
        195                 200                 205

Leu Glu Leu Gln Leu Lys Leu Asn His Pro Glu Ser Ser Gln Leu Phe
    210                 215                 220

Ala Lys Leu Leu Gln Lys Met Thr Asp Leu Arg Gln Ile Val Thr Glu
225                 230                 235                 240

His Val Gln Leu Leu Gln Val Ile Lys Lys Thr Glu Thr Asp Met Ser
                245                 250                 255

Leu His Pro Leu Leu Gln Glu Ile Tyr Lys Asp Leu
            260                 265


<210>  150
<211>  268
<212>  PRT
<213>  Homo sapiens

<400>  150

Ala Asp Leu Lys Ala Phe Ser Lys His Ile Tyr Asn Ala Tyr Leu Lys
1               5                   10                  15

Asn Phe Asn Met Thr Lys Lys Lys Ala Arg Ser Ile Leu Thr Gly Lys
            20                  25                  30

Ala Ser His Thr Ala Pro Phe Val Ile His Asp Ile Glu Thr Leu Trp
        35                  40                  45

Gln Ala Glu Lys Gly Leu Val Trp Lys Gln Leu Val Asn Gly Leu Pro
    50                  55                  60

Pro Tyr Lys Glu Ile Ser Val His Val Phe Tyr Arg Cys Gln Cys Thr
65                  70                  75                  80

Thr Val Glu Thr Val Arg Glu Leu Thr Glu Phe Ala Lys Ser Ile Pro
                85                  90                  95

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

Gly Val His Glu Ala Ile Phe Ala Met Leu Ala Ser Ile Val Asn Lys
        115                 120                 125
```

```
Asp Gly Leu Leu Val Ala Asn Gly Ser Gly Phe Val Thr Arg Glu Phe
    130                 135                 140

Leu Arg Ser Leu Arg Lys Pro Phe Ser Asp Ile Ile Glu Pro Lys Phe
145                 150                 155                 160

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

Ala Leu Phe Ile Ala Ala Ile Ile Leu Cys Gly Asp Arg Pro Gly Leu
            180                 185                 190

Met Asn Val Pro Arg Val Glu Ala Ile Gln Asp Thr Ile Leu Arg Ala
        195                 200                 205

Leu Glu Phe His Leu Gln Ala Asn His Pro Asp Ala Gln Tyr Leu Phe
    210                 215                 220

Pro Lys Leu Leu Gln Lys Met Ala Asp Leu Arg Gln Leu Val Thr Glu
225                 230                 235                 240

His Ala Gln Met Met Gln Arg Ile Lys Lys Thr Glu Thr Glu Thr Ser
                245                 250                 255

Leu His Pro Leu Leu Gln Glu Ile Tyr Lys Asp Met
            260                 265
```

<210> 151
<211> 268
<212> PRT
<213> Homo sapiens

<400> 151

```
Ala Asp Leu Arg Ala Leu Ala Lys His Leu Tyr Asp Ser Tyr Ile Lys
1               5                   10                  15

Ser Phe Pro Leu Thr Lys Ala Lys Ala Arg Ala Ile Leu Thr Gly Lys
            20                  25                  30

Thr Thr Asp Lys Ser Pro Phe Val Ile Tyr Asp Met Asn Ser Leu Arg
        35                  40                  45

Met Gly Glu Asp Gln Ile Lys Cys Lys His Ala Ser Pro Leu Gln Glu
    50                  55                  60

Gln Asn Lys Glu Val Ala Ile Arg Ile Phe Gln Arg Cys Gln Phe Arg
65                  70                  75                  80

Ser Val Glu Ala Val Gln Glu Ile Thr Glu Phe Ala Lys Asn Ile Pro
                85                  90                  95

Gly Phe Val Asn Leu Asp Leu Asn Asp Gln Val Thr Leu Leu Lys Tyr
```

100 105 110

Gly Val His Glu Ile Ile Tyr Thr Leu Leu Ala Ser Leu Met Asn Lys
115 120 125

Asp Gly Val Leu Ile Ser Asp Gly Gln Gly Phe Met Thr Arg Glu Phe
130 135 140

Leu Lys Ser Leu Arg Lys Pro Phe Cys Asp Phe Met Glu Pro Lys Phe
145 150 155 160

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

Ala Ile Phe Ile Ala Val Ile Ile Leu Ser Gly Asp Arg Pro Gly Leu
180 185 190

Leu Asn Val Lys Pro Ile Glu Asp Ile Gln Asp Asn Leu Leu Gln Ala
195 200 205

Leu Glu Leu Gln Leu Lys Leu Asn His Pro Glu Ser Ser Gln Leu Phe
210 215 220

Ala Lys Leu Leu Gln Lys Met Thr Asp Leu Arg Gln Ile Val Thr Glu
225 230 235 240

His Val Gln Leu Leu Gln Ile Ile Lys Lys Thr Glu Thr Asp Met Ser
245 250 255

Leu His Pro Leu Leu Gln Glu Ile Tyr Lys Asp Leu
260 265

<210> 152
<211> 302
<212> PRT
<213> Homo sapiens

<400> 152

Ala Asp Leu Arg Ala Leu Ala Arg His Leu Tyr Glu Ala Tyr Leu Lys
1 5 10 15

Tyr Phe Pro Leu Thr Lys Ala Lys Ala Arg Ala Ile Leu Ser Gly Lys
20 25 30

Thr Gly Asp Asn Ala Pro Phe Val Ile His Asp Ile Lys Ser Leu Met
35 40 45

Glu Gly Glu Gln Phe Ile Asn Cys Arg Gln Met Pro Ile Gln Glu Gln
50 55 60

Gln Gln Ala Ser Val Leu Thr Ala Thr His Gly Gly Leu Thr Glu His
65 70 75 80

```
His Met Gly Ser Asp Tyr Gly Val Trp Gly Thr Thr Ser Ile Ser Gly
                85                  90                  95

Gln Glu Pro Gln Asn Ala Leu Glu Leu Arg Phe Phe Gln Ser Cys Gln
            100                 105                 110

Ser Arg Ser Ala Glu Ala Val Arg Glu Val Thr Glu Phe Ala Lys Ser
        115                 120                 125

Ile Pro Gly Phe Thr Asp Leu Asp Leu Asn Asp Gln Val Thr Leu Leu
    130                 135                 140

Lys Tyr Gly Val Ile Glu Val Leu Ile Ile Met Met Ser Pro Leu Met
145                 150                 155                 160

Asn Lys Asp Gly Thr Leu Ile Ser Tyr Gly Gln Ile Phe Met Thr Arg
                165                 170                 175

Glu Phe Leu Lys Ser Leu Arg Lys Pro Phe Cys Gln Met Met Glu Pro
            180                 185                 190

Lys Phe Glu Phe Ser Val Lys Phe Asn Thr Leu Glu Leu Asp Asp Ser
        195                 200                 205

Asp Met Ala Leu Phe Leu Val Val Ile Ile Leu Ser Gly Asp Arg Pro
    210                 215                 220

Gly Leu Leu Asn Val Lys Pro Ile Glu Gln Leu Gln Glu Thr Val Leu
225                 230                 235                 240

His Ser Leu Glu Leu Gln Leu Lys Leu Asn His Pro Asp Ser Leu Gln
                245                 250                 255

Leu Phe Ala Lys Leu Leu Gln Lys Met Thr Asp Leu Arg Gln Ile Val
            260                 265                 270

Thr Asp His Val His Leu Ile Gln Leu Leu Lys Lys Thr Glu Val Asp
        275                 280                 285

Met Cys Leu His Pro Leu Leu Gln Glu Ile Met Lys Asp Leu
    290                 295                 300
```

<210> 153
<211> 242
<212> PRT
<213> Homo sapiens

<400> 153

```
Thr Lys Leu Val Ser Pro Cys Asp Glu Met Leu Thr Pro Asp Leu Lys
1               5                  10                  15
```

```
Ala Arg Leu Leu Phe Ala Ser Gln Val Phe Lys Lys Asn Ile Gly Lys
            20                  25                  30

Asp Lys Pro Thr Ile Tyr Lys Asn Val Ile Gly Ser Lys Ile Val Gln
        35                  40                  45

Ile Leu Tyr Ser Asp Phe Gln Ala Arg Val Val Asn Gly Ile Cys Glu
    50                  55                  60

Leu Thr Glu Phe Ala Lys Arg Leu Pro Asn Phe His Asp Ile Ser Leu
65                  70                  75                  80

Gln Asp Gln Val Ile Leu Leu Lys Tyr Gly Ser Tyr Glu Thr Met Phe
                85                  90                  95

Val Leu Phe Ser Arg Leu Ile Tyr Gly Glu Gly Met Ile Leu Pro Lys
            100                 105                 110

Ser Asn Ile Tyr Val Thr Phe Asn Phe Val Tyr Gln Leu Gly Val Ala
        115                 120                 125

Gly Asp Ile Met Lys Ser Lys Phe Leu Phe Ala Lys Lys Met Leu Ala
    130                 135                 140

Leu Glu Leu Thr Asp Asp Glu Met Ala Leu Phe Val Ala Met Ile Ile
145                 150                 155                 160

Leu Cys Pro Asp Arg Pro Glu Ile Asn Asp Arg Lys Leu Val Glu Arg
                165                 170                 175

Ile Gln Glu Lys Val Leu Phe Ala Leu Glu Tyr Gln Leu Ser Ile Ser
            180                 185                 190

His Pro His Lys Pro Arg Leu Phe Ala His Leu Leu Leu Lys Met Ala
        195                 200                 205

Glu Leu Arg Glu Leu Val Ser Lys His Val Val Met Val Gln Lys Leu
    210                 215                 220

Ala Asp Ala Lys Asp Phe Val Pro Pro Leu Leu Cys Glu Ile Met Gln
225                 230                 235                 240

Asp Met
```

<210> 154
<211> 267
<212> PRT
<213> Homo sapiens

<400> 154

```
Ser Asp Leu Asp Val Leu Ser Gln Leu Ile His Ser Ser Tyr Met Asn
1               5                  10                  15

Thr Phe Thr Met Thr Lys Lys Arg Ala Arg Asp Ile Leu Thr Gly Arg
            20                  25                  30

Asn Ser Ile Ser Pro Phe Val Ile His Asp Met Asp Thr Leu Trp Gln
        35                  40                  45

Ala Glu Gln Gly Thr Val Trp Glu Gln Leu Pro Thr Gln Asn Leu Thr
    50                  55                  60

Gly Thr Glu Ile Gly Val His Val Phe Tyr Arg Cys Gln Cys Thr Ser
65                  70                  75                  80

Val Glu Thr Val Arg Ala Leu Thr Asp Phe Ala Lys Arg Ile Pro Gly
                85                  90                  95

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

Val His Glu Ala Ile Phe Cys Met Leu Ala Ser Leu Met Asn Lys Asp
        115                 120                 125

Gly Leu Leu Val Ala Gly Gly Arg Gly Phe Val Thr Arg Glu Phe Leu
    130                 135                 140

Arg Ser Leu Arg Gln Pro Phe Cys His Ile Met Glu Pro Lys Phe His
145                 150                 155                 160

Phe Ala Ser Lys Phe Asn Ala Leu Glu Leu Asn Asp Ser Asp Leu Ala
                165                 170                 175

Leu Phe Val Ala Ser Ile Ile Leu Cys Gly Asp Arg Pro Gly Leu Ile
            180                 185                 190

Asn Pro Ser Gln Val Glu Asp Ile Gln Glu Gly Ile Leu Gly Ala Leu
        195                 200                 205

Arg Arg His Leu Lys Ala Ser His Thr Asp Ala Pro Phe Leu Phe Pro
    210                 215                 220

Lys Leu Leu His Lys Met Ala Asp Leu Arg Gln Leu Val Thr Glu His
225                 230                 235                 240

Ala Glu Leu Val Gln Ser Ile Lys Arg Thr Glu Ser Ser Ala Ala Leu
                245                 250                 255

His Pro Leu Leu Gln Glu Ile Tyr Arg Asp Met
            260                 265
```

<210> 155
<211> 242
<212> PRT
<213> Homo sapiens

<400> 155

Arg Ile His Ser Ile Tyr Ile Asn Met Trp Met Gly Gln Phe Ile Ser
1 5 10 15

Met Pro Val Gly Ser Arg Ala Thr Arg Ser Lys Glu Pro Asn Gly Lys
20 25 30

Thr Glu Asp His Lys Ser Met Lys Glu Leu Thr Glu Lys Glu Ala Leu
35 40 45

Thr Lys Phe Cys Arg Gly Ala Leu Leu Ala Ile Ile Glu Ser Leu Ala
50 55 60

Lys Phe Ala Lys Lys Leu Gln Glu Phe Lys Asn Leu Asp Leu Asn Asp
65 70 75 80

Gln Val Cys Leu Leu Lys His Ala Ala Phe Glu Val Ala Leu Ile Ala
85 90 95

Thr Ser Ser Arg Tyr Ala Ser Glu Gly Leu Trp Phe Pro Thr Asp Gly
100 105 110

Val Tyr Phe Thr Lys Lys Met Leu Glu Gln Leu Glu Ile Ser Phe Phe
115 120 125

Asp Gly Lys Phe Lys Phe Phe Glu Lys Met Lys Lys Leu Asn Leu Thr
130 135 140

Glu Arg Glu Leu Ala Leu Phe Cys Val Leu Ser Leu Thr Ser Pro Asp
145 150 155 160

Arg Asp Glu Leu Ile Glu Arg Asp Glu Val Glu Lys Phe Gln Glu Gln
165 170 175

Val Leu Glu Ala Ile Gln Ile Glu Leu Arg Thr Asn His Ser Asn His
180 185 190

Arg Met Leu Leu Pro Arg Leu Leu Ser Leu Leu Val Asp Leu Arg Gln
195 200 205

Leu Val Leu Asp His Ile Lys Gln Val Gln Gln Leu Met Leu Met Asp
210 215 220

Asp Pro Ser Tyr Ser Gly Pro Pro Pro Leu Ile Lys Glu Ile Phe Gly
225 230 235 240

Leu Tyr

<210> 156
<211> 260
<212> PRT
<213> Homo sapiens

<400> 156

Val Asp Ser Ile Ala Gln Gln Phe Asn Asp Ile Val Cys Ala Met Thr
1 5 10 15

Gln Glu Asp Leu Glu Lys Phe Trp Lys Arg Cys Ser Arg Pro Phe Thr
20 25 30

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

Lys Asp Gly Pro Pro Gln Glu Ile Thr Ser Arg Ala Glu Met Ala Gln
50 55 60

Gln Cys Phe Val Ser Met Glu Val Thr Ile Glu Lys Phe Ala Thr Phe
65 70 75 80

Ala Lys Gln Leu Pro Glu Phe Arg Arg Leu Ser Ser Ser Asp Gln Leu
85 90 95

Thr Leu Phe Lys Gly Ala Ala Leu Glu Val Cys Ala Thr Leu Ser Ala
100 105 110

Ser Arg Tyr Tyr His Gly Val Tyr Arg Phe Pro Glu Ile Asn Thr Tyr
115 120 125

Ile Arg Arg Asp Val Ala Glu Asn Ser Pro Phe Gly Lys Val Thr Thr
130 135 140

Tyr Thr Thr Glu Met Met Phe Tyr Glu Met Phe Asn Glu Leu Gly Leu
145 150 155 160

Thr Asp Lys Glu Lys Ala Val Phe Cys Thr Phe Leu Leu Tyr Ser Pro
165 170 175

Asp Arg Glu Gly Leu Val Asp Arg Glu Val Val Glu Arg His Gln Glu
180 185 190

His Leu Ala Gln Ile Leu Tyr Leu Glu Val Lys Lys Asn His Pro Asp
195 200 205

Arg Ser Asn Leu Tyr Ala Lys Leu Met Asp Val Ala Val Ala Leu Arg
210 215 220

Thr Leu Val Pro Asp His Leu Ala Arg Leu Glu Gln Ile Lys Met Arg
225 230 235 240

Cys Asn Gly His Leu Pro Ala Glu Pro Ser Pro Leu Leu Asn Glu Val
245 250 255

Tyr Gly Ser Ile
260

<210> 157
<211> 341
<212> PRT
<213> Homo sapiens

<400> 157

Ser Asp Leu Arg Ser Leu Ala Arg Leu Val Gln Glu Ala Tyr Leu Arg
1 5 10 15

Ile Phe Pro Leu Ser Lys Ala Lys Ala Gln Ala Ile Leu Ala Gly Lys
20 25 30

Val Gln Asn Asn Ala Val Val Ile His Asp His Glu Ser Leu Ala Gln
35 40 45

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

His Gly Ser Ile Gly Val Asn Ile Ala Ser Val Gly Gly Gly Cys Gly
65 70 75 80

Gly Ala Arg Gly Gly Thr Ile Cys Asp Gly Arg Gly Gly Pro Cys Asp
85 90 95

Ser Thr Thr Arg Gly Arg Val Leu Gly Thr Asp Cys Val Phe Ile Thr
100 105 110

Ala Asn Ser Val Thr Asp Thr Glu Leu Ala Ala Asp Ala Glu Gly Asn
115 120 125

Arg Ser Ser Asp Gln Glu Val Thr Pro Pro Arg Gly Ala Ala Glu Ile
130 135 140

Arg Ile Phe Asn Arg Cys His Tyr Arg Leu Val Glu Ala Val Arg Glu
145 150 155 160

Val Thr Glu Phe Ala Lys Ser Ile Pro Gly Phe Met Ile Leu Asp Leu
165 170 175

Asn Asp Gln Val Thr Leu Leu Lys Tyr Gly Val Tyr Glu Val Ile Phe
180 185 190

Ala Met Leu Ala Ala Gln Ile Asn Lys Asp Gly Leu Leu Ile Ala Tyr
195 200 205

Gly Ser Ala Phe Ile Thr Arg Glu Phe Leu Arg Ser Leu Arg Ser Pro
210 215 220

Phe Cys His Ile Met Glu Pro Lys Phe Glu Phe Ser Ile Arg Phe Asn
225 230 235 240

Ala Leu Ser Leu Asp Gly Thr Asp Leu Ala Leu Tyr Met Ala Ala Ile
245 250 255

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

Arg Ile Gln Asp Arg Ile Leu Gln Ala Leu Asp Leu Gln Leu Arg Lys
275 280 285

Thr His Pro Glu Ser Pro Phe Leu Phe Pro Lys Leu Leu Gln Lys Leu
290 295 300

Ser Asp Leu Arg Gln Leu Val Thr Glu His Ala Gln Met Val His Asn
305 310 315 320

Ile Arg Lys Thr Glu Ala Asp Thr Ala Leu Pro Pro Leu Leu Gln Glu
325 330 335

Ile Phe Lys Asp Met
340

<210> 158
<211> 778
<212> PRT
<213> Homo sapiens

<400> 158

Met Asp Ser Lys Glu Ser Leu Thr Pro Gly Arg Glu Glu Asn Pro Ser
1 5 10 15

Ser Val Leu Ala Gln Glu Arg Gly Asp Val Met Asp Phe Tyr Lys Thr
20 25 30

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

Ala Val Ala Ser Gln Ser Asp Ser Lys Gln Arg Arg Leu Leu Val Asp
50 55 60

Phe Pro Lys Gly Ser Val Ser Asn Ala Gln Gln Pro Asp Leu Ser Lys
65 70 75 80

Ala Val Ser Leu Ser Met Gly Leu Tyr Met Gly Glu Thr Glu Thr Lys
85 90 95

```
Val Met Gly Asn Asp Leu Gly Phe Pro Gln Gln Gly Gln Ile Ser Leu
            100                 105                 110

Ser Ser Gly Glu Thr Asp Leu Lys Leu Leu Glu Glu Ser Ile Ala Asn
        115                 120                 125

Leu Asn Arg Ser Thr Ser Val Pro Glu Asn Pro Lys Ser Ser Ala Ser
    130                 135                 140

Thr Ala Val Ser Ala Ala Pro Thr Glu Lys Glu Phe Pro Lys Thr His
145                 150                 155                 160

Ser Asp Val Ser Ser Glu Gln Gln His Leu Lys Gly Gln Thr Gly Thr
                165                 170                 175

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

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

Asn Glu Ser Pro Trp Arg Ser Asp Leu Leu Ile Asp Glu Asn Cys Leu
    210                 215                 220

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

Ser Asn Glu Asp Cys Lys Pro Leu Ile Leu Pro Asp Thr Lys Pro Lys
                245                 250                 255

Ile Lys Asp Asn Gly Asp Leu Val Leu Ser Ser Pro Ser Asn Val Thr
            260                 265                 270

Leu Pro Gln Val Lys Thr Glu Lys Glu Asp Phe Ile Glu Leu Cys Thr
        275                 280                 285

Pro Gly Val Ile Lys Gln Glu Lys Leu Gly Thr Val Tyr Cys Gln Ala
    290                 295                 300

Ser Phe Pro Gly Ala Asn Ile Ile Gly Asn Lys Met Ser Ala Ile Ser
305                 310                 315                 320

Val His Gly Val Ser Thr Ser Gly Gly Gln Met Tyr His Tyr Asp Met
                325                 330                 335

Asn Thr Ala Ser Leu Ser Gln Gln Gln Asp Gln Lys Pro Ile Phe Asn
            340                 345                 350

Val Ile Pro Pro Ile Pro Val Gly Ser Glu Asn Trp Asn Arg Cys Gln
        355                 360                 365
```

```
Gly Ser Gly Asp Asp Asn Leu Thr Ser Leu Gly Thr Leu Asn Phe Pro
    370                 375                 380

Gly Arg Thr Val Phe Ser Asn Gly Tyr Ser Ser Pro Ser Met Arg Pro
385                 390                 395                 400

Asp Val Ser Ser Pro Pro Ser Ser Ser Ser Thr Ala Thr Thr Gly Pro
                405                 410                 415

Pro Pro Lys Leu Cys Leu Val Cys Ser Asp Glu Ala Ser Gly Cys His
            420                 425                 430

Tyr Gly Val Leu Thr Cys Gly Ser Cys Lys Val Phe Phe Lys Arg Ala
        435                 440                 445

Val Glu Gly Arg Gln His Asn Tyr Leu Cys Ala Gly Arg Asn Asp Cys
    450                 455                 460

Ile Ile Asp Lys Ile Arg Arg Lys Asn Cys Pro Ala Cys Arg Tyr Arg
465                 470                 475                 480

Lys Cys Leu Gln Ala Gly Met Asn Leu Glu Ala Arg Lys Thr Lys Lys
                485                 490                 495

Lys Ile Lys Gly Ile Gln Gln Ala Thr Thr Gly Val Ser Gln Glu Thr
            500                 505                 510

Ser Glu Asn Pro Gly Asn Lys Thr Ile Val Pro Ala Thr Leu Pro Gln
        515                 520                 525

Leu Thr Pro Thr Leu Val Ser Leu Leu Glu Val Ile Glu Pro Glu Val
    530                 535                 540

Leu Tyr Ala Gly Tyr Asp Ser Ser Val Pro Asp Ser Thr Trp Arg Ile
545                 550                 555                 560

Met Thr Thr Leu Asn Met Leu Gly Gly Arg Gln Val Ile Ala Ala Val
                565                 570                 575

Lys Trp Ala Lys Ala Ile Pro Gly Phe Arg Asn Leu His Leu Asp Asp
            580                 585                 590

Gln Met Thr Leu Leu Gln Tyr Ser Trp Met Phe Leu Met Ala Phe Ala
        595                 600                 605

Leu Gly Trp Arg Ser Tyr Arg Gln Ser Ser Ala Asn Leu Leu Cys Phe
    610                 615                 620

Ala Pro Asp Leu Ile Ile Asn Glu Gln Arg Met Thr Leu Pro Cys Met
625                 630                 635                 640
```

Tyr Asp Gln Cys Lys His Met Leu Tyr Val Ser Ser Glu Leu His Arg
645 650 655

Leu Gln Val Ser Tyr Glu Glu Tyr Leu Cys Met Lys Thr Leu Leu Leu
660 665 670

Leu Ser Ser Val Pro Lys Asp Gly Leu Lys Ser Gln Glu Leu Phe Asp
675 680 685

Glu Ile Arg Met Thr Tyr Ile Lys Glu Leu Gly Lys Ala Ile Val Lys
690 695 700

Arg Glu Gly Asn Ser Ser Gln Asn Trp Gln Arg Phe Tyr Gln Leu Thr
705 710 715 720

Lys Leu Leu Asp Ser Met His Glu Val Val Glu Asn Leu Leu Asn Tyr
725 730 735

Cys Phe Gln Thr Phe Leu Asp Lys Thr Met Ser Ile Glu Phe Pro Glu
740 745 750

Met Leu Ala Glu Ile Ile Thr Asn Gln Ile Pro Lys Tyr Ser Asn Gly
755 760 765

Asn Ile Lys Lys Leu Leu Phe His Gln Lys
770 775

<210> 159
<211> 247
<212> PRT
<213> Homo sapiens

<400> 159

Thr Leu Val Ser Leu Leu Glu Val Ile Glu Pro Glu Val Leu Tyr Ala
1 5 10 15

Gly Tyr Asp Ser Ser Val Pro Asp Ser Thr Trp Arg Ile Met Thr Thr
20 25 30

Leu Asn Met Leu Gly Gly Arg Gln Val Ile Ala Ala Val Lys Trp Ala
35 40 45

Lys Ala Ile Pro Gly Phe Arg Asn Leu His Leu Asp Asp Gln Met Thr
50 55 60

Leu Leu Gln Tyr Ser Trp Met Phe Leu Met Ala Phe Ala Leu Gly Trp
65 70 75 80

Arg Ser Tyr Arg Gln Ser Ser Ala Asn Leu Leu Cys Phe Ala Pro Asp
85 90 95

Leu Ile Ile Asn Glu Gln Arg Met Thr Leu Pro Cys Met Tyr Asp Gln

100 105 110

Cys Lys His Met Leu Tyr Val Ser Ser Glu Leu His Arg Leu Gln Val
115 120 125

Ser Tyr Glu Glu Tyr Leu Cys Met Lys Thr Leu Leu Leu Leu Ser Ser
130 135 140

Val Pro Lys Asp Gly Leu Lys Ser Gln Glu Leu Phe Asp Glu Ile Arg
145 150 155 160

Met Thr Tyr Ile Lys Glu Leu Gly Lys Ala Ile Val Lys Arg Glu Gly
165 170 175

Asn Ser Ser Gln Asn Trp Gln Arg Phe Tyr Gln Leu Thr Lys Leu Leu
180 185 190

Asp Ser Met His Glu Val Val Glu Asn Leu Leu Asn Tyr Cys Phe Gln
195 200 205

Thr Phe Leu Asp Lys Thr Met Ser Ile Glu Phe Pro Glu Met Leu Ala
210 215 220

Glu Ile Ile Thr Asn Gln Ile Pro Lys Tyr Ser Asn Gly Asn Ile Lys
225 230 235 240

Lys Leu Leu Phe His Gln Lys
245

<210> 160
<211> 247
<212> PRT
<213> Homo sapiens

<400> 160

Thr Leu Val Ser Leu Leu Glu Val Ile Glu Pro Glu Val Leu Tyr Ala
1 5 10 15

Gly Tyr Asp Ser Ser Val Pro Asp Ser Thr Trp Arg Ile Met Thr Thr
20 25 30

Leu Asn Met Leu Gly Gly Arg Gln Val Ile Ala Ala Val Lys Trp Ala
35 40 45

Lys Ala Ile Pro Gly Phe Arg Asn Leu His Leu Asp Asp Gln Met Thr
50 55 60

Leu Leu Gln Tyr Ser Trp Met Ser Leu Met Ala Phe Ala Leu Gly Trp
65 70 75 80

Arg Ser Tyr Arg Gln Ser Ser Ala Asn Leu Leu Cys Phe Ala Pro Asp
85 90 95

```
Leu Ile Ile Asn Glu Gln Arg Met Thr Leu Pro Asp Met Tyr Asp Gln
            100                 105                 110

Cys Lys His Met Leu Tyr Val Ser Ser Glu Leu His Arg Leu Gln Val
        115                 120                 125

Ser Tyr Glu Glu Tyr Leu Cys Met Lys Thr Leu Leu Leu Leu Ser Ser
    130                 135                 140

Val Pro Lys Asp Gly Leu Lys Ser Gln Glu Leu Phe Asp Glu Ile Arg
145                 150                 155                 160

Met Thr Tyr Ile Lys Glu Leu Gly Lys Ala Ile Val Lys Arg Glu Gly
                165                 170                 175

Asn Ser Ser Gln Asn Trp Gln Arg Phe Tyr Gln Leu Thr Lys Leu Leu
            180                 185                 190

Asp Ser Met His Glu Val Val Glu Asn Leu Leu Asn Tyr Cys Phe Gln
        195                 200                 205

Thr Phe Leu Asp Lys Thr Met Ser Ile Glu Phe Pro Glu Met Leu Ala
    210                 215                 220

Glu Ile Ile Thr Asn Gln Ile Pro Lys Tyr Ser Asn Gly Asn Ile Lys
225                 230                 235                 240

Lys Leu Leu Phe His Gln Lys
                245
```

<210> 161
<211> 247
<212> PRT
<213> Homo sapiens

<400> 161

```
Thr Leu Val Ser Leu Leu Glu Val Ile Glu Pro Glu Val Leu Tyr Ser
1               5                   10                  15

Gly Tyr Asp Ser Thr Leu Pro Asp Ser Ser Trp Arg Ile Met Ser Thr
            20                  25                  30

Leu Asn Met Leu Gly Gly Arg Gln Val Val Ala Ala Val Lys Trp Ala
        35                  40                  45

Lys Ala Ile Pro Gly Phe Arg Asn Leu His Leu Asp Asp Gln Met Thr
    50                  55                  60

Leu Leu Gln Tyr Ser Trp Met Phe Leu Met Ala Phe Ala Leu Gly Trp
65                  70                  75                  80
```

```
Arg Ser Tyr Lys Gln Ser Asn Gly Asn Leu Leu Cys Phe Ala Pro Asp
                85                  90                  95

Leu Ile Ile Asn Glu Gln Arg Met Asn Leu Pro Cys Met Tyr Glu Gln
            100                 105                 110

Cys Lys His Met Leu Met Val Ala Arg Glu Leu Ser Arg Leu Gln Val
        115                 120                 125

Ser Tyr Glu Glu Tyr Leu Cys Met Lys Thr Leu Leu Leu Leu Ser Thr
    130                 135                 140

Ile Pro Lys Glu Gly Leu Lys Ser Gln Thr Leu Phe Glu Glu Ile Arg
145                 150                 155                 160

Met Thr Tyr Ile Lys Glu Leu Gly Lys Ala Ile Val Lys Arg Glu Gly
                165                 170                 175

Asn Ser Ser Gln Asn Trp Gln Arg Phe Tyr Gln Leu Thr Lys Leu Leu
            180                 185                 190

Asp Ser Met His Asp Val Val Glu Asn Leu Leu Ser Phe Cys Phe Gln
        195                 200                 205

Thr Phe Leu Asp Lys Ser Met Ser Ile Glu Phe Pro Glu Met Leu Ala
    210                 215                 220

Glu Ile Ile Ser Asn Gln Ile Pro Lys Tyr Ser Asn Gly Asn Ile Lys
225                 230                 235                 240

Lys Leu Leu Phe His Gln Lys
                245
```

<210> 162
<211> 247
<212> PRT
<213> Homo sapiens

<400> 162

```
Thr Leu Ile Ser Leu Leu Glu Val Ile Glu Pro Glu Val Leu Tyr Ser
1               5                   10                  15

Gly Tyr Asp Ser Ser Ile Pro Asp Thr Thr Arg Arg Leu Met Ser Ser
            20                  25                  30

Leu Asn Met Leu Gly Gly Arg Gln Val Val Ser Ala Val Arg Trp Ala
        35                  40                  45

Lys Ala Ile Pro Gly Phe Arg Asn Leu His Leu Asp Asp Gln Met Thr
    50                  55                  60
```

Leu Leu Gln Tyr Ser Trp Met Phe Leu Met Val Phe Ala Leu Gly Trp
65 70 75 80

Arg Ser Tyr Lys Gln Thr Asn Gly Ser Ile Leu Tyr Phe Ala Pro Asp
85 90 95

Leu Val Ile Thr Glu Asp Arg Met His Leu Pro Phe Met Gln Glu Arg
100 105 110

Cys Gln Glu Met Leu Lys Ile Ala Gly Glu Met Ser Ser Leu Gln Ile
115 120 125

Ser Tyr Asp Glu Tyr Leu Cys Met Lys Val Leu Leu Leu Met Cys Thr
130 135 140

Ile Pro Lys Glu Gly Leu Lys Ser His Ala Leu Phe Glu Glu Ile Arg
145 150 155 160

Met Thr Tyr Ile Lys Glu Leu Gly Lys Ala Ile Val Lys Arg Glu Gly
165 170 175

Asn Ser Ser Gln Asn Trp Gln Arg Phe Tyr Gln Leu Thr Lys Leu Leu
180 185 190

Asp Ser Met His Glu Val Ala Glu Asn Leu Leu Ala Phe Cys Phe Leu
195 200 205

Ser Phe Leu Asp Lys Ser Met Ser Ile Glu Phe Pro Asp Met Leu Ser
210 215 220

Glu Ile Ile Ser Asn Gln Ile Pro Lys Tyr Ser Ser Gly Asn Leu Lys
225 230 235 240

Lys Leu Leu Phe His Gln Lys
245

<210> 163
<211> 247
<212> PRT
<213> Homo sapiens

<400> 163

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

Gly Tyr Asp Ser Thr Leu Pro Asp Thr Ser Ser Arg Leu Met Ser Thr
20 25 30

Leu Asn Arg Leu Gly Gly Gln Gln Val Val Ser Ala Val Lys Trp Ala
35 40 45

Lys Ser Leu Pro Gly Phe Arg Asn Leu His Leu Asp Asp Gln Met Ile

50 55 60

Leu Leu Gln Cys Ser Trp Leu Phe Leu Met Ser Phe Ser Leu Gly Trp
65 70 75 80

Arg Ser Tyr Gln Gln Cys Asn Gly Ser Met Leu Cys Phe Ala Pro Asp
85 90 95

Leu Val Ile Asn Glu Glu Arg Met Arg Leu Pro Phe Met Asn Asp Gln
100 105 110

Cys Glu Lys Met Leu Arg Ile Cys Arg Glu Phe Val Arg Leu Gln Leu
115 120 125

Ser His Glu Glu Tyr Leu Cys Met Lys Val Leu Leu Leu Leu Ser Thr
130 135 140

Val Pro Lys Asp Gly Leu Lys Ser Gln Ala Val Phe Asp Glu Ile Arg
145 150 155 160

Met Thr Tyr Ile Lys Glu Leu Gly Lys Ala Ile Val Lys Arg Glu Glu
165 170 175

Asn Pro Ser Gln Asn Trp Gln Arg Phe Tyr Gln Leu Thr Lys Leu Leu
180 185 190

Asp Ser Met Gln Glu Met Val Glu Gly Leu Ile Lys Phe Cys Phe Tyr
195 200 205

Thr Phe Val Asn Lys Thr Leu Ser Val Glu Phe Pro Glu Met Leu Val
210 215 220

Glu Ile Ile Thr Asn Gln Ile Pro Lys Phe Gln Glu Gly Gly Ile Lys
225 230 235 240

Ala Leu Leu Phe His Gln Lys
245

<210> 164
<211> 247
<212> PRT
<213> Homo sapiens

<400> 164

Thr Leu Val Ser Leu Leu Glu Val Ile Glu Pro Glu Val Leu Tyr Ala
1 5 10 15

Gly Tyr Asp Ser Ser Val Pro Asp Ser Thr Trp Arg Ile Met Thr Thr
20 25 30

Leu Asn Met Leu Gly Gly Arg Gln Val Ile Ala Ala Val Lys Trp Ala
35 40 45

```
Lys Ala Ile Pro Gly Phe Arg Asn Leu His Leu Asp Asp Gln Met Thr
    50                  55                  60

Leu Leu Gln Tyr Ser Trp Met Tyr Leu Met Ala Phe Ala Leu Gly Trp
65                  70                  75                  80

Arg Ser Tyr Arg Gln Ser Ser Ala Asn Leu Leu Cys Phe Ala Pro Asp
                85                  90                  95

Leu Ile Ile Asn Glu Gln Arg Met Thr Leu Pro Gly Met Tyr Asp Gln
            100                 105                 110

Cys Lys His Met Leu Tyr Val Ser Ser Glu Leu His Arg Leu Gln Val
        115                 120                 125

Ser Tyr Glu Glu Tyr Leu Cys Met Lys Thr Leu Leu Leu Leu Ser Ser
    130                 135                 140

Val Pro Lys Asp Gly Leu Lys Ser Gln Glu Leu Phe Asp Glu Ile Arg
145                 150                 155                 160

Met Thr Tyr Ile Lys Glu Leu Gly Lys Ala Ile Val Lys Arg Glu Gly
                165                 170                 175

Asn Ser Ser Gln Asn Trp Gln Arg Phe Tyr Gln Leu Thr Lys Leu Leu
            180                 185                 190

Asp Ser Met His Glu Val Val Glu Asn Leu Leu Asn Tyr Cys Phe Gln
        195                 200                 205

Thr Phe Leu Asp Lys Thr Met Ser Ile Glu Phe Pro Glu Met Leu Ala
    210                 215                 220

Glu Ile Ile Thr Asn Gln Ile Pro Lys Tyr Ser Asn Gly Asn Ile Lys
225                 230                 235                 240

Lys Leu Leu Phe His Gln Lys
                245
```

<210> 165
<211> 247
<212> PRT
<213> Homo sapiens

<400> 165

```
Thr Leu Val Ser Leu Leu Glu Val Ile Glu Pro Glu Val Leu Tyr Ala
1               5                   10                  15

Gly Tyr Asp Ser Ser Val Pro Asp Ser Thr Trp Arg Ile Met Thr Thr
            20                  25                  30
```

```
Leu Asn Met Leu Gly Gly Arg Gln Val Ile Ala Ala Val Lys Trp Ala
        35                  40                  45

Lys Ala Ile Pro Gly Phe Arg Asn Leu His Leu Asp Asp Gln Met Thr
    50                  55                  60

Leu Leu Gln Tyr Ser Trp Met Ser Leu Met Ala Phe Ala Leu Gly Trp
65                  70                  75                  80

Arg Ser Tyr Arg Gln Ser Ser Ala Asn Leu Leu Cys Phe Ala Pro Asp
                85                  90                  95

Leu Ile Ile Asn Glu Gln Arg Met Thr Leu Pro Cys Met Tyr Asp Gln
            100                 105                 110

Cys Lys His Met Leu Tyr Val Ser Ser Glu Leu His Arg Leu Gln Val
        115                 120                 125

Ser Tyr Glu Glu Tyr Leu Cys Met Lys Thr Leu Leu Leu Leu Ser Ser
    130                 135                 140

Val Pro Lys Asp Gly Leu Lys Ser Gln Glu Leu Phe Asp Glu Ile Arg
145                 150                 155                 160

Met Thr Tyr Ile Lys Glu Leu Gly Lys Ala Ile Val Lys Arg Glu Gly
                165                 170                 175

Asn Ser Ser Gln Asn Trp Gln Arg Phe Tyr Gln Leu Thr Lys Leu Leu
            180                 185                 190

Asp Ser Met His Glu Val Val Glu Asn Leu Leu Asn Tyr Cys Phe Gln
        195                 200                 205

Thr Phe Leu Asp Lys Thr Met Ser Ile Glu Phe Pro Glu Met Leu Ala
    210                 215                 220

Glu Ile Ile Thr Asn Gln Ile Pro Lys Tyr Ser Asn Gly Asn Ile Lys
225                 230                 235                 240

Lys Leu Leu Phe His Gln Lys
                245
```

<210> 166
<211> 247
<212> PRT
<213> Homo sapiens

<400> 166

```
Thr Leu Val Ser Leu Leu Glu Val Ile Glu Pro Glu Val Leu Tyr Ala
1               5                   10                  15
```

```
Gly Tyr Asp Ser Ser Val Pro Asp Ser Thr Trp Arg Ile Met Thr Thr
            20                  25                  30

Leu Asn Met Leu Gly Gly Arg Gln Val Ile Ala Ala Val Lys Trp Ala
        35                  40                  45

Lys Ala Ile Pro Gly Phe Arg Asn Leu His Leu Asp Asp Gln Met Thr
    50                  55                  60

Leu Leu Gln Tyr Ser Trp Met Ser Leu Met Ala Phe Ala Leu Gly Trp
65                  70                  75                  80

Arg Ser Tyr Arg Gln Ser Ser Ala Asn Leu Leu Cys Phe Ala Pro Asp
                85                  90                  95

Leu Ile Ile Asn Glu Gln Arg Met Thr Leu Pro Cys Met Tyr Asp Gln
            100                 105                 110

Cys Lys His Met Leu Tyr Val Ser Ser Glu Leu His Arg Leu Gln Val
        115                 120                 125

Ser Tyr Glu Glu Tyr Leu Cys Met Lys Thr Leu Leu Leu Leu Ser Ser
    130                 135                 140

Val Pro Lys Asp Gly Leu Lys Ser Gln Glu Leu Phe Asp Glu Ile Arg
145                 150                 155                 160

Met Thr Tyr Ile Lys Glu Leu Gly Lys Ala Ile Val Lys Arg Glu Gly
                165                 170                 175

Asn Ser Ser Gln Asn Trp Gln Arg Phe Tyr Gln Leu Thr Lys Leu Leu
            180                 185                 190

Asp Ser Met His Glu Val Val Glu Asn Leu Leu Asn Tyr Cys Phe Gln
        195                 200                 205

Thr Phe Leu Asp Lys Thr Met Ser Ile Glu Phe Pro Glu Met Leu Ala
    210                 215                 220

Glu Ile Ile Thr Asn Gln Ile Pro Lys Tyr Ser Asn Gly Asn Ile Lys
225                 230                 235                 240

Lys Leu Leu Phe His Gln Lys
                245
```

<210> 167
<211> 427
<212> PRT
<213> Homo sapiens

<400> 167

```
Met Glu Ala Met Ala Ala Ser Thr Ser Leu Pro Asp Pro Gly Asp Phe
```

1 5 10 15

Asp Arg Asn Val Pro Arg Ile Cys Gly Val Cys Gly Asp Arg Ala Thr
20 25 30

Gly Phe His Phe Asn Ala Met Thr Cys Glu Gly Cys Lys Gly Phe Phe
35 40 45

Arg Arg Ser Met Lys Arg Lys Ala Leu Phe Thr Cys Pro Phe Asn Gly
50 55 60

Asp Cys Arg Ile Thr Lys Asp Asn Arg Arg His Cys Gln Ala Cys Arg
65 70 75 80

Leu Lys Arg Cys Val Asp Ile Gly Met Met Lys Glu Phe Ile Leu Thr
85 90 95

Asp Glu Glu Val Gln Arg Lys Arg Glu Met Ile Leu Lys Arg Lys Glu
100 105 110

Glu Glu Ala Leu Lys Asp Ser Leu Arg Pro Lys Leu Ser Glu Glu Gln
115 120 125

Gln Arg Ile Ile Ala Ile Leu Leu Asp Ala His His Lys Thr Tyr Asp
130 135 140

Pro Thr Tyr Ser Asp Phe Cys Gln Phe Arg Pro Pro Val Arg Val Asn
145 150 155 160

Asp Gly Gly Gly Ser His Pro Ser Arg Pro Asn Ser Arg His Thr Pro
165 170 175

Ser Phe Ser Gly Asp Ser Ser Ser Ser Cys Ser Asp His Cys Ile Thr
180 185 190

Ser Ser Asp Met Met Asp Ser Ser Ser Phe Ser Asn Leu Asp Leu Ser
195 200 205

Glu Glu Asp Ser Asp Asp Pro Ser Val Thr Leu Glu Leu Ser Gln Leu
210 215 220

Ser Met Leu Pro His Leu Ala Asp Leu Val Ser Tyr Ser Ile Gln Lys
225 230 235 240

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

Glu Asp Gln Ile Val Leu Leu Lys Ser Ser Ala Ile Glu Val Ile Met
260 265 270

Leu Arg Ser Asn Glu Ser Phe Thr Met Asp Asp Met Ser Trp Thr Cys

275 280 285

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

His Ser Leu Glu Leu Ile Glu Pro Leu Ile Lys Phe Gln Val Gly Leu
305 310 315 320

Lys Lys Leu Asn Leu His Glu Glu Glu His Val Leu Leu Met Ala Ile
325 330 335

Cys Ile Val Ser Pro Asp Arg Pro Gly Val Gln Asp Ala Ala Leu Ile
340 345 350

Glu Ala Ile Gln Asp Arg Leu Ser Asn Thr Leu Gln Thr Tyr Ile Arg
355 360 365

Cys Arg His Pro Pro Pro Gly Ser His Leu Leu Tyr Ala Lys Met Ile
370 375 380

Gln Lys Leu Ala Asp Leu Arg Ser Leu Asn Glu Glu His Ser Lys Gln
385 390 395 400

Tyr Arg Cys Leu Ser Phe Gln Pro Glu Cys Ser Met Lys Leu Thr Pro
405 410 415

Leu Val Leu Glu Val Phe Gly Asn Glu Ile Ser
420 425

<210> 168
<211> 305
<212> PRT
<213> Homo sapiens

<400> 168

Glu Leu Ser Glu Glu Gln Gln Arg Ile Ile Ala Ile Leu Leu Asp Ala
1 5 10 15

His His Lys Thr Tyr Asp Pro Thr Tyr Ser Asp Phe Cys Gln Phe Arg
20 25 30

Pro Pro Val Arg Val Asn Asp Gly Gly Gly Ser His Pro Ser Arg Pro
35 40 45

Asn Ser Arg His Thr Pro Ser Phe Ser Gly Asp Ser Ser Ser Ser Cys
50 55 60

Ser Asp His Cys Ile Thr Ser Ser Asp Met Met Asp Ser Ser Ser Phe
65 70 75 80

Ser Asn Leu Asp Leu Ser Glu Glu Asp Ser Asp Asp Pro Ser Val Thr
85 90 95

```
Leu Glu Leu Ser Gln Leu Ser Met Leu Pro His Leu Ala Asp Leu Val
            100                 105                 110

Ser Tyr Ser Ile Gln Lys Val Ile Gly Phe Ala Lys Met Ile Pro Gly
        115                 120                 125

Phe Arg Asp Leu Thr Ser Glu Asp Gln Ile Val Leu Leu Lys Ser Ser
    130                 135                 140

Ala Ile Glu Val Ile Met Leu Arg Ser Asn Glu Ser Phe Thr Met Asp
145                 150                 155                 160

Asp Met Ser Trp Thr Cys Gly Asn Gln Asp Tyr Lys Tyr Arg Val Ser
                165                 170                 175

Asp Val Thr Lys Ala Gly His Ser Leu Glu Leu Ile Glu Pro Leu Ile
            180                 185                 190

Lys Phe Gln Val Gly Leu Lys Lys Leu Asn Leu His Glu Glu Glu His
        195                 200                 205

Val Leu Leu Met Ala Ile Cys Ile Val Ser Pro Asp Arg Pro Gly Val
    210                 215                 220

Gln Asp Ala Ala Leu Ile Glu Ala Ile Gln Asp Arg Leu Ser Asn Thr
225                 230                 235                 240

Leu Gln Thr Tyr Ile Arg Cys Arg His Pro Pro Pro Gly Ser His Leu
                245                 250                 255

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

Glu Glu His Ser Lys Gln Tyr Arg Cys Leu Ser Phe Gln Pro Glu Cys
        275                 280                 285

Ser Met Lys Leu Thr Pro Leu Val Leu Glu Val Phe Gly Asn Glu Ile
    290                 295                 300

Ser
305


<210>  169
<211>  297
<212>  PRT
<213>  Homo sapiens

<400>  169

Leu Ser Asp Glu Gln Met Gln Ile Ile Asn Ser Leu Val Glu Ala His
1               5                   10                  15
```

```
His Lys Thr Tyr Asp Asp Ser Tyr Ser Asp Phe Val Arg Phe Arg Pro
            20                  25                  30

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

Leu His Ser Leu Ser Asp Ala Ser Ser Asp Ser Phe Asn His Ser Pro
    50                  55                  60

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

Gln Asp Ser Gly Ser Pro Asp Ser Ser Glu Glu Asp Gln Gln Ser Arg
                85                  90                  95

Leu Ser Met Leu Pro His Leu Ala Asp Leu Val Ser Tyr Ser Ile Gln
            100                 105                 110

Lys Val Ile Gly Phe Ala Lys Met Ile Pro Gly Phe Arg Asp Leu Thr
        115                 120                 125

Ala Glu Asp Gln Ile Ala Leu Leu Lys Ser Ser Ala Ile Glu Ile Ile
    130                 135                 140

Met Leu Arg Ser Asn Gln Ser Phe Ser Leu Glu Asp Met Ser Trp Ser
145                 150                 155                 160

Cys Gly Gly Pro Asp Phe Lys Tyr Cys Ile Asn Asp Val Thr Lys Ala
                165                 170                 175

Gly His Thr Leu Glu Leu Leu Glu Pro Leu Val Lys Phe Gln Val Gly
            180                 185                 190

Leu Lys Lys Leu Lys Leu His Glu Glu Glu His Val Leu Leu Met Ala
        195                 200                 205

Ile Cys Leu Leu Ser Pro Asp Arg Pro Gly Val Gln Asp His Val Arg
    210                 215                 220

Ile Glu Ala Leu Gln Asp Arg Leu Cys Asp Val Leu Gln Ala Tyr Ile
225                 230                 235                 240

Arg Ile Gln His Pro Gly Gly Arg Leu Leu Tyr Ala Lys Met Ile Gln
                245                 250                 255

Lys Leu Ala Asp Leu Arg Ser Leu Asn Glu Glu His Ser Lys Gln Tyr
            260                 265                 270

Arg Ser Leu Ser Phe Gln Pro Glu His Ser Met Gln Leu Thr Pro Leu
        275                 280                 285
```

Val Leu Glu Val Phe Gly Ser Glu Val
290 295

<210> 170
<211> 252
<212> PRT
<213> Homo sapiens

<400> 170

Leu Ser Glu Glu Gln Gln Arg Ile Ile Ala Ile Leu Leu Asp Ala His
1 5 10 15

His Lys Thr Tyr Asp Pro Thr Tyr Ser Asp Phe Cys Gln Phe Arg Pro
20 25 30

Pro Val Arg Val Asn Asp Gly Gly Gly Ser Val Thr Leu Glu Leu Ser
35 40 45

Gln Leu Ser Met Leu Pro His Leu Ala Asp Leu Val Ser Tyr Ser Ile
50 55 60

Gln Lys Val Ile Gly Phe Ala Lys Met Ile Pro Gly Phe Arg Asp Leu
65 70 75 80

Thr Ser Glu Asp Gln Ile Val Leu Leu Lys Ser Ser Ala Ile Glu Val
85 90 95

Ile Met Leu Arg Ser Asn Glu Ser Phe Thr Met Asp Asp Met Ser Trp
100 105 110

Thr Cys Gly Asn Gln Asp Tyr Lys Tyr Arg Val Ser Asp Val Thr Lys
115 120 125

Ala Gly His Ser Leu Glu Leu Ile Glu Pro Leu Ile Lys Phe Gln Val
130 135 140

Gly Leu Lys Lys Leu Asn Leu His Glu Glu Glu His Val Leu Leu Met
145 150 155 160

Ala Ile Cys Ile Val Ser Pro Asp Arg Pro Gly Val Gln Asp Ala Ala
165 170 175

Leu Ile Glu Ala Ile Gln Asp Arg Leu Ser Asn Thr Leu Gln Thr Tyr
180 185 190

Ile Arg Cys Arg His Pro Pro Pro Gly Ser His Leu Leu Tyr Ala Lys
195 200 205

Met Ile Gln Lys Leu Ala Asp Leu Arg Ser Leu Asn Glu Glu His Ser
210 215 220

Lys Gln Tyr Arg Cys Leu Ser Phe Gln Pro Glu Cys Ser Met Lys Leu
225 230 235 240

Thr Pro Leu Val Leu Glu Val Phe Gly Asn Glu Ile
245 250

<210> 171
<211> 297
<212> PRT
<213> Homo sapiens

<400> 171

Ile Ser Asp Glu Gln Gln Lys Met Ile Asp Ile Leu Leu Glu Ala His
1 5 10 15

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

Pro Val Arg Glu Asn Val Asp Pro Phe Arg Arg Ile Thr Arg Ser Ser
35 40 45

Ser Val His Thr Gln Gly Ser Pro Ser Glu Asp Ser Asp Val Phe Thr
50 55 60

Ser Ser Pro Asp Ser Ser Glu His Gly Phe Phe Ser Ala Ser Leu Phe
65 70 75 80

Gly Gln Phe Glu Tyr Ser Ser Met Gly Gly Lys Ser Gly Glu Leu Ser
85 90 95

Met Leu Pro His Ile Ala Asp Leu Val Ser Tyr Ser Ile Gln Lys Ile
100 105 110

Ile Gly Phe Ala Lys Met Ile Pro Gly Phe Arg Asp Leu Ile Ala Glu
115 120 125

Asp Gln Ile Ala Leu Leu Lys Ser Ser Val Ile Glu Val Ile Met Leu
130 135 140

Arg Ser Asn Gln Ser Phe Ser Leu Asp Asp Met Ser Trp Thr Cys Gly
145 150 155 160

Ser Glu Asp Phe Lys Tyr Lys Val Asp Asp Val Thr Gln Ala Gly His
165 170 175

Asn Met Glu Leu Leu Glu Pro Leu Val Lys Phe Gln Val Gly Leu Lys
180 185 190

Lys Leu Asp Leu His Glu Glu Glu His Val Leu Leu Met Ala Ile Cys
195 200 205

Ile Leu Ser Pro Asp Arg Pro Gly Leu Gln Asp Lys Ala Leu Val Glu

210 215 220

Ser Ile Gln Asp Arg Leu Ser Ser Thr Leu Gln Thr Tyr Ile Leu Cys
225 230 235 240

Lys His Pro Pro Pro Gly Ser Arg Leu Leu Tyr Ala Lys Met Ile Gln
245 250 255

Lys Leu Ala Asp Leu Arg Ser Leu Asn Glu Glu His Ser Lys Gln Tyr
260 265 270

Arg Ser Ile Ser Phe Leu Pro Glu His Ser Met Lys Leu Thr Pro Leu
275 280 285

Met Leu Glu Val Phe Ser Asp Glu Ile
290 295

<210> 172
<211> 304
<212> PRT
<213> Homo sapiens

<400> 172

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

His Lys Thr Phe Asp Thr Thr Tyr Ser Asp Phe Asn Lys Phe Arg Pro
20 25 30

Pro Val Arg Ser Lys Phe Ser Ser Arg Met Ala Thr His Ser Ser Ser
35 40 45

Val Val Ser Gln Asp Phe Ser Ser Glu Asp Ser Asn Asp Val Phe Gly
50 55 60

Ser Asp Ala Phe Ala Ala Phe Pro Glu Pro Met Glu Pro Gln Met Phe
65 70 75 80

Ser Asn Leu Asp Leu Ser Glu Glu Ser Asp Glu Ser Pro Ser Met Asn
85 90 95

Ile Glu Leu Pro His Leu Pro Met Leu Pro His Leu Ala Asp Leu Val
100 105 110

Ser Tyr Ser Ile Gln Lys Val Ile Gly Phe Ala Lys Met Ile Pro Gly
115 120 125

Phe Arg Asp Leu Thr Ala Glu Asp Gln Ile Ala Leu Leu Lys Ser Ser
130 135 140

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

```
Asp Met Ser Trp Thr Cys Gly Ser Asn Asp Phe Lys Tyr Lys Val Ser
                165                 170                 175

Asp Val Thr Gln Ala Gly His Ser Met Asp Leu Leu Glu Pro Leu Val
            180                 185                 190

Lys Phe Gln Val Gly Leu Lys Lys Leu Asn Leu His Glu Glu Glu His
        195                 200                 205

Val Leu Leu Met Ala Ile Cys Ile Leu Ser Pro Asp Arg Pro Gly Val
    210                 215                 220

Gln Asp Thr Ser Leu Val Glu Ser Ile Gln Asp Arg Leu Ser Asp Ile
225                 230                 235                 240

Leu Gln Thr Tyr Ile Arg Cys Arg His Pro Pro Pro Gly Ser Arg Leu
                245                 250                 255

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

Glu Glu His Ser Lys Gln Tyr Arg Cys Leu Ser Phe Gln Pro Glu His
        275                 280                 285

Ser Met Gln Leu Thr Pro Leu Val Leu Glu Val Phe Gly Asn Glu Ile
    290                 295                 300
```

<210> 173
<211> 410
<212> PRT
<213> Homo sapiens

<400> 173

```
Met Glu Gln Lys Pro Ser Lys Val Glu Cys Gly Ser Asp Pro Glu Glu
1               5                   10                  15

Asn Ser Ala Arg Ser Pro Asp Gly Lys Arg Lys Arg Lys Asn Gly Gln
            20                  25                  30

Cys Ser Leu Lys Thr Ser Met Ser Gly Tyr Ile Pro Ser Tyr Leu Asp
        35                  40                  45

Lys Asp Glu Gln Cys Val Val Cys Gly Asp Lys Ala Thr Gly Tyr His
    50                  55                  60

Tyr Arg Cys Ile Thr Cys Glu Gly Cys Lys Gly Phe Phe Arg Arg Thr
65                  70                  75                  80

Ile Gln Lys Asn Leu His Pro Thr Tyr Ser Cys Lys Tyr Asp Ser Cys
                85                  90                  95
```

```
Cys Val Ile Asp Lys Ile Thr Arg Asn Gln Cys Gln Leu Cys Arg Phe
            100                 105                 110

Lys Lys Cys Ile Ala Val Gly Met Ala Met Asp Leu Val Leu Asp Asp
        115                 120                 125

Ser Lys Arg Val Ala Lys Arg Lys Leu Ile Glu Gln Asn Arg Glu Arg
    130                 135                 140

Arg Arg Lys Glu Glu Met Ile Arg Ser Leu Gln Gln Arg Pro Glu Pro
145                 150                 155                 160

Thr Pro Glu Glu Trp Asp Leu Ile His Ile Ala Thr Glu Ala His Arg
                165                 170                 175

Ser Thr Asn Ala Gln Gly Ser His Trp Lys Gln Arg Arg Lys Phe Leu
            180                 185                 190

Pro Asp Asp Ile Gly Gln Ser Pro Ile Val Ser Met Pro Asp Gly Asp
        195                 200                 205

Lys Val Asp Leu Glu Ala Phe Ser Glu Phe Thr Lys Ile Ile Thr Pro
    210                 215                 220

Ala Ile Thr Arg Val Val Asp Phe Ala Lys Lys Leu Pro Thr Phe Ser
225                 230                 235                 240

Glu Leu Pro Cys Glu Asp Gln Ile Ile Leu Leu Lys Gly Cys Cys Met
                245                 250                 255

Glu Ile Met Ser Leu Arg Ala Ala Val Arg Tyr Asp Pro Glu Ser Asp
            260                 265                 270

Thr Leu Thr Leu Ser Gly Glu Met Ala Val Lys Arg Glu Gln Leu Lys
        275                 280                 285

Asn Gly Gly Leu Gly Val Val Ser Asp Ala Ile Phe Glu Leu Gly Lys
    290                 295                 300

Ser Leu Ser Ala Phe Asn Leu Asp Asp Thr Glu Val Ala Leu Leu Gln
305                 310                 315                 320

Ala Val Leu Leu Met Ser Thr Asp Arg Ser Gly Leu Leu Cys Val Asp
                325                 330                 335

Lys Ile Glu Lys Ser Gln Glu Ala Tyr Leu Leu Ala Phe Glu His Tyr
            340                 345                 350

Val Asn His Arg Lys His Asn Ile Pro His Phe Trp Pro Lys Gln Leu
        355                 360                 365
```

Met Lys Val Thr Asp Leu Arg Met Ile Gly Ala Cys His Ala Ser Arg
370 375 380

Phe Leu His Met Lys Val Glu Cys Pro Thr Glu Leu Phe Pro Pro Leu
385 390 395 400

Phe Leu Glu Val Phe Glu Asp Gln Glu Val
405 410

<210> 174
<211> 243
<212> PRT
<213> Homo sapiens

<400> 174

Pro Glu Glu Trp Asp Leu Ile His Ile Ala Thr Glu Ala His Arg Ser
1 5 10 15

Thr Asn Ala Gln Gly Ser His Trp Lys Gln Arg Arg Lys Phe Leu Pro
20 25 30

Asp Asp Ile Gly Gln Ser Pro Ile Val Ser Met Pro Asp Gly Asp Lys
35 40 45

Val Asp Leu Glu Ala Phe Ser Glu Phe Thr Lys Ile Ile Thr Pro Ala
50 55 60

Ile Thr Arg Val Val Asp Phe Ala Lys Lys Leu Pro Thr Phe Ser Glu
65 70 75 80

Leu Pro Cys Glu Asp Gln Ile Ile Leu Leu Lys Gly Cys Cys Met Glu
85 90 95

Ile Met Ser Leu Arg Ala Ala Val Arg Tyr Asp Pro Glu Ser Asp Thr
100 105 110

Leu Thr Leu Ser Gly Glu Met Ala Val Lys Arg Glu Gln Leu Lys Asn
115 120 125

Gly Gly Leu Gly Val Val Ser Asp Ala Ile Phe Glu Leu Gly Lys Ser
130 135 140

Leu Ser Ala Phe Asn Leu Asp Asp Thr Glu Val Ala Leu Leu Gln Ala
145 150 155 160

Val Leu Leu Met Ser Thr Asp Arg Ser Gly Leu Leu Cys Val Asp Lys
165 170 175

Ile Glu Lys Ser Gln Glu Ala Tyr Leu Leu Ala Phe Glu His Tyr Val
180 185 190

Asn His Arg Lys His Asn Ile Pro His Phe Trp Pro Lys Gln Leu Met
195 200 205

Lys Val Thr Asp Leu Arg Met Ile Gly Ala Cys His Ala Ser Arg Phe
210 215 220

Leu His Met Lys Val Glu Cys Pro Thr Glu Leu Phe Pro Pro Leu Phe
225 230 235 240

Leu Glu Val

<210> 175
<211> 243
<212> PRT
<213> Homo sapiens

<400> 175

Asp Glu Glu Trp Glu Leu Ile Lys Thr Val Thr Glu Ala His Val Ala
1 5 10 15

Thr Asn Ala Gln Gly Ser His Trp Lys Gln Lys Arg Lys Phe Leu Pro
20 25 30

Glu Asp Ile Gly Gln Ala Pro Ile Val Asn Ala Pro Glu Gly Gly Lys
35 40 45

Val Asp Leu Glu Ala Phe Ser His Phe Thr Lys Ile Ile Thr Pro Ala
50 55 60

Ile Thr Arg Val Val Asp Phe Ala Lys Lys Leu Pro Met Phe Cys Glu
65 70 75 80

Leu Pro Cys Glu Asp Gln Ile Ile Leu Leu Lys Gly Cys Cys Met Glu
85 90 95

Ile Met Ser Leu Arg Ala Ala Val Arg Tyr Asp Pro Glu Ser Glu Thr
100 105 110

Leu Thr Leu Asn Gly Glu Met Ala Val Thr Arg Gly Gln Leu Lys Asn
115 120 125

Gly Gly Leu Gly Val Val Ser Asp Ala Ile Phe Asp Leu Gly Met Ser
130 135 140

Leu Ser Ser Phe Asn Leu Asp Asp Thr Glu Val Ala Leu Leu Gln Ala
145 150 155 160

Val Leu Leu Met Ser Ser Asp Arg Pro Gly Leu Ala Cys Val Glu Arg
165 170 175

Ile Glu Lys Tyr Gln Asp Ser Phe Leu Leu Ala Phe Glu His Tyr Ile

180 185 190

Asn Tyr Arg Lys His His Val Thr His Phe Trp Pro Lys Leu Leu Met
195 200 205

Lys Val Thr Asp Leu Arg Met Ile Gly Ala Cys His Ala Ser Arg Phe
210 215 220

Leu His Met Lys Val Glu Cys Pro Thr Glu Leu Phe Pro Pro Leu Phe
225 230 235 240

Leu Glu Val

<210> 176
<211> 243
<212> PRT
<213> Homo sapiens

<400> 176

Asp Glu Glu Trp Glu Leu Ile Lys Thr Val Thr Glu Ala His Val Ala
1 5 10 15

Thr Asn Ala Gln Gly Ser His Trp Lys Gln Lys Arg Lys Phe Leu Pro
20 25 30

Glu Asp Ile Gly Gln Ala Pro Ile Val Asn Ala Pro Glu Gly Gly Lys
35 40 45

Val Asp Leu Glu Ala Phe Ser His Phe Thr Lys Ile Ile Thr Pro Ala
50 55 60

Ile Thr Arg Val Val Asp Phe Ala Lys Lys Leu Pro Met Phe Cys Glu
65 70 75 80

Leu Pro Cys Glu Asp Gln Ile Ile Leu Leu Lys Gly Cys Cys Met Glu
85 90 95

Ile Met Ser Leu Arg Ala Ala Val Arg Tyr Asp Pro Glu Ser Glu Thr
100 105 110

Leu Thr Leu Asn Gly Glu Met Ala Val Thr Arg Gly Gln Leu Lys Asn
115 120 125

Gly Gly Leu Gly Val Val Ser Asp Ala Ile Phe Asp Leu Gly Met Ser
130 135 140

Leu Ser Ser Phe Asn Leu Asp Asp Thr Glu Val Ala Leu Leu Gln Ala
145 150 155 160

Val Leu Leu Met Ser Ser Asp Arg Pro Gly Leu Ala Cys Val Glu Arg
165 170 175

```
Ile Glu Lys Tyr Gln Asp Ser Phe Leu Leu Ala Phe Glu His Tyr Ile
            180                 185                 190

Asn Tyr Arg Lys His His Val Thr His Phe Trp Pro Lys Leu Leu Met
        195                 200                 205

Lys Val Thr Asp Leu Arg Met Ile Gly Ala Cys His Ala Ser Arg Phe
    210                 215                 220

Leu His Met Lys Val Glu Cys Pro Thr Glu Leu Phe Pro Pro Leu Phe
225                 230                 235                 240

Leu Glu Val
```

<210> 177
<211> 243
<212> PRT
<213> Homo sapiens

<400> 177

```
Asp Glu Glu Trp Glu Leu Ile Lys Thr Val Thr Glu Ala His Val Ala
1               5                   10                  15

Thr Asn Ala Gln Gly Ser His Trp Lys Gln Lys Arg Lys Phe Leu Pro
            20                  25                  30

Glu Asp Ile Gly Gln Ala Pro Ile Val Asn Ala Pro Glu Gly Gly Lys
        35                  40                  45

Val Asp Leu Glu Ala Phe Ser His Phe Thr Lys Ile Ile Thr Pro Ala
    50                  55                  60

Ile Thr Arg Val Val Asp Phe Ala Lys Lys Leu Pro Met Phe Cys Glu
65                  70                  75                  80

Leu Pro Cys Glu Asp Gln Ile Ile Leu Leu Lys Gly Cys Cys Met Glu
                85                  90                  95

Ile Met Ser Leu Arg Ala Ala Val Arg Tyr Asp Pro Glu Ser Glu Thr
            100                 105                 110

Leu Thr Leu Asn Gly Glu Met Ala Val Thr Arg Gly Gln Leu Lys Asn
        115                 120                 125

Gly Gly Leu Gly Val Val Ser Asp Ala Ile Phe Arg Leu Gly Met Ser
    130                 135                 140

Leu Ser Ser Phe Asn Leu Asp Asp Thr Glu Val Ala Leu Leu Gln Ala
145                 150                 155                 160
```

Val Leu Leu Met Ser Ser Asp Arg Pro Gly Leu Ala Cys Val Glu Arg
165 170 175

Ile Glu Lys Tyr Gln Asp Ser Phe Leu Leu Ala Phe Glu His Tyr Ile
180 185 190

Asn Tyr Arg Lys His His Val Thr His Phe Trp Pro Lys Leu Leu Met
195 200 205

Lys Val Thr Asp Leu Arg Met Ile Gly Ala Cys His Ala Ser Arg Phe
210 215 220

Leu His Met Lys Val Glu Cys Pro Thr Glu Leu Phe Pro Pro Leu Phe
225 230 235 240

Leu Glu Val

<210> 178
<211> 243
<212> PRT
<213> Homo sapiens

<400> 178

Asp Glu Glu Trp Glu Leu Ile Lys Thr Val Thr Glu Ala His Val Ala
1 5 10 15

Thr Asn Ala Gln Gly Ser His Trp Lys Gln Lys Arg Lys Phe Leu Pro
20 25 30

Glu Asp Ile Gly Gln Ala Pro Ile Val Asn Ala Pro Glu Gly Gly Lys
35 40 45

Val Asp Leu Glu Ala Phe Ser His Phe Thr Lys Ile Ile Thr Pro Ala
50 55 60

Ile Thr Arg Val Val Asp Phe Ala Lys Lys Leu Pro Met Phe Cys Glu
65 70 75 80

Leu Pro Cys Glu Asp Gln Ile Ile Leu Leu Lys Gly Cys Cys Met Glu
85 90 95

Ile Met Ser Leu Arg Ala Ala Val Arg Tyr Asp Pro Glu Ser Glu Thr
100 105 110

Leu Thr Leu Asn Gly Glu Met Ala Val Thr Arg Gly Gln Leu Lys Asn
115 120 125

Gly Gly Leu Gly Val Val Ser Asp Ala Ile Phe Arg Leu Gly Met Ser
130 135 140

Leu Ser Ser Phe Asn Leu Asp Asp Thr Glu Val Ala Leu Leu Gln Ala
145 150 155 160

Val Leu Leu Met Ser Ser Asp Arg Pro Gly Leu Ala Cys Val Glu Arg
165 170 175

Ile Glu Lys Tyr Gln Asp Ser Phe Leu Leu Ala Phe Glu His Tyr Ile
180 185 190

Asn Tyr Arg Lys His His Val Thr His Phe Trp Pro Lys Leu Leu Met
195 200 205

Lys Val Thr Asp Leu Arg Met Ile Gly Ala Cys His Ala Ser Arg Phe
210 215 220

Leu His Met Lys Val Glu Cys Pro Thr Glu Leu Phe Pro Pro Leu Phe
225 230 235 240

Leu Glu Val

<210> 179
<211> 241
<212> PRT
<213> Homo sapiens

<400> 179

Thr Cys Pro Lys Lys Val Asn Arg Tyr Tyr Leu Asn Gly Ser Pro Lys
1 5 10 15

Pro Gly Met Pro Val Pro Glu Ala Pro Arg Pro Pro Val Val Gln Asn
20 25 30

Gly Val Val Arg Glu Ala Asp Ser Ser Gly Ala Met Asp Asp Asp Met
35 40 45

Val Asp Gln Asp Ile Phe Ser His Leu Ala Glu Val Ile Thr Pro Ala
50 55 60

Ile Ile Lys Val Val Glu Phe Ala Lys Gln Ile Pro Gly Phe Thr Lys
65 70 75 80

Leu Val Pro Asp Asp Gln Val Ala Leu Leu Lys Asn Cys Cys Phe Glu
85 90 95

Val Met Cys Leu Arg Ala Ala Ser Arg Phe Asp Lys Gln Arg Arg Thr
100 105 110

Ile Thr Met Phe Gly Gly Leu Thr Val Thr Lys Glu Gln Val Ser Gln
115 120 125

Gly Gly Leu Gly Arg Leu Ala Glu Pro Leu Phe Glu Phe Ala Glu Gly

130 135 140

Leu Ser Gln Leu His Leu Asp Asp Thr Glu Val Ala Leu Leu Ala Ala
145 150 155 160

Leu Leu Val Val Ala Asp Arg Pro Gly Val Gln Asp Gln Glu Ser Ile
165 170 175

Asp Arg Leu Gln Asp Ile Ile Leu Thr Ala Tyr Lys Asn Tyr Ile Thr
180 185 190

Arg Gln Arg Pro His Gln Pro Val Leu Trp Gly Lys Ile Leu Met Lys
195 200 205

Val Thr Asp Leu Arg Ala Leu Ser Val Ala His Ala Glu Gln Val Lys
210 215 220

Leu Val Lys Met Glu Cys Thr Asn Asp Ile Pro Pro Leu Phe Leu Glu
225 230 235 240

Met

<210> 180
<211> 243
<212> PRT
<213> Homo sapiens

<400> 180

Ala Glu Glu Trp Glu Leu Ile His Val Val Thr Glu Ala His Arg Ser
1 5 10 15

Thr Asn Ala Gln Gly Ser His Trp Lys Gln Lys Arg Lys Phe Leu Pro
20 25 30

Glu Asp Ile Gly Gln Ser Pro Met Ala Ser Met Pro Asp Gly Asp Lys
35 40 45

Val Asp Leu Glu Ala Phe Ser Glu Phe Thr Lys Ile Ile Thr Pro Ala
50 55 60

Ile Thr Arg Val Val Asp Phe Ala Lys Lys Leu Pro Met Phe Ser Glu
65 70 75 80

Leu Pro Cys Glu Asp Gln Ile Ile Leu Leu Lys Gly Cys Cys Met Glu
85 90 95

Ile Met Ser Leu Arg Ala Ala Val Arg Tyr Asp Pro Glu Ser Glu Thr
100 105 110

Leu Thr Leu Ser Gly Glu Met Ala Val Lys Arg Glu Gln Leu Lys Asn
115 120 125

Gly Gly Leu Gly Val Val Ser Asp Ala Ile Phe Asp Leu Gly Lys Ser
130 135 140

Leu Ser Ala Phe Asn Leu Asp Asp Thr Glu Val Ala Leu Leu Gln Ala
145 150 155 160

Val Leu Leu Met Ser Ser Asp Arg Thr Gly Leu Ile Cys Val Asp Lys
165 170 175

Ile Glu Lys Cys Gln Glu Thr Tyr Leu Leu Ala Phe Glu His Tyr Ile
180 185 190

Asn Tyr Arg Lys His Asn Ile Pro His Phe Trp Pro Lys Leu Leu Met
195 200 205

Lys Val Thr Asp Leu Arg Met Ile Gly Ala Cys His Ala Ser Arg Phe
210 215 220

Leu His Met Lys Val Glu Cys Pro Thr Glu Leu Phe Pro Pro Leu Phe
225 230 235 240

Leu Glu Val

<210> 181
<211> 243
<212> PRT
<213> Homo sapiens

<400> 181

Ser Glu Glu Trp Glu Leu Ile Arg Ile Val Thr Glu Ala His Arg Ser
1 5 10 15

Thr Asn Ala Gln Gly Ser His Trp Lys Gln Arg Arg Lys Phe Leu Pro
20 25 30

Glu Asp Ile Gly Gln Ser Pro Met Ala Ser Met Pro Asp Gly Asp Lys
35 40 45

Val Asp Leu Glu Ala Phe Ser Glu Phe Thr Lys Ile Ile Thr Pro Ala
50 55 60

Ile Thr Arg Val Val Asp Phe Ala Lys Lys Leu Pro Met Phe Ser Glu
65 70 75 80

Leu Thr Cys Glu Asp Gln Ile Ile Leu Leu Lys Gly Cys Cys Met Glu
85 90 95

Ile Met Ser Leu Arg Ala Ala Val Arg Tyr Asp Pro Asp Ser Glu Thr
100 105 110

Leu Thr Leu Ser Gly Glu Met Ala Val Lys Arg Glu Gln Leu Lys Asn
115 120 125

Gly Gly Leu Gly Val Val Ser Asp Ala Ile Phe Asp Leu Gly Arg Ser
130 135 140

Leu Ala Ala Phe Asn Leu Asp Asp Thr Glu Val Ala Leu Leu Gln Ala
145 150 155 160

Val Leu Leu Met Ser Ser Asp Arg Thr Gly Leu Ile Cys Thr Asp Lys
165 170 175

Ile Glu Lys Cys Gln Glu Thr Tyr Leu Leu Ala Phe Glu His Tyr Ile
180 185 190

Asn His Arg Lys His Asn Ile Pro His Phe Trp Pro Lys Leu Leu Met
195 200 205

Lys Val Thr Asp Leu Arg Met Ile Gly Ala Cys His Ala Ser Arg Phe
210 215 220

Leu His Met Lys Val Glu Cys Pro Thr Glu Leu Phe Pro Pro Leu Phe
225 230 235 240

Leu Glu Val

<210> 182
<211> 280
<212> PRT
<213> Homo sapiens

<400> 182

Ser Asp Pro Ser Gly Leu Ile Pro Asp Pro Leu Leu Asp Ser Arg Ala
1 5 10 15

Thr Ser Ser Thr Phe Pro Gln Leu Leu Thr Cys Pro Ile Leu Arg Pro
20 25 30

Gly Phe Ser Arg Pro Ala Asp Ala Pro Pro Asp Lys Ile Gly Gln Ser
35 40 45

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

Ser Glu Phe Thr Lys Ile Ile Thr Pro Ala Ile Thr Arg Val Val Asp
65 70 75 80

Phe Ala Lys Lys Leu Pro Met Phe Ser Glu Leu Pro Cys Glu Asp Gln
85 90 95

```
Ile Ile Leu Leu Lys Gly Cys Cys Met Glu Ile Met Ser Leu Arg Ala
            100                 105                 110

Ala Met Arg Tyr Asp Pro Glu Ser Glu Thr Leu Thr Leu Ser Gly Glu
        115                 120                 125

Met Ala Val Lys Arg Glu Gln Leu Lys Asn Gly Gly Leu Gly Val Val
    130                 135                 140

Ser Asp Ala Ile Phe Asp Leu Gly Lys Ser Leu Ala Gln Phe Asn Leu
145                 150                 155                 160

Asp Asp Thr Glu Val Ala Leu Leu Gln Ala Val Leu Leu Met Ser Ser
                165                 170                 175

Gly Asn Arg Arg Arg Gly Arg Pro Arg Pro Ser Pro Ala Pro Gly Ser
            180                 185                 190

Thr Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Asp Arg Ser Gly Leu
        195                 200                 205

Thr Cys Thr Asp Lys Ile Glu Lys Cys Gln Glu Thr Tyr Leu Leu Ala
    210                 215                 220

Phe Glu His Tyr Ile Asn Tyr Arg Lys His Asn Ile Pro His Phe Trp
225                 230                 235                 240

Pro Lys Leu Leu Met Lys Val Thr Asp Leu Arg Met Ile Gly Ala Cys
                245                 250                 255

His Ala Ser Arg Phe Leu His Met Lys Val Glu Cys Pro Asn Glu Leu
            260                 265                 270

Phe Pro Pro Leu Phe Leu Glu Val
        275                 280


<210>  183
<211>  231
<212>  PRT
<213>  Homo sapiens

<400>  183

Asp His Glu Glu Ala Leu Ile Arg Ala Ile Leu Val Ala His Lys Gln
1               5                   10                  15

Thr Ser His Met Tyr Arg Arg Glu Ser Ser Ser Gly Glu Glu Ser Glu
            20                  25                  30

Pro Asp Ser Lys Lys Gln Lys Leu Glu Asp Glu Lys Pro Leu Ser Glu
        35                  40                  45

Ile Met Thr Pro Ser Ile Val Lys Val Val Glu Phe Ala Lys Arg Ile
```

50 55 60

Pro Gly Phe Thr Gly Leu His His Asp Asp Gln Ile Leu Leu Leu Lys
65 70 75 80

Thr Cys Cys Met Glu Ile Met Cys Leu Arg Val Ala Gln Lys Phe Asp
85 90 95

Pro Asp Ser Gln Lys Leu Ile Leu Ser Asn Gly Leu Arg Val Gly Lys
100 105 110

Ser Asp Met Asp His Gly Val Leu Ser Glu Leu Ile Glu Pro Ile Phe
115 120 125

Asp Phe Ala Val Ser Met Ser Arg Leu Gln Leu Thr Glu Thr Glu Met
130 135 140

Ala Leu Leu Ala Ala Val Leu Leu Ile Ala Gly Asp Arg Pro Gly Leu
145 150 155 160

Lys Glu Ala Lys Leu Val Glu Thr Leu Gln Asp Ser Leu Leu Thr Ala
165 170 175

Phe Gln His Phe Ile Asn Glu Ser Arg Pro Lys Thr Pro Val His Trp
180 185 190

Ala Lys Ile Leu Met Lys Ile Thr Asp Leu Arg Thr Ile Ser Ala Arg
195 200 205

His Ala Glu Arg Ile Met Cys Ile Lys Leu Asp Arg Pro Asn Glu Ile
210 215 220

Pro Gln Ile Phe Leu Glu Met
225 230

<210> 184
<211> 243
<212> PRT
<213> Homo sapiens

<400> 184

Asp Glu Glu Trp Glu Leu Ile Lys Thr Val Thr Glu Ala His Val Ala
1 5 10 15

Thr Asn Ala Gln Gly Ser His Trp Lys Gln Lys Arg Lys Phe Leu Pro
20 25 30

Glu Asp Ile Gly Gln Ala Pro Ile Val Asn Ala Pro Glu Gly Gly Lys
35 40 45

Val Asp Leu Glu Ala Phe Ser His Phe Thr Lys Ile Ile Thr Pro Ala
50 55 60

```
Ile Thr Arg Val Val Asp Phe Ala Lys Lys Leu Pro Met Phe Cys Glu
65                  70                  75                  80

Leu Pro Cys Glu Asp Gln Ile Ile Leu Leu Lys Gly Cys Cys Met Glu
                85                  90                  95

Ile Met Ser Leu Arg Ala Ala Val Arg Tyr Asp Pro Glu Ser Glu Thr
            100                 105                 110

Leu Thr Leu Asn Gly Glu Met Ala Val Thr Arg Gly Gln Leu Lys Asn
        115                 120                 125

Gly Gly Leu Gly Val Val Ser Asp Ala Ile Phe Asp Leu Gly Met Ser
    130                 135                 140

Leu Ser Ser Phe Asn Leu Asp Asp Thr Glu Val Ala Leu Leu Gln Ala
145                 150                 155                 160

Val Leu Leu Met Ser Ser Asp Arg Pro Gly Leu Ala Cys Val Glu Arg
                165                 170                 175

Ile Glu Lys Tyr Gln Asp Ser Phe Leu Leu Ala Phe Glu His Tyr Ile
            180                 185                 190

Asn Tyr Arg Lys His His Val Thr His Phe Trp Pro Lys Leu Leu Met
        195                 200                 205

Lys Val Thr Asp Leu Arg Met Ile Gly Ala Cys His Ala Ser Arg Phe
    210                 215                 220

Leu His Met Lys Val Glu Cys Pro Thr Glu Leu Phe Pro Pro Leu Phe
225                 230                 235                 240

Leu Glu Val
```

<210> 185
<211> 252
<212> PRT
<213> Homo sapiens

<400> 185

```
Gln Glu Glu Trp Glu Met Ile Arg Val Val Thr Glu Ala His Met Ala
1               5                   10                  15

Thr Asn Ala Gln Gly Asn His Trp Lys Gln Lys Arg Lys Phe Leu Ser
            20                  25                  30

Ala Val Gly Val Lys Glu Ala Lys Pro Glu Asp Ile Gly Ser Ala Pro
        35                  40                  45
```

```
Ile Val Asn Ala Pro Glu Gly Asn Lys Val Asp Ile Glu Ala Phe Ser
    50                  55                  60

Gln Phe Thr Lys Ile Ile Thr Pro Ala Ile Thr Arg Val Val Asp Phe
65                  70                  75                  80

Ala Lys Lys Leu Pro Met Phe Cys Glu Leu Pro Cys Glu Asp Gln Ile
                85                  90                  95

Ile Leu Leu Lys Gly Cys Cys Met Glu Ile Met Ser Leu Arg Ala Ala
            100                 105                 110

Val Arg Tyr Asp Pro Glu Ser Asp Thr Leu Thr Leu Asn Gly Glu Met
        115                 120                 125

Ala Val Thr Arg Gly Gln Leu Lys Asn Gly Gly Leu Gly Val Val Ser
    130                 135                 140

Asp Ala Ile Phe Asp Leu Gly Val Ser Leu Ser Ser Phe Asn Leu Asp
145                 150                 155                 160

Asp Ser Glu Val Ala Leu Leu Gln Ala Val Ile Leu Leu Ser Ser Asp
                165                 170                 175

Arg Pro Gly Leu Thr Ser Val Glu Arg Ile Glu Arg Cys Gln Glu Glu
            180                 185                 190

Phe Leu Leu Ala Phe Glu His Tyr Ile Asn Tyr Arg Lys His Lys Val
        195                 200                 205

Ala His Phe Trp Pro Lys Leu Leu Met Lys Val Thr Asp Leu Arg Met
    210                 215                 220

Ile Gly Ala Cys His Ala Ser Arg Phe Leu His Met Lys Val Glu Cys
225                 230                 235                 240

Pro Thr Glu Leu Phe Pro Pro Leu Phe Leu Glu Val
                245                 250


<210>  186
<211>  448
<212>  PRT
<213>  Homo sapiens

<400>  186

Met Phe Asp Cys Met Asp Val Leu Ser Val Ser Pro Gly Gln Ile Leu
1               5                   10                  15

Asp Phe Tyr Thr Ala Ser Pro Ser Ser Cys Met Leu Gln Glu Lys Ala
            20                  25                  30
```

```
Leu Lys Ala Cys Phe Ser Gly Leu Thr Gln Thr Glu Trp Gln His Arg
        35                  40                  45

His Thr Ala Gln Ser Ile Glu Thr Gln Ser Thr Ser Ser Glu Glu Leu
    50                  55                  60

Val Pro Ser Pro Pro Ser Pro Leu Pro Pro Pro Arg Val Tyr Lys Pro
65                  70                  75                  80

Cys Phe Val Cys Gln Asp Lys Ser Ser Gly Tyr His Tyr Gly Val Ser
                85                  90                  95

Ala Cys Glu Gly Cys Lys Gly Phe Phe Arg Arg Ser Ile Gln Lys Asn
            100                 105                 110

Met Ile Tyr Thr Cys His Arg Asp Lys Asn Cys Val Ile Asn Lys Val
        115                 120                 125

Thr Arg Asn Arg Cys Gln Tyr Cys Arg Leu Gln Lys Cys Phe Glu Val
    130                 135                 140

Gly Met Ser Lys Glu Ser Val Arg Asn Asp Arg Asn Lys Lys Lys Lys
145                 150                 155                 160

Glu Thr Ser Lys Gln Glu Cys Thr Glu Ser Tyr Glu Met Thr Ala Glu
                165                 170                 175

Leu Asp Asp Leu Thr Glu Lys Ile Arg Lys Ala His Gln Glu Thr Phe
            180                 185                 190

Pro Ser Leu Cys Gln Leu Gly Lys Tyr Thr Thr Asn Ser Ser Ala Asp
        195                 200                 205

His Arg Val Arg Leu Asp Leu Gly Leu Trp Asp Lys Phe Ser Glu Leu
    210                 215                 220

Ala Thr Lys Cys Ile Ile Lys Ile Val Glu Phe Ala Lys Arg Leu Pro
225                 230                 235                 240

Gly Phe Thr Gly Leu Thr Ile Ala Asp Gln Ile Thr Leu Leu Lys Ala
                245                 250                 255

Ala Cys Leu Asp Ile Leu Ile Leu Arg Ile Cys Thr Arg Tyr Thr Pro
            260                 265                 270

Glu Gln Asp Thr Met Thr Phe Ser Asp Gly Leu Thr Leu Asn Arg Thr
        275                 280                 285

Gln Met His Asn Ala Gly Phe Gly Pro Leu Thr Asp Leu Val Phe Thr
    290                 295                 300
```

Phe Ala Asn Gln Leu Leu Pro Leu Glu Met Asp Asp Thr Glu Thr Gly
305 310 315 320

Leu Leu Ser Ala Ile Cys Leu Ile Cys Gly Asp Arg Gln Asp Leu Glu
325 330 335

Glu Pro Thr Lys Val Asp Lys Leu Gln Glu Pro Leu Leu Glu Ala Leu
340 345 350

Lys Ile Tyr Ile Arg Lys Arg Arg Pro Ser Lys Pro His Met Phe Pro
355 360 365

Lys Ile Leu Met Lys Ile Thr Asp Leu Arg Ser Ile Ser Ala Lys Gly
370 375 380

Ala Glu Arg Val Ile Thr Leu Lys Met Glu Ile Pro Gly Ser Met Pro
385 390 395 400

Pro Leu Ile Gln Glu Met Leu Glu Asn Ser Glu Gly His Glu Pro Leu
405 410 415

Thr Pro Ser Ser Ser Gly Asn Thr Ala Glu His Ser Pro Ser Ile Ser
420 425 430

Pro Ser Ser Val Glu Asn Ser Gly Val Ser Gln Ser Pro Leu Val Gln
435 440 445

<210> 187
<211> 231
<212> PRT
<213> Homo sapiens

<400> 187

Asp Leu Thr Glu Lys Ile Arg Lys Ala His Gln Glu Thr Phe Pro Ser
1 5 10 15

Leu Cys Gln Leu Gly Lys Tyr Thr Thr Asn Ser Ser Ala Asp His Arg
20 25 30

Val Arg Leu Asp Leu Gly Leu Trp Asp Lys Phe Ser Glu Leu Ala Thr
35 40 45

Lys Cys Ile Ile Lys Ile Val Glu Phe Ala Lys Arg Leu Pro Gly Phe
50 55 60

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

Leu Asp Ile Leu Ile Leu Arg Ile Cys Thr Arg Tyr Thr Pro Glu Gln
85 90 95

Asp Thr Met Thr Phe Ser Asp Gly Leu Thr Leu Asn Arg Thr Gln Met

100 105 110

His Asn Ala Gly Phe Gly Pro Leu Thr Asp Leu Val Phe Thr Phe Ala
115 120 125

Asn Gln Leu Leu Pro Leu Glu Met Asp Asp Thr Glu Thr Gly Leu Leu
130 135 140

Ser Ala Ile Cys Leu Ile Cys Gly Asp Arg Gln Asp Leu Glu Glu Pro
145 150 155 160

Thr Lys Val Asp Lys Leu Gln Glu Pro Leu Leu Glu Ala Leu Lys Ile
165 170 175

Tyr Ile Arg Lys Arg Arg Pro Ser Lys Pro His Met Phe Pro Lys Ile
180 185 190

Leu Met Lys Ile Thr Asp Leu Arg Ser Ile Ser Ala Lys Gly Ala Glu
195 200 205

Arg Val Ile Thr Leu Lys Met Glu Ile Pro Gly Ser Met Pro Pro Leu
210 215 220

Ile Gln Glu Met Leu Glu Asn
225 230

<210> 188
<211> 231
<212> PRT
<213> Homo sapiens

<400> 188

Asp Leu Thr Glu Lys Ile Arg Lys Ala His Gln Glu Thr Phe Pro Ser
1 5 10 15

Leu Cys Gln Leu Gly Lys Tyr Thr Thr Asn Ser Ser Ala Asp His Arg
20 25 30

Val Arg Leu Asp Leu Gly Leu Trp Asp Lys Phe Ser Glu Leu Ala Thr
35 40 45

Lys Cys Ile Ile Lys Ile Val Glu Phe Ala Lys Arg Leu Pro Gly Phe
50 55 60

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

Leu Asp Ile Leu Ile Leu Arg Ile Cys Thr Arg Tyr Thr Pro Glu Gln
85 90 95

Asp Thr Met Thr Phe Ser Asp Gly Leu Thr Leu Asn Arg Thr Gln Met
100 105 110

```
His Asn Ala Gly Phe Gly Pro Leu Thr Asp Leu Val Phe Thr Phe Ala
        115                 120                 125

Asn Gln Leu Leu Pro Leu Glu Met Asp Asp Thr Glu Thr Gly Leu Leu
    130                 135                 140

Ser Ala Ile Cys Leu Ile Cys Gly Asp Arg Gln Asp Leu Glu Glu Pro
145                 150                 155                 160

Thr Lys Val Asp Lys Leu Gln Glu Pro Leu Leu Glu Ala Leu Lys Ile
                165                 170                 175

Tyr Ile Arg Lys Arg Arg Pro Ser Lys Pro His Met Phe Pro Lys Ile
            180                 185                 190

Leu Met Lys Ile Thr Asp Leu Arg Ser Ile Ser Ala Lys Gly Ala Glu
        195                 200                 205

Arg Val Ile Thr Leu Lys Met Glu Ile Pro Gly Ser Met Pro Pro Leu
    210                 215                 220

Ile Gln Glu Met Leu Glu Asn
225                 230


<210>  189
<211>  235
<212>  PRT
<213>  Homo sapiens

<400>  189

Ala Leu Val Thr Ser Val His Lys Phe His Val Glu Thr Phe Pro Leu
1               5                   10                  15

Ser Ser Glu Leu Lys Lys Tyr Gln Ile Pro Ser Pro Pro Ile Val Lys
            20                  25                  30

Asp Thr Ser Ala Lys Thr Asp Ser Asn Leu Trp Glu Lys Phe Ala Glu
        35                  40                  45

Leu Ser Thr Lys Cys Ile Val Lys Ile Val Glu Phe Ala Lys Gly Ile
    50                  55                  60

Pro Gly Phe Gln Asp Phe Thr Ile Ala Asp Gln Ile Thr Leu Leu Lys
65                  70                  75                  80

Cys Ala Cys Leu Glu Val Leu Phe Leu Arg Ile Cys Ser Arg Phe Ser
                85                  90                  95

Pro Glu His Asp Thr Met Thr Phe Ser Asp Gly Leu Thr Leu Thr Arg
            100                 105                 110
```

```
Lys Gln Met Arg Val Cys Gly Phe Gly Pro Ile Thr Glu Gln Val Phe
        115                 120                 125

Ser Phe Ala Gln Ser Leu His Pro Leu Asn Ala Asp Ala Thr Glu Ile
    130                 135                 140

Gly Leu Leu Ser Ala Ile Cys Leu Val Ser Ala Asp Arg Val Asp Leu
145                 150                 155                 160

Glu Glu Pro Asp Lys Val Glu Leu Leu Gln Glu Ser Leu Val Glu Gly
                165                 170                 175

Leu Lys Tyr Tyr Ala Arg Lys Arg Arg Pro His Thr Pro Gln Val Phe
            180                 185                 190

Pro Lys Leu Ile Ile Lys Ile Ser Asp Leu Arg Ser Ile Ser Leu Lys
        195                 200                 205

Gly Ala Asp Arg Val Val Thr Val Lys Thr Glu Ile Pro Cys Gly Ala
    210                 215                 220

Met Pro Pro Leu Met Ser Glu Met Leu Glu Asn
225                 230                 235


<210>  190
<211>  231
<212>  PRT
<213>  Homo sapiens

<400>  190

Asp Leu Thr Glu Lys Ile Arg Lys Ala His Gln Glu Thr Phe Pro Ser
1               5                   10                  15

Leu Cys Gln Leu Gly Lys Tyr Thr Thr Asn Ser Ser Ala Asp His Arg
            20                  25                  30

Val Arg Leu Asp Leu Gly Leu Trp Asp Lys Phe Ser Glu Leu Ala Thr
        35                  40                  45

Lys Cys Ile Ile Lys Ile Val Glu Phe Ala Lys Arg Leu Pro Gly Phe
    50                  55                  60

Thr Ser Leu Thr Ile Ala Asp Gln Ile Thr Leu Leu Lys Ala Ala Cys
65                  70                  75                  80

Leu Asp Ile Leu Ile Leu Arg Ile Cys Thr Arg Tyr Thr Pro Glu Gln
                85                  90                  95

Asp Thr Met Thr Phe Ser Asp Gly Leu Thr Leu Asn Arg Thr Gln Met
            100                 105                 110
```

His Asn Ala Gly Phe Gly Pro Leu Thr Asp Leu Val Phe Thr Phe Ala
115 120 125

Asn Gln Leu Leu Pro Leu Glu Met Asp Asp Thr Glu Thr Gly Leu Leu
130 135 140

Ser Ala Ile Cys Leu Ile Cys Gly Asp Arg Gln Asp Leu Glu Glu Pro
145 150 155 160

Met Lys Val Asp Lys Leu Gln Glu Pro Leu Leu Glu Ala Leu Lys Ile
165 170 175

Tyr Ile Arg Lys Arg Arg Pro Asn Lys Pro His Met Phe Pro Lys Ile
180 185 190

Leu Met Lys Ile Thr Asp Leu Arg Ser Ile Ser Ala Lys Gly Ala Glu
195 200 205

Arg Val Ile Thr Leu Lys Met Glu Ile Pro Gly Ser Met Pro Pro Leu
210 215 220

Ile Gln Glu Met Leu Glu Asn
225 230

<210> 191
<211> 231
<212> PRT
<213> Homo sapiens

<400> 191

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

Leu Cys Gln Leu Gly Lys Tyr Thr Thr Asn Ser Ser Ala Asp Gln Arg
20 25 30

Val Gln Leu Asp Leu Gly Leu Trp Asp Lys Phe Ser Glu Leu Ser Thr
35 40 45

Lys Cys Ile Ile Lys Ile Val Glu Phe Ala Lys Arg Leu Pro Gly Phe
50 55 60

Thr Thr Leu Thr Ile Ala Asp Gln Ile Thr Leu Leu Lys Ser Ala Cys
65 70 75 80

Leu Asp Ile Leu Met Leu Arg Ile Cys Thr Arg Tyr Thr Pro Glu Gln
85 90 95

Asp Thr Met Thr Phe Ser Asp Gly Leu Thr Leu Asn Arg Thr Gln Met
100 105 110

His Asn Ala Gly Phe Gly Pro Leu Thr Asp Leu Val Phe Ser Phe Ala

115 120 125

Asp Gln Leu Leu Pro Leu Glu Met Asp Asp Thr Glu Thr Gly Leu Leu
130 135 140

Ser Ala Ile Cys Leu Ile Cys Gly Asp Arg Met Asp Leu Glu Glu Pro
145 150 155 160

Glu Lys Val Glu Lys Leu Gln Glu Pro Leu Leu Glu Ala Leu Lys Phe
165 170 175

Tyr Ala Arg Arg Arg Arg Pro Asp Lys Pro Tyr Met Phe Pro Arg Met
180 185 190

Leu Met Lys Ile Thr Asp Leu Arg Gly Ile Ser Thr Lys Gly Ala Glu
195 200 205

Arg Ala Ile Thr Leu Lys Leu Glu Ile Pro Gly Pro Met Pro Pro Leu
210 215 220

Ile Arg Glu Met Leu Glu Asn
225 230

<210> 192
<211> 231
<212> PRT
<213> Homo sapiens

<400> 192

Glu Leu Val Asn Lys Val Ser Lys Ala His Gln Glu Thr Phe Pro Ser
1 5 10 15

Leu Cys Gln Leu Gly Lys Tyr Thr Thr Asn Ser Ser Ser Asp His Arg
20 25 30

Ile Gln Leu Asp Leu Gly Leu Trp Asp Lys Phe Ser Glu Leu Ser Thr
35 40 45

Lys Cys Ile Ile Lys Ile Val Glu Phe Ala Lys Arg Leu Pro Gly Phe
50 55 60

Thr Thr Leu Thr Ile Ala Asp Gln Ile Thr Leu Leu Lys Ser Ala Cys
65 70 75 80

Leu Asp Ile Leu Met Leu Arg Ile Cys Thr Arg Tyr Thr Pro Glu Gln
85 90 95

Asp Thr Met Thr Phe Ser Asp Gly Leu Thr Leu Asn Arg Thr Gln Met
100 105 110

His Asn Ala Gly Phe Gly Pro Leu Thr Asp Leu Val Phe Ala Phe Ala
115 120 125

Gly Gln Leu Leu Pro Leu Glu Met Asp Asp Thr Glu Thr Gly Leu Leu
130 135 140

Ser Ala Ile Cys Leu Ile Cys Gly Asp Arg Met Asp Leu Glu Glu Pro
145 150 155 160

Glu Arg Val Asp Arg Leu Gln Glu Pro Leu Leu Glu Ala Leu Lys Ile
165 170 175

Tyr Ala Arg Arg Arg Arg Pro Asn Lys Pro His Met Phe Pro Arg Met
180 185 190

Leu Met Lys Ile Thr Asp Leu Arg Gly Ile Ser Thr Lys Gly Ala Glu
195 200 205

Arg Ala Ile Thr Leu Lys Met Glu Ile Pro Gly Pro Met Pro Pro Leu
210 215 220

Ile Arg Glu Met Leu Glu Asn
225 230

<210> 193
<211> 229
<212> PRT
<213> Homo sapiens

<400> 193

Asp Ile Leu Gln Glu Val Leu Arg Ala His Arg Asp Thr Phe Pro Gln
1 5 10 15

Arg Pro Leu His Pro Ile His Asn Ala Val Ser Ala Gly Asn Ile Asp
20 25 30

Ile Asp Met Val Met Phe Asp Tyr Val Thr Asp Met Ser Ser Arg Ala
35 40 45

Ile Val Met Val Val Asp Phe Ala Lys Lys Leu Pro Gly Phe Leu Ser
50 55 60

Leu Ser Thr Gln Asp Gln Ile Thr Leu Leu Lys Ala Ser Cys Leu Asp
65 70 75 80

Ile Met Ile Leu Arg Ile Cys Ser Arg Phe Asn Pro Gln Asp Ala Ser
85 90 95

Val Thr Phe Thr Thr Gly Leu Thr Leu Thr Gln Gly Gln Leu Lys Ala
100 105 110

Gly Gly Phe Gly Ser Leu Leu Asp Val Ile Phe Thr Phe Ala Ser Ser
115 120 125

```
Leu Ser Arg Met His Ile Asp Glu Thr Glu Ile Ala Leu Leu Ser Ala
    130                 135                 140

Ile Cys Leu Ile Ser Glu Asp Arg Thr Gly Leu Glu Asp Ala Pro Arg
145                 150                 155                 160

Ile Glu Lys Met Gln Glu Pro Leu Leu Glu Gly Leu Arg Leu Tyr Val
                165                 170                 175

Arg Lys Arg Arg Pro Lys Glu Ser His Phe Phe Ala Lys Leu Leu Met
            180                 185                 190

Lys Ile Thr Asp Leu Arg Cys Ile Ser Val Lys Ser Ala Glu Lys Val
        195                 200                 205

Phe Asp Met Lys Val Glu Phe Val Lys Glu Met Pro Ala Leu Ile Ser
    210                 215                 220

Glu Met Ile Asp Lys
225
```

<210> 194
<211> 231
<212> PRT
<213> Homo sapiens

<400> 194

```
Thr Ile Ile Thr Thr Val Arg Glu Ala His Met Ala Thr Leu Pro Asp
1               5                   10                  15

Met Gly Lys Leu Pro Lys Tyr Lys Val Lys Asn Ala Ala Glu Gln Arg
            20                  25                  30

Gly Pro Thr Asp Ile Glu Leu Trp Gln His Phe Ser Asp Leu Cys Thr
        35                  40                  45

Glu Thr Ile Ile Lys Ile Val Gln Phe Ala Lys Lys Val Pro Gly Phe
    50                  55                  60

Thr Thr Phe Gly Thr Ala Asp Gln Ile Thr Leu Leu Lys Ala Ala Cys
65                  70                  75                  80

Leu Asp Ile Leu Ile Leu Arg Leu Ala Thr Arg Leu Asp Lys Glu Ser
                85                  90                  95

Asp Thr Val Thr Phe Ile Asn Gly Met Met Leu Ser Arg Thr Gln Met
            100                 105                 110

His Asn Ala Gly Phe Gly Pro Leu Thr Asp Gly Val Phe Thr Phe Ala
        115                 120                 125
```

Glu Gly Met Gln Lys Leu Leu Phe Asp Glu Thr Glu Ile Gly Leu Met
130 135 140

Cys Ser Ile Cys Leu Val Cys Gly Asp Arg Gln Gly Leu Glu Asp Ile
145 150 155 160

Gln Arg Ala Glu Asn Leu Gln Glu Pro Leu Leu Glu Ala Leu Lys Ala
165 170 175

Tyr Ser Arg Arg Arg Ile Pro Asp Asp Pro Gln Arg Phe Pro Lys Met
180 185 190

Ile Met Lys Ile Thr Asp Leu Arg Ser Ile Ser Ser Lys Gly Ala Glu
195 200 205

Arg Val Ile Thr Leu Lys Met Glu Leu Ser Ser Pro Met Pro Pro Leu
210 215 220

Ile Ala Glu Ile Trp Glu Lys
225 230

<210> 195
<211> 231
<212> PRT
<213> Homo sapiens

<400> 195

Asp Leu Thr Glu Lys Ile Arg Lys Ala His Gln Glu Thr Phe Pro Ser
1 5 10 15

Leu Cys Gln Leu Gly Lys Tyr Thr Thr Asn Ser Ser Ala Asp His Arg
20 25 30

Val Arg Leu Asp Leu Gly Leu Trp Asp Lys Phe Ser Glu Leu Ala Thr
35 40 45

Lys Cys Ile Ile Lys Ile Val Glu Phe Ala Lys Arg Leu Pro Gly Phe
50 55 60

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

Leu Asp Ile Leu Ile Leu Arg Ile Cys Thr Arg Tyr Thr Pro Glu Gln
85 90 95

Asp Thr Met Thr Phe Ser Asp Gly Leu Thr Leu Asn Arg Thr Gln Met
100 105 110

His Asn Ala Gly Phe Gly Pro Leu Thr Asp Leu Val Phe Thr Phe Ala
115 120 125

Asn Gln Leu Leu Pro Leu Glu Met Asp Asp Thr Glu Thr Gly Leu Leu

130 135 140

Ser Ala Ile Cys Leu Ile Cys Gly Asp Arg Gln Asp Leu Glu Glu Pro
145 150 155 160

Thr Lys Val Asp Lys Leu Gln Glu Pro Leu Leu Glu Ala Leu Lys Ile
165 170 175

Tyr Ile Arg Lys Arg Arg Pro Ser Lys Pro His Met Phe Pro Lys Ile
180 185 190

Leu Met Lys Ile Thr Asp Leu Arg Ser Ile Ser Ala Lys Gly Ala Glu
195 200 205

Arg Val Ile Thr Leu Lys Met Glu Ile Pro Gly Ser Met Pro Pro Leu
210 215 220

Ile Gln Glu Met Leu Glu Asn
225 230

<210> 196
<211> 231
<212> PRT
<213> Homo sapiens

<400> 196

Glu Leu Ile Glu Lys Val Arg Lys Ala His Gln Glu Thr Phe Pro Ala
1 5 10 15

Leu Cys Gln Leu Gly Lys Tyr Thr Thr Asn Asn Ser Ser Glu Gln Arg
20 25 30

Val Ser Leu Asp Ile Asp Leu Trp Asp Lys Phe Ser Glu Leu Ser Thr
35 40 45

Lys Cys Ile Ile Lys Thr Val Glu Phe Ala Lys Gln Leu Pro Gly Phe
50 55 60

Thr Thr Leu Thr Ile Ala Asp Gln Ile Thr Leu Leu Lys Ala Ala Cys
65 70 75 80

Leu Asp Ile Leu Ile Leu Arg Ile Cys Thr Arg Tyr Thr Pro Glu Gln
85 90 95

Asp Thr Met Thr Phe Ser Asp Gly Leu Thr Leu Asn Arg Thr Gln Met
100 105 110

His Asn Ala Gly Phe Gly Pro Leu Thr Asp Leu Val Phe Ala Phe Ala
115 120 125

Asn Gln Leu Leu Pro Leu Glu Met Asp Asp Ala Glu Thr Gly Leu Leu
130 135 140

```
Ser Ala Ile Cys Leu Ile Cys Gly Asp Arg Gln Asp Leu Glu Gln Pro
145                 150                 155                 160

Asp Arg Val Asp Met Leu Gln Glu Pro Leu Leu Glu Ala Leu Lys Val
                165                 170                 175

Tyr Val Arg Lys Arg Arg Pro Ser Arg Pro His Met Phe Pro Lys Met
            180                 185                 190

Leu Met Lys Ile Thr Asp Leu Arg Ser Ile Ser Ala Lys Gly Ala Glu
        195                 200                 205

Arg Val Ile Thr Leu Lys Met Glu Ile Pro Gly Ser Met Pro Pro Leu
    210                 215                 220

Ile Gln Glu Met Leu Glu Asn
225                 230


<210>  197
<211>  512
<212>  PRT
<213>  Homo sapiens

<400>  197

Met Gly Cys Ile Lys Ser Lys Gly Lys Asp Ser Leu Ser Asp Asp Gly
1               5                   10                  15

Val Asp Leu Lys Thr Gln Pro Val Arg Asn Thr Glu Arg Thr Ile Tyr
            20                  25                  30

Val Arg Asp Pro Thr Ser Asn Lys Gln Gln Arg Pro Val Pro Glu Ser
        35                  40                  45

Gln Leu Leu Pro Gly Gln Arg Phe Gln Thr Lys Asp Pro Glu Glu Gln
    50                  55                  60

Gly Asp Ile Val Val Ala Leu Tyr Pro Tyr Asp Gly Ile His Pro Asp
65                  70                  75                  80

Asp Leu Ser Phe Lys Lys Gly Glu Lys Met Lys Val Leu Glu Glu His
                85                  90                  95

Gly Glu Trp Trp Lys Ala Lys Ser Leu Leu Thr Lys Lys Glu Gly Phe
            100                 105                 110

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

Trp Phe Phe Lys Asp Ile Thr Arg Lys Asp Ala Glu Arg Gln Leu Leu
    130                 135                 140
```

```
Ala Pro Gly Asn Ser Ala Gly Ala Phe Leu Ile Arg Glu Ser Glu Thr
145                 150                 155                 160

Leu Lys Gly Ser Phe Ser Leu Ser Val Arg Asp Phe Asp Pro Val His
                165                 170                 175

Gly Asp Val Ile Lys His Tyr Lys Ile Arg Ser Leu Asp Asn Gly Gly
            180                 185                 190

Tyr Tyr Ile Ser Pro Arg Ile Thr Phe Pro Cys Ile Ser Asp Met Ile
        195                 200                 205

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

Ala Cys Ile Ser Pro Lys Pro Gln Lys Pro Trp Asp Lys Asp Ala Trp
225                 230                 235                 240

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

Gln Phe Gly Glu Val Trp Met Gly Tyr Tyr Asn Asn Ser Thr Lys Val
            260                 265                 270

Ala Val Lys Thr Leu Lys Pro Gly Thr Met Ser Val Gln Ala Phe Leu
        275                 280                 285

Glu Glu Ala Asn Leu Met Lys Thr Leu Gln His Asp Lys Leu Val Arg
    290                 295                 300

Leu Tyr Ala Val Val Thr Arg Glu Glu Pro Ile Tyr Ile Ile Thr Glu
305                 310                 315                 320

Tyr Met Ala Lys Gly Ser Leu Leu Asp Phe Leu Lys Ser Asp Glu Gly
                325                 330                 335

Gly Lys Val Leu Leu Pro Lys Leu Ile Asp Phe Ser Ala Gln Ile Ala
            340                 345                 350

Glu Gly Met Ala Tyr Ile Glu Arg Lys Asn Tyr Ile His Arg Asp Leu
        355                 360                 365

Arg Ala Ala Asn Val Leu Val Ser Glu Ser Leu Met Cys Lys Ile Ala
    370                 375                 380

Asp Phe Gly Leu Ala Arg Val Ile Glu Asp Asn Glu Tyr Thr Ala Arg
385                 390                 395                 400

Glu Gly Ala Lys Phe Pro Ile Lys Trp Thr Ala Pro Glu Ala Ile Asn
                405                 410                 415
```

Phe Gly Cys Phe Thr Ile Lys Ser Asp Val Trp Ser Phe Gly Ile Leu
420 425 430

Leu Tyr Glu Ile Val Thr Tyr Gly Lys Ile Pro Tyr Pro Gly Arg Thr
435 440 445

Asn Ala Asp Val Met Thr Ala Leu Ser Gln Gly Tyr Arg Met Pro Arg
450 455 460

Val Glu Asn Cys Pro Asp Glu Leu Tyr Asp Ile Met Lys Met Cys Trp
465 470 475 480

Lys Glu Lys Ala Glu Glu Arg Pro Thr Phe Asp Tyr Leu Gln Ser Val
485 490 495

Leu Asp Asp Phe Tyr Thr Ala Thr Glu Gly Gln Tyr Gln Gln Gln Pro
500 505 510

<210> 198
<211> 183
<212> PRT
<213> Homo sapiens

<400> 198

Tyr Gln Lys Gln Ala Asp Gly Leu Cys Arg Arg Leu Glu Lys Ala Cys
1 5 10 15

Ile Ser Pro Lys Pro Gln Lys Pro Trp Asp Lys Asp Ala Trp Glu Ile
20 25 30

Pro Arg Glu Ser Ile Lys Leu Val Lys Arg Leu Gly Ala Gly Gln Phe
35 40 45

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

Lys Thr Leu Lys Pro Gly Thr Met Ser Val Gln Ala Phe Leu Glu Glu
65 70 75 80

Ala Asn Leu Met Lys Thr Leu Gln His Asp Lys Leu Val Arg Leu Tyr
85 90 95

Ala Val Val Thr Arg Glu Glu Pro Ile Tyr Ile Ile Thr Glu Tyr Met
100 105 110

Ala Lys Gly Ser Leu Leu Asp Phe Leu Lys Ser Asp Glu Gly Gly Lys
115 120 125

Val Leu Leu Pro Lys Leu Ile Asp Phe Ser Ala Gln Ile Ala Glu Gly
130 135 140

Met Ala Tyr Ile Glu Arg Lys Asn Tyr Ile His Arg Asp Leu Arg Ala
145 150 155 160

Ala Asn Val Leu Val Ser Glu Ser Leu Met Cys Lys Ile Ala Asp Phe
165 170 175

Gly Leu Ala Arg Val Ile Glu
180

<210> 199
<211> 119
<212> PRT
<213> Homo sapiens

<400> 199

Asp Asn Glu Tyr Thr Ala Arg Glu Gly Ala Lys Phe Pro Ile Lys Trp
1 5 10 15

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

Val Trp Ser Phe Gly Ile Leu Leu Tyr Glu Ile Val Thr Tyr Gly Lys
35 40 45

Ile Pro Tyr Pro Gly Arg Thr Asn Ala Asp Val Met Thr Ala Leu Ser
50 55 60

Gln Gly Tyr Arg Met Pro Arg Val Glu Asn Cys Pro Asp Glu Leu Tyr
65 70 75 80

Asp Ile Met Lys Met Cys Trp Lys Glu Lys Ala Glu Glu Arg Pro Thr
85 90 95

Phe Asp Tyr Leu Gln Ser Val Leu Asp Asp Phe Tyr Thr Ala Thr Glu
100 105 110

Gly Gln Tyr Gln Gln Gln Pro
115

<210> 200
<211> 1055
<212> PRT
<213> Homo sapiens

<400> 200

Met Ala Ala Ala Tyr Leu Asp Pro Asn Leu Asn His Thr Pro Ser Ser
1 5 10 15

Ser Thr Lys Thr His Leu Gly Thr Gly Thr Glu Arg Ser Pro Gly Ala
20 25 30

Met Glu Arg Val Leu Lys Val Phe His Tyr Phe Glu Ser Ser Asn Glu
35 40 45

```
Pro Thr Thr Trp Ala Ser Ile Ile Arg His Gly Asp Ala Thr Asp Val
    50                  55                  60

Arg Gly Ile Ile Gln Lys Ile Val Asp Ser His Lys Val Lys His Val
65                  70                  75                  80

Ala Cys Tyr Gly Phe Arg Leu Ser His Leu Arg Ser Glu Glu Val His
                85                  90                  95

Trp Leu His Val Asp Met Gly Val Ser Ser Val Arg Glu Lys Tyr Glu
            100                 105                 110

Leu Ala His Pro Pro Glu Glu Trp Lys Tyr Glu Leu Arg Ile Arg Tyr
        115                 120                 125

Leu Pro Lys Gly Phe Leu Asn Gln Phe Thr Glu Asp Lys Pro Thr Leu
    130                 135                 140

Asn Phe Phe Tyr Gln Gln Val Lys Ser Asp Tyr Met Leu Glu Ile Ala
145                 150                 155                 160

Asp Gln Val Asp Gln Asp Ile Ala Leu Lys Leu Gly Cys Leu Glu Ile
                165                 170                 175

Arg Arg Ser Tyr Trp Glu Met Arg Gly Asn Ala Leu Glu Lys Lys Ser
            180                 185                 190

Asn Tyr Glu Val Leu Glu Lys Asp Val Gly Leu Lys Arg Phe Phe Pro
        195                 200                 205

Lys Ser Leu Leu Asp Ser Val Lys Ala Lys Thr Leu Arg Lys Leu Ile
    210                 215                 220

Gln Gln Thr Phe Arg Gln Phe Ala Asn Leu Asn Arg Glu Glu Ser Ile
225                 230                 235                 240

Leu Lys Phe Phe Glu Ile Leu Ser Pro Val Tyr Arg Phe Asp Lys Glu
                245                 250                 255

Cys Phe Lys Cys Ala Leu Gly Ser Ser Trp Ile Ile Ser Val Glu Leu
            260                 265                 270

Ala Ile Gly Pro Glu Glu Gly Ile Ser Tyr Leu Thr Asp Lys Gly Cys
        275                 280                 285

Asn Pro Thr His Leu Ala Asp Phe Asn Gln Val Gln Thr Ile Gln Tyr
    290                 295                 300

Ser Asn Ser Glu Asp Lys Asp Arg Lys Gly Met Leu Gln Leu Lys Ile
305                 310                 315                 320
```

```
Ala Gly Ala Pro Glu Pro Leu Thr Val Thr Ala Pro Ser Leu Thr Ile
                325                 330                 335

Ala Glu Asn Met Ala Asp Leu Ile Asp Gly Tyr Cys Arg Leu Val Asn
            340                 345                 350

Gly Ala Thr Gln Ser Phe Ile Ile Arg Pro Gln Lys Glu Gly Glu Arg
        355                 360                 365

Ala Leu Pro Ser Ile Pro Lys Leu Ala Asn Asn Glu Lys Gln Gly Met
    370                 375                 380

Arg Thr His Ala Val Ser Val Ser Glu Thr Asp Asp Tyr Ala Glu Ile
385                 390                 395                 400

Ile Asp Glu Glu Asp Thr Tyr Thr Met Pro Ser Thr Arg Asp Tyr Glu
                405                 410                 415

Ile Gln Arg Glu Arg Ile Glu Leu Gly Arg Cys Ile Gly Glu Gly Gln
            420                 425                 430

Phe Gly Asp Val His Gln Gly Val Tyr Leu Ser Pro Glu Asn Pro Ala
        435                 440                 445

Leu Ala Val Ala Ile Lys Thr Cys Lys Asn Cys Thr Ser Asp Ser Val
    450                 455                 460

Arg Glu Lys Phe Leu Gln Glu Ala Leu Thr Met Arg Gln Phe Asp His
465                 470                 475                 480

Pro His Ile Val Lys Leu Ile Gly Val Ile Thr Glu Asn Pro Val Trp
                485                 490                 495

Ile Ile Met Glu Leu Cys Thr Leu Gly Glu Leu Arg Ser Phe Leu Gln
            500                 505                 510

Val Arg Lys Tyr Ser Leu Asp Leu Ala Ser Leu Ile Leu Tyr Ala Tyr
        515                 520                 525

Gln Leu Ser Thr Ala Leu Ala Tyr Leu Glu Ser Lys Arg Phe Val His
    530                 535                 540

Arg Asp Ile Ala Ala Arg Asn Val Leu Val Ser Ser Asn Asp Cys Val
545                 550                 555                 560

Lys Leu Gly Asp Phe Gly Leu Ser Arg Tyr Met Glu Asp Ser Thr Tyr
                565                 570                 575

Tyr Lys Ala Ser Lys Gly Lys Leu Pro Ile Lys Trp Met Ala Pro Glu
            580                 585                 590
```

```
Ser Ile Asn Phe Arg Arg Phe Thr Ser Ala Ser Asp Val Trp Met Phe
        595                 600                 605

Gly Val Cys Met Trp Glu Ile Leu Met His Gly Val Lys Pro Phe Gln
    610                 615                 620

Gly Val Lys Asn Asn Asp Val Ile Gly Arg Ile Glu Asn Gly Glu Arg
625                 630                 635                 640

Leu Pro Met Pro Pro Asn Cys Pro Pro Thr Leu Tyr Ser Leu Met Thr
                645                 650                 655

Lys Cys Trp Ala Tyr Asp Pro Ser Arg Arg Pro Arg Phe Thr Glu Leu
            660                 665                 670

Lys Ala Gln Leu Ser Thr Ile Leu Glu Glu Glu Lys Val Gln Gln Glu
        675                 680                 685

Glu Arg Met Arg Met Glu Ser Arg Arg Gln Ala Thr Val Ser Trp Asp
    690                 695                 700

Ser Gly Gly Ser Asp Glu Ala Pro Pro Lys Pro Ser Arg Pro Gly Tyr
705                 710                 715                 720

Pro Ser Pro Arg Ser Ser Glu Gly Phe Tyr Pro Ser Pro Gln His Met
                725                 730                 735

Val Gln Thr Asn His Tyr Gln Ile Ser Gly Tyr Pro Gly Ser His Gly
            740                 745                 750

Ile Pro Ala Met Ala Gly Ser Ile Tyr Pro Gly Gln Ala Ser Leu Leu
        755                 760                 765

Asp Gln Thr Glu Leu Trp Asn His Arg Pro Gln Glu Met Ser Met Trp
    770                 775                 780

Gln Pro Ser Val Glu Asp Ser Ala Ala Leu Asp Leu Arg Gly Met Gly
785                 790                 795                 800

Gln Val Leu Pro Pro His Leu Met Glu Glu Arg Leu Ile Arg Gln Gln
                805                 810                 815

Gln Glu Met Glu Glu Asp Gln Arg Trp Leu Glu Lys Glu Glu Arg Phe
            820                 825                 830

Leu Lys Pro Asp Val Arg Leu Ser Arg Gly Ser Ile Asp Arg Glu Asp
        835                 840                 845

Gly Ser Phe Gln Gly Pro Thr Gly Asn Gln His Ile Tyr Gln Pro Val
    850                 855                 860
```

```
Gly Lys Pro Asp Pro Ala Ala Pro Pro Lys Lys Pro Pro Arg Pro Gly
865                 870                 875                 880

Ala Pro Gly His Leu Ser Asn Leu Ser Ser Ile Ser Ser Pro Ala Glu
                885                 890                 895

Ser Tyr Asn Glu Gly Val Lys Pro Trp Arg Leu Gln Pro Gln Glu Ile
            900                 905                 910

Ser Pro Pro Pro Thr Ala Asn Leu Asp Arg Ser Asn Asp Lys Val Tyr
        915                 920                 925

Glu Asn Val Thr Gly Leu Val Lys Ala Val Ile Glu Met Ser Ser Lys
    930                 935                 940

Ile Gln Pro Ala Pro Pro Glu Glu Tyr Val Pro Met Val Lys Glu Val
945                 950                 955                 960

Gly Leu Ala Leu Arg Thr Leu Leu Ala Thr Val Asp Glu Thr Ile Pro
                965                 970                 975

Ile Leu Pro Ala Ser Thr His Arg Glu Ile Glu Met Ala Gln Lys Leu
            980                 985                 990

Leu Asn Ser Asp Leu Gly Glu Leu  Ile Ser Lys Met Lys  Leu Ala Gln
        995                 1000                1005

Gln Tyr  Val Met Thr Ser Leu  Gln Gln Glu Tyr Lys  Lys Gln Met
    1010                1015                1020

Leu Thr  Ala Ala His Ala Leu  Ala Val Asp Ala Lys  Asn Leu Leu
    1025                1030                1035

Asp Val  Ile Asp Gln Ala Arg  Leu Lys Met Leu Gly  Gln Thr Arg
    1040                1045                1050

Pro His
    1055


<210>  201
<211>  472
<212>  PRT
<213>  Homo sapiens

<400>  201

Met Gly Ser Lys Met Asn Leu Ile Glu His Ser His Leu Pro Thr Thr
1               5                   10                  15

Asp Glu Phe Ser Phe Ser Glu Asn Leu Phe Gly Val Leu Thr Glu Gln
            20                  25                  30
```

```
Val Ala Gly Pro Leu Gly Gln Asn Leu Glu Val Glu Pro Tyr Ser Gln
        35                  40                  45

Tyr Ser Asn Val Gln Phe Pro Gln Val Gln Pro Gln Ile Ser Ser Ser
    50                  55                  60

Ser Tyr Tyr Ser Asn Leu Gly Phe Tyr Pro Gln Gln Pro Glu Glu Trp
65                  70                  75                  80

Tyr Ser Pro Gly Ile Tyr Glu Leu Arg Arg Met Pro Ala Glu Thr Leu
                85                  90                  95

Tyr Gln Gly Glu Thr Glu Val Ala Glu Met Pro Val Thr Lys Lys Pro
            100                 105                 110

Arg Met Gly Ala Ser Ala Gly Arg Ile Lys Gly Asp Glu Leu Cys Val
        115                 120                 125

Val Cys Gly Asp Arg Ala Ser Gly Tyr His Tyr Asn Ala Leu Thr Cys
    130                 135                 140

Glu Gly Cys Lys Gly Phe Phe Arg Arg Ser Ile Thr Lys Asn Ala Val
145                 150                 155                 160

Tyr Lys Cys Lys Asn Gly Gly Asn Cys Val Met Asp Met Tyr Met Arg
                165                 170                 175

Arg Lys Cys Gln Glu Cys Arg Leu Arg Lys Cys Lys Glu Met Gly Met
            180                 185                 190

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

Arg Lys Asn Val Lys Gln His Ala Asp Gln Thr Val Asn Glu Asp Ser
    210                 215                 220

Glu Gly Arg Asp Leu Arg Gln Val Thr Ser Thr Thr Lys Ser Cys Arg
225                 230                 235                 240

Glu Lys Thr Glu Leu Thr Pro Asp Gln Gln Thr Leu Leu His Phe Ile
                245                 250                 255

Met Asp Ser Tyr Asn Lys Gln Arg Met Pro Gln Glu Ile Thr Asn Lys
            260                 265                 270

Ile Leu Lys Glu Glu Phe Ser Ala Glu Glu Asn Phe Leu Ile Leu Thr
        275                 280                 285

Glu Met Ala Thr Asn His Val Gln Val Leu Val Glu Phe Thr Lys Lys
    290                 295                 300
```

```
Leu Pro Gly Phe Gln Thr Leu Asp His Glu Asp Gln Ile Ala Leu Leu
305                 310                 315                 320

Lys Gly Ser Ala Val Glu Ala Met Phe Leu Arg Ser Ala Glu Ile Phe
                325                 330                 335

Asn Lys Lys Leu Pro Ser Gly His Ser Asp Leu Leu Glu Glu Arg Ile
            340                 345                 350

Arg Asn Ser Gly Ile Ser Asp Glu Tyr Ile Thr Pro Met Phe Ser Phe
        355                 360                 365

Tyr Lys Ser Ile Gly Glu Leu Lys Met Thr Gln Glu Glu Tyr Ala Leu
    370                 375                 380

Leu Thr Ala Ile Val Ile Leu Ser Pro Asp Arg Gln Tyr Ile Lys Asp
385                 390                 395                 400

Arg Glu Ala Val Glu Lys Leu Gln Glu Pro Leu Leu Asp Val Leu Gln
                405                 410                 415

Lys Leu Cys Lys Ile His Gln Pro Glu Asn Pro Gln His Phe Ala Cys
            420                 425                 430

Leu Leu Gly Arg Leu Thr Glu Leu Arg Thr Phe Asn His His His Ala
        435                 440                 445

Glu Met Leu Met Ser Trp Arg Val Asn Asp His Lys Phe Thr Pro Leu
    450                 455                 460

Leu Cys Glu Ile Trp Asp Val Gln
465                 470
```

<210> 202
<211> 236
<212> PRT
<213> Homo sapiens

<400> 202

```
Lys Ser Cys Arg Glu Lys Thr Glu Leu Thr Pro Asp Gln Gln Thr Leu
1               5                   10                  15

Leu His Phe Ile Met Asp Ser Tyr Asn Lys Gln Arg Met Pro Gln Glu
            20                  25                  30

Ile Thr Asn Lys Ile Leu Lys Glu Glu Phe Ser Ala Glu Glu Asn Phe
        35                  40                  45

Leu Ile Leu Thr Glu Met Ala Thr Asn His Val Gln Val Leu Val Glu
    50                  55                  60
```

Phe Thr Lys Lys Leu Pro Gly Phe Gln Thr Leu Asp His Glu Asp Gln
65 70 75 80

Ile Ala Leu Leu Lys Gly Ser Ala Val Glu Ala Met Phe Leu Arg Ser
85 90 95

Ala Glu Ile Phe Asn Lys Lys Leu Pro Ser Gly His Ser Asp Leu Leu
100 105 110

Glu Glu Arg Ile Arg Asn Ser Gly Ile Ser Asp Glu Tyr Ile Thr Pro
115 120 125

Met Phe Ser Phe Tyr Lys Ser Ile Gly Glu Leu Lys Met Thr Gln Glu
130 135 140

Glu Tyr Ala Leu Leu Thr Ala Ile Val Ile Leu Ser Pro Asp Arg Gln
145 150 155 160

Tyr Ile Lys Asp Arg Glu Ala Val Glu Lys Leu Gln Glu Pro Leu Leu
165 170 175

Asp Val Leu Gln Lys Leu Cys Lys Ile His Gln Pro Glu Asn Pro Gln
180 185 190

His Phe Ala Cys Leu Leu Gly Arg Leu Thr Glu Leu Arg Thr Phe Asn
195 200 205

His His His Ala Glu Met Leu Met Ser Trp Arg Val Asn Asp His Lys
210 215 220

Phe Thr Pro Leu Leu Cys Glu Ile Trp Asp Val Gln
225 230 235

<210> 203
<211> 447
<212> PRT
<213> Homo sapiens

<400> 203

Met Ser Leu Trp Leu Gly Ala Pro Val Pro Asp Ile Pro Pro Asp Ser
1 5 10 15

Ala Val Glu Leu Trp Lys Pro Gly Ala Gln Asp Ala Ser Ser Gln Ala
20 25 30

Gln Gly Gly Ser Ser Cys Ile Leu Arg Glu Glu Ala Arg Met Pro His
35 40 45

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

Ala Leu Leu Thr Arg Ala Glu Pro Pro Ser Glu Pro Thr Glu Ile Arg

65 70 75 80

Pro Gln Lys Arg Lys Lys Gly Pro Ala Pro Lys Met Leu Gly Asn Glu
85 90 95

Leu Cys Ser Val Cys Gly Asp Lys Ala Ser Gly Phe His Tyr Asn Val
100 105 110

Leu Ser Cys Glu Gly Cys Lys Gly Phe Phe Arg Arg Ser Val Ile Lys
115 120 125

Gly Ala His Tyr Ile Cys His Ser Gly Gly His Cys Pro Met Asp Thr
130 135 140

Tyr Met Arg Arg Lys Cys Gln Glu Cys Arg Leu Arg Lys Cys Arg Gln
145 150 155 160

Ala Gly Met Arg Glu Glu Cys Val Leu Ser Glu Glu Gln Ile Arg Leu
165 170 175

Lys Lys Leu Lys Arg Gln Glu Glu Glu Gln Ala His Ala Thr Ser Leu
180 185 190

Pro Pro Arg Ala Ser Ser Pro Pro Gln Ile Leu Pro Gln Leu Ser Pro
195 200 205

Glu Gln Leu Gly Met Ile Glu Lys Leu Val Ala Ala Gln Gln Gln Cys
210 215 220

Asn Arg Arg Ser Phe Ser Asp Arg Leu Arg Val Thr Pro Trp Pro Met
225 230 235 240

Ala Pro Asp Pro His Ser Arg Glu Ala Arg Gln Gln Arg Phe Ala His
245 250 255

Phe Thr Glu Leu Ala Ile Val Ser Val Gln Glu Ile Val Asp Phe Ala
260 265 270

Lys Gln Leu Pro Gly Phe Leu Gln Leu Ser Arg Glu Asp Gln Ile Ala
275 280 285

Leu Leu Lys Thr Ser Ala Ile Glu Val Met Leu Leu Glu Thr Ser Arg
290 295 300

Arg Tyr Asn Pro Gly Ser Glu Ser Ile Thr Phe Leu Lys Asp Phe Ser
305 310 315 320

Tyr Asn Arg Glu Asp Phe Ala Lys Ala Gly Leu Gln Val Glu Phe Ile
325 330 335

Asn Pro Ile Phe Glu Phe Ser Arg Ala Met Asn Glu Leu Gln Leu Asn

340 345 350

Asp Ala Glu Phe Ala Leu Leu Ile Ala Ile Ser Ile Phe Ser Ala Asp
355 360 365

Arg Pro Asn Val Gln Asp Gln Leu Gln Val Glu Arg Leu Gln His Thr
370 375 380

Tyr Val Glu Ala Leu His Ala Tyr Val Ser Ile His His Pro His Asp
385 390 395 400

Arg Leu Met Phe Pro Arg Met Leu Met Lys Leu Val Ser Leu Arg Thr
405 410 415

Leu Ser Ser Val His Ser Glu Gln Val Phe Ala Leu Arg Leu Gln Asp
420 425 430

Lys Lys Leu Pro Pro Leu Leu Ser Glu Ile Trp Asp Val His Glu
435 440 445

<210> 204
<211> 266
<212> PRT
<213> Homo sapiens

<400> 204

Gln Glu Glu Glu Gln Ala His Ala Thr Ser Leu Pro Pro Arg Ala Ser
1 5 10 15

Ser Pro Pro Gln Ile Leu Pro Gln Leu Ser Pro Glu Gln Leu Gly Met
20 25 30

Ile Glu Lys Leu Val Ala Ala Gln Gln Gln Cys Asn Arg Arg Ser Phe
35 40 45

Ser Asp Arg Leu Arg Val Thr Pro Trp Pro Met Ala Pro Asp Pro His
50 55 60

Ser Arg Glu Ala Arg Gln Gln Arg Phe Ala His Phe Thr Glu Leu Ala
65 70 75 80

Ile Val Ser Val Gln Glu Ile Val Asp Phe Ala Lys Gln Leu Pro Gly
85 90 95

Phe Leu Gln Leu Ser Arg Glu Asp Gln Ile Ala Leu Leu Lys Thr Ser
100 105 110

Ala Ile Glu Val Met Leu Leu Glu Thr Ser Arg Arg Tyr Asn Pro Gly
115 120 125

Ser Glu Ser Ile Thr Phe Leu Lys Asp Phe Ser Tyr Asn Arg Glu Asp
130 135 140

```
Phe Ala Lys Ala Gly Leu Gln Val Glu Phe Ile Asn Pro Ile Phe Glu
145                 150                 155                 160

Phe Ser Arg Ala Met Asn Glu Leu Gln Leu Asn Asp Ala Glu Phe Ala
                165                 170                 175

Leu Leu Ile Ala Ile Ser Ile Phe Ser Ala Asp Arg Pro Asn Val Gln
            180                 185                 190

Asp Gln Leu Gln Val Glu Arg Leu Gln His Thr Tyr Val Glu Ala Leu
        195                 200                 205

His Ala Tyr Val Ser Ile His His Pro His Asp Arg Leu Met Phe Pro
    210                 215                 220

Arg Met Leu Met Lys Leu Val Ser Leu Arg Thr Leu Ser Ser Val His
225                 230                 235                 240

Ser Glu Gln Val Phe Ala Leu Arg Leu Gln Asp Lys Lys Leu Pro Pro
                245                 250                 255

Leu Leu Ser Glu Ile Trp Asp Val His Glu
            260                 265


<210>  205
<211>  497
<212>  PRT
<213>  Homo sapiens

<400>  205

Met Arg Thr Gln Ile Glu Val Ile Pro Cys Lys Ile Cys Gly Asp Lys
1               5                   10                  15

Ser Ser Gly Ile His Tyr Gly Val Ile Thr Cys Glu Gly Cys Lys Gly
            20                  25                  30

Phe Phe Arg Arg Ser Gln Arg Cys Asn Ala Ala Tyr Ser Cys Thr Arg
        35                  40                  45

Gln Gln Asn Cys Pro Ile Asp Arg Thr Ser Arg Asn Arg Cys Gln His
    50                  55                  60

Cys Arg Leu Gln Lys Cys Leu Ala Leu Gly Met Ser Arg Asp Ala Val
65                  70                  75                  80

Lys Phe Gly Arg Met Ser Lys Lys Gln Arg Asp Ser Leu His Ala Glu
                85                  90                  95

Val Gln Lys Gln Leu Gln Gln Arg Gln Gln Gln Gln Gln Glu Pro Val
            100                 105                 110
```

```
Val Lys Thr Pro Pro Ala Gly Ala Gln Gly Ala Asp Thr Leu Thr Tyr
        115                 120                 125

Thr Leu Gly Leu Pro Asp Gly Gln Leu Pro Leu Gly Ser Ser Pro Asp
    130                 135                 140

Leu Pro Glu Ala Ser Ala Cys Pro Pro Gly Leu Leu Lys Ala Ser Gly
145                 150                 155                 160

Ser Gly Pro Ser Tyr Ser Asn Asn Leu Ala Lys Ala Gly Leu Asn Gly
                165                 170                 175

Ala Ser Cys His Leu Glu Tyr Ser Pro Glu Arg Gly Lys Ala Glu Gly
            180                 185                 190

Arg Glu Ser Phe Tyr Ser Thr Gly Ser Gln Leu Thr Pro Asp Arg Cys
        195                 200                 205

Gly Leu Arg Phe Glu Glu His Arg His Pro Gly Leu Gly Glu Leu Gly
    210                 215                 220

Gln Gly Pro Asp Ser Tyr Gly Ser Pro Ser Phe Arg Ser Thr Pro Glu
225                 230                 235                 240

Ala Pro Tyr Ala Ser Leu Thr Glu Ile Glu His Leu Val Gln Ser Val
                245                 250                 255

Cys Lys Ser Tyr Arg Glu Thr Cys Gln Leu Arg Leu Glu Asp Leu Leu
            260                 265                 270

Arg Gln Arg Ser Asn Ile Phe Ser Arg Glu Glu Val Thr Gly Tyr Gln
        275                 280                 285

Arg Lys Ser Met Trp Glu Met Trp Glu Arg Cys Ala His His Leu Thr
    290                 295                 300

Glu Ala Ile Gln Tyr Val Val Glu Phe Ala Lys Arg Leu Ser Gly Phe
305                 310                 315                 320

Met Glu Leu Cys Gln Asn Asp Gln Ile Val Leu Leu Lys Ala Gly Ala
                325                 330                 335

Met Glu Val Val Leu Val Arg Met Cys Arg Ala Tyr Asn Ala Asp Asn
            340                 345                 350

Arg Thr Val Phe Phe Glu Gly Lys Tyr Gly Gly Met Glu Leu Phe Arg
        355                 360                 365

Ala Leu Gly Cys Ser Glu Leu Ile Ser Ser Ile Phe Asp Phe Ser His
    370                 375                 380
```

```
Ser Leu Ser Ala Leu His Phe Ser Glu Asp Glu Ile Ala Leu Tyr Thr
385                 390                 395                 400

Ala Leu Val Leu Ile Asn Ala His Arg Pro Gly Leu Gln Glu Lys Arg
                405                 410                 415

Lys Val Glu Gln Leu Gln Tyr Asn Leu Glu Leu Ala Phe His His His
            420                 425                 430

Leu Cys Lys Thr His Arg Gln Ser Ile Leu Ala Lys Leu Pro Pro Lys
        435                 440                 445

Gly Lys Leu Arg Ser Leu Cys Ser Gln His Val Glu Arg Leu Gln Ile
    450                 455                 460

Phe Gln His Leu His Pro Ile Val Val Gln Ala Ala Phe Pro Pro Leu
465                 470                 475                 480

Tyr Lys Glu Leu Phe Ser Thr Glu Thr Glu Ser Pro Val Gly Leu Ser
                485                 490                 495

Lys
```

<210> 206
<211> 261
<212> PRT
<213> Homo sapiens

<400> 206

```
Ser Thr Pro Glu Ala Pro Tyr Ala Ser Leu Thr Glu Ile Glu His Leu
1               5                   10                  15

Val Gln Ser Val Cys Lys Ser Tyr Arg Glu Thr Cys Gln Leu Arg Leu
            20                  25                  30

Glu Asp Leu Leu Arg Gln Arg Ser Asn Ile Phe Ser Arg Glu Glu Val
        35                  40                  45

Thr Gly Tyr Gln Arg Lys Ser Met Trp Glu Met Trp Glu Arg Cys Ala
    50                  55                  60

His His Leu Thr Glu Ala Ile Gln Tyr Val Val Glu Phe Ala Lys Arg
65                  70                  75                  80

Leu Ser Gly Phe Met Glu Leu Cys Gln Asn Asp Gln Ile Val Leu Leu
                85                  90                  95

Lys Ala Gly Ala Met Glu Val Val Leu Val Arg Met Cys Arg Ala Tyr
            100                 105                 110
```

```
Asn Ala Asp Asn Arg Thr Val Phe Phe Glu Gly Lys Tyr Gly Gly Met
        115                 120                 125

Glu Leu Phe Arg Ala Leu Gly Cys Ser Glu Leu Ile Ser Ser Ile Phe
    130                 135                 140

Asp Phe Ser His Ser Leu Ser Ala Leu His Phe Ser Glu Asp Glu Ile
145                 150                 155                 160

Ala Leu Tyr Thr Ala Leu Val Leu Ile Asn Ala His Arg Pro Gly Leu
                165                 170                 175

Gln Glu Lys Arg Lys Val Glu Gln Leu Gln Tyr Asn Leu Glu Leu Ala
            180                 185                 190

Phe His His His Leu Cys Lys Thr His Arg Gln Ser Ile Leu Ala Lys
        195                 200                 205

Leu Pro Pro Lys Gly Lys Leu Arg Ser Leu Cys Ser Gln His Val Glu
    210                 215                 220

Arg Leu Gln Ile Phe Gln His Leu His Pro Ile Val Val Gln Ala Ala
225                 230                 235                 240

Phe Pro Pro Leu Tyr Lys Glu Leu Phe Ser Thr Glu Thr Glu Ser Pro
                245                 250                 255

Val Gly Leu Ser Lys
            260
```

<210> 207
<211> 462
<212> PRT
<213> Homo sapiens

<400> 207

```
Met Asp Thr Lys His Phe Leu Pro Leu Asp Phe Ser Thr Gln Val Asn
1               5                   10                  15

Ser Ser Leu Thr Ser Pro Thr Gly Arg Gly Ser Met Ala Ala Pro Ser
            20                  25                  30

Leu His Pro Ser Leu Gly Pro Gly Ile Gly Ser Pro Gly Gln Leu His
        35                  40                  45

Ser Pro Ile Ser Thr Leu Ser Ser Pro Ile Asn Gly Met Gly Pro Pro
    50                  55                  60

Phe Ser Val Ile Ser Ser Pro Met Gly Pro His Ser Met Ser Val Pro
65                  70                  75                  80

Thr Thr Pro Thr Leu Gly Phe Ser Thr Gly Ser Pro Gln Leu Ser Ser
```

85 90 95

Pro Met Asn Pro Val Ser Ser Ser Glu Asp Ile Lys Pro Pro Leu Gly
100 105 110

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

Ser Phe Thr Lys His Ile Cys Ala Ile Cys Gly Asp Arg Ser Ser Gly
130 135 140

Lys His Tyr Gly Val Tyr Ser Cys Glu Gly Cys Lys Gly Phe Phe Lys
145 150 155 160

Arg Thr Val Arg Lys Asp Leu Thr Tyr Thr Cys Arg Asp Asn Lys Asp
165 170 175

Cys Leu Ile Asp Lys Arg Gln Arg Asn Arg Cys Gln Tyr Cys Arg Tyr
180 185 190

Gln Lys Cys Leu Ala Met Gly Met Lys Arg Glu Ala Val Gln Glu Glu
195 200 205

Arg Gln Arg Gly Lys Asp Arg Asn Glu Asn Glu Val Glu Ser Thr Ser
210 215 220

Ser Ala Asn Glu Asp Met Pro Val Glu Arg Ile Leu Glu Ala Glu Leu
225 230 235 240

Ala Val Glu Pro Lys Thr Glu Thr Tyr Val Glu Ala Asn Met Gly Leu
245 250 255

Asn Pro Ser Ser Pro Asn Asp Pro Val Thr Asn Ile Cys Gln Ala Ala
260 265 270

Asp Lys Gln Leu Phe Thr Leu Val Glu Trp Ala Lys Arg Ile Pro His
275 280 285

Phe Ser Glu Leu Pro Leu Asp Asp Gln Val Ile Leu Leu Arg Ala Gly
290 295 300

Trp Asn Glu Leu Leu Ile Ala Ser Phe Ser His Arg Ser Ile Ala Val
305 310 315 320

Lys Asp Gly Ile Leu Leu Ala Thr Gly Leu His Val His Arg Asn Ser
325 330 335

Ala His Ser Ala Gly Val Gly Ala Ile Phe Asp Arg Val Leu Thr Glu
340 345 350

Leu Val Ser Lys Met Arg Asp Met Gln Met Asp Lys Thr Glu Leu Gly

355 360 365

Cys Leu Arg Ala Ile Val Leu Phe Asn Pro Asp Ser Lys Gly Leu Ser
370 375 380

Asn Pro Ala Glu Val Glu Ala Leu Arg Glu Lys Val Tyr Ala Ser Leu
385 390 395 400

Glu Ala Tyr Cys Lys His Lys Tyr Pro Glu Gln Pro Gly Arg Phe Ala
405 410 415

Lys Leu Leu Leu Arg Leu Pro Ala Leu Arg Ser Ile Gly Leu Lys Cys
420 425 430

Leu Glu His Leu Phe Phe Phe Lys Leu Ile Gly Asp Thr Pro Ile Asp
435 440 445

Thr Phe Leu Met Glu Met Leu Glu Ala Pro His Gln Met Thr
450 455 460

<210> 208
<211> 238
<212> PRT
<213> Homo sapiens

<400> 208

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

Ala Val Glu Pro Lys Thr Glu Thr Tyr Val Glu Ala Asn Met Gly Leu
20 25 30

Asn Pro Ser Ser Pro Asn Asp Pro Val Thr Asn Ile Cys Gln Ala Ala
35 40 45

Asp Lys Gln Leu Phe Thr Leu Val Glu Trp Ala Lys Arg Ile Pro His
50 55 60

Phe Ser Glu Leu Pro Leu Asp Asp Gln Val Ile Leu Leu Arg Ala Gly
65 70 75 80

Trp Asn Glu Leu Leu Ile Ala Ser Phe Ser His Arg Ser Ile Ala Val
85 90 95

Lys Asp Gly Ile Leu Leu Ala Thr Gly Leu His Val His Arg Asn Ser
100 105 110

Ala His Ser Ala Gly Val Gly Ala Ile Phe Asp Arg Val Leu Thr Glu
115 120 125

Leu Val Ser Lys Met Arg Asp Met Gln Met Asp Lys Thr Glu Leu Gly
130 135 140

```
Cys Leu Arg Ala Ile Val Leu Phe Asn Pro Asp Ser Lys Gly Leu Ser
145                 150                 155                 160

Asn Pro Ala Glu Val Glu Ala Leu Arg Glu Lys Val Tyr Ala Ser Leu
                165                 170                 175

Glu Ala Tyr Cys Lys His Lys Tyr Pro Glu Gln Pro Gly Arg Phe Ala
            180                 185                 190

Lys Leu Leu Leu Arg Leu Pro Ala Leu Arg Ser Ile Gly Leu Lys Cys
        195                 200                 205

Leu Glu His Leu Phe Phe Phe Lys Leu Ile Gly Asp Thr Pro Ile Asp
    210                 215                 220

Thr Phe Leu Met Glu Met Leu Glu Ala Pro His Gln Met Thr
225                 230                 235
```

<210> 209
<211> 434
<212> PRT
<213> Homo sapiens

<400> 209

```
Met Glu Val Arg Pro Lys Glu Ser Trp Asn His Ala Asp Phe Val His
1               5                   10                  15

Cys Glu Asp Thr Glu Ser Val Pro Gly Lys Pro Ser Val Asn Ala Asp
            20                  25                  30

Glu Glu Val Gly Gly Pro Gln Ile Cys Arg Val Cys Gly Asp Lys Ala
        35                  40                  45

Thr Gly Tyr His Phe Asn Val Met Thr Cys Glu Gly Cys Lys Gly Phe
    50                  55                  60

Phe Arg Arg Ala Met Lys Arg Asn Ala Arg Leu Arg Cys Pro Phe Arg
65                  70                  75                  80

Lys Gly Ala Cys Glu Ile Thr Arg Lys Thr Arg Arg Gln Cys Gln Ala
                85                  90                  95

Cys Arg Leu Arg Lys Cys Leu Glu Ser Gly Met Lys Lys Glu Met Ile
            100                 105                 110

Met Ser Asp Glu Ala Val Glu Glu Arg Arg Ala Leu Ile Lys Arg Lys
        115                 120                 125

Lys Ser Glu Arg Thr Gly Thr Gln Pro Leu Gly Val Gln Gly Leu Thr
    130                 135                 140
```

```
Glu Glu Gln Arg Met Met Ile Arg Glu Leu Met Asp Ala Gln Met Lys
145                 150                 155                 160

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

Val Leu Ser Ser Gly Cys Glu Leu Pro Glu Ser Leu Gln Ala Pro Ser
            180                 185                 190

Arg Glu Glu Ala Ala Lys Trp Ser Gln Val Arg Lys Asp Leu Cys Ser
        195                 200                 205

Leu Lys Val Ser Leu Gln Leu Arg Gly Glu Asp Gly Ser Val Trp Asn
    210                 215                 220

Tyr Lys Pro Pro Ala Asp Ser Gly Gly Lys Glu Ile Phe Ser Leu Leu
225                 230                 235                 240

Pro His Met Ala Asp Met Ser Thr Tyr Met Phe Lys Gly Ile Ile Ser
                245                 250                 255

Phe Ala Lys Val Ile Ser Tyr Phe Arg Asp Leu Pro Ile Glu Asp Gln
            260                 265                 270

Ile Ser Leu Leu Lys Gly Ala Ala Phe Glu Leu Cys Gln Leu Arg Phe
        275                 280                 285

Asn Thr Val Phe Asn Ala Glu Thr Gly Thr Trp Glu Cys Gly Arg Leu
    290                 295                 300

Ser Tyr Cys Leu Glu Asp Thr Ala Gly Gly Phe Gln Gln Leu Leu Leu
305                 310                 315                 320

Glu Pro Met Leu Lys Phe His Tyr Met Leu Lys Lys Leu Gln Leu His
                325                 330                 335

Glu Glu Glu Tyr Val Leu Met Gln Ala Ile Ser Leu Phe Ser Pro Asp
            340                 345                 350

Arg Pro Gly Val Leu Gln His Arg Val Val Asp Gln Leu Gln Glu Gln
        355                 360                 365

Phe Ala Ile Thr Leu Lys Ser Tyr Ile Glu Cys Asn Arg Pro Gln Pro
    370                 375                 380

Ala His Arg Phe Leu Phe Leu Lys Ile Met Ala Met Leu Thr Glu Leu
385                 390                 395                 400

Arg Ser Ile Asn Ala Gln His Thr Gln Arg Leu Leu Arg Ile Gln Asp
                405                 410                 415
```

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Ile His Pro Phe Ala Thr Pro Leu Met Gln Glu Leu Phe Gly Ile Thr
            420                 425                 430


Gly Ser



<210>  210
<211>  305
<212>  PRT
<213>  Homo sapiens

<400>  210

Ser Glu Arg Thr Gly Thr Gln Pro Leu Gly Val Gln Gly Leu Thr Glu
1               5                   10                  15


Glu Gln Arg Met Met Ile Arg Glu Leu Met Asp Ala Gln Met Lys Thr
            20                  25                  30


Phe Asp Thr Thr Phe Ser His Phe Lys Asn Phe Arg Leu Pro Gly Val
        35                  40                  45


Leu Ser Ser Gly Cys Glu Leu Pro Glu Ser Leu Gln Ala Pro Ser Arg
    50                  55                  60


Glu Glu Ala Ala Lys Trp Ser Gln Val Arg Lys Asp Leu Cys Ser Leu
65                  70                  75                  80


Lys Val Ser Leu Gln Leu Arg Gly Glu Asp Gly Ser Val Trp Asn Tyr
                85                  90                  95


Lys Pro Pro Ala Asp Ser Gly Gly Lys Glu Ile Phe Ser Leu Leu Pro
            100                 105                 110


His Met Ala Asp Met Ser Thr Tyr Met Phe Lys Gly Ile Ile Ser Phe
        115                 120                 125


Ala Lys Val Ile Ser Tyr Phe Arg Asp Leu Pro Ile Glu Asp Gln Ile
    130                 135                 140


Ser Leu Leu Lys Gly Ala Ala Phe Glu Leu Cys Gln Leu Arg Phe Asn
145                 150                 155                 160


Thr Val Phe Asn Ala Glu Thr Gly Thr Trp Glu Cys Gly Arg Leu Ser
                165                 170                 175


Tyr Cys Leu Glu Asp Thr Ala Gly Gly Phe Gln Gln Leu Leu Leu Glu
            180                 185                 190


Pro Met Leu Lys Phe His Tyr Met Leu Lys Lys Leu Gln Leu His Glu
        195                 200                 205
```

Glu Glu Tyr Val Leu Met Gln Ala Ile Ser Leu Phe Ser Pro Asp Arg
210 215 220

Pro Gly Val Leu Gln His Arg Val Val Asp Gln Leu Gln Glu Gln Phe
225 230 235 240

Ala Ile Thr Leu Lys Ser Tyr Ile Glu Cys Asn Arg Pro Gln Pro Ala
245 250 255

His Arg Phe Leu Phe Leu Lys Ile Met Ala Met Leu Thr Glu Leu Arg
260 265 270

Ser Ile Asn Ala Gln His Thr Gln Arg Leu Leu Arg Ile Gln Asp Ile
275 280 285

His Pro Phe Ala Thr Pro Leu Met Gln Glu Leu Phe Gly Ile Thr Gly
290 295 300

Ser
305

<210> 211
<211> 19
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 211

Arg Cys Arg Glu Arg Arg Arg Asn Glu Arg Leu Arg Arg Glu Ser Val
1 5 10 15

Arg Pro Val

<210> 212
<211> 29
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 212

Arg Lys Gly Arg Met Met Asp Val Lys Lys Cys Gly Ile Gln Asp Thr
1 5 10 15

Asn Ser Lys Lys Gln Ser Asp Thr His Leu Glu Glu Thr
20 25

<210> 213
<211> 32
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 213

Lys Lys Arg His Met Ala Ser Tyr Ser Met Cys Ser Asp Pro Ser Thr
1 5 10 15

Arg Asp Pro Pro Gly Arg Pro Glu Pro Tyr Val Glu Val Tyr Leu Ile
20 25 30

<210> 214
<211> 35
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 214

Thr Lys Lys Lys Tyr Ser Ser Ser Val His Asp Pro Asn Gly Glu Tyr
1 5 10 15

Met Phe Met Arg Ala Val Asn Thr Ala Lys Lys Ser Arg Leu Thr Asp
20 25 30

Val Thr Leu
35

<210> 215
<211> 35
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 215

Met Glu Glu Ser Val Val Arg Pro Ser Val Phe Val Val Asp Gly Gln
1 5 10 15

Thr Asp Ile Pro Phe Thr Arg Leu Gly Arg Ser His Arg Arg Gln Ser
20 25 30

Cys Ser Val
35

<210> 216
<211> 39
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 216

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

Tyr Val Lys Met Pro Pro Thr Glu Pro Glu Cys Glu Lys Gln Phe Gln
20 25 30

Pro Tyr Phe Ile Pro Ile Asn
35

<210> 217
<211> 40
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 217

Ala Arg Thr Gln Ile Lys Lys Leu Cys Ser Trp Arg Asp Lys Asn Ser
1 5 10 15

Ala Ala Cys Val Val Tyr Glu Asp Met Ser His Ser Arg Cys Asn Thr
20 25 30

Leu Ser Ser Pro Asn Gln Tyr Gln
35 40

<210> 218
<211> 42
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 218

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
1 5 10 15

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
20 25 30

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu
35 40

<210> 219
<211> 43
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 219

Trp Val Arg Ser Lys Arg Ser Arg Leu Leu His Ser Asp Tyr Met Asn
1 5 10 15

Met Thr Pro Arg Arg Pro Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr
20 25 30

Ala Pro Pro Arg Asp Phe Ala Ala Tyr Arg Ser
35 40

<210> 220
<211> 49
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 220

His Gln Arg Arg Lys Tyr Arg Ser Asn Lys Gly Glu Ser Pro Val Glu
1 5 10 15

Pro Ala Glu Pro Cys His Tyr Ser Cys Pro Arg Glu Glu Glu Gly Ser
20 25 30

Thr Ile Pro Ile Gln Glu Asp Tyr Arg Lys Pro Glu Pro Ala Cys Ser
35 40 45

Pro

<210> 221
<211> 51
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 221

Arg Arg Gln Trp Arg Pro Arg Arg Phe Ser Ala Leu Glu Gln Gly Ile
1 5 10 15

His Pro Pro Gln Ala Gln Ser Lys Ile Glu Glu Leu Glu Gln Glu Pro
20 25 30

Glu Pro Glu Pro Glu Pro Glu Pro Glu Pro Glu Pro Glu Pro Glu Pro
35 40 45

Glu Gln Leu
50

<210> 222
<211> 54
<212> PRT
<213> Artificial sequence

<220>

<223> synthetic amino acid sequence

<400> 222

His Ile Trp Gln Leu Arg Ser Gln Cys Met Trp Pro Arg Glu Thr Gln
1 5 10 15

Leu Leu Leu Glu Val Pro Pro Ser Thr Glu Asp Ala Arg Ser Cys Gln
20 25 30

Phe Pro Glu Glu Glu Arg Gly Glu Arg Ser Ala Glu Glu Lys Gly Arg
35 40 45

Leu Gly Asp Leu Trp Val
50

<210> 223
<211> 61
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 223

Asn Arg Arg Arg Arg Arg Glu Arg Arg Asp Leu Phe Thr Glu Ser Trp
1 5 10 15

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

Gln Pro Thr Asn Gln Ser Met Asp Asp Thr Arg Glu Asp Ile Tyr Val
35 40 45

Asn Tyr Pro Thr Phe Ser Arg Arg Pro Lys Thr Arg Val
50 55 60

<210> 224
<211> 62
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 224

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

Glu Pro Gln Glu Ile Asn Phe Pro Asp Asp Leu Pro Gly Ser Asn Thr
20 25 30

Ala Ala Pro Val Gln Glu Thr Leu His Gly Cys Gln Pro Val Thr Gln
35 40 45

Glu Asp Gly Lys Glu Ser Arg Ile Ser Val Gln Glu Arg Gln
50 55 60

<210> 225
<211> 77
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 225

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

Ser Leu Ala Asn Leu Pro Pro Ser Gly Leu Ala Asn Ala Val Ala Glu
20 25 30

Gly Ile Arg Ser Glu Glu Asn Ile Tyr Thr Ile Glu Glu Asn Val Tyr
35 40 45

Glu Val Glu Glu Pro Asn Glu Tyr Tyr Cys Tyr Val Ser Ser Arg Gln
50 55 60

Gln Pro Ser Gln Pro Leu Gly Cys Arg Phe Ala Met Pro
65 70 75

<210> 226
<211> 80
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 226

Arg Lys Lys Lys Ala Leu Arg Ile His Ser Val Glu Gly Asp Leu Arg
1 5 10 15

Arg Lys Ser Ala Gly Gln Glu Glu Trp Ser Pro Ser Ala Pro Ser Pro
20 25 30

Pro Gly Ser Cys Val Gln Ala Glu Ala Ala Pro Ala Gly Leu Cys Gly
35 40 45

Glu Gln Arg Gly Glu Asp Cys Ala Glu Leu His Asp Tyr Phe Asn Val
50 55 60

Leu Ser Tyr Arg Ser Leu Gly Asn Cys Ser Phe Phe Thr Glu Thr Gly
65 70 75 80

<210> 227
<211> 83
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 227

Lys Leu Arg Lys Ala His Val Ile Trp Lys Lys Glu Asn Glu Val Ser
1 5 10 15

Glu His Thr Leu Glu Ser Tyr Arg Ser Arg Ser Asn Asn Glu Glu Thr
20 25 30

Ser Ser Glu Glu Lys Asn Gly Gln Ser Ser His Pro Met Arg Cys Met
35 40 45

Asn Tyr Ile Thr Lys Leu Tyr Ser Glu Ala Lys Thr Lys Arg Lys Glu
50 55 60

Asn Val Gln His Ser Lys Leu Glu Glu Lys His Ile Gln Val Pro Glu
65 70 75 80

Ser Ile Val

<210> 228
<211> 98
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 228

Ile Cys Ser Arg Ala Ala Arg Gly Thr Ile Gly Ala Arg Arg Thr Gly
1 5 10 15

Gln Pro Leu Lys Glu Asp Pro Ser Ala Val Pro Val Phe Ser Val Asp
20 25 30

Tyr Gly Glu Leu Asp Phe Gln Trp Arg Glu Lys Thr Pro Glu Pro Pro
35 40 45

Val Pro Cys Val Pro Glu Gln Thr Glu Tyr Ala Thr Ile Val Phe Pro
50 55 60

Ser Gly Met Gly Thr Ser Ser Pro Ala Arg Arg Gly Ser Ala Asp Gly
65 70 75 80

Pro Arg Ser Ala Gln Pro Leu Arg Pro Glu Asp Gly His Cys Ser Trp
85 90 95

Pro Leu

<210> 229
<211> 101
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 229

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His Arg Gln Asn Gln Ile Lys Gln Gly Pro Pro Arg Ser Lys Asp Glu
1               5                   10                  15


Glu Gln Lys Pro Gln Gln Arg Pro Asp Leu Ala Val Asp Val Leu Glu
            20                  25                  30


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


Glu Thr Asp Thr Ser Ala Leu Ala Ala Gly Ser Ser Gln Glu Val Thr
    50                  55                  60


Tyr Ala Gln Leu Asp His Trp Ala Leu Thr Gln Arg Thr Ala Arg Ala
65                  70                  75                  80


Val Ser Pro Gln Ser Thr Lys Pro Met Ala Glu Ser Ile Thr Tyr Ala
                85                  90                  95


Ala Val Ala Arg His
            100
```

<210> 230
<211> 107
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 230

```
Cys Cys Arg Lys Lys Arg Arg Glu Glu Lys Tyr Glu Lys Glu Val His
1               5                   10                  15


His Asp Ile Arg Glu Asp Val Pro Pro Pro Lys Ser Arg Thr Ser Thr
            20                  25                  30


Ala Arg Ser Tyr Ile Gly Ser Asn His Ser Ser Leu Gly Ser Met Ser
        35                  40                  45


Pro Ser Asn Met Glu Gly Tyr Ser Lys Thr Gln Tyr Asn Gln Val Pro
    50                  55                  60


Ser Glu Asp Phe Glu Arg Thr Pro Gln Ser Pro Thr Leu Pro Pro Ala
65                  70                  75                  80
```

Lys Val Ala Ala Pro Asn Leu Ser Arg Met Gly Ala Ile Pro Val Met
85 90 95

Ile Pro Ala Gln Ser Lys Asp Gly Ser Ile Val
100 105

<210> 231
<211> 114
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 231

Cys Cys Leu Arg Arg His Gln Gly Lys Gln Asn Glu Leu Ser Asp Thr
1 5 10 15

Ala Gly Arg Glu Ile Asn Leu Val Asp Ala His Leu Lys Ser Glu Gln
20 25 30

Thr Glu Ala Ser Thr Arg Gln Asn Ser Gln Val Leu Leu Ser Glu Thr
35 40 45

Gly Ile Tyr Asp Asn Asp Pro Asp Leu Cys Phe Arg Met Gln Glu Gly
50 55 60

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

Val Tyr Ala Ser Leu Asn His Ser Val Ile Gly Pro Asn Ser Arg Leu
85 90 95

Ala Arg Asn Val Lys Glu Ala Pro Thr Glu Tyr Ala Ser Ile Cys Val
100 105 110

Arg Ser

<210> 232
<211> 117
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 232

Thr Lys Arg Lys Lys Gln Arg Ser Arg Arg Asn Asp Glu Glu Leu Glu
1 5 10 15

Thr Arg Ala His Arg Val Ala Thr Glu Glu Arg Gly Arg Lys Pro His
20 25 30

Gln Ile Pro Ala Ser Thr Pro Gln Asn Pro Ala Thr Ser Gln His Pro
35 40 45

Pro Pro Pro Pro Gly His Arg Ser Gln Ala Pro Ser His Arg Pro Pro
50 55 60

Pro Pro Gly His Arg Val Gln His Gln Pro Gln Lys Arg Pro Pro Ala
65 70 75 80

Pro Ser Gly Thr Gln Val His Gln Gln Lys Gly Pro Pro Leu Pro Arg
85 90 95

Pro Arg Val Gln Pro Lys Pro Pro His Gly Ala Ala Glu Asn Ser Leu
100 105 110

Ser Pro Ser Ser Asn
115

<210> 233
<211> 120
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 233

Trp Arg Arg Lys Arg Lys Glu Lys Gln Ser Glu Thr Ser Pro Lys Glu
1 5 10 15

Phe Leu Thr Ile Tyr Glu Asp Val Lys Asp Leu Lys Thr Arg Arg Asn
20 25 30

His Glu Gln Glu Gln Thr Phe Pro Gly Gly Gly Ser Thr Ile Tyr Ser
35 40 45

Met Ile Gln Ser Gln Ser Ser Ala Pro Thr Ser Gln Glu Pro Ala Tyr
50 55 60

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

Arg Asn His Ser Pro Ser Phe Asn Ser Thr Ile Tyr Glu Val Ile Gly
85 90 95

Lys Ser Gln Pro Lys Ala Gln Asn Pro Ala Arg Leu Ser Arg Lys Glu
100 105 110

Leu Glu Asn Phe Asp Val Tyr Ser
115 120

<210> 234
<211> 187

<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 234

Arg Arg Ala Cys Arg Lys Arg Ile Arg Gln Lys Leu His Leu Cys Tyr
1 5 10 15

Pro Val Gln Thr Ser Gln Pro Lys Leu Glu Leu Val Asp Ser Arg Pro
20 25 30

Arg Arg Ser Ser Thr Gln Leu Arg Ser Gly Ala Ser Val Thr Glu Pro
35 40 45

Val Ala Glu Glu Arg Gly Leu Met Ser Gln Pro Leu Met Glu Thr Cys
50 55 60

His Ser Val Gly Ala Ala Tyr Leu Glu Ser Leu Pro Leu Gln Asp Ala
65 70 75 80

Ser Pro Ala Gly Gly Pro Ser Ser Pro Arg Asp Leu Pro Glu Pro Arg
85 90 95

Val Ser Thr Glu His Thr Asn Asn Lys Ile Glu Lys Ile Tyr Ile Met
100 105 110

Lys Ala Asp Thr Val Ile Val Gly Thr Val Lys Ala Glu Leu Pro Glu
115 120 125

Gly Arg Gly Leu Ala Gly Pro Ala Glu Pro Glu Leu Glu Glu Glu Leu
130 135 140

Glu Ala Asp His Thr Pro His Tyr Pro Glu Gln Glu Thr Glu Pro Pro
145 150 155 160

Leu Gly Ser Cys Ser Asp Val Met Leu Ser Val Glu Glu Glu Gly Lys
165 170 175

Glu Asp Pro Leu Pro Thr Ala Ala Ser Gly Lys
180 185

<210> 235
<211> 108
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 235

Thr Tyr Arg His Cys Trp Pro His Lys Pro Leu Val Thr Ala Asp Glu
1 5 10 15

Ala Gly Met Glu Ala Leu Thr Pro Pro Pro Ala Thr His Leu Ser Pro
            20   25   30

Leu Asp Ser Ala His Thr Leu Leu Ala Pro Pro Asp Ser Ser Glu Lys
        35   40   45

Ile Cys Thr Val Gln Leu Val Gly Asn Ser Trp Thr Pro Gly Tyr Pro
    50   55   60

Glu Thr Gln Glu Ala Leu Cys Pro Gln Val Thr Trp Ser Trp Asp Gln
65   70   75   80

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

Glu Ser Pro Ala Gly Ser Pro Ala Met Met Leu Gln
            100   105

<210> 236
<211> 42
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 236

Ala Leu Tyr Leu Leu Arg Arg Asp Gln Arg Leu Pro Pro Asp Ala His
1   5   10   15

Lys Pro Pro Gly Gly Gly Ser Phe Arg Thr Pro Ile Gln Glu Glu Gln
            20   25   30

Ala Asp Ala His Ser Thr Leu Ala Lys Ile
        35   40

<210> 237
<211> 51
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 237

Met Gly Trp Ile Arg Gly Arg Arg Ser Arg His Ser Trp Glu Met Ser
1   5   10   15

Glu Phe His Asn Tyr Asn Leu Asp Leu Lys Lys Ser Asp Phe Ser Thr
            20   25   30

Arg Trp Gln Lys Gln Arg Cys Pro Val Val Lys Ser Lys Cys Arg Glu
        35   40   45

Asn Ala Ser
    50

<210> 238
<211> 48
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 238

Lys Lys Tyr Phe Phe Lys Lys Glu Val Gln Gln Leu Ser Val Ser Phe
1   5   10   15

Ser Ser Leu Gln Ile Lys Ala Leu Gln Asn Ala Val Glu Lys Glu Val
            20   25   30

Gln Ala Glu Asp Asn Ile Tyr Ile Glu Asn Ser Leu Tyr Ala Thr Asp
        35   40   45

<210> 239
<211> 22
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 239

Ser Gly Phe Leu Gln Glu Lys Val Trp Val Met Leu Val Thr Ser Leu
1   5   10   15

Val Ala Leu Gln Ala Leu
            20

<210> 240
<211> 85
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 240

Ser Trp Arg Arg Arg Gln Arg Arg Leu Arg Gly Ala Ser Ser Ala Glu
1   5   10   15

Ala Pro Asp Gly Asp Lys Asp Ala Pro Glu Pro Leu Asp Lys Val Ile
            20   25   30

Ile Leu Ser Pro Gly Ile Ser Asp Ala Thr Ala Pro Ala Trp Pro Pro
        35   40   45

Pro Gly Glu Asp Pro Gly Thr Thr Pro Pro Gly His Ser Val Pro Val
50 55 60

Pro Ala Thr Glu Leu Gly Ser Thr Glu Leu Val Thr Thr Lys Thr Ala
65 70 75 80

Gly Pro Glu Gln Gln
85

<210> 241
<211> 111
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 241

Ala Cys Phe Leu Lys Lys Arg Gly Asp Pro Cys Ser Cys Gln Pro Arg
1 5 10 15

Ser Arg Pro Arg Gln Ser Pro Ala Lys Ser Ser Gln Asp His Ala Met
20 25 30

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

Ser Phe Cys Phe Pro Glu Cys Arg Ala Pro Thr Gln Glu Ser Ala Val
50 55 60

Thr Pro Gly Thr Pro Asp Pro Thr Cys Ala Gly Arg Trp Gly Cys His
65 70 75 80

Thr Arg Thr Thr Val Leu Gln Pro Cys Pro His Ile Pro Asp Ser Gly
85 90 95

Leu Gly Ile Val Cys Val Pro Ala Gln Glu Gly Gly Pro Gly Ala
100 105 110

<210> 242
<211> 95
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 242

Met Ala Glu Ala Ile Thr Tyr Ala Asp Leu Arg Phe Val Lys Ala Pro
1 5 10 15

Leu Lys Lys Ser Ile Ser Ser Arg Leu Gly Gln Asp Pro Gly Ala Asp
20 25 30

Asp Asp Gly Glu Ile Thr Tyr Glu Asn Val Gln Val Pro Ala Val Leu
35 40 45

Gly Val Pro Ser Ser Leu Ala Ser Ser Val Leu Gly Asp Lys Ala Ala
50 55 60

Val Lys Ser Glu Gln Pro Thr Ala Ser Trp Arg Ala Val Thr Ser Pro
65 70 75 80

Ala Val Gly Arg Ile Leu Pro Cys Arg Thr Thr Cys Leu Arg Tyr
85 90 95

<210> 243
<211> 141
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 243

Lys Leu Gln Arg Arg Trp Lys Arg Thr Gln Ser Gln Gln Gly Leu Gln
1 5 10 15

Glu Asn Ser Ser Gly Gln Ser Phe Phe Val Arg Asn Lys Lys Val Arg
20 25 30

Arg Ala Pro Leu Ser Glu Gly Pro His Ser Leu Gly Cys Tyr Asn Pro
35 40 45

Met Met Glu Asp Gly Ile Ser Tyr Thr Thr Leu Arg Phe Pro Glu Met
50 55 60

Asn Ile Pro Arg Thr Gly Asp Ala Glu Ser Ser Glu Met Gln Arg Pro
65 70 75 80

Pro Pro Asp Cys Asp Asp Thr Val Thr Tyr Ser Ala Leu His Lys Arg
85 90 95

Gln Val Gly Asp Tyr Glu Asn Val Ile Pro Asp Phe Pro Glu Asp Glu
100 105 110

Gly Ile His Tyr Ser Glu Leu Ile Gln Phe Gly Val Gly Glu Arg Pro
115 120 125

Gln Ala Gln Glu Asn Val Asp Tyr Val Ile Leu Lys His
130 135 140

<210> 244
<211> 45
<212> PRT
<213> Artificial sequence

<220>

<223> synthetic amino acid sequence

<400> 244

Arg Lys Trp Cys Gln Tyr Gln Lys Glu Ile Met Glu Arg Pro Pro Pro
1 5 10 15

Phe Lys Pro Pro Pro Pro Pro Ile Lys Tyr Thr Cys Ile Gln Glu Pro
20 25 30

Asn Glu Ser Asp Leu Pro Tyr His Glu Met Glu Thr Leu
35 40 45

<210> 245
<211> 84
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 245

Leu Arg Lys Arg Arg Asp Ser Leu Ser Leu Ser Thr Gln Arg Thr Gln
1 5 10 15

Gly Pro Ala Glu Ser Ala Arg Asn Leu Glu Tyr Val Ser Val Ser Pro
20 25 30

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

Glu Ile Trp Thr Pro Arg Glu Asn Asp Thr Ile Thr Ile Tyr Ser Thr
50 55 60

Ile Asn His Ser Lys Glu Ser Lys Pro Thr Phe Ser Arg Ala Thr Ala
65 70 75 80

Leu Asp Asn Val

<210> 246
<211> 88
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 246

Trp Phe Leu Lys Arg Glu Arg Gln Glu Glu Tyr Ile Glu Glu Lys Lys
1 5 10 15

Arg Val Asp Ile Cys Arg Glu Thr Pro Asn Ile Cys Pro His Ser Gly
20 25 30

```
Glu Asn Thr Glu Tyr Asp Thr Ile Pro His Thr Asn Arg Thr Ile Leu
        35                  40                  45

Lys Glu Asp Pro Ala Asn Thr Val Tyr Ser Thr Val Glu Ile Pro Lys
    50                  55                  60

Lys Met Glu Asn Pro His Ser Leu Leu Thr Met Pro Asp Thr Pro Arg
65                  70                  75                  80

Leu Phe Ala Tyr Glu Asn Val Ile
                85
```

<210> 247
<211> 82
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 247

```
Lys Thr His Arg Arg Lys Ala Ala Arg Thr Ala Val Gly Arg Asn Asp
1               5                   10                  15

Thr His Pro Thr Thr Gly Ser Ala Ser Pro Lys His Gln Lys Lys Ser
            20                  25                  30

Lys Leu His Gly Pro Thr Glu Thr Ser Ser Cys Ser Gly Ala Ala Pro
        35                  40                  45

Thr Val Glu Met Asp Glu Glu Leu His Tyr Ala Ser Leu Asn Phe His
    50                  55                  60

Gly Met Asn Pro Ser Lys Asp Thr Ser Thr Glu Tyr Ser Glu Val Arg
65                  70                  75                  80

Thr Gln
```

<210> 248
<211> 38
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 248

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Met Thr Asp Ser Val Ile Tyr Ser Met Leu Glu Leu Pro Thr Ala Thr
1               5                   10                  15

Gln Ala Gln Asn Asp Tyr Gly Pro Gln Gln Lys Ser Ser Ser Ser Arg
            20                  25                  30
```

Pro Ser Cys Ser Cys Leu
        35

<210> 249
<211> 45
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 249

Met Asp Gln Gln Ala Ile Tyr Ala Glu Leu Asn Leu Pro Thr Asp Ser
1   5   10   15

Gly Pro Glu Ser Ser Ser Pro Ser Ser Leu Pro Arg Asp Val Cys Gln
            20   25   30

Gly Ser Pro Trp His Gln Phe Ala Leu Lys Leu Ser Cys
        35   40   45

<210> 250
<211> 168
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 250

Leu Arg His Arg Arg Gln Gly Lys His Trp Thr Ser Thr Gln Arg Lys
1   5   10   15

Ala Asp Phe Gln His Pro Ala Gly Ala Val Gly Pro Glu Pro Thr Asp
            20   25   30

Arg Gly Leu Gln Trp Arg Ser Ser Pro Ala Ala Asp Ala Gln Glu Glu
        35   40   45

Asn Leu Tyr Ala Ala Val Lys His Thr Gln Pro Glu Asp Gly Val Glu
    50   55   60

Met Asp Thr Arg Ser Pro His Asp Glu Asp Pro Gln Ala Val Thr Tyr
65   70   75   80

Ala Glu Val Lys His Ser Arg Pro Arg Arg Glu Met Ala Ser Pro Pro
                85   90   95

Ser Pro Leu Ser Gly Glu Phe Leu Asp Thr Lys Asp Arg Gln Ala Glu
            100   105   110

Glu Asp Arg Gln Met Asp Thr Glu Ala Ala Ala Ser Glu Ala Pro Gln
        115   120   125

Asp Val Thr Tyr Ala Gln Leu His Ser Leu Thr Leu Arg Arg Glu Ala
130 135 140

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

Ile Tyr Ala Thr Leu Ala Ile His
165

<210> 251
<211> 83
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 251

Arg Trp Cys Ser Asn Lys Lys Asn Ala Ala Val Met Asp Gln Glu Ser
1 5 10 15

Ala Gly Asn Arg Thr Ala Asn Ser Glu Asp Ser Asp Glu Gln Asp Pro
20 25 30

Gln Glu Val Thr Tyr Thr Gln Leu Asn His Cys Val Phe Thr Gln Arg
35 40 45

Lys Ile Thr Arg Pro Ser Gln Arg Pro Lys Thr Pro Pro Thr Asp Ile
50 55 60

Ile Val Tyr Thr Glu Leu Pro Asn Ala Glu Ser Arg Ser Lys Val Val
65 70 75 80

Ser Cys Pro

<210> 252
<211> 84
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 252

His Leu Trp Cys Ser Asn Lys Lys Asn Ala Ala Val Met Asp Gln Glu
1 5 10 15

Pro Ala Gly Asn Arg Thr Ala Asn Ser Glu Asp Ser Asp Glu Gln Asp
20 25 30

Pro Glu Glu Val Thr Tyr Ala Gln Leu Asp His Cys Val Phe Thr Gln
35 40 45

Arg Lys Ile Thr Arg Pro Ser Gln Arg Pro Lys Thr Pro Pro Thr Asp
50 55 60

Thr Ile Leu Tyr Thr Glu Leu Pro Asn Ala Lys Pro Arg Ser Lys Val
65 70 75 80

Val Ser Cys Pro

<210> 253
<211> 10
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 253

Met Ala Val Phe Lys Thr Thr Leu Trp Arg
1 5 10

<210> 254
<211> 29
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 254

Lys Gly Ser Gln Arg Val Pro Glu Glu Pro Gly Glu Gln Pro Ile Tyr
1 5 10 15

Met Asn Phe Ser Glu Pro Leu Thr Lys Asp Met Ala Thr
20 25

<210> 255
<211> 11
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 255

Val Asn Arg Pro Gln Trp Ala Pro Pro Gly Arg
1 5 10

<210> 256
<211> 8
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 256

Val Thr Leu Arg Ser Phe Val Pro
1 5

<210> 257
<211> 35
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 257

Ala Ala Trp His Gly Gln Lys Pro Gly Thr His Pro Pro Ser Glu Leu
1 5 10 15

Asp Cys Gly His Asp Pro Gly Tyr Gln Leu Gln Thr Leu Pro Gly Leu
20 25 30

Arg Asp Thr
35

<210> 258
<211> 32
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 258

Gln His Ser Gln Arg Ser Pro Pro Arg Cys Ser Gln Glu Ala Asn Ser
1 5 10 15

Arg Lys Asp Asn Ala Pro Phe Arg Val Val Glu Pro Trp Glu Gln Ile
20 25 30

<210> 259
<211> 168
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 259

Gln His Trp Arg Gln Gly Lys His Arg Thr Leu Ala Gln Arg Gln Ala
1 5 10 15

Asp Phe Gln Arg Pro Pro Gly Ala Ala Glu Pro Glu Pro Lys Asp Gly
20 25 30

Gly Leu Gln Arg Arg Ser Ser Pro Ala Ala Asp Val Gln Gly Glu Asn
35 40 45

Phe Cys Ala Ala Val Lys Asn Thr Gln Pro Glu Asp Gly Val Glu Met
50 55 60

```
Asp Thr Arg Gln Ser Pro His Asp Glu Asp Pro Gln Ala Val Thr Tyr
65                  70                  75                  80

Ala Lys Val Lys His Ser Arg Pro Arg Arg Glu Met Ala Ser Pro Pro
                85                  90                  95

Ser Pro Leu Ser Gly Glu Phe Leu Asp Thr Lys Asp Arg Gln Ala Glu
            100                 105                 110

Glu Asp Arg Gln Met Asp Thr Glu Ala Ala Ala Ser Glu Ala Pro Gln
        115                 120                 125

Asp Val Thr Tyr Ala Gln Leu His Ser Phe Thr Leu Arg Gln Lys Ala
    130                 135                 140

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

Val Tyr Ala Thr Leu Ala Ile His
                165
```

<210> 260
<211> 116
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 260

```
Leu Arg His Arg Arg Gln Gly Lys His Trp Thr Ser Thr Gln Arg Lys
1               5                   10                  15

Ala Asp Phe Gln His Pro Ala Gly Ala Val Gly Pro Glu Pro Thr Asp
            20                  25                  30

Arg Gly Leu Gln Trp Arg Ser Ser Pro Ala Ala Asp Ala Gln Glu Glu
        35                  40                  45

Asn Leu Tyr Ala Ala Val Lys Asp Thr Gln Pro Glu Asp Gly Val Glu
    50                  55                  60

Met Asp Thr Arg Ala Ala Ala Ser Glu Ala Pro Gln Asp Val Thr Tyr
65                  70                  75                  80

Ala Gln Leu His Ser Leu Thr Leu Arg Arg Lys Ala Thr Glu Pro Pro
                85                  90                  95

Pro Ser Gln Glu Arg Glu Pro Pro Ala Glu Pro Ser Ile Tyr Ala Thr
            100                 105                 110
```

Leu Ala Ile His
        115

<210> 261
<211> 128
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 261

Met Ala Lys Arg Lys Gln Gly Asn Arg Leu Gly Val Cys Gly Arg Phe
1   5   10   15

Leu Ser Ser Arg Val Ser Gly Met Asn Pro Ser Ser Val Val His His
            20   25   30

Val Ser Asp Ser Gly Pro Ala Ala Glu Leu Pro Leu Asp Val Pro His
        35   40   45

Ile Arg Leu Asp Ser Pro Pro Ser Phe Asp Asn Thr Thr Tyr Thr Ser
    50   55   60

Leu Pro Leu Asp Ser Pro Ser Gly Lys Pro Ser Leu Pro Ala Pro Ser
65   70   75   80

Ser Leu Pro Pro Leu Pro Pro Lys Val Leu Val Cys Ser Lys Pro Val
                85   90   95

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

Ser Cys Gly Pro Ala Gln Asn Pro Pro Asn Asn Gln Thr Pro Ser Ser
        115   120   125

<210> 262
<211> 61
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 262

Lys Val Asn Gly Cys Arg Lys Tyr Lys Leu Asn Lys Thr Glu Ser Thr
1   5   10   15

Pro Val Val Glu Glu Asp Glu Met Gln Pro Tyr Ala Ser Tyr Thr Glu
            20   25   30

Lys Asn Asn Pro Leu Tyr Asp Thr Thr Asn Lys Val Lys Ala Ser Glu
        35   40   45

Ala Leu Gln Ser Glu Val Asp Thr Asp Leu His Thr Leu
50 55 60

<210> 263
<211> 98
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 263

Arg Met Phe Gln Lys Trp Ile Lys Ala Gly Asp His Ser Glu Leu Ser
1 5 10 15

Gln Asn Pro Lys Gln Ala Ala Thr Gln Ser Glu Leu His Tyr Ala Asn
20 25 30

Leu Glu Leu Leu Met Trp Pro Leu Gln Glu Lys Pro Ala Pro Pro Arg
35 40 45

Glu Val Glu Val Glu Tyr Ser Thr Val Ala Ser Pro Arg Glu Glu Leu
50 55 60

His Tyr Ala Ser Val Val Phe Asp Ser Asn Thr Asn Arg Ile Ala Ala
65 70 75 80

Gln Arg Pro Arg Glu Glu Glu Pro Asp Ser Asp Tyr Ser Val Ile Arg
85 90 95

Lys Thr

<210> 264
<211> 113
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 264

Trp Arg Met Met Lys Tyr Gln Gln Lys Ala Ala Gly Met Ser Pro Glu
1 5 10 15

Gln Val Leu Gln Pro Leu Glu Gly Asp Leu Cys Tyr Ala Asp Leu Thr
20 25 30

Leu Gln Leu Ala Gly Thr Ser Pro Gln Lys Ala Thr Thr Lys Leu Ser
35 40 45

Ser Ala Gln Val Asp Gln Val Glu Val Glu Tyr Val Thr Met Ala Ser
50 55 60

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

Asp Gln Glu Pro Thr Tyr Cys Asn Met Gly His Leu Ser Ser His Leu
85 90 95

Pro Gly Arg Gly Pro Glu Glu Pro Thr Glu Tyr Ser Thr Ile Ser Arg
100 105 110

Pro

<210> 265
<211> 37
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 265

Met Ser Asp Ser Lys Glu Pro Arg Leu Gln Gln Leu Gly Leu Leu Glu
1 5 10 15

Glu Glu Gln Leu Arg Gly Leu Gly Phe Arg Gln Thr Arg Gly Tyr Lys
20 25 30

Ser Leu Ala Gly Cys
35

<210> 266
<211> 29
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 266

Arg Lys Ser Ser Gly Gly Lys Gly Gly Ser Tyr Ser Gln Ala Ala Cys
1 5 10 15

Ser Asp Ser Ala Gln Gly Ser Asp Val Ser Leu Thr Ala
20 25

<210> 267
<211> 95
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 267

Leu Pro Lys Tyr Lys Thr Arg Lys Ala Met Arg Asn Asn Val Pro Arg
1 5 10 15

Asp Arg Gly Asp Thr Ala Met Glu Val Gly Ile Tyr Ala Asn Ile Leu
20 25 30

Glu Lys Gln Ala Lys Glu Glu Ser Val Pro Glu Val Gly Ser Arg Pro
35 40 45

Cys Val Ser Thr Ala Gln Asp Glu Ala Lys His Ser Gln Glu Leu Gln
50 55 60

Tyr Ala Thr Pro Val Phe Gln Glu Val Ala Pro Arg Glu Gln Glu Ala
65 70 75 80

Cys Asp Ser Tyr Lys Ser Gly Tyr Val Tyr Ser Glu Leu Asn Phe
85 90 95

<210> 268
<211> 178
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 268

Arg Arg Arg His Arg Gly Lys Phe Arg Lys Asp Val Gln Lys Glu Lys
1 5 10 15

Asp Leu Gln Leu Ser Ser Gly Ala Glu Glu Pro Ile Thr Arg Lys Gly
20 25 30

Glu Leu Gln Lys Arg Pro Asn Pro Ala Ala Ala Thr Gln Glu Glu Ser
35 40 45

Leu Tyr Ala Ser Val Glu Asp Met Gln Thr Glu Asp Gly Val Glu Leu
50 55 60

Asn Ser Trp Thr Pro Pro Glu Glu Asp Pro Gln Gly Glu Thr Tyr Ala
65 70 75 80

Gln Val Lys Pro Ser Arg Leu Arg Lys Ala Gly His Val Ser Pro Ser
85 90 95

Val Met Ser Arg Glu Gln Leu Asn Thr Glu Tyr Glu Gln Ala Glu Glu
100 105 110

Gly Gln Gly Ala Asn Asn Gln Ala Ala Glu Ser Gly Glu Ser Gln Asp
115 120 125

Val Thr Tyr Ala Gln Leu Cys Ser Arg Thr Leu Arg Gln Gly Ala Ala
130 135 140

Ala Ser Pro Leu Ser Gln Ala Gly Glu Ala Pro Glu Glu Pro Ser Val
145 150 155 160

Tyr Ala Thr Leu Ala Ala Ala Arg Pro Glu Ala Val Pro Lys Asp Met
165 170 175

Glu Gln

<210> 269
<211> 42
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 269

Ser Ala Gly Ser Ala Gly Ser Ala Gly Ser Ala Gly Ser Ala Gly Ser
1 5 10 15

Ala Gly Ser Ala Gly Ser Ala Gly Ser Ala Gly Ser Ala Gly Ser Ala
20 25 30

Gly Ser Ala Gly Ser Ala Gly Ser Ala Gly
35 40

<210> 270
<211> 42
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 270

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
1 5 10 15

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
20 25 30

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu
35 40

<210> 271
<211> 42
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 271

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
1 5 10 15

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
20 25 30

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu
35 40

<210> 272
<211> 42
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 272

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
1 5 10 15

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
20 25 30

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu
35 40

<210> 273
<211> 93
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 273

Lys Lys Leu Val Lys Lys Phe Arg Gln Lys Lys Gln Arg Gln Trp Ile
1 5 10 15

Gly Pro Thr Gly Met Asn Gln Asn Met Ser Phe His Arg Asn His Thr
20 25 30

Ala Thr Val Arg Ser His Ala Glu Asn Pro Thr Ala Ser His Val Asp
35 40 45

Asn Glu Tyr Ser Gln Pro Pro Arg Asn Ser His Leu Ser Ala Tyr Pro
50 55 60

Ala Leu Glu Gly Ala Leu His Arg Ser Ser Met Gln Pro Asp Asn Ser
65 70 75 80

Ser Asp Ser Asp Tyr Asp Leu His Gly Ala Gln Arg Leu
85 90

<210> 274
<211> 118

<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 274

Lys Cys Tyr Phe Leu Arg Lys Ala Lys Ala Lys Gln Met Pro Val Glu
1 5 10 15

Met Ser Arg Pro Ala Val Pro Leu Leu Asn Ser Asn Asn Glu Lys Met
20 25 30

Ser Asp Pro Asn Met Glu Ala Asn Ser His Tyr Gly His Asn Asp Asp
35 40 45

Val Arg Asn His Ala Met Lys Pro Ile Asn Asp Asn Lys Glu Pro Leu
50 55 60

Asn Ser Asp Val Gln Tyr Thr Glu Val Gln Val Ser Ser Ala Glu Ser
65 70 75 80

His Lys Asp Leu Gly Lys Lys Asp Thr Glu Thr Val Tyr Ser Glu Val
85 90 95

Arg Lys Ala Val Pro Asp Ala Val Glu Ser Arg Tyr Ser Arg Thr Glu
100 105 110

Gly Ser Leu Asp Gly Thr
115

<210> 275
<211> 74
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 275

His Phe Gly Lys Thr Gly Arg Ala Ser Asp Gln Arg Asp Leu Thr Glu
1 5 10 15

His Lys Pro Ser Val Ser Asn His Thr Gln Asp His Ser Asn Asp Pro
20 25 30

Pro Asn Lys Met Asn Glu Val Thr Tyr Ser Thr Leu Asn Phe Glu Ala
35 40 45

Gln Gln Pro Thr Gln Pro Thr Ser Ala Ser Pro Ser Leu Thr Ala Thr
50 55 60

Glu Ile Ile Tyr Ser Glu Val Lys Lys Gln
65 70

<210> 276
<211> 112
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 276

Asp Val Val Cys Thr Gly Trp Leu Arg Lys Ser Pro Pro Glu Lys Lys
1 5 10 15

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

Arg Met Ser Gly Asp Pro Asp Val Leu Glu Tyr Tyr Lys Asn Asp His
35 40 45

Ser Lys Lys Pro Leu Arg Ile Ile Asn Leu Asn Phe Cys Glu Gln Val
50 55 60

Asp Ala Gly Leu Thr Phe Asn Lys Lys Glu Leu Gln Asp Ser Phe Val
65 70 75 80

Phe Asp Ile Lys Thr Ser Glu Arg Thr Phe Tyr Leu Val Ala Glu Thr
85 90 95

Glu Glu Asp Met Asn Lys Trp Val Gln Ser Ile Cys Gln Ile Cys Gly
100 105 110

<210> 277
<211> 116
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 277

Ala Val Met Glu Gly Pro Leu Phe Leu Gln Ser Gln Arg Phe Gly Thr
1 5 10 15

Lys Arg Trp Arg Lys Thr Trp Ala Val Leu Tyr Pro Ala Ser Pro His
20 25 30

Gly Val Ala Arg Leu Glu Phe Phe Asp His Lys Gly Ser Ser Ser Gly
35 40 45

Gly Gly Arg Gly Ser Ser Arg Arg Leu Asp Cys Lys Val Ile Arg Leu
50 55 60

Ala Glu Cys Val Ser Val Ala Pro Val Thr Val Glu Thr Pro Pro Glu
65 70 75 80

```
Pro Gly Ala Thr Ala Phe Arg Leu Asp Thr Ala Gln Arg Ser His Leu
                85                  90                  95

Leu Ala Ala Asp Ala Pro Ser Ser Ala Ala Trp Val Gln Thr Leu Cys
            100                 105                 110

Arg Asn Ala Phe
        115


<210>  278
<211>  111
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic amino acid sequence

<400>  278

Gly Ala Val Lys Gln Gly Phe Leu Tyr Leu Gln Gln Gln Gln Thr Phe
1               5                   10                  15

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

Cys Ala Leu Ala Arg Leu Glu Leu Gln Glu Gly Pro Glu Lys Pro Arg
        35                  40                  45

Arg Cys Glu Ala Ala Arg Lys Val Ile Arg Leu Ser Asp Cys Leu Arg
    50                  55                  60

Val Ala Glu Ala Gly Gly Glu Ala Ser Ser Pro Arg Asp Thr Ser Ala
65                  70                  75                  80

Phe Phe Leu Glu Thr Lys Glu Arg Leu Tyr Leu Leu Ala Ala Pro Ala
                85                  90                  95

Ala Glu Arg Gly Asp Trp Val Gln Ala Ile Cys Leu Leu Ala Phe
            100                 105                 110


<210>  279
<211>  1368
<212>  PRT
<213>  Streptococcus pyogenes

<400>  279

Met Asp Lys Lys Tyr Ser Ile Gly Leu Asp Ile Gly Thr Asn Ser Val
1               5                   10                  15

Gly Trp Ala Val Ile Thr Asp Asp Tyr Lys Val Pro Ser Lys Lys Phe
            20                  25                  30

Lys Val Leu Gly Asn Thr Asp Arg His Ser Ile Lys Lys Asn Leu Ile
```

35 40 45

Gly Ala Leu Leu Phe Asp Ser Gly Glu Thr Ala Glu Ala Thr Arg Leu
50 55 60

Lys Arg Thr Ala Arg Arg Arg Tyr Thr Arg Arg Lys Asn Arg Ile Cys
65 70 75 80

Tyr Leu Gln Glu Ile Phe Ser Asn Glu Met Ala Lys Val Asp Asp Ser
85 90 95

Phe Phe His Arg Leu Glu Glu Ser Phe Leu Val Glu Glu Asp Lys Lys
100 105 110

His Glu Arg His Pro Ile Phe Gly Asn Ile Val Asp Glu Val Ala Tyr
115 120 125

His Glu Lys Tyr Pro Thr Ile Tyr His Leu Arg Lys Lys Leu Val Asp
130 135 140

Ser Thr Asp Lys Ala Asp Leu Arg Leu Ile Tyr Leu Ala Leu Ala His
145 150 155 160

Met Ile Lys Phe Arg Gly His Phe Leu Ile Glu Gly Asp Leu Asn Pro
165 170 175

Asp Asn Ser Asp Val Asp Lys Leu Phe Ile Gln Leu Val Gln Thr Tyr
180 185 190

Asn Gln Leu Phe Glu Glu Asn Pro Ile Asn Ala Ser Gly Val Asp Ala
195 200 205

Lys Ala Ile Leu Ser Ala Arg Leu Ser Lys Ser Arg Arg Leu Glu Asn
210 215 220

Leu Ile Ala Gln Leu Pro Gly Glu Lys Lys Asn Ser Leu Phe Gly Asn
225 230 235 240

Leu Ile Ala Leu Ser Leu Gly Leu Thr Pro Asn Phe Lys Ser Asn Phe
245 250 255

Asp Leu Ala Glu Asp Ala Lys Leu Gln Leu Ser Lys Asp Thr Tyr Asp
260 265 270

Asp Asp Leu Asp Asn Leu Leu Ala Gln Ile Gly Asp Gln Tyr Ala Asp
275 280 285

Leu Phe Leu Ala Ala Lys Asn Leu Ser Asp Ala Ile Leu Leu Ser Asp
290 295 300

Ile Leu Arg Val Asn Thr Glu Ile Thr Lys Ala Pro Leu Ser Ala Ser

305 310 315 320

Met Ile Lys Arg Tyr Asp Glu His His Gln Asp Leu Thr Leu Leu Lys
325 330 335

Ala Leu Val Arg Gln Gln Leu Pro Glu Lys Tyr Lys Glu Ile Phe Phe
340 345 350

Asp Gln Ser Lys Asn Gly Tyr Ala Gly Tyr Ile Asp Gly Gly Ala Ser
355 360 365

Gln Glu Glu Phe Tyr Lys Phe Ile Lys Pro Ile Leu Glu Lys Met Asp
370 375 380

Gly Thr Glu Glu Leu Leu Val Lys Leu Asn Arg Glu Asp Leu Leu Arg
385 390 395 400

Lys Gln Arg Thr Phe Asp Asn Gly Ser Ile Pro His Gln Ile His Leu
405 410 415

Gly Glu Leu His Ala Ile Leu Arg Arg Gln Glu Asp Phe Tyr Pro Phe
420 425 430

Leu Lys Asp Asn Arg Glu Lys Ile Glu Lys Ile Leu Thr Phe Arg Ile
435 440 445

Pro Tyr Tyr Val Gly Pro Leu Ala Arg Gly Asn Ser Arg Phe Ala Trp
450 455 460

Met Thr Arg Lys Ser Glu Glu Thr Ile Thr Pro Trp Asn Phe Glu Glu
465 470 475 480

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

Asn Phe Asp Lys Asn Leu Pro Asn Glu Lys Val Leu Pro Lys His Ser
500 505 510

Leu Leu Tyr Glu Tyr Phe Thr Val Tyr Asn Glu Leu Thr Lys Val Lys
515 520 525

Tyr Val Thr Glu Gly Met Arg Lys Pro Ala Phe Leu Ser Gly Glu Gln
530 535 540

Lys Lys Ala Ile Val Asp Leu Leu Phe Lys Thr Asn Arg Lys Val Thr
545 550 555 560

Val Lys Gln Leu Lys Glu Asp Tyr Phe Lys Lys Ile Glu Cys Phe Asp
565 570 575

Ser Val Glu Ile Ser Gly Val Glu Asp Arg Phe Asn Ala Ser Leu Gly

580 585 590

Thr Tyr His Asp Leu Leu Lys Ile Ile Lys Asp Lys Asp Phe Leu Asp
595 600 605

Asn Glu Glu Asn Glu Asp Ile Leu Glu Asp Ile Val Leu Thr Leu Thr
610 615 620

Leu Phe Glu Asp Arg Glu Met Ile Glu Glu Arg Leu Lys Thr Tyr Ala
625 630 635 640

His Leu Phe Asp Asp Lys Val Met Lys Gln Leu Lys Arg Arg Arg Tyr
645 650 655

Thr Gly Trp Gly Arg Leu Ser Arg Lys Leu Ile Asn Gly Ile Arg Asp
660 665 670

Lys Gln Ser Gly Lys Thr Ile Leu Asp Phe Leu Lys Ser Asp Gly Phe
675 680 685

Ala Asn Arg Asn Phe Met Gln Leu Ile His Asp Asp Ser Leu Thr Phe
690 695 700

Lys Glu Asp Ile Gln Lys Ala Gln Val Ser Gly Gln Gly Asp Ser Leu
705 710 715 720

His Glu His Ile Ala Asn Leu Ala Gly Ser Pro Ala Ile Lys Lys Gly
725 730 735

Ile Leu Gln Thr Val Lys Val Val Asp Glu Leu Val Lys Val Met Gly
740 745 750

Arg His Lys Pro Glu Asn Ile Val Ile Glu Met Ala Arg Glu Asn Gln
755 760 765

Thr Thr Gln Lys Gly Gln Lys Asn Ser Arg Glu Arg Met Lys Arg Ile
770 775 780

Glu Glu Gly Ile Lys Glu Leu Gly Ser Gln Ile Leu Lys Glu His Pro
785 790 795 800

Val Glu Asn Thr Gln Leu Gln Asn Glu Lys Leu Tyr Leu Tyr Tyr Leu
805 810 815

Gln Asn Gly Arg Asp Met Tyr Val Asp Gln Glu Leu Asp Ile Asn Arg
820 825 830

Leu Ser Asp Tyr Asp Val Asp His Ile Val Pro Gln Ser Phe Leu Lys
835 840 845

Asp Asp Ser Ile Asp Asn Lys Val Leu Thr Arg Ser Asp Lys Asn Arg

```
    850                 855                 860

Gly Lys Ser Asp Asn Val Pro Ser Glu Glu Val Val Lys Lys Met Lys
865                 870                 875                 880

Asn Tyr Trp Arg Gln Leu Leu Asn Ala Lys Leu Ile Thr Gln Arg Lys
                885                 890                 895

Phe Asp Asn Leu Thr Lys Ala Glu Arg Gly Gly Leu Ser Glu Leu Asp
            900                 905                 910

Lys Ala Gly Phe Ile Lys Arg Gln Leu Val Glu Thr Arg Gln Ile Thr
        915                 920                 925

Lys His Val Ala Gln Ile Leu Asp Ser Arg Met Asn Thr Lys Tyr Asp
    930                 935                 940

Glu Asn Asp Lys Leu Ile Arg Glu Val Lys Val Ile Thr Leu Lys Ser
945                 950                 955                 960

Lys Leu Val Ser Asp Phe Arg Lys Asp Phe Gln Phe Tyr Lys Val Arg
                965                 970                 975

Glu Ile Asn Asn Tyr His His Ala His Asp Ala Tyr Leu Asn Ala Val
            980                 985                 990

Val Gly Thr Ala Leu Ile Lys Lys  Tyr Pro Lys Leu Glu  Ser Glu Phe
        995                 1000                1005

Val Tyr  Gly Asp Tyr Lys Val  Tyr Asp Val Arg Lys  Met Ile Ala
    1010                1015                1020

Lys Ser  Glu Gln Glu Ile Gly  Lys Ala Thr Ala Lys  Tyr Phe Phe
    1025                1030                1035

Tyr Ser  Asn Ile Met Asn Phe  Phe Lys Thr Glu Ile  Thr Leu Ala
    1040                1045                1050

Asn Gly  Glu Ile Arg Lys Arg  Pro Leu Ile Glu Thr  Asn Gly Glu
    1055                1060                1065

Thr Gly  Glu Ile Val Trp Asp  Lys Gly Arg Asp Phe  Ala Thr Val
    1070                1075                1080

Arg Lys  Val Leu Ser Met Pro  Gln Val Asn Ile Val  Lys Lys Thr
    1085                1090                1095

Glu Val  Gln Thr Gly Gly Phe  Ser Lys Glu Ser Ile  Leu Pro Lys
    1100                1105                1110

Arg Asn  Ser Asp Lys Leu Ile  Ala Arg Lys Lys Asp  Trp Asp Pro
```

1115 1120 1125

Lys Lys Tyr Gly Gly Phe Asp Ser Pro Thr Val Ala Tyr Ser Val
1130 1135 1140

Leu Val Val Ala Lys Val Glu Lys Gly Lys Ser Lys Lys Leu Lys
1145 1150 1155

Ser Val Lys Glu Leu Leu Gly Ile Thr Ile Met Glu Arg Ser Ser
1160 1165 1170

Phe Glu Lys Asn Pro Ile Asp Phe Leu Glu Ala Lys Gly Tyr Lys
1175 1180 1185

Glu Val Lys Lys Asp Leu Ile Ile Lys Leu Pro Lys Tyr Ser Leu
1190 1195 1200

Phe Glu Leu Glu Asn Gly Arg Lys Arg Met Leu Ala Ser Ala Gly
1205 1210 1215

Glu Leu Gln Lys Gly Asn Glu Leu Ala Leu Pro Ser Lys Tyr Val
1220 1225 1230

Asn Phe Leu Tyr Leu Ala Ser His Tyr Glu Lys Leu Lys Gly Ser
1235 1240 1245

Pro Glu Asp Asn Glu Gln Lys Gln Leu Phe Val Glu Gln His Lys
1250 1255 1260

His Tyr Leu Asp Glu Ile Ile Glu Gln Ile Ser Glu Phe Ser Lys
1265 1270 1275

Arg Val Ile Leu Ala Asp Ala Asn Leu Asp Lys Val Leu Ser Ala
1280 1285 1290

Tyr Asn Lys His Arg Asp Lys Pro Ile Arg Glu Gln Ala Glu Asn
1295 1300 1305

Ile Ile His Leu Phe Thr Leu Thr Asn Leu Gly Ala Pro Ala Ala
1310 1315 1320

Phe Lys Tyr Phe Asp Thr Thr Ile Asp Arg Lys Arg Tyr Thr Ser
1325 1330 1335

Thr Lys Glu Val Leu Asp Ala Thr Leu Ile His Gln Ser Ile Thr
1340 1345 1350

Gly Leu Tyr Glu Thr Arg Ile Asp Leu Ser Gln Leu Gly Gly Asp
1355 1360 1365

<210> 280

<211> 1441
<212> PRT
<213> Homo sapiens

<400> 280

Met Ser Gly Leu Gly Asp Ser Ser Ser Asp Pro Ala Asn Pro Asp Ser
1 5 10 15

His Lys Arg Lys Gly Ser Pro Cys Asp Thr Leu Ala Ser Ser Thr Glu
20 25 30

Lys Arg Arg Arg Glu Gln Glu Asn Lys Tyr Leu Glu Glu Leu Ala Glu
35 40 45

Leu Leu Ser Ala Asn Ile Ser Asp Ile Asp Ser Leu Ser Val Lys Pro
50 55 60

Asp Lys Cys Lys Ile Leu Lys Lys Thr Val Asp Gln Ile Gln Leu Met
65 70 75 80

Lys Arg Met Glu Gln Glu Lys Ser Thr Thr Asp Asp Asp Val Gln Lys
85 90 95

Ser Asp Ile Ser Ser Ser Ser Gln Gly Val Ile Glu Lys Glu Ser Leu
100 105 110

Gly Pro Leu Leu Leu Glu Ala Leu Asp Gly Phe Phe Phe Val Val Asn
115 120 125

Cys Glu Gly Arg Ile Val Phe Val Ser Glu Asn Val Thr Ser Tyr Leu
130 135 140

Gly Tyr Asn Gln Glu Glu Leu Met Asn Thr Ser Val Tyr Ser Ile Leu
145 150 155 160

His Val Gly Asp His Ala Glu Phe Val Lys Asn Leu Leu Pro Lys Ser
165 170 175

Leu Val Asn Gly Val Pro Trp Pro Gln Glu Ala Thr Arg Arg Asn Ser
180 185 190

His Thr Phe Asn Cys Arg Met Leu Ile His Pro Pro Asp Glu Pro Gly
195 200 205

Thr Glu Asn Gln Glu Ala Cys Gln Arg Tyr Glu Val Met Gln Cys Phe
210 215 220

Thr Val Ser Gln Pro Lys Ser Ile Gln Glu Asp Gly Glu Asp Phe Gln
225 230 235 240

Ser Cys Leu Ile Cys Ile Ala Arg Arg Leu Pro Arg Pro Pro Ala Ile
245 250 255

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

Ile Ser Ile Asp Thr Ser Ser Leu Arg Ala Ala Gly Arg Thr Gly Trp
        275                 280                 285

Glu Asp Leu Val Arg Lys Cys Ile Tyr Ala Phe Phe Gln Pro Gln Gly
    290                 295                 300

Arg Glu Pro Ser Tyr Ala Arg Gln Leu Phe Gln Glu Val Met Thr Arg
305                 310                 315                 320

Gly Thr Ala Ser Ser Pro Ser Tyr Arg Phe Ile Leu Asn Asp Gly Thr
                325                 330                 335

Met Leu Ser Ala His Thr Lys Cys Lys Leu Cys Tyr Pro Gln Ser Pro
            340                 345                 350

Asp Met Gln Pro Phe Ile Met Gly Ile His Ile Ile Asp Arg Glu His
        355                 360                 365

Ser Gly Leu Ser Pro Gln Asp Asp Thr Asn Ser Gly Met Ser Ile Pro
    370                 375                 380

Arg Val Asn Pro Ser Val Asn Pro Ser Ile Ser Pro Ala His Gly Val
385                 390                 395                 400

Ala Arg Ser Ser Thr Leu Pro Pro Ser Asn Ser Asn Met Val Ser Thr
                405                 410                 415

Arg Ile Asn Arg Gln Gln Ser Ser Asp Leu His Ser Ser Ser His Ser
            420                 425                 430

Asn Ser Ser Asn Ser Gln Gly Ser Phe Gly Cys Ser Pro Gly Ser Gln
        435                 440                 445

Ile Val Ala Asn Val Ala Leu Asn Gln Gly Gln Ala Ser Ser Gln Ser
    450                 455                 460

Ser Asn Pro Ser Leu Asn Leu Asn Asn Ser Pro Met Glu Gly Thr Gly
465                 470                 475                 480

Ile Ser Leu Ala Gln Phe Met Ser Pro Arg Arg Gln Val Thr Ser Gly
                485                 490                 495

Leu Ala Thr Arg Pro Arg Met Pro Asn Asn Ser Phe Pro Pro Asn Ile
            500                 505                 510

Ser Thr Leu Ser Ser Pro Val Gly Met Thr Ser Ser Ala Cys Asn Asn
        515                 520                 525
```

```
Asn Asn Arg Ser Tyr Ser Asn Ile Pro Val Thr Ser Leu Gln Gly Met
    530                 535                 540

Asn Glu Gly Pro Asn Asn Ser Val Gly Phe Ser Ala Ser Ser Pro Val
545                 550                 555                 560

Leu Arg Gln Met Ser Ser Gln Asn Ser Pro Ser Arg Leu Asn Ile Gln
                565                 570                 575

Pro Ala Lys Ala Glu Ser Lys Asp Asn Lys Glu Ile Ala Ser Ile Leu
            580                 585                 590

Asn Glu Met Ile Gln Ser Asp Asn Ser Ser Ser Asp Gly Lys Pro Leu
        595                 600                 605

Asp Ser Gly Leu Leu His Asn Asn Asp Arg Leu Ser Asp Gly Asp Ser
    610                 615                 620

Lys Tyr Ser Gln Thr Ser His Lys Leu Val Gln Leu Leu Thr Thr Thr
625                 630                 635                 640

Ala Glu Gln Gln Leu Arg His Ala Asp Ile Asp Thr Ser Cys Lys Asp
                645                 650                 655

Val Leu Ser Cys Thr Gly Thr Ser Asn Ser Ala Ser Ala Asn Ser Ser
            660                 665                 670

Gly Gly Ser Cys Pro Ser Ser His Ser Ser Leu Thr Glu Arg His Lys
        675                 680                 685

Ile Leu His Arg Leu Leu Gln Glu Gly Ser Pro Ser Asp Ile Thr Thr
    690                 695                 700

Leu Ser Val Glu Pro Asp Lys Lys Asp Ser Ala Ser Thr Ser Val Ser
705                 710                 715                 720

Val Thr Gly Gln Val Gln Gly Asn Ser Ser Ile Lys Leu Glu Leu Asp
                725                 730                 735

Ala Ser Lys Lys Lys Glu Ser Lys Asp His Gln Leu Leu Arg Tyr Leu
            740                 745                 750

Leu Asp Lys Asp Glu Lys Asp Leu Arg Ser Thr Pro Asn Leu Ser Leu
        755                 760                 765

Asp Asp Val Lys Val Lys Val Glu Lys Lys Glu Gln Met Asp Pro Cys
    770                 775                 780

Asn Thr Asn Pro Thr Pro Met Thr Lys Pro Thr Pro Glu Glu Ile Lys
785                 790                 795                 800
```

```
Leu Glu Ala Gln Ser Gln Phe Thr Ala Asp Leu Asp Gln Phe Asp Gln
                805                 810                 815

Leu Leu Pro Thr Leu Glu Lys Ala Ala Gln Leu Pro Gly Leu Cys Glu
            820                 825                 830

Thr Asp Arg Met Asp Gly Ala Val Thr Ser Val Thr Ile Lys Ser Glu
        835                 840                 845

Ile Leu Pro Ala Ser Leu Gln Ser Ala Thr Ala Arg Pro Thr Ser Arg
    850                 855                 860

Leu Asn Arg Leu Pro Glu Leu Glu Leu Glu Ala Ile Asp Asn Gln Phe
865                 870                 875                 880

Gly Gln Pro Gly Thr Gly Asp Gln Ile Pro Trp Thr Asn Asn Thr Val
                885                 890                 895

Thr Ala Ile Asn Gln Ser Lys Ser Glu Asp Gln Cys Ile Ser Ser Gln
            900                 905                 910

Leu Asp Glu Leu Leu Cys Pro Pro Thr Thr Val Glu Gly Arg Asn Asp
        915                 920                 925

Glu Lys Ala Leu Leu Glu Gln Leu Val Ser Phe Leu Ser Gly Lys Asp
    930                 935                 940

Glu Thr Glu Leu Ala Glu Leu Asp Arg Ala Leu Gly Ile Asp Lys Leu
945                 950                 955                 960

Val Gln Gly Gly Gly Leu Asp Val Leu Ser Glu Arg Phe Pro Pro Gln
                965                 970                 975

Gln Ala Thr Pro Pro Leu Ile Met Glu Glu Arg Pro Asn Leu Tyr Ser
            980                 985                 990

Gln Pro Tyr Ser Ser Pro Ser Pro  Thr Ala Asn Leu Pro  Ser Pro Phe
        995                 1000                1005

Gln Gly  Met Val Arg Gln Lys  Pro Ser Leu Gly Thr  Met Pro Val
    1010                1015                1020

Gln Val  Thr Pro Pro Arg Gly  Ala Phe Ser Pro Gly  Met Gly Met
    1025                1030                1035

Gln Pro  Arg Gln Thr Leu Asn  Arg Pro Pro Ala Ala  Pro Asn Gln
    1040                1045                1050

Leu Arg  Leu Gln Leu Gln Gln  Arg Leu Gln Gly Gln  Gln Gln Leu
    1055                1060                1065
```

```
Ile His  Gln Asn Arg Gln Ala  Ile Leu Asn Gln Phe  Ala Ala Thr
    1070                1075                1080

Ala Pro  Val Gly Ile Asn Met  Arg Ser Gly Met Gln  Gln Gln Ile
    1085                1090                1095

Thr Pro  Gln Pro Pro Leu Asn  Ala Gln Met Leu Ala  Gln Arg Gln
    1100                1105                1110

Arg Glu  Leu Tyr Ser Gln Gln  His Arg Gln Arg Gln  Leu Ile Gln
    1115                1120                1125

Gln Gln  Arg Ala Met Leu Met  Arg Gln Gln Ser Phe  Gly Asn Asn
    1130                1135                1140

Leu Pro  Pro Ser Ser Gly Leu  Pro Val Gln Met Gly  Asn Pro Arg
    1145                1150                1155

Leu Pro  Gln Gly Ala Pro Gln  Gln Phe Pro Tyr Pro  Pro Asn Tyr
    1160                1165                1170

Gly Thr  Asn Pro Gly Thr Pro  Pro Ala Ser Thr Ser  Pro Phe Ser
    1175                1180                1185

Gln Leu  Ala Ala Asn Pro Glu  Ala Ser Leu Ala Asn  Arg Asn Ser
    1190                1195                1200

Met Val  Ser Arg Gly Met Thr  Gly Asn Ile Gly Gly  Gln Phe Gly
    1205                1210                1215

Thr Gly  Ile Asn Pro Gln Met  Gln Gln Asn Val Phe  Gln Tyr Pro
    1220                1225                1230

Gly Ala  Gly Met Val Pro Gln  Gly Glu Ala Asn Phe  Ala Pro Ser
    1235                1240                1245

Leu Ser  Pro Gly Ser Ser Met  Val Pro Met Pro Ile  Pro Pro Pro
    1250                1255                1260

Gln Ser  Ser Leu Leu Gln Gln  Thr Pro Pro Ala Ser  Gly Tyr Gln
    1265                1270                1275

Ser Pro  Asp Met Lys Ala Trp  Gln Gln Gly Ala Ile  Gly Asn Asn
    1280                1285                1290

Asn Val  Phe Ser Gln Ala Val  Gln Asn Gln Pro Thr  Pro Ala Gln
    1295                1300                1305

Pro Gly  Val Tyr Asn Asn Met  Ser Ile Thr Val Ser  Met Ala Gly
    1310                1315                1320
```

Gly Asn Thr Asn Val Gln Asn Met Asn Pro Met Met Ala Gln Met
1325 1330 1335

Gln Met Ser Ser Leu Gln Met Pro Gly Met Asn Thr Val Cys Pro
1340 1345 1350

Glu Gln Ile Asn Asp Pro Ala Leu Arg His Thr Gly Leu Tyr Cys
1355 1360 1365

Asn Gln Leu Ser Ser Thr Asp Leu Leu Lys Thr Glu Ala Asp Gly
1370 1375 1380

Thr Gln Gln Val Gln Gln Val Gln Val Phe Ala Asp Val Gln Cys
1385 1390 1395

Thr Val Asn Leu Val Gly Gly Asp Pro Tyr Leu Asn Gln Pro Gly
1400 1405 1410

Pro Leu Gly Thr Gln Lys Pro Thr Ser Gly Pro Gln Thr Pro Gln
1415 1420 1425

Ala Gln Gln Lys Ser Leu Leu Gln Gln Leu Leu Thr Glu
1430 1435 1440

<210> 281
<211> 1464
<212> PRT
<213> Homo sapiens

<400> 281

Met Ser Gly Met Gly Glu Asn Thr Ser Asp Pro Ser Arg Ala Glu Thr
1 5 10 15

Arg Lys Arg Lys Glu Cys Pro Asp Gln Leu Gly Pro Ser Pro Lys Arg
20 25 30

Asn Thr Glu Lys Arg Asn Arg Glu Gln Glu Asn Lys Tyr Ile Glu Glu
35 40 45

Leu Ala Glu Leu Ile Phe Ala Asn Phe Asn Asp Ile Asp Asn Phe Asn
50 55 60

Phe Lys Pro Asp Lys Cys Ala Ile Leu Lys Glu Thr Val Lys Gln Ile
65 70 75 80

Arg Gln Ile Lys Glu Gln Glu Lys Ala Ala Ala Ala Asn Ile Asp Glu
85 90 95

Val Gln Lys Ser Asp Val Ser Ser Thr Gly Gln Gly Val Ile Asp Lys
100 105 110

```
Asp Ala Leu Gly Pro Met Met Leu Glu Ala Leu Asp Gly Phe Phe Phe
        115                 120                 125

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

Gln Tyr Leu Arg Tyr Asn Gln Glu Glu Leu Met Asn Lys Ser Val Tyr
145                 150                 155                 160

Ser Ile Leu His Val Gly Asp His Thr Glu Phe Val Lys Asn Leu Leu
                165                 170                 175

Pro Lys Ser Ile Val Asn Gly Gly Ser Trp Ser Gly Glu Pro Pro Arg
            180                 185                 190

Arg Asn Ser His Thr Phe Asn Cys Arg Met Leu Val Lys Pro Leu Pro
        195                 200                 205

Asp Ser Glu Glu Glu Gly His Asp Asn Gln Glu Ala His Gln Lys Tyr
    210                 215                 220

Glu Thr Met Gln Cys Phe Ala Val Ser Gln Pro Lys Ser Ile Lys Glu
225                 230                 235                 240

Glu Gly Glu Asp Leu Gln Ser Cys Leu Ile Cys Val Ala Arg Arg Val
                245                 250                 255

Pro Met Lys Glu Arg Pro Val Leu Pro Ser Ser Glu Ser Phe Thr Thr
            260                 265                 270

Arg Gln Asp Leu Gln Gly Lys Ile Thr Ser Leu Asp Thr Ser Thr Met
        275                 280                 285

Arg Ala Ala Met Lys Pro Gly Trp Glu Asp Leu Val Arg Arg Cys Ile
    290                 295                 300

Gln Lys Phe His Ala Gln His Glu Gly Glu Ser Val Ser Tyr Ala Lys
305                 310                 315                 320

Arg His His His Glu Val Leu Arg Gln Gly Leu Ala Phe Ser Gln Ile
                325                 330                 335

Tyr Arg Phe Ser Leu Ser Asp Gly Thr Leu Val Ala Ala Gln Thr Lys
            340                 345                 350

Ser Lys Leu Ile Arg Ser Gln Thr Thr Asn Glu Pro Gln Leu Val Ile
        355                 360                 365

Ser Leu His Met Leu His Arg Glu Gln Asn Val Cys Val Met Asn Pro
    370                 375                 380
```

```
Asp Leu Thr Gly Gln Thr Met Gly Lys Pro Leu Asn Pro Ile Ser Ser
385                 390                 395                 400

Asn Ser Pro Ala His Gln Ala Leu Cys Ser Gly Asn Pro Gly Gln Asp
                405                 410                 415

Met Thr Leu Ser Ser Asn Ile Asn Phe Pro Ile Asn Gly Pro Lys Glu
            420                 425                 430

Gln Met Gly Met Pro Met Gly Arg Phe Gly Gly Ser Gly Gly Met Asn
        435                 440                 445

His Val Ser Gly Met Gln Ala Thr Thr Pro Gln Gly Ser Asn Tyr Ala
    450                 455                 460

Leu Lys Met Asn Ser Pro Ser Gln Ser Ser Pro Gly Met Asn Pro Gly
465                 470                 475                 480

Gln Pro Thr Ser Met Leu Ser Pro Arg His Arg Met Ser Pro Gly Val
                485                 490                 495

Ala Gly Ser Pro Arg Ile Pro Pro Ser Gln Phe Ser Pro Ala Gly Ser
            500                 505                 510

Leu His Ser Pro Val Gly Val Cys Ser Ser Thr Gly Asn Ser His Ser
        515                 520                 525

Tyr Thr Asn Ser Ser Leu Asn Ala Leu Gln Ala Leu Ser Glu Gly His
    530                 535                 540

Gly Val Ser Leu Gly Ser Ser Leu Ala Ser Pro Asp Leu Lys Met Gly
545                 550                 555                 560

Asn Leu Gln Asn Ser Pro Val Asn Met Asn Pro Pro Pro Leu Ser Lys
                565                 570                 575

Met Gly Ser Leu Asp Ser Lys Asp Cys Phe Gly Leu Tyr Gly Glu Pro
            580                 585                 590

Ser Glu Gly Thr Thr Gly Gln Ala Glu Ser Ser Cys His Pro Gly Glu
        595                 600                 605

Gln Lys Glu Thr Asn Asp Pro Asn Leu Pro Pro Ala Val Ser Ser Glu
    610                 615                 620

Arg Ala Asp Gly Gln Ser Arg Leu His Asp Ser Lys Gly Gln Thr Lys
625                 630                 635                 640

Leu Leu Gln Leu Leu Thr Thr Lys Ser Asp Gln Met Glu Pro Ser Pro
                645                 650                 655
```

```
Leu Ala Ser Ser Leu Ser Asp Thr Asn Lys Asp Ser Thr Gly Ser Leu
            660                 665                 670

Pro Gly Ser Gly Ser Thr His Gly Thr Ser Leu Lys Glu Lys His Lys
        675                 680                 685

Ile Leu His Arg Leu Leu Gln Asp Ser Ser Ser Pro Val Asp Leu Ala
    690                 695                 700

Lys Leu Thr Ala Glu Ala Thr Gly Lys Asp Leu Ser Gln Glu Ser Ser
705                 710                 715                 720

Ser Thr Ala Pro Gly Ser Glu Val Thr Ile Lys Gln Glu Pro Val Ser
                725                 730                 735

Pro Lys Lys Lys Glu Asn Ala Leu Leu Arg Tyr Leu Leu Asp Lys Asp
            740                 745                 750

Asp Thr Lys Asp Ile Gly Leu Pro Glu Ile Thr Pro Lys Leu Glu Arg
        755                 760                 765

Leu Asp Ser Lys Thr Asp Pro Ala Ser Asn Thr Lys Leu Ile Ala Met
    770                 775                 780

Lys Thr Glu Lys Glu Glu Met Ser Phe Glu Pro Gly Asp Gln Pro Gly
785                 790                 795                 800

Ser Glu Leu Asp Asn Leu Glu Glu Ile Leu Asp Asp Leu Gln Asn Ser
                805                 810                 815

Gln Leu Pro Gln Leu Phe Pro Asp Thr Arg Pro Gly Ala Pro Ala Gly
            820                 825                 830

Ser Val Asp Lys Gln Ala Ile Ile Asn Asp Leu Met Gln Leu Thr Ala
        835                 840                 845

Glu Asn Ser Pro Val Thr Pro Val Gly Ala Gln Lys Thr Ala Leu Arg
    850                 855                 860

Ile Ser Gln Ser Thr Phe Asn Asn Pro Arg Pro Gly Gln Leu Gly Arg
865                 870                 875                 880

Leu Leu Pro Asn Gln Asn Leu Pro Leu Asp Ile Thr Leu Gln Ser Pro
                885                 890                 895

Thr Gly Ala Gly Pro Phe Pro Pro Ile Arg Asn Ser Ser Pro Tyr Ser
            900                 905                 910

Val Ile Pro Gln Pro Gly Met Met Gly Asn Gln Gly Met Ile Gly Asn
        915                 920                 925
```

```
Gln Gly Asn Leu Gly Asn Ser Ser Thr Gly Met Ile Gly Asn Ser Ala
    930                 935                 940

Ser Arg Pro Thr Met Pro Ser Gly Glu Trp Ala Pro Gln Ser Ser Ala
945                 950                 955                 960

Val Arg Val Thr Cys Ala Ala Thr Thr Ser Ala Met Asn Arg Pro Val
                965                 970                 975

Gln Gly Gly Met Ile Arg Asn Pro Ala Ala Ser Ile Pro Met Arg Pro
            980                 985                 990

Ser Ser Gln Pro Gly Gln Arg Gln  Thr Leu Gln Ser Gln  Val Met Asn
        995                 1000                1005

Ile Gly  Pro Ser Glu Leu Glu  Met Asn Met Gly Gly  Pro Gln Tyr
    1010                1015                1020

Ser Gln  Gln Gln Ala Pro Pro  Asn Gln Thr Ala Pro  Trp Pro Glu
    1025                1030                1035

Ser Ile  Leu Pro Ile Asp Gln  Ala Ser Phe Ala Ser  Gln Asn Arg
    1040                1045                1050

Gln Pro  Phe Gly Ser Ser Pro  Asp Asp Leu Leu Cys  Pro His Pro
    1055                1060                1065

Ala Ala  Glu Ser Pro Ser Asp  Glu Gly Ala Leu Leu  Asp Gln Leu
    1070                1075                1080

Tyr Leu  Ala Leu Arg Asn Phe  Asp Gly Leu Glu Glu  Ile Asp Arg
    1085                1090                1095

Ala Leu  Gly Ile Pro Glu Leu  Val Ser Gln Ser Gln  Ala Val Asp
    1100                1105                1110

Pro Glu  Gln Phe Ser Ser Gln  Asp Ser Asn Ile Met  Leu Glu Gln
    1115                1120                1125

Lys Ala  Pro Val Phe Pro Gln  Gln Tyr Ala Ser Gln  Ala Gln Met
    1130                1135                1140

Ala Gln  Gly Ser Tyr Ser Pro  Met Gln Asp Pro Asn  Phe His Thr
    1145                1150                1155

Met Gly  Gln Arg Pro Ser Tyr  Ala Thr Leu Arg Met  Gln Pro Arg
    1160                1165                1170

Pro Gly  Leu Arg Pro Thr Gly  Leu Val Gln Asn Gln  Pro Asn Gln
    1175                1180                1185
```

```
Leu Arg  Leu Gln Leu Gln His  Arg Leu Gln Ala Gln  Gln Asn Arg
    1190                1195                1200

Gln Pro  Leu Met Asn Gln Ile  Ser Asn Val Ser Asn  Val Asn Leu
    1205                1210                1215

Thr Leu  Arg Pro Gly Val Pro  Thr Gln Ala Pro Ile  Asn Ala Gln
    1220                1225                1230

Met Leu  Ala Gln Arg Gln Arg  Glu Ile Leu Asn Gln  His Leu Arg
    1235                1240                1245

Gln Arg  Gln Met His Gln Gln  Gln Gln Val Gln Gln  Arg Thr Leu
    1250                1255                1260

Met Met  Arg Gly Gln Gly Leu  Asn Met Thr Pro Ser  Met Val Ala
    1265                1270                1275

Pro Ser  Gly Met Pro Ala Thr  Met Ser Asn Pro Arg  Ile Pro Gln
    1280                1285                1290

Ala Asn  Ala Gln Gln Phe Pro  Phe Pro Pro Asn Tyr  Gly Ile Ser
    1295                1300                1305

Gln Gln  Pro Asp Pro Gly Phe  Thr Gly Ala Thr Thr  Pro Gln Ser
    1310                1315                1320

Pro Leu  Met Ser Pro Arg Met  Ala His Thr Gln Ser  Pro Met Met
    1325                1330                1335

Gln Gln  Ser Gln Ala Asn Pro  Ala Tyr Gln Ala Pro  Ser Asp Ile
    1340                1345                1350

Asn Gly  Trp Ala Gln Gly Asn  Met Gly Gly Asn Ser  Met Phe Ser
    1355                1360                1365

Gln Gln  Ser Pro Pro His Phe  Gly Gln Gln Ala Asn  Thr Ser Met
    1370                1375                1380

Tyr Ser  Asn Asn Met Asn Ile  Asn Val Ser Met Ala  Thr Asn Thr
    1385                1390                1395

Gly Gly  Met Ser Ser Met Asn  Gln Met Thr Gly Gln  Ile Ser Met
    1400                1405                1410

Thr Ser  Val Thr Ser Val Pro  Thr Ser Gly Leu Ser  Ser Met Gly
    1415                1420                1425

Pro Glu  Gln Val Asn Asp Pro  Ala Leu Arg Gly Gly  Asn Leu Phe
    1430                1435                1440
```

Pro Asn Gln Leu Pro Gly Met Asp Met Ile Lys Gln Glu Gly Asp
1445 1450 1455

Thr Thr Arg Lys Tyr Cys
1460

<210> 282
<211> 1420
<212> PRT
<213> Homo sapiens

<400> 282

Met Ser Gly Leu Gly Glu Asn Leu Asp Pro Leu Ala Ser Asp Ser Arg
1 5 10 15

Lys Arg Lys Leu Pro Cys Asp Thr Pro Gly Gln Gly Leu Thr Cys Ser
20 25 30

Gly Glu Lys Arg Arg Arg Glu Gln Glu Ser Lys Tyr Ile Glu Glu Leu
35 40 45

Ala Glu Leu Ile Ser Ala Asn Leu Ser Asp Ile Asp Asn Phe Asn Val
50 55 60

Lys Pro Asp Lys Cys Ala Ile Leu Lys Glu Thr Val Arg Gln Ile Arg
65 70 75 80

Gln Ile Lys Glu Gln Gly Lys Thr Ile Ser Asn Asp Asp Asp Val Gln
85 90 95

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

Leu Gly Pro Leu Leu Leu Gln Ala Leu Asp Gly Phe Leu Phe Val Val
115 120 125

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

Leu Gln Tyr Lys Gln Glu Asp Leu Val Asn Thr Ser Val Tyr Asn Ile
145 150 155 160

Leu His Glu Glu Asp Arg Lys Asp Phe Leu Lys Asn Leu Pro Lys Ser
165 170 175

Thr Val Asn Gly Val Ser Trp Thr Asn Glu Thr Gln Arg Gln Lys Ser
180 185 190

His Thr Phe Asn Cys Arg Met Leu Met Lys Thr Pro His Asp Ile Leu
195 200 205

```
Glu Asp Ile Asn Ala Ser Pro Glu Met Arg Gln Arg Tyr Glu Thr Met
    210                 215                 220

Gln Cys Phe Ala Leu Ser Gln Pro Arg Ala Met Met Glu Glu Gly Glu
225                 230                 235                 240

Asp Leu Gln Ser Cys Met Ile Cys Val Ala Arg Arg Ile Thr Thr Gly
                245                 250                 255

Glu Arg Thr Phe Pro Ser Asn Pro Glu Ser Phe Ile Thr Arg His Asp
            260                 265                 270

Leu Ser Gly Lys Val Val Asn Ile Asp Thr Asn Ser Leu Arg Ser Ser
        275                 280                 285

Met Arg Pro Gly Phe Glu Asp Ile Ile Arg Arg Cys Ile Gln Arg Phe
    290                 295                 300

Phe Ser Leu Asn Asp Gly Gln Ser Trp Ser Gln Lys Arg His Tyr Gln
305                 310                 315                 320

Glu Ala Tyr Leu Asn Gly His Ala Glu Thr Pro Val Tyr Arg Phe Ser
                325                 330                 335

Leu Ala Asp Gly Thr Ile Val Thr Ala Gln Thr Lys Ser Lys Leu Phe
            340                 345                 350

Arg Asn Pro Val Thr Asn Asp Arg His Gly Phe Val Ser Thr His Phe
        355                 360                 365

Leu Gln Arg Glu Gln Asn Gly Tyr Arg Pro Asn Pro Asn Pro Val Gly
    370                 375                 380

Gln Gly Ile Arg Pro Pro Met Ala Gly Cys Asn Ser Ser Val Gly Gly
385                 390                 395                 400

Met Ser Met Ser Pro Asn Gln Gly Leu Gln Met Pro Ser Ser Arg Ala
                405                 410                 415

Tyr Gly Leu Ala Asp Pro Ser Thr Thr Gly Gln Met Ser Gly Ala Arg
            420                 425                 430

Tyr Gly Gly Ser Ser Asn Ile Ala Ser Leu Thr Pro Gly Pro Gly Met
        435                 440                 445

Gln Ser Pro Ser Ser Tyr Gln Asn Asn Asn Tyr Gly Leu Asn Met Ser
    450                 455                 460

Ser Pro Pro His Gly Ser Pro Gly Leu Ala Pro Asn Gln Gln Asn Ile
465                 470                 475                 480
```

```
Met Ile Ser Pro Arg Asn Arg Gly Ser Pro Lys Ile Ala Ser His Gln
                485                 490                 495

Phe Ser Pro Val Ala Gly Val His Ser Pro Met Ala Ser Ser Gly Asn
            500                 505                 510

Thr Gly Asn His Ser Phe Ser Ser Ser Ser Leu Ser Ala Leu Gln Ala
        515                 520                 525

Ile Ser Glu Gly Val Gly Thr Ser Leu Leu Ser Thr Leu Ser Ser Pro
    530                 535                 540

Gly Pro Lys Leu Asp Asn Ser Pro Asn Met Asn Ile Thr Gln Pro Ser
545                 550                 555                 560

Lys Val Ser Asn Gln Asp Ser Lys Ser Pro Leu Gly Phe Tyr Cys Asp
                565                 570                 575

Gln Asn Pro Val Glu Ser Ser Met Cys Gln Ser Asn Ser Arg Asp His
            580                 585                 590

Leu Ser Asp Lys Glu Ser Lys Glu Ser Ser Val Glu Gly Ala Glu Asn
        595                 600                 605

Gln Arg Gly Pro Leu Glu Ser Lys Gly His Lys Lys Leu Leu Gln Leu
    610                 615                 620

Leu Thr Cys Ser Ser Asp Asp Arg Gly His Ser Ser Leu Thr Asn Ser
625                 630                 635                 640

Pro Leu Asp Ser Ser Cys Lys Glu Ser Ser Val Ser Val Thr Ser Pro
                645                 650                 655

Ser Gly Val Ser Ser Ser Thr Ser Gly Gly Val Ser Ser Thr Ser Asn
            660                 665                 670

Met His Gly Ser Leu Leu Gln Glu Lys His Arg Ile Leu His Lys Leu
        675                 680                 685

Leu Gln Asn Gly Asn Ser Pro Ala Glu Val Ala Lys Ile Thr Ala Glu
    690                 695                 700

Ala Thr Gly Lys Asp Thr Ser Ser Ile Thr Ser Cys Gly Asp Gly Asn
705                 710                 715                 720

Val Val Lys Gln Glu Gln Leu Ser Pro Lys Lys Lys Glu Asn Asn Ala
                725                 730                 735

Leu Leu Arg Tyr Leu Leu Asp Arg Asp Asp Pro Ser Asp Ala Leu Ser
            740                 745                 750
```

```
Lys Glu Leu Gln Pro Gln Val Glu Gly Val Asp Asn Lys Met Ser Gln
        755                 760                 765

Cys Thr Ser Ser Thr Ile Pro Ser Ser Ser Gln Glu Lys Asp Pro Lys
    770                 775                 780

Ile Lys Thr Glu Thr Ser Glu Glu Gly Ser Gly Asp Leu Asp Asn Leu
785                 790                 795                 800

Asp Ala Ile Leu Gly Asp Leu Thr Ser Ser Asp Phe Tyr Asn Asn Ser
                805                 810                 815

Ile Ser Ser Asn Gly Ser His Leu Gly Thr Lys Gln Gln Val Phe Gln
            820                 825                 830

Gly Thr Asn Ser Leu Gly Leu Lys Ser Ser Gln Ser Val Gln Ser Ile
        835                 840                 845

Arg Pro Pro Tyr Asn Arg Ala Val Ser Leu Asp Ser Pro Val Ser Val
    850                 855                 860

Gly Ser Ser Pro Pro Val Lys Asn Ile Ser Ala Phe Pro Met Leu Pro
865                 870                 875                 880

Lys Gln Pro Met Leu Gly Gly Asn Pro Arg Met Met Asp Ser Gln Glu
                885                 890                 895

Asn Tyr Gly Ser Ser Met Gly Gly Pro Asn Arg Asn Val Thr Val Thr
            900                 905                 910

Gln Thr Pro Ser Ser Gly Asp Trp Gly Leu Pro Asn Ser Lys Ala Gly
        915                 920                 925

Arg Met Glu Pro Met Asn Ser Asn Ser Met Gly Arg Pro Gly Gly Asp
    930                 935                 940

Tyr Asn Thr Ser Leu Pro Arg Pro Ala Leu Gly Gly Ser Ile Pro Thr
945                 950                 955                 960

Leu Pro Leu Arg Ser Asn Ser Ile Pro Gly Ala Arg Pro Val Leu Gln
                965                 970                 975

Gln Gln Gln Gln Met Leu Gln Met Arg Pro Gly Glu Ile Pro Met Gly
            980                 985                 990

Met Gly Ala Asn Pro Tyr Gly Gln  Ala Ala Ala Ser Asn  Gln Leu Gly
        995                 1000                1005

Ser Trp  Pro Asp Gly Met Leu  Ser Met Glu Gln Val  Ser His Gly
    1010                1015                1020
```

```
Thr Gln  Asn Arg Pro Leu Leu  Arg Asn Ser Leu Asp  Asp Leu Val
    1025                1030                1035

Gly Pro  Pro Ser Asn Leu Glu  Gly Gln Ser Asp Glu  Arg Ala Leu
    1040                1045                1050

Leu Asp  Gln Leu His Thr Leu  Leu Ser Asn Thr Asp  Ala Thr Gly
    1055                1060                1065

Leu Glu  Glu Ile Asp Arg Ala  Leu Gly Ile Pro Glu  Leu Val Asn
    1070                1075                1080

Gln Gly  Gln Ala Leu Glu Pro  Lys Gln Asp Ala Phe  Gln Gly Gln
    1085                1090                1095

Glu Ala  Ala Val Met Met Asp  Gln Lys Ala Gly Leu  Tyr Gly Gln
    1100                1105                1110

Thr Tyr  Pro Ala Gln Gly Pro  Pro Met Gln Gly Gly  Phe His Leu
    1115                1120                1125

Gln Gly  Gln Ser Pro Ser Phe  Asn Ser Met Met Asn  Gln Met Asn
    1130                1135                1140

Gln Gln  Gly Asn Phe Pro Leu  Gln Gly Met His Pro  Arg Ala Asn
    1145                1150                1155

Ile Met  Arg Pro Arg Thr Asn  Thr Pro Lys Gln Leu  Arg Met Gln
    1160                1165                1170

Leu Gln  Gln Arg Leu Gln Gly  Gln Gln Phe Leu Asn  Gln Ser Arg
    1175                1180                1185

Gln Ala  Leu Glu Leu Lys Met  Glu Asn Pro Thr Ala  Gly Gly Ala
    1190                1195                1200

Ala Val  Met Arg Pro Met Met  Gln Pro Gln Gln Gly  Phe Leu Asn
    1205                1210                1215

Ala Gln  Met Val Ala Gln Arg  Ser Arg Glu Leu Leu  Ser His His
    1220                1225                1230

Phe Arg  Gln Gln Arg Val Ala  Met Met Met Gln Gln  Gln Gln Gln
    1235                1240                1245

Gln Gln  Gln Gln Gln Gln Gln  Gln Gln Gln Gln Gln  Gln Gln Gln
    1250                1255                1260

Gln Gln  Gln Gln Gln Gln Gln  Gln Gln Thr Gln Ala  Phe Ser Pro
    1265                1270                1275
```

Pro Pro Asn Val Thr Ala Ser Pro Ser Met Asp Gly Leu Leu Ala
1280 1285 1290

Gly Pro Thr Met Pro Gln Ala Pro Pro Gln Gln Phe Pro Tyr Gln
1295 1300 1305

Pro Asn Tyr Gly Met Gly Gln Gln Pro Asp Pro Ala Phe Gly Arg
1310 1315 1320

Val Ser Ser Pro Pro Asn Ala Met Met Ser Ser Arg Met Gly Pro
1325 1330 1335

Ser Gln Asn Pro Met Met Gln His Pro Gln Ala Ala Ser Ile Tyr
1340 1345 1350

Gln Ser Ser Glu Met Lys Gly Trp Pro Ser Gly Asn Leu Ala Arg
1355 1360 1365

Asn Ser Ser Phe Ser Gln Gln Gln Phe Ala His Gln Gly Asn Pro
1370 1375 1380

Ala Val Tyr Ser Met Val His Met Asn Gly Ser Ser Gly His Met
1385 1390 1395

Gly Gln Met Asn Met Asn Pro Met Pro Met Ser Gly Met Pro Met
1400 1405 1410

Gly Pro Asp Gln Lys Tyr Cys
1415 1420

<210> 283
<211> 798
<212> PRT
<213> Homo sapiens

<400> 283

Met Ala Trp Asp Met Cys Asn Gln Asp Ser Glu Ser Val Trp Ser Asp
1 5 10 15

Ile Glu Cys Ala Ala Leu Val Gly Glu Asp Gln Pro Leu Cys Pro Asp
20 25 30

Leu Pro Glu Leu Asp Leu Ser Glu Leu Asp Val Asn Asp Leu Asp Thr
35 40 45

Asp Ser Phe Leu Gly Gly Leu Lys Trp Cys Ser Asp Gln Ser Glu Ile
50 55 60

Ile Ser Asn Gln Tyr Asn Asn Glu Pro Ser Asn Ile Phe Glu Lys Ile
65 70 75 80

Asp Glu Glu Asn Glu Ala Asn Leu Leu Ala Val Leu Thr Glu Thr Leu

85 90 95

Asp Ser Leu Pro Val Asp Glu Asp Gly Leu Pro Ser Phe Asp Ala Leu
100 105 110

Thr Asp Gly Asp Val Thr Thr Asp Asn Glu Ala Ser Pro Ser Ser Met
115 120 125

Pro Asp Gly Thr Pro Pro Pro Gln Glu Ala Glu Glu Pro Ser Leu Leu
130 135 140

Lys Lys Leu Leu Leu Ala Pro Ala Asn Thr Gln Leu Ser Tyr Asn Glu
145 150 155 160

Cys Ser Gly Leu Ser Thr Gln Asn His Ala Asn His Asn His Arg Ile
165 170 175

Arg Thr Asn Pro Ala Ile Val Lys Thr Glu Asn Ser Trp Ser Asn Lys
180 185 190

Ala Lys Ser Ile Cys Gln Gln Gln Lys Pro Gln Arg Arg Pro Cys Ser
195 200 205

Glu Leu Leu Lys Tyr Leu Thr Thr Asn Asp Asp Pro Pro His Thr Lys
210 215 220

Pro Thr Glu Asn Arg Asn Ser Ser Arg Asp Lys Cys Thr Ser Lys Lys
225 230 235 240

Lys Ser His Thr Gln Ser Gln Ser Gln His Leu Gln Ala Lys Pro Thr
245 250 255

Thr Leu Ser Leu Pro Leu Thr Pro Glu Ser Pro Asn Asp Pro Lys Gly
260 265 270

Ser Pro Phe Glu Asn Lys Thr Ile Glu Arg Thr Leu Ser Val Glu Leu
275 280 285

Ser Gly Thr Ala Gly Leu Thr Pro Pro Thr Thr Pro Pro His Lys Ala
290 295 300

Asn Gln Asp Asn Pro Phe Arg Ala Ser Pro Lys Leu Lys Ser Ser Cys
305 310 315 320

Lys Thr Val Val Pro Pro Pro Ser Lys Lys Pro Arg Tyr Ser Glu Ser
325 330 335

Ser Gly Thr Gln Gly Asn Asn Ser Thr Lys Lys Gly Pro Glu Gln Ser
340 345 350

Glu Leu Tyr Ala Gln Leu Ser Lys Ser Ser Val Leu Thr Gly Gly His

```
        355                 360                 365

Glu Glu Arg Lys Thr Lys Arg Pro Ser Leu Arg Leu Phe Gly Asp His
    370                 375                 380

Asp Tyr Cys Gln Ser Ile Asn Ser Lys Thr Glu Ile Leu Ile Asn Ile
385                 390                 395                 400

Ser Gln Glu Leu Gln Asp Ser Arg Gln Leu Glu Asn Lys Asp Val Ser
                405                 410                 415

Ser Asp Trp Gln Gly Gln Ile Cys Ser Ser Thr Asp Ser Asp Gln Cys
            420                 425                 430

Tyr Leu Arg Glu Thr Leu Glu Ala Ser Lys Gln Val Ser Pro Cys Ser
        435                 440                 445

Thr Arg Lys Gln Leu Gln Asp Gln Glu Ile Arg Ala Glu Leu Asn Lys
    450                 455                 460

His Phe Gly His Pro Ser Gln Ala Val Phe Asp Asp Glu Ala Asp Lys
465                 470                 475                 480

Thr Gly Glu Leu Arg Asp Ser Asp Phe Ser Asn Glu Gln Phe Ser Lys
                485                 490                 495

Leu Pro Met Phe Ile Asn Ser Gly Leu Ala Met Asp Gly Leu Phe Asp
            500                 505                 510

Asp Ser Glu Asp Glu Ser Asp Lys Leu Ser Tyr Pro Trp Asp Gly Thr
        515                 520                 525

Gln Ser Tyr Ser Leu Phe Asn Val Ser Pro Ser Cys Ser Ser Phe Asn
    530                 535                 540

Ser Pro Cys Arg Asp Ser Val Ser Pro Pro Lys Ser Leu Phe Ser Gln
545                 550                 555                 560

Arg Pro Gln Arg Met Arg Ser Arg Ser Arg Ser Phe Ser Arg His Arg
                565                 570                 575

Ser Cys Ser Arg Ser Pro Tyr Ser Arg Ser Arg Ser Arg Ser Pro Gly
            580                 585                 590

Ser Arg Ser Ser Ser Arg Ser Cys Tyr Tyr Tyr Glu Ser Ser His Tyr
        595                 600                 605

Arg His Arg Thr His Arg Asn Ser Pro Leu Tyr Val Arg Ser Arg Ser
    610                 615                 620

Arg Ser Pro Tyr Ser Arg Arg Pro Arg Tyr Asp Ser Tyr Glu Glu Tyr
```

625 630 635 640

Gln His Glu Arg Leu Lys Arg Glu Glu Tyr Arg Arg Glu Tyr Glu Lys
645 650 655

Arg Glu Ser Glu Arg Ala Lys Gln Arg Glu Arg Gln Arg Gln Lys Ala
660 665 670

Ile Glu Glu Arg Arg Val Ile Tyr Val Gly Lys Ile Arg Pro Asp Thr
675 680 685

Thr Arg Thr Glu Leu Arg Asp Arg Phe Glu Val Phe Gly Glu Ile Glu
690 695 700

Glu Cys Thr Val Asn Leu Arg Asp Asp Gly Asp Ser Tyr Gly Phe Ile
705 710 715 720

Thr Tyr Arg Tyr Thr Cys Asp Ala Phe Ala Ala Leu Glu Asn Gly Tyr
725 730 735

Thr Leu Arg Arg Ser Asn Glu Thr Asp Phe Glu Leu Tyr Phe Cys Gly
740 745 750

Arg Lys Gln Phe Phe Lys Ser Asn Tyr Ala Asp Leu Asp Ser Asn Ser
755 760 765

Asp Asp Phe Asp Pro Ala Ser Thr Lys Ser Lys Tyr Asp Ser Leu Asp
770 775 780

Phe Asp Ser Leu Leu Lys Glu Ala Gln Arg Ser Leu Arg Arg
785 790 795

<210> 284
<211> 1023
<212> PRT
<213> Homo sapiens

<400> 284

Met Ala Gly Asn Asp Cys Gly Ala Leu Leu Asp Glu Glu Leu Ser Ser
1 5 10 15

Phe Phe Leu Asn Tyr Leu Ala Asp Thr Gln Gly Gly Gly Ser Gly Glu
20 25 30

Glu Gln Leu Tyr Ala Asp Phe Pro Glu Leu Asp Leu Ser Gln Leu Asp
35 40 45

Ala Ser Asp Phe Asp Ser Ala Thr Cys Phe Gly Glu Leu Gln Trp Cys
50 55 60

Pro Glu Asn Ser Glu Thr Glu Pro Asn Gln Tyr Ser Pro Asp Asp Ser
65 70 75 80

```
Glu Leu Phe Gln Ile Asp Ser Glu Asn Glu Ala Leu Leu Ala Glu Leu
                85                  90                  95

Thr Lys Thr Leu Asp Asp Ile Pro Glu Asp Asp Val Gly Leu Ala Ala
            100                 105                 110

Phe Pro Ala Leu Asp Gly Gly Asp Ala Leu Ser Cys Thr Ser Ala Ser
        115                 120                 125

Pro Ala Pro Ser Ser Ala Pro Pro Ser Pro Ala Pro Glu Lys Pro Ser
    130                 135                 140

Ala Pro Ala Pro Glu Val Asp Glu Leu Ser Leu Leu Gln Lys Leu Leu
145                 150                 155                 160

Leu Ala Thr Ser Tyr Pro Thr Ser Ser Ser Asp Thr Gln Lys Glu Gly
                165                 170                 175

Thr Ala Trp Arg Gln Ala Gly Leu Arg Ser Lys Ser Gln Arg Pro Cys
            180                 185                 190

Val Lys Ala Asp Ser Thr Gln Asp Lys Lys Ala Pro Met Met Gln Ser
        195                 200                 205

Gln Ser Arg Ser Cys Thr Glu Leu His Lys His Leu Thr Ser Ala Gln
    210                 215                 220

Cys Cys Leu Gln Asp Arg Gly Leu Gln Pro Pro Cys Leu Gln Ser Pro
225                 230                 235                 240

Arg Leu Pro Ala Lys Glu Asp Lys Glu Pro Gly Glu Asp Cys Pro Ser
                245                 250                 255

Pro Gln Pro Ala Pro Ala Ser Pro Arg Asp Ser Leu Ala Leu Gly Arg
            260                 265                 270

Ala Asp Pro Gly Ala Pro Val Ser Gln Glu Asp Met Gln Ala Met Val
        275                 280                 285

Gln Leu Ile Arg Tyr Met His Thr Tyr Cys Leu Pro Gln Arg Lys Leu
    290                 295                 300

Pro Pro Gln Thr Pro Glu Pro Leu Pro Lys Ala Cys Ser Asn Pro Ser
305                 310                 315                 320

Gln Gln Val Arg Ser Arg Pro Trp Ser Arg His His Ser Lys Ala Ser
                325                 330                 335

Trp Ala Glu Phe Ser Ile Leu Arg Glu Leu Leu Ala Gln Asp Val Leu
            340                 345                 350
```

```
Cys Asp Val Ser Lys Pro Tyr Arg Leu Ala Thr Pro Val Tyr Ala Ser
        355                 360                 365

Leu Thr Pro Arg Ser Arg Pro Arg Pro Pro Lys Asp Ser Gln Ala Ser
    370                 375                 380

Pro Gly Arg Pro Ser Ser Val Glu Glu Val Arg Ile Ala Ala Ser Pro
385                 390                 395                 400

Lys Ser Thr Gly Pro Arg Pro Ser Leu Arg Pro Leu Arg Leu Glu Val
                405                 410                 415

Lys Arg Glu Val Arg Arg Pro Ala Arg Leu Gln Gln Gln Glu Glu Glu
            420                 425                 430

Asp Glu Glu Glu Glu Glu Glu Glu Glu Glu Glu Glu Lys Glu Glu Glu
        435                 440                 445

Glu Glu Trp Gly Arg Lys Arg Pro Gly Arg Gly Leu Pro Trp Thr Lys
    450                 455                 460

Leu Gly Arg Lys Leu Glu Ser Ser Val Cys Pro Val Arg Arg Ser Arg
465                 470                 475                 480

Arg Leu Asn Pro Glu Leu Gly Pro Trp Leu Thr Phe Ala Asp Glu Pro
                485                 490                 495

Leu Val Pro Ser Glu Pro Gln Gly Ala Leu Pro Ser Leu Cys Leu Ala
            500                 505                 510

Pro Lys Ala Tyr Asp Val Glu Arg Glu Leu Gly Ser Pro Thr Asp Glu
        515                 520                 525

Asp Ser Gly Gln Asp Gln Gln Leu Leu Arg Gly Pro Gln Ile Pro Ala
    530                 535                 540

Leu Glu Ser Pro Cys Glu Ser Gly Cys Gly Asp Met Asp Glu Asp Pro
545                 550                 555                 560

Ser Cys Pro Gln Leu Pro Pro Arg Asp Ser Pro Arg Cys Leu Met Leu
                565                 570                 575

Ala Leu Ser Gln Ser Asp Pro Thr Phe Gly Lys Lys Ser Phe Glu Gln
            580                 585                 590

Thr Leu Thr Val Glu Leu Cys Gly Thr Ala Gly Leu Thr Pro Pro Thr
        595                 600                 605

Thr Pro Pro Tyr Lys Pro Thr Glu Glu Asp Pro Phe Lys Pro Asp Ile
    610                 615                 620
```

```
Lys His Ser Leu Gly Lys Glu Ile Ala Leu Ser Leu Pro Ser Pro Glu
625                 630                 635                 640

Gly Leu Ser Leu Lys Ala Thr Pro Gly Ala Ala His Lys Leu Pro Lys
                645                 650                 655

Lys His Pro Glu Arg Ser Glu Leu Leu Ser His Leu Arg His Ala Thr
            660                 665                 670

Ala Gln Pro Ala Ser Gln Ala Gly Gln Lys Arg Pro Phe Ser Cys Ser
        675                 680                 685

Phe Gly Asp His Asp Tyr Cys Gln Val Leu Arg Pro Glu Gly Val Leu
    690                 695                 700

Gln Arg Lys Val Leu Arg Ser Trp Glu Pro Ser Gly Val His Leu Glu
705                 710                 715                 720

Asp Trp Pro Gln Gln Gly Ala Pro Trp Ala Glu Ala Gln Ala Pro Gly
                725                 730                 735

Arg Glu Glu Asp Arg Ser Cys Asp Ala Gly Ala Pro Pro Lys Asp Ser
            740                 745                 750

Thr Leu Leu Arg Asp His Glu Ile Arg Ala Ser Leu Thr Lys His Phe
        755                 760                 765

Gly Leu Leu Glu Thr Ala Leu Glu Glu Glu Asp Leu Ala Ser Cys Lys
    770                 775                 780

Ser Pro Glu Tyr Asp Thr Val Phe Glu Asp Ser Ser Ser Ser Ser Gly
785                 790                 795                 800

Glu Ser Ser Phe Leu Pro Glu Glu Glu Glu Glu Glu Gly Glu Glu Glu
                805                 810                 815

Glu Glu Asp Asp Glu Glu Glu Asp Ser Gly Val Ser Pro Thr Cys Ser
            820                 825                 830

Asp His Cys Pro Tyr Gln Ser Pro Pro Ser Lys Ala Asn Arg Gln Leu
        835                 840                 845

Cys Ser Arg Ser Arg Ser Ser Ser Gly Ser Ser Pro Cys His Ser Trp
    850                 855                 860

Ser Pro Ala Thr Arg Arg Asn Phe Arg Cys Glu Ser Arg Gly Pro Cys
865                 870                 875                 880

Ser Asp Arg Thr Pro Ser Ile Arg His Ala Arg Lys Arg Arg Glu Lys
                885                 890                 895
```

Ala Ile Gly Glu Gly Arg Val Val Tyr Ile Gln Asn Leu Ser Ser Asp
900 905 910

Met Ser Ser Arg Glu Leu Lys Arg Arg Phe Glu Val Phe Gly Glu Ile
915 920 925

Glu Glu Cys Glu Val Leu Thr Arg Asn Arg Arg Gly Glu Lys Tyr Gly
930 935 940

Phe Ile Thr Tyr Arg Cys Ser Glu His Ala Ala Leu Ser Leu Thr Lys
945 950 955 960

Gly Ala Ala Leu Arg Lys Arg Asn Glu Pro Ser Phe Gln Leu Ser Tyr
965 970 975

Gly Gly Leu Arg His Phe Cys Trp Pro Arg Tyr Thr Asp Tyr Asp Ser
980 985 990

Asn Ser Glu Glu Ala Leu Pro Ala Ser Gly Lys Ser Lys Tyr Glu Ala
995 1000 1005

Met Asp Phe Asp Ser Leu Leu Lys Glu Ala Gln Gln Ser Leu His
1010 1015 1020

<210> 285
<211> 1664
<212> PRT
<213> Homo sapiens

<400> 285

Met Ala Ala Arg Arg Gly Arg Arg Asp Gly Val Ala Pro Pro Pro Ser
1 5 10 15

Gly Gly Pro Gly Pro Asp Pro Gly Gly Gly Ala Arg Gly Ser Gly Trp
20 25 30

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

Gly Glu Gln Val Leu Leu His Glu Glu Ala Gly Asp Ser Gly Phe Val
50 55 60

Ser Leu Ser Arg Leu Gly Pro Ser Leu Arg Asp Lys Asp Leu Glu Met
65 70 75 80

Glu Glu Leu Met Leu Gln Asp Glu Thr Leu Leu Gly Thr Met Gln Ser
85 90 95

Tyr Met Asp Ala Ser Leu Ile Ser Leu Ile Glu Asp Phe Gly Ser Leu
100 105 110

```
Gly Glu Ser Arg Leu Ser Leu Glu Asp Gln Asn Glu Val Ser Leu Leu
        115                 120                 125

Thr Ala Leu Thr Glu Ile Leu Asp Asn Ala Asp Ser Glu Asn Leu Ser
    130                 135                 140

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

Gly Ser Ser Leu His Lys Leu Leu Thr Leu Ser Arg Thr Pro Pro Glu
                165                 170                 175

Arg Asp Leu Ile Thr Pro Val Asp Pro Leu Gly Pro Ser Thr Gly Ser
            180                 185                 190

Ser Arg Gly Ser Gly Val Glu Met Ser Leu Pro Asp Pro Ser Trp Asp
        195                 200                 205

Phe Ser Pro Pro Ser Phe Leu Glu Thr Ser Ser Pro Lys Leu Pro Ser
    210                 215                 220

Trp Arg Pro Pro Arg Ser Arg Pro Arg Trp Gly Gln Ser Pro Pro Pro
225                 230                 235                 240

Gln Gln Arg Ser Asp Gly Glu Glu Glu Glu Glu Val Ala Ser Phe Ser
                245                 250                 255

Gly Gln Ile Leu Ala Gly Glu Leu Asp Asn Cys Val Ser Ser Ile Pro
            260                 265                 270

Asp Phe Pro Met His Leu Ala Cys Pro Glu Glu Glu Asp Lys Ala Thr
        275                 280                 285

Ala Ala Glu Met Ala Val Pro Ala Ala Gly Asp Glu Ser Ile Ser Ser
    290                 295                 300

Leu Ser Glu Leu Val Arg Ala Met His Pro Tyr Cys Leu Pro Asn Leu
305                 310                 315                 320

Thr His Leu Ala Ser Leu Glu Asp Glu Leu Gln Glu Gln Pro Asp Asp
                325                 330                 335

Leu Thr Leu Pro Glu Gly Cys Val Val Leu Glu Ile Val Gly Gln Ala
            340                 345                 350

Ala Thr Ala Gly Asp Asp Leu Glu Ile Pro Val Val Val Arg Gln Val
        355                 360                 365

Ser Pro Gly Pro Arg Pro Val Leu Leu Asp Asp Ser Leu Glu Thr Ser
    370                 375                 380
```

```
Ser Ala Leu Gln Leu Leu Met Pro Thr Leu Glu Ser Glu Thr Glu Ala
385                 390                 395                 400

Ala Val Pro Lys Val Thr Leu Cys Ser Glu Lys Glu Gly Leu Ser Leu
                405                 410                 415

Asn Ser Glu Glu Lys Leu Asp Ser Ala Cys Leu Leu Lys Pro Arg Glu
            420                 425                 430

Val Val Glu Pro Val Val Pro Lys Glu Pro Gln Asn Pro Pro Ala Asn
        435                 440                 445

Ala Ala Pro Gly Ser Gln Arg Ala Arg Lys Gly Arg Lys Lys Lys Ser
    450                 455                 460

Lys Glu Gln Pro Ala Ala Cys Val Glu Gly Tyr Ala Arg Arg Leu Arg
465                 470                 475                 480

Ser Ser Ser Arg Gly Gln Ser Thr Val Gly Thr Glu Val Thr Ser Gln
                485                 490                 495

Val Asp Asn Leu Gln Lys Gln Pro Gln Glu Glu Leu Gln Lys Glu Ser
            500                 505                 510

Gly Pro Leu Gln Gly Lys Gly Lys Pro Arg Ala Trp Ala Arg Ala Trp
        515                 520                 525

Ala Ala Ala Leu Glu Asn Ser Ser Pro Lys Asn Leu Glu Arg Ser Ala
    530                 535                 540

Gly Gln Ser Ser Pro Ala Lys Glu Gly Pro Leu Asp Leu Tyr Pro Lys
545                 550                 555                 560

Leu Ala Asp Thr Ile Gln Thr Asn Pro Ile Pro Thr His Leu Ser Leu
                565                 570                 575

Val Asp Ser Ala Gln Ala Ser Pro Met Pro Val Asp Ser Val Glu Ala
            580                 585                 590

Asp Pro Thr Ala Val Gly Pro Val Leu Ala Gly Pro Val Pro Val Asp
        595                 600                 605

Pro Gly Leu Val Asp Leu Ala Ser Thr Ser Ser Glu Leu Val Glu Pro
    610                 615                 620

Leu Pro Ala Glu Pro Val Leu Ile Asn Pro Val Leu Ala Asp Ser Ala
625                 630                 635                 640

Ala Val Asp Pro Ala Val Val Pro Ile Ser Asp Asn Leu Pro Pro Val
                645                 650                 655
```

```
Asp Ala Val Pro Ser Gly Pro Ala Pro Val Asp Leu Ala Leu Val Asp
            660                 665                 670

Pro Val Pro Asn Asp Leu Thr Pro Val Asp Pro Val Leu Val Lys Ser
        675                 680                 685

Arg Pro Thr Asp Pro Arg Arg Gly Ala Val Ser Ser Ala Leu Gly Gly
    690                 695                 700

Ser Ala Pro Gln Leu Leu Val Glu Ser Glu Ser Leu Asp Pro Pro Lys
705                 710                 715                 720

Thr Ile Ile Pro Glu Val Lys Glu Val Val Asp Ser Leu Lys Ile Glu
                725                 730                 735

Ser Gly Thr Ser Ala Thr Thr His Glu Ala Arg Pro Arg Pro Leu Ser
            740                 745                 750

Leu Ser Glu Tyr Arg Arg Arg Arg Gln Gln Arg Gln Ala Glu Thr Glu
        755                 760                 765

Glu Arg Ser Pro Gln Pro Pro Thr Gly Lys Trp Pro Ser Leu Pro Glu
    770                 775                 780

Thr Pro Thr Gly Leu Ala Asp Ile Pro Cys Leu Val Ile Pro Pro Ala
785                 790                 795                 800

Pro Ala Lys Lys Thr Ala Leu Gln Arg Ser Pro Glu Thr Pro Leu Glu
                805                 810                 815

Ile Cys Leu Val Pro Val Gly Pro Ser Pro Ala Ser Pro Ser Pro Glu
            820                 825                 830

Pro Pro Val Ser Lys Pro Val Ala Ser Ser Pro Thr Glu Gln Val Pro
        835                 840                 845

Ser Gln Glu Met Pro Leu Leu Ala Arg Pro Ser Pro Pro Val Gln Ser
    850                 855                 860

Val Ser Pro Ala Val Pro Thr Pro Pro Ser Met Ser Ala Ala Leu Pro
865                 870                 875                 880

Phe Pro Ala Gly Gly Leu Gly Met Pro Pro Ser Leu Pro Pro Pro Pro
                885                 890                 895

Leu Gln Pro Pro Ser Leu Pro Leu Ser Met Gly Pro Val Leu Pro Asp
            900                 905                 910

Pro Phe Thr His Tyr Ala Pro Leu Pro Ser Trp Pro Cys Tyr Pro His
        915                 920                 925
```

```
Val Ser Pro Ser Gly Tyr Pro Cys Leu Pro Pro Pro Thr Val Pro
    930                 935                 940

Leu Val Ser Gly Thr Pro Gly Ala Tyr Ala Val Pro Pro Thr Cys Ser
945                 950                 955                 960

Val Pro Trp Ala Pro Pro Pro Ala Pro Val Ser Pro Tyr Ser Ser Thr
                965                 970                 975

Cys Thr Tyr Gly Pro Leu Gly Trp Gly Pro Gly Pro Gln His Ala Pro
            980                 985                 990

Phe Trp Ser Thr Val Pro Pro Pro  Pro Leu Pro Pro Ala  Ser Ile Gly
        995                 1000                1005

Arg Ala  Val Pro Gln Pro Lys  Met Glu Ser Arg Gly  Thr Pro Ala
    1010                1015                1020

Gly Pro  Pro Glu Asn Val Leu  Pro Leu Ser Met Ala  Pro Pro Leu
    1025                1030                1035

Ser Leu  Gly Leu Pro Gly His  Gly Ala Pro Gln Thr  Glu Pro Thr
    1040                1045                1050

Lys Val  Glu Val Lys Pro Val  Pro Ala Ser Pro His  Pro Lys His
    1055                1060                1065

Lys Val  Ser Ala Leu Val Gln  Ser Pro Gln Met Lys  Ala Leu Ala
    1070                1075                1080

Cys Val  Ser Ala Glu Gly Val  Thr Val Glu Glu Pro  Ala Ser Glu
    1085                1090                1095

Arg Leu  Lys Pro Glu Thr Gln  Glu Thr Arg Pro Arg  Glu Lys Pro
    1100                1105                1110

Pro Leu  Pro Ala Thr Lys Ala  Val Pro Thr Pro Arg  Gln Ser Thr
    1115                1120                1125

Val Pro  Lys Leu Pro Ala Val  His Pro Ala Arg Leu  Arg Lys Leu
    1130                1135                1140

Ser Phe  Leu Pro Thr Pro Arg  Thr Gln Gly Ser Glu  Asp Val Val
    1145                1150                1155

Gln Ala  Phe Ile Ser Glu Ile  Gly Ile Glu Ala Ser  Asp Leu Ser
    1160                1165                1170

Ser Leu  Leu Glu Gln Phe Glu  Lys Ser Glu Ala Lys  Lys Glu Cys
    1175                1180                1185
```

```
Pro Pro  Pro Ala Pro Ala Asp  Ser Leu Ala Val Gly  Asn Ser Gly
    1190                1195                1200

Gly Val  Asp Ile Pro Gln Glu  Lys Arg Pro Leu Asp  Arg Leu Gln
    1205                1210                1215

Ala Pro  Glu Leu Ala Asn Val  Ala Gly Leu Thr Pro  Pro Ala Thr
    1220                1225                1230

Pro Pro  His Gln Leu Trp Lys  Pro Leu Ala Ala Val  Ser Leu Leu
    1235                1240                1245

Ala Lys  Ala Lys Ser Pro Lys  Ser Thr Ala Gln Glu  Gly Thr Leu
    1250                1255                1260

Lys Pro  Glu Gly Val Thr Glu  Ala Lys His Pro Ala  Ala Val Arg
    1265                1270                1275

Leu Gln  Glu Gly Val His Gly  Pro Ser Arg Val His  Val Gly Ser
    1280                1285                1290

Gly Asp  His Asp Tyr Cys Val  Arg Ser Arg Thr Pro  Pro Lys Lys
    1295                1300                1305

Met Pro  Ala Leu Val Ile Pro  Glu Val Gly Ser Arg  Trp Asn Val
    1310                1315                1320

Lys Arg  His Gln Asp Ile Thr  Ile Lys Pro Val Leu  Ser Leu Gly
    1325                1330                1335

Pro Ala  Ala Pro Pro Pro Pro  Cys Ile Ala Ala Ser  Arg Glu Pro
    1340                1345                1350

Leu Asp  His Arg Thr Ser Ser  Glu Gln Ala Asp Pro  Ser Ala Pro
    1355                1360                1365

Cys Leu  Ala Pro Ser Ser Leu  Leu Ser Pro Glu Ala  Ser Pro Cys
    1370                1375                1380

Arg Asn  Asp Met Asn Thr Arg  Thr Pro Pro Glu Pro  Ser Ala Lys
    1385                1390                1395

Gln Arg  Ser Met Arg Cys Tyr  Arg Lys Ala Cys Arg  Ser Ala Ser
    1400                1405                1410

Pro Ser  Ser Gln Gly Trp Gln  Gly Arg Arg Gly Arg  Asn Ser Arg
    1415                1420                1425

Ser Val  Ser Ser Gly Ser Asn  Arg Thr Ser Glu Ala  Ser Ser Ser
    1430                1435                1440
```

```
Ser Ser  Ser Ser Ser Ser Ser  Ser Arg Ser Arg Ser  Arg Ser Leu
    1445                1450                1455

Ser Pro  Pro His Lys Arg Trp  Arg Arg Ser Ser Cys  Ser Ser Ser
    1460                1465                1470

Gly Arg  Ser Arg Arg Cys Ser  Ser Ser Ser Ser Ser  Ser Ser Ser
    1475                1480                1485

Ser Ser  Ser Ser Ser Ser Ser  Ser Ser Ser Ser Arg  Ser Arg Ser
    1490                1495                1500

Arg Ser  Pro Ser Pro Arg Arg  Arg Ser Asp Arg Arg  Arg Arg Tyr
    1505                1510                1515

Ser Ser  Tyr Arg Ser His Asp  His Tyr Gln Arg Gln  Arg Val Leu
    1520                1525                1530

Gln Lys  Glu Arg Ala Ile Glu  Glu Arg Arg Val Val  Phe Ile Gly
    1535                1540                1545

Lys Ile  Pro Gly Arg Met Thr  Arg Ser Glu Leu Lys  Gln Arg Phe
    1550                1555                1560

Ser Val  Phe Gly Glu Ile Glu  Glu Cys Thr Ile His  Phe Arg Val
    1565                1570                1575

Gln Gly  Asp Asn Tyr Gly Phe  Val Thr Tyr Arg Tyr  Ala Glu Glu
    1580                1585                1590

Ala Phe  Ala Ala Ile Glu Ser  Gly His Lys Leu Arg  Gln Ala Asp
    1595                1600                1605

Glu Gln  Pro Phe Asp Leu Cys  Phe Gly Gly Arg Arg  Gln Phe Cys
    1610                1615                1620

Lys Arg  Ser Tyr Ser Asp Leu  Asp Ser Asn Arg Glu  Asp Phe Asp
    1625                1630                1635

Pro Ala  Pro Val Lys Ser Lys  Phe Asp Ser Leu Asp  Phe Asp Thr
    1640                1645                1650

Leu Leu  Lys Gln Ala Gln Lys  Asn Leu Arg Arg
    1655                1660
```

<210> 286
<211> 1581
<212> PRT
<213> Homo sapiens

<400> 286

```
Met Lys Ala Gln Gly Glu Thr Glu Glu Ser Glu Lys Leu Ser Lys Met
1               5                  10                  15

Ser Ser Leu Leu Glu Arg Leu His Ala Lys Phe Asn Gln Asn Arg Pro
            20                  25                  30

Trp Ser Glu Thr Ile Lys Leu Val Arg Gln Val Met Glu Lys Arg Val
        35                  40                  45

Val Met Ser Ser Gly Gly His Gln His Leu Val Ser Cys Leu Glu Thr
    50                  55                  60

Leu Gln Lys Ala Leu Lys Val Thr Ser Leu Pro Ala Met Thr Asp Arg
65                  70                  75                  80

Leu Glu Ser Ile Ala Arg Gln Asn Gly Leu Gly Ser His Leu Ser Ala
                85                  90                  95

Ser Gly Thr Glu Cys Tyr Ile Thr Ser Asp Met Phe Tyr Val Glu Val
            100                 105                 110

Gln Leu Asp Pro Ala Gly Gln Leu Cys Asp Val Lys Val Ala His His
        115                 120                 125

Gly Glu Asn Pro Val Ser Cys Pro Glu Leu Val Gln Gln Leu Arg Glu
    130                 135                 140

Lys Asn Phe Asp Glu Phe Ser Lys His Leu Lys Gly Leu Val Asn Leu
145                 150                 155                 160

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

Leu Gln Ser Leu Glu Gln Asp Leu Ser Lys Met Ala Ile Met Tyr Trp
            180                 185                 190

Lys Ala Thr Asn Ala Gly Pro Leu Asp Lys Ile Leu His Gly Ser Val
        195                 200                 205

Gly Tyr Leu Thr Pro Arg Ser Gly Gly His Leu Met Asn Leu Lys Tyr
    210                 215                 220

Tyr Val Ser Pro Ser Asp Leu Leu Asp Asp Lys Thr Ala Ser Pro Ile
225                 230                 235                 240

Ile Leu His Glu Asn Asn Val Ser Arg Ser Leu Gly Met Asn Ala Ser
                245                 250                 255

Val Thr Ile Glu Gly Thr Ser Ala Val Tyr Lys Leu Pro Ile Ala Pro
            260                 265                 270
```

```
Leu Ile Met Gly Ser His Pro Val Asp Asn Lys Trp Thr Pro Ser Phe
        275                 280                 285

Ser Ser Ile Thr Ser Ala Asn Ser Val Asp Leu Pro Ala Cys Phe Phe
    290                 295                 300

Leu Lys Phe Pro Gln Pro Ile Pro Val Ser Arg Ala Phe Val Gln Lys
305                 310                 315                 320

Leu Gln Asn Cys Thr Gly Ile Pro Leu Phe Glu Thr Gln Pro Thr Tyr
                325                 330                 335

Ala Pro Leu Tyr Glu Leu Ile Thr Gln Phe Glu Leu Ser Lys Asp Pro
            340                 345                 350

Asp Pro Ile Pro Leu Asn His Asn Met Arg Phe Tyr Ala Ala Leu Pro
        355                 360                 365

Gly Gln Gln His Cys Tyr Phe Leu Asn Lys Asp Ala Pro Leu Pro Asp
    370                 375                 380

Gly Arg Ser Leu Gln Gly Thr Leu Val Ser Lys Ile Thr Phe Gln His
385                 390                 395                 400

Pro Gly Arg Val Pro Leu Ile Leu Asn Leu Ile Arg His Gln Val Ala
                405                 410                 415

Tyr Asn Thr Leu Ile Gly Ser Cys Val Lys Arg Thr Ile Leu Lys Glu
            420                 425                 430

Asp Ser Pro Gly Leu Leu Gln Phe Glu Val Cys Pro Leu Ser Glu Ser
        435                 440                 445

Arg Phe Ser Val Ser Phe Gln His Pro Val Asn Asp Ser Leu Val Cys
    450                 455                 460

Val Val Met Asp Val Gln Asp Ser Thr His Val Ser Cys Lys Leu Tyr
465                 470                 475                 480

Lys Gly Leu Ser Asp Ala Leu Ile Cys Thr Asp Asp Phe Ile Ala Lys
                485                 490                 495

Val Val Gln Arg Cys Met Ser Ile Pro Val Thr Met Arg Ala Ile Arg
            500                 505                 510

Arg Lys Ala Glu Thr Ile Gln Ala Asp Thr Pro Ala Leu Ser Leu Ile
        515                 520                 525

Ala Glu Thr Val Glu Asp Met Val Lys Lys Asn Leu Pro Pro Ala Ser
    530                 535                 540
```

```
Ser Pro Gly Tyr Gly Met Thr Thr Gly Asn Asn Pro Met Ser Gly Thr
545                 550                 555                 560

Thr Thr Pro Thr Asn Thr Phe Pro Gly Gly Pro Ile Thr Thr Leu Phe
                565                 570                 575

Asn Met Ser Met Ser Ile Lys Asp Arg His Glu Ser Val Gly His Gly
            580                 585                 590

Glu Asp Phe Ser Lys Val Ser Gln Asn Pro Ile Leu Thr Ser Leu Leu
        595                 600                 605

Gln Ile Thr Gly Asn Gly Gly Ser Thr Ile Gly Ser Ser Pro Thr Pro
    610                 615                 620

Pro His His Thr Pro Pro Pro Val Ser Ser Met Ala Gly Asn Thr Lys
625                 630                 635                 640

Asn His Pro Met Leu Met Asn Leu Leu Lys Asp Asn Pro Ala Gln Asp
                645                 650                 655

Phe Ser Thr Leu Tyr Gly Ser Ser Pro Leu Glu Arg Gln Asn Ser Ser
            660                 665                 670

Ser Gly Ser Pro Arg Met Glu Ile Cys Ser Gly Ser Asn Lys Thr Lys
        675                 680                 685

Lys Lys Lys Ser Ser Arg Leu Pro Pro Glu Lys Pro Lys His Gln Thr
    690                 695                 700

Glu Asp Asp Phe Gln Arg Glu Leu Phe Ser Met Asp Val Asp Ser Gln
705                 710                 715                 720

Asn Pro Ile Phe Asp Val Asn Met Thr Ala Asp Thr Leu Asp Thr Pro
                725                 730                 735

His Ile Thr Pro Ala Pro Ser Gln Cys Ser Thr Pro Pro Thr Thr Tyr
            740                 745                 750

Pro Gln Pro Val Pro His Pro Gln Pro Ser Ile Gln Arg Met Val Arg
        755                 760                 765

Leu Ser Ser Ser Asp Ser Ile Gly Pro Asp Val Thr Asp Ile Leu Ser
    770                 775                 780

Asp Ile Ala Glu Glu Ala Ser Lys Leu Pro Ser Thr Ser Asp Asp Cys
785                 790                 795                 800

Pro Ala Ile Gly Thr Pro Leu Arg Asp Ser Ser Ser Ser Gly His Ser
                805                 810                 815
```

```
Gln Ser Thr Leu Phe Asp Ser Asp Val Phe Gln Thr Asn Asn Asn Glu
            820                 825                 830

Asn Pro Tyr Thr Asp Pro Ala Asp Leu Ile Ala Asp Ala Ala Gly Ser
        835                 840                 845

Pro Ser Ser Asp Ser Pro Thr Asn His Phe Phe His Asp Gly Val Asp
    850                 855                 860

Phe Asn Pro Asp Leu Leu Asn Ser Gln Ser Gln Ser Gly Phe Gly Glu
865                 870                 875                 880

Glu Tyr Phe Asp Glu Ser Ser Gln Ser Gly Asp Asn Asp Asp Phe Lys
                885                 890                 895

Gly Phe Ala Ser Gln Ala Leu Asn Thr Leu Gly Val Pro Met Leu Gly
            900                 905                 910

Gly Asp Asn Gly Glu Thr Lys Phe Lys Gly Asn Asn Gln Ala Asp Thr
        915                 920                 925

Val Asp Phe Ser Ile Ile Ser Val Ala Gly Lys Ala Leu Ala Pro Ala
    930                 935                 940

Asp Leu Met Glu His His Ser Gly Ser Gln Gly Pro Leu Leu Thr Thr
945                 950                 955                 960

Gly Asp Leu Gly Lys Glu Lys Thr Gln Lys Arg Val Lys Glu Gly Asn
                965                 970                 975

Gly Thr Ser Asn Ser Thr Leu Ser Gly Pro Gly Leu Asp Ser Lys Pro
            980                 985                 990

Gly Lys Arg Ser Arg Thr Pro Ser  Asn Asp Gly Lys Ser  Lys Asp Lys
        995                 1000                1005

Pro Pro  Lys Arg Lys Lys Ala  Asp Thr Glu Gly Lys  Ser Pro Ser
    1010                1015                1020

His Ser  Ser Ser Asn Arg Pro  Phe Thr Pro Pro Thr  Ser Thr Gly
    1025                1030                1035

Gly Ser  Lys Ser Pro Gly Ser  Ala Gly Arg Ser Gln  Thr Pro Pro
    1040                1045                1050

Gly Val  Ala Thr Pro Pro Ile  Pro Lys Ile Thr Ile  Gln Ile Pro
    1055                1060                1065

Lys Gly  Thr Val Met Val Gly  Lys Pro Ser Ser His  Ser Gln Tyr
    1070                1075                1080
```

```
Thr Ser  Ser Gly Ser Val Ser  Ser Ser Gly Ser Lys  Ser His His
    1085                1090                1095

Ser His  Ser Ser Ser Ser Ser  Ser Ser Ala Ser Thr  Ser Gly Lys
    1100                1105                1110

Met Lys  Ser Ser Lys Ser Glu  Gly Ser Ser Ser Ser  Lys Leu Ser
    1115                1120                1125

Ser Ser  Met Tyr Ser Ser Gln  Gly Ser Ser Gly Ser  Ser Gln Ser
    1130                1135                1140

Lys Asn  Ser Ser Gln Ser Gly  Gly Lys Pro Gly Ser  Ser Pro Ile
    1145                1150                1155

Thr Lys  His Gly Leu Ser Ser  Gly Ser Ser Ser Thr  Lys Met Lys
    1160                1165                1170

Pro Gln  Gly Lys Pro Ser Ser  Leu Met Asn Pro Ser  Leu Ser Lys
    1175                1180                1185

Pro Asn  Ile Ser Pro Ser His  Ser Arg Pro Pro Gly  Gly Ser Asp
    1190                1195                1200

Lys Leu  Ala Ser Pro Met Lys  Pro Val Pro Gly Thr  Pro Pro Ser
    1205                1210                1215

Ser Lys  Ala Lys Ser Pro Ile  Ser Ser Gly Ser Gly  Gly Ser His
    1220                1225                1230

Met Ser  Gly Thr Ser Ser Ser  Ser Gly Met Lys Ser  Ser Ser Gly
    1235                1240                1245

Leu Gly  Ser Ser Gly Ser Leu  Ser Gln Lys Thr Pro  Pro Ser Ser
    1250                1255                1260

Asn Ser  Cys Thr Ala Ser Ser  Ser Ser Phe Ser Ser  Ser Gly Ser
    1265                1270                1275

Ser Met  Ser Ser Ser Gln Asn  Gln His Gly Ser Ser  Lys Gly Lys
    1280                1285                1290

Ser Pro  Ser Arg Asn Lys Lys  Pro Ser Leu Thr Ala  Val Ile Asp
    1295                1300                1305

Lys Leu  Lys His Gly Val Val  Thr Ser Gly Pro Gly  Gly Glu Asp
    1310                1315                1320

Pro Leu  Asp Gly Gln Met Gly  Val Ser Thr Asn Ser  Ser Ser His
    1325                1330                1335
```

```
Pro Met  Ser Ser Lys His Asn  Met Ser Gly Gly Glu  Phe Gln Gly
    1340                1345                1350

Lys Arg  Glu Lys Ser Asp Lys  Asp Lys Ser Lys Val  Ser Thr Ser
    1355                1360                1365

Gly Ser  Ser Val Asp Ser Ser  Lys Lys Thr Ser Glu  Ser Lys Asn
    1370                1375                1380

Val Gly  Ser Thr Gly Val Ala  Lys Ile Ile Ile Ser  Lys His Asp
    1385                1390                1395

Gly Gly  Ser Pro Ser Ile Lys  Ala Lys Val Thr Leu  Gln Lys Pro
    1400                1405                1410

Gly Glu  Ser Ser Gly Glu Gly  Leu Arg Pro Gln Met  Ala Ser Ser
    1415                1420                1425

Lys Asn  Tyr Gly Ser Pro Leu  Ile Ser Gly Ser Thr  Pro Lys His
    1430                1435                1440

Glu Arg  Gly Ser Pro Ser His  Ser Lys Ser Pro Ala  Tyr Thr Pro
    1445                1450                1455

Gln Asn  Leu Asp Ser Glu Ser  Glu Ser Gly Ser Ser  Ile Ala Glu
    1460                1465                1470

Lys Ser  Tyr Gln Asn Ser Pro  Ser Ser Asp Asp Gly  Ile Arg Pro
    1475                1480                1485

Leu Pro  Glu Tyr Ser Thr Glu  Lys His Lys Lys His  Lys Lys Glu
    1490                1495                1500

Lys Lys  Lys Val Lys Asp Lys  Asp Arg Asp Arg Asp  Arg Asp Lys
    1505                1510                1515

Asp Arg  Asp Lys Lys Lys Ser  His Ser Ile Lys Pro  Glu Ser Trp
    1520                1525                1530

Ser Lys  Ser Pro Ile Ser Ser  Asp Gln Ser Leu Ser  Met Thr Ser
    1535                1540                1545

Asn Thr  Ile Leu Ser Ala Asp  Arg Pro Ser Arg Leu  Ser Pro Asp
    1550                1555                1560

Phe Met  Ile Gly Glu Glu Asp  Asp Asp Leu Met Asp  Val Ala Leu
    1565                1570                1575

Ile Gly  Asn
    1580
```

<210> 287
<211> 2063
<212> PRT
<213> Homo sapiens

<400> 287

Met Val Leu Asp Asp Leu Pro Asn Leu Glu Asp Ile Tyr Thr Ser Leu
1 5 10 15

Cys Ser Ser Thr Met Glu Asp Ser Glu Met Asp Phe Asp Ser Gly Leu
20 25 30

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

Phe Val Ala Phe Lys Gly Asn Ile Asp Asp Lys Asp Phe Lys Trp Lys
50 55 60

Leu Asp Ala Ile Leu Lys Asn Val Pro Asn Leu Leu His Met Glu Ser
65 70 75 80

Ser Lys Leu Lys Val Gln Lys Val Glu Pro Trp Asn Ser Val Arg Val
85 90 95

Thr Phe Asn Ile Pro Arg Glu Ala Ala Glu Arg Leu Arg Ile Leu Ala
100 105 110

Gln Ser Asn Asn Gln Gln Leu Arg Asp Leu Gly Ile Leu Ser Val Gln
115 120 125

Ile Glu Gly Glu Gly Ala Ile Asn Leu Ala Leu Ala Gln Asn Arg Ser
130 135 140

Gln Asp Val Arg Met Asn Gly Pro Met Gly Ala Gly Asn Ser Val Arg
145 150 155 160

Met Glu Ala Gly Phe Pro Met Ala Ser Gly Pro Gly Ile Ile Arg Met
165 170 175

Asn Asn Pro Ala Thr Val Met Ile Pro Pro Gly Gly Asn Val Ser Ser
180 185 190

Ser Met Met Ala Pro Gly Pro Asn Pro Glu Leu Gln Pro Arg Thr Pro
195 200 205

Arg Pro Ala Ser Gln Ser Asp Ala Met Asp Pro Leu Leu Ser Gly Leu
210 215 220

His Ile Gln Gln Gln Ser His Pro Ser Gly Ser Leu Ala Pro Pro His
225 230 235 240

His Pro Met Gln Pro Val Ser Val Asn Arg Gln Met Asn Pro Ala Asn

245 250 255

Phe Pro Gln Leu Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln
260 265 270

Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln Leu Gln Ala
275 280 285

Arg Pro Pro Gln Gln His Gln Gln Gln Gln Pro Gln Gly Ile Arg Pro
290 295 300

Gln Phe Thr Ala Pro Thr Gln Val Pro Val Pro Pro Gly Trp Asn Gln
305 310 315 320

Leu Pro Ser Gly Ala Leu Gln Pro Pro Pro Ala Gln Gly Ser Leu Gly
325 330 335

Thr Met Thr Ala Asn Gln Gly Trp Lys Lys Ala Pro Leu Pro Gly Pro
340 345 350

Met Gln Gln Gln Leu Gln Ala Arg Pro Ser Leu Ala Thr Val Gln Thr
355 360 365

Pro Ser His Pro Pro Pro Pro Tyr Pro Phe Gly Ser Gln Gln Ala Ser
370 375 380

Gln Ala His Thr Asn Phe Pro Gln Met Ser Asn Pro Gly Gln Phe Thr
385 390 395 400

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

Pro Leu Gln Gln Pro His Leu Thr Asn Lys Ser Pro Ala Ser Ser Pro
420 425 430

Ser Ser Phe Gln Gln Gly Ser Pro Ala Ser Ser Pro Thr Val Asn Gln
435 440 445

Thr Gln Gln Gln Met Gly Pro Arg Pro Pro Gln Asn Asn Pro Leu Pro
450 455 460

Gln Gly Phe Gln Gln Pro Val Ser Ser Pro Gly Arg Asn Pro Met Val
465 470 475 480

Gln Gln Gly Asn Val Pro Pro Asn Phe Met Val Met Gln Gln Gln Pro
485 490 495

Pro Asn Gln Gly Pro Gln Ser Leu His Pro Gly Leu Gly Gly Met Pro
500 505 510

Lys Arg Leu Pro Pro Gly Phe Ser Ala Gly Gln Ala Asn Pro Asn Phe

515 520 525

Met Gln Gly Gln Val Pro Ser Thr Thr Ala Thr Thr Pro Gly Asn Ser
530 535 540

Gly Ala Pro Gln Leu Gln Ala Asn Gln Asn Val Gln His Ala Gly Gly
545 550 555 560

Gln Gly Ala Gly Pro Pro Gln Asn Gln Met Gln Val Ser His Gly Pro
565 570 575

Pro Asn Met Met Gln Pro Ser Leu Met Gly Ile His Gly Asn Met Asn
580 585 590

Asn Gln Gln Ala Gly Thr Ser Gly Val Pro Gln Val Asn Leu Ser Asn
595 600 605

Met Gln Gly Gln Pro Gln Gln Gly Pro Pro Ser Gln Leu Met Gly Met
610 615 620

His Gln Gln Ile Val Pro Ser Gln Gly Gln Met Val Gln Gln Gln Gly
625 630 635 640

Thr Leu Asn Pro Gln Asn Pro Met Ile Leu Ser Arg Ala Gln Leu Met
645 650 655

Pro Gln Gly Gln Met Met Val Asn Pro Pro Ser Gln Asn Leu Gly Pro
660 665 670

Ser Pro Gln Arg Met Thr Pro Pro Lys Gln Met Leu Ser Gln Gln Gly
675 680 685

Pro Gln Met Met Ala Pro His Asn Gln Met Met Gly Pro Gln Gly Gln
690 695 700

Val Leu Leu Gln Gln Asn Pro Met Ile Glu Gln Ile Met Thr Asn Gln
705 710 715 720

Met Gln Gly Asn Lys Gln Gln Phe Asn Thr Gln Asn Gln Ser Asn Val
725 730 735

Met Pro Gly Pro Ala Gln Ile Met Arg Gly Pro Thr Pro Asn Met Gln
740 745 750

Gly Asn Met Val Gln Phe Thr Gly Gln Met Ser Gly Gln Met Leu Pro
755 760 765

Gln Gln Gly Pro Val Asn Asn Ser Pro Ser Gln Val Met Gly Ile Gln
770 775 780

Gly Gln Val Leu Arg Pro Pro Gly Pro Ser Pro His Met Ala Gln Gln

785 790 795 800

His Gly Asp Pro Ala Thr Thr Ala Asn Asn Asp Val Ser Leu Ser Gln
805 810 815

Met Met Pro Asp Val Ser Ile Gln Gln Thr Asn Met Val Pro Pro His
820 825 830

Val Gln Ala Met Gln Gly Asn Ser Ala Ser Gly Asn His Phe Ser Gly
835 840 845

His Gly Met Ser Phe Asn Ala Pro Phe Ser Gly Ala Pro Asn Gly Asn
850 855 860

Gln Met Ser Cys Gly Gln Asn Pro Gly Phe Pro Val Asn Lys Asp Val
865 870 875 880

Thr Leu Thr Ser Pro Leu Leu Val Asn Leu Leu Gln Ser Asp Ile Ser
885 890 895

Ala Gly His Phe Gly Val Asn Asn Lys Gln Asn Asn Thr Asn Ala Asn
900 905 910

Lys Pro Lys Lys Lys Lys Pro Pro Arg Lys Lys Lys Asn Ser Gln Gln
915 920 925

Asp Leu Asn Thr Pro Asp Thr Arg Pro Ala Gly Leu Glu Glu Ala Asp
930 935 940

Gln Pro Pro Leu Pro Gly Glu Gln Gly Ile Asn Leu Asp Asn Ser Gly
945 950 955 960

Pro Lys Leu Pro Glu Phe Ser Asn Arg Pro Pro Gly Tyr Pro Ser Gln
965 970 975

Pro Val Glu Gln Arg Pro Leu Gln Gln Met Pro Pro Gln Leu Met Gln
980 985 990

His Val Ala Pro Pro Pro Gln Pro Pro Gln Gln Gln Pro Gln Pro Gln
995 1000 1005

Leu Pro Gln Gln Gln Gln Pro Pro Pro Pro Ser Gln Pro Gln Ser
1010 1015 1020

Gln Gln Gln Gln Gln Gln Gln Gln Met Met Met Met Leu Met
1025 1030 1035

Met Gln Gln Asp Pro Lys Ser Val Arg Leu Pro Val Ser Gln Asn
1040 1045 1050

Val His Pro Pro Arg Gly Pro Leu Asn Pro Asp Ser Gln Arg Met

1055 1060 1065

Pro Met Gln Gln Ser Gly Ser Val Pro Val Met Val Ser Leu Gln
1070 1075 1080

Gly Pro Ala Ser Val Pro Pro Ser Pro Asp Lys Gln Arg Met Pro
1085 1090 1095

Met Pro Val Asn Thr Pro Leu Gly Ser Asn Ser Arg Lys Met Val
1100 1105 1110

Tyr Gln Glu Ser Pro Gln Asn Pro Ser Ser Ser Pro Leu Ala Glu
1115 1120 1125

Met Ala Ser Leu Pro Glu Ala Ser Gly Ser Glu Ala Pro Ser Val
1130 1135 1140

Pro Gly Gly Pro Asn Asn Met Pro Ser His Val Val Leu Pro Gln
1145 1150 1155

Asn Gln Leu Met Met Thr Gly Pro Lys Pro Gly Pro Ser Pro Leu
1160 1165 1170

Ser Ala Thr Gln Gly Ala Thr Pro Gln Gln Pro Pro Val Asn Ser
1175 1180 1185

Leu Pro Ser Ser His Gly His His Phe Pro Asn Val Ala Ala Pro
1190 1195 1200

Thr Gln Thr Ser Arg Pro Lys Thr Pro Asn Arg Ala Ser Pro Arg
1205 1210 1215

Pro Tyr Tyr Pro Gln Thr Pro Asn Asn Arg Pro Pro Ser Thr Glu
1220 1225 1230

Pro Ser Glu Ile Ser Leu Ser Pro Glu Arg Leu Asn Ala Ser Ile
1235 1240 1245

Ala Gly Leu Phe Pro Pro Gln Ile Asn Ile Pro Leu Pro Pro Arg
1250 1255 1260

Pro Asn Leu Asn Arg Gly Phe Asp Gln Gln Gly Leu Asn Pro Thr
1265 1270 1275

Thr Leu Lys Ala Ile Gly Gln Ala Pro Ser Asn Leu Thr Met Asn
1280 1285 1290

Pro Ser Asn Phe Ala Thr Pro Gln Thr His Lys Leu Asp Ser Val
1295 1300 1305

Val Val Asn Ser Gly Lys Gln Ser Asn Ser Gly Ala Thr Lys Arg

1310 1315 1320

Ala Ser Pro Ser Asn Ser Arg Arg Ser Ser Pro Gly Ser Ser Arg
1325 1330 1335

Lys Thr Thr Pro Ser Pro Gly Arg Gln Asn Ser Lys Ala Pro Lys
1340 1345 1350

Leu Thr Leu Ala Ser Gln Thr Asn Ala Ala Leu Leu Gln Asn Val
1355 1360 1365

Glu Leu Pro Arg Asn Val Leu Val Ser Pro Thr Pro Leu Ala Asn
1370 1375 1380

Pro Pro Val Pro Gly Ser Phe Pro Asn Asn Ser Gly Leu Asn Pro
1385 1390 1395

Gln Asn Ser Thr Val Ser Val Ala Ala Val Gly Gly Val Val Glu
1400 1405 1410

Asp Asn Lys Glu Ser Leu Asn Val Pro Gln Asp Ser Asp Cys Gln
1415 1420 1425

Asn Ser Gln Ser Arg Lys Glu Gln Val Asn Ile Glu Leu Lys Ala
1430 1435 1440

Val Pro Ala Gln Glu Val Lys Met Val Val Pro Glu Asp Gln Ser
1445 1450 1455

Lys Lys Asp Gly Gln Pro Ser Asp Pro Asn Lys Leu Pro Ser Val
1460 1465 1470

Glu Glu Asn Lys Asn Leu Val Ser Pro Ala Met Arg Glu Ala Pro
1475 1480 1485

Thr Ser Leu Ser Gln Leu Leu Asp Asn Ser Gly Ala Pro Asn Val
1490 1495 1500

Thr Ile Lys Pro Pro Gly Leu Thr Asp Leu Glu Val Thr Pro Pro
1505 1510 1515

Val Val Ser Gly Glu Asp Leu Lys Lys Ala Ser Val Ile Pro Thr
1520 1525 1530

Leu Gln Asp Leu Ser Ser Ser Lys Glu Pro Ser Asn Ser Leu Asn
1535 1540 1545

Leu Pro His Ser Asn Glu Leu Cys Ser Ser Leu Val His Pro Glu
1550 1555 1560

Leu Ser Glu Val Ser Ser Asn Val Ala Pro Ser Ile Pro Pro Val

1565 1570 1575

Met Ser Arg Pro Val Ser Ser Ser Ser Ile Ser Thr Pro Leu Pro
1580 1585 1590

Pro Asn Gln Ile Thr Val Phe Val Thr Ser Asn Pro Ile Thr Thr
1595 1600 1605

Ser Ala Asn Thr Ser Ala Ala Leu Pro Thr His Leu Gln Ser Ala
1610 1615 1620

Leu Met Ser Thr Val Val Thr Met Pro Asn Ala Gly Ser Lys Val
1625 1630 1635

Met Val Ser Glu Gly Gln Ser Ala Ala Gln Ser Asn Ala Arg Pro
1640 1645 1650

Gln Phe Ile Thr Pro Val Phe Ile Asn Ser Ser Ser Ile Ile Gln
1655 1660 1665

Val Met Lys Gly Ser Gln Pro Ser Thr Ile Pro Ala Ala Pro Leu
1670 1675 1680

Thr Thr Asn Ser Gly Leu Met Pro Pro Ser Val Ala Val Val Gly
1685 1690 1695

Pro Leu His Ile Pro Gln Asn Ile Lys Phe Ser Ser Ala Pro Val
1700 1705 1710

Pro Pro Asn Ala Leu Ser Ser Ser Pro Ala Pro Asn Ile Gln Thr
1715 1720 1725

Gly Arg Pro Leu Val Leu Ser Ser Arg Ala Thr Pro Val Gln Leu
1730 1735 1740

Pro Ser Pro Pro Cys Thr Ser Ser Pro Val Val Pro Ser His Pro
1745 1750 1755

Pro Val Gln Gln Val Lys Glu Leu Asn Pro Asp Glu Ala Ser Pro
1760 1765 1770

Gln Val Asn Thr Ser Ala Asp Gln Asn Thr Leu Pro Ser Ser Gln
1775 1780 1785

Ser Thr Thr Met Val Ser Pro Leu Leu Thr Asn Ser Pro Gly Ser
1790 1795 1800

Ser Gly Asn Arg Arg Ser Pro Val Ser Ser Ser Lys Gly Lys Gly
1805 1810 1815

Lys Val Asp Lys Ile Gly Gln Ile Leu Leu Thr Lys Ala Cys Lys

1820 1825 1830

Lys Val Thr Gly Ser Leu Glu Lys Gly Glu Glu Gln Tyr Gly Ala
1835 1840 1845

Asp Gly Glu Thr Glu Gly Gln Gly Leu Asp Thr Thr Ala Pro Gly
1850 1855 1860

Leu Met Gly Thr Glu Gln Leu Ser Thr Glu Leu Asp Ser Lys Thr
1865 1870 1875

Pro Thr Pro Pro Ala Pro Thr Leu Leu Lys Met Thr Ser Ser Pro
1880 1885 1890

Val Gly Pro Gly Thr Ala Ser Ala Gly Pro Ser Leu Pro Gly Gly
1895 1900 1905

Ala Leu Pro Thr Ser Val Arg Ser Ile Val Thr Thr Leu Val Pro
1910 1915 1920

Ser Glu Leu Ile Ser Ala Val Pro Thr Thr Lys Ser Asn His Gly
1925 1930 1935

Gly Ile Ala Ser Glu Ser Leu Ala Gly Gly Leu Val Glu Glu Lys
1940 1945 1950

Val Gly Ser His Pro Glu Leu Leu Pro Ser Ile Ala Pro Ser Gln
1955 1960 1965

Asn Leu Val Ser Lys Glu Thr Ser Thr Thr Ala Leu Gln Ala Ser
1970 1975 1980

Val Ala Arg Pro Glu Leu Glu Val Asn Ala Ala Ile Val Ser Gly
1985 1990 1995

Gln Ser Ser Glu Pro Lys Glu Ile Val Glu Lys Ser Lys Ile Pro
2000 2005 2010

Gly Arg Arg Asn Ser Arg Thr Glu Glu Pro Thr Val Ala Ser Glu
2015 2020 2025

Ser Val Glu Asn Gly His Arg Lys Arg Ser Ser Arg Pro Ala Ser
2030 2035 2040

Ala Ser Ser Ser Thr Lys Asp Ile Thr Ser Ala Val Gln Ser Lys
2045 2050 2055

Arg Arg Lys Ser Lys
2060

<210> 288

<211> 2442
<212> PRT
<213> Homo sapiens

<400> 288

```
Met Ala Glu Asn Leu Leu Asp Gly Pro Pro Asn Pro Lys Arg Ala Lys
1               5                  10                  15

Leu Ser Ser Pro Gly Phe Ser Ala Asn Asp Ser Thr Asp Phe Gly Ser
            20                  25                  30

Leu Phe Asp Leu Glu Asn Asp Leu Pro Asp Glu Leu Ile Pro Asn Gly
        35                  40                  45

Gly Glu Leu Gly Leu Leu Asn Ser Gly Asn Leu Val Pro Asp Ala Ala
    50                  55                  60

Ser Lys His Lys Gln Leu Ser Glu Leu Leu Arg Gly Gly Ser Gly Ser
65                  70                  75                  80

Ser Ile Asn Pro Gly Ile Gly Asn Val Ser Ala Ser Ser Pro Val Gln
                85                  90                  95

Gln Gly Leu Gly Gly Gln Ala Gln Gly Gln Pro Asn Ser Ala Asn Met
            100                 105                 110

Ala Ser Leu Ser Ala Met Gly Lys Ser Pro Leu Ser Gln Gly Asp Ser
        115                 120                 125

Ser Ala Pro Ser Leu Pro Lys Gln Ala Ala Ser Thr Ser Gly Pro Thr
    130                 135                 140

Pro Ala Ala Ser Gln Ala Leu Asn Pro Gln Ala Gln Lys Gln Val Gly
145                 150                 155                 160

Leu Ala Thr Ser Ser Pro Ala Thr Ser Gln Thr Gly Pro Gly Ile Cys
                165                 170                 175

Met Asn Ala Asn Phe Asn Gln Thr His Pro Gly Leu Leu Asn Ser Asn
            180                 185                 190

Ser Gly His Ser Leu Ile Asn Gln Ala Ser Gln Gly Gln Ala Gln Val
        195                 200                 205

Met Asn Gly Ser Leu Gly Ala Ala Gly Arg Gly Arg Gly Ala Gly Met
    210                 215                 220

Pro Tyr Pro Thr Pro Ala Met Gln Gly Ala Ser Ser Ser Val Leu Ala
225                 230                 235                 240

Glu Thr Leu Thr Gln Val Ser Pro Gln Met Thr Gly His Ala Gly Leu
                245                 250                 255
```

```
Asn Thr Ala Gln Ala Gly Gly Met Ala Lys Met Gly Ile Thr Gly Asn
            260                 265                 270

Thr Ser Pro Phe Gly Gln Pro Phe Ser Gln Ala Gly Gly Gln Pro Met
        275                 280                 285

Gly Ala Thr Gly Val Asn Pro Gln Leu Ala Ser Lys Gln Ser Met Val
    290                 295                 300

Asn Ser Leu Pro Thr Phe Pro Thr Asp Ile Lys Asn Thr Ser Val Thr
305                 310                 315                 320

Asn Val Pro Asn Met Ser Gln Met Gln Thr Ser Val Gly Ile Val Pro
                325                 330                 335

Thr Gln Ala Ile Ala Thr Gly Pro Thr Ala Asp Pro Glu Lys Arg Lys
            340                 345                 350

Leu Ile Gln Gln Gln Leu Val Leu Leu Leu His Ala His Lys Cys Gln
        355                 360                 365

Arg Arg Glu Gln Ala Asn Gly Glu Val Arg Ala Cys Ser Leu Pro His
    370                 375                 380

Cys Arg Thr Met Lys Asn Val Leu Asn His Met Thr His Cys Gln Ala
385                 390                 395                 400

Gly Lys Ala Cys Gln Val Ala His Cys Ala Ser Ser Arg Gln Ile Ile
                405                 410                 415

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

Leu Lys Asn Ala Ser Asp Lys Arg Asn Gln Gln Thr Ile Leu Gly Ser
        435                 440                 445

Pro Ala Ser Gly Ile Gln Asn Thr Ile Gly Ser Val Gly Thr Gly Gln
    450                 455                 460

Gln Asn Ala Thr Ser Leu Ser Asn Pro Asn Pro Ile Asp Pro Ser Ser
465                 470                 475                 480

Met Gln Arg Ala Tyr Ala Ala Leu Gly Leu Pro Tyr Met Asn Gln Pro
                485                 490                 495

Gln Thr Gln Leu Gln Pro Gln Val Pro Gly Gln Gln Pro Ala Gln Pro
            500                 505                 510

Gln Thr His Gln Gln Met Arg Thr Leu Asn Pro Leu Gly Asn Asn Pro
        515                 520                 525
```

```
Met Asn Ile Pro Ala Gly Gly Ile Thr Thr Asp Gln Gln Pro Pro Asn
    530                 535                 540

Leu Ile Ser Glu Ser Ala Leu Pro Thr Ser Leu Gly Ala Thr Asn Pro
545                 550                 555                 560

Leu Met Asn Asp Gly Ser Asn Ser Gly Asn Ile Gly Thr Leu Ser Thr
                565                 570                 575

Ile Pro Thr Ala Ala Pro Pro Ser Ser Thr Gly Val Arg Lys Gly Trp
            580                 585                 590

His Glu His Val Thr Gln Asp Leu Arg Ser His Leu Val His Lys Leu
        595                 600                 605

Val Gln Ala Ile Phe Pro Thr Pro Asp Pro Ala Ala Leu Lys Asp Arg
    610                 615                 620

Arg Met Glu Asn Leu Val Ala Tyr Ala Lys Lys Val Glu Gly Asp Met
625                 630                 635                 640

Tyr Glu Ser Ala Asn Ser Arg Asp Glu Tyr Tyr His Leu Leu Ala Glu
                645                 650                 655

Lys Ile Tyr Lys Ile Gln Lys Glu Leu Glu Glu Lys Arg Arg Ser Arg
            660                 665                 670

Leu His Lys Gln Gly Ile Leu Gly Asn Gln Pro Ala Leu Pro Ala Pro
        675                 680                 685

Gly Ala Gln Pro Pro Val Ile Pro Gln Ala Gln Pro Val Arg Pro Pro
    690                 695                 700

Asn Gly Pro Leu Ser Leu Pro Val Asn Arg Met Gln Val Ser Gln Gly
705                 710                 715                 720

Met Asn Ser Phe Asn Pro Met Ser Leu Gly Asn Val Gln Leu Pro Gln
                725                 730                 735

Ala Pro Met Gly Pro Arg Ala Ala Ser Pro Met Asn His Ser Val Gln
            740                 745                 750

Met Asn Ser Met Gly Ser Val Pro Gly Met Ala Ile Ser Pro Ser Arg
        755                 760                 765

Met Pro Gln Pro Pro Asn Met Met Gly Ala His Thr Asn Asn Met Met
    770                 775                 780

Ala Gln Ala Pro Ala Gln Ser Gln Phe Leu Pro Gln Asn Gln Phe Pro
785                 790                 795                 800
```

```
Ser Ser Ser Gly Ala Met Ser Val Gly Met Gly Gln Pro Pro Ala Gln
                805                 810                 815

Thr Gly Val Ser Gln Gly Gln Val Pro Gly Ala Ala Leu Pro Asn Pro
            820                 825                 830

Leu Asn Met Leu Gly Pro Gln Ala Ser Gln Leu Pro Cys Pro Pro Val
        835                 840                 845

Thr Gln Ser Pro Leu His Pro Thr Pro Pro Pro Ala Ser Thr Ala Ala
    850                 855                 860

Gly Met Pro Ser Leu Gln His Thr Thr Pro Pro Gly Met Thr Pro Pro
865                 870                 875                 880

Gln Pro Ala Ala Pro Thr Gln Pro Ser Thr Pro Val Ser Ser Ser Gly
                885                 890                 895

Gln Thr Pro Thr Pro Thr Pro Gly Ser Val Pro Ser Ala Thr Gln Thr
            900                 905                 910

Gln Ser Thr Pro Thr Val Gln Ala Ala Ala Gln Ala Gln Val Thr Pro
        915                 920                 925

Gln Pro Gln Thr Pro Val Gln Pro Pro Ser Val Ala Thr Pro Gln Ser
    930                 935                 940

Ser Gln Gln Gln Pro Thr Pro Val His Ala Gln Pro Pro Gly Thr Pro
945                 950                 955                 960

Leu Ser Gln Ala Ala Ala Ser Ile Asp Asn Arg Val Pro Thr Pro Ser
                965                 970                 975

Ser Val Ala Ser Ala Glu Thr Asn Ser Gln Gln Pro Gly Pro Asp Val
            980                 985                 990

Pro Val Leu Glu Met Lys Thr Glu  Thr Gln Ala Glu Asp  Thr Glu Pro
        995                 1000                1005

Asp Pro  Gly Glu Ser Lys Gly  Glu Pro Arg Ser Glu  Met Met Glu
    1010                1015                1020

Glu Asp  Leu Gln Gly Ala Ser  Gln Val Lys Glu Glu  Thr Asp Ile
    1025                1030                1035

Ala Glu  Gln Lys Ser Glu Pro  Met Glu Val Asp Glu  Lys Lys Pro
    1040                1045                1050

Glu Val  Lys Val Glu Val Lys  Glu Glu Glu Glu Ser  Ser Ser Asn
    1055                1060                1065
```

```
Gly Thr  Ala Ser Gln Ser Thr  Ser Pro Ser Gln Pro  Arg Lys Lys
    1070                 1075                 1080

Ile Phe  Lys Pro Glu Glu Leu  Arg Gln Ala Leu Met  Pro Thr Leu
    1085                 1090                 1095

Glu Ala  Leu Tyr Arg Gln Asp  Pro Glu Ser Leu Pro  Phe Arg Gln
    1100                 1105                 1110

Pro Val  Asp Pro Gln Leu Leu  Gly Ile Pro Asp Tyr  Phe Asp Ile
    1115                 1120                 1125

Val Lys  Asn Pro Met Asp Leu  Ser Thr Ile Lys Arg  Lys Leu Asp
    1130                 1135                 1140

Thr Gly  Gln Tyr Gln Glu Pro  Trp Gln Tyr Val Asp  Asp Val Trp
    1145                 1150                 1155

Leu Met  Phe Asn Asn Ala Trp  Leu Tyr Asn Arg Lys  Thr Ser Arg
    1160                 1165                 1170

Val Tyr  Lys Phe Cys Ser Lys  Leu Ala Glu Val Phe  Glu Gln Glu
    1175                 1180                 1185

Ile Asp  Pro Val Met Gln Ser  Leu Gly Tyr Cys Cys  Gly Arg Lys
    1190                 1195                 1200

Tyr Glu  Phe Ser Pro Gln Thr  Leu Cys Cys Tyr Gly  Lys Gln Leu
    1205                 1210                 1215

Cys Thr  Ile Pro Arg Asp Ala  Ala Tyr Tyr Ser Tyr  Gln Asn Arg
    1220                 1225                 1230

Tyr His  Phe Cys Glu Lys Cys  Phe Thr Glu Ile Gln  Gly Glu Asn
    1235                 1240                 1245

Val Thr  Leu Gly Asp Asp Pro  Ser Gln Pro Gln Thr  Thr Ile Ser
    1250                 1255                 1260

Lys Asp  Gln Phe Glu Lys Lys  Lys Asn Asp Thr Leu  Asp Pro Glu
    1265                 1270                 1275

Pro Phe  Val Asp Cys Lys Glu  Cys Gly Arg Lys Met  His Gln Ile
    1280                 1285                 1290

Cys Val  Leu His Tyr Asp Ile  Ile Trp Pro Ser Gly  Phe Val Cys
    1295                 1300                 1305

Asp Asn  Cys Leu Lys Lys Thr  Gly Arg Pro Arg Lys  Glu Asn Lys
    1310                 1315                 1320
```

```
Phe Ser  Ala Lys Arg Leu Gln  Thr Thr Arg Leu Gly  Asn His Leu
    1325                 1330                 1335

Glu Asp  Arg Val Asn Lys Phe  Leu Arg Arg Gln Asn  His Pro Glu
    1340                 1345                 1350

Ala Gly  Glu Val Phe Val Arg  Val Val Ala Ser Ser  Asp Lys Thr
    1355                 1360                 1365

Val Glu  Val Lys Pro Gly Met  Lys Ser Arg Phe Val  Asp Ser Gly
    1370                 1375                 1380

Glu Met  Ser Glu Ser Phe Pro  Tyr Arg Thr Lys Ala  Leu Phe Ala
    1385                 1390                 1395

Phe Glu  Glu Ile Asp Gly Val  Asp Val Cys Phe Phe  Gly Met His
    1400                 1405                 1410

Val Gln  Glu Tyr Gly Ser Asp  Cys Pro Pro Pro Asn  Thr Arg Arg
    1415                 1420                 1425

Val Tyr  Ile Ser Tyr Leu Asp  Ser Ile His Phe Phe  Arg Pro Arg
    1430                 1435                 1440

Cys Leu  Arg Thr Ala Val Tyr  His Glu Ile Leu Ile  Gly Tyr Leu
    1445                 1450                 1455

Glu Tyr  Val Lys Lys Leu Gly  Tyr Val Thr Gly His  Ile Trp Ala
    1460                 1465                 1470

Cys Pro  Pro Ser Glu Gly Asp  Asp Tyr Ile Phe His  Cys His Pro
    1475                 1480                 1485

Pro Asp  Gln Lys Ile Pro Lys  Pro Lys Arg Leu Gln  Glu Trp Tyr
    1490                 1495                 1500

Lys Lys  Met Leu Asp Lys Ala  Phe Ala Glu Arg Ile  Ile His Asp
    1505                 1510                 1515

Tyr Lys  Asp Ile Phe Lys Gln  Ala Thr Glu Asp Arg  Leu Thr Ser
    1520                 1525                 1530

Ala Lys  Glu Leu Pro Tyr Phe  Glu Gly Asp Phe Trp  Pro Asn Val
    1535                 1540                 1545

Leu Glu  Glu Ser Ile Lys Glu  Leu Glu Gln Glu Glu  Glu Glu Arg
    1550                 1555                 1560

Lys Lys  Glu Glu Ser Thr Ala  Ala Ser Glu Thr Thr  Glu Gly Ser
    1565                 1570                 1575
```

```
Gln Gly  Asp Ser Lys Asn Ala  Lys Lys Lys Asn Asn  Lys Lys Thr
    1580                 1585                 1590

Asn Lys  Asn Lys Ser Ser Ile  Ser Arg Ala Asn Lys  Lys Lys Pro
    1595                 1600                 1605

Ser Met  Pro Asn Val Ser Asn  Asp Leu Ser Gln Lys  Leu Tyr Ala
    1610                 1615                 1620

Thr Met  Glu Lys His Lys Glu  Val Phe Phe Val Ile  His Leu His
    1625                 1630                 1635

Ala Gly  Pro Val Ile Asn Thr  Leu Pro Pro Ile Val  Asp Pro Asp
    1640                 1645                 1650

Pro Leu  Leu Ser Cys Asp Leu  Met Asp Gly Arg Asp  Ala Phe Leu
    1655                 1660                 1665

Thr Leu  Ala Arg Asp Lys His  Trp Glu Phe Ser Ser  Leu Arg Arg
    1670                 1675                 1680

Ser Lys  Trp Ser Thr Leu Cys  Met Leu Val Glu Leu  His Thr Gln
    1685                 1690                 1695

Gly Gln  Asp Arg Phe Val Tyr  Thr Cys Asn Glu Cys  Lys His His
    1700                 1705                 1710

Val Glu  Thr Arg Trp His Cys  Thr Val Cys Glu Asp  Tyr Asp Leu
    1715                 1720                 1725

Cys Ile  Asn Cys Tyr Asn Thr  Lys Ser His Ala His  Lys Met Val
    1730                 1735                 1740

Lys Trp  Gly Leu Gly Leu Asp  Asp Glu Gly Ser Ser  Gln Gly Glu
    1745                 1750                 1755

Pro Gln  Ser Lys Ser Pro Gln  Glu Ser Arg Arg Leu  Ser Ile Gln
    1760                 1765                 1770

Arg Cys  Ile Gln Ser Leu Val  His Ala Cys Gln Cys  Arg Asn Ala
    1775                 1780                 1785

Asn Cys  Ser Leu Pro Ser Cys  Gln Lys Met Lys Arg  Val Val Gln
    1790                 1795                 1800

His Thr  Lys Gly Cys Lys Arg  Lys Thr Asn Gly Gly  Cys Pro Val
    1805                 1810                 1815

Cys Lys  Gln Leu Ile Ala Leu  Cys Cys Tyr His Ala  Lys His Cys
    1820                 1825                 1830
```

```
Gln Glu  Asn Lys Cys Pro Val  Pro Phe Cys Leu Asn  Ile Lys His
    1835                 1840                 1845

Lys Leu  Arg Gln Gln Gln Ile  Gln His Arg Leu Gln  Gln Ala Gln
    1850                 1855                 1860

Leu Met  Arg Arg Arg Met Ala  Thr Met Asn Thr Arg  Asn Val Pro
    1865                 1870                 1875

Gln Gln  Ser Leu Pro Ser Pro  Thr Ser Ala Pro Pro  Gly Thr Pro
    1880                 1885                 1890

Thr Gln  Gln Pro Ser Thr Pro  Gln Thr Pro Gln Pro  Pro Ala Gln
    1895                 1900                 1905

Pro Gln  Pro Ser Pro Val Ser  Met Ser Pro Ala Gly  Phe Pro Ser
    1910                 1915                 1920

Val Ala  Arg Thr Gln Pro Pro  Thr Thr Val Ser Thr  Gly Lys Pro
    1925                 1930                 1935

Thr Ser  Gln Val Pro Ala Pro  Pro Pro Pro Ala Gln  Pro Pro Pro
    1940                 1945                 1950

Ala Ala  Val Glu Ala Ala Arg  Gln Ile Glu Arg Glu  Ala Gln Gln
    1955                 1960                 1965

Gln Gln  His Leu Tyr Arg Val  Asn Ile Asn Asn Ser  Met Pro Pro
    1970                 1975                 1980

Gly Arg  Thr Gly Met Gly Thr  Pro Gly Ser Gln Met  Ala Pro Val
    1985                 1990                 1995

Ser Leu  Asn Val Pro Arg Pro  Asn Gln Val Ser Gly  Pro Val Met
    2000                 2005                 2010

Pro Ser  Met Pro Pro Gly Gln  Trp Gln Gln Ala Pro  Leu Pro Gln
    2015                 2020                 2025

Gln Gln  Pro Met Pro Gly Leu  Pro Arg Pro Val Ile  Ser Met Gln
    2030                 2035                 2040

Ala Gln  Ala Ala Val Ala Gly  Pro Arg Met Pro Ser  Val Gln Pro
    2045                 2050                 2055

Pro Arg  Ser Ile Ser Pro Ser  Ala Leu Gln Asp Leu  Leu Arg Thr
    2060                 2065                 2070

Leu Lys  Ser Pro Ser Ser Pro  Gln Gln Gln Gln Gln  Val Leu Asn
    2075                 2080                 2085
```

```
Ile Leu  Lys Ser Asn Pro Gln  Leu Met Ala Ala Phe  Ile Lys Gln
    2090                 2095                 2100

Arg Thr  Ala Lys Tyr Val Ala  Asn Gln Pro Gly Met  Gln Pro Gln
    2105                 2110                 2115

Pro Gly  Leu Gln Ser Gln Pro  Gly Met Gln Pro Gln  Pro Gly Met
    2120                 2125                 2130

His Gln  Gln Pro Ser Leu Gln  Asn Leu Asn Ala Met  Gln Ala Gly
    2135                 2140                 2145

Val Pro  Arg Pro Gly Val Pro  Pro Gln Gln Gln Ala  Met Gly Gly
    2150                 2155                 2160

Leu Asn  Pro Gln Gly Gln Ala  Leu Asn Ile Met Asn  Pro Gly His
    2165                 2170                 2175

Asn Pro  Asn Met Ala Ser Met  Asn Pro Gln Tyr Arg  Glu Met Leu
    2180                 2185                 2190

Arg Arg  Gln Leu Leu Gln Gln  Gln Gln Gln Gln Gln  Gln Gln Gln
    2195                 2200                 2205

Gln Gln  Gln Gln Gln Gln Gln  Gln Gly Ser Ala Gly  Met Ala Gly
    2210                 2215                 2220

Gly Met  Ala Gly His Gly Gln  Phe Gln Gln Pro Gln  Gly Pro Gly
    2225                 2230                 2235

Gly Tyr  Pro Pro Ala Met Gln  Gln Gln Gln Arg Met  Gln Gln His
    2240                 2245                 2250

Leu Pro  Leu Gln Gly Ser Ser  Met Gly Gln Met Ala  Ala Gln Met
    2255                 2260                 2265

Gly Gln  Leu Gly Gln Met Gly  Gln Pro Gly Leu Gly  Ala Asp Ser
    2270                 2275                 2280

Thr Pro  Asn Ile Gln Gln Ala  Leu Gln Gln Arg Ile  Leu Gln Gln
    2285                 2290                 2295

Gln Gln  Met Lys Gln Gln Ile  Gly Ser Pro Gly Gln  Pro Asn Pro
    2300                 2305                 2310

Met Ser  Pro Gln Gln His Met  Leu Ser Gly Gln Pro  Gln Ala Ser
    2315                 2320                 2325

His Leu  Pro Gly Gln Gln Ile  Ala Thr Ser Leu Ser  Asn Gln Val
    2330                 2335                 2340
```

```
Arg Ser  Pro Ala Pro Val Gln  Ser Pro Arg Pro Gln  Ser Gln Pro
    2345                 2350                 2355

Pro His  Ser Ser Pro Ser Pro  Arg Ile Gln Pro Gln  Pro Ser Pro
    2360                 2365                 2370

His His  Val Ser Pro Gln Thr  Gly Ser Pro His Pro  Gly Leu Ala
    2375                 2380                 2385

Val Thr  Met Ala Ser Ser Ile  Asp Gln Gly His Leu  Gly Asn Pro
    2390                 2395                 2400

Glu Gln  Ser Ala Met Leu Pro  Gln Leu Asn Thr Pro  Ser Arg Ser
    2405                 2410                 2415

Ala Leu  Ser Ser Glu Leu Ser  Leu Val Gly Asp Thr  Thr Gly Asp
    2420                 2425                 2430

Thr Leu  Glu Lys Phe Val Glu  Gly Leu
    2435                 2440
```

<210> 289
<211> 2414
<212> PRT
<213> Homo sapiens

<400> 289

```
Met Ala Glu Asn Val Val Glu Pro Gly Pro Pro Ser Ala Lys Arg Pro
1               5                  10                  15

Lys Leu Ser Ser Pro Ala Leu Ser Ala Ser Ala Ser Asp Gly Thr Asp
            20                  25                  30

Phe Gly Ser Leu Phe Asp Leu Glu His Asp Leu Pro Asp Glu Leu Ile
        35                  40                  45

Asn Ser Thr Glu Leu Gly Leu Thr Asn Gly Gly Asp Ile Asn Gln Leu
    50                  55                  60

Gln Thr Ser Leu Gly Met Val Gln Asp Ala Ala Ser Lys His Lys Gln
65                  70                  75                  80

Leu Ser Glu Leu Leu Arg Ser Gly Ser Ser Pro Asn Leu Asn Met Gly
                85                  90                  95

Val Gly Gly Pro Gly Gln Val Met Ala Ser Gln Ala Gln Gln Ser Ser
            100                 105                 110

Pro Gly Leu Gly Leu Ile Asn Ser Met Val Lys Ser Pro Met Thr Gln
        115                 120                 125
```

```
Ala Gly Leu Thr Ser Pro Asn Met Gly Met Gly Thr Ser Gly Pro Asn
    130                 135                 140

Gln Gly Pro Thr Gln Ser Thr Gly Met Met Asn Ser Pro Val Asn Gln
145                 150                 155                 160

Pro Ala Met Gly Met Asn Thr Gly Met Asn Ala Gly Met Asn Pro Gly
                165                 170                 175

Met Leu Ala Ala Gly Asn Gly Gln Gly Ile Met Pro Asn Gln Val Met
            180                 185                 190

Asn Gly Ser Ile Gly Ala Gly Arg Gly Arg Gln Asn Met Gln Tyr Pro
        195                 200                 205

Asn Pro Gly Met Gly Ser Ala Gly Asn Leu Leu Thr Glu Pro Leu Gln
    210                 215                 220

Gln Gly Ser Pro Gln Met Gly Gly Gln Thr Gly Leu Arg Gly Pro Gln
225                 230                 235                 240

Pro Leu Lys Met Gly Met Met Asn Asn Pro Asn Pro Tyr Gly Ser Pro
                245                 250                 255

Tyr Thr Gln Asn Pro Gly Gln Gln Ile Gly Ala Ser Gly Leu Gly Leu
            260                 265                 270

Gln Ile Gln Thr Lys Thr Val Leu Ser Asn Asn Leu Ser Pro Phe Ala
        275                 280                 285

Met Asp Lys Lys Ala Val Pro Gly Gly Gly Met Pro Asn Met Gly Gln
    290                 295                 300

Gln Pro Ala Pro Gln Val Gln Gln Pro Gly Leu Val Thr Pro Val Ala
305                 310                 315                 320

Gln Gly Met Gly Ser Gly Ala His Thr Ala Asp Pro Glu Lys Arg Lys
                325                 330                 335

Leu Ile Gln Gln Gln Leu Val Leu Leu Leu His Ala His Lys Cys Gln
            340                 345                 350

Arg Arg Glu Gln Ala Asn Gly Glu Val Arg Gln Cys Asn Leu Pro His
        355                 360                 365

Cys Arg Thr Met Lys Asn Val Leu Asn His Met Thr His Cys Gln Ser
    370                 375                 380

Gly Lys Ser Cys Gln Val Ala His Cys Ala Ser Ser Arg Gln Ile Ile
385                 390                 395                 400
```

```
Ser His Trp Lys Asn Cys Thr Arg His Asp Cys Pro Val Cys Leu Pro
                405                 410                 415

Leu Lys Asn Ala Gly Asp Lys Arg Asn Gln Gln Pro Ile Leu Thr Gly
            420                 425                 430

Ala Pro Val Gly Leu Gly Asn Pro Ser Ser Leu Gly Val Gly Gln Gln
        435                 440                 445

Ser Ala Pro Asn Leu Ser Thr Val Ser Gln Ile Asp Pro Ser Ser Ile
    450                 455                 460

Glu Arg Ala Tyr Ala Ala Leu Gly Leu Pro Tyr Gln Val Asn Gln Met
465                 470                 475                 480

Pro Thr Gln Pro Gln Val Gln Ala Lys Asn Gln Gln Asn Gln Gln Pro
                485                 490                 495

Gly Gln Ser Pro Gln Gly Met Arg Pro Met Ser Asn Met Ser Ala Ser
            500                 505                 510

Pro Met Gly Val Asn Gly Gly Val Gly Val Gln Thr Pro Ser Leu Leu
        515                 520                 525

Ser Asp Ser Met Leu His Ser Ala Ile Asn Ser Gln Asn Pro Met Met
    530                 535                 540

Ser Glu Asn Ala Ser Val Pro Ser Leu Gly Pro Met Pro Thr Ala Ala
545                 550                 555                 560

Gln Pro Ser Thr Thr Gly Ile Arg Lys Gln Trp His Glu Asp Ile Thr
                565                 570                 575

Gln Asp Leu Arg Asn His Leu Val His Lys Leu Val Gln Ala Ile Phe
            580                 585                 590

Pro Thr Pro Asp Pro Ala Ala Leu Lys Asp Arg Arg Met Glu Asn Leu
        595                 600                 605

Val Ala Tyr Ala Arg Lys Val Glu Gly Asp Met Tyr Glu Ser Ala Asn
    610                 615                 620

Asn Arg Ala Glu Tyr Tyr His Leu Leu Ala Glu Lys Ile Tyr Lys Ile
625                 630                 635                 640

Gln Lys Glu Leu Glu Glu Lys Arg Arg Thr Arg Leu Gln Lys Gln Asn
                645                 650                 655

Met Leu Pro Asn Ala Ala Gly Met Val Pro Val Ser Met Asn Pro Gly
            660                 665                 670
```

```
Pro Asn Met Gly Gln Pro Gln Pro Gly Met Thr Ser Asn Gly Pro Leu
        675                 680                 685

Pro Asp Pro Ser Met Ile Arg Gly Ser Val Pro Asn Gln Met Met Pro
    690                 695                 700

Arg Ile Thr Pro Gln Ser Gly Leu Asn Gln Phe Gly Gln Met Ser Met
705                 710                 715                 720

Ala Gln Pro Pro Ile Val Pro Arg Gln Thr Pro Pro Leu Gln His His
                725                 730                 735

Gly Gln Leu Ala Gln Pro Gly Ala Leu Asn Pro Pro Met Gly Tyr Gly
            740                 745                 750

Pro Arg Met Gln Gln Pro Ser Asn Gln Gly Gln Phe Leu Pro Gln Thr
        755                 760                 765

Gln Phe Pro Ser Gln Gly Met Asn Val Thr Asn Ile Pro Leu Ala Pro
    770                 775                 780

Ser Ser Gly Gln Ala Pro Val Ser Gln Ala Gln Met Ser Ser Ser Ser
785                 790                 795                 800

Cys Pro Val Asn Ser Pro Ile Met Pro Pro Gly Ser Gln Gly Ser His
                805                 810                 815

Ile His Cys Pro Gln Leu Pro Gln Pro Ala Leu His Gln Asn Ser Pro
            820                 825                 830

Ser Pro Val Pro Ser Arg Thr Pro Thr Pro His His Thr Pro Pro Ser
        835                 840                 845

Ile Gly Ala Gln Gln Pro Pro Ala Thr Thr Ile Pro Ala Pro Val Pro
    850                 855                 860

Thr Pro Pro Ala Met Pro Pro Gly Pro Gln Ser Gln Ala Leu His Pro
865                 870                 875                 880

Pro Pro Arg Gln Thr Pro Thr Pro Pro Thr Thr Gln Leu Pro Gln Gln
                885                 890                 895

Val Gln Pro Ser Leu Pro Ala Ala Pro Ser Ala Asp Gln Pro Gln Gln
            900                 905                 910

Gln Pro Arg Ser Gln Gln Ser Thr Ala Ala Ser Val Pro Thr Pro Thr
        915                 920                 925

Ala Pro Leu Leu Pro Pro Gln Pro Ala Thr Pro Leu Ser Gln Pro Ala
    930                 935                 940
```

```
Val Ser Ile Glu Gly Gln Val Ser Asn Pro Pro Ser Thr Ser Ser Thr
945                 950                 955                 960

Glu Val Asn Ser Gln Ala Ile Ala Glu Lys Gln Pro Ser Gln Glu Val
                965                 970                 975

Lys Met Glu Ala Lys Met Glu Val Asp Gln Pro Glu Pro Ala Asp Thr
            980                 985                 990

Gln Pro Glu Asp Ile Ser Glu Ser  Lys Val Glu Asp Cys  Lys Met Glu
        995                 1000                1005

Ser Thr  Glu Thr Glu Glu Arg  Ser Thr Glu Leu Lys  Thr Glu Ile
    1010                1015                1020

Lys Glu  Glu Glu Asp Gln Pro  Ser Thr Ser Ala Thr  Gln Ser Ser
    1025                1030                1035

Pro Ala  Pro Gly Gln Ser Lys  Lys Lys Ile Phe Lys  Pro Glu Glu
    1040                1045                1050

Leu Arg  Gln Ala Leu Met Pro  Thr Leu Glu Ala Leu  Tyr Arg Gln
    1055                1060                1065

Asp Pro  Glu Ser Leu Pro Phe  Arg Gln Pro Val Asp  Pro Gln Leu
    1070                1075                1080

Leu Gly  Ile Pro Asp Tyr Phe  Asp Ile Val Lys Ser  Pro Met Asp
    1085                1090                1095

Leu Ser  Thr Ile Lys Arg Lys  Leu Asp Thr Gly Gln  Tyr Gln Glu
    1100                1105                1110

Pro Trp  Gln Tyr Val Asp Asp  Ile Trp Leu Met Phe  Asn Asn Ala
    1115                1120                1125

Trp Leu  Tyr Asn Arg Lys Thr  Ser Arg Val Tyr Lys  Tyr Cys Ser
    1130                1135                1140

Lys Leu  Ser Glu Val Phe Glu  Gln Glu Ile Asp Pro  Val Met Gln
    1145                1150                1155

Ser Leu  Gly Tyr Cys Cys Gly  Arg Lys Leu Glu Phe  Ser Pro Gln
    1160                1165                1170

Thr Leu  Cys Cys Tyr Gly Lys  Gln Leu Cys Thr Ile  Pro Arg Asp
    1175                1180                1185

Ala Thr  Tyr Tyr Ser Tyr Gln  Asn Arg Tyr His Phe  Cys Glu Lys
    1190                1195                1200
```

```
Cys Phe  Asn Glu Ile Gln Gly  Glu Ser Val Ser Leu  Gly Asp Asp
    1205                 1210                 1215

Pro Ser  Gln Pro Gln Thr Thr  Ile Asn Lys Glu Gln  Phe Ser Lys
    1220                 1225                 1230

Arg Lys  Asn Asp Thr Leu Asp  Pro Glu Leu Phe Val  Glu Cys Thr
    1235                 1240                 1245

Glu Cys  Gly Arg Lys Met His  Gln Ile Cys Val Leu  His His Glu
    1250                 1255                 1260

Ile Ile  Trp Pro Ala Gly Phe  Val Cys Asp Gly Cys  Leu Lys Lys
    1265                 1270                 1275

Ser Ala  Arg Thr Arg Lys Glu  Asn Lys Phe Ser Ala  Lys Arg Leu
    1280                 1285                 1290

Pro Ser  Thr Arg Leu Gly Thr  Phe Leu Glu Asn Arg  Val Asn Asp
    1295                 1300                 1305

Phe Leu  Arg Arg Gln Asn His  Pro Glu Ser Gly Glu  Val Thr Val
    1310                 1315                 1320

Arg Val  Val His Ala Ser Asp  Lys Thr Val Glu Val  Lys Pro Gly
    1325                 1330                 1335

Met Lys  Ala Arg Phe Val Asp  Ser Gly Glu Met Ala  Glu Ser Phe
    1340                 1345                 1350

Pro Tyr  Arg Thr Lys Ala Leu  Phe Ala Phe Glu Glu  Ile Asp Gly
    1355                 1360                 1365

Val Asp  Leu Cys Phe Phe Gly  Met His Val Gln Glu  Tyr Gly Ser
    1370                 1375                 1380

Asp Cys  Pro Pro Pro Asn Gln  Arg Arg Val Tyr Ile  Ser Tyr Leu
    1385                 1390                 1395

Asp Ser  Val His Phe Phe Arg  Pro Lys Cys Leu Arg  Thr Ala Val
    1400                 1405                 1410

Tyr His  Glu Ile Leu Ile Gly  Tyr Leu Glu Tyr Val  Lys Lys Leu
    1415                 1420                 1425

Gly Tyr  Thr Thr Gly His Ile  Trp Ala Cys Pro Pro  Ser Glu Gly
    1430                 1435                 1440

Asp Asp  Tyr Ile Phe His Cys  His Pro Pro Asp Gln  Lys Ile Pro
    1445                 1450                 1455
```

```
Lys Pro  Lys Arg Leu Gln Glu  Trp Tyr Lys Lys Met  Leu Asp Lys
    1460                1465                1470

Ala Val  Ser Glu Arg Ile Val  His Asp Tyr Lys Asp  Ile Phe Lys
    1475                1480                1485

Gln Ala  Thr Glu Asp Arg Leu  Thr Ser Ala Lys Glu  Leu Pro Tyr
    1490                1495                1500

Phe Glu  Gly Asp Phe Trp Pro  Asn Val Leu Glu Glu  Ser Ile Lys
    1505                1510                1515

Glu Leu  Glu Gln Glu Glu Glu  Glu Arg Lys Arg Glu  Glu Asn Thr
    1520                1525                1530

Ser Asn  Glu Ser Thr Asp Val  Thr Lys Gly Asp Ser  Lys Asn Ala
    1535                1540                1545

Lys Lys  Lys Asn Asn Lys Lys  Thr Ser Lys Asn Lys  Ser Ser Leu
    1550                1555                1560

Ser Arg  Gly Asn Lys Lys Lys  Pro Gly Met Pro Asn  Val Ser Asn
    1565                1570                1575

Asp Leu  Ser Gln Lys Leu Tyr  Ala Thr Met Glu Lys  His Lys Glu
    1580                1585                1590

Val Phe  Phe Val Ile Arg Leu  Ile Ala Gly Pro Ala  Ala Asn Ser
    1595                1600                1605

Leu Pro  Pro Ile Val Asp Pro  Asp Pro Leu Ile Pro  Cys Asp Leu
    1610                1615                1620

Met Asp  Gly Arg Asp Ala Phe  Leu Thr Leu Ala Arg  Asp Lys His
    1625                1630                1635

Leu Glu  Phe Ser Ser Leu Arg  Arg Ala Gln Trp Ser  Thr Met Cys
    1640                1645                1650

Met Leu  Val Glu Leu His Thr  Gln Ser Gln Asp Arg  Phe Val Tyr
    1655                1660                1665

Thr Cys  Asn Glu Cys Lys His  His Val Glu Thr Arg  Trp His Cys
    1670                1675                1680

Thr Val  Cys Glu Asp Tyr Asp  Leu Cys Ile Thr Cys  Tyr Asn Thr
    1685                1690                1695

Lys Asn  His Asp His Lys Met  Glu Lys Leu Gly Leu  Gly Leu Asp
    1700                1705                1710
```

```
Asp Glu  Ser Asn Asn Gln Gln  Ala Ala Ala Thr Gln  Ser Pro Gly
    1715                1720                1725

Asp Ser  Arg Arg Leu Ser Ile  Gln Arg Cys Ile Gln  Ser Leu Val
    1730                1735                1740

His Ala  Cys Gln Cys Arg Asn  Ala Asn Cys Ser Leu  Pro Ser Cys
    1745                1750                1755

Gln Lys  Met Lys Arg Val Val  Gln His Thr Lys Gly  Cys Lys Arg
    1760                1765                1770

Lys Thr  Asn Gly Gly Cys Pro  Ile Cys Lys Gln Leu  Ile Ala Leu
    1775                1780                1785

Cys Cys  Tyr His Ala Lys His  Cys Gln Glu Asn Lys  Cys Pro Val
    1790                1795                1800

Pro Phe  Cys Leu Asn Ile Lys  Gln Lys Leu Arg Gln  Gln Gln Leu
    1805                1810                1815

Gln His  Arg Leu Gln Gln Ala  Gln Met Leu Arg Arg  Arg Met Ala
    1820                1825                1830

Ser Met  Gln Arg Thr Gly Val  Val Gly Gln Gln Gln  Gly Leu Pro
    1835                1840                1845

Ser Pro  Thr Pro Ala Thr Pro  Thr Thr Pro Thr Gly  Gln Gln Pro
    1850                1855                1860

Thr Thr  Pro Gln Thr Pro Gln  Pro Thr Ser Gln Pro  Gln Pro Thr
    1865                1870                1875

Pro Pro  Asn Ser Met Pro Pro  Tyr Leu Pro Arg Thr  Gln Ala Ala
    1880                1885                1890

Gly Pro  Val Ser Gln Gly Lys  Ala Ala Gly Gln Val  Thr Pro Pro
    1895                1900                1905

Thr Pro  Pro Gln Thr Ala Gln  Pro Pro Leu Pro Gly  Pro Pro Pro
    1910                1915                1920

Ala Ala  Val Glu Met Ala Met  Gln Ile Gln Arg Ala  Ala Glu Thr
    1925                1930                1935

Gln Arg  Gln Met Ala His Val  Gln Ile Phe Gln Arg  Pro Ile Gln
    1940                1945                1950

His Gln  Met Pro Pro Met Thr  Pro Met Ala Pro Met  Gly Met Asn
    1955                1960                1965
```

```
Pro Pro  Pro Met Thr Arg Gly  Pro Ser Gly His Leu  Glu Pro Gly
    1970                1975                1980

Met Gly  Pro Thr Gly Met Gln  Gln Gln Pro Pro Trp  Ser Gln Gly
    1985                1990                1995

Gly Leu  Pro Gln Pro Gln Gln  Leu Gln Ser Gly Met  Pro Arg Pro
    2000                2005                2010

Ala Met  Met Ser Val Ala Gln  His Gly Gln Pro Leu  Asn Met Ala
    2015                2020                2025

Pro Gln  Pro Gly Leu Gly Gln  Val Gly Ile Ser Pro  Leu Lys Pro
    2030                2035                2040

Gly Thr  Val Ser Gln Gln Ala  Leu Gln Asn Leu Leu  Arg Thr Leu
    2045                2050                2055

Arg Ser  Pro Ser Ser Pro Leu  Gln Gln Gln Gln Val  Leu Ser Ile
    2060                2065                2070

Leu His  Ala Asn Pro Gln Leu  Leu Ala Ala Phe Ile  Lys Gln Arg
    2075                2080                2085

Ala Ala  Lys Tyr Ala Asn Ser  Asn Pro Gln Pro Ile  Pro Gly Gln
    2090                2095                2100

Pro Gly  Met Pro Gln Gly Gln  Pro Gly Leu Gln Pro  Pro Thr Met
    2105                2110                2115

Pro Gly  Gln Gln Gly Val His  Ser Asn Pro Ala Met  Gln Asn Met
    2120                2125                2130

Asn Pro  Met Gln Ala Gly Val  Gln Arg Ala Gly Leu  Pro Gln Gln
    2135                2140                2145

Gln Pro  Gln Gln Gln Leu Gln  Pro Pro Met Gly Gly  Met Ser Pro
    2150                2155                2160

Gln Ala  Gln Gln Met Asn Met  Asn His Asn Thr Met  Pro Ser Gln
    2165                2170                2175

Phe Arg  Asp Ile Leu Arg Arg  Gln Gln Met Met Gln  Gln Gln Gln
    2180                2185                2190

Gln Gln  Gly Ala Gly Pro Gly  Ile Gly Pro Gly Met  Ala Asn His
    2195                2200                2205

Asn Gln  Phe Gln Gln Pro Gln  Gly Val Gly Tyr Pro  Pro Gln Gln
    2210                2215                2220
```

```
Gln Gln  Arg Met Gln His His  Met Gln Gln Met Gln  Gln Gly Asn
    2225                 2230                 2235

Met Gly  Gln Ile Gly Gln Leu  Pro Gln Ala Leu Gly  Ala Glu Ala
    2240                 2245                 2250

Gly Ala  Ser Leu Gln Ala Tyr  Gln Gln Arg Leu Leu  Gln Gln Gln
    2255                 2260                 2265

Met Gly  Ser Pro Val Gln Pro  Asn Pro Met Ser Pro  Gln Gln His
    2270                 2275                 2280

Met Leu  Pro Asn Gln Ala Gln  Ser Pro His Leu Gln  Gly Gln Gln
    2285                 2290                 2295

Ile Pro  Asn Ser Leu Ser Asn  Gln Val Arg Ser Pro  Gln Pro Val
    2300                 2305                 2310

Pro Ser  Pro Arg Pro Gln Ser  Gln Pro Pro His Ser  Ser Pro Ser
    2315                 2320                 2325

Pro Arg  Met Gln Pro Gln Pro  Ser Pro His His Val  Ser Pro Gln
    2330                 2335                 2340

Thr Ser  Ser Pro His Pro Gly  Leu Val Ala Ala Gln  Ala Asn Pro
    2345                 2350                 2355

Met Glu  Gln Gly His Phe Ala  Ser Pro Asp Gln Asn  Ser Met Leu
    2360                 2365                 2370

Ser Gln  Leu Ala Ser Asn Pro  Gly Met Ala Asn Leu  His Gly Ala
    2375                 2380                 2385

Ser Ala  Thr Asp Leu Gly Leu  Ser Thr Asp Asn Ser  Asp Leu Asn
    2390                 2395                 2400

Ser Asn  Leu Ser Gln Ser Thr  Leu Asp Ile His
    2405                 2410
```

<210> 290
<211> 579
<212> PRT
<213> Homo sapiens

<400> 290

```
Met Asn Thr Ala Pro Ser Arg Pro Ser Pro Thr Arg Arg Asp Pro Tyr
1               5                  10                  15

Gly Phe Gly Asp Ser Arg Asp Ser Arg Arg Asp Arg Ser Pro Ile Arg
            20                  25                  30
```

```
Gly Ser Pro Arg Arg Glu Pro Arg Asp Gly Arg Asn Gly Arg Asp Ala
        35                  40                  45

Arg Asp Ser Arg Asp Ile Arg Asp Pro Arg Asp Leu Arg Asp His Arg
    50                  55                  60

His Ser Arg Asp Leu Arg Asp His Arg Asp Ser Arg Ser Val Arg Asp
65                  70                  75                  80

Val Arg Asp Val Arg Asp Leu Arg Asp Phe Arg Asp Leu Arg Asp Ser
                85                  90                  95

Arg Asp Phe Arg Asp Gln Arg Asp Pro Met Tyr Asp Arg Tyr Arg Asp
            100                 105                 110

Met Arg Asp Ser Arg Asp Pro Met Tyr Arg Arg Glu Gly Ser Tyr Asp
        115                 120                 125

Arg Tyr Leu Arg Met Asp Asp Tyr Cys Arg Arg Lys Asp Asp Ser Tyr
    130                 135                 140

Phe Asp Arg Tyr Arg Asp Ser Phe Asp Gly Arg Gly Pro Pro Gly Pro
145                 150                 155                 160

Glu Ser Gln Ser Arg Ala Lys Glu Arg Leu Lys Arg Glu Glu Arg Arg
                165                 170                 175

Arg Glu Glu Leu Tyr Arg Gln Tyr Phe Glu Glu Ile Gln Arg Arg Phe
            180                 185                 190

Asp Ala Glu Arg Pro Val Asp Cys Ser Val Ile Val Val Asn Lys Gln
        195                 200                 205

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

Met Val Val Asp Leu Ile Phe Leu Asn Thr Glu Val Ser Leu Ser Gln
225                 230                 235                 240

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

Thr Gln Gln His Gln Ile His Arg Ser Cys Thr Val Asn Ile Met Phe
            260                 265                 270

Gly Thr Pro Gln Glu His Arg Asn Met Pro Gln Ala Asp Ala Met Val
        275                 280                 285

Leu Val Ala Arg Asn Tyr Glu Arg Tyr Lys Asn Glu Cys Arg Glu Lys
    290                 295                 300
```

```
Glu Arg Glu Glu Ile Ala Arg Gln Ala Ala Lys Met Ala Asp Glu Ala
305                 310                 315                 320

Ile Leu Gln Glu Arg Glu Arg Gly Gly Pro Glu Glu Gly Val Arg Gly
                325                 330                 335

Gly His Pro Pro Ala Ile Gln Ser Leu Ile Asn Leu Leu Ala Asp Asn
            340                 345                 350

Arg Tyr Leu Thr Ala Glu Glu Thr Asp Lys Ile Ile Asn Tyr Leu Arg
        355                 360                 365

Glu Arg Lys Glu Arg Leu Met Arg Ser Ser Thr Asp Ser Leu Pro Gly
    370                 375                 380

Pro Ile Ser Arg Gln Pro Leu Gly Ala Thr Ser Gly Ala Ser Leu Lys
385                 390                 395                 400

Thr Gln Pro Ser Ser Gln Pro Leu Gln Ser Gly Gln Val Leu Pro Ser
                405                 410                 415

Ala Thr Pro Thr Pro Ser Ala Pro Pro Thr Ser Gln Gln Glu Leu Gln
            420                 425                 430

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

Ser Ser Ala Ser Pro Ser Val Ala Ala Gly Asn Thr Pro Asn Gln Asn
    450                 455                 460

Phe Ser Thr Ala Ala Asn Ser Gln Pro Gln Gln Arg Ser Gln Ala Ser
465                 470                 475                 480

Gly Asn Gln Pro Pro Ser Ile Leu Gly Gln Gly Gly Ser Ala Gln Asn
                485                 490                 495

Met Gly Pro Arg Pro Gly Ala Pro Ser Gln Gly Leu Phe Gly Gln Pro
            500                 505                 510

Ser Ser Arg Leu Ala Pro Ala Ser Asn Met Thr Ser Gln Arg Pro Val
        515                 520                 525

Ser Ser Thr Gly Ile Asn Phe Asp Asn Pro Ser Val Gln Lys Ala Leu
    530                 535                 540

Asp Thr Leu Ile Gln Ser Gly Pro Ala Leu Ser His Leu Val Ser Gln
545                 550                 555                 560

Thr Thr Ala Gln Met Gly Gln Pro Gln Ala Pro Met Gly Ser Tyr Gln
                565                 570                 575
```

Arg His Tyr

<210> 291
<211> 614
<212> PRT
<213> Homo sapiens

<400> 291

Met Asn Thr Phe Gln Asp Gln Ser Gly Ser Ser Ser Asn Arg Glu Pro
1 5 10 15

Leu Leu Arg Cys Ser Asp Ala Arg Arg Asp Leu Glu Leu Ala Ile Gly
20 25 30

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

Lys Ala Gln Ile His Ser Cys Ile Ser Arg His Leu Glu Cys Leu Arg
50 55 60

Ser Arg Glu Val Trp Leu Tyr Glu Gln Val Asp Leu Ile Tyr Gln Leu
65 70 75 80

Lys Glu Glu Thr Leu Gln Gln Gln Ala Gln Gln Leu Tyr Ser Leu Leu
85 90 95

Gly Gln Phe Asn Cys Leu Thr His Gln Leu Glu Cys Thr Gln Asn Lys
100 105 110

Asp Leu Ala Asn Gln Val Ser Val Cys Leu Glu Arg Leu Gly Ser Leu
115 120 125

Thr Leu Lys Pro Glu Asp Ser Thr Val Leu Leu Phe Glu Ala Asp Thr
130 135 140

Ile Thr Leu Arg Gln Thr Ile Thr Thr Phe Gly Ser Leu Lys Thr Ile
145 150 155 160

Gln Ile Pro Glu His Leu Met Ala His Ala Ser Ser Ala Asn Ile Gly
165 170 175

Pro Phe Leu Glu Lys Arg Gly Cys Ile Ser Met Pro Glu Gln Lys Ser
180 185 190

Ala Ser Gly Ile Val Ala Val Pro Phe Ser Glu Trp Leu Leu Gly Ser
195 200 205

Lys Pro Ala Ser Gly Tyr Gln Ala Pro Tyr Ile Pro Ser Thr Asp Pro
210 215 220

Gln Asp Trp Leu Thr Gln Lys Gln Thr Leu Glu Asn Ser Gln Thr Ser

225 230 235 240

Ser Arg Ala Cys Asn Phe Phe Asn Asn Val Gly Gly Asn Leu Lys Gly
245 250 255

Leu Glu Asn Trp Leu Leu Lys Ser Glu Lys Ser Ser Tyr Gln Lys Cys
260 265 270

Asn Ser His Ser Thr Thr Ser Ser Phe Ser Ile Glu Met Glu Lys Val
275 280 285

Gly Asp Gln Glu Leu Pro Asp Gln Asp Glu Met Asp Leu Ser Asp Trp
290 295 300

Leu Val Thr Pro Gln Glu Ser His Lys Leu Arg Lys Pro Glu Asn Gly
305 310 315 320

Ser Arg Glu Thr Ser Glu Lys Phe Lys Leu Leu Phe Gln Ser Tyr Asn
325 330 335

Val Asn Asp Trp Leu Val Lys Thr Asp Ser Cys Thr Asn Cys Gln Gly
340 345 350

Asn Gln Pro Lys Gly Val Glu Ile Glu Asn Leu Gly Asn Leu Lys Cys
355 360 365

Leu Asn Asp His Leu Glu Ala Lys Lys Pro Leu Ser Thr Pro Ser Met
370 375 380

Val Thr Glu Asp Trp Leu Val Gln Asn His Gln Asp Pro Cys Lys Val
385 390 395 400

Glu Glu Val Cys Arg Ala Asn Glu Pro Cys Thr Ser Phe Ala Glu Cys
405 410 415

Val Cys Asp Glu Asn Cys Glu Lys Glu Ala Leu Tyr Lys Trp Leu Leu
420 425 430

Lys Lys Glu Gly Lys Asp Lys Asn Gly Met Pro Val Glu Pro Lys Pro
435 440 445

Glu Pro Glu Lys His Lys Asp Ser Leu Asn Met Trp Leu Cys Pro Arg
450 455 460

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

Arg Ile Ala Asp Ser Phe Gln Val Ile Lys Asn Ser Pro Leu Ser Glu
485 490 495

Trp Leu Ile Arg Pro Pro Tyr Lys Glu Gly Ser Pro Lys Glu Val Pro

500 505 510

Gly Thr Glu Asp Arg Ala Gly Lys Gln Lys Phe Lys Ser Pro Met Asn
515 520 525

Thr Ser Trp Cys Ser Phe Asn Thr Ala Asp Trp Val Leu Pro Gly Lys
530 535 540

Lys Met Gly Asn Leu Ser Gln Leu Ser Ser Gly Glu Asp Lys Trp Leu
545 550 555 560

Leu Arg Lys Lys Ala Gln Glu Val Leu Leu Asn Ser Pro Leu Gln Glu
565 570 575

Glu His Asn Phe Pro Pro Asp His Tyr Gly Leu Pro Ala Val Cys Asp
580 585 590

Leu Phe Ala Cys Met Gln Leu Lys Val Asp Lys Glu Lys Trp Leu Tyr
595 600 605

Arg Thr Pro Leu Gln Met
610

<210> 292
<211> 1016
<212> PRT
<213> Homo sapiens

<400> 292

Met Glu Val Ala Val Glu Lys Ala Val Ala Ala Ala Ala Ala Ala Ser
1 5 10 15

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

Ala Glu Ser Arg Gln Gly Pro Asp Ser Glu Arg Gly Gly Glu Ala Ala
35 40 45

Arg Leu Asn Leu Leu Asp Thr Cys Ala Val Cys His Gln Asn Ile Gln
50 55 60

Ser Arg Ala Pro Lys Leu Leu Pro Cys Leu His Ser Phe Cys Gln Arg
65 70 75 80

Cys Leu Pro Ala Pro Gln Arg Tyr Leu Met Leu Pro Ala Pro Met Leu
85 90 95

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

Ser Gly Ser Ser Pro Phe Ala Thr Gln Val Gly Val Ile Arg Cys Pro
115 120 125

```
Val Cys Ser Gln Glu Cys Ala Glu Arg His Ile Ile Asp Asn Phe Phe
    130                 135                 140

Val Lys Asp Thr Thr Glu Val Pro Ser Ser Thr Val Glu Lys Ser Asn
145                 150                 155                 160

Gln Val Cys Thr Ser Cys Glu Asp Asn Ala Glu Ala Asn Gly Phe Cys
                165                 170                 175

Val Glu Cys Val Glu Trp Leu Cys Lys Thr Cys Ile Arg Ala His Gln
            180                 185                 190

Arg Val Lys Phe Thr Lys Asp His Thr Val Arg Gln Lys Glu Glu Val
        195                 200                 205

Ser Pro Glu Ala Val Gly Val Thr Ser Gln Arg Pro Val Phe Cys Pro
    210                 215                 220

Phe His Lys Lys Glu Gln Leu Lys Leu Tyr Cys Glu Thr Cys Asp Lys
225                 230                 235                 240

Leu Thr Cys Arg Asp Cys Gln Leu Leu Glu His Lys Glu His Arg Tyr
                245                 250                 255

Gln Phe Ile Glu Glu Ala Phe Gln Asn Gln Lys Val Ile Ile Asp Thr
            260                 265                 270

Leu Ile Thr Lys Leu Met Glu Lys Thr Lys Tyr Ile Lys Phe Thr Gly
        275                 280                 285

Asn Gln Ile Gln Asn Arg Ile Ile Glu Val Asn Gln Asn Gln Lys Gln
    290                 295                 300

Val Glu Gln Asp Ile Lys Val Ala Ile Phe Thr Leu Met Val Glu Ile
305                 310                 315                 320

Asn Lys Lys Gly Lys Ala Leu Leu His Gln Leu Glu Ser Leu Ala Lys
                325                 330                 335

Asp His Arg Met Lys Leu Met Gln Gln Gln Gln Glu Val Ala Gly Leu
            340                 345                 350

Ser Lys Gln Leu Glu His Val Met His Phe Ser Lys Trp Ala Val Ser
        355                 360                 365

Ser Gly Ser Ser Thr Ala Leu Leu Tyr Ser Lys Arg Leu Ile Thr Tyr
    370                 375                 380

Arg Leu Arg His Leu Leu Arg Ala Arg Cys Asp Ala Ser Pro Val Thr
385                 390                 395                 400
```

```
Asn Asn Thr Ile Gln Phe His Cys Asp Pro Ser Phe Trp Ala Gln Asn
                405                 410                 415

Ile Ile Asn Leu Gly Ser Leu Val Ile Glu Asp Lys Glu Ser Gln Pro
            420                 425                 430

Gln Met Pro Lys Gln Asn Pro Val Val Glu Gln Asn Ser Gln Pro Pro
        435                 440                 445

Ser Gly Leu Ser Ser Asn Gln Leu Ser Lys Phe Pro Thr Gln Ile Ser
    450                 455                 460

Leu Ala Gln Leu Arg Leu Gln His Met Gln Gln Gln Pro Pro Pro
465                 470                 475                 480

Arg Leu Ile Asn Phe Gln Asn His Ser Pro Lys Pro Asn Gly Pro Val
                485                 490                 495

Leu Pro Pro His Pro Gln Gln Leu Arg Tyr Pro Pro Asn Gln Asn Ile
            500                 505                 510

Pro Arg Gln Ala Ile Lys Pro Asn Pro Leu Gln Met Ala Phe Leu Ala
        515                 520                 525

Gln Gln Ala Ile Lys Gln Trp Gln Ile Ser Ser Gly Gln Gly Thr Pro
    530                 535                 540

Ser Thr Thr Asn Ser Thr Ser Ser Thr Pro Ser Ser Pro Thr Ile Thr
545                 550                 555                 560

Ser Ala Ala Gly Tyr Asp Gly Lys Ala Phe Gly Ser Pro Met Ile Asp
                565                 570                 575

Leu Ser Ser Pro Val Gly Gly Ser Tyr Asn Leu Pro Ser Leu Pro Asp
            580                 585                 590

Ile Asp Cys Ser Ser Thr Ile Met Leu Asp Asn Ile Val Arg Lys Asp
        595                 600                 605

Thr Asn Ile Asp His Gly Gln Pro Arg Pro Pro Ser Asn Arg Thr Val
    610                 615                 620

Gln Ser Pro Asn Ser Ser Val Pro Ser Pro Gly Leu Ala Gly Pro Val
625                 630                 635                 640

Thr Met Thr Ser Val His Pro Pro Ile Arg Ser Pro Ser Ala Ser Ser
                645                 650                 655

Val Gly Ser Arg Gly Ser Ser Gly Ser Ser Ser Lys Pro Ala Gly Ala
            660                 665                 670
```

```
Asp Ser Thr His Lys Val Pro Val Val Met Leu Glu Pro Ile Arg Ile
        675                 680                 685

Lys Gln Glu Asn Ser Gly Pro Pro Glu Asn Tyr Asp Phe Pro Val Val
    690                 695                 700

Ile Val Lys Gln Glu Ser Asp Glu Glu Ser Arg Pro Gln Asn Ala Asn
705                 710                 715                 720

Tyr Pro Arg Ser Ile Leu Thr Ser Leu Leu Leu Asn Ser Ser Gln Ser
                725                 730                 735

Ser Thr Ser Glu Glu Thr Val Leu Arg Ser Asp Ala Pro Asp Ser Thr
            740                 745                 750

Gly Asp Gln Pro Gly Leu His Gln Asp Asn Ser Ser Asn Gly Lys Ser
        755                 760                 765

Glu Trp Leu Asp Pro Ser Gln Lys Ser Pro Leu His Val Gly Glu Thr
    770                 775                 780

Arg Lys Glu Asp Asp Pro Asn Glu Asp Trp Cys Ala Val Cys Gln Asn
785                 790                 795                 800

Gly Gly Glu Leu Leu Cys Cys Glu Lys Cys Pro Lys Val Phe His Leu
                805                 810                 815

Ser Cys His Val Pro Thr Leu Thr Asn Phe Pro Ser Gly Glu Trp Ile
            820                 825                 830

Cys Thr Phe Cys Arg Asp Leu Ser Lys Pro Glu Val Glu Tyr Asp Cys
        835                 840                 845

Asp Ala Pro Ser His Asn Ser Glu Lys Lys Lys Thr Glu Gly Leu Val
    850                 855                 860

Lys Leu Thr Pro Ile Asp Lys Arg Lys Cys Glu Arg Leu Leu Leu Phe
865                 870                 875                 880

Leu Tyr Cys His Glu Met Ser Leu Ala Phe Gln Asp Pro Val Pro Leu
                885                 890                 895

Thr Val Pro Asp Tyr Tyr Lys Ile Ile Lys Asn Pro Met Asp Leu Ser
            900                 905                 910

Thr Ile Lys Lys Arg Leu Gln Glu Asp Tyr Ser Met Tyr Ser Lys Pro
        915                 920                 925

Glu Asp Phe Val Ala Asp Phe Arg Leu Ile Phe Gln Asn Cys Ala Glu
    930                 935                 940
```

```
Phe Asn Glu Pro Asp Ser Glu Val Ala Asn Ala Gly Ile Lys Leu Glu
945                 950                 955                 960


Asn Tyr Phe Glu Glu Leu Leu Lys Asn Leu Tyr Pro Glu Lys Arg Phe
                965                 970                 975


Pro Lys Pro Glu Phe Arg Asn Glu Ser Glu Asp Asn Lys Phe Ser Asp
            980                 985                 990


Asp Ser Asp Asp Asp Phe Val Gln  Pro Arg Lys Lys Arg  Leu Lys Ser
        995                 1000                1005


Ile Glu  Glu Arg Gln Leu Leu  Lys
    1010                1015


<210>  293
<211>  2696
<212>  PRT
<213>  Homo sapiens

<400>  293

Met Asp Gln Thr Cys Glu Leu Pro Arg Arg Asn Cys Leu Leu Pro Phe
1               5                   10                  15


Ser Asn Pro Val Asn Leu Asp Ala Pro Glu Asp Lys Asp Ser Pro Phe
            20                  25                  30


Gly Asn Gly Gln Ser Asn Phe Ser Glu Pro Leu Asn Gly Cys Thr Met
        35                  40                  45


Gln Leu Ser Thr Val Ser Gly Thr Ser Gln Asn Ala Tyr Gly Gln Asp
    50                  55                  60


Ser Pro Ser Cys Tyr Ile Pro Leu Arg Arg Leu Gln Asp Leu Ala Ser
65                  70                  75                  80


Met Ile Asn Val Glu Tyr Leu Asn Gly Ser Ala Asp Gly Ser Glu Ser
                85                  90                  95


Phe Gln Asp Pro Glu Lys Ser Asp Ser Arg Ala Gln Thr Pro Ile Val
            100                 105                 110


Cys Thr Ser Leu Ser Pro Gly Gly Pro Thr Ala Leu Ala Met Lys Gln
        115                 120                 125


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


Thr Ile Lys Asn Gly Phe Leu His Phe Glu Asn Phe Thr Cys Val Asp
145                 150                 155                 160
```

```
Asp Ala Asp Val Asp Ser Glu Met Asp Pro Glu Gln Pro Val Thr Glu
                165                 170                 175

Asp Glu Ser Ile Glu Glu Ile Phe Glu Glu Thr Gln Thr Asn Ala Thr
            180                 185                 190

Cys Asn Tyr Glu Thr Lys Ser Glu Asn Gly Val Lys Val Ala Met Gly
        195                 200                 205

Ser Glu Gln Asp Ser Thr Pro Glu Ser Arg His Gly Ala Val Lys Ser
    210                 215                 220

Pro Phe Leu Pro Leu Ala Pro Gln Thr Glu Thr Gln Lys Asn Lys Gln
225                 230                 235                 240

Arg Asn Glu Val Asp Gly Ser Asn Glu Lys Ala Ala Leu Leu Pro Ala
                245                 250                 255

Pro Phe Ser Leu Gly Asp Thr Asn Ile Thr Ile Glu Glu Gln Leu Asn
            260                 265                 270

Ser Ile Asn Leu Ser Phe Gln Asp Asp Pro Asp Ser Ser Thr Ser Thr
        275                 280                 285

Leu Gly Asn Met Leu Glu Leu Pro Gly Thr Ser Ser Ser Ser Thr Ser
    290                 295                 300

Gln Glu Leu Pro Phe Cys Gln Pro Lys Lys Lys Ser Thr Pro Leu Lys
305                 310                 315                 320

Tyr Glu Val Gly Asp Leu Ile Trp Ala Lys Phe Lys Arg Arg Pro Trp
                325                 330                 335

Trp Pro Cys Arg Ile Cys Ser Asp Pro Leu Ile Asn Thr His Ser Lys
            340                 345                 350

Met Lys Val Ser Asn Arg Arg Pro Tyr Arg Gln Tyr Tyr Val Glu Ala
        355                 360                 365

Phe Gly Asp Pro Ser Glu Arg Ala Trp Val Ala Gly Lys Ala Ile Val
    370                 375                 380

Met Phe Glu Gly Arg His Gln Phe Glu Glu Leu Pro Val Leu Arg Arg
385                 390                 395                 400

Arg Gly Lys Gln Lys Glu Lys Gly Tyr Arg His Lys Val Pro Gln Lys
                405                 410                 415

Ile Leu Ser Lys Trp Glu Ala Ser Val Gly Leu Ala Glu Gln Tyr Asp
            420                 425                 430
```

```
Val Pro Lys Gly Ser Lys Asn Arg Lys Cys Ile Pro Gly Ser Ile Lys
        435                 440                 445

Leu Asp Ser Glu Glu Asp Met Pro Phe Glu Asp Cys Thr Asn Asp Pro
    450                 455                 460

Glu Ser Glu His Asp Leu Leu Leu Asn Gly Cys Leu Lys Ser Leu Ala
465                 470                 475                 480

Phe Asp Ser Glu His Ser Ala Asp Glu Lys Glu Lys Pro Cys Ala Lys
                485                 490                 495

Ser Arg Ala Arg Lys Ser Ser Asp Asn Pro Lys Arg Thr Ser Val Lys
            500                 505                 510

Lys Gly His Ile Gln Phe Glu Ala His Lys Asp Glu Arg Arg Gly Lys
        515                 520                 525

Ile Pro Glu Asn Leu Gly Leu Asn Phe Ile Ser Gly Asp Ile Ser Asp
    530                 535                 540

Thr Gln Ala Ser Asn Glu Leu Ser Arg Ile Ala Asn Ser Leu Thr Gly
545                 550                 555                 560

Ser Asn Thr Ala Pro Gly Ser Phe Leu Phe Ser Ser Cys Gly Lys Asn
                565                 570                 575

Thr Ala Lys Lys Glu Phe Glu Thr Ser Asn Gly Asp Ser Leu Leu Gly
            580                 585                 590

Leu Pro Glu Gly Ala Leu Ile Ser Lys Cys Ser Arg Glu Lys Asn Lys
        595                 600                 605

Pro Gln Arg Ser Leu Val Cys Gly Ser Lys Val Lys Leu Cys Tyr Ile
    610                 615                 620

Gly Ala Gly Asp Glu Glu Lys Arg Ser Asp Ser Ile Ser Ile Cys Thr
625                 630                 635                 640

Thr Ser Asp Asp Gly Ser Ser Asp Leu Asp Pro Ile Glu His Ser Ser
                645                 650                 655

Glu Ser Asp Asn Ser Val Leu Glu Ile Pro Asp Ala Phe Asp Arg Thr
            660                 665                 670

Glu Asn Met Leu Ser Met Gln Lys Asn Glu Lys Ile Lys Tyr Ser Arg
        675                 680                 685

Phe Ala Ala Thr Asn Thr Arg Val Lys Ala Lys Gln Lys Pro Leu Ile
    690                 695                 700
```

```
Ser Asn Ser His Thr Asp His Leu Met Gly Cys Thr Lys Ser Ala Glu
705                 710                 715                 720

Pro Gly Thr Glu Thr Ser Gln Val Asn Leu Ser Asp Leu Lys Ala Ser
                725                 730                 735

Thr Leu Val His Lys Pro Gln Ser Asp Phe Thr Asn Asp Ala Leu Ser
            740                 745                 750

Pro Lys Phe Asn Leu Ser Ser Ser Ile Ser Ser Glu Asn Ser Leu Ile
        755                 760                 765

Lys Gly Gly Ala Ala Asn Gln Ala Leu Leu His Ser Lys Ser Lys Gln
    770                 775                 780

Pro Lys Phe Arg Ser Ile Lys Cys Lys His Lys Glu Asn Pro Val Met
785                 790                 795                 800

Ala Glu Pro Pro Val Ile Asn Glu Glu Cys Ser Leu Lys Cys Cys Ser
                805                 810                 815

Ser Asp Thr Lys Gly Ser Pro Leu Ala Ser Ile Ser Lys Ser Gly Lys
            820                 825                 830

Val Asp Gly Leu Lys Leu Leu Asn Asn Met His Glu Lys Thr Arg Asp
        835                 840                 845

Ser Ser Asp Ile Glu Thr Ala Val Val Lys His Val Leu Ser Glu Leu
    850                 855                 860

Lys Glu Leu Ser Tyr Arg Ser Leu Gly Glu Asp Val Ser Asp Ser Gly
865                 870                 875                 880

Thr Ser Lys Pro Ser Lys Pro Leu Leu Phe Ser Ser Ala Ser Ser Gln
                885                 890                 895

Asn His Ile Pro Ile Glu Pro Asp Tyr Lys Phe Ser Thr Leu Leu Met
            900                 905                 910

Met Leu Lys Asp Met His Asp Ser Lys Thr Lys Glu Gln Arg Leu Met
        915                 920                 925

Thr Ala Gln Asn Leu Val Ser Tyr Arg Ser Pro Gly Arg Gly Asp Cys
    930                 935                 940

Ser Thr Asn Ser Pro Val Gly Val Ser Lys Val Leu Val Ser Gly Gly
945                 950                 955                 960

Ser Thr His Asn Ser Glu Lys Lys Gly Asp Gly Thr Gln Asn Ser Ala
                965                 970                 975
```

```
Asn Pro Ser Pro Ser Gly Gly Asp Ser Ala Leu Ser Gly Glu Leu Ser
            980                 985                 990

Ala Ser Leu Pro Gly Leu Leu Ser  Asp Lys Arg Asp Leu  Pro Ala Ser
        995                 1000                1005

Gly Lys  Ser Arg Ser Asp Cys  Val Thr Arg Arg Asn  Cys Gly Arg
    1010                1015                1020

Ser Lys  Pro Ser Ser Lys Leu  Arg Asp Ala Phe Ser  Ala Gln Met
    1025                1030                1035

Val Lys  Asn Thr Val Asn Arg  Lys Ala Leu Lys Thr  Glu Arg Lys
    1040                1045                1050

Arg Lys  Leu Asn Gln Leu Pro  Ser Val Thr Leu Asp  Ala Val Leu
    1055                1060                1065

Gln Gly  Asp Arg Glu Arg Gly  Gly Ser Leu Arg Gly  Gly Ala Glu
    1070                1075                1080

Asp Pro  Ser Lys Glu Asp Pro  Leu Gln Ile Met Gly  His Leu Thr
    1085                1090                1095

Ser Glu  Asp Gly Asp His Phe  Ser Asp Val His Phe  Asp Ser Lys
    1100                1105                1110

Val Lys  Gln Ser Asp Pro Gly  Lys Ile Ser Glu Lys  Gly Leu Ser
    1115                1120                1125

Phe Glu  Asn Gly Lys Gly Pro  Glu Leu Asp Ser Val  Met Asn Ser
    1130                1135                1140

Glu Asn  Asp Glu Leu Asn Gly  Val Asn Gln Val Val  Pro Lys Lys
    1145                1150                1155

Arg Trp  Gln Arg Leu Asn Gln  Arg Arg Thr Lys Pro  Arg Lys Arg
    1160                1165                1170

Met Asn  Arg Phe Lys Glu Lys  Glu Asn Ser Glu Cys  Ala Phe Arg
    1175                1180                1185

Val Leu  Leu Pro Ser Asp Pro  Val Gln Glu Gly Arg  Asp Glu Phe
    1190                1195                1200

Pro Glu  His Arg Thr Pro Ser  Ala Ser Ile Leu Glu  Glu Pro Leu
    1205                1210                1215

Thr Glu  Gln Asn His Ala Asp  Cys Leu Asp Ser Ala  Gly Pro Arg
    1220                1225                1230
```

```
Leu Asn  Val Cys Asp Lys Ser  Ser Ala Ser Ile Gly  Asp Met Glu
    1235                 1240                 1245

Lys Glu  Pro Gly Ile Pro Ser  Leu Thr Pro Gln Ala  Glu Leu Pro
    1250                 1255                 1260

Glu Pro  Ala Val Arg Ser Glu  Lys Lys Arg Leu Arg  Lys Pro Ser
    1265                 1270                 1275

Lys Trp  Leu Leu Glu Tyr Thr  Glu Glu Tyr Asp Gln  Ile Phe Ala
    1280                 1285                 1290

Pro Lys  Lys Lys Gln Lys Lys  Val Gln Glu Gln Val  His Lys Val
    1295                 1300                 1305

Ser Ser  Arg Cys Glu Glu Glu  Ser Leu Leu Ala Arg  Gly Arg Ser
    1310                 1315                 1320

Ser Ala  Gln Asn Lys Gln Val  Asp Glu Asn Ser Leu  Ile Ser Thr
    1325                 1330                 1335

Lys Glu  Glu Pro Pro Val Leu  Glu Arg Glu Ala Pro  Phe Leu Glu
    1340                 1345                 1350

Gly Pro  Leu Ala Gln Ser Glu  Leu Gly Gly Gly His  Ala Glu Leu
    1355                 1360                 1365

Pro Gln  Leu Thr Leu Ser Val  Pro Val Ala Pro Glu  Val Ser Pro
    1370                 1375                 1380

Arg Pro  Ala Leu Glu Ser Glu  Glu Leu Leu Val Lys  Thr Pro Gly
    1385                 1390                 1395

Asn Tyr  Glu Ser Lys Arg Gln  Arg Lys Pro Thr Lys  Lys Leu Leu
    1400                 1405                 1410

Glu Ser  Asn Asp Leu Asp Pro  Gly Phe Met Pro Lys  Lys Gly Asp
    1415                 1420                 1425

Leu Gly  Leu Ser Lys Lys Cys  Tyr Glu Ala Gly His  Leu Glu Asn
    1430                 1435                 1440

Gly Ile  Thr Glu Ser Cys Ala  Thr Ser Tyr Ser Lys  Asp Phe Gly
    1445                 1450                 1455

Gly Gly  Thr Thr Lys Ile Phe  Asp Lys Pro Arg Lys  Arg Lys Arg
    1460                 1465                 1470

Gln Arg  His Ala Ala Ala Lys  Met Gln Cys Lys Lys  Val Lys Asn
    1475                 1480                 1485
```

```
Asp Asp  Ser Ser Lys Glu Ile  Pro Gly Ser Glu Gly  Glu Leu Met
    1490                 1495                 1500

Pro His  Arg Thr Ala Thr Ser  Pro Lys Glu Thr Val  Glu Glu Gly
    1505                 1510                 1515

Val Glu  His Asp Pro Gly Met  Pro Ala Ser Lys Lys  Met Gln Gly
    1520                 1525                 1530

Glu Arg  Gly Gly Gly Ala Ala  Leu Lys Glu Asn Val  Cys Gln Asn
    1535                 1540                 1545

Cys Glu  Lys Leu Gly Glu Leu  Leu Leu Cys Glu Ala  Gln Cys Cys
    1550                 1555                 1560

Gly Ala  Phe His Leu Glu Cys  Leu Gly Leu Thr Glu  Met Pro Arg
    1565                 1570                 1575

Gly Lys  Phe Ile Cys Asn Glu  Cys Arg Thr Gly Ile  His Thr Cys
    1580                 1585                 1590

Phe Val  Cys Lys Gln Ser Gly  Glu Asp Val Lys Arg  Cys Leu Leu
    1595                 1600                 1605

Pro Leu  Cys Gly Lys Phe Tyr  His Glu Glu Cys Val  Gln Lys Tyr
    1610                 1615                 1620

Pro Pro  Thr Val Met Gln Asn  Lys Gly Phe Arg Cys  Ser Leu His
    1625                 1630                 1635

Ile Cys  Ile Thr Cys His Ala  Ala Asn Pro Ala Asn  Val Ser Ala
    1640                 1645                 1650

Ser Lys  Gly Arg Leu Met Arg  Cys Val Arg Cys Pro  Val Ala Tyr
    1655                 1660                 1665

His Ala  Asn Asp Phe Cys Leu  Ala Ala Gly Ser Lys  Ile Leu Ala
    1670                 1675                 1680

Ser Asn  Ser Ile Ile Cys Pro  Asn His Phe Thr Pro  Arg Arg Gly
    1685                 1690                 1695

Cys Arg  Asn His Glu His Val  Asn Val Ser Trp Cys  Phe Val Cys
    1700                 1705                 1710

Ser Glu  Gly Gly Ser Leu Leu  Cys Cys Asp Ser Cys  Pro Ala Ala
    1715                 1720                 1725

Phe His  Arg Glu Cys Leu Asn  Ile Asp Ile Pro Glu  Gly Asn Trp
    1730                 1735                 1740
```

```
Tyr Cys  Asn Asp Cys Lys Ala  Gly Lys Lys Pro His  Tyr Arg Glu
    1745                1750                1755

Ile Val  Trp Val Lys Val Gly  Arg Tyr Arg Trp Trp  Pro Ala Glu
    1760                1765                1770

Ile Cys  His Pro Arg Ala Val  Pro Ser Asn Ile Asp  Lys Met Arg
    1775                1780                1785

His Asp  Val Gly Glu Phe Pro  Val Leu Phe Phe Gly  Ser Asn Asp
    1790                1795                1800

Tyr Leu  Trp Thr His Gln Ala  Arg Val Phe Pro Tyr  Met Glu Gly
    1805                1810                1815

Asp Val  Ser Ser Lys Asp Lys  Met Gly Lys Gly Val  Asp Gly Thr
    1820                1825                1830

Tyr Lys  Lys Ala Leu Gln Glu  Ala Ala Ala Arg Phe  Glu Glu Leu
    1835                1840                1845

Lys Ala  Gln Lys Glu Leu Arg  Gln Leu Gln Glu Asp  Arg Lys Asn
    1850                1855                1860

Asp Lys  Lys Pro Pro Pro Tyr  Lys His Ile Lys Val  Asn Arg Pro
    1865                1870                1875

Ile Gly  Arg Val Gln Ile Phe  Thr Ala Asp Leu Ser  Glu Ile Pro
    1880                1885                1890

Arg Cys  Asn Cys Lys Ala Thr  Asp Glu Asn Pro Cys  Gly Ile Asp
    1895                1900                1905

Ser Glu  Cys Ile Asn Arg Met  Leu Leu Tyr Glu Cys  His Pro Thr
    1910                1915                1920

Val Cys  Pro Ala Gly Gly Arg  Cys Gln Asn Gln Cys  Phe Ser Lys
    1925                1930                1935

Arg Gln  Tyr Pro Glu Val Glu  Ile Phe Arg Thr Leu  Gln Arg Gly
    1940                1945                1950

Trp Gly  Leu Arg Thr Lys Thr  Asp Ile Lys Lys Gly  Glu Phe Val
    1955                1960                1965

Asn Glu  Tyr Val Gly Glu Leu  Ile Asp Glu Glu Glu  Cys Arg Ala
    1970                1975                1980

Arg Ile  Arg Tyr Ala Gln Glu  His Asp Ile Thr Asn  Phe Tyr Met
    1985                1990                1995
```

```
Leu Thr  Leu Asp Lys Asp Arg  Ile Ile Asp Ala Gly  Pro Lys Gly
    2000                2005                2010

Asn Tyr  Ala Arg Phe Met Asn  His Cys Cys Gln Pro  Asn Cys Glu
    2015                2020                2025

Thr Gln  Lys Trp Ser Val Asn  Gly Asp Thr Arg Val  Gly Leu Phe
    2030                2035                2040

Ala Leu  Ser Asp Ile Lys Ala  Gly Thr Glu Leu Thr  Phe Asn Tyr
    2045                2050                2055

Asn Leu  Glu Cys Leu Gly Asn  Gly Lys Thr Val Cys  Lys Cys Gly
    2060                2065                2070

Ala Pro  Asn Cys Ser Gly Phe  Leu Gly Val Arg Pro  Lys Asn Gln
    2075                2080                2085

Pro Ile  Ala Thr Glu Glu Lys  Ser Lys Lys Phe Lys  Lys Lys Gln
    2090                2095                2100

Gln Gly  Lys Arg Arg Thr Gln  Gly Glu Ile Thr Lys  Glu Arg Glu
    2105                2110                2115

Asp Glu  Cys Phe Ser Cys Gly  Asp Ala Gly Gln Leu  Val Ser Cys
    2120                2125                2130

Lys Lys  Pro Gly Cys Pro Lys  Val Tyr His Ala Asp  Cys Leu Asn
    2135                2140                2145

Leu Thr  Lys Arg Pro Ala Gly  Lys Trp Glu Cys Pro  Trp His Gln
    2150                2155                2160

Cys Asp  Ile Cys Gly Lys Glu  Ala Ala Ser Phe Cys  Glu Met Cys
    2165                2170                2175

Pro Ser  Ser Phe Cys Lys Gln  His Arg Glu Gly Met  Leu Phe Ile
    2180                2185                2190

Ser Lys  Leu Asp Gly Arg Leu  Ser Cys Thr Glu His  Asp Pro Cys
    2195                2200                2205

Gly Pro  Asn Pro Leu Glu Pro  Gly Glu Ile Arg Glu  Tyr Val Pro
    2210                2215                2220

Pro Pro  Val Pro Leu Pro Pro  Gly Pro Ser Thr His  Leu Ala Glu
    2225                2230                2235

Gln Ser  Thr Gly Met Ala Ala  Gln Ala Pro Lys Met  Ser Asp Lys
    2240                2245                2250
```

```
Pro Pro  Ala Asp Thr Asn Gln  Met Leu Ser Leu Ser  Lys Lys Ala
    2255                 2260                 2265

Leu Ala  Gly Thr Cys Gln Arg  Pro Leu Leu Pro Glu  Arg Pro Leu
    2270                 2275                 2280

Glu Arg  Thr Asp Ser Arg Pro  Gln Pro Leu Asp Lys  Val Arg Asp
    2285                 2290                 2295

Leu Ala  Gly Ser Gly Thr Lys  Ser Gln Ser Leu Val  Ser Ser Gln
    2300                 2305                 2310

Arg Pro  Leu Asp Arg Pro Pro  Ala Val Ala Gly Pro  Arg Pro Gln
    2315                 2320                 2325

Leu Ser  Asp Lys Pro Ser Pro  Val Thr Ser Pro Ser  Ser Ser Pro
    2330                 2335                 2340

Ser Val  Arg Ser Gln Pro Leu  Glu Arg Pro Leu Gly  Thr Ala Asp
    2345                 2350                 2355

Pro Arg  Leu Asp Lys Ser Ile  Gly Ala Ala Ser Pro  Arg Pro Gln
    2360                 2365                 2370

Ser Leu  Glu Lys Thr Ser Val  Pro Thr Gly Leu Arg  Leu Pro Pro
    2375                 2380                 2385

Pro Asp  Arg Leu Leu Ile Thr  Ser Ser Pro Lys Pro  Gln Thr Ser
    2390                 2395                 2400

Asp Arg  Pro Thr Asp Lys Pro  His Ala Ser Leu Ser  Gln Arg Leu
    2405                 2410                 2415

Pro Pro  Pro Glu Lys Val Leu  Ser Ala Val Val Gln  Thr Leu Val
    2420                 2425                 2430

Ala Lys  Glu Lys Ala Leu Arg  Pro Val Asp Gln Asn  Thr Gln Ser
    2435                 2440                 2445

Lys Asn  Arg Ala Ala Leu Val  Met Asp Leu Ile Asp  Leu Thr Pro
    2450                 2455                 2460

Arg Gln  Lys Glu Arg Ala Ala  Ser Pro His Gln Val  Thr Pro Gln
    2465                 2470                 2475

Ala Asp  Glu Lys Met Pro Val  Leu Glu Ser Ser Ser  Trp Pro Ala
    2480                 2485                 2490

Ser Lys  Gly Leu Gly His Met  Pro Arg Ala Val Glu  Lys Gly Cys
    2495                 2500                 2505
```

```
Val Ser  Asp Pro Leu Gln Thr  Ser Gly Lys Ala Ala  Ala Pro Ser
    2510                 2515                 2520

Glu Asp  Pro Trp Gln Ala Val  Lys Ser Leu Thr Gln  Ala Arg Leu
    2525                 2530                 2535

Leu Ser  Gln Pro Pro Ala Lys  Ala Phe Leu Tyr Glu  Pro Thr Thr
    2540                 2545                 2550

Gln Ala  Ser Gly Arg Ala Ser  Ala Gly Ala Glu Gln  Thr Pro Gly
    2555                 2560                 2565

Pro Leu  Ser Gln Ser Pro Gly  Leu Val Lys Gln Ala  Lys Gln Met
    2570                 2575                 2580

Val Gly  Gly Gln Gln Leu Pro  Ala Leu Ala Ala Lys  Ser Gly Gln
    2585                 2590                 2595

Ser Phe  Arg Ser Leu Gly Lys  Ala Pro Ala Ser Leu  Pro Thr Glu
    2600                 2605                 2610

Glu Lys  Lys Leu Val Thr Thr  Glu Gln Ser Pro Trp  Ala Leu Gly
    2615                 2620                 2625

Lys Ala  Ser Ser Arg Ala Gly  Leu Trp Pro Ile Val  Ala Gly Gln
    2630                 2635                 2640

Thr Leu  Ala Gln Ser Cys Trp  Ser Ala Gly Ser Thr  Gln Thr Leu
    2645                 2650                 2655

Ala Gln  Thr Cys Trp Ser Leu  Gly Arg Gly Gln Asp  Pro Lys Pro
    2660                 2665                 2670

Glu Gln  Asn Thr Leu Pro Ala  Leu Asn Gln Ala Pro  Ser Ser His
    2675                 2680                 2685

Lys Cys  Ala Glu Ser Glu Gln  Lys
    2690                 2695
```

<210> 294
<211> 951
<212> PRT
<213> Homo sapiens

<400> 294

```
Met Ala Thr Gly Thr Gly Lys His Lys Leu Leu Ser Thr Gly Pro Thr
1               5                  10                  15

Glu Pro Trp Ser Ile Arg Glu Lys Leu Cys Leu Ala Ser Ser Val Met
            20                  25                  30
```

```
Arg Ser Gly Asp Gln Asn Trp Val Ser Val Ser Arg Ala Ile Lys Pro
        35                  40                  45

Phe Ala Glu Pro Gly Arg Pro Pro Asp Trp Phe Ser Gln Lys His Cys
    50                  55                  60

Ala Ser Gln Tyr Ser Glu Leu Leu Glu Thr Thr Glu Thr Pro Lys Arg
65                  70                  75                  80

Lys Arg Gly Glu Lys Gly Glu Val Val Glu Thr Val Glu Asp Val Ile
                85                  90                  95

Val Arg Lys Leu Thr Ala Glu Arg Val Glu Glu Leu Lys Lys Val Ile
            100                 105                 110

Lys Glu Thr Gln Glu Arg Tyr Arg Arg Leu Lys Arg Asp Ala Glu Leu
        115                 120                 125

Ile Gln Ala Gly His Met Asp Ser Arg Leu Asp Glu Leu Cys Asn Asp
    130                 135                 140

Ile Ala Thr Lys Lys Lys Leu Glu Glu Glu Glu Ala Glu Val Lys Arg
145                 150                 155                 160

Lys Ala Thr Asp Ala Ala Tyr Gln Ala Arg Gln Ala Val Lys Thr Pro
                165                 170                 175

Pro Arg Arg Leu Pro Thr Val Met Val Arg Ser Pro Ile Asp Ser Ala
            180                 185                 190

Ser Pro Gly Gly Asp Tyr Pro Leu Gly Asp Leu Thr Pro Thr Thr Met
        195                 200                 205

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

Val Thr Ser Phe Pro Gly Ile Pro Asp Thr Leu Pro Pro Gly Ser Ala
225                 230                 235                 240

Pro Leu Glu Ala Pro Met Thr Pro Val Thr Asp Asp Ser Pro Gln Lys
                245                 250                 255

Lys Met Leu Gly Gln Lys Ala Thr Pro Pro Pro Ser Pro Leu Leu Ser
            260                 265                 270

Glu Leu Leu Lys Lys Gly Ser Leu Leu Pro Thr Ser Pro Arg Leu Val
        275                 280                 285

Asn Glu Ser Glu Met Ala Val Ala Ser Gly His Leu Asn Ser Thr Gly
    290                 295                 300
```

```
Val Leu Leu Glu Val Gly Gly Val Leu Pro Met Ile His Gly Gly Glu
305                 310                 315                 320

Ile Gln Gln Thr Pro Asn Thr Val Ala Ala Ser Pro Ala Ala Ser Gly
                325                 330                 335

Ala Pro Thr Leu Ser Arg Leu Leu Glu Ala Gly Pro Thr Gln Phe Thr
            340                 345                 350

Thr Pro Leu Ala Ser Phe Thr Thr Val Ala Ser Glu Pro Pro Val Lys
        355                 360                 365

Leu Val Pro Pro Pro Val Glu Ser Val Ser Gln Ala Thr Ile Val Met
    370                 375                 380

Met Pro Ala Leu Pro Ala Pro Ser Ser Ala Pro Ala Val Ser Thr Thr
385                 390                 395                 400

Glu Ser Val Ala Pro Val Ser Gln Pro Asp Asn Cys Val Pro Met Glu
                405                 410                 415

Ala Val Gly Asp Pro His Thr Val Thr Val Ser Met Asp Ser Ser Glu
            420                 425                 430

Ile Ser Met Ile Ile Asn Ser Ile Lys Glu Glu Cys Phe Arg Ser Gly
        435                 440                 445

Val Ala Glu Ala Pro Val Gly Ser Lys Ala Pro Ser Ile Asp Gly Lys
    450                 455                 460

Glu Glu Leu Asp Leu Ala Glu Lys Met Asp Ile Ala Val Ser Tyr Thr
465                 470                 475                 480

Gly Glu Glu Leu Asp Phe Glu Thr Val Gly Asp Ile Ile Ala Ile Ile
                485                 490                 495

Glu Asp Lys Val Asp Asp His Pro Glu Val Leu Asp Val Ala Ala Val
            500                 505                 510

Glu Ala Ala Leu Ser Phe Cys Glu Glu Asn Asp Asp Pro Gln Ser Leu
        515                 520                 525

Pro Gly Pro Trp Glu His Pro Ile Gln Gln Glu Arg Asp Lys Pro Val
    530                 535                 540

Pro Leu Pro Ala Pro Glu Met Thr Val Lys Gln Glu Arg Leu Asp Phe
545                 550                 555                 560

Glu Glu Thr Glu Asn Lys Gly Ile His Glu Leu Val Asp Ile Arg Glu
                565                 570                 575
```

```
Pro Ser Ala Glu Ile Lys Val Glu Pro Ala Glu Pro Glu Pro Val Ile
            580                 585                 590

Ser Gly Ala Glu Ile Val Ala Gly Val Val Pro Ala Thr Ser Met Glu
        595                 600                 605

Pro Pro Glu Leu Arg Ser Gln Asp Leu Asp Glu Glu Leu Gly Ser Thr
    610                 615                 620

Ala Ala Gly Glu Ile Val Glu Ala Asp Val Ala Ile Gly Lys Gly Asp
625                 630                 635                 640

Glu Thr Pro Leu Thr Asn Val Lys Thr Glu Ala Ser Pro Glu Ser Met
                645                 650                 655

Leu Ser Pro Ser His Gly Ser Asn Pro Ile Glu Asp Pro Leu Glu Ala
            660                 665                 670

Glu Thr Gln His Lys Phe Glu Met Ser Asp Ser Leu Lys Glu Glu Ser
        675                 680                 685

Gly Thr Ile Phe Gly Ser Gln Ile Lys Asp Ala Pro Gly Glu Asp Glu
    690                 695                 700

Glu Glu Asp Gly Val Ser Glu Ala Ala Ser Leu Glu Glu Pro Lys Glu
705                 710                 715                 720

Glu Asp Gln Gly Glu Gly Tyr Leu Ser Glu Met Asp Asn Glu Pro Pro
                725                 730                 735

Val Ser Glu Ser Asp Asp Gly Phe Ser Ile His Asn Ala Thr Leu Gln
            740                 745                 750

Ser His Thr Leu Ala Asp Ser Ile Pro Ser Ser Pro Ala Ser Ser Gln
        755                 760                 765

Phe Ser Val Cys Ser Glu Asp Gln Glu Ala Ile Gln Ala Gln Lys Ile
    770                 775                 780

Trp Lys Lys Ala Ile Met Leu Val Trp Arg Ala Ala Ala Asn His Arg
785                 790                 795                 800

Tyr Ala Asn Val Phe Leu Gln Pro Val Thr Asp Asp Ile Ala Pro Gly
                805                 810                 815

Tyr His Ser Ile Val Gln Arg Pro Met Asp Leu Ser Thr Ile Lys Lys
            820                 825                 830

Asn Ile Glu Asn Gly Leu Ile Arg Ser Thr Ala Glu Phe Gln Arg Asp
        835                 840                 845
```

Ile Met Leu Met Phe Gln Asn Ala Val Met Tyr Asn Ser Ser Asp His
850 855 860

Asp Val Tyr His Met Ala Val Glu Met Gln Arg Asp Val Leu Glu Gln
865 870 875 880

Ile Gln Gln Phe Leu Ala Thr Gln Leu Ile Met Gln Thr Ser Glu Ser
885 890 895

Gly Ile Ser Ala Lys Ser Leu Arg Gly Arg Asp Ser Thr Arg Lys Gln
900 905 910

Asp Ala Ser Glu Lys Asp Ser Val Pro Met Gly Ser Pro Ala Phe Leu
915 920 925

Leu Ser Leu Phe Asp Gly Gly Thr Arg Gly Arg Arg Cys Ala Ile Glu
930 935 940

Ala Asp Met Lys Met Lys Lys
945 950

<210> 295
<211> 513
<212> PRT
<213> Homo sapiens

<400> 295

Met Ala Glu Val Gly Glu Ile Ile Glu Gly Cys Arg Leu Pro Val Leu
1 5 10 15

Arg Arg Asn Gln Asp Asn Glu Asp Glu Trp Pro Leu Ala Glu Ile Leu
20 25 30

Ser Val Lys Asp Ile Ser Gly Arg Lys Leu Phe Tyr Val His Tyr Ile
35 40 45

Asp Phe Asn Lys Arg Leu Asp Glu Trp Val Thr His Glu Arg Leu Asp
50 55 60

Leu Lys Lys Ile Gln Phe Pro Lys Lys Glu Ala Lys Thr Pro Thr Lys
65 70 75 80

Asn Gly Leu Pro Gly Ser Arg Pro Gly Ser Pro Glu Arg Glu Val Pro
85 90 95

Ala Ser Ala Gln Ala Ser Gly Lys Thr Leu Pro Ile Pro Val Gln Ile
100 105 110

Thr Leu Arg Phe Asn Leu Pro Lys Glu Arg Glu Ala Ile Pro Gly Gly
115 120 125

Glu Pro Asp Gln Pro Leu Ser Ser Ser Ser Cys Leu Gln Pro Asn His

130 135 140

Arg Ser Thr Lys Arg Lys Val Glu Val Val Ser Pro Ala Thr Pro Val
145 150 155 160

Pro Ser Glu Thr Ala Pro Ala Ser Val Phe Pro Gln Asn Gly Ala Ala
165 170 175

Arg Arg Ala Val Ala Ala Gln Pro Gly Arg Lys Arg Lys Ser Asn Cys
180 185 190

Leu Gly Thr Asp Glu Asp Ser Gln Asp Ser Ser Asp Gly Ile Pro Ser
195 200 205

Ala Pro Arg Met Thr Gly Ser Leu Val Ser Asp Arg Ser His Asp Asp
210 215 220

Ile Val Thr Arg Met Lys Asn Ile Glu Cys Ile Glu Leu Gly Arg His
225 230 235 240

Arg Leu Lys Pro Trp Tyr Phe Ser Pro Tyr Pro Gln Glu Leu Thr Thr
245 250 255

Leu Pro Val Leu Tyr Leu Cys Glu Phe Cys Leu Lys Tyr Gly Arg Ser
260 265 270

Leu Lys Cys Leu Gln Arg His Leu Thr Lys Cys Asp Leu Arg His Pro
275 280 285

Pro Gly Asn Glu Ile Tyr Arg Lys Gly Thr Ile Ser Phe Phe Glu Ile
290 295 300

Asp Gly Arg Lys Asn Lys Ser Tyr Ser Gln Asn Leu Cys Leu Leu Ala
305 310 315 320

Lys Cys Phe Leu Asp His Lys Thr Leu Tyr Tyr Asp Thr Asp Pro Phe
325 330 335

Leu Phe Tyr Val Met Thr Glu Tyr Asp Cys Lys Gly Phe His Ile Val
340 345 350

Gly Tyr Phe Ser Lys Glu Lys Glu Ser Thr Glu Asp Tyr Asn Val Ala
355 360 365

Cys Ile Leu Thr Leu Pro Pro Tyr Gln Arg Arg Gly Tyr Gly Lys Leu
370 375 380

Leu Ile Glu Phe Ser Tyr Glu Leu Ser Lys Val Glu Gly Lys Thr Gly
385 390 395 400

Thr Pro Glu Lys Pro Leu Ser Asp Leu Gly Leu Leu Ser Tyr Arg Ser

405 410 415

Tyr Trp Ser Gln Thr Ile Leu Glu Ile Leu Met Gly Leu Lys Ser Glu
420 425 430

Ser Gly Glu Arg Pro Gln Ile Thr Ile Asn Glu Ile Ser Glu Ile Thr
435 440 445

Ser Ile Lys Lys Glu Asp Val Ile Ser Thr Leu Gln Tyr Leu Asn Leu
450 455 460

Ile Asn Tyr Tyr Lys Gly Gln Tyr Ile Leu Thr Leu Ser Glu Asp Ile
465 470 475 480

Val Asp Gly His Glu Arg Ala Met Leu Lys Arg Leu Leu Arg Ile Asp
485 490 495

Ser Lys Cys Leu His Phe Thr Pro Lys Asp Trp Ser Lys Arg Gly Lys
500 505 510

Trp

<210> 296
<211> 942
<212> PRT
<213> Homo sapiens

<400> 296

Met Asp Thr Lys Glu Glu Lys Lys Glu Arg Lys Gln Ser Tyr Phe Ala
1 5 10 15

Arg Leu Lys Lys Lys Lys Gln Ala Lys Gln Asn Ala Glu Thr Ala Ser
20 25 30

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

Val Leu Glu Pro Asp Lys Cys Asn Ile Ala Val Glu Glu Glu Tyr Met
50 55 60

Thr Asp Glu Lys Lys Lys Arg Lys Ser Asn Gln Leu Lys Glu Ile Arg
65 70 75 80

Arg Thr Glu Leu Lys Arg Tyr Tyr Ser Ile Asp Asp Asn Gln Asn Lys
85 90 95

Thr His Asp Lys Lys Glu Lys Lys Met Val Val Gln Lys Pro His Gly
100 105 110

Thr Met Glu Tyr Thr Ala Gly Asn Gln Asp Thr Leu Asn Ser Ile Ala
115 120 125

```
Leu Lys Phe Asn Ile Thr Pro Asn Lys Leu Val Glu Leu Asn Lys Leu
    130                 135                 140

Phe Thr His Thr Ile Val Pro Gly Gln Val Leu Phe Val Pro Asp Ala
145                 150                 155                 160

Asn Ser Pro Ser Ser Thr Leu Arg Leu Ser Ser Ser Ser Pro Gly Ala
                165                 170                 175

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

Ala Asp Leu Ala Arg Lys Ala Leu Lys Pro Ile Glu Arg Val Leu Ser
        195                 200                 205

Ser Thr Ser Glu Glu Asp Glu Pro Gly Val Val Lys Phe Leu Lys Met
    210                 215                 220

Asn Cys Arg Tyr Phe Thr Asp Gly Lys Gly Val Val Gly Gly Val Met
225                 230                 235                 240

Ile Val Thr Pro Asn Asn Ile Met Phe Asp Pro His Lys Ser Asp Pro
                245                 250                 255

Leu Val Ile Glu Asn Gly Cys Glu Glu Tyr Gly Leu Ile Cys Pro Met
            260                 265                 270

Glu Glu Val Val Ser Ile Ala Leu Tyr Asn Asp Ile Ser His Met Lys
        275                 280                 285

Ile Lys Asp Ala Leu Pro Ser Asp Leu Pro Gln Asp Leu Cys Pro Leu
    290                 295                 300

Tyr Arg Pro Gly Glu Trp Glu Asp Leu Ala Ser Glu Lys Asp Ile Asn
305                 310                 315                 320

Pro Phe Ser Lys Phe Lys Ser Ile Asn Lys Glu Lys Arg Gln Gln Asn
                325                 330                 335

Gly Glu Lys Ile Met Thr Ser Asp Ser Arg Pro Ile Val Pro Leu Glu
            340                 345                 350

Lys Ser Thr Gly His Thr Pro Thr Lys Pro Ser Gly Ser Ser Val Ser
        355                 360                 365

Glu Lys Leu Lys Lys Leu Asp Ser Ser Arg Glu Thr Ser His Gly Ser
    370                 375                 380

Pro Thr Val Thr Lys Leu Ser Lys Glu Pro Ser Asp Thr Ser Ser Ala
385                 390                 395                 400
```

```
Phe Glu Ser Thr Ala Lys Glu Asn Phe Leu Gly Glu Asp Asp Asp Phe
                405                 410                 415

Val Asp Leu Glu Glu Leu Ser Ser Gln Thr Gly Gly Gly Met His Lys
            420                 425                 430

Lys Asp Thr Leu Lys Glu Cys Leu Ser Leu Asp Pro Glu Glu Arg Lys
        435                 440                 445

Lys Ala Glu Ser Gln Ile Asn Asn Ser Ala Val Glu Met Gln Val Gln
    450                 455                 460

Ser Ala Leu Ala Phe Leu Gly Thr Glu Asn Asp Val Glu Leu Lys Gly
465                 470                 475                 480

Ala Leu Asp Leu Glu Thr Cys Glu Lys Gln Asp Ile Met Pro Glu Val
                485                 490                 495

Asp Lys Gln Ser Gly Ser Pro Glu Ser Arg Val Glu Asn Thr Leu Asn
            500                 505                 510

Ile His Glu Asp Leu Asp Lys Val Lys Leu Ile Glu Tyr Tyr Leu Thr
        515                 520                 525

Lys Asn Lys Glu Gly Pro Gln Val Ser Glu Asn Leu Gln Lys Thr Glu
    530                 535                 540

Leu Ser Asp Gly Lys Ser Ile Glu Pro Gly Gly Ile Asp Ile Thr Leu
545                 550                 555                 560

Ser Ser Ser Leu Ser Gln Ala Gly Asp Pro Ile Thr Glu Gly Asn Lys
                565                 570                 575

Glu Pro Asp Lys Thr Trp Val Lys Lys Gly Glu Pro Leu Pro Val Lys
            580                 585                 590

Leu Asn Ser Ser Thr Glu Ala Asn Val Ile Lys Glu Ala Leu Asp Ser
        595                 600                 605

Ser Leu Glu Ser Thr Leu Asp Asn Ser Cys Gln Gly Ala Gln Met Asp
    610                 615                 620

Asn Lys Ser Glu Val Gln Leu Trp Leu Leu Lys Arg Ile Gln Val Pro
625                 630                 635                 640

Ile Glu Asp Ile Leu Pro Ser Lys Glu Glu Lys Ser Lys Thr Pro Pro
                645                 650                 655

Met Phe Leu Cys Ile Lys Val Gly Lys Pro Met Arg Lys Ser Phe Ala
            660                 665                 670
```

```
Thr His Thr Ala Ala Met Val Gln Gln Tyr Gly Lys Arg Arg Lys Gln
        675                 680                 685

Pro Glu Tyr Trp Phe Ala Val Pro Arg Glu Arg Val Asp His Leu Tyr
    690                 695                 700

Thr Phe Phe Val Gln Trp Ser Pro Asp Val Tyr Gly Lys Asp Ala Lys
705                 710                 715                 720

Glu Gln Gly Phe Val Val Val Glu Lys Glu Glu Leu Asn Met Ile Asp
                725                 730                 735

Asn Phe Phe Ser Glu Pro Thr Thr Lys Ser Trp Glu Ile Ile Thr Val
            740                 745                 750

Glu Glu Ala Lys Arg Arg Lys Ser Thr Cys Ser Tyr Tyr Glu Asp Glu
        755                 760                 765

Asp Glu Glu Val Leu Pro Val Leu Arg Pro His Ser Ala Leu Leu Glu
    770                 775                 780

Asn Met His Ile Glu Gln Leu Ala Arg Arg Leu Pro Ala Arg Val Gln
785                 790                 795                 800

Gly Tyr Pro Trp Arg Leu Ala Tyr Ser Thr Leu Glu His Gly Thr Ser
                805                 810                 815

Leu Lys Thr Leu Tyr Arg Lys Ser Ala Ser Leu Asp Ser Pro Val Leu
            820                 825                 830

Leu Val Ile Lys Asp Met Asp Asn Gln Ile Phe Gly Ala Tyr Ala Thr
        835                 840                 845

His Pro Phe Lys Phe Ser Asp His Tyr Tyr Gly Thr Gly Glu Thr Phe
    850                 855                 860

Leu Tyr Thr Phe Ser Pro His Phe Lys Val Phe Lys Trp Ser Gly Glu
865                 870                 875                 880

Asn Ser Tyr Phe Ile Asn Gly Asp Ile Ser Ser Leu Glu Leu Gly Gly
                885                 890                 895

Gly Gly Gly Arg Phe Gly Leu Trp Leu Asp Ala Asp Leu Tyr His Gly
            900                 905                 910

Arg Ser Asn Ser Cys Ser Thr Phe Asn Asn Asp Ile Leu Ser Lys Lys
        915                 920                 925

Glu Asp Phe Ile Val Gln Asp Leu Glu Val Trp Ala Phe Asp
    930                 935                 940
```

<210> 297
<211> 281
<212> PRT
<213> Homo sapiens

<400> 297

```
Met Leu Phe Ile Phe Pro Leu Ser Leu Pro Trp Arg Pro Ser Cys Trp
1               5                   10                  15

Lys Glu Ser Cys Ser Thr Gly Gln Arg Gln Ala Gly Arg Ser Arg Glu
            20                  25                  30

Asp Ser Val Thr Pro Pro Pro Ser Ser Pro Trp Pro Thr Pro Pro Ala
        35                  40                  45

Gly Ala Met Ser Thr Lys Gln Glu Ala Arg Arg Asp Glu Gly Glu Ala
    50                  55                  60

Arg Thr Arg Gly Gln Glu Ala Gln Leu Arg Asp Arg Ala His Leu Ser
65                  70                  75                  80

Gln Gln Arg Arg Leu Lys Gln Ala Thr Gln Phe Leu His Lys Asp Ser
                85                  90                  95

Ala Asp Leu Leu Pro Leu Asp Ser Leu Lys Arg Leu Gly Thr Ser Lys
            100                 105                 110

Asp Leu Gln Pro Arg Ser Val Ile Gln Arg Arg Leu Val Glu Gly Asn
        115                 120                 125

Pro Asn Trp Leu Gln Gly Glu Pro Pro Arg Met Gln Asp Leu Ile His
    130                 135                 140

Gly Gln Glu Ser Arg Arg Lys Thr Ser Arg Thr Glu Ile Pro Ala Leu
145                 150                 155                 160

Leu Val Asn Cys Lys Cys Gln Asp Gln Leu Leu Arg Val Ala Val Asp
                165                 170                 175

Thr Gly Thr Gln Tyr Asn Arg Ile Ser Ala Gly Cys Leu Ser Arg Leu
            180                 185                 190

Gly Leu Glu Lys Arg Val Leu Lys Ala Ser Ala Gly Asp Leu Ala Pro
        195                 200                 205

Gly Pro Pro Thr Gln Val Glu Gln Leu Glu Leu Gln Leu Gly Gln Glu
    210                 215                 220

Thr Val Val Cys Ser Ala Gln Val Val Asp Ala Glu Ser Pro Glu Phe
225                 230                 235                 240
```

```
Cys Leu Gly Leu Gln Thr Leu Leu Ser Leu Lys Cys Cys Ile Asp Leu
                245                 250                 255


Glu His Gly Val Leu Arg Leu Lys Ala Pro Phe Ser Glu Leu Pro Phe
            260                 265                 270


Leu Pro Leu Tyr Gln Glu Pro Gly Gln
        275                 280


<210>  298
<211>  433
<212>  PRT
<213>  Homo sapiens

<400>  298

Met Gln Arg Met Ile Gln Gln Phe Ala Ala Glu Tyr Thr Ser Lys Asn
1               5                   10                  15


Ser Ser Thr Gln Asp Pro Ser Gln Pro Asn Ser Thr Lys Asn Gln Ser
            20                  25                  30


Leu Pro Lys Ala Ser Pro Val Thr Thr Ser Pro Thr Ala Ala Thr Thr
        35                  40                  45


Gln Asn Pro Val Leu Ser Lys Leu Leu Met Ala Asp Gln Asp Ser Pro
    50                  55                  60


Leu Asp Leu Thr Val Arg Lys Ser Gln Ser Glu Pro Ser Glu Gln Asp
65                  70                  75                  80


Gly Val Leu Asp Leu Ser Thr Lys Lys Ser Pro Cys Ala Gly Ser Thr
                85                  90                  95


Ser Leu Ser His Ser Pro Gly Cys Ser Ser Thr Gln Gly Asn Gly Arg
            100                 105                 110


Pro Gly Arg Pro Ser Gln Tyr Arg Pro Asp Gly Leu Arg Ser Gly Asp
        115                 120                 125


Gly Val Pro Pro Arg Ser Leu Gln Asp Gly Thr Arg Glu Gly Phe Gly
    130                 135                 140


His Ser Thr Ser Leu Lys Val Pro Leu Ala Arg Ser Leu Gln Ile Ser
145                 150                 155                 160


Glu Glu Leu Leu Ser Arg Asn Gln Leu Ser Thr Ala Ala Ser Leu Gly
                165                 170                 175


Pro Ser Gly Leu Gln Asn His Gly Gln His Leu Ile Leu Ser Arg Glu
            180                 185                 190
```

```
Ala Ser Trp Ala Lys Pro His Tyr Glu Phe Asn Leu Ser Arg Met Lys
        195                 200                 205

Phe Arg Gly Asn Gly Ala Leu Ser Asn Ile Ser Asp Leu Pro Phe Leu
    210                 215                 220

Ala Glu Asn Ser Ala Phe Pro Lys Met Ala Leu Gln Ala Lys Gln Asp
225                 230                 235                 240

Gly Lys Lys Asp Val Ser His Ser Ser Pro Val Asp Leu Lys Ile Pro
                245                 250                 255

Gln Val Arg Gly Met Asp Leu Ser Trp Glu Ser Arg Thr Gly Asp Gln
            260                 265                 270

Tyr Ser Tyr Ser Ser Leu Val Met Gly Ser Gln Thr Glu Ser Ala Leu
        275                 280                 285

Ser Lys Lys Leu Arg Ala Ile Leu Pro Lys Gln Ser Arg Lys Ser Met
    290                 295                 300

Leu Asp Ala Gly Pro Asp Ser Trp Gly Ser Asp Ala Glu Gln Ser Thr
305                 310                 315                 320

Ser Gly Gln Pro Tyr Pro Thr Ser Asp Gln Glu Gly Asp Pro Gly Ser
                325                 330                 335

Lys Gln Pro Arg Lys Lys Arg Gly Arg Tyr Arg Gln Tyr Asn Ser Glu
            340                 345                 350

Ile Leu Glu Glu Ala Ile Ser Val Val Met Ser Gly Lys Met Ser Val
        355                 360                 365

Ser Lys Ala Gln Ser Ile Tyr Gly Ile Pro His Ser Thr Leu Glu Tyr
    370                 375                 380

Lys Val Lys Glu Arg Leu Gly Thr Leu Lys Asn Pro Pro Lys Lys Lys
385                 390                 395                 400

Met Lys Leu Met Arg Ser Glu Gly Pro Asp Val Ser Val Lys Ile Glu
                405                 410                 415

Leu Asp Pro Gln Gly Glu Ala Ala Gln Ser Ala Asn Glu Ser Lys Asn
            420                 425                 430

Glu
```

<210> 299
<211> 2440
<212> PRT
<213> Homo sapiens

<400> 299

```
Met Ser Ser Ser Gly Tyr Pro Pro Asn Gln Gly Ala Phe Ser Thr Glu
1               5                  10                  15

Gln Ser Arg Tyr Pro Pro His Ser Val Gln Tyr Thr Phe Pro Asn Thr
            20                  25                  30

Arg His Gln Gln Glu Phe Ala Val Pro Asp Tyr Arg Ser Ser His Leu
        35                  40                  45

Glu Val Ser Gln Ala Ser Gln Leu Leu Gln Gln Gln Gln Gln Gln Gln
    50                  55                  60

Leu Arg Arg Arg Pro Ser Leu Leu Ser Glu Phe His Pro Gly Ser Asp
65                  70                  75                  80

Arg Pro Gln Glu Arg Arg Thr Ser Tyr Glu Pro Phe His Pro Gly Pro
                85                  90                  95

Ser Pro Val Asp His Asp Ser Leu Glu Ser Lys Arg Pro Arg Leu Glu
            100                 105                 110

Gln Val Ser Asp Ser His Phe Gln Arg Val Ser Ala Ala Val Leu Pro
        115                 120                 125

Leu Val His Pro Leu Pro Glu Gly Leu Arg Ala Ser Ala Asp Ala Lys
    130                 135                 140

Lys Asp Pro Ala Phe Gly Gly Lys His Glu Ala Pro Ser Ser Pro Ile
145                 150                 155                 160

Ser Gly Gln Pro Cys Gly Asp Asp Gln Asn Ala Ser Pro Ser Lys Leu
                165                 170                 175

Ser Lys Glu Glu Leu Ile Gln Ser Met Asp Arg Val Asp Arg Glu Ile
            180                 185                 190

Ala Lys Val Glu Gln Gln Ile Leu Lys Leu Lys Lys Lys Gln Gln Gln
        195                 200                 205

Leu Glu Glu Glu Ala Ala Lys Pro Pro Glu Pro Glu Lys Pro Val Ser
    210                 215                 220

Pro Pro Pro Val Glu Gln Lys His Arg Ser Ile Val Gln Ile Ile Tyr
225                 230                 235                 240

Asp Glu Asn Arg Lys Lys Ala Glu Glu Ala His Lys Ile Phe Glu Gly
                245                 250                 255

Leu Gly Pro Lys Val Glu Leu Pro Leu Tyr Asn Gln Pro Ser Asp Thr
```

260 265 270

Lys Val Tyr His Glu Asn Ile Lys Thr Asn Gln Val Met Arg Lys Lys
275 280 285

Leu Ile Leu Phe Phe Lys Arg Arg Asn His Ala Arg Lys Gln Arg Glu
290 295 300

Gln Lys Ile Cys Gln Arg Tyr Asp Gln Leu Met Glu Ala Trp Glu Lys
305 310 315 320

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

Lys Thr Arg Glu Tyr Tyr Glu Lys Gln Phe Pro Glu Ile Arg Lys Gln
340 345 350

Arg Glu Gln Gln Glu Arg Phe Gln Arg Val Gly Gln Arg Gly Ala Gly
355 360 365

Leu Ser Ala Thr Ile Ala Arg Ser Glu His Glu Ile Ser Glu Ile Ile
370 375 380

Asp Gly Leu Ser Glu Gln Glu Asn Asn Glu Lys Gln Met Arg Gln Leu
385 390 395 400

Ser Val Ile Pro Pro Met Met Phe Asp Ala Glu Gln Arg Arg Val Lys
405 410 415

Phe Ile Asn Met Asn Gly Leu Met Glu Asp Pro Met Lys Val Tyr Lys
420 425 430

Asp Arg Gln Phe Met Asn Val Trp Thr Asp His Glu Lys Glu Ile Phe
435 440 445

Lys Asp Lys Phe Ile Gln His Pro Lys Asn Phe Gly Leu Ile Ala Ser
450 455 460

Tyr Leu Glu Arg Lys Ser Val Pro Asp Cys Val Leu Tyr Tyr Tyr Leu
465 470 475 480

Thr Lys Lys Asn Glu Asn Tyr Lys Ala Leu Val Arg Arg Asn Tyr Gly
485 490 495

Lys Arg Arg Gly Arg Asn Gln Gln Ile Ala Arg Pro Ser Gln Glu Glu
500 505 510

Lys Val Glu Glu Lys Glu Glu Asp Lys Ala Glu Lys Thr Glu Lys Lys
515 520 525

Glu Glu Glu Lys Lys Asp Glu Glu Glu Lys Asp Glu Lys Glu Asp Ser

530 535 540

Lys Glu Asn Thr Lys Glu Lys Asp Lys Ile Asp Gly Thr Ala Glu Glu
545 550 555 560

Thr Glu Glu Arg Glu Gln Ala Thr Pro Arg Gly Arg Lys Thr Ala Asn
565 570 575

Ser Gln Gly Arg Arg Lys Gly Arg Ile Thr Arg Ser Met Thr Asn Glu
580 585 590

Ala Ala Ala Ala Ser Ala Ala Ala Ala Ala Ala Thr Glu Glu Pro Pro
595 600 605

Pro Pro Leu Pro Pro Pro Pro Glu Pro Ile Ser Thr Glu Pro Val Glu
610 615 620

Thr Ser Arg Trp Thr Glu Glu Glu Met Glu Val Ala Lys Lys Gly Leu
625 630 635 640

Val Glu His Gly Arg Asn Trp Ala Ala Ile Ala Lys Met Val Gly Thr
645 650 655

Lys Ser Glu Ala Gln Cys Lys Asn Phe Tyr Phe Asn Tyr Lys Arg Arg
660 665 670

His Asn Leu Asp Asn Leu Leu Gln Gln His Lys Gln Lys Thr Ser Arg
675 680 685

Lys Pro Arg Glu Glu Arg Asp Val Ser Gln Cys Glu Ser Val Ala Ser
690 695 700

Thr Val Ser Ala Gln Glu Asp Glu Asp Ile Glu Ala Ser Asn Glu Glu
705 710 715 720

Glu Asn Pro Glu Asp Ser Glu Val Glu Ala Val Lys Pro Ser Glu Asp
725 730 735

Ser Pro Glu Asn Ala Thr Ser Arg Gly Asn Thr Glu Pro Ala Val Glu
740 745 750

Leu Glu Pro Thr Thr Glu Thr Ala Pro Ser Thr Ser Pro Ser Leu Ala
755 760 765

Val Pro Ser Thr Lys Pro Ala Glu Asp Glu Ser Val Glu Thr Gln Val
770 775 780

Asn Asp Ser Ile Ser Ala Glu Thr Ala Glu Gln Met Asp Val Asp Gln
785 790 795 800

Gln Glu His Ser Ala Glu Glu Gly Ser Val Cys Asp Pro Pro Pro Ala

805 810 815

Thr Lys Ala Asp Ser Val Asp Val Glu Val Arg Val Pro Glu Asn His
820 825 830

Ala Ser Lys Val Glu Gly Asp Asn Thr Lys Glu Arg Asp Leu Asp Arg
835 840 845

Ala Ser Glu Lys Val Glu Pro Arg Asp Glu Asp Leu Val Val Ala Gln
850 855 860

Gln Ile Asn Ala Gln Arg Pro Glu Pro Gln Ser Asp Asn Asp Ser Ser
865 870 875 880

Ala Thr Cys Ser Ala Asp Glu Asp Val Asp Gly Glu Pro Glu Arg Gln
885 890 895

Arg Met Phe Pro Met Asp Ser Lys Pro Ser Leu Leu Asn Pro Thr Gly
900 905 910

Ser Ile Leu Val Ser Ser Pro Leu Lys Pro Asn Pro Leu Asp Leu Pro
915 920 925

Gln Leu Gln His Arg Ala Ala Val Ile Pro Pro Met Val Ser Cys Thr
930 935 940

Pro Cys Asn Ile Pro Ile Gly Thr Pro Val Ser Gly Tyr Ala Leu Tyr
945 950 955 960

Gln Arg His Ile Lys Ala Met His Glu Ser Ala Leu Leu Glu Glu Gln
965 970 975

Arg Gln Arg Gln Glu Gln Ile Asp Leu Glu Cys Arg Ser Ser Thr Ser
980 985 990

Pro Cys Gly Thr Ser Lys Ser Pro Asn Arg Glu Trp Glu Val Leu Gln
995 1000 1005

Pro Ala Pro His Gln Val Ile Thr Asn Leu Pro Glu Gly Val Arg
1010 1015 1020

Leu Pro Thr Thr Arg Pro Thr Arg Pro Pro Pro Pro Leu Ile Pro
1025 1030 1035

Ser Ser Lys Thr Thr Val Ala Ser Glu Lys Pro Ser Phe Ile Met
1040 1045 1050

Gly Gly Ser Ile Ser Gln Gly Thr Pro Gly Thr Tyr Leu Thr Ser
1055 1060 1065

His Asn Gln Ala Ser Tyr Thr Gln Glu Thr Pro Lys Pro Ser Val

1070 1075 1080

Gly Ser Ile Ser Leu Gly Leu Pro Arg Gln Gln Glu Ser Ala Lys
1085 1090 1095

Ser Ala Thr Leu Pro Tyr Ile Lys Gln Glu Glu Phe Ser Pro Arg
1100 1105 1110

Ser Gln Asn Ser Gln Pro Glu Gly Leu Leu Val Arg Ala Gln His
1115 1120 1125

Glu Gly Val Val Arg Gly Thr Ala Gly Ala Ile Gln Glu Gly Ser
1130 1135 1140

Ile Thr Arg Gly Thr Pro Thr Ser Lys Ile Ser Val Glu Ser Ile
1145 1150 1155

Pro Ser Leu Arg Gly Ser Ile Thr Gln Gly Thr Pro Ala Leu Pro
1160 1165 1170

Gln Thr Gly Ile Pro Thr Glu Ala Leu Val Lys Gly Ser Ile Ser
1175 1180 1185

Arg Met Pro Ile Glu Asp Ser Ser Pro Glu Lys Gly Arg Glu Glu
1190 1195 1200

Ala Ala Ser Lys Gly His Val Ile Tyr Glu Gly Lys Ser Gly His
1205 1210 1215

Ile Leu Ser Tyr Asp Asn Ile Lys Asn Ala Arg Glu Gly Thr Arg
1220 1225 1230

Ser Pro Arg Thr Ala His Glu Ile Ser Leu Lys Arg Ser Tyr Glu
1235 1240 1245

Ser Val Glu Gly Asn Ile Lys Gln Gly Met Ser Met Arg Glu Ser
1250 1255 1260

Pro Val Ser Ala Pro Leu Glu Gly Leu Ile Cys Arg Ala Leu Pro
1265 1270 1275

Arg Gly Ser Pro His Ser Asp Leu Lys Glu Arg Thr Val Leu Ser
1280 1285 1290

Gly Ser Ile Met Gln Gly Thr Pro Arg Ala Thr Thr Glu Ser Phe
1295 1300 1305

Glu Asp Gly Leu Lys Tyr Pro Lys Gln Ile Lys Arg Glu Ser Pro
1310 1315 1320

Pro Ile Arg Ala Phe Glu Gly Ala Ile Thr Lys Gly Lys Pro Tyr

1325 1330 1335

Asp Gly Ile Thr Thr Ile Lys Glu Met Gly Arg Ser Ile His Glu
1340 1345 1350

Ile Pro Arg Gln Asp Ile Leu Thr Gln Glu Ser Arg Lys Thr Pro
1355 1360 1365

Glu Val Val Gln Ser Thr Arg Pro Ile Ile Glu Gly Ser Ile Ser
1370 1375 1380

Gln Gly Thr Pro Ile Lys Phe Asp Asn Asn Ser Gly Gln Ser Ala
1385 1390 1395

Ile Lys His Asn Val Lys Ser Leu Ile Thr Gly Pro Ser Lys Leu
1400 1405 1410

Ser Arg Gly Met Pro Pro Leu Glu Ile Val Pro Glu Asn Ile Lys
1415 1420 1425

Val Val Glu Arg Gly Lys Tyr Glu Asp Val Lys Ala Gly Glu Thr
1430 1435 1440

Val Arg Ser Arg His Thr Ser Val Val Ser Ser Gly Pro Ser Val
1445 1450 1455

Leu Arg Ser Thr Leu His Glu Ala Pro Lys Ala Gln Leu Ser Pro
1460 1465 1470

Gly Ile Tyr Asp Asp Thr Ser Ala Arg Arg Thr Pro Val Ser Tyr
1475 1480 1485

Gln Asn Thr Met Ser Arg Gly Ser Pro Met Met Asn Arg Thr Ser
1490 1495 1500

Asp Val Thr Ile Ser Ser Asn Lys Ser Thr Asn His Glu Arg Lys
1505 1510 1515

Ser Thr Leu Thr Pro Thr Gln Arg Glu Ser Ile Pro Ala Lys Ser
1520 1525 1530

Pro Val Pro Gly Val Asp Pro Val Val Ser His Ser Pro Phe Asp
1535 1540 1545

Pro His His Arg Gly Ser Thr Ala Gly Glu Val Tyr Arg Ser His
1550 1555 1560

Leu Pro Thr His Leu Asp Pro Ala Met Pro Phe His Arg Ala Leu
1565 1570 1575

Asp Pro Ala Ala Ala Ala Tyr Leu Phe Gln Arg Gln Leu Ser Pro

1580 1585 1590

Thr Pro Gly Tyr Pro Ser Gln Tyr Gln Leu Tyr Ala Met Glu Asn
1595 1600 1605

Thr Arg Gln Thr Ile Leu Asn Asp Tyr Ile Thr Ser Gln Gln Met
1610 1615 1620

Gln Val Asn Leu Arg Pro Asp Val Ala Arg Gly Leu Ser Pro Arg
1625 1630 1635

Glu Gln Pro Leu Gly Leu Pro Tyr Pro Ala Thr Arg Gly Ile Ile
1640 1645 1650

Asp Leu Thr Asn Met Pro Pro Thr Ile Leu Val Pro His Pro Gly
1655 1660 1665

Gly Thr Ser Thr Pro Pro Met Asp Arg Ile Thr Tyr Ile Pro Gly
1670 1675 1680

Thr Gln Ile Thr Phe Pro Pro Arg Pro Tyr Asn Ser Ala Ser Met
1685 1690 1695

Ser Pro Gly His Pro Thr His Leu Ala Ala Ala Ala Ser Ala Glu
1700 1705 1710

Arg Glu Arg Glu Arg Glu Arg Glu Lys Glu Arg Glu Arg Glu Arg
1715 1720 1725

Ile Ala Ala Ala Ser Ser Asp Leu Tyr Leu Arg Pro Gly Ser Glu
1730 1735 1740

Gln Pro Gly Arg Pro Gly Ser His Gly Tyr Val Arg Ser Pro Ser
1745 1750 1755

Pro Ser Val Arg Thr Gln Glu Thr Met Leu Gln Gln Arg Pro Ser
1760 1765 1770

Val Phe Gln Gly Thr Asn Gly Thr Ser Val Ile Thr Pro Leu Asp
1775 1780 1785

Pro Thr Ala Gln Leu Arg Ile Met Pro Leu Pro Ala Gly Gly Pro
1790 1795 1800

Ser Ile Ser Gln Gly Leu Pro Ala Ser Arg Tyr Asn Thr Ala Ala
1805 1810 1815

Asp Ala Leu Ala Ala Leu Val Asp Ala Ala Ala Ser Ala Pro Gln
1820 1825 1830

Met Asp Val Ser Lys Thr Lys Glu Ser Lys His Glu Ala Ala Arg

1835 1840 1845

Leu Glu Glu Asn Leu Arg Ser Arg Ser Ala Ala Val Ser Glu Gln
1850 1855 1860

Gln Gln Leu Glu Gln Lys Thr Leu Glu Val Glu Lys Arg Ser Val
1865 1870 1875

Gln Cys Leu Tyr Thr Ser Ser Ala Phe Pro Ser Gly Lys Pro Gln
1880 1885 1890

Pro His Ser Ser Val Val Tyr Ser Glu Ala Gly Lys Asp Lys Gly
1895 1900 1905

Pro Pro Pro Lys Ser Arg Tyr Glu Glu Glu Leu Arg Thr Arg Gly
1910 1915 1920

Lys Thr Thr Ile Thr Ala Ala Asn Phe Ile Asp Val Ile Ile Thr
1925 1930 1935

Arg Gln Ile Ala Ser Asp Lys Asp Ala Arg Glu Arg Gly Ser Gln
1940 1945 1950

Ser Ser Asp Ser Ser Ser Ser Leu Ser Ser His Arg Tyr Glu Thr
1955 1960 1965

Pro Ser Asp Ala Ile Glu Val Ile Ser Pro Ala Ser Ser Pro Ala
1970 1975 1980

Pro Pro Gln Glu Lys Leu Gln Thr Tyr Gln Pro Glu Val Val Lys
1985 1990 1995

Ala Asn Gln Ala Glu Asn Asp Pro Thr Arg Gln Tyr Glu Gly Pro
2000 2005 2010

Leu His His Tyr Arg Pro Gln Gln Glu Ser Pro Ser Pro Gln Gln
2015 2020 2025

Gln Leu Pro Pro Ser Ser Gln Ala Glu Gly Met Gly Gln Val Pro
2030 2035 2040

Arg Thr His Arg Leu Ile Thr Leu Ala Asp His Ile Cys Gln Ile
2045 2050 2055

Ile Thr Gln Asp Phe Ala Arg Asn Gln Val Ser Ser Gln Thr Pro
2060 2065 2070

Gln Gln Pro Pro Thr Ser Thr Phe Gln Asn Ser Pro Ser Ala Leu
2075 2080 2085

Val Ser Thr Pro Val Arg Thr Lys Thr Ser Asn Arg Tyr Ser Pro

2090 2095 2100

Glu Ser Gln Ala Gln Ser Val His His Gln Arg Pro Gly Ser Arg
2105 2110 2115

Val Ser Pro Glu Asn Leu Val Asp Lys Ser Arg Gly Ser Arg Pro
2120 2125 2130

Gly Lys Ser Pro Glu Arg Ser His Val Ser Ser Glu Pro Tyr Glu
2135 2140 2145

Pro Ile Ser Pro Pro Gln Val Pro Val Val His Glu Lys Gln Asp
2150 2155 2160

Ser Leu Leu Leu Leu Ser Gln Arg Gly Ala Glu Pro Ala Glu Gln
2165 2170 2175

Arg Asn Asp Ala Arg Ser Pro Gly Ser Ile Ser Tyr Leu Pro Ser
2180 2185 2190

Phe Phe Thr Lys Leu Glu Asn Thr Ser Pro Met Val Lys Ser Lys
2195 2200 2205

Lys Gln Glu Ile Phe Arg Lys Leu Asn Ser Ser Gly Gly Gly Asp
2210 2215 2220

Ser Asp Met Ala Ala Ala Gln Pro Gly Thr Glu Ile Phe Asn Leu
2225 2230 2235

Pro Ala Val Thr Thr Ser Gly Ser Val Ser Ser Arg Gly His Ser
2240 2245 2250

Phe Ala Asp Pro Ala Ser Asn Leu Gly Leu Glu Asp Ile Ile Arg
2255 2260 2265

Lys Ala Leu Met Gly Ser Phe Asp Asp Lys Val Glu Asp His Gly
2270 2275 2280

Val Val Met Ser Gln Pro Met Gly Val Val Pro Gly Thr Ala Asn
2285 2290 2295

Thr Ser Val Val Thr Ser Gly Glu Thr Arg Arg Glu Glu Gly Asp
2300 2305 2310

Pro Ser Pro His Ser Gly Gly Val Cys Lys Pro Lys Leu Ile Ser
2315 2320 2325

Lys Ser Asn Ser Arg Lys Ser Lys Ser Pro Ile Pro Gly Gln Gly
2330 2335 2340

Tyr Leu Gly Thr Glu Arg Pro Ser Ser Val Ser Ser Val His Ser

2345 2350 2355

Glu Gly Asp Tyr His Arg Gln Thr Pro Gly Trp Ala Trp Glu Asp
2360 2365 2370

Arg Pro Ser Ser Thr Gly Ser Thr Gln Phe Pro Tyr Asn Pro Leu
2375 2380 2385

Thr Met Arg Met Leu Ser Ser Thr Pro Pro Thr Pro Ile Ala Cys
2390 2395 2400

Ala Pro Ser Ala Val Asn Gln Ala Ala Pro His Gln Gln Asn Arg
2405 2410 2415

Ile Trp Glu Arg Glu Pro Ala Pro Leu Leu Ser Ala Gln Tyr Glu
2420 2425 2430

Thr Leu Ser Asp Ser Asp Asp
2435 2440

<210> 300
<211> 2514
<212> PRT
<213> Homo sapiens

<400> 300

Met Ser Gly Ser Thr Gln Pro Val Ala Gln Thr Trp Arg Ala Thr Glu
1 5 10 15

Pro Arg Tyr Pro Pro His Ser Leu Ser Tyr Pro Val Gln Ile Ala Arg
20 25 30

Thr His Thr Asp Val Gly Leu Leu Glu Tyr Gln His His Ser Arg Asp
35 40 45

Tyr Ala Ser His Leu Ser Pro Gly Ser Ile Ile Gln Pro Gln Arg Arg
50 55 60

Arg Pro Ser Leu Leu Ser Glu Phe Gln Pro Gly Asn Glu Arg Ser Gln
65 70 75 80

Glu Leu His Leu Arg Pro Glu Ser His Ser Tyr Leu Pro Glu Leu Gly
85 90 95

Lys Ser Glu Met Glu Phe Ile Glu Ser Lys Arg Pro Arg Leu Glu Leu
100 105 110

Leu Pro Asp Pro Leu Leu Arg Pro Ser Pro Leu Leu Ala Thr Gly Gln
115 120 125

Pro Ala Gly Ser Glu Asp Leu Thr Lys Asp Arg Ser Leu Thr Gly Lys
130 135 140

```
Leu Glu Pro Val Ser Pro Pro Ser Pro Pro His Thr Asp Pro Glu Leu
145                 150                 155                 160

Glu Leu Val Pro Pro Arg Leu Ser Lys Glu Glu Leu Ile Gln Asn Met
                165                 170                 175

Asp Arg Val Asp Arg Glu Ile Thr Met Val Glu Gln Gln Ile Ser Lys
            180                 185                 190

Leu Lys Lys Lys Gln Gln Gln Leu Glu Glu Glu Ala Ala Lys Pro Pro
        195                 200                 205

Glu Pro Glu Lys Pro Val Ser Pro Pro Pro Ile Glu Ser Lys His Arg
    210                 215                 220

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

Ala His Arg Ile Leu Glu Gly Leu Gly Pro Gln Val Glu Leu Pro Leu
                245                 250                 255

Tyr Asn Gln Pro Ser Asp Thr Arg Gln Tyr His Glu Asn Ile Lys Ile
            260                 265                 270

Asn Gln Ala Met Arg Lys Lys Leu Ile Leu Tyr Phe Lys Arg Arg Asn
        275                 280                 285

His Ala Arg Lys Gln Trp Glu Gln Lys Phe Cys Gln Arg Tyr Asp Gln
    290                 295                 300

Leu Met Glu Ala Trp Glu Lys Lys Val Glu Arg Ile Glu Asn Asn Pro
305                 310                 315                 320

Arg Arg Arg Ala Lys Glu Ser Lys Val Arg Glu Tyr Tyr Glu Lys Gln
                325                 330                 335

Phe Pro Glu Ile Arg Lys Gln Arg Glu Leu Gln Glu Arg Met Gln Ser
            340                 345                 350

Arg Val Gly Gln Arg Gly Ser Gly Leu Ser Met Ser Ala Ala Arg Ser
        355                 360                 365

Glu His Glu Val Ser Glu Ile Ile Asp Gly Leu Ser Glu Gln Glu Asn
    370                 375                 380

Leu Glu Lys Gln Met Arg Gln Leu Ala Val Ile Pro Pro Met Leu Tyr
385                 390                 395                 400

Asp Ala Asp Gln Gln Arg Ile Lys Phe Ile Asn Met Asn Gly Leu Met
                405                 410                 415
```

```
Ala Asp Pro Met Lys Val Tyr Lys Asp Arg Gln Val Met Asn Met Trp
            420                 425                 430

Ser Glu Gln Glu Lys Glu Thr Phe Arg Glu Lys Phe Met Gln His Pro
        435                 440                 445

Lys Asn Phe Gly Leu Ile Ala Ser Phe Leu Glu Arg Lys Thr Val Ala
    450                 455                 460

Glu Cys Val Leu Tyr Tyr Tyr Leu Thr Lys Lys Asn Glu Asn Tyr Lys
465                 470                 475                 480

Ser Leu Val Arg Arg Ser Tyr Arg Arg Arg Gly Lys Ser Gln Gln Gln
                485                 490                 495

Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln Pro Met
            500                 505                 510

Pro Arg Ser Ser Gln Glu Glu Lys Asp Glu Lys Glu Lys Glu Lys Glu
        515                 520                 525

Ala Glu Lys Glu Glu Glu Lys Pro Glu Val Glu Asn Asp Lys Glu Asp
    530                 535                 540

Leu Leu Lys Glu Lys Thr Asp Asp Thr Ser Gly Glu Asp Asn Asp Glu
545                 550                 555                 560

Lys Glu Ala Val Ala Ser Lys Gly Arg Lys Thr Ala Asn Ser Gln Gly
                565                 570                 575

Arg Arg Lys Gly Arg Ile Thr Arg Ser Met Ala Asn Glu Ala Asn Ser
            580                 585                 590

Glu Glu Ala Ile Thr Pro Gln Gln Ser Ala Glu Leu Ala Ser Met Glu
        595                 600                 605

Leu Asn Glu Ser Ser Arg Trp Thr Glu Glu Glu Met Glu Thr Ala Lys
    610                 615                 620

Lys Gly Leu Leu Glu His Gly Arg Asn Trp Ser Ala Ile Ala Arg Met
625                 630                 635                 640

Val Gly Ser Lys Thr Val Ser Gln Cys Lys Asn Phe Tyr Phe Asn Tyr
                645                 650                 655

Lys Lys Arg Gln Asn Leu Asp Glu Ile Leu Gln Gln His Lys Leu Lys
            660                 665                 670

Met Glu Lys Glu Arg Asn Ala Arg Arg Lys Lys Lys Lys Ala Pro Ala
        675                 680                 685
```

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Ala Ala Ser Glu Glu Ala Ala Phe Pro Pro Val Val Glu Asp Glu Glu
    690                 695                 700

Met Glu Ala Ser Gly Val Ser Gly Asn Glu Glu Glu Met Val Glu Glu
705                 710                 715                 720

Ala Glu Ala Leu His Ala Ser Gly Asn Glu Val Pro Arg Gly Glu Cys
                725                 730                 735

Ser Gly Pro Ala Thr Val Asn Asn Ser Ser Asp Thr Glu Ser Ile Pro
            740                 745                 750

Ser Pro His Thr Glu Ala Ala Lys Asp Thr Gly Gln Asn Gly Pro Lys
        755                 760                 765

Pro Pro Ala Thr Leu Gly Ala Asp Gly Pro Pro Pro Gly Pro Pro Thr
    770                 775                 780

Pro Pro Pro Glu Asp Ile Pro Ala Pro Thr Glu Pro Thr Pro Ala Ser
785                 790                 795                 800

Glu Ala Thr Gly Ala Pro Thr Pro Pro Pro Ala Pro Pro Ser Pro Ser
                805                 810                 815

Ala Pro Pro Pro Val Val Pro Lys Glu Glu Lys Glu Glu Glu Thr Ala
            820                 825                 830

Ala Ala Pro Pro Val Glu Glu Gly Glu Glu Gln Lys Pro Pro Ala Ala
        835                 840                 845

Glu Glu Leu Ala Val Asp Thr Gly Lys Ala Glu Glu Pro Val Lys Ser
    850                 855                 860

Glu Cys Thr Glu Glu Ala Glu Glu Gly Pro Ala Lys Gly Lys Asp Ala
865                 870                 875                 880

Glu Ala Ala Glu Ala Thr Ala Glu Gly Ala Leu Lys Ala Glu Lys Lys
                885                 890                 895

Glu Gly Gly Ser Gly Arg Ala Thr Thr Ala Lys Ser Ser Gly Ala Pro
            900                 905                 910

Gln Asp Ser Asp Ser Ser Ala Thr Cys Ser Ala Asp Glu Val Asp Glu
        915                 920                 925

Ala Glu Gly Gly Asp Lys Asn Arg Leu Leu Ser Pro Arg Pro Ser Leu
    930                 935                 940

Leu Thr Pro Thr Gly Asp Pro Arg Ala Asn Ala Ser Pro Gln Lys Pro
945                 950                 955                 960
```

```
Leu Asp Leu Lys Gln Leu Lys Gln Arg Ala Ala Ala Ile Pro Pro Ile
               965                 970                 975

Gln Val Thr Lys Val His Glu Pro Pro Arg Glu Asp Ala Ala Pro Thr
           980                 985                 990

Lys Pro Ala Pro Pro Ala Pro Pro  Pro Pro Gln Asn Leu  Gln Pro Glu
       995                 1000                1005

Ser Asp  Ala Pro Gln Gln Pro  Gly Ser Ser Pro Arg  Gly Lys Ser
    1010                1015                1020

Arg Ser  Pro Ala Pro Pro Ala  Asp Lys Glu Ala Phe  Ala Ala Glu
    1025                1030                1035

Ala Gln  Lys Leu Pro Gly Asp  Pro Pro Cys Trp Thr  Ser Gly Leu
    1040                1045                1050

Pro Phe  Pro Val Pro Pro Arg  Glu Val Ile Lys Ala  Ser Pro His
    1055                1060                1065

Ala Pro  Asp Pro Ser Ala Phe  Ser Tyr Ala Pro Pro  Gly His Pro
    1070                1075                1080

Leu Pro  Leu Gly Leu His Asp  Thr Ala Arg Pro Val  Leu Pro Arg
    1085                1090                1095

Pro Pro  Thr Ile Ser Asn Pro  Pro Pro Leu Ile Ser  Ser Ala Lys
    1100                1105                1110

His Pro  Ser Val Leu Glu Arg  Gln Ile Gly Ala Ile  Ser Gln Gly
    1115                1120                1125

Met Ser  Val Gln Leu His Val  Pro Tyr Ser Glu His  Ala Lys Ala
    1130                1135                1140

Pro Val  Gly Pro Val Thr Met  Gly Leu Pro Leu Pro  Met Asp Pro
    1145                1150                1155

Lys Lys  Leu Ala Pro Phe Ser  Gly Val Lys Gln Glu  Gln Leu Ser
    1160                1165                1170

Pro Arg  Gly Gln Ala Gly Pro  Pro Glu Ser Leu Gly  Val Pro Thr
    1175                1180                1185

Ala Gln  Glu Ala Ser Val Leu  Arg Gly Thr Ala Leu  Gly Ser Val
    1190                1195                1200

Pro Gly  Gly Ser Ile Thr Lys  Gly Ile Pro Ser Thr  Arg Val Pro
    1205                1210                1215
```

```
Ser Asp  Ser Ala Ile Thr Tyr  Arg Gly Ser Ile Thr  His Gly Thr
    1220                 1225                 1230

Pro Ala  Asp Val Leu Tyr Lys  Gly Thr Ile Thr Arg  Ile Ile Gly
    1235                 1240                 1245

Glu Asp  Ser Pro Ser Arg Leu  Asp Arg Gly Arg Glu  Asp Ser Leu
    1250                 1255                 1260

Pro Lys  Gly His Val Ile Tyr  Glu Gly Lys Lys Gly  His Val Leu
    1265                 1270                 1275

Ser Tyr  Glu Gly Gly Met Ser  Val Thr Gln Cys Ser  Lys Glu Asp
    1280                 1285                 1290

Gly Arg  Ser Ser Ser Gly Pro  Pro His Glu Thr Ala  Ala Pro Lys
    1295                 1300                 1305

Arg Thr  Tyr Asp Met Met Glu  Gly Arg Val Gly Arg  Ala Ile Ser
    1310                 1315                 1320

Ser Ala  Ser Ile Glu Gly Leu  Met Gly Arg Ala Ile  Pro Pro Glu
    1325                 1330                 1335

Arg His  Ser Pro His His Leu  Lys Glu Gln His His  Ile Arg Gly
    1340                 1345                 1350

Ser Ile  Thr Gln Gly Ile Pro  Arg Ser Tyr Val Glu  Ala Gln Glu
    1355                 1360                 1365

Asp Tyr  Leu Arg Arg Glu Ala  Lys Leu Leu Lys Arg  Glu Gly Thr
    1370                 1375                 1380

Pro Pro  Pro Pro Pro Pro Ser  Arg Asp Leu Thr Glu  Ala Tyr Lys
    1385                 1390                 1395

Thr Gln  Ala Leu Gly Pro Leu  Lys Leu Lys Pro Ala  His Glu Gly
    1400                 1405                 1410

Leu Val  Ala Thr Val Lys Glu  Ala Gly Arg Ser Ile  His Glu Ile
    1415                 1420                 1425

Pro Arg  Glu Glu Leu Arg His  Thr Pro Glu Leu Pro  Leu Ala Pro
    1430                 1435                 1440

Arg Pro  Leu Lys Glu Gly Ser  Ile Thr Gln Gly Thr  Pro Leu Lys
    1445                 1450                 1455

Tyr Asp  Thr Gly Ala Ser Thr  Thr Gly Ser Lys Lys  His Asp Val
    1460                 1465                 1470
```

```
Arg Ser  Leu Ile Gly Ser Pro  Gly Arg Thr Phe Pro  Pro Val His
    1475                 1480                 1485

Pro Leu  Asp Val Met Ala Asp  Ala Arg Ala Leu Glu  Arg Ala Cys
    1490                 1495                 1500

Tyr Glu  Glu Ser Leu Lys Ser  Arg Pro Gly Thr Ala  Ser Ser Ser
    1505                 1510                 1515

Gly Gly  Ser Ile Ala Arg Gly  Ala Pro Val Ile Val  Pro Glu Leu
    1520                 1525                 1530

Gly Lys  Pro Arg Gln Ser Pro  Leu Thr Tyr Glu Asp  His Gly Ala
    1535                 1540                 1545

Pro Phe  Ala Gly His Leu Pro  Arg Gly Ser Pro Val  Thr Thr Arg
    1550                 1555                 1560

Glu Pro  Thr Pro Arg Leu Gln  Glu Gly Ser Leu Ser  Ser Ser Lys
    1565                 1570                 1575

Ala Ser  Gln Asp Arg Lys Leu  Thr Ser Thr Pro Arg  Glu Ile Ala
    1580                 1585                 1590

Lys Ser  Pro His Ser Thr Val  Pro Glu His His Pro  His Pro Ile
    1595                 1600                 1605

Ser Pro  Tyr Glu His Leu Leu  Arg Gly Val Ser Gly  Val Asp Leu
    1610                 1615                 1620

Tyr Arg  Ser His Ile Pro Leu  Ala Phe Asp Pro Thr  Ser Ile Pro
    1625                 1630                 1635

Arg Gly  Ile Pro Leu Asp Ala  Ala Ala Ala Tyr Tyr  Leu Pro Arg
    1640                 1645                 1650

His Leu  Ala Pro Asn Pro Thr  Tyr Pro His Leu Tyr  Pro Pro Tyr
    1655                 1660                 1665

Leu Ile  Arg Gly Tyr Pro Asp  Thr Ala Ala Leu Glu  Asn Arg Gln
    1670                 1675                 1680

Thr Ile  Ile Asn Asp Tyr Ile  Thr Ser Gln Gln Met  His His Asn
    1685                 1690                 1695

Ala Ala  Thr Ala Met Ala Gln  Arg Ala Asp Met Leu  Arg Gly Leu
    1700                 1705                 1710

Ser Pro  Arg Glu Ser Ser Leu  Ala Leu Asn Tyr Ala  Ala Gly Pro
    1715                 1720                 1725
```

```
Arg Gly  Ile Ile Asp Leu Ser  Gln Val Pro His Leu  Pro Val Leu
    1730                1735                1740

Val Pro  Pro Thr Pro Gly Thr  Pro Ala Thr Ala Met  Asp Arg Leu
    1745                1750                1755

Ala Tyr  Leu Pro Thr Ala Pro  Gln Pro Phe Ser Ser  Arg His Ser
    1760                1765                1770

Ser Ser  Pro Leu Ser Pro Gly  Gly Pro Thr His Leu  Thr Lys Pro
    1775                1780                1785

Thr Thr  Thr Ser Ser Ser Glu  Arg Glu Arg Asp Arg  Asp Arg Glu
    1790                1795                1800

Arg Asp  Arg Asp Arg Glu Arg  Glu Lys Ser Ile Leu  Thr Ser Thr
    1805                1810                1815

Thr Thr  Val Glu His Ala Pro  Ile Trp Arg Pro Gly  Thr Glu Gln
    1820                1825                1830

Ser Ser  Gly Ser Ser Gly Gly  Gly Gly Gly Ser Ser  Ser Arg Pro
    1835                1840                1845

Ala Ser  His Ser His Ala His  Gln His Ser Pro Ile  Ser Pro Arg
    1850                1855                1860

Thr Gln  Asp Ala Leu Gln Gln  Arg Pro Ser Val Leu  His Asn Thr
    1865                1870                1875

Gly Met  Lys Gly Ile Ile Thr  Ala Val Glu Pro Ser  Thr Pro Thr
    1880                1885                1890

Val Leu  Arg Ser Thr Ser Thr  Ser Ser Pro Val Arg  Pro Ala Ala
    1895                1900                1905

Thr Phe  Pro Pro Ala Thr His  Cys Pro Leu Gly Gly  Thr Leu Asp
    1910                1915                1920

Gly Val  Tyr Pro Thr Leu Met  Glu Pro Val Leu Leu  Pro Lys Glu
    1925                1930                1935

Ala Pro  Arg Val Ala Arg Pro  Glu Arg Pro Arg Ala  Asp Thr Gly
    1940                1945                1950

His Ala  Phe Leu Ala Lys Pro  Pro Ala Arg Ser Gly  Leu Glu Pro
    1955                1960                1965

Ala Ser  Ser Pro Ser Lys Gly  Ser Glu Pro Arg Pro  Leu Val Pro
    1970                1975                1980
```

```
Pro Val  Ser Gly His Ala Thr  Ile Ala Arg Thr Pro  Ala Lys Asn
    1985                 1990                 1995

Leu Ala  Pro His His Ala Ser  Pro Asp Pro Pro Ala  Pro Pro Ala
    2000                 2005                 2010

Ser Ala  Ser Asp Pro His Arg  Glu Lys Thr Gln Ser  Lys Pro Phe
    2015                 2020                 2025

Ser Ile  Gln Glu Leu Glu Leu  Arg Ser Leu Gly Tyr  His Gly Ser
    2030                 2035                 2040

Ser Tyr  Ser Pro Glu Gly Val  Glu Pro Val Ser Pro  Val Ser Ser
    2045                 2050                 2055

Pro Ser  Leu Thr His Asp Lys  Gly Leu Pro Lys His  Leu Glu Glu
    2060                 2065                 2070

Leu Asp  Lys Ser His Leu Glu  Gly Glu Leu Arg Pro  Lys Gln Pro
    2075                 2080                 2085

Gly Pro  Val Lys Leu Gly Gly  Glu Ala Ala His Leu  Pro His Leu
    2090                 2095                 2100

Arg Pro  Leu Pro Glu Ser Gln  Pro Ser Ser Ser Pro  Leu Leu Gln
    2105                 2110                 2115

Thr Ala  Pro Gly Val Lys Gly  His Gln Arg Val Val  Thr Leu Ala
    2120                 2125                 2130

Gln His  Ile Ser Glu Val Ile  Thr Gln Asp Tyr Thr  Arg His His
    2135                 2140                 2145

Pro Gln  Gln Leu Ser Ala Pro  Leu Pro Ala Pro Leu  Tyr Ser Phe
    2150                 2155                 2160

Pro Gly  Ala Ser Cys Pro Val  Leu Asp Leu Arg Arg  Pro Pro Ser
    2165                 2170                 2175

Asp Leu  Tyr Leu Pro Pro Pro  Asp His Gly Ala Pro  Ala Arg Gly
    2180                 2185                 2190

Ser Pro  His Ser Glu Gly Gly  Lys Arg Ser Pro Glu  Pro Asn Lys
    2195                 2200                 2205

Thr Ser  Val Leu Gly Gly Gly  Glu Asp Gly Ile Glu  Pro Val Ser
    2210                 2215                 2220

Pro Pro  Glu Gly Met Thr Glu  Pro Gly His Ser Arg  Ser Ala Val
    2225                 2230                 2235
```

```
Tyr Pro  Leu Leu Tyr Arg Asp  Gly Glu Gln Thr Glu  Pro Ser Arg
    2240                 2245                 2250

Met Gly  Ser Lys Ser Pro Gly  Asn Thr Ser Gln Pro  Pro Ala Phe
    2255                 2260                 2265

Phe Ser  Lys Leu Thr Glu Ser  Asn Ser Ala Met Val  Lys Ser Lys
    2270                 2275                 2280

Lys Gln  Glu Ile Asn Lys Lys  Leu Asn Thr His Asn  Arg Asn Glu
    2285                 2290                 2295

Pro Glu  Tyr Asn Ile Ser Gln  Pro Gly Thr Glu Ile  Phe Asn Met
    2300                 2305                 2310

Pro Ala  Ile Thr Gly Thr Gly  Leu Met Thr Tyr Arg  Ser Gln Ala
    2315                 2320                 2325

Val Gln  Glu His Ala Ser Thr  Asn Met Gly Leu Glu  Ala Ile Ile
    2330                 2335                 2340

Arg Lys  Ala Leu Met Gly Lys  Tyr Asp Gln Trp Glu  Glu Ser Pro
    2345                 2350                 2355

Pro Leu  Ser Ala Asn Ala Phe  Asn Pro Leu Asn Ala  Ser Ala Ser
    2360                 2365                 2370

Leu Pro  Ala Ala Met Pro Ile  Thr Ala Ala Asp Gly  Arg Ser Asp
    2375                 2380                 2385

His Thr  Leu Thr Ser Pro Gly  Gly Gly Gly Lys Ala  Lys Val Ser
    2390                 2395                 2400

Gly Arg  Pro Ser Ser Arg Lys  Ala Lys Ser Pro Ala  Pro Gly Leu
    2405                 2410                 2415

Ala Ser  Gly Asp Arg Pro Pro  Ser Val Ser Ser Val  His Ser Glu
    2420                 2425                 2430

Gly Asp  Cys Asn Arg Arg Thr  Pro Leu Thr Asn Arg  Val Trp Glu
    2435                 2440                 2445

Asp Arg  Pro Ser Ser Ala Gly  Ser Thr Pro Phe Pro  Tyr Asn Pro
    2450                 2455                 2460

Leu Ile  Met Arg Leu Gln Ala  Gly Val Met Ala Ser  Pro Pro Pro
    2465                 2470                 2475

Pro Gly  Leu Pro Ala Gly Ser  Gly Pro Leu Ala Gly  Pro His His
    2480                 2485                 2490
```

Ala Trp Asp Glu Glu Pro Lys Pro Leu Leu Cys Ser Gln Tyr Glu
2495 2500 2505

Thr Leu Ser Asp Ser Glu
2510

<210> 301
<211> 1158
<212> PRT
<213> Homo sapiens

<400> 301

Met Thr His Gly Glu Glu Leu Gly Ser Asp Val His Gln Asp Ser Ile
1 5 10 15

Val Leu Thr Tyr Leu Glu Gly Leu Leu Met His Gln Ala Ala Gly Gly
20 25 30

Ser Gly Thr Ala Val Asp Lys Lys Ser Ala Gly His Asn Glu Glu Asp
35 40 45

Gln Asn Phe Asn Ile Ser Gly Ser Ala Phe Pro Thr Cys Gln Ser Asn
50 55 60

Gly Pro Val Leu Asn Thr His Thr Tyr Gln Gly Ser Gly Met Leu His
65 70 75 80

Leu Lys Lys Ala Arg Leu Leu Gln Ser Ser Glu Asp Trp Asn Ala Ala
85 90 95

Lys Arg Lys Arg Leu Ser Asp Ser Ile Met Asn Leu Asn Val Lys Lys
100 105 110

Glu Ala Leu Leu Ala Gly Met Val Asp Ser Val Pro Lys Gly Lys Gln
115 120 125

Asp Ser Thr Leu Leu Ala Ser Leu Leu Gln Ser Phe Ser Ser Arg Leu
130 135 140

Gln Thr Val Ala Leu Ser Gln Gln Ile Arg Gln Ser Leu Lys Glu Gln
145 150 155 160

Gly Tyr Ala Leu Ser His Asp Ser Leu Lys Val Glu Lys Asp Leu Arg
165 170 175

Cys Tyr Gly Val Ala Ser Ser His Leu Lys Thr Leu Leu Lys Lys Ser
180 185 190

Lys Val Lys Asp Gln Lys Pro Asp Thr Asn Leu Pro Asp Val Thr Lys
195 200 205

```
Asn Leu Ile Arg Asp Arg Phe Ala Glu Ser Pro His His Val Gly Gln
    210                 215                 220

Ser Gly Thr Lys Val Met Ser Glu Pro Leu Ser Cys Ala Ala Arg Leu
225                 230                 235                 240

Gln Ala Val Ala Ser Met Val Glu Lys Arg Ala Ser Pro Ala Thr Ser
                245                 250                 255

Pro Lys Pro Ser Val Ala Cys Ser Gln Leu Ala Leu Leu Leu Ser Ser
            260                 265                 270

Glu Ala His Leu Gln Gln Tyr Ser Arg Glu His Ala Leu Lys Thr Gln
        275                 280                 285

Asn Ala Asn Gln Ala Ala Ser Glu Arg Leu Ala Ala Met Ala Arg Leu
    290                 295                 300

Gln Glu Asn Gly Gln Lys Asp Val Gly Ser Tyr Gln Leu Pro Lys Gly
305                 310                 315                 320

Met Ser Ser His Leu Asn Gly Gln Ala Arg Thr Ser Ser Ser Lys Leu
                325                 330                 335

Met Ala Ser Lys Ser Ser Ala Thr Val Phe Gln Asn Pro Met Gly Ile
            340                 345                 350

Ile Pro Ser Ser Pro Lys Asn Ala Gly Tyr Lys Asn Ser Leu Glu Arg
        355                 360                 365

Asn Asn Ile Lys Gln Ala Ala Asn Asn Ser Leu Leu Leu His Leu Leu
    370                 375                 380

Lys Ser Gln Thr Ile Pro Lys Pro Met Asn Gly His Ser His Ser Glu
385                 390                 395                 400

Arg Gly Ser Ile Phe Glu Glu Ser Ser Thr Pro Thr Thr Ile Asp Glu
                405                 410                 415

Tyr Ser Asp Asn Asn Pro Ser Phe Thr Asp Asp Ser Ser Gly Asp Glu
            420                 425                 430

Ser Ser Tyr Ser Asn Cys Val Pro Ile Asp Leu Ser Cys Lys His Arg
        435                 440                 445

Thr Glu Lys Ser Glu Ser Asp Gln Pro Val Ser Leu Asp Asn Phe Thr
    450                 455                 460

Gln Ser Leu Leu Asn Thr Trp Asp Pro Lys Val Pro Asp Val Asp Ile
465                 470                 475                 480
```

```
Lys Glu Asp Gln Asp Thr Ser Lys Asn Ser Lys Leu Asn Ser His Gln
                485                 490                 495

Lys Val Thr Leu Leu Gln Leu Leu Leu Gly His Lys Asn Glu Glu Asn
            500                 505                 510

Val Glu Lys Asn Thr Ser Pro Gln Gly Val His Asn Asp Val Ser Lys
        515                 520                 525

Phe Asn Thr Gln Asn Tyr Ala Arg Thr Ser Val Ile Glu Ser Pro Ser
    530                 535                 540

Thr Asn Arg Thr Thr Pro Val Ser Thr Pro Pro Leu Leu Thr Ser Ser
545                 550                 555                 560

Lys Ala Gly Ser Pro Ile Asn Leu Ser Gln His Ser Leu Val Ile Lys
                565                 570                 575

Trp Asn Ser Pro Pro Tyr Val Cys Ser Thr Gln Ser Glu Lys Leu Thr
            580                 585                 590

Asn Thr Ala Ser Asn His Ser Met Asp Leu Thr Lys Ser Lys Asp Pro
        595                 600                 605

Pro Gly Glu Lys Pro Ala Gln Asn Glu Gly Ala Gln Asn Ser Ala Thr
    610                 615                 620

Phe Ser Ala Ser Lys Leu Leu Gln Asn Leu Ala Gln Cys Gly Met Gln
625                 630                 635                 640

Ser Ser Met Ser Val Glu Glu Gln Arg Pro Ser Lys Gln Leu Leu Thr
                645                 650                 655

Gly Asn Thr Asp Lys Pro Ile Gly Met Ile Asp Arg Leu Asn Ser Pro
            660                 665                 670

Leu Leu Ser Asn Lys Thr Asn Ala Val Glu Glu Asn Lys Ala Phe Ser
        675                 680                 685

Ser Gln Pro Thr Gly Pro Glu Pro Gly Leu Ser Gly Ser Glu Ile Glu
    690                 695                 700

Asn Leu Leu Glu Arg Arg Thr Val Leu Gln Leu Leu Leu Gly Asn Pro
705                 710                 715                 720

Asn Lys Gly Lys Ser Glu Lys Lys Glu Lys Thr Pro Leu Arg Asp Glu
                725                 730                 735

Ser Thr Gln Glu His Ser Glu Arg Ala Leu Ser Glu Gln Ile Leu Met
            740                 745                 750
```

```
Val Lys Ile Lys Ser Glu Pro Cys Asp Asp Leu Gln Ile Pro Asn Thr
        755                 760                 765

Asn Val His Leu Ser His Asp Ala Lys Ser Ala Pro Phe Leu Gly Met
    770                 775                 780

Ala Pro Ala Val Gln Arg Ser Ala Pro Ala Leu Pro Val Ser Glu Asp
785                 790                 795                 800

Phe Lys Ser Glu Pro Val Ser Pro Gln Asp Phe Ser Phe Ser Lys Asn
                805                 810                 815

Gly Leu Leu Ser Arg Leu Leu Arg Gln Asn Gln Asp Ser Tyr Leu Ala
            820                 825                 830

Asp Asp Ser Asp Arg Ser His Arg Asn Asn Glu Met Ala Leu Leu Glu
        835                 840                 845

Ser Lys Asn Leu Cys Met Val Pro Lys Lys Arg Lys Leu Tyr Thr Glu
    850                 855                 860

Pro Leu Glu Asn Pro Phe Lys Lys Met Lys Asn Asn Ile Val Asp Ala
865                 870                 875                 880

Ala Asn Asn His Ser Ala Pro Glu Val Leu Tyr Gly Ser Leu Leu Asn
                885                 890                 895

Gln Glu Glu Leu Lys Phe Ser Arg Asn Asp Leu Glu Phe Lys Tyr Pro
            900                 905                 910

Ala Gly His Gly Ser Ala Ser Glu Ser Glu His Arg Ser Trp Ala Arg
        915                 920                 925

Glu Ser Lys Ser Phe Asn Val Leu Lys Gln Leu Leu Leu Ser Glu Asn
    930                 935                 940

Cys Val Arg Asp Leu Ser Pro His Arg Ser Asn Ser Val Ala Asp Ser
945                 950                 955                 960

Lys Lys Lys Gly His Lys Asn Asn Val Thr Asn Ser Lys Pro Glu Phe
                965                 970                 975

Ser Ile Ser Ser Leu Asn Gly Leu Met Tyr Ser Ser Thr Gln Pro Ser
            980                 985                 990

Ser Cys Met Asp Asn Arg Thr Phe  Ser Tyr Pro Gly Val  Val Lys Thr
        995                 1000                1005

Pro Val  Ser Pro Thr Phe Pro  Glu His Leu Gly Cys  Ala Gly Ser
    1010                1015                1020
```

```
Arg Pro  Glu Ser Gly Leu Leu  Asn Gly Cys Ser Met  Pro Ser Glu
    1025                1030                1035

Lys Gly  Pro Ile Lys Trp Val  Ile Thr Asp Ala Glu  Lys Asn Glu
    1040                1045                1050

Tyr Glu  Lys Asp Ser Pro Arg  Leu Thr Lys Thr Asn  Pro Ile Leu
    1055                1060                1065

Tyr Tyr  Met Leu Gln Lys Gly  Gly Asn Ser Val Thr  Ser Arg Glu
    1070                1075                1080

Thr Gln  Asp Lys Asp Ile Trp  Arg Glu Ala Ser Ser  Ala Glu Ser
    1085                1090                1095

Val Ser  Gln Val Thr Ala Lys  Glu Glu Leu Leu Pro  Thr Ala Glu
    1100                1105                1110

Thr Lys  Ala Ser Phe Phe Asn  Leu Arg Ser Pro Tyr  Asn Ser His
    1115                1120                1125

Met Gly  Asn Asn Ala Ser Arg  Pro His Ser Ala Asn  Gly Glu Val
    1130                1135                1140

Tyr Gly  Leu Leu Gly Ser Val  Leu Thr Ile Lys Lys  Glu Ser Glu
    1145                1150                1155
```

<210> 302
<211> 2080
<212> PRT
<213> Homo sapiens

<400> 302

```
Met Ser Ser Ser Pro Ser Arg Ser Ala Ala Asp Ile Tyr Ile Arg Glu
1               5                   10                  15

Tyr Phe His Ser His Val Ser Gly Gly His Pro Glu Ala Thr Pro Leu
            20                  25                  30

Arg Val Met Tyr Thr Asp Arg Pro Leu Ser Gln Thr Asp Pro Val Thr
        35                  40                  45

Leu Gln Tyr Cys Cys Leu Thr Asp Asp Arg Gln Ala Phe Arg Pro Pro
    50                  55                  60

Thr Arg Ala Glu Leu Ala Arg His Arg Val Val Val Thr Thr Thr Ser
65                  70                  75                  80

Gln Ala Arg Glu Leu Arg Val Pro Val Gly Phe Phe Ser His Ile Leu
                85                  90                  95
```

```
Ile Asp Glu Ala Ala Gln Met Leu Glu Cys Glu Ala Leu Thr Pro Leu
            100                 105                 110

Ala Tyr Ala Ser His Gly Thr Arg Leu Val Leu Ala Gly Asp His Met
        115                 120                 125

Gln Val Thr Pro Arg Leu Phe Ser Val Ala Arg Ala Arg Ala Ala Glu
    130                 135                 140

His Thr Leu Leu His Arg Leu Phe Leu Cys Tyr Gln Gln Glu Thr His
145                 150                 155                 160

Glu Val Ala Arg Gln Ser Arg Leu Val Phe His Glu Asn Tyr Arg Cys
                165                 170                 175

Thr Asp Ala Ile Val Ser Phe Ile Ser Arg His Phe Tyr Val Ala Lys
            180                 185                 190

Gly Asn Pro Ile His Ala Arg Gly Lys Val Pro Pro His Pro Arg His
        195                 200                 205

Tyr Pro Leu Met Phe Cys His Val Ala Gly Ser Pro Asp Arg Asp Met
    210                 215                 220

Ser Met Ala Ser Trp Leu Asn Leu Ala Glu Ile Ala Gln Val Val Glu
225                 230                 235                 240

Lys Val Gln Glu Ala Tyr Asn Thr Trp Pro Ser Cys Trp Gly Gly Arg
                245                 250                 255

Glu Gln Arg Cys Ile Cys Val Val Ser His Gly Ala Gln Val Ser Ala
            260                 265                 270

Leu Arg Gln Glu Leu Arg Arg Arg Asp Leu Gly Gln Val Ser Val Gly
        275                 280                 285

Ser Phe Glu Ile Leu Pro Gly Arg Gln Phe Arg Val Val Val Leu Ser
    290                 295                 300

Thr Val His Thr Cys Gln Ser Leu Leu Ser Pro Gly Ala Leu Ala Pro
305                 310                 315                 320

Glu Phe Phe Thr Asp Ala Arg Val Leu Asn Thr Val Leu Thr Arg Ala
                325                 330                 335

Gln Ser Gln Leu Val Val Val Gly Asp Ala Val Ala Leu Cys Ser Phe
            340                 345                 350

Gly Ala Cys Gly Lys Leu Trp Glu Ser Phe Ile Arg Glu Cys Val Glu
        355                 360                 365
```

```
Arg His Ser Val Cys Pro Glu Gly Leu Ser Met Glu Gln Val Glu Gln
    370                 375                 380

Gly Val Ala Gln Arg Arg Arg Trp Pro Pro Arg Gly Thr Gln Ala Gly
385                 390                 395                 400

Ala Ala Gly Asn Trp Glu Ala Ala Pro Glu Pro Val Gly Asp Leu Ala
                405                 410                 415

Glu Glu Gln Ala Ala Val Val Thr Ala Met Val Lys Ala Glu Pro Gly
            420                 425                 430

Asp Glu Ala Leu Ser Pro Ala Ser Arg Asp Ile Thr Ala Thr Thr Ala
        435                 440                 445

Gln Thr Glu Ala Ala Ala Ala Pro Ala Gly Asp Ala Val Lys Glu Asp
    450                 455                 460

Val Val Pro Gly Ala Cys Ala Ala Gly Ala Ala Ala Ala Ala Gly Val
465                 470                 475                 480

Glu Ser Thr Glu Ala Glu Asp Ala Glu Ala Asp Phe Trp Pro Trp Asp
                485                 490                 495

Gly Glu Leu Asn Ala Asp Asp Ala Ile Leu Arg Glu Leu Leu Asp Glu
            500                 505                 510

Ser Gln Lys Val Met Val Thr Val Gly Glu Asp Gly Leu Leu Asp Thr
        515                 520                 525

Val Ala Arg Pro Glu Ser Leu Gln Gln Ala Arg Leu Tyr Glu Asn Leu
    530                 535                 540

Pro Pro Ala Ala Leu Arg Lys Leu Leu His Ala Glu Pro Glu Arg Tyr
545                 550                 555                 560

Arg His Cys Ser Phe Val Pro Glu Thr Phe Glu Arg Ala Ser Ala Ile
                565                 570                 575

Pro Leu Asp Asp Ala Ser Ser Gly Pro Ile Gln Val Arg Gly Arg Leu
            580                 585                 590

Asp Cys Gly Met Ala Phe Ala Gly Asp Glu Val Leu Val Gln Leu Leu
        595                 600                 605

Ser Gly Asp Lys Ala Pro Glu Gly Arg Leu Arg Gly Arg Val Leu Gly
    610                 615                 620

Val Leu Lys Arg Lys Arg His Glu Leu Ala Phe Val Cys Arg Met Asp
625                 630                 635                 640
```

```
Thr Trp Asp Pro Arg Ile Met Val Pro Ile Asn Gly Ser Val Thr Lys
                645                 650                 655

Ile Phe Val Ala Glu Leu Lys Asp Pro Ser Gln Val Pro Ile Tyr Ser
            660                 665                 670

Leu Arg Lys Gly Arg Leu Gln Arg Val Gly Leu Glu Arg Leu Thr Ala
        675                 680                 685

Glu Ala Arg His Ser Arg Leu Phe Trp Val Gln Ile Val Leu Trp Arg
    690                 695                 700

Gln Gly Phe Tyr Tyr Pro Leu Gly Ile Val Arg Glu Val Leu Pro Glu
705                 710                 715                 720

Ala Ser Thr Trp Glu Gln Gly Leu Arg Ile Leu Gly Leu Glu Tyr Ser
                725                 730                 735

Leu Arg Val Pro Pro Ser Asp Gln Ala Thr Ile Thr Lys Val Leu Gln
            740                 745                 750

Lys Tyr His Thr Glu Leu Gly Arg Val Ala Gly Arg Arg Glu Asp Cys
        755                 760                 765

Arg Ala Phe Leu Thr Phe Thr Val Asp Pro Gln Gly Ala Cys Asn Leu
    770                 775                 780

Asp Asp Ala Leu Ser Val Arg Asp Leu Gly Pro Arg Cys Glu Val Ala
785                 790                 795                 800

Val His Ile Thr Asp Val Ala Ser Phe Val Pro Arg Asp Gly Val Leu
                805                 810                 815

Asp Val Glu Ala Arg Arg Gln Gly Ala Ala Phe Tyr Ala Pro Gly Arg
            820                 825                 830

Glu Pro Val Pro Met Leu Pro Ala Ser Leu Cys Gln Asp Val Leu Ser
        835                 840                 845

Leu Leu Pro Gly Arg Asp Arg Leu Ala Ile Ser Leu Phe Leu Thr Met
    850                 855                 860

Glu Lys Ala Ser Gly Gln Leu Lys Ser Leu Arg Phe Ala Pro Ser Val
865                 870                 875                 880

Val Gln Ser Asp Arg Gln Leu Ser Tyr Glu Glu Ala Glu Glu Val Ile
                885                 890                 895

Arg Gln His Pro Gly Ala Gly Arg Glu Leu Pro Ala Arg Leu Asp Ser
            900                 905                 910
```

```
Val Asp Ala Cys Val Val Ala Ala Cys Tyr Phe Ser Arg Leu Leu Arg
        915                 920                 925

Arg His Arg Leu Arg Ser Asp Cys Phe Tyr Glu Gln Pro Asp Glu Asp
    930                 935                 940

Gly Thr Leu Gly Phe Arg Ala Ala His Ile Met Val Lys Glu Tyr Met
945                 950                 955                 960

Ile Gln Phe Asn Arg Leu Val Ala Glu Phe Leu Val Gly Ser Glu Cys
                965                 970                 975

Thr Arg Thr Val Thr Pro Leu Arg Trp Gln Pro Ala Pro Arg Ser Gln
            980                 985                 990

Gln Leu Lys Ala Leu Cys Glu Lys  His Gly Asp Arg Val  Pro Leu Ser
        995                 1000                1005

Leu His  Leu Gly His His Leu  His Gly Gly Gly Gly  Ser Pro Pro
    1010                1015                1020

Asp Thr  Arg Leu His Leu Leu  Ala Ser Leu Trp Lys  Gln Val Gln
    1025                1030                1035

Phe Ala  Ala Arg Thr Gln Asp  Tyr Glu Gln Met Val  Asp Leu Val
    1040                1045                1050

Thr Thr  Asp Asp Met His Pro  Phe Leu Ala Pro Ala  Gly Arg Asp
    1055                1060                1065

Leu Arg  Lys Ala Leu Glu Arg  Ser Ala Phe Gly Arg  Cys Ala Arg
    1070                1075                1080

Gly His  Gln Gln Gln Gly Gly  His Tyr Ser Leu Gln  Val Asp Trp
    1085                1090                1095

Tyr Thr  Trp Ala Thr Ser Pro  Ile Arg Arg Tyr Leu  Asp Val Val
    1100                1105                1110

Leu Gln  Arg Gln Ile Leu Leu  Ala Leu Gly His Gly  Gly Ser Ala
    1115                1120                1125

Tyr Ser  Ala Arg Asp Ile Asp  Gly Leu Cys Gln Ala  Phe Ser Leu
    1130                1135                1140

Gln His  Ala Leu Ala Gln Ser  Tyr Gln Arg Arg Ala  Arg Ser Leu
    1145                1150                1155

His Leu  Ala Val Gln Leu Lys  Ala Gln Pro Leu Asp  Lys Leu Gly
    1160                1165                1170
```

```
Phe Val  Val Asp Val Glu Ala  Gly Ser Arg Cys Phe  Arg Leu Leu
    1175                1180                1185

Phe Pro  Ser Asn Arg Glu Thr  Leu Pro Asp Pro Cys  Pro Val Pro
    1190                1195                1200

Tyr Gly  Ser Leu Gln Leu Ala  Glu His Pro His Ala  Leu Ala Gly
    1205                1210                1215

Arg Pro  Gly Leu Arg Leu Leu  Trp Arg Arg Arg Val  Tyr Ser Ala
    1220                1225                1230

Gln Gly  Ser Ser Pro Pro Leu  Pro Leu Pro Gly Thr  Val Pro Asp
    1235                1240                1245

Pro His  Thr Leu Ala Val Glu  Thr Ala Leu Trp Lys  Gln Leu Leu
    1250                1255                1260

Glu Leu  Val Glu Leu Gln Arg  Trp Pro Glu Ala Ala  Ala Leu Ile
    1265                1270                1275

Gln Glu  Lys Gly Glu Ala Ser  Gln Arg Arg Glu Leu  Val Gln Val
    1280                1285                1290

Gln Arg  Ser His Cys Gly His  Phe Leu Glu Val Ala  Arg Glu Leu
    1295                1300                1305

Gly Ser  Gly Asp Thr Leu Gln  Val Gln Leu Gly Thr  Ser Leu Gln
    1310                1315                1320

His Gly  Phe Leu Val Pro Ser  Pro Gln Leu Trp Thr  Val Ala Pro
    1325                1330                1335

Gly Phe  Ser Leu Cys Leu Glu  His Val Glu Arg Pro  Gly Asp Cys
    1340                1345                1350

Phe Ser  Gly Arg Val Tyr Arg  Ala Pro Arg Asp Arg  Tyr Arg Asp
    1355                1360                1365

Val Asp  Glu Tyr Ala Cys Val  Trp Glu Pro Phe Cys  Ala Leu Glu
    1370                1375                1380

Ser Ala  Thr Gly Ala Val Ala  Glu Asn Asp Ser Val  Thr Leu Gln
    1385                1390                1395

His Leu  Ser Val Ser Trp Glu  Ala Ser Arg Thr Pro  Gln Gly Gln
    1400                1405                1410

Leu Gln  Gly Ala Phe Arg Leu  Glu Ala Ala Phe Leu  Glu Glu Asn
    1415                1420                1425
```

```
Cys Ala  Asp Ile Asn Phe Ser  Cys Cys Tyr Leu Cys  Ile Arg Leu
    1430                 1435                 1440

Glu Gly  Leu Pro Ala Pro Thr  Ala Ser Pro Arg Pro  Gly Pro Ser
    1445                 1450                 1455

Ser Leu  Gly Pro Gly Leu Asn  Val Asp Pro Gly Thr  Tyr Thr Trp
    1460                 1465                 1470

Val Ala  His Gly Gln Thr Gln  Asp Trp Asp Gln Glu  Arg Arg Ala
    1475                 1480                 1485

Asp Arg  Gln Glu Ala Pro Arg  Arg Val His Leu Phe  Val His His
    1490                 1495                 1500

Met Gly  Met Glu Lys Val Pro  Glu Glu Val Leu Arg  Pro Gly Thr
    1505                 1510                 1515

Leu Phe  Thr Val Glu Leu Leu  Pro Lys Gln Leu Pro  Asp Leu Arg
    1520                 1525                 1530

Lys Glu  Glu Ala Val Arg Gly  Leu Glu Glu Ala Ser  Pro Leu Val
    1535                 1540                 1545

Thr Ser  Ile Ala Leu Gly Arg  Pro Val Pro Gln Pro  Leu Cys Arg
    1550                 1555                 1560

Val Ile  Pro Ser Arg Phe Leu  Glu Arg Gln Thr Tyr  Asn Ile Pro
    1565                 1570                 1575

Gly Gly  Arg His Lys Leu Asn  Pro Ser Gln Asn Val  Ala Val Arg
    1580                 1585                 1590

Glu Ala  Leu Glu Lys Pro Phe  Thr Val Ile Gln Gly  Pro Pro Gly
    1595                 1600                 1605

Thr Gly  Lys Thr Ile Val Gly  Leu His Ile Val Phe  Trp Phe His
    1610                 1615                 1620

Lys Ser  Asn Gln Glu Gln Val  Gln Pro Gly Gly Pro  Pro Arg Gly
    1625                 1630                 1635

Glu Lys  Arg Leu Gly Gly Pro  Cys Ile Leu Tyr Cys  Gly Pro Ser
    1640                 1645                 1650

Asn Lys  Ser Val Asp Val Leu  Ala Gly Leu Leu Leu  Arg Arg Met
    1655                 1660                 1665

Glu Leu  Lys Pro Leu Arg Val  Tyr Ser Glu Gln Ala  Glu Ala Ser
    1670                 1675                 1680
```

```
Glu Phe  Pro Val Pro Arg Val  Gly Ser Arg Lys Leu  Leu Arg Lys
    1685                1690                1695

Ser Pro  Arg Glu Gly Arg Pro  Asn Gln Ser Leu Arg  Ser Ile Thr
    1700                1705                1710

Leu His  His Arg Ile Arg Gln  Ala Pro Asn Pro Tyr  Ser Ser Glu
    1715                1720                1725

Ile Lys  Ala Phe Asp Thr Arg  Leu Gln Arg Gly Glu  Leu Phe Ser
    1730                1735                1740

Arg Glu  Asp Leu Val Trp Tyr  Lys Lys Val Leu Trp  Glu Ala Arg
    1745                1750                1755

Lys Phe  Glu Leu Asp Arg His  Glu Val Ile Leu Cys  Thr Cys Ser
    1760                1765                1770

Cys Ala  Ala Ser Ala Ser Leu  Lys Ile Leu Asp Val  Arg Gln Ile
    1775                1780                1785

Leu Val  Asp Glu Ala Gly Met  Ala Thr Glu Pro Glu  Thr Leu Ile
    1790                1795                1800

Pro Leu  Val Gln Phe Pro Gln  Ala Glu Lys Val Val  Leu Leu Gly
    1805                1810                1815

Asp His  Lys Gln Leu Arg Pro  Val Val Lys Asn Glu  Arg Leu Gln
    1820                1825                1830

Asn Leu  Gly Leu Asp Arg Ser  Leu Phe Glu Arg Tyr  His Glu Asp
    1835                1840                1845

Ala His  Met Leu Asp Thr Gln  Tyr Arg Met His Glu  Gly Ile Cys
    1850                1855                1860

Ala Phe  Pro Ser Val Ala Phe  Tyr Lys Ser Lys Leu  Lys Thr Trp
    1865                1870                1875

Gln Gly  Leu Arg Arg Pro Pro  Ser Val Leu Gly His  Ala Gly Lys
    1880                1885                1890

Glu Ser  Cys Pro Val Ile Phe  Gly His Val Gln Gly  His Glu Arg
    1895                1900                1905

Ser Leu  Leu Val Ser Thr Asp  Glu Gly Asn Glu Asn  Ser Lys Ala
    1910                1915                1920

Asn Leu  Glu Glu Val Ala Glu  Val Val Arg Ile Thr  Lys Gln Leu
    1925                1930                1935
```

Thr Leu Gly Arg Thr Val Glu Pro Gln Asp Ile Ala Val Leu Thr
1940 1945 1950

Pro Tyr Asn Ala Gln Ala Ser Glu Ile Ser Lys Ala Leu Arg Arg
1955 1960 1965

Glu Gly Ile Ala Gly Val Ala Val Ser Ser Ile Thr Lys Ser Gln
1970 1975 1980

Gly Ser Glu Trp Arg Tyr Val Leu Val Ser Thr Val Arg Thr Cys
1985 1990 1995

Ala Lys Ser Asp Leu Asp Gln Arg Pro Thr Lys Ser Trp Leu Lys
2000 2005 2010

Lys Phe Leu Gly Phe Val Val Asp Pro Asn Gln Val Asn Val Ala
2015 2020 2025

Val Thr Arg Ala Gln Glu Gly Leu Cys Leu Ile Gly Asp His Leu
2030 2035 2040

Leu Leu Arg Cys Cys Pro Leu Trp Arg Ser Leu Leu Asp Phe Cys
2045 2050 2055

Glu Ala Gln Gln Thr Leu Val Pro Ala Gly Gln Val Arg Val Cys
2060 2065 2070

Arg Arg Pro Thr Met Pro Ser
2075 2080

<210> 303
<211> 380
<212> PRT
<213> Homo sapiens

<400> 303

Met Ala Phe Val Cys Leu Ala Ile Gly Cys Leu Tyr Thr Phe Leu Ile
1 5 10 15

Ser Thr Thr Phe Gly Cys Thr Ser Ser Ser Asp Thr Glu Ile Lys Val
20 25 30

Asn Pro Pro Gln Asp Phe Glu Ile Val Asp Pro Gly Tyr Leu Gly Tyr
35 40 45

Leu Tyr Leu Gln Trp Gln Pro Pro Leu Ser Leu Asp His Phe Lys Glu
50 55 60

Cys Thr Val Glu Tyr Glu Leu Lys Tyr Arg Asn Ile Gly Ser Glu Thr
65 70 75 80

Trp Lys Thr Ile Ile Thr Lys Asn Leu His Tyr Lys Asp Gly Phe Asp

85 90 95

Leu Asn Lys Gly Ile Glu Ala Lys Ile His Thr Leu Leu Pro Trp Gln
100 105 110

Cys Thr Asn Gly Ser Glu Val Gln Ser Ser Trp Ala Glu Thr Thr Tyr
115 120 125

Trp Ile Ser Pro Gln Gly Ile Pro Glu Thr Lys Val Gln Asp Met Asp
130 135 140

Cys Val Tyr Tyr Asn Trp Gln Tyr Leu Leu Cys Ser Trp Lys Pro Gly
145 150 155 160

Ile Gly Val Leu Leu Asp Thr Asn Tyr Asn Leu Phe Tyr Trp Tyr Glu
165 170 175

Gly Leu Asp His Ala Leu Gln Cys Val Asp Tyr Ile Lys Ala Asp Gly
180 185 190

Gln Asn Ile Gly Cys Arg Phe Pro Tyr Leu Glu Ala Ser Asp Tyr Lys
195 200 205

Asp Phe Tyr Ile Cys Val Asn Gly Ser Ser Glu Asn Lys Pro Ile Arg
210 215 220

Ser Ser Tyr Phe Thr Phe Gln Leu Gln Asn Ile Val Lys Pro Leu Pro
225 230 235 240

Pro Val Tyr Leu Thr Phe Thr Arg Glu Ser Ser Cys Glu Ile Lys Leu
245 250 255

Lys Trp Ser Ile Pro Leu Gly Pro Ile Pro Ala Arg Cys Phe Asp Tyr
260 265 270

Glu Ile Glu Ile Arg Glu Asp Asp Thr Thr Leu Val Thr Ala Thr Val
275 280 285

Glu Asn Glu Thr Tyr Thr Leu Lys Thr Thr Asn Glu Thr Arg Gln Leu
290 295 300

Cys Phe Val Val Arg Ser Lys Val Asn Ile Tyr Cys Ser Asp Asp Gly
305 310 315 320

Ile Trp Ser Glu Trp Ser Asp Lys Gln Cys Trp Glu Gly Glu Asp Leu
325 330 335

Ser Lys Lys Thr Leu Leu Arg Phe Trp Leu Pro Phe Gly Phe Ile Leu
340 345 350

Ile Leu Val Ile Phe Val Thr Gly Leu Leu Leu Arg Lys Pro Asn Thr

355 360 365

Tyr Pro Lys Met Ile Pro Glu Phe Phe Cys Asp Thr
370 375 380

<210> 304
<211> 272
<212> PRT
<213> Homo sapiens

<400> 304

Met Asp Ser Tyr Leu Leu Met Trp Gly Leu Leu Thr Phe Ile Met Val
1 5 10 15

Pro Gly Cys Gln Ala Glu Leu Cys Asp Asp Pro Pro Glu Ile Pro
20 25 30

His Ala Thr Phe Lys Ala Met Ala Tyr Lys Glu Gly Thr Met Leu Asn
35 40 45

Cys Glu Cys Lys Arg Gly Phe Arg Arg Ile Lys Ser Gly Ser Leu Tyr
50 55 60

Met Leu Cys Thr Gly Asn Ser Ser His Ser Ser Trp Asp Asn Gln Cys
65 70 75 80

Gln Cys Thr Ser Ser Ala Thr Arg Asn Thr Thr Lys Gln Val Thr Pro
85 90 95

Gln Pro Glu Glu Gln Lys Glu Arg Lys Thr Thr Glu Met Gln Ser Pro
100 105 110

Met Gln Pro Val Asp Gln Ala Ser Leu Pro Gly His Cys Arg Glu Pro
115 120 125

Pro Pro Trp Glu Asn Glu Ala Thr Glu Arg Ile Tyr His Phe Val Val
130 135 140

Gly Gln Met Val Tyr Tyr Gln Cys Val Gln Gly Tyr Arg Ala Leu His
145 150 155 160

Arg Gly Pro Ala Glu Ser Val Cys Lys Met Thr His Gly Lys Thr Arg
165 170 175

Trp Thr Gln Pro Gln Leu Ile Cys Thr Gly Glu Met Glu Thr Ser Gln
180 185 190

Phe Pro Gly Glu Glu Lys Pro Gln Ala Ser Pro Glu Gly Arg Pro Glu
195 200 205

Ser Glu Thr Ser Cys Leu Val Thr Thr Thr Asp Phe Gln Ile Gln Thr
210 215 220

```
Glu Met Ala Ala Thr Met Glu Thr Ser Ile Phe Thr Thr Glu Tyr Gln
225                 230                 235                 240

Val Ala Val Ala Gly Cys Val Phe Leu Leu Ile Ser Val Leu Leu Leu
                245                 250                 255

Ser Gly Leu Thr Trp Gln Arg Arg Gln Arg Lys Ser Arg Arg Thr Ile
            260                 265                 270
```

<210> 305
<211> 551
<212> PRT
<213> Homo sapiens

<400> 305

```
Met Ala Ala Pro Ala Leu Ser Trp Arg Leu Pro Leu Leu Ile Leu Leu
1               5                   10                  15

Leu Pro Leu Ala Thr Ser Trp Ala Ser Ala Ala Val Asn Gly Thr Ser
            20                  25                  30

Gln Phe Thr Cys Phe Tyr Asn Ser Arg Ala Asn Ile Ser Cys Val Trp
        35                  40                  45

Ser Gln Asp Gly Ala Leu Gln Asp Thr Ser Cys Gln Val His Ala Trp
    50                  55                  60

Pro Asp Arg Arg Arg Trp Asn Gln Thr Cys Glu Leu Leu Pro Val Ser
65                  70                  75                  80

Gln Ala Ser Trp Ala Cys Asn Leu Ile Leu Gly Ala Pro Asp Ser Gln
                85                  90                  95

Lys Leu Thr Thr Val Asp Ile Val Thr Leu Arg Val Leu Cys Arg Glu
            100                 105                 110

Gly Val Arg Trp Arg Val Met Ala Ile Gln Asp Phe Lys Pro Phe Glu
        115                 120                 125

Asn Leu Arg Leu Met Ala Pro Ile Ser Leu Gln Val Val His Val Glu
    130                 135                 140

Thr His Arg Cys Asn Ile Ser Trp Glu Ile Ser Gln Ala Ser His Tyr
145                 150                 155                 160

Phe Glu Arg His Leu Glu Phe Glu Ala Arg Thr Leu Ser Pro Gly His
                165                 170                 175

Thr Trp Glu Glu Ala Pro Leu Leu Thr Leu Lys Gln Lys Gln Glu Trp
            180                 185                 190
```

```
Ile Cys Leu Glu Thr Leu Thr Pro Asp Thr Gln Tyr Glu Phe Gln Val
        195                 200                 205

Arg Val Lys Pro Leu Gln Gly Glu Phe Thr Thr Trp Ser Pro Trp Ser
    210                 215                 220

Gln Pro Leu Ala Phe Arg Thr Lys Pro Ala Ala Leu Gly Lys Asp Thr
225                 230                 235                 240

Ile Pro Trp Leu Gly His Leu Leu Val Gly Leu Ser Gly Ala Phe Gly
                245                 250                 255

Phe Ile Ile Leu Val Tyr Leu Leu Ile Asn Cys Arg Asn Thr Gly Pro
            260                 265                 270

Trp Leu Lys Lys Val Leu Lys Cys Asn Thr Pro Asp Pro Ser Lys Phe
        275                 280                 285

Phe Ser Gln Leu Ser Ser Glu His Gly Gly Asp Val Gln Lys Trp Leu
    290                 295                 300

Ser Ser Pro Phe Pro Ser Ser Ser Phe Ser Pro Gly Gly Leu Ala Pro
305                 310                 315                 320

Glu Ile Ser Pro Leu Glu Val Leu Glu Arg Asp Lys Val Thr Gln Leu
                325                 330                 335

Leu Leu Gln Gln Asp Lys Val Pro Glu Pro Ala Ser Leu Ser Ser Asn
            340                 345                 350

His Ser Leu Thr Ser Cys Phe Thr Asn Gln Gly Tyr Phe Phe Phe His
        355                 360                 365

Leu Pro Asp Ala Leu Glu Ile Glu Ala Cys Gln Val Tyr Phe Thr Tyr
    370                 375                 380

Asp Pro Tyr Ser Glu Glu Asp Pro Asp Glu Gly Val Ala Gly Ala Pro
385                 390                 395                 400

Thr Gly Ser Ser Pro Gln Pro Leu Gln Pro Leu Ser Gly Glu Asp Asp
                405                 410                 415

Ala Tyr Cys Thr Phe Pro Ser Arg Asp Asp Leu Leu Leu Phe Ser Pro
            420                 425                 430

Ser Leu Leu Gly Gly Pro Ser Pro Pro Ser Thr Ala Pro Gly Gly Ser
        435                 440                 445

Gly Ala Gly Glu Glu Arg Met Pro Pro Ser Leu Gln Glu Arg Val Pro
    450                 455                 460
```

```
Arg Asp Trp Asp Pro Gln Pro Leu Gly Pro Pro Thr Pro Gly Val Pro
465                 470                 475                 480

Asp Leu Val Asp Phe Gln Pro Pro Pro Glu Leu Val Leu Arg Glu Ala
                485                 490                 495

Gly Glu Glu Val Pro Asp Ala Gly Pro Arg Glu Gly Val Ser Phe Pro
            500                 505                 510

Trp Ser Arg Pro Pro Gly Gln Gly Glu Phe Arg Ala Leu Asn Ala Arg
        515                 520                 525

Leu Pro Leu Asn Thr Asp Ala Tyr Leu Ser Leu Gln Glu Leu Gln Gly
    530                 535                 540

Gln Asp Pro Thr His Leu Val
545                 550


<210>  306
<211>  369
<212>  PRT
<213>  Homo sapiens

<400>  306

Met Leu Lys Pro Ser Leu Pro Phe Thr Ser Leu Leu Phe Leu Gln Leu
1               5                   10                  15

Pro Leu Leu Gly Val Gly Leu Asn Thr Thr Ile Leu Thr Pro Asn Gly
            20                  25                  30

Asn Glu Asp Thr Thr Ala Asp Phe Phe Leu Thr Thr Met Pro Thr Asp
        35                  40                  45

Ser Leu Ser Val Ser Thr Leu Pro Leu Pro Glu Val Gln Cys Phe Val
    50                  55                  60

Phe Asn Val Glu Tyr Met Asn Cys Thr Trp Asn Ser Ser Ser Glu Pro
65                  70                  75                  80

Gln Pro Thr Asn Leu Thr Leu His Tyr Trp Tyr Lys Asn Ser Asp Asn
                85                  90                  95

Asp Lys Val Gln Lys Cys Ser His Tyr Leu Phe Ser Glu Glu Ile Thr
            100                 105                 110

Ser Gly Cys Gln Leu Gln Lys Lys Glu Ile His Leu Tyr Gln Thr Phe
        115                 120                 125

Val Val Gln Leu Gln Asp Pro Arg Glu Pro Arg Arg Gln Ala Thr Gln
    130                 135                 140
```

```
Met Leu Lys Leu Gln Asn Leu Val Ile Pro Trp Ala Pro Glu Asn Leu
145                 150                 155                 160

Thr Leu His Lys Leu Ser Glu Ser Gln Leu Glu Leu Asn Trp Asn Asn
                165                 170                 175

Arg Phe Leu Asn His Cys Leu Glu His Leu Val Gln Tyr Arg Thr Asp
            180                 185                 190

Trp Asp His Ser Trp Thr Glu Gln Ser Val Asp Tyr Arg His Lys Phe
        195                 200                 205

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

Ser Arg Phe Asn Pro Leu Cys Gly Ser Ala Gln His Trp Ser Glu Trp
225                 230                 235                 240

Ser His Pro Ile His Trp Gly Ser Asn Thr Ser Lys Glu Asn Pro Phe
                245                 250                 255

Leu Phe Ala Leu Glu Ala Val Val Ile Ser Val Gly Ser Met Gly Leu
            260                 265                 270

Ile Ile Ser Leu Leu Cys Val Tyr Phe Trp Leu Glu Arg Thr Met Pro
        275                 280                 285

Arg Ile Pro Thr Leu Lys Asn Leu Glu Asp Leu Val Thr Glu Tyr His
    290                 295                 300

Gly Asn Phe Ser Ala Trp Ser Gly Val Ser Lys Gly Leu Ala Glu Ser
305                 310                 315                 320

Leu Gln Pro Asp Tyr Ser Glu Arg Leu Cys Leu Val Ser Glu Ile Pro
                325                 330                 335

Pro Lys Gly Gly Ala Leu Gly Glu Gly Pro Gly Ala Ser Pro Cys Asn
            340                 345                 350

Gln His Ser Pro Tyr Trp Ala Pro Pro Cys Tyr Thr Leu Lys Pro Glu
        355                 360                 365

Thr
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<210> 307
<211> 825
<212> PRT
<213> Homo sapiens

<400> 307

```
Met Gly Trp Leu Cys Ser Gly Leu Leu Phe Pro Val Ser Cys Leu Val
```

1 5 10 15

Leu Leu Gln Val Ala Ser Ser Gly Asn Met Lys Val Leu Gln Glu Pro
20 25 30

Thr Cys Val Ser Asp Tyr Met Ser Ile Ser Thr Cys Glu Trp Lys Met
35 40 45

Asn Gly Pro Thr Asn Cys Ser Thr Glu Leu Arg Leu Leu Tyr Gln Leu
50 55 60

Val Phe Leu Leu Ser Glu Ala His Thr Cys Ile Pro Glu Asn Asn Gly
65 70 75 80

Gly Ala Gly Cys Val Cys His Leu Leu Met Asp Asp Val Val Ser Ala
85 90 95

Asp Asn Tyr Thr Leu Asp Leu Trp Ala Gly Gln Gln Leu Leu Trp Lys
100 105 110

Gly Ser Phe Lys Pro Ser Glu His Val Lys Pro Arg Ala Pro Gly Asn
115 120 125

Leu Thr Val His Thr Asn Val Ser Asp Thr Leu Leu Leu Thr Trp Ser
130 135 140

Asn Pro Tyr Pro Pro Asp Asn Tyr Leu Tyr Asn His Leu Thr Tyr Ala
145 150 155 160

Val Asn Ile Trp Ser Glu Asn Asp Pro Ala Asp Phe Arg Ile Tyr Asn
165 170 175

Val Thr Tyr Leu Glu Pro Ser Leu Arg Ile Ala Ala Ser Thr Leu Lys
180 185 190

Ser Gly Ile Ser Tyr Arg Ala Arg Val Arg Ala Trp Ala Gln Cys Tyr
195 200 205

Asn Thr Thr Trp Ser Glu Trp Ser Pro Ser Thr Lys Trp His Asn Ser
210 215 220

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

Cys Ile Val Ile Leu Ala Val Cys Leu Leu Cys Tyr Val Ser Ile Thr
245 250 255

Lys Ile Lys Lys Glu Trp Trp Asp Gln Ile Pro Asn Pro Ala Arg Ser
260 265 270

Arg Leu Val Ala Ile Ile Ile Gln Asp Ala Gln Gly Ser Gln Trp Glu

275 280 285

Lys Arg Ser Arg Gly Gln Glu Pro Ala Lys Cys Pro His Trp Lys Asn
290 295 300

Cys Leu Thr Lys Leu Leu Pro Cys Phe Leu Glu His Asn Met Lys Arg
305 310 315 320

Asp Glu Asp Pro His Lys Ala Ala Lys Glu Met Pro Phe Gln Gly Ser
325 330 335

Gly Lys Ser Ala Trp Cys Pro Val Glu Ile Ser Lys Thr Val Leu Trp
340 345 350

Pro Glu Ser Ile Ser Val Val Arg Cys Val Glu Leu Phe Glu Ala Pro
355 360 365

Val Glu Cys Glu Glu Glu Glu Glu Val Glu Glu Glu Lys Gly Ser Phe
370 375 380

Cys Ala Ser Pro Glu Ser Ser Arg Asp Asp Phe Gln Glu Gly Arg Glu
385 390 395 400

Gly Ile Val Ala Arg Leu Thr Glu Ser Leu Phe Leu Asp Leu Leu Gly
405 410 415

Glu Glu Asn Gly Gly Phe Cys Gln Gln Asp Met Gly Glu Ser Cys Leu
420 425 430

Leu Pro Pro Ser Gly Ser Thr Ser Ala His Met Pro Trp Asp Glu Phe
435 440 445

Pro Ser Ala Gly Pro Lys Glu Ala Pro Pro Trp Gly Lys Glu Gln Pro
450 455 460

Leu His Leu Glu Pro Ser Pro Pro Ala Ser Pro Thr Gln Ser Pro Asp
465 470 475 480

Asn Leu Thr Cys Thr Glu Thr Pro Leu Val Ile Ala Gly Asn Pro Ala
485 490 495

Tyr Arg Ser Phe Ser Asn Ser Leu Ser Gln Ser Pro Cys Pro Arg Glu
500 505 510

Leu Gly Pro Asp Pro Leu Leu Ala Arg His Leu Glu Glu Val Glu Pro
515 520 525

Glu Met Pro Cys Val Pro Gln Leu Ser Glu Pro Thr Thr Val Pro Gln
530 535 540

Pro Glu Pro Glu Thr Trp Glu Gln Ile Leu Arg Arg Asn Val Leu Gln

545 550 555 560

His Gly Ala Ala Ala Ala Pro Val Ser Ala Pro Thr Ser Gly Tyr Gln
565 570 575

Glu Phe Val His Ala Val Glu Gln Gly Gly Thr Gln Ala Ser Ala Val
580 585 590

Val Gly Leu Gly Pro Pro Gly Glu Ala Gly Tyr Lys Ala Phe Ser Ser
595 600 605

Leu Leu Ala Ser Ser Ala Val Ser Pro Glu Lys Cys Gly Phe Gly Ala
610 615 620

Ser Ser Gly Glu Glu Gly Tyr Lys Pro Phe Gln Asp Leu Ile Pro Gly
625 630 635 640

Cys Pro Gly Asp Pro Ala Pro Val Pro Val Pro Leu Phe Thr Phe Gly
645 650 655

Leu Asp Arg Glu Pro Pro Arg Ser Pro Gln Ser Ser His Leu Pro Ser
660 665 670

Ser Ser Pro Glu His Leu Gly Leu Glu Pro Gly Glu Lys Val Glu Asp
675 680 685

Met Pro Lys Pro Pro Leu Pro Gln Glu Gln Ala Thr Asp Pro Leu Val
690 695 700

Asp Ser Leu Gly Ser Gly Ile Val Tyr Ser Ala Leu Thr Cys His Leu
705 710 715 720

Cys Gly His Leu Lys Gln Cys His Gly Gln Glu Asp Gly Gly Gln Thr
725 730 735

Pro Val Met Ala Ser Pro Cys Cys Gly Cys Cys Cys Gly Asp Arg Ser
740 745 750

Ser Pro Pro Thr Thr Pro Leu Arg Ala Pro Asp Pro Ser Pro Gly Gly
755 760 765

Val Pro Leu Glu Ala Ser Leu Cys Pro Ala Ser Leu Ala Pro Ser Gly
770 775 780

Ile Ser Glu Lys Ser Lys Ser Ser Ser Ser Phe His Pro Ala Pro Gly
785 790 795 800

Asn Ala Gln Ser Ser Ser Gln Thr Pro Lys Ile Val Asn Phe Val Ser
805 810 815

Val Gly Pro Thr Tyr Met Arg Val Ser

820 825

<210> 308
<211> 459
<212> PRT
<213> Homo sapiens

<400> 308

Met Thr Ile Leu Gly Thr Thr Phe Gly Met Val Phe Ser Leu Leu Gln
1 5 10 15

Val Val Ser Gly Glu Ser Gly Tyr Ala Gln Asn Gly Asp Leu Glu Asp
20 25 30

Ala Glu Leu Asp Asp Tyr Ser Phe Ser Cys Tyr Ser Gln Leu Glu Val
35 40 45

Asn Gly Ser Gln His Ser Leu Thr Cys Ala Phe Glu Asp Pro Asp Val
50 55 60

Asn Ile Thr Asn Leu Glu Phe Glu Ile Cys Gly Ala Leu Val Glu Val
65 70 75 80

Lys Cys Leu Asn Phe Arg Lys Leu Gln Glu Ile Tyr Phe Ile Glu Thr
85 90 95

Lys Lys Phe Leu Leu Ile Gly Lys Ser Asn Ile Cys Val Lys Val Gly
100 105 110

Glu Lys Ser Leu Thr Cys Lys Lys Ile Asp Leu Thr Thr Ile Val Lys
115 120 125

Pro Glu Ala Pro Phe Asp Leu Ser Val Val Tyr Arg Glu Gly Ala Asn
130 135 140

Asp Phe Val Val Thr Phe Asn Thr Ser His Leu Gln Lys Lys Tyr Val
145 150 155 160

Lys Val Leu Met His Asp Val Ala Tyr Arg Gln Glu Lys Asp Glu Asn
165 170 175

Lys Trp Thr His Val Asn Leu Ser Ser Thr Lys Leu Thr Leu Leu Gln
180 185 190

Arg Lys Leu Gln Pro Ala Ala Met Tyr Glu Ile Lys Val Arg Ser Ile
195 200 205

Pro Asp His Tyr Phe Lys Gly Phe Trp Ser Glu Trp Ser Pro Ser Tyr
210 215 220

Tyr Phe Arg Thr Pro Glu Ile Asn Asn Ser Ser Gly Glu Met Asp Pro
225 230 235 240

```
Ile Leu Leu Thr Ile Ser Ile Leu Ser Phe Phe Ser Val Ala Leu Leu
                245                 250                 255

Val Ile Leu Ala Cys Val Leu Trp Lys Lys Arg Ile Lys Pro Ile Val
            260                 265                 270

Trp Pro Ser Leu Pro Asp His Lys Lys Thr Leu Glu His Leu Cys Lys
        275                 280                 285

Lys Pro Arg Lys Asn Leu Asn Val Ser Phe Asn Pro Glu Ser Phe Leu
    290                 295                 300

Asp Cys Gln Ile His Arg Val Asp Asp Ile Gln Ala Arg Asp Glu Val
305                 310                 315                 320

Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu
                325                 330                 335

Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu
            340                 345                 350

Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr
        355                 360                 365

Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser
    370                 375                 380

Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val
385                 390                 395                 400

Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro
                405                 410                 415

Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala
            420                 425                 430

Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala
        435                 440                 445

Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln
    450                 455


<210>  309
<211>  521
<212>  PRT
<213>  Homo sapiens

<400>  309

Met Gly Leu Gly Arg Cys Ile Trp Glu Gly Trp Thr Leu Glu Ser Glu
1               5                   10                  15
```

```
Ala Leu Arg Arg Asp Met Gly Thr Trp Leu Leu Ala Cys Ile Cys Ile
            20                  25                  30

Cys Thr Cys Val Cys Leu Gly Val Ser Val Thr Gly Glu Gly Gln Gly
        35                  40                  45

Pro Arg Ser Arg Thr Phe Thr Cys Leu Thr Asn Asn Ile Leu Arg Ile
    50                  55                  60

Asp Cys His Trp Ser Ala Pro Glu Leu Gly Gln Gly Ser Ser Pro Trp
65                  70                  75                  80

Leu Leu Phe Thr Ser Asn Gln Ala Pro Gly Gly Thr His Lys Cys Ile
                85                  90                  95

Leu Arg Gly Ser Glu Cys Thr Val Val Leu Pro Pro Glu Ala Val Leu
            100                 105                 110

Val Pro Ser Asp Asn Phe Thr Ile Thr Phe His His Cys Met Ser Gly
        115                 120                 125

Arg Glu Gln Val Ser Leu Val Asp Pro Glu Tyr Leu Pro Arg Arg His
    130                 135                 140

Val Lys Leu Asp Pro Pro Ser Asp Leu Gln Ser Asn Ile Ser Ser Gly
145                 150                 155                 160

His Cys Ile Leu Thr Trp Ser Ile Ser Pro Ala Leu Glu Pro Met Thr
                165                 170                 175

Thr Leu Leu Ser Tyr Glu Leu Ala Phe Lys Lys Gln Glu Glu Ala Trp
            180                 185                 190

Glu Gln Ala Gln His Arg Asp His Ile Val Gly Val Thr Trp Leu Ile
        195                 200                 205

Leu Glu Ala Phe Glu Leu Asp Pro Gly Phe Ile His Glu Ala Arg Leu
    210                 215                 220

Arg Val Gln Met Ala Thr Leu Glu Asp Asp Val Val Glu Glu Glu Arg
225                 230                 235                 240

Tyr Thr Gly Gln Trp Ser Glu Trp Ser Gln Pro Val Cys Phe Gln Ala
                245                 250                 255

Pro Gln Arg Gln Gly Pro Leu Ile Pro Pro Trp Gly Trp Pro Gly Asn
            260                 265                 270

Thr Leu Val Ala Val Ser Ile Phe Leu Leu Leu Thr Gly Pro Thr Tyr
        275                 280                 285
```

```
Leu Leu Phe Lys Leu Ser Pro Arg Val Lys Arg Ile Phe Tyr Gln Asn
    290                 295                 300

Val Pro Ser Pro Ala Met Phe Phe Gln Pro Leu Tyr Ser Val His Asn
305                 310                 315                 320

Gly Asn Phe Gln Thr Trp Met Gly Ala His Gly Ala Gly Val Leu Leu
                325                 330                 335

Ser Gln Asp Cys Ala Gly Thr Pro Gln Gly Ala Leu Glu Pro Cys Val
            340                 345                 350

Gln Glu Ala Thr Ala Leu Leu Thr Cys Gly Pro Ala Arg Pro Trp Lys
        355                 360                 365

Ser Val Ala Leu Glu Glu Glu Gln Glu Gly Pro Gly Thr Arg Leu Pro
    370                 375                 380

Gly Asn Leu Ser Ser Glu Asp Val Leu Pro Ala Gly Cys Thr Glu Trp
385                 390                 395                 400

Arg Val Gln Thr Leu Ala Tyr Leu Pro Gln Glu Asp Trp Ala Pro Thr
                405                 410                 415

Ser Leu Thr Arg Pro Ala Pro Pro Asp Ser Glu Gly Ser Arg Ser Ser
            420                 425                 430

Ser Ser Ser Ser Ser Ser Asn Asn Asn Asn Tyr Cys Ala Leu Gly Cys
        435                 440                 445

Tyr Gly Gly Trp His Leu Ser Ala Leu Pro Gly Asn Thr Gln Ser Ser
    450                 455                 460

Gly Pro Ile Pro Ala Leu Ala Cys Gly Leu Ser Cys Asp His Gln Gly
465                 470                 475                 480

Leu Glu Thr Gln Gln Gly Val Ala Trp Val Leu Ala Gly His Cys Gln
                485                 490                 495

Arg Pro Gly Leu His Glu Asp Leu Gln Gly Met Leu Leu Pro Ser Val
            500                 505                 510

Leu Ser Lys Ala Arg Ser Trp Thr Phe
        515                 520
```

<210> 310
<211> 427
<212> PRT
<213> Homo sapiens

<400> 310

```
Met Glu Trp Pro Ala Arg Leu Cys Gly Leu Trp Ala Leu Leu Leu Cys
1               5                  10                  15

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

Pro Pro Val Thr Asn Leu Ser Val Ser Val Glu Asn Leu Cys Thr Val
        35                  40                  45

Ile Trp Thr Trp Asn Pro Pro Glu Gly Ala Ser Ser Asn Cys Ser Leu
    50                  55                  60

Trp Tyr Phe Ser His Phe Gly Asp Lys Gln Asp Lys Lys Ile Ala Pro
65                  70                  75                  80

Glu Thr Arg Arg Ser Ile Glu Val Pro Leu Asn Glu Arg Ile Cys Leu
                85                  90                  95

Gln Val Gly Ser Gln Cys Ser Thr Asn Glu Ser Glu Lys Pro Ser Ile
            100                 105                 110

Leu Val Glu Lys Cys Ile Ser Pro Pro Glu Gly Asp Pro Glu Ser Ala
        115                 120                 125

Val Thr Glu Leu Gln Cys Ile Trp His Asn Leu Ser Tyr Met Lys Cys
    130                 135                 140

Ser Trp Leu Pro Gly Arg Asn Thr Ser Pro Asp Thr Asn Tyr Thr Leu
145                 150                 155                 160

Tyr Tyr Trp His Arg Ser Leu Glu Lys Ile His Gln Cys Glu Asn Ile
                165                 170                 175

Phe Arg Glu Gly Gln Tyr Phe Gly Cys Ser Phe Asp Leu Thr Lys Val
            180                 185                 190

Lys Asp Ser Ser Phe Glu Gln His Ser Val Gln Ile Met Val Lys Asp
        195                 200                 205

Asn Ala Gly Lys Ile Lys Pro Ser Phe Asn Ile Val Pro Leu Thr Ser
    210                 215                 220

Arg Val Lys Pro Asp Pro Pro His Ile Lys Asn Leu Ser Phe His Asn
225                 230                 235                 240

Asp Asp Leu Tyr Val Gln Trp Glu Asn Pro Gln Asn Phe Ile Ser Arg
                245                 250                 255

Cys Leu Phe Tyr Glu Val Glu Val Asn Asn Ser Gln Thr Glu Thr His
            260                 265                 270
```

```
Asn Val Phe Tyr Val Gln Glu Ala Lys Cys Glu Asn Pro Glu Phe Glu
        275                 280                 285

Arg Asn Val Glu Asn Thr Ser Cys Phe Met Val Pro Gly Val Leu Pro
    290                 295                 300

Asp Thr Leu Asn Thr Val Arg Ile Arg Val Lys Thr Asn Lys Leu Cys
305                 310                 315                 320

Tyr Glu Asp Asp Lys Leu Trp Ser Asn Trp Ser Gln Glu Met Ser Ile
                325                 330                 335

Gly Lys Lys Arg Asn Ser Thr Leu Tyr Ile Thr Met Leu Leu Ile Val
            340                 345                 350

Pro Val Ile Val Ala Gly Ala Ile Ile Val Leu Leu Leu Tyr Leu Lys
        355                 360                 365

Arg Leu Lys Ile Ile Ile Phe Pro Pro Ile Pro Asp Pro Gly Lys Ile
    370                 375                 380

Phe Lys Glu Met Phe Gly Asp Gln Asn Asp Asp Thr Leu His Trp Lys
385                 390                 395                 400

Lys Tyr Asp Ile Tyr Glu Lys Gln Thr Lys Glu Glu Thr Asp Ser Val
                405                 410                 415

Val Leu Ile Glu Asn Leu Lys Lys Ala Ser Gln
            420                 425


<210>  311
<211>  231
<212>  PRT
<213>  Homo sapiens

<400>  311

Met Ser Val Glu His Ala Asp Ile Trp Val Lys Ser Tyr Ser Leu Tyr
1               5                   10                  15

Ser Arg Glu Arg Tyr Ile Cys Asn Ser Gly Phe Lys Arg Lys Ala Gly
            20                  25                  30

Thr Ser Ser Leu Thr Glu Cys Val Leu Asn Lys Ala Thr Asn Val Ala
        35                  40                  45

His Trp Thr Thr Pro Ser Leu Lys Cys Ile Arg Asp Pro Ala Leu Val
    50                  55                  60

His Gln Arg Pro Ala Pro Pro Ser Thr Val Thr Thr Ala Gly Val Thr
65                  70                  75                  80

Pro Gln Pro Glu Ser Leu Ser Pro Ser Gly Lys Glu Pro Ala Ala Ser
```

85 90 95

Ser Pro Ser Ser Asn Asn Thr Ala Ala Thr Thr Ala Ala Ile Val Pro
100 105 110

Gly Ser Gln Leu Met Pro Ser Lys Ser Pro Ser Thr Gly Thr Thr Glu
115 120 125

Ile Ser Ser His Glu Ser Ser His Gly Thr Pro Ser Gln Thr Thr Ala
130 135 140

Lys Asn Trp Glu Leu Thr Ala Ser Ala Ser His Gln Pro Pro Gly Val
145 150 155 160

Tyr Pro Gln Gly His Ser Asp Thr Thr Val Ala Ile Ser Thr Ser Thr
165 170 175

Val Leu Leu Cys Gly Leu Ser Ala Val Ser Leu Leu Ala Cys Tyr Leu
180 185 190

Lys Ser Arg Gln Thr Pro Pro Leu Ala Ser Val Glu Met Glu Ala Met
195 200 205

Glu Ala Leu Pro Val Thr Trp Gly Thr Ser Ser Arg Asp Glu Asp Leu
210 215 220

Glu Asn Cys Ser His His Leu
225 230

<210> 312
<211> 538
<212> PRT
<213> Homo sapiens

<400> 312

Met Pro Arg Gly Trp Ala Ala Pro Leu Leu Leu Leu Leu Leu Gln Gly
1 5 10 15

Gly Trp Gly Cys Pro Asp Leu Val Cys Tyr Thr Asp Tyr Leu Gln Thr
20 25 30

Val Ile Cys Ile Leu Glu Met Trp Asn Leu His Pro Ser Thr Leu Thr
35 40 45

Leu Thr Trp Gln Asp Gln Tyr Glu Glu Leu Lys Asp Glu Ala Thr Ser
50 55 60

Cys Ser Leu His Arg Ser Ala His Asn Ala Thr His Ala Thr Tyr Thr
65 70 75 80

Cys His Met Asp Val Phe His Phe Met Ala Asp Asp Ile Phe Ser Val
85 90 95

```
Asn Ile Thr Asp Gln Ser Gly Asn Tyr Ser Gln Glu Cys Gly Ser Phe
            100                 105                 110

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

Thr Phe Ser Gly Gln Tyr Asn Ile Ser Trp Arg Ser Asp Tyr Glu Asp
    130                 135                 140

Pro Ala Phe Tyr Met Leu Lys Gly Lys Leu Gln Tyr Glu Leu Gln Tyr
145                 150                 155                 160

Arg Asn Arg Gly Asp Pro Trp Ala Val Ser Pro Arg Arg Lys Leu Ile
                165                 170                 175

Ser Val Asp Ser Arg Ser Val Ser Leu Leu Pro Leu Glu Phe Arg Lys
            180                 185                 190

Asp Ser Ser Tyr Glu Leu Gln Val Arg Ala Gly Pro Met Pro Gly Ser
        195                 200                 205

Ser Tyr Gln Gly Thr Trp Ser Glu Trp Ser Asp Pro Val Ile Phe Gln
    210                 215                 220

Thr Gln Ser Glu Glu Leu Lys Glu Gly Trp Asn Pro His Leu Leu Leu
225                 230                 235                 240

Leu Leu Leu Leu Val Ile Val Phe Ile Pro Ala Phe Trp Ser Leu Lys
                245                 250                 255

Thr His Pro Leu Trp Arg Leu Trp Lys Lys Ile Trp Ala Val Pro Ser
            260                 265                 270

Pro Glu Arg Phe Phe Met Pro Leu Tyr Lys Gly Cys Ser Gly Asp Phe
        275                 280                 285

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

Pro Trp Ser Pro Glu Val Pro Ser Thr Leu Glu Val Tyr Ser Cys His
305                 310                 315                 320

Pro Pro Arg Ser Pro Ala Lys Arg Leu Gln Leu Thr Glu Leu Gln Glu
                325                 330                 335

Pro Ala Glu Leu Val Glu Ser Asp Gly Val Pro Lys Pro Ser Phe Trp
            340                 345                 350

Pro Thr Ala Gln Asn Ser Gly Gly Ser Ala Tyr Ser Glu Glu Arg Asp
        355                 360                 365
```

```
Arg Pro Tyr Gly Leu Val Ser Ile Asp Thr Val Thr Val Leu Asp Ala
    370                 375                 380

Glu Gly Pro Cys Thr Trp Pro Cys Ser Cys Glu Asp Asp Gly Tyr Pro
385                 390                 395                 400

Ala Leu Asp Leu Asp Ala Gly Leu Glu Pro Ser Pro Gly Leu Glu Asp
                405                 410                 415

Pro Leu Leu Asp Ala Gly Thr Thr Val Leu Ser Cys Gly Cys Val Ser
            420                 425                 430

Ala Gly Ser Pro Gly Leu Gly Gly Pro Leu Gly Ser Leu Leu Asp Arg
        435                 440                 445

Leu Lys Pro Pro Leu Ala Asp Gly Glu Asp Trp Ala Gly Gly Leu Pro
    450                 455                 460

Trp Gly Gly Arg Ser Pro Gly Gly Val Ser Glu Ser Glu Ala Gly Ser
465                 470                 475                 480

Pro Leu Ala Gly Leu Asp Met Asp Thr Phe Asp Ser Gly Phe Val Gly
                485                 490                 495

Ser Asp Cys Ser Ser Pro Val Glu Cys Asp Phe Thr Ser Pro Gly Asp
            500                 505                 510

Glu Gly Pro Pro Arg Ser Tyr Leu Arg Gln Trp Val Val Ile Pro Pro
        515                 520                 525

Pro Leu Ser Ser Pro Gly Pro Gln Ala Ser
    530                 535


<210>  313
<211>  259
<212>  PRT
<213>  Homo sapiens

<400>  313

Met Val Tyr Tyr Leu Lys Pro Ser Ser Pro Lys His Val Arg Phe Ser
1               5                   10                  15

Trp His Gln Asp Ala Val Thr Val Thr Cys Ser Asp Leu Ser Tyr Gly
            20                  25                  30

Asp Leu Leu Tyr Glu Val Gln Tyr Arg Ser Pro Phe Asp Thr Glu Trp
        35                  40                  45

Gln Ser Lys Gln Glu Asn Thr Cys Asn Val Thr Ile Glu Gly Leu Asp
    50                  55                  60
```

```
Ala Glu Lys Cys Tyr Ser Phe Trp Val Arg Val Lys Ala Met Glu Asp
65                  70                  75                  80

Val Tyr Gly Pro Asp Thr Tyr Pro Ser Asp Trp Ser Glu Val Thr Cys
                85                  90                  95

Trp Gln Arg Gly Glu Ile Arg Asp Ala Cys Ala Glu Thr Pro Thr Pro
            100                 105                 110

Pro Lys Pro Lys Leu Ser Lys Phe Ile Leu Ile Ser Ser Leu Ala Ile
        115                 120                 125

Leu Leu Met Val Ser Leu Leu Leu Leu Ser Leu Trp Lys Leu Trp Arg
    130                 135                 140

Val Lys Lys Phe Leu Ile Pro Ser Val Pro Asp Pro Lys Ser Ile Phe
145                 150                 155                 160

Pro Gly Leu Phe Glu Ile His Gln Gly Asn Phe Gln Glu Trp Ile Thr
                165                 170                 175

Asp Thr Gln Asn Val Ala His Leu His Lys Met Ala Gly Ala Glu Gln
            180                 185                 190

Glu Ser Gly Pro Glu Glu Pro Leu Val Val Gln Leu Ala Lys Thr Glu
        195                 200                 205

Ala Glu Ser Pro Arg Met Leu Asp Pro Gln Thr Glu Glu Lys Glu Ala
    210                 215                 220

Ser Gly Gly Ser Leu Gln Leu Pro His Gln Pro Leu Gln Gly Gly Asp
225                 230                 235                 240

Val Val Thr Ile Gly Gly Phe Thr Phe Val Met Asn Asp Arg Ser Tyr
                245                 250                 255

Val Ala Leu
```

<210> 314
<211> 300
<212> PRT
<213> Homo sapiens

<400> 314

```
Met Val Leu Leu Trp Leu Thr Leu Leu Leu Ile Ala Leu Pro Cys Leu
1               5                   10                  15

Leu Gln Thr Lys Glu Gly Gly Lys Pro Trp Ala Gly Ala Glu Asn Leu
            20                  25                  30
```

```
Thr Cys Trp Ile His Asp Val Asp Phe Leu Ser Cys Ser Trp Ala Val
        35                  40                  45

Gly Pro Gly Ala Pro Ala Asp Val Gln Tyr Asp Leu Tyr Leu Asn Val
    50                  55                  60

Ala Asn Arg Arg Gln Gln Tyr Glu Cys Leu His Tyr Lys Thr Asp Ala
65                  70                  75                  80

Gln Gly Thr Arg Ile Gly Cys Arg Phe Asp Asp Ile Ser Arg Leu Ser
                85                  90                  95

Ser Gly Ser Gln Ser Ser His Ile Leu Val Arg Gly Arg Ser Ala Ala
            100                 105                 110

Phe Gly Ile Pro Cys Thr Asp Lys Phe Val Val Phe Ser Gln Ile Glu
        115                 120                 125

Ile Leu Thr Pro Pro Asn Met Thr Ala Lys Cys Asn Lys Thr His Ser
    130                 135                 140

Phe Met His Trp Lys Met Arg Ser His Phe Asn Arg Lys Phe Arg Tyr
145                 150                 155                 160

Glu Leu Gln Ile Gln Lys Arg Met Gln Pro Val Ile Thr Glu Gln Val
                165                 170                 175

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

Gln Ile Arg Ala Arg Glu Arg Val Tyr Glu Phe Leu Ser Ala Trp Ser
        195                 200                 205

Thr Pro Gln Arg Phe Glu Cys Asp Gln Glu Glu Gly Ala Asn Thr Arg
    210                 215                 220

Ala Trp Arg Thr Ser Leu Leu Ile Ala Leu Gly Thr Leu Leu Ala Leu
225                 230                 235                 240

Val Cys Val Phe Val Ile Cys Arg Arg Tyr Leu Val Met Gln Arg Leu
                245                 250                 255

Phe Pro Arg Ile Pro His Met Lys Asp Pro Ile Gly Asp Ser Phe Gln
            260                 265                 270

Asn Asp Lys Leu Val Val Trp Glu Ala Gly Lys Ala Gly Leu Glu Glu
        275                 280                 285

Cys Leu Val Thr Glu Val Gln Val Val Gln Lys Thr
    290                 295                 300
```

<210> 315
<211> 420
<212> PRT
<213> Homo sapiens

<400> 315

Met Ile Ile Val Ala His Val Leu Leu Ile Leu Leu Gly Ala Thr Glu
1 5 10 15

Ile Leu Gln Ala Asp Leu Leu Pro Asp Glu Lys Ile Ser Leu Leu Pro
20 25 30

Pro Val Asn Phe Thr Ile Lys Val Thr Gly Leu Ala Gln Val Leu Leu
35 40 45

Gln Trp Lys Pro Asn Pro Asp Gln Glu Gln Arg Asn Val Asn Leu Glu
50 55 60

Tyr Gln Val Lys Ile Asn Ala Pro Lys Glu Asp Asp Tyr Glu Thr Arg
65 70 75 80

Ile Thr Glu Ser Lys Cys Val Thr Ile Leu His Lys Gly Phe Ser Ala
85 90 95

Ser Val Arg Thr Ile Leu Gln Asn Asp His Ser Leu Leu Ala Ser Ser
100 105 110

Trp Ala Ser Ala Glu Leu His Ala Pro Pro Gly Ser Pro Gly Thr Ser
115 120 125

Ile Val Asn Leu Thr Cys Thr Thr Asn Thr Thr Glu Asp Asn Tyr Ser
130 135 140

Arg Leu Arg Ser Tyr Gln Val Ser Leu His Cys Thr Trp Leu Val Gly
145 150 155 160

Thr Asp Ala Pro Glu Asp Thr Gln Tyr Phe Leu Tyr Tyr Arg Tyr Gly
165 170 175

Ser Trp Thr Glu Glu Cys Gln Glu Tyr Ser Lys Asp Thr Leu Gly Arg
180 185 190

Asn Ile Ala Cys Trp Phe Pro Arg Thr Phe Ile Leu Ser Lys Gly Arg
195 200 205

Asp Trp Leu Ala Val Leu Val Asn Gly Ser Ser Lys His Ser Ala Ile
210 215 220

Arg Pro Phe Asp Gln Leu Phe Ala Leu His Ala Ile Asp Gln Ile Asn
225 230 235 240

Pro Pro Leu Asn Val Thr Ala Glu Ile Glu Gly Thr Arg Leu Ser Ile

245 250 255

Gln Trp Glu Lys Pro Val Ser Ala Phe Pro Ile His Cys Phe Asp Tyr
260 265 270

Glu Val Lys Ile His Asn Thr Arg Asn Gly Tyr Leu Gln Ile Glu Lys
275 280 285

Leu Met Thr Asn Ala Phe Ile Ser Ile Ile Asp Asp Leu Ser Lys Tyr
290 295 300

Asp Val Gln Val Arg Ala Ala Val Ser Ser Met Cys Arg Glu Ala Gly
305 310 315 320

Leu Trp Ser Glu Trp Ser Gln Pro Ile Tyr Val Gly Asn Asp Glu His
325 330 335

Lys Pro Leu Arg Glu Trp Phe Val Ile Val Ile Met Ala Thr Ile Cys
340 345 350

Phe Ile Leu Leu Ile Leu Ser Leu Ile Cys Lys Ile Cys His Leu Trp
355 360 365

Ile Lys Leu Phe Pro Pro Ile Pro Ala Pro Lys Ser Asn Ile Lys Asp
370 375 380

Leu Phe Val Thr Thr Asn Tyr Glu Lys Ala Gly Ser Ser Glu Thr Glu
385 390 395 400

Ile Glu Val Ile Cys Tyr Ile Glu Lys Pro Gly Val Glu Thr Leu Glu
405 410 415

Asp Ser Val Phe
420

<210> 316
<211> 400
<212> PRT
<213> Homo sapiens

<400> 316

Met Leu Leu Leu Val Thr Ser Leu Leu Leu Cys Glu Leu Pro His Pro
1 5 10 15

Ala Phe Leu Leu Ile Pro Glu Lys Ser Asp Leu Arg Thr Val Ala Pro
20 25 30

Ala Ser Ser Leu Asn Val Arg Phe Asp Ser Arg Thr Met Asn Leu Ser
35 40 45

Trp Asp Cys Gln Glu Asn Thr Thr Phe Ser Lys Cys Phe Leu Thr Asp
50 55 60

```
Lys Lys Asn Arg Val Val Glu Pro Arg Leu Ser Asn Asn Glu Cys Ser
65                  70                  75                  80

Cys Thr Phe Arg Glu Ile Cys Leu His Glu Gly Val Thr Phe Glu Val
                85                  90                  95

His Val Asn Thr Ser Gln Arg Gly Phe Gln Gln Lys Leu Leu Tyr Pro
            100                 105                 110

Asn Ser Gly Arg Glu Gly Thr Ala Ala Gln Asn Phe Ser Cys Phe Ile
        115                 120                 125

Tyr Asn Ala Asp Leu Met Asn Cys Thr Trp Ala Arg Gly Pro Thr Ala
    130                 135                 140

Pro Arg Asp Val Gln Tyr Phe Leu Tyr Ile Arg Asn Ser Lys Arg Arg
145                 150                 155                 160

Arg Glu Ile Arg Cys Pro Tyr Tyr Ile Gln Asp Ser Gly Thr His Val
                165                 170                 175

Gly Cys His Leu Asp Asn Leu Ser Gly Leu Thr Ser Arg Asn Tyr Phe
            180                 185                 190

Leu Val Asn Gly Thr Ser Arg Glu Ile Gly Ile Gln Phe Phe Asp Ser
        195                 200                 205

Leu Leu Asp Thr Lys Lys Ile Glu Arg Phe Asn Pro Pro Ser Asn Val
    210                 215                 220

Thr Val Arg Cys Asn Thr Thr His Cys Leu Val Arg Trp Lys Gln Pro
225                 230                 235                 240

Arg Thr Tyr Gln Lys Leu Ser Tyr Leu Asp Phe Gln Tyr Gln Leu Asp
                245                 250                 255

Val His Arg Lys Asn Thr Gln Pro Gly Thr Glu Asn Leu Leu Ile Asn
            260                 265                 270

Val Ser Gly Asp Leu Glu Asn Arg Tyr Asn Phe Pro Ser Ser Glu Pro
        275                 280                 285

Arg Ala Lys His Ser Val Lys Ile Arg Ala Ala Asp Val Arg Ile Leu
    290                 295                 300

Asn Trp Ser Ser Trp Ser Glu Ala Ile Glu Phe Gly Ser Asp Asp Gly
305                 310                 315                 320

Asn Leu Gly Ser Val Tyr Ile Tyr Val Leu Leu Ile Val Gly Thr Leu
                325                 330                 335
```

Val Cys Gly Ile Val Leu Gly Phe Leu Phe Lys Arg Phe Leu Arg Ile
340 345 350

Gln Arg Leu Phe Pro Pro Val Pro Gln Ile Lys Asp Lys Leu Asn Asp
355 360 365

Asn His Glu Val Glu Asp Glu Ile Ile Trp Glu Glu Phe Thr Pro Glu
370 375 380

Glu Gly Lys Gly Tyr Arg Glu Glu Val Leu Thr Val Lys Glu Ile Thr
385 390 395 400

<210> 317
<211> 897
<212> PRT
<213> Homo sapiens

<400> 317

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

Trp Glu Arg Ser Leu Ala Gly Ala Glu Glu Thr Ile Pro Leu Gln Thr
20 25 30

Leu Arg Cys Tyr Asn Asp Tyr Thr Ser His Ile Thr Cys Arg Trp Ala
35 40 45

Asp Thr Gln Asp Ala Gln Arg Leu Val Asn Val Thr Leu Ile Arg Arg
50 55 60

Val Asn Glu Asp Leu Leu Glu Pro Val Ser Cys Asp Leu Ser Asp Asp
65 70 75 80

Met Pro Trp Ser Ala Cys Pro His Pro Arg Cys Val Pro Arg Arg Cys
85 90 95

Val Ile Pro Cys Gln Ser Phe Val Val Thr Asp Val Asp Tyr Phe Ser
100 105 110

Phe Gln Pro Asp Arg Pro Leu Gly Thr Arg Leu Thr Val Thr Leu Thr
115 120 125

Gln His Val Gln Pro Pro Glu Pro Arg Asp Leu Gln Ile Ser Thr Asp
130 135 140

Gln Asp His Phe Leu Leu Thr Trp Ser Val Ala Leu Gly Ser Pro Gln
145 150 155 160

Ser His Trp Leu Ser Pro Gly Asp Leu Glu Phe Glu Val Val Tyr Lys
165 170 175

```
Arg Leu Gln Asp Ser Trp Glu Asp Ala Ala Ile Leu Leu Ser Asn Thr
            180                 185                 190

Ser Gln Ala Thr Leu Gly Pro Glu His Leu Met Pro Ser Ser Thr Tyr
        195                 200                 205

Val Ala Arg Val Arg Thr Arg Leu Ala Pro Gly Ser Arg Leu Ser Gly
    210                 215                 220

Arg Pro Ser Lys Trp Ser Pro Glu Val Cys Trp Asp Ser Gln Pro Gly
225                 230                 235                 240

Asp Glu Ala Gln Pro Gln Asn Leu Glu Cys Phe Phe Asp Gly Ala Ala
                245                 250                 255

Val Leu Ser Cys Ser Trp Glu Val Arg Lys Glu Val Ala Ser Ser Val
            260                 265                 270

Ser Phe Gly Leu Phe Tyr Lys Pro Ser Pro Asp Ala Gly Glu Glu Glu
        275                 280                 285

Cys Ser Pro Val Leu Arg Glu Gly Leu Gly Ser Leu His Thr Arg His
    290                 295                 300

His Cys Gln Ile Pro Val Pro Asp Pro Ala Thr His Gly Gln Tyr Ile
305                 310                 315                 320

Val Ser Val Gln Pro Arg Arg Ala Glu Lys His Ile Lys Ser Ser Val
                325                 330                 335

Asn Ile Gln Met Ala Pro Pro Ser Leu Asn Val Thr Lys Asp Gly Asp
            340                 345                 350

Ser Tyr Ser Leu Arg Trp Glu Thr Met Lys Met Arg Tyr Glu His Ile
        355                 360                 365

Asp His Thr Phe Glu Ile Gln Tyr Arg Lys Asp Thr Ala Thr Trp Lys
    370                 375                 380

Asp Ser Lys Thr Glu Thr Leu Gln Asn Ala His Ser Met Ala Leu Pro
385                 390                 395                 400

Ala Leu Glu Pro Ser Thr Arg Tyr Trp Ala Arg Val Arg Val Arg Thr
                405                 410                 415

Ser Arg Thr Gly Tyr Asn Gly Ile Trp Ser Glu Trp Ser Glu Ala Arg
            420                 425                 430

Ser Trp Asp Thr Glu Ser Val Leu Pro Met Trp Val Leu Ala Leu Ile
        435                 440                 445
```

```
Val Ile Phe Leu Thr Ile Ala Val Leu Leu Ala Leu Arg Phe Cys Gly
    450                 455                 460

Ile Tyr Gly Tyr Arg Leu Arg Arg Lys Trp Glu Glu Lys Ile Pro Asn
465                 470                 475                 480

Pro Ser Lys Ser His Leu Phe Gln Asn Gly Ser Ala Glu Leu Trp Pro
                485                 490                 495

Pro Gly Ser Met Ser Ala Phe Thr Ser Gly Ser Pro Pro His Gln Gly
            500                 505                 510

Pro Trp Gly Ser Arg Phe Pro Glu Leu Glu Gly Val Phe Pro Val Gly
        515                 520                 525

Phe Gly Asp Ser Glu Val Ser Pro Leu Thr Ile Glu Asp Pro Lys His
    530                 535                 540

Val Cys Asp Pro Pro Ser Gly Pro Asp Thr Thr Pro Ala Ala Ser Asp
545                 550                 555                 560

Leu Pro Thr Glu Gln Pro Pro Ser Pro Gln Pro Gly Pro Pro Ala Ala
                565                 570                 575

Ser His Thr Pro Glu Lys Gln Ala Ser Ser Phe Asp Phe Asn Gly Pro
            580                 585                 590

Tyr Leu Gly Pro Pro His Ser Arg Ser Leu Pro Asp Ile Leu Gly Gln
        595                 600                 605

Pro Glu Pro Pro Gln Glu Gly Gly Ser Gln Lys Ser Pro Pro Pro Gly
    610                 615                 620

Ser Leu Glu Tyr Leu Cys Leu Pro Ala Gly Gly Gln Val Gln Leu Val
625                 630                 635                 640

Pro Leu Ala Gln Ala Met Gly Pro Gly Gln Ala Val Glu Val Glu Arg
                645                 650                 655

Arg Pro Ser Gln Gly Ala Ala Gly Ser Pro Ser Leu Glu Ser Gly Gly
            660                 665                 670

Gly Pro Ala Pro Pro Ala Leu Gly Pro Arg Val Gly Gly Gln Asp Gln
        675                 680                 685

Lys Asp Ser Pro Val Ala Ile Pro Met Ser Ser Gly Asp Thr Glu Asp
    690                 695                 700

Pro Gly Val Ala Ser Gly Tyr Val Ser Ser Ala Asp Leu Val Phe Thr
705                 710                 715                 720
```

```
Pro Asn Ser Gly Ala Ser Ser Val Ser Leu Val Pro Ser Leu Gly Leu
                725                 730                 735

Pro Ser Asp Gln Thr Pro Ser Leu Cys Pro Gly Leu Ala Ser Gly Pro
            740                 745                 750

Pro Gly Ala Pro Gly Pro Val Lys Ser Gly Phe Glu Gly Tyr Val Glu
        755                 760                 765

Leu Pro Pro Ile Glu Gly Arg Ser Pro Arg Ser Pro Arg Asn Asn Pro
    770                 775                 780

Val Pro Pro Glu Ala Lys Ser Pro Val Leu Asn Pro Gly Glu Arg Pro
785                 790                 795                 800

Ala Asp Val Ser Pro Thr Ser Pro Gln Pro Glu Gly Leu Leu Val Leu
                805                 810                 815

Gln Gln Val Gly Asp Tyr Cys Phe Leu Pro Gly Leu Gly Pro Gly Pro
            820                 825                 830

Leu Ser Leu Arg Ser Lys Pro Ser Ser Pro Gly Pro Gly Pro Glu Ile
        835                 840                 845

Lys Asn Leu Asp Gln Ala Phe Gln Val Lys Lys Pro Pro Gly Gln Ala
    850                 855                 860

Val Pro Gln Val Pro Val Ile Gln Leu Phe Lys Ala Leu Lys Gln Gln
865                 870                 875                 880

Asp Tyr Leu Ser Leu Pro Pro Trp Glu Val Asn Lys Pro Gly Glu Val
                885                 890                 895

Cys
```

<210> 318
<211> 896
<212> PRT
<213> Homo sapiens

<400> 318

```
Met Ile Cys Gln Lys Phe Cys Val Val Leu Leu His Trp Glu Phe Ile
1               5                   10                  15

Tyr Val Ile Thr Ala Phe Asn Leu Ser Tyr Pro Ile Thr Pro Trp Arg
            20                  25                  30

Phe Lys Leu Ser Cys Met Pro Pro Asn Ser Thr Tyr Asp Tyr Phe Leu
        35                  40                  45
```

```
Leu Pro Ala Gly Leu Ser Lys Asn Thr Ser Asn Ser Asn Gly His Tyr
    50                  55                  60

Glu Thr Ala Val Glu Pro Lys Phe Asn Ser Ser Gly Thr His Phe Ser
65                  70                  75                  80

Asn Leu Ser Lys Thr Thr Phe His Cys Cys Phe Arg Ser Glu Gln Asp
                85                  90                  95

Arg Asn Cys Ser Leu Cys Ala Asp Asn Ile Glu Gly Lys Thr Phe Val
            100                 105                 110

Ser Thr Val Asn Ser Leu Val Phe Gln Gln Ile Asp Ala Asn Trp Asn
        115                 120                 125

Ile Gln Cys Trp Leu Lys Gly Asp Leu Lys Leu Phe Ile Cys Tyr Val
    130                 135                 140

Glu Ser Leu Phe Lys Asn Leu Phe Arg Asn Tyr Asn Tyr Lys Val His
145                 150                 155                 160

Leu Leu Tyr Val Leu Pro Glu Val Leu Glu Asp Ser Pro Leu Val Pro
                165                 170                 175

Gln Lys Gly Ser Phe Gln Met Val His Cys Asn Cys Ser Val His Glu
            180                 185                 190

Cys Cys Glu Cys Leu Val Pro Val Pro Thr Ala Lys Leu Asn Asp Thr
        195                 200                 205

Leu Leu Met Cys Leu Lys Ile Thr Ser Gly Gly Val Ile Phe Gln Ser
    210                 215                 220

Pro Leu Met Ser Val Gln Pro Ile Asn Met Val Lys Pro Asp Pro Pro
225                 230                 235                 240

Leu Gly Leu His Met Glu Ile Thr Asp Asp Gly Asn Leu Lys Ile Ser
                245                 250                 255

Trp Ser Ser Pro Pro Leu Val Pro Phe Pro Leu Gln Tyr Gln Val Lys
            260                 265                 270

Tyr Ser Glu Asn Ser Thr Thr Val Ile Arg Glu Ala Asp Lys Ile Val
        275                 280                 285

Ser Ala Thr Ser Leu Leu Val Asp Ser Ile Leu Pro Gly Ser Ser Tyr
    290                 295                 300

Glu Val Gln Val Arg Gly Lys Arg Leu Asp Gly Pro Gly Ile Trp Ser
305                 310                 315                 320
```

```
Asp Trp Ser Thr Pro Arg Val Phe Thr Thr Gln Asp Val Ile Tyr Phe
                325                 330                 335

Pro Pro Lys Ile Leu Thr Ser Val Gly Ser Asn Val Ser Phe His Cys
            340                 345                 350

Ile Tyr Lys Lys Glu Asn Lys Ile Val Pro Ser Lys Glu Ile Val Trp
        355                 360                 365

Trp Met Asn Leu Ala Glu Lys Ile Pro Gln Ser Gln Tyr Asp Val Val
    370                 375                 380

Ser Asp His Val Ser Lys Val Thr Phe Phe Asn Leu Asn Glu Thr Lys
385                 390                 395                 400

Pro Arg Gly Lys Phe Thr Tyr Asp Ala Val Tyr Cys Cys Asn Glu His
                405                 410                 415

Glu Cys His His Arg Tyr Ala Glu Leu Tyr Val Ile Asp Val Asn Ile
            420                 425                 430

Asn Ile Ser Cys Glu Thr Asp Gly Tyr Leu Thr Lys Met Thr Cys Arg
        435                 440                 445

Trp Ser Thr Ser Thr Ile Gln Ser Leu Ala Glu Ser Thr Leu Gln Leu
    450                 455                 460

Arg Tyr His Arg Ser Ser Leu Tyr Cys Ser Asp Ile Pro Ser Ile His
465                 470                 475                 480

Pro Ile Ser Glu Pro Lys Asp Cys Tyr Leu Gln Ser Asp Gly Phe Tyr
                485                 490                 495

Glu Cys Ile Phe Gln Pro Ile Phe Leu Leu Ser Gly Tyr Thr Met Trp
            500                 505                 510

Ile Arg Ile Asn His Ser Leu Gly Ser Leu Asp Ser Pro Pro Thr Cys
        515                 520                 525

Val Leu Pro Asp Ser Val Val Lys Pro Leu Pro Pro Ser Ser Val Lys
    530                 535                 540

Ala Glu Ile Thr Ile Asn Ile Gly Leu Leu Lys Ile Ser Trp Glu Lys
545                 550                 555                 560

Pro Val Phe Pro Glu Asn Asn Leu Gln Phe Gln Ile Arg Tyr Gly Leu
                565                 570                 575

Ser Gly Lys Glu Val Gln Trp Lys Met Tyr Glu Val Tyr Asp Ala Lys
            580                 585                 590
```

```
Ser Lys Ser Val Ser Leu Pro Val Pro Asp Leu Cys Ala Val Tyr Ala
        595                 600                 605

Val Gln Val Arg Cys Lys Arg Leu Asp Gly Leu Gly Tyr Trp Ser Asn
    610                 615                 620

Trp Ser Asn Pro Ala Tyr Thr Val Val Met Asp Ile Lys Val Pro Met
625                 630                 635                 640

Arg Gly Pro Glu Phe Trp Arg Ile Ile Asn Gly Asp Thr Met Lys Lys
                645                 650                 655

Glu Lys Asn Val Thr Leu Leu Trp Lys Pro Leu Met Lys Asn Asp Ser
            660                 665                 670

Leu Cys Ser Val Gln Arg Tyr Val Ile Asn His His Thr Ser Cys Asn
        675                 680                 685

Gly Thr Trp Ser Glu Asp Val Gly Asn His Thr Lys Phe Thr Phe Leu
    690                 695                 700

Trp Thr Glu Gln Ala His Thr Val Thr Val Leu Ala Ile Asn Ser Ile
705                 710                 715                 720

Gly Ala Ser Val Ala Asn Phe Asn Leu Thr Phe Ser Trp Pro Met Ser
                725                 730                 735

Lys Val Asn Ile Val Gln Ser Leu Ser Ala Tyr Pro Leu Asn Ser Ser
            740                 745                 750

Cys Val Ile Val Ser Trp Ile Leu Ser Pro Ser Asp Tyr Lys Leu Met
        755                 760                 765

Tyr Phe Ile Ile Glu Trp Lys Asn Leu Asn Glu Asp Gly Glu Ile Lys
    770                 775                 780

Trp Leu Arg Ile Ser Ser Ser Val Lys Lys Tyr Tyr Ile His Asp His
785                 790                 795                 800

Phe Ile Pro Ile Glu Lys Tyr Gln Phe Ser Leu Tyr Pro Ile Phe Met
                805                 810                 815

Glu Gly Val Gly Lys Pro Lys Ile Ile Asn Ser Phe Thr Gln Asp Asp
            820                 825                 830

Ile Glu Lys His Gln Ser Asp Ala Gly Leu Tyr Val Ile Val Pro Val
        835                 840                 845

Ile Ile Ser Ser Ser Ile Leu Leu Leu Gly Thr Leu Leu Ile Ser His
    850                 855                 860
```

Gln Arg Met Lys Lys Leu Phe Trp Glu Asp Val Pro Asn Pro Lys Asn
865 870 875 880

Cys Ser Trp Ala Gln Gly Leu Asn Phe Gln Lys Arg Thr Asp Ile Leu
885 890 895

<210> 319
<211> 468
<212> PRT
<213> Homo sapiens

<400> 319

Met Leu Ala Val Gly Cys Ala Leu Leu Ala Ala Leu Leu Ala Ala Pro
1 5 10 15

Gly Ala Ala Leu Ala Pro Arg Arg Cys Pro Ala Gln Glu Val Ala Arg
20 25 30

Gly Val Leu Thr Ser Leu Pro Gly Asp Ser Val Thr Leu Thr Cys Pro
35 40 45

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

Pro Ala Ala Gly Ser His Pro Ser Arg Trp Ala Gly Met Gly Arg Arg
65 70 75 80

Leu Leu Leu Arg Ser Val Gln Leu His Asp Ser Gly Asn Tyr Ser Cys
85 90 95

Tyr Arg Ala Gly Arg Pro Ala Gly Thr Val His Leu Leu Val Asp Val
100 105 110

Pro Pro Glu Glu Pro Gln Leu Ser Cys Phe Arg Lys Ser Pro Leu Ser
115 120 125

Asn Val Val Cys Glu Trp Gly Pro Arg Ser Thr Pro Ser Leu Thr Thr
130 135 140

Lys Ala Val Leu Leu Val Arg Lys Phe Gln Asn Ser Pro Ala Glu Asp
145 150 155 160

Phe Gln Glu Pro Cys Gln Tyr Ser Gln Glu Ser Gln Lys Phe Ser Cys
165 170 175

Gln Leu Ala Val Pro Glu Gly Asp Ser Ser Phe Tyr Ile Val Ser Met
180 185 190

Cys Val Ala Ser Ser Val Gly Ser Lys Phe Ser Lys Thr Gln Thr Phe
195 200 205

Gln Gly Cys Gly Ile Leu Gln Pro Asp Pro Pro Ala Asn Ile Thr Val

210 215 220

Thr Ala Val Ala Arg Asn Pro Arg Trp Leu Ser Val Thr Trp Gln Asp
225 230 235 240

Pro His Ser Trp Asn Ser Ser Phe Tyr Arg Leu Arg Phe Glu Leu Arg
245 250 255

Tyr Arg Ala Glu Arg Ser Lys Thr Phe Thr Thr Trp Met Val Lys Asp
260 265 270

Leu Gln His His Cys Val Ile His Asp Ala Trp Ser Gly Leu Arg His
275 280 285

Val Val Gln Leu Arg Ala Gln Glu Glu Phe Gly Gln Gly Glu Trp Ser
290 295 300

Glu Trp Ser Pro Glu Ala Met Gly Thr Pro Trp Thr Glu Ser Arg Ser
305 310 315 320

Pro Pro Ala Glu Asn Glu Val Ser Thr Pro Met Gln Ala Leu Thr Thr
325 330 335

Asn Lys Asp Asp Asp Asn Ile Leu Phe Arg Asp Ser Ala Asn Ala Thr
340 345 350

Ser Leu Pro Val Gln Asp Ser Ser Ser Val Pro Leu Pro Thr Phe Leu
355 360 365

Val Ala Gly Gly Ser Leu Ala Phe Gly Thr Leu Leu Cys Ile Ala Ile
370 375 380

Val Leu Arg Phe Lys Lys Thr Trp Lys Leu Arg Ala Leu Lys Glu Gly
385 390 395 400

Lys Thr Ser Met His Pro Pro Tyr Ser Leu Gly Gln Leu Val Pro Glu
405 410 415

Arg Pro Arg Pro Thr Pro Val Leu Val Pro Leu Ile Ser Pro Pro Val
420 425 430

Ser Pro Ser Ser Leu Gly Ser Asp Asn Thr Ser Ser His Asn Arg Pro
435 440 445

Asp Ala Arg Asp Pro Arg Ser Pro Tyr Asp Ile Ser Asn Thr Asp Tyr
450 455 460

Phe Phe Pro Arg
465

<210> 320

<211> 857
<212> PRT
<213> Homo sapiens

<400> 320

Met Leu Thr Leu Gln Thr Trp Leu Val Gln Ala Leu Phe Ile Phe Leu
1 5 10 15

Thr Thr Glu Ser Thr Gly Glu Leu Leu Asp Pro Cys Gly Tyr Ile Ser
20 25 30

Pro Glu Ser Pro Val Val Gln Leu His Ser Asn Phe Thr Ala Val Cys
35 40 45

Val Leu Lys Glu Lys Cys Met Asp Tyr Phe His Val Asn Ala Asn Tyr
50 55 60

Ile Val Trp Lys Thr Asn His Phe Thr Ile Pro Lys Glu Gln Tyr Thr
65 70 75 80

Ile Ile Asn Arg Thr Ala Ser Ser Val Thr Phe Thr Asp Ile Ala Ser
85 90 95

Leu Asn Ile Gln Leu Thr Cys Asn Ile Leu Thr Phe Gly Gln Leu Glu
100 105 110

Gln Asn Val Tyr Gly Ile Thr Ile Ile Ser Gly Leu Pro Pro Glu Lys
115 120 125

Pro Lys Asn Leu Ser Cys Ile Val Asn Glu Gly Lys Lys Met Arg Cys
130 135 140

Glu Trp Asp Gly Gly Arg Glu Thr His Leu Glu Thr Asn Phe Thr Leu
145 150 155 160

Lys Ser Glu Trp Ala Thr His Lys Phe Ala Asp Cys Lys Ala Lys Arg
165 170 175

Asp Thr Pro Thr Ser Cys Thr Val Asp Tyr Ser Thr Val Tyr Phe Val
180 185 190

Asn Ile Glu Val Trp Val Glu Ala Glu Asn Ala Leu Gly Lys Val Thr
195 200 205

Ser Asp His Ile Asn Phe Asp Pro Val Tyr Lys Val Lys Pro Asn Pro
210 215 220

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

Lys Leu Thr Trp Thr Asn Pro Ser Ile Lys Ser Val Ile Ile Leu Lys
245 250 255

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

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

Leu Lys Pro Phe Thr Glu Tyr Val Phe Arg Ile Arg Cys Met Lys Glu
    290                 295                 300

Asp Gly Lys Gly Tyr Trp Ser Asp Trp Ser Glu Glu Ala Ser Gly Ile
305                 310                 315                 320

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

Asp Pro Ser His Thr Gln Gly Tyr Arg Thr Val Gln Leu Val Trp Lys
            340                 345                 350

Thr Leu Pro Pro Phe Glu Ala Asn Gly Lys Ile Leu Asp Tyr Glu Val
        355                 360                 365

Thr Leu Thr Arg Trp Lys Ser His Leu Gln Asn Tyr Thr Val Asn Ala
    370                 375                 380

Thr Lys Leu Thr Val Asn Leu Thr Asn Asp Arg Tyr Leu Ala Thr Leu
385                 390                 395                 400

Thr Val Arg Asn Leu Val Gly Lys Ser Asp Ala Ala Val Leu Thr Ile
                405                 410                 415

Pro Ala Cys Asp Phe Gln Gly Asn Leu Ala Glu Ser Lys Cys Tyr Leu
            420                 425                 430

Ile Thr Val Thr Pro Val Tyr Ala Asp Gly Pro Gly Ser Pro Glu Ser
        435                 440                 445

Ile Lys Ala Tyr Leu Lys Gln Ala Pro Pro Ser Lys Gly Pro Thr Val
    450                 455                 460

Arg Thr Lys Lys Val Gly Lys Asn Glu Ala Val Leu Glu Trp Asp Gln
465                 470                 475                 480

Leu Pro Val Asp Val Gln Asn Gly Phe Ile Arg Asn Tyr Thr Ile Phe
                485                 490                 495

Tyr Arg Thr Ile Ile Gly Asn Glu Thr Ala Val Asn Val Asp Ser Ser
            500                 505                 510

His Thr Glu Tyr Thr Leu Ser Ser Leu Thr Ser Asp Thr Leu Tyr Met
        515                 520                 525
```

```
Val Arg Met Ala Ala Tyr Thr Asp Glu Gly Gly Lys Asp Gly Pro Glu
    530                 535                 540

Phe Thr Phe Thr Thr Pro Lys Phe Ala Gln Gly Glu Ile Glu Ala Ile
545                 550                 555                 560

Val Val Pro Val Cys Leu Ala Phe Leu Leu Thr Thr Leu Leu Gly Val
                565                 570                 575

Leu Phe Cys Phe Asn Lys Arg Asp Leu Ile Lys Lys His Ile Trp Pro
            580                 585                 590

Asn Val Pro Asp Pro Ser Lys Ser His Ile Ala Gln Trp Ser Pro His
        595                 600                 605

Thr Pro Pro Arg His Asn Phe Asn Ser Lys Asp Gln Met Tyr Ser Asp
    610                 615                 620

Gly Asn Phe Thr Asp Val Ser Val Val Glu Ile Glu Ala Asn Asp Lys
625                 630                 635                 640

Lys Pro Phe Pro Glu Asp Leu Lys Ser Leu Asp Leu Phe Lys Lys Glu
                645                 650                 655

Lys Ile Asn Thr Glu Gly His Ser Ser Gly Ile Gly Gly Ser Ser Cys
            660                 665                 670

Met Ser Ser Ser Arg Pro Ser Ile Ser Ser Ser Asp Glu Asn Glu Ser
        675                 680                 685

Ser Gln Asn Thr Ser Ser Thr Val Gln Tyr Ser Thr Val Val His Ser
    690                 695                 700

Gly Tyr Arg His Gln Val Pro Ser Val Gln Val Phe Ser Arg Ser Glu
705                 710                 715                 720

Ser Thr Gln Pro Leu Leu Asp Ser Glu Glu Arg Pro Glu Asp Leu Gln
                725                 730                 735

Leu Val Asp His Val Asp Gly Gly Asp Gly Ile Leu Pro Arg Gln Gln
            740                 745                 750

Tyr Phe Lys Gln Asn Cys Ser Gln His Glu Ser Ser Pro Asp Ile Ser
        755                 760                 765

His Phe Glu Arg Ser Lys Gln Val Ser Ser Val Asn Glu Glu Asp Phe
    770                 775                 780

Val Arg Leu Lys Gln Gln Ile Ser Asp His Ile Ser Gln Ser Cys Gly
785                 790                 795                 800
```

Ser Gly Gln Met Lys Met Phe Gln Glu Val Ser Ala Ala Asp Ala Phe
805 810 815

Gly Pro Gly Thr Glu Gly Gln Val Glu Arg Phe Glu Thr Val Gly Met
820 825 830

Glu Ala Ala Thr Asp Glu Gly Met Pro Lys Ser Tyr Leu Pro Gln Thr
835 840 845

Val Arg Gln Gly Gly Tyr Met Pro Gln
850 855

<210> 321
<211> 422
<212> PRT
<213> Homo sapiens

<400> 321

Met Ser Ser Ser Cys Ser Gly Leu Ser Arg Val Leu Val Ala Val Ala
1 5 10 15

Thr Ala Leu Val Ser Ala Ser Ser Pro Cys Pro Gln Ala Trp Gly Pro
20 25 30

Pro Gly Val Gln Tyr Gly Gln Pro Gly Arg Ser Val Lys Leu Cys Cys
35 40 45

Pro Gly Val Thr Ala Gly Asp Pro Val Ser Trp Phe Arg Asp Gly Glu
50 55 60

Pro Lys Leu Leu Gln Gly Pro Asp Ser Gly Leu Gly His Glu Leu Val
65 70 75 80

Leu Ala Gln Ala Asp Ser Thr Asp Glu Gly Thr Tyr Ile Cys Gln Thr
85 90 95

Leu Asp Gly Ala Leu Gly Gly Thr Val Thr Leu Gln Leu Gly Tyr Pro
100 105 110

Pro Ala Arg Pro Val Val Ser Cys Gln Ala Ala Asp Tyr Glu Asn Phe
115 120 125

Ser Cys Thr Trp Ser Pro Ser Gln Ile Ser Gly Leu Pro Thr Arg Tyr
130 135 140

Leu Thr Ser Tyr Arg Lys Lys Thr Val Leu Gly Ala Asp Ser Gln Arg
145 150 155 160

Arg Ser Pro Ser Thr Gly Pro Trp Pro Cys Pro Gln Asp Pro Leu Gly
165 170 175

Ala Ala Arg Cys Val Val His Gly Ala Glu Phe Trp Ser Gln Tyr Arg
180 185 190

Ile Asn Val Thr Glu Val Asn Pro Leu Gly Ala Ser Thr Arg Leu Leu
195 200 205

Asp Val Ser Leu Gln Ser Ile Leu Arg Pro Asp Pro Pro Gln Gly Leu
210 215 220

Arg Val Glu Ser Val Pro Gly Tyr Pro Arg Arg Leu Arg Ala Ser Trp
225 230 235 240

Thr Tyr Pro Ala Ser Trp Pro Cys Gln Pro His Phe Leu Leu Lys Phe
245 250 255

Arg Leu Gln Tyr Arg Pro Ala Gln His Pro Ala Trp Ser Thr Val Glu
260 265 270

Pro Ala Gly Leu Glu Glu Val Ile Thr Asp Ala Val Ala Gly Leu Pro
275 280 285

His Ala Val Arg Val Ser Ala Arg Asp Phe Leu Asp Ala Gly Thr Trp
290 295 300

Ser Thr Trp Ser Pro Glu Ala Trp Gly Thr Pro Ser Thr Gly Thr Ile
305 310 315 320

Pro Lys Glu Ile Pro Ala Trp Gly Gln Leu His Thr Gln Pro Glu Val
325 330 335

Glu Pro Gln Val Asp Ser Pro Ala Pro Pro Arg Pro Ser Leu Gln Pro
340 345 350

His Pro Arg Leu Leu Asp His Arg Asp Ser Val Glu Gln Val Ala Val
355 360 365

Leu Ala Ser Leu Gly Ile Leu Ser Phe Leu Gly Leu Val Ala Gly Ala
370 375 380

Leu Ala Leu Gly Leu Trp Leu Arg Leu Arg Arg Gly Gly Lys Asp Gly
385 390 395 400

Ser Pro Lys Pro Gly Phe Leu Ala Ser Val Ile Pro Val Asp Arg Arg
405 410 415

Pro Gly Ala Pro Asn Leu
420

<210> 322
<211> 636
<212> PRT

<213> Homo sapiens

<400> 322

```
Met Arg Gly Gly Arg Gly Ala Pro Phe Trp Leu Trp Pro Leu Pro Lys
1               5                  10                  15

Leu Ala Leu Leu Pro Leu Leu Trp Val Leu Phe Gln Arg Thr Arg Pro
            20                  25                  30

Gln Gly Ser Ala Gly Pro Leu Gln Cys Tyr Gly Val Gly Pro Leu Gly
        35                  40                  45

Asp Leu Asn Cys Ser Trp Glu Pro Leu Gly Asp Leu Gly Ala Pro Ser
    50                  55                  60

Glu Leu His Leu Gln Ser Gln Lys Tyr Arg Ser Asn Lys Thr Gln Thr
65                  70                  75                  80

Val Ala Val Ala Ala Gly Arg Ser Trp Val Ala Ile Pro Arg Glu Gln
                85                  90                  95

Leu Thr Met Ser Asp Lys Leu Leu Val Trp Gly Thr Lys Ala Gly Gln
            100                 105                 110

Pro Leu Trp Pro Pro Val Phe Val Asn Leu Glu Thr Gln Met Lys Pro
        115                 120                 125

Asn Ala Pro Arg Leu Gly Pro Asp Val Asp Phe Ser Glu Asp Asp Pro
    130                 135                 140

Leu Glu Ala Thr Val His Trp Ala Pro Pro Thr Trp Pro Ser His Lys
145                 150                 155                 160

Val Leu Ile Cys Gln Phe His Tyr Arg Arg Cys Gln Glu Ala Ala Trp
                165                 170                 175

Thr Leu Leu Glu Pro Glu Leu Lys Thr Ile Pro Leu Thr Pro Val Glu
            180                 185                 190

Ile Gln Asp Leu Glu Leu Ala Thr Gly Tyr Lys Val Tyr Gly Arg Cys
        195                 200                 205

Arg Met Glu Lys Glu Glu Asp Leu Trp Gly Glu Trp Ser Pro Ile Leu
    210                 215                 220

Ser Phe Gln Thr Pro Pro Ser Ala Pro Lys Asp Val Trp Val Ser Gly
225                 230                 235                 240

Asn Leu Cys Gly Thr Pro Gly Gly Glu Glu Pro Leu Leu Leu Trp Lys
                245                 250                 255
```

```
Ala Pro Gly Pro Cys Val Gln Val Ser Tyr Lys Val Trp Phe Trp Val
            260                 265                 270

Gly Gly Arg Glu Leu Ser Pro Glu Gly Ile Thr Cys Cys Cys Ser Leu
        275                 280                 285

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

Ser Trp Glu Pro Leu Thr Asn Leu Ser Leu Val Cys Leu Asp Ser Ala
305                 310                 315                 320

Ser Ala Pro Arg Ser Val Ala Val Ser Ser Ile Ala Gly Ser Thr Glu
                325                 330                 335

Leu Leu Val Thr Trp Gln Pro Gly Pro Gly Glu Pro Leu Glu His Val
            340                 345                 350

Val Asp Trp Ala Arg Asp Gly Asp Pro Leu Glu Lys Leu Asn Trp Val
        355                 360                 365

Arg Leu Pro Pro Gly Asn Leu Ser Ala Leu Leu Pro Gly Asn Phe Thr
    370                 375                 380

Val Gly Val Pro Tyr Arg Ile Thr Val Thr Ala Val Ser Ala Ser Gly
385                 390                 395                 400

Leu Ala Ser Ala Ser Ser Val Trp Gly Phe Arg Glu Glu Leu Ala Pro
                405                 410                 415

Leu Val Gly Pro Thr Leu Trp Arg Leu Gln Asp Ala Pro Pro Gly Thr
            420                 425                 430

Pro Ala Ile Ala Trp Gly Glu Val Pro Arg His Gln Leu Arg Gly His
        435                 440                 445

Leu Thr His Tyr Thr Leu Cys Ala Gln Ser Gly Thr Ser Pro Ser Val
    450                 455                 460

Cys Met Asn Val Ser Gly Asn Thr Gln Ser Val Thr Leu Pro Asp Leu
465                 470                 475                 480

Pro Trp Gly Pro Cys Glu Leu Trp Val Thr Ala Ser Thr Ile Ala Gly
                485                 490                 495

Gln Gly Pro Pro Gly Pro Ile Leu Arg Leu His Leu Pro Asp Asn Thr
            500                 505                 510

Leu Arg Trp Lys Val Leu Pro Gly Ile Leu Phe Leu Trp Gly Leu Phe
        515                 520                 525
```

```
Leu Leu Gly Cys Gly Leu Ser Leu Ala Thr Ser Gly Arg Cys Tyr His
    530                 535                 540

Leu Arg His Lys Val Leu Pro Arg Trp Val Trp Glu Lys Val Pro Asp
545                 550                 555                 560

Pro Ala Asn Ser Ser Ser Gly Gln Pro His Met Glu Gln Val Pro Glu
                565                 570                 575

Ala Gln Pro Leu Gly Asp Leu Pro Ile Leu Glu Val Glu Glu Met Glu
            580                 585                 590

Pro Pro Pro Val Met Glu Ser Ser Gln Pro Ala Gln Ala Thr Ala Pro
        595                 600                 605

Leu Asp Ser Gly Tyr Glu Lys His Phe Leu Pro Thr Pro Glu Glu Leu
    610                 615                 620

Gly Leu Leu Gly Pro Pro Arg Pro Gln Val Leu Ala
625                 630                 635
```

<210> 323
<211> 745
<212> PRT
<213> Homo sapiens

<400> 323

```
Met Lys Leu Ser Pro Gln Pro Ser Cys Val Asn Leu Gly Met Met Trp
1               5                   10                  15

Thr Trp Ala Leu Trp Met Leu Pro Ser Leu Cys Lys Phe Ser Leu Ala
            20                  25                  30

Ala Leu Pro Ala Lys Pro Glu Asn Ile Ser Cys Val Tyr Tyr Tyr Arg
        35                  40                  45

Lys Asn Leu Thr Cys Thr Trp Ser Pro Gly Lys Glu Thr Ser Tyr Thr
    50                  55                  60

Gln Tyr Thr Val Lys Arg Thr Tyr Ala Phe Gly Glu Lys His Asp Asn
65                  70                  75                  80

Cys Thr Thr Asn Ser Ser Thr Ser Glu Asn Arg Ala Ser Cys Ser Phe
                85                  90                  95

Phe Leu Pro Arg Ile Thr Ile Pro Asp Asn Tyr Thr Ile Glu Val Glu
            100                 105                 110

Ala Glu Asn Gly Asp Gly Val Ile Lys Ser His Met Thr Tyr Trp Arg
        115                 120                 125

Leu Glu Asn Ile Ala Lys Thr Glu Pro Pro Lys Ile Phe Arg Val Lys
```

130 135 140

Pro Val Leu Gly Ile Lys Arg Met Ile Gln Ile Glu Trp Ile Lys Pro
145 150 155 160

Glu Leu Ala Pro Val Ser Ser Asp Leu Lys Tyr Thr Leu Arg Phe Arg
165 170 175

Thr Val Asn Ser Thr Ser Trp Met Glu Val Asn Phe Ala Lys Asn Arg
180 185 190

Lys Asp Lys Asn Gln Thr Tyr Asn Leu Thr Gly Leu Gln Pro Phe Thr
195 200 205

Glu Tyr Val Ile Ala Leu Arg Cys Ala Val Lys Glu Ser Lys Phe Trp
210 215 220

Ser Asp Trp Ser Gln Glu Lys Met Gly Met Thr Glu Glu Glu Ala Pro
225 230 235 240

Cys Gly Leu Glu Leu Trp Arg Val Leu Lys Pro Ala Glu Ala Asp Gly
245 250 255

Arg Arg Pro Val Arg Leu Leu Trp Lys Lys Ala Arg Gly Ala Pro Val
260 265 270

Leu Glu Lys Thr Leu Gly Tyr Asn Ile Trp Tyr Tyr Pro Glu Ser Asn
275 280 285

Thr Asn Leu Thr Glu Thr Met Asn Thr Thr Asn Gln Gln Leu Glu Leu
290 295 300

His Leu Gly Gly Glu Ser Phe Trp Val Ser Met Ile Ser Tyr Asn Ser
305 310 315 320

Leu Gly Lys Ser Pro Val Ala Thr Leu Arg Ile Pro Ala Ile Gln Glu
325 330 335

Lys Ser Phe Gln Cys Ile Glu Val Met Gln Ala Cys Val Ala Glu Asp
340 345 350

Gln Leu Val Val Lys Trp Gln Ser Ser Ala Leu Asp Val Asn Thr Trp
355 360 365

Met Ile Glu Trp Phe Pro Asp Val Asp Ser Glu Pro Thr Thr Leu Ser
370 375 380

Trp Glu Ser Val Ser Gln Ala Thr Asn Trp Thr Ile Gln Gln Asp Lys
385 390 395 400

Leu Lys Pro Phe Trp Cys Tyr Asn Ile Ser Val Tyr Pro Met Leu His

405 410 415

Asp Lys Val Gly Glu Pro Tyr Ser Ile Gln Ala Tyr Ala Lys Glu Gly
420 425 430

Val Pro Ser Glu Gly Pro Glu Thr Lys Val Glu Asn Ile Gly Val Lys
435 440 445

Thr Val Thr Ile Thr Trp Lys Glu Ile Pro Lys Ser Glu Arg Lys Gly
450 455 460

Ile Ile Cys Asn Tyr Thr Ile Phe Tyr Gln Ala Glu Gly Gly Lys Gly
465 470 475 480

Phe Ser Lys Thr Val Asn Ser Ser Ile Leu Gln Tyr Gly Leu Glu Ser
485 490 495

Leu Lys Arg Lys Thr Ser Tyr Ile Val Gln Val Met Ala Ser Thr Ser
500 505 510

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

Ser Val Phe Glu Ile Ile Leu Ile Thr Ser Leu Ile Gly Gly Gly Leu
530 535 540

Leu Ile Leu Ile Ile Leu Thr Val Ala Tyr Gly Leu Lys Lys Pro Asn
545 550 555 560

Lys Leu Thr His Leu Cys Trp Pro Thr Val Pro Asn Pro Ala Glu Ser
565 570 575

Ser Ile Ala Thr Trp His Gly Asp Asp Phe Lys Asp Lys Leu Asn Leu
580 585 590

Lys Glu Ser Asp Asp Ser Val Asn Thr Glu Asp Arg Ile Leu Lys Pro
595 600 605

Cys Ser Thr Pro Ser Asp Lys Leu Val Ile Asp Lys Leu Val Val Asn
610 615 620

Phe Gly Asn Val Leu Gln Glu Ile Phe Thr Asp Glu Ala Arg Thr Gly
625 630 635 640

Gln Glu Asn Asn Leu Gly Gly Glu Lys Asn Gly Tyr Val Thr Cys Pro
645 650 655

Phe Arg Pro Asp Cys Pro Leu Gly Lys Ser Phe Glu Glu Leu Pro Val
660 665 670

Ser Pro Glu Ile Pro Pro Arg Lys Ser Gln Tyr Leu Arg Ser Arg Met

675 680 685

Pro Glu Gly Thr Arg Pro Glu Ala Lys Glu Gln Leu Leu Phe Ser Gly
690 695 700

Gln Ser Leu Val Pro Asp His Leu Cys Glu Glu Gly Ala Pro Asn Pro
705 710 715 720

Tyr Leu Lys Asn Ser Val Thr Ala Arg Glu Phe Leu Val Ser Glu Lys
725 730 735

Leu Pro Glu His Thr Lys Gly Glu Val
740 745

<210> 324
<211> 372
<212> PRT
<213> Homo sapiens

<400> 324

Met Ala Ala Pro Val Pro Trp Ala Cys Cys Ala Val Leu Ala Ala Ala
1 5 10 15

Ala Ala Val Val Tyr Ala Gln Arg His Ser Pro Gln Glu Ala Pro His
20 25 30

Val Gln Tyr Glu Arg Leu Gly Ser Asp Val Thr Leu Pro Cys Gly Thr
35 40 45

Ala Asn Trp Asp Ala Ala Val Thr Trp Arg Val Asn Gly Thr Asp Leu
50 55 60

Ala Pro Asp Leu Leu Asn Gly Ser Gln Leu Val Leu His Gly Leu Glu
65 70 75 80

Leu Gly His Ser Gly Leu Tyr Ala Cys Phe His Arg Asp Ser Trp His
85 90 95

Leu Arg His Gln Val Leu Leu His Val Gly Leu Pro Pro Arg Glu Pro
100 105 110

Val Leu Ser Cys Arg Ser Asn Thr Tyr Pro Lys Gly Phe Tyr Cys Ser
115 120 125

Trp His Leu Pro Thr Pro Thr Tyr Ile Pro Asn Thr Phe Asn Val Thr
130 135 140

Val Leu His Gly Ser Lys Ile Met Val Cys Glu Lys Asp Pro Ala Leu
145 150 155 160

Lys Asn Arg Cys His Ile Arg Tyr Met His Leu Phe Ser Thr Ile Lys
165 170 175

```
Tyr Lys Val Ser Ile Ser Val Ser Asn Ala Leu Gly His Asn Ala Thr
            180                 185                 190

Ala Ile Thr Phe Asp Glu Phe Thr Ile Val Lys Pro Asp Pro Pro Glu
        195                 200                 205

Asn Val Val Ala Arg Pro Val Pro Ser Asn Pro Arg Arg Leu Glu Val
    210                 215                 220

Thr Trp Gln Thr Pro Ser Thr Trp Pro Asp Pro Glu Ser Phe Pro Leu
225                 230                 235                 240

Lys Phe Phe Leu Arg Tyr Arg Pro Leu Ile Leu Asp Gln Trp Gln His
                245                 250                 255

Val Glu Leu Ser Asp Gly Thr Ala His Thr Ile Thr Asp Ala Tyr Ala
            260                 265                 270

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

Thr Trp Ser Asp Trp Ser Val Ala Ala His Ala Thr Pro Trp Thr Glu
    290                 295                 300

Glu Pro Arg His Leu Thr Thr Glu Ala Gln Ala Ala Glu Thr Thr Thr
305                 310                 315                 320

Ser Thr Thr Ser Ser Leu Ala Pro Pro Pro Thr Thr Lys Ile Cys Asp
                325                 330                 335

Pro Gly Glu Leu Gly Ser Gly Gly Gly Pro Ser Ala Pro Phe Leu Val
            340                 345                 350

Ser Val Pro Ile Thr Leu Ala Leu Ala Ala Ala Ala Ala Thr Ala Ser
        355                 360                 365

Ser Leu Leu Ile
    370


<210>  325
<211>  1097
<212>  PRT
<213>  Homo sapiens

<400>  325

Met Met Asp Ile Tyr Val Cys Leu Lys Arg Pro Ser Trp Met Val Asp
1               5                   10                  15

Asn Lys Arg Met Arg Thr Ala Ser Asn Phe Gln Trp Leu Leu Ser Thr
            20                  25                  30
```

```
Phe Ile Leu Leu Tyr Leu Met Asn Gln Val Asn Ser Gln Lys Lys Gly
        35                  40                  45

Ala Pro His Asp Leu Lys Cys Val Thr Asn Asn Leu Gln Val Trp Asn
    50                  55                  60

Cys Ser Trp Lys Ala Pro Ser Gly Thr Gly Arg Gly Thr Asp Tyr Glu
65                  70                  75                  80

Val Cys Ile Glu Asn Arg Ser Arg Ser Cys Tyr Gln Leu Glu Lys Thr
                85                  90                  95

Ser Ile Lys Ile Pro Ala Leu Ser His Gly Asp Tyr Glu Ile Thr Ile
            100                 105                 110

Asn Ser Leu His Asp Phe Gly Ser Ser Thr Ser Lys Phe Thr Leu Asn
        115                 120                 125

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

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

Gly Ser Val Phe Pro His Arg Ser Asn Val Ile Trp Glu Ile Lys Val
                165                 170                 175

Leu Arg Lys Glu Ser Met Glu Leu Val Lys Leu Val Thr His Asn Thr
            180                 185                 190

Thr Leu Asn Gly Lys Asp Thr Leu His His Trp Ser Trp Ala Ser Asp
        195                 200                 205

Met Pro Leu Glu Cys Ala Ile His Phe Val Glu Ile Arg Cys Tyr Ile
    210                 215                 220

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

Val Lys Asn Ile Ser Trp Ile Pro Asp Ser Gln Thr Lys Val Phe Pro
                245                 250                 255

Gln Asp Lys Val Ile Leu Val Gly Ser Asp Ile Thr Phe Cys Cys Val
            260                 265                 270

Ser Gln Glu Lys Val Leu Ser Ala Leu Ile Gly His Thr Asn Cys Pro
        275                 280                 285

Leu Ile His Leu Asp Gly Glu Asn Val Ala Ile Lys Ile Arg Asn Ile
    290                 295                 300
```

```
Ser Val Ser Ala Ser Ser Gly Thr Asn Val Val Phe Thr Thr Glu Asp
305                 310                 315                 320

Asn Ile Phe Gly Thr Val Ile Phe Ala Gly Tyr Pro Pro Asp Thr Pro
                325                 330                 335

Gln Gln Leu Asn Cys Glu Thr His Asp Leu Lys Glu Ile Ile Cys Ser
            340                 345                 350

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

Tyr Thr Leu Val Glu Ser Phe Ser Gly Lys Tyr Val Arg Leu Lys Arg
    370                 375                 380

Ala Glu Ala Pro Thr Asn Glu Ser Tyr Gln Leu Leu Phe Gln Met Leu
385                 390                 395                 400

Pro Asn Gln Glu Ile Tyr Asn Phe Thr Leu Asn Ala His Asn Pro Leu
                405                 410                 415

Gly Arg Ser Gln Ser Thr Ile Leu Val Asn Ile Thr Glu Lys Val Tyr
            420                 425                 430

Pro His Thr Pro Thr Ser Phe Lys Val Lys Asp Ile Asn Ser Thr Ala
        435                 440                 445

Val Lys Leu Ser Trp His Leu Pro Gly Asn Phe Ala Lys Ile Asn Phe
    450                 455                 460

Leu Cys Glu Ile Glu Ile Lys Lys Ser Asn Ser Val Gln Glu Gln Arg
465                 470                 475                 480

Asn Val Thr Ile Lys Gly Val Glu Asn Ser Ser Tyr Leu Val Ala Leu
                485                 490                 495

Asp Lys Leu Asn Pro Tyr Thr Leu Tyr Thr Phe Arg Ile Arg Cys Ser
            500                 505                 510

Thr Glu Thr Phe Trp Lys Trp Ser Lys Trp Ser Asn Lys Lys Gln His
        515                 520                 525

Leu Thr Thr Glu Ala Ser Pro Ser Lys Gly Pro Asp Thr Trp Arg Glu
    530                 535                 540

Trp Ser Ser Asp Gly Lys Asn Leu Ile Ile Tyr Trp Lys Pro Leu Pro
545                 550                 555                 560

Ile Asn Glu Ala Asn Gly Lys Ile Leu Ser Tyr Asn Val Ser Cys Ser
                565                 570                 575
```

```
Ser Asp Glu Glu Thr Gln Ser Leu Ser Glu Ile Pro Asp Pro Gln His
            580                 585                 590

Lys Ala Glu Ile Arg Leu Asp Lys Asn Asp Tyr Ile Ile Ser Val Val
        595                 600                 605

Ala Lys Asn Ser Val Gly Ser Ser Pro Pro Ser Lys Ile Ala Ser Met
    610                 615                 620

Glu Ile Pro Asn Asp Asp Leu Lys Ile Glu Gln Val Val Gly Met Gly
625                 630                 635                 640

Lys Gly Ile Leu Leu Thr Trp His Tyr Asp Pro Asn Met Thr Cys Asp
                645                 650                 655

Tyr Val Ile Lys Trp Cys Asn Ser Ser Arg Ser Glu Pro Cys Leu Met
            660                 665                 670

Asp Trp Arg Lys Val Pro Ser Asn Ser Thr Glu Thr Val Ile Glu Ser
        675                 680                 685

Asp Glu Phe Arg Pro Gly Ile Arg Tyr Asn Phe Phe Leu Tyr Gly Cys
    690                 695                 700

Arg Asn Gln Gly Tyr Gln Leu Leu Arg Ser Met Ile Gly Tyr Ile Glu
705                 710                 715                 720

Glu Leu Ala Pro Ile Val Ala Pro Asn Phe Thr Val Glu Asp Thr Ser
                725                 730                 735

Ala Asp Ser Ile Leu Val Lys Trp Glu Asp Ile Pro Val Glu Glu Leu
            740                 745                 750

Arg Gly Phe Leu Arg Gly Tyr Leu Phe Tyr Phe Gly Lys Gly Glu Arg
        755                 760                 765

Asp Thr Ser Lys Met Arg Val Leu Glu Ser Gly Arg Ser Asp Ile Lys
    770                 775                 780

Val Lys Asn Ile Thr Asp Ile Ser Gln Lys Thr Leu Arg Ile Ala Asp
785                 790                 795                 800

Leu Gln Gly Lys Thr Ser Tyr His Leu Val Leu Arg Ala Tyr Thr Asp
                805                 810                 815

Gly Gly Val Gly Pro Glu Lys Ser Met Tyr Val Val Thr Lys Glu Asn
            820                 825                 830

Ser Val Gly Leu Ile Ile Ala Ile Leu Ile Pro Val Ala Val Ala Val
        835                 840                 845
```

```
Ile Val Gly Val Val Thr Ser Ile Leu Cys Tyr Arg Lys Arg Glu Trp
    850                 855                 860

Ile Lys Glu Thr Phe Tyr Pro Asp Ile Pro Asn Pro Glu Asn Cys Lys
865                 870                 875                 880

Ala Leu Gln Phe Gln Lys Ser Val Cys Glu Gly Ser Ser Ala Leu Lys
                885                 890                 895

Thr Leu Glu Met Asn Pro Cys Thr Pro Asn Asn Val Glu Val Leu Glu
            900                 905                 910

Thr Arg Ser Ala Phe Pro Lys Ile Glu Asp Thr Glu Ile Ile Ser Pro
        915                 920                 925

Val Ala Glu Arg Pro Glu Asp Arg Ser Asp Ala Glu Pro Glu Asn His
    930                 935                 940

Val Val Val Ser Tyr Cys Pro Pro Ile Ile Glu Glu Glu Ile Pro Asn
945                 950                 955                 960

Pro Ala Ala Asp Glu Ala Gly Gly Thr Ala Gln Val Ile Tyr Ile Asp
                965                 970                 975

Val Gln Ser Met Tyr Gln Pro Gln Ala Lys Pro Glu Glu Glu Gln Glu
            980                 985                 990

Asn Asp Pro Val Gly Gly Ala Gly  Tyr Lys Pro Gln Met  His Leu Pro
        995                 1000                1005

Ile Asn  Ser Thr Val Glu Asp  Ile Ala Ala Glu Glu  Asp Leu Asp
    1010                1015                1020

Lys Thr  Ala Gly Tyr Arg Pro  Gln Ala Asn Val Asn  Thr Trp Asn
    1025                1030                1035

Leu Val  Ser Pro Asp Ser Pro  Arg Ser Ile Asp Ser  Asn Ser Glu
    1040                1045                1050

Ile Val  Ser Phe Gly Ser Pro  Cys Ser Ile Asn Ser  Arg Gln Phe
    1055                1060                1065

Leu Ile  Pro Pro Lys Asp Glu  Asp Ser Pro Lys Ser  Asn Gly Gly
    1070                1075                1080

Gly Trp  Ser Phe Thr Asn Phe  Phe Gln Asn Lys Pro  Asn Asp
    1085                1090                1095

<210>  326
<211>  342
<212>  PRT
```

<213> Homo sapiens

<400> 326

```
Met Ala Leu Phe Ala Val Phe Gln Thr Thr Phe Phe Leu Thr Leu Leu
1               5                  10                  15

Ser Leu Arg Thr Tyr Gln Ser Glu Val Leu Ala Glu Arg Leu Pro Leu
            20                  25                  30

Thr Pro Val Ser Leu Lys Val Ser Thr Asn Ser Thr Arg Gln Ser Leu
        35                  40                  45

His Leu Gln Trp Thr Val His Asn Leu Pro Tyr His Gln Glu Leu Lys
    50                  55                  60

Met Val Phe Gln Ile Gln Ile Ser Arg Ile Glu Thr Ser Asn Val Ile
65                  70                  75                  80

Trp Val Gly Asn Tyr Ser Thr Thr Val Lys Trp Asn Gln Val Leu His
                85                  90                  95

Trp Ser Trp Glu Ser Glu Leu Pro Leu Glu Cys Ala Thr His Phe Val
            100                 105                 110

Arg Ile Lys Ser Leu Val Asp Asp Ala Lys Phe Pro Glu Pro Asn Phe
        115                 120                 125

Trp Ser Asn Trp Ser Ser Trp Glu Glu Val Ser Val Gln Asp Ser Thr
    130                 135                 140

Gly Gln Asp Ile Leu Phe Val Phe Pro Lys Asp Lys Leu Val Glu Glu
145                 150                 155                 160

Gly Thr Asn Val Thr Ile Cys Tyr Val Ser Arg Asn Ile Gln Asn Asn
                165                 170                 175

Val Ser Cys Tyr Leu Glu Gly Lys Gln Ile His Gly Glu Gln Leu Asp
            180                 185                 190

Pro His Val Thr Ala Phe Asn Leu Asn Ser Val Pro Phe Ile Arg Asn
        195                 200                 205

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

Gly Met Lys Gly Ile Val Leu Phe Val Ser Lys Val Leu Glu Glu Pro
225                 230                 235                 240

Lys Asp Phe Ser Cys Glu Thr Glu Asp Phe Lys Thr Leu His Cys Thr
                245                 250                 255
```

Trp Asp Pro Gly Thr Asp Thr Ala Leu Gly Trp Ser Lys Gln Pro Ser
260 265 270

Gln Ser Tyr Thr Leu Phe Glu Ser Phe Ser Gly Glu Lys Lys Leu Cys
275 280 285

Thr His Lys Asn Trp Cys Asn Trp Gln Ile Thr Gln Asp Ser Gln Glu
290 295 300

Thr Tyr Asn Phe Thr Leu Ile Ala Glu Asn Tyr Leu Arg Lys Arg Ser
305 310 315 320

Val Asn Ile Leu Phe Asn Leu Thr His Arg Gly Glu Thr Arg Val Val
325 330 335

Thr Ala His Arg Gly His
340

<210> 327
<211> 660
<212> PRT
<213> Homo sapiens

<400> 327

Met Glu Pro Leu Val Thr Trp Val Val Pro Leu Leu Phe Leu Phe Leu
1 5 10 15

Leu Ser Arg Gln Gly Ala Ala Cys Arg Thr Ser Glu Cys Cys Phe Gln
20 25 30

Asp Pro Pro Tyr Pro Asp Ala Asp Ser Gly Ser Ala Ser Gly Pro Arg
35 40 45

Asp Leu Arg Cys Tyr Arg Ile Ser Ser Asp Arg Tyr Glu Cys Ser Trp
50 55 60

Gln Tyr Glu Gly Pro Thr Ala Gly Val Ser His Phe Leu Arg Cys Cys
65 70 75 80

Leu Ser Ser Gly Arg Cys Cys Tyr Phe Ala Ala Gly Ser Ala Thr Arg
85 90 95

Leu Gln Phe Ser Asp Gln Ala Gly Val Ser Val Leu Tyr Thr Val Thr
100 105 110

Leu Trp Val Glu Ser Trp Ala Arg Asn Gln Thr Glu Lys Ser Pro Glu
115 120 125

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

Asp Ile Lys Val Ser Lys Leu Ala Gly Gln Leu Arg Met Glu Trp Glu

145 150 155 160

Thr Pro Asp Asn Gln Val Gly Ala Glu Val Gln Phe Arg His Arg Thr
165 170 175

Pro Ser Ser Pro Trp Lys Leu Gly Asp Cys Gly Pro Gln Asp Asp Asp
180 185 190

Thr Glu Ser Cys Leu Cys Pro Leu Glu Met Asn Val Ala Gln Glu Phe
195 200 205

Gln Leu Arg Arg Arg Gln Leu Gly Ser Gln Gly Ser Ser Trp Ser Lys
210 215 220

Trp Ser Ser Pro Val Cys Val Pro Pro Glu Asn Pro Pro Gln Pro Gln
225 230 235 240

Val Arg Phe Ser Val Glu Gln Leu Gly Gln Asp Gly Arg Arg Arg Leu
245 250 255

Thr Leu Lys Glu Gln Pro Thr Gln Leu Glu Leu Pro Glu Gly Cys Gln
260 265 270

Gly Leu Ala Pro Gly Thr Glu Val Thr Tyr Arg Leu Gln Leu His Met
275 280 285

Leu Ser Cys Pro Cys Lys Ala Lys Ala Thr Arg Thr Leu His Leu Gly
290 295 300

Lys Met Pro Tyr Leu Ser Gly Ala Ala Tyr Asn Val Ala Val Ile Ser
305 310 315 320

Ser Asn Gln Phe Gly Pro Gly Leu Asn Gln Thr Trp His Ile Pro Ala
325 330 335

Asp Thr His Thr Glu Pro Val Ala Leu Asn Ile Ser Val Gly Thr Asn
340 345 350

Gly Thr Thr Met Tyr Trp Pro Ala Arg Ala Gln Ser Met Thr Tyr Cys
355 360 365

Ile Glu Trp Gln Pro Val Gly Gln Asp Gly Gly Leu Ala Thr Cys Ser
370 375 380

Leu Thr Ala Pro Gln Asp Pro Asp Pro Ala Gly Met Ala Thr Tyr Ser
385 390 395 400

Trp Ser Arg Glu Ser Gly Ala Met Gly Gln Glu Lys Cys Tyr Tyr Ile
405 410 415

Thr Ile Phe Ala Ser Ala His Pro Glu Lys Leu Thr Leu Trp Ser Thr

420 425 430

Val Leu Ser Thr Tyr His Phe Gly Gly Asn Ala Ser Ala Ala Gly Thr
435 440 445

Pro His His Val Ser Val Lys Asn His Ser Leu Asp Ser Val Ser Val
450 455 460

Asp Trp Ala Pro Ser Leu Leu Ser Thr Cys Pro Gly Val Leu Lys Glu
465 470 475 480

Tyr Val Val Arg Cys Arg Asp Glu Asp Ser Lys Gln Val Ser Glu His
485 490 495

Pro Val Gln Pro Thr Glu Thr Gln Val Thr Leu Ser Gly Leu Arg Ala
500 505 510

Gly Val Ala Tyr Thr Val Gln Val Arg Ala Asp Thr Ala Trp Leu Arg
515 520 525

Gly Val Trp Ser Gln Pro Gln Arg Phe Ser Ile Glu Val Gln Val Ser
530 535 540

Asp Trp Leu Ile Phe Phe Ala Ser Leu Gly Ser Phe Leu Ser Ile Leu
545 550 555 560

Leu Val Gly Val Leu Gly Tyr Leu Gly Leu Asn Arg Ala Ala Arg His
565 570 575

Leu Cys Pro Pro Leu Pro Thr Pro Cys Ala Ser Ser Ala Ile Glu Phe
580 585 590

Pro Gly Gly Lys Glu Thr Trp Gln Trp Ile Asn Pro Val Asp Phe Gln
595 600 605

Glu Glu Ala Ser Leu Gln Glu Ala Leu Val Val Glu Met Ser Trp Asp
610 615 620

Lys Gly Glu Arg Thr Glu Pro Leu Glu Lys Thr Glu Leu Pro Glu Gly
625 630 635 640

Ala Pro Glu Leu Ala Leu Asp Thr Glu Leu Ser Leu Glu Asp Gly Asp
645 650 655

Arg Cys Asp Arg
660

<210> 328
<211> 659
<212> PRT
<213> Homo sapiens

<400> 328

```
Met Ala His Thr Phe Arg Gly Cys Ser Leu Ala Phe Met Phe Ile Ile
1               5                  10                  15

Thr Trp Leu Leu Ile Lys Ala Lys Ile Asp Ala Cys Lys Arg Gly Asp
            20                  25                  30

Val Thr Val Lys Pro Ser His Val Ile Leu Leu Gly Ser Thr Val Asn
        35                  40                  45

Ile Thr Cys Ser Leu Lys Pro Arg Gln Gly Cys Phe His Tyr Ser Arg
    50                  55                  60

Arg Asn Lys Leu Ile Leu Tyr Lys Phe Asp Arg Arg Ile Asn Phe His
65                  70                  75                  80

His Gly His Ser Leu Asn Ser Gln Val Thr Gly Leu Pro Leu Gly Thr
                85                  90                  95

Thr Leu Phe Val Cys Lys Leu Ala Cys Ile Asn Ser Asp Glu Ile Gln
            100                 105                 110

Ile Cys Gly Ala Glu Ile Phe Val Gly Val Ala Pro Glu Gln Pro Gln
        115                 120                 125

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

Trp Glu Arg Gly Arg Asp Thr His Leu Tyr Thr Glu Tyr Thr Leu Gln
145                 150                 155                 160

Leu Ser Gly Pro Lys Asn Leu Thr Trp Gln Lys Gln Cys Lys Asp Ile
                165                 170                 175

Tyr Cys Asp Tyr Leu Asp Phe Gly Ile Asn Leu Thr Pro Glu Ser Pro
            180                 185                 190

Glu Ser Asn Phe Thr Ala Lys Val Thr Ala Val Asn Ser Leu Gly Ser
        195                 200                 205

Ser Ser Ser Leu Pro Ser Thr Phe Thr Phe Leu Asp Ile Val Arg Pro
    210                 215                 220

Leu Pro Pro Trp Asp Ile Arg Ile Lys Phe Gln Lys Ala Ser Val Ser
225                 230                 235                 240

Arg Cys Thr Leu Tyr Trp Arg Asp Glu Gly Leu Val Leu Leu Asn Arg
                245                 250                 255

Leu Arg Tyr Arg Pro Ser Asn Ser Arg Leu Trp Asn Met Val Asn Val
            260                 265                 270
```

```
Thr Lys Ala Lys Gly Arg His Asp Leu Leu Asp Leu Lys Pro Phe Thr
        275                 280                 285

Glu Tyr Glu Phe Gln Ile Ser Ser Lys Leu His Leu Tyr Lys Gly Ser
    290                 295                 300

Trp Ser Asp Trp Ser Glu Ser Leu Arg Ala Gln Thr Pro Glu Glu Glu
305                 310                 315                 320

Pro Thr Gly Met Leu Asp Val Trp Tyr Met Lys Arg His Ile Asp Tyr
                325                 330                 335

Ser Arg Gln Gln Ile Ser Leu Phe Trp Lys Asn Leu Ser Val Ser Glu
            340                 345                 350

Ala Arg Gly Lys Ile Leu His Tyr Gln Val Thr Leu Gln Glu Leu Thr
        355                 360                 365

Gly Gly Lys Ala Met Thr Gln Asn Ile Thr Gly His Thr Ser Trp Thr
    370                 375                 380

Thr Val Ile Pro Arg Thr Gly Asn Trp Ala Val Ala Val Ser Ala Ala
385                 390                 395                 400

Asn Ser Lys Gly Ser Ser Leu Pro Thr Arg Ile Asn Ile Met Asn Leu
                405                 410                 415

Cys Glu Ala Gly Leu Leu Ala Pro Arg Gln Val Ser Ala Asn Ser Glu
            420                 425                 430

Gly Met Asp Asn Ile Leu Val Thr Trp Gln Pro Pro Arg Lys Asp Pro
        435                 440                 445

Ser Ala Val Gln Glu Tyr Val Val Glu Trp Arg Glu Leu His Pro Gly
    450                 455                 460

Gly Asp Thr Gln Val Pro Leu Asn Trp Leu Arg Ser Arg Pro Tyr Asn
465                 470                 475                 480

Val Ser Ala Leu Ile Ser Glu Asn Ile Lys Ser Tyr Ile Cys Tyr Glu
                485                 490                 495

Ile Arg Val Tyr Ala Leu Ser Gly Asp Gln Gly Gly Cys Ser Ser Ile
            500                 505                 510

Leu Gly Asn Ser Lys His Lys Ala Pro Leu Ser Gly Pro His Ile Asn
        515                 520                 525

Ala Ile Thr Glu Glu Lys Gly Ser Ile Leu Ile Ser Trp Asn Ser Ile
    530                 535                 540
```

Pro Val Gln Glu Gln Met Gly Cys Leu Leu His Tyr Arg Ile Tyr Trp
545 550 555 560

Lys Glu Arg Asp Ser Asn Ser Gln Pro Gln Leu Cys Glu Ile Pro Tyr
565 570 575

Arg Val Ser Gln Asn Ser His Pro Ile Asn Ser Leu Gln Pro Arg Val
580 585 590

Thr Tyr Val Leu Trp Met Thr Ala Leu Thr Ala Ala Gly Glu Ser Ser
595 600 605

His Gly Asn Glu Arg Glu Phe Cys Leu Gln Gly Lys Ala Asn Trp Met
610 615 620

Ala Phe Val Ala Pro Ser Ile Cys Ile Ala Ile Ile Met Val Gly Ile
625 630 635 640

Phe Ser Thr His Tyr Phe Gln Gln Lys Arg Arg His Ser Cys Pro Trp
645 650 655

Thr Gly Ser

<210> 329
<211> 629
<212> PRT
<213> Homo sapiens

<400> 329

Met Asn Gln Val Thr Ile Gln Trp Asp Ala Val Ile Ala Leu Tyr Ile
1 5 10 15

Leu Phe Ser Trp Cys His Gly Gly Ile Thr Asn Ile Asn Cys Ser Gly
20 25 30

His Ile Trp Val Glu Pro Ala Thr Ile Phe Lys Met Gly Met Asn Ile
35 40 45

Ser Ile Tyr Cys Gln Ala Ala Ile Lys Asn Cys Gln Pro Arg Lys Leu
50 55 60

His Phe Tyr Lys Asn Gly Ile Lys Glu Arg Phe Gln Ile Thr Arg Ile
65 70 75 80

Asn Lys Thr Thr Ala Arg Leu Trp Tyr Lys Asn Phe Leu Glu Pro His
85 90 95

Ala Ser Met Tyr Cys Thr Ala Glu Cys Pro Lys His Phe Gln Glu Thr
100 105 110

```
Leu Ile Cys Gly Lys Asp Ile Ser Ser Gly Tyr Pro Pro Asp Ile Pro
        115                 120                 125

Asp Glu Val Thr Cys Val Ile Tyr Glu Tyr Ser Gly Asn Met Thr Cys
    130                 135                 140

Thr Trp Asn Ala Gly Lys Leu Thr Tyr Ile Asp Thr Lys Tyr Val Val
145                 150                 155                 160

His Val Lys Ser Leu Glu Thr Glu Glu Glu Gln Gln Tyr Leu Thr Ser
                165                 170                 175

Ser Tyr Ile Asn Ile Ser Thr Asp Ser Leu Gln Gly Gly Lys Lys Tyr
            180                 185                 190

Leu Val Trp Val Gln Ala Ala Asn Ala Leu Gly Met Glu Glu Ser Lys
        195                 200                 205

Gln Leu Gln Ile His Leu Asp Asp Ile Val Ile Pro Ser Ala Ala Val
    210                 215                 220

Ile Ser Arg Ala Glu Thr Ile Asn Ala Thr Val Pro Lys Thr Ile Ile
225                 230                 235                 240

Tyr Trp Asp Ser Gln Thr Thr Ile Glu Lys Val Ser Cys Glu Met Arg
                245                 250                 255

Tyr Lys Ala Thr Thr Asn Gln Thr Trp Asn Val Lys Glu Phe Asp Thr
            260                 265                 270

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

Lys Tyr Val Phe Gln Val Arg Cys Gln Glu Thr Gly Lys Arg Tyr Trp
    290                 295                 300

Gln Pro Trp Ser Ser Leu Phe Phe His Lys Thr Pro Glu Thr Val Pro
305                 310                 315                 320

Gln Val Thr Ser Lys Ala Phe Gln His Asp Thr Trp Asn Ser Gly Leu
                325                 330                 335

Thr Val Ala Ser Ile Ser Thr Gly His Leu Thr Ser Asp Asn Arg Gly
            340                 345                 350

Asp Ile Gly Leu Leu Leu Gly Met Ile Val Phe Ala Val Met Leu Ser
        355                 360                 365

Ile Leu Ser Leu Ile Gly Ile Phe Asn Arg Ser Phe Arg Thr Gly Ile
    370                 375                 380
```

```
Lys Arg Arg Ile Leu Leu Leu Ile Pro Lys Trp Leu Tyr Glu Asp Ile
385                 390                 395                 400

Pro Asn Met Lys Asn Ser Asn Val Val Lys Met Leu Gln Glu Asn Ser
                405                 410                 415

Glu Leu Met Asn Asn Asn Ser Ser Glu Gln Val Leu Tyr Val Asp Pro
            420                 425                 430

Met Ile Thr Glu Ile Lys Glu Ile Phe Ile Pro Glu His Lys Pro Thr
        435                 440                 445

Asp Tyr Lys Lys Glu Asn Thr Gly Pro Leu Glu Thr Arg Asp Tyr Pro
    450                 455                 460

Gln Asn Ser Leu Phe Asp Asn Thr Thr Val Val Tyr Ile Pro Asp Leu
465                 470                 475                 480

Asn Thr Gly Tyr Lys Pro Gln Ile Ser Asn Phe Leu Pro Glu Gly Ser
                485                 490                 495

His Leu Ser Asn Asn Asn Glu Ile Thr Ser Leu Thr Leu Lys Pro Pro
            500                 505                 510

Val Asp Ser Leu Asp Ser Gly Asn Asn Pro Arg Leu Gln Lys His Pro
        515                 520                 525

Asn Phe Ala Phe Ser Val Ser Ser Val Asn Ser Leu Ser Asn Thr Ile
    530                 535                 540

Phe Leu Gly Glu Leu Ser Leu Ile Leu Asn Gln Gly Glu Cys Ser Ser
545                 550                 555                 560

Pro Asp Ile Gln Asn Ser Val Glu Glu Glu Thr Thr Met Leu Leu Glu
                565                 570                 575

Asn Asp Ser Pro Ser Glu Thr Ile Pro Glu Gln Thr Leu Leu Pro Asp
            580                 585                 590

Glu Phe Val Ser Cys Leu Gly Ile Val Asn Glu Glu Leu Pro Ser Ile
        595                 600                 605

Asn Thr Tyr Phe Pro Gln Asn Ile Leu Glu Ser His Phe Asn Arg Ile
    610                 615                 620

Ser Leu Leu Glu Lys
625
```

<210> 330
<211> 508
<212> PRT

<213> Homo sapiens

<400> 330

```
Met Asp His Leu Gly Ala Ser Leu Trp Pro Gln Val Gly Ser Leu Cys
1               5                  10                  15

Leu Leu Leu Ala Gly Ala Ala Trp Ala Pro Pro Pro Asn Leu Pro Asp
            20                  25                  30

Pro Lys Phe Glu Ser Lys Ala Ala Leu Leu Ala Ala Arg Gly Pro Glu
        35                  40                  45

Glu Leu Leu Cys Phe Thr Glu Arg Leu Glu Asp Leu Val Cys Phe Trp
    50                  55                  60

Glu Glu Ala Ala Ser Ala Gly Val Gly Pro Gly Asn Tyr Ser Phe Ser
65                  70                  75                  80

Tyr Gln Leu Glu Asp Glu Pro Trp Lys Leu Cys Arg Leu His Gln Ala
                85                  90                  95

Pro Thr Ala Arg Gly Ala Val Arg Phe Trp Cys Ser Leu Pro Thr Ala
            100                 105                 110

Asp Thr Ser Ser Phe Val Pro Leu Glu Leu Arg Val Thr Ala Ala Ser
        115                 120                 125

Gly Ala Pro Arg Tyr His Arg Val Ile His Ile Asn Glu Val Val Leu
    130                 135                 140

Leu Asp Ala Pro Val Gly Leu Val Ala Arg Leu Ala Asp Glu Ser Gly
145                 150                 155                 160

His Val Val Leu Arg Trp Leu Pro Pro Pro Glu Thr Pro Met Thr Ser
                165                 170                 175

His Ile Arg Tyr Glu Val Asp Val Ser Ala Gly Asn Gly Ala Gly Ser
            180                 185                 190

Val Gln Arg Val Glu Ile Leu Glu Gly Arg Thr Glu Cys Val Leu Ser
        195                 200                 205

Asn Leu Arg Gly Arg Thr Arg Tyr Thr Phe Ala Val Arg Ala Arg Met
    210                 215                 220

Ala Glu Pro Ser Phe Gly Gly Phe Trp Ser Ala Trp Ser Glu Pro Val
225                 230                 235                 240

Ser Leu Leu Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser
                245                 250                 255
```

```
Leu Ile Leu Val Val Ile Leu Val Leu Leu Thr Val Leu Ala Leu Leu
            260                 265                 270

Ser His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser
        275                 280                 285

Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe
    290                 295                 300

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

Thr Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu
                325                 330                 335

Arg Cys Trp Gly Thr Met Gln Ala Val Glu Pro Gly Thr Asp Asp Glu
            340                 345                 350

Gly Pro Leu Leu Glu Pro Val Gly Ser Glu His Ala Gln Asp Thr Tyr
        355                 360                 365

Leu Val Leu Asp Lys Trp Leu Leu Pro Arg Asn Pro Pro Ser Glu Asp
    370                 375                 380

Leu Pro Gly Pro Gly Gly Ser Val Asp Ile Val Ala Met Asp Glu Gly
385                 390                 395                 400

Ser Glu Ala Ser Ser Cys Ser Ser Ala Leu Ala Ser Lys Pro Ser Pro
                405                 410                 415

Glu Gly Ala Ser Ala Ala Ser Phe Glu Tyr Thr Ile Leu Asp Pro Ser
            420                 425                 430

Ser Gln Leu Leu Arg Pro Trp Thr Leu Cys Pro Glu Leu Pro Pro Thr
        435                 440                 445

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

Ser Thr Asp Tyr Ser Ser Gly Asp Ser Gln Gly Ala Gln Gly Gly Leu
465                 470                 475                 480

Ser Asp Gly Pro Tyr Ser Asn Pro Tyr Glu Asn Ser Leu Ile Pro Ala
                485                 490                 495

Ala Glu Pro Leu Pro Pro Ser Tyr Val Ala Cys Ser
            500                 505
```

<210> 331
<211> 836
<212> PRT
<213> Homo sapiens

<400> 331

```
Met Ala Arg Leu Gly Asn Cys Ser Leu Thr Trp Ala Ala Leu Ile Ile
1               5                  10                  15

Leu Leu Leu Pro Gly Ser Leu Glu Glu Cys Gly His Ile Ser Val Ser
            20                  25                  30

Ala Pro Ile Val His Leu Gly Asp Pro Ile Thr Ala Ser Cys Ile Ile
        35                  40                  45

Lys Gln Asn Cys Ser His Leu Asp Pro Glu Pro Gln Ile Leu Trp Arg
    50                  55                  60

Leu Gly Ala Glu Leu Gln Pro Gly Gly Arg Gln Gln Arg Leu Ser Asp
65                  70                  75                  80

Gly Thr Gln Glu Ser Ile Ile Thr Leu Pro His Leu Asn His Thr Gln
                85                  90                  95

Ala Phe Leu Ser Cys Cys Leu Asn Trp Gly Asn Ser Leu Gln Ile Leu
            100                 105                 110

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

Leu Ser Cys Leu Met Asn Leu Thr Thr Ser Ser Leu Ile Cys Gln Trp
    130                 135                 140

Glu Pro Gly Pro Glu Thr His Leu Pro Thr Ser Phe Thr Leu Lys Ser
145                 150                 155                 160

Phe Lys Ser Arg Gly Asn Cys Gln Thr Gln Gly Asp Ser Ile Leu Asp
                165                 170                 175

Cys Val Pro Lys Asp Gly Gln Ser His Cys Cys Ile Pro Arg Lys His
            180                 185                 190

Leu Leu Leu Tyr Gln Asn Met Gly Ile Trp Val Gln Ala Glu Asn Ala
        195                 200                 205

Leu Gly Thr Ser Met Ser Pro Gln Leu Cys Leu Asp Pro Met Asp Val
    210                 215                 220

Val Lys Leu Glu Pro Pro Met Leu Arg Thr Met Asp Pro Ser Pro Glu
225                 230                 235                 240

Ala Ala Pro Pro Gln Ala Gly Cys Leu Gln Leu Cys Trp Glu Pro Trp
                245                 250                 255

Gln Pro Gly Leu His Ile Asn Gln Lys Cys Glu Leu Arg His Lys Pro
```

260 265 270

Gln Arg Gly Glu Ala Ser Trp Ala Leu Val Gly Pro Leu Pro Leu Glu
275 280 285

Ala Leu Gln Tyr Glu Leu Cys Gly Leu Leu Pro Ala Thr Ala Tyr Thr
290 295 300

Leu Gln Ile Arg Cys Ile Arg Trp Pro Leu Pro Gly His Trp Ser Asp
305 310 315 320

Trp Ser Pro Ser Leu Glu Leu Arg Thr Thr Glu Arg Ala Pro Thr Val
325 330 335

Arg Leu Asp Thr Trp Trp Arg Gln Arg Gln Leu Asp Pro Arg Thr Val
340 345 350

Gln Leu Phe Trp Lys Pro Val Pro Leu Glu Glu Asp Ser Gly Arg Ile
355 360 365

Gln Gly Tyr Val Val Ser Trp Arg Pro Ser Gly Gln Ala Gly Ala Ile
370 375 380

Leu Pro Leu Cys Asn Thr Thr Glu Leu Ser Cys Thr Phe His Leu Pro
385 390 395 400

Ser Glu Ala Gln Glu Val Ala Leu Val Ala Tyr Asn Ser Ala Gly Thr
405 410 415

Ser Arg Pro Thr Pro Val Val Phe Ser Glu Ser Arg Gly Pro Ala Leu
420 425 430

Thr Arg Leu His Ala Met Ala Arg Asp Pro His Ser Leu Trp Val Gly
435 440 445

Trp Glu Pro Pro Asn Pro Trp Pro Gln Gly Tyr Val Ile Glu Trp Gly
450 455 460

Leu Gly Pro Pro Ser Ala Ser Asn Ser Asn Lys Thr Trp Arg Met Glu
465 470 475 480

Gln Asn Gly Arg Ala Thr Gly Phe Leu Leu Lys Glu Asn Ile Arg Pro
485 490 495

Phe Gln Leu Tyr Glu Ile Ile Val Thr Pro Leu Tyr Gln Asp Thr Met
500 505 510

Gly Pro Ser Gln His Val Tyr Ala Tyr Ser Gln Glu Met Ala Pro Ser
515 520 525

His Ala Pro Glu Leu His Leu Lys His Ile Gly Lys Thr Trp Ala Gln

530 535 540

Leu Glu Trp Val Pro Glu Pro Pro Glu Leu Gly Lys Ser Pro Leu Thr
545 550 555 560

His Tyr Thr Ile Phe Trp Thr Asn Ala Gln Asn Gln Ser Phe Ser Ala
565 570 575

Ile Leu Asn Ala Ser Ser Arg Gly Phe Val Leu His Gly Leu Glu Pro
580 585 590

Ala Ser Leu Tyr His Ile His Leu Met Ala Ala Ser Gln Ala Gly Ala
595 600 605

Thr Asn Ser Thr Val Leu Thr Leu Met Thr Leu Thr Pro Glu Gly Ser
610 615 620

Glu Leu His Ile Ile Leu Gly Leu Phe Gly Leu Leu Leu Leu Leu Thr
625 630 635 640

Cys Leu Cys Gly Thr Ala Trp Leu Cys Cys Ser Pro Asn Arg Lys Asn
645 650 655

Pro Leu Trp Pro Ser Val Pro Asp Pro Ala His Ser Ser Leu Gly Ser
660 665 670

Trp Val Pro Thr Ile Met Glu Glu Asp Ala Phe Gln Leu Pro Gly Leu
675 680 685

Gly Thr Pro Pro Ile Thr Lys Leu Thr Val Leu Glu Glu Asp Glu Lys
690 695 700

Lys Pro Val Pro Trp Glu Ser His Asn Ser Ser Glu Thr Cys Gly Leu
705 710 715 720

Pro Thr Leu Val Gln Thr Tyr Val Leu Gln Gly Asp Pro Arg Ala Val
725 730 735

Ser Thr Gln Pro Gln Ser Gln Ser Gly Thr Ser Asp Gln Val Leu Tyr
740 745 750

Gly Gln Leu Leu Gly Ser Pro Thr Ser Pro Gly Pro Gly His Tyr Leu
755 760 765

Arg Cys Asp Ser Thr Gln Pro Leu Leu Ala Gly Leu Thr Pro Ser Pro
770 775 780

Lys Ser Tyr Glu Asn Leu Trp Phe Gln Ala Ser Pro Leu Gly Thr Leu
785 790 795 800

Val Thr Pro Ala Pro Ser Gln Glu Asp Asp Cys Val Phe Gly Pro Leu

805 810 815

Leu Asn Phe Pro Leu Leu Gln Gly Ile Arg Val His Gly Met Glu Ala
820 825 830

Leu Gly Ser Phe
835

<210> 332
<211> 638
<212> PRT
<213> Homo sapiens

<400> 332

Met Asp Leu Trp Gln Leu Leu Leu Thr Leu Ala Leu Ala Gly Ser Ser
1 5 10 15

Asp Ala Phe Ser Gly Ser Glu Ala Thr Ala Ala Ile Leu Ser Arg Ala
20 25 30

Pro Trp Ser Leu Gln Ser Val Asn Pro Gly Leu Lys Thr Asn Ser Ser
35 40 45

Lys Glu Pro Lys Phe Thr Lys Cys Arg Ser Pro Glu Arg Glu Thr Phe
50 55 60

Ser Cys His Trp Thr Asp Glu Val His His Gly Thr Lys Asn Leu Gly
65 70 75 80

Pro Ile Gln Leu Phe Tyr Thr Arg Arg Asn Thr Gln Glu Trp Thr Gln
85 90 95

Glu Trp Lys Glu Cys Pro Asp Tyr Val Ser Ala Gly Glu Asn Ser Cys
100 105 110

Tyr Phe Asn Ser Ser Phe Thr Ser Ile Trp Ile Pro Tyr Cys Ile Lys
115 120 125

Leu Thr Ser Asn Gly Gly Thr Val Asp Glu Lys Cys Phe Ser Val Asp
130 135 140

Glu Ile Val Gln Pro Asp Pro Pro Ile Ala Leu Asn Trp Thr Leu Leu
145 150 155 160

Asn Val Ser Leu Thr Gly Ile His Ala Asp Ile Gln Val Arg Trp Glu
165 170 175

Ala Pro Arg Asn Ala Asp Ile Gln Lys Gly Trp Met Val Leu Glu Tyr
180 185 190

Glu Leu Gln Tyr Lys Glu Val Asn Glu Thr Lys Trp Lys Met Met Asp
195 200 205

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Pro Ile Leu Thr Thr Ser Val Pro Val Tyr Ser Leu Lys Val Asp Lys
    210                 215                 220

Glu Tyr Glu Val Arg Val Arg Ser Lys Gln Arg Asn Ser Gly Asn Tyr
225                 230                 235                 240

Gly Glu Phe Ser Glu Val Leu Tyr Val Thr Leu Pro Gln Met Ser Gln
                245                 250                 255

Phe Thr Cys Glu Glu Asp Phe Tyr Phe Pro Trp Leu Leu Ile Ile Ile
            260                 265                 270

Phe Gly Ile Phe Gly Leu Thr Val Met Leu Phe Val Phe Leu Phe Ser
        275                 280                 285

Lys Gln Gln Arg Ile Lys Met Leu Ile Leu Pro Pro Val Pro Val Pro
    290                 295                 300

Lys Ile Lys Gly Ile Asp Pro Asp Leu Leu Lys Glu Gly Lys Leu Glu
305                 310                 315                 320

Glu Val Asn Thr Ile Leu Ala Ile His Asp Ser Tyr Lys Pro Glu Phe
                325                 330                 335

His Ser Asp Asp Ser Trp Val Glu Phe Ile Glu Leu Asp Ile Asp Glu
            340                 345                 350

Pro Asp Glu Lys Thr Glu Glu Ser Asp Thr Asp Arg Leu Leu Ser Ser
        355                 360                 365

Asp His Glu Lys Ser His Ser Asn Leu Gly Val Lys Asp Gly Asp Ser
    370                 375                 380

Gly Arg Thr Ser Cys Cys Glu Pro Asp Ile Leu Glu Thr Asp Phe Asn
385                 390                 395                 400

Ala Asn Asp Ile His Glu Gly Thr Ser Glu Val Ala Gln Pro Gln Arg
                405                 410                 415

Leu Lys Gly Glu Ala Asp Leu Leu Cys Leu Asp Gln Lys Asn Gln Asn
            420                 425                 430

Asn Ser Pro Tyr His Asp Ala Cys Pro Ala Thr Gln Gln Pro Ser Val
        435                 440                 445

Ile Gln Ala Glu Lys Asn Lys Pro Gln Pro Leu Pro Thr Glu Gly Ala
    450                 455                 460

Glu Ser Thr His Gln Ala Ala His Ile Gln Leu Ser Asn Pro Ser Ser
465                 470                 475                 480
```

```
Leu Ser Asn Ile Asp Phe Tyr Ala Gln Val Ser Asp Ile Thr Pro Ala
                485                 490                 495

Gly Ser Val Val Leu Ser Pro Gly Gln Lys Asn Lys Ala Gly Met Ser
            500                 505                 510

Gln Cys Asp Met His Pro Glu Met Val Ser Leu Cys Gln Glu Asn Phe
        515                 520                 525

Leu Met Asp Asn Ala Tyr Phe Cys Glu Ala Asp Ala Lys Lys Cys Ile
    530                 535                 540

Pro Val Ala Pro His Ile Lys Val Glu Ser His Ile Gln Pro Ser Leu
545                 550                 555                 560

Asn Gln Glu Asp Ile Tyr Ile Thr Thr Glu Ser Leu Thr Thr Ala Ala
                565                 570                 575

Gly Arg Pro Gly Thr Gly Glu His Val Pro Gly Ser Glu Met Pro Val
            580                 585                 590

Pro Asp Tyr Thr Ser Ile His Ile Val Gln Ser Pro Gln Gly Leu Ile
        595                 600                 605

Leu Asn Ala Thr Ala Leu Pro Leu Pro Asp Lys Glu Phe Leu Ser Ser
    610                 615                 620

Cys Gly Tyr Val Ser Thr Asp Gln Leu Asn Lys Ile Met Pro
625                 630                 635


<210>  333
<211>  622
<212>  PRT
<213>  Homo sapiens

<400>  333

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

Leu Asn Thr Cys Leu Leu Asn Gly Gln Leu Pro Pro Gly Lys Pro Glu
            20                  25                  30

Ile Phe Lys Cys Arg Ser Pro Asn Lys Glu Thr Phe Thr Cys Trp Trp
        35                  40                  45

Arg Pro Gly Thr Asp Gly Gly Leu Pro Thr Asn Tyr Ser Leu Thr Tyr
    50                  55                  60

His Arg Glu Gly Glu Thr Leu Met His Glu Cys Pro Asp Tyr Ile Thr
65                  70                  75                  80
```

```
Gly Gly Pro Asn Ser Cys His Phe Gly Lys Gln Tyr Thr Ser Met Trp
                85                  90                  95

Arg Thr Tyr Ile Met Met Val Asn Ala Thr Asn Gln Met Gly Ser Ser
            100                 105                 110

Phe Ser Asp Glu Leu Tyr Val Asp Val Thr Tyr Ile Val Gln Pro Asp
        115                 120                 125

Pro Pro Leu Glu Leu Ala Val Glu Val Lys Gln Pro Glu Asp Arg Lys
    130                 135                 140

Pro Tyr Leu Trp Ile Lys Trp Ser Pro Pro Thr Leu Ile Asp Leu Lys
145                 150                 155                 160

Thr Gly Trp Phe Thr Leu Leu Tyr Glu Ile Arg Leu Lys Pro Glu Lys
                165                 170                 175

Ala Ala Glu Trp Glu Ile His Phe Ala Gly Gln Gln Thr Glu Phe Lys
            180                 185                 190

Ile Leu Ser Leu His Pro Gly Gln Lys Tyr Leu Val Gln Val Arg Cys
        195                 200                 205

Lys Pro Asp His Gly Tyr Trp Ser Ala Trp Ser Pro Ala Thr Phe Ile
    210                 215                 220

Gln Ile Pro Ser Asp Phe Thr Met Asn Asp Thr Thr Val Trp Ile Ser
225                 230                 235                 240

Val Ala Val Leu Ser Ala Val Ile Cys Leu Ile Ile Val Trp Ala Val
                245                 250                 255

Ala Leu Lys Gly Tyr Ser Met Val Thr Cys Ile Phe Pro Pro Val Pro
            260                 265                 270

Gly Pro Lys Ile Lys Gly Phe Asp Ala His Leu Leu Glu Lys Gly Lys
        275                 280                 285

Ser Glu Glu Leu Leu Ser Ala Leu Gly Cys Gln Asp Phe Pro Pro Thr
    290                 295                 300

Ser Asp Tyr Glu Asp Leu Leu Val Glu Tyr Leu Glu Val Asp Asp Ser
305                 310                 315                 320

Glu Asp Gln His Leu Met Ser Val His Ser Lys Glu His Pro Ser Gln
                325                 330                 335

Gly Met Lys Pro Thr Tyr Leu Asp Pro Asp Thr Asp Ser Gly Arg Gly
            340                 345                 350
```

```
Ser Cys Asp Ser Pro Ser Leu Leu Ser Glu Lys Cys Glu Glu Pro Gln
        355                 360                 365

Ala Asn Pro Ser Thr Phe Tyr Asp Pro Glu Val Ile Glu Lys Pro Glu
    370                 375                 380

Asn Pro Glu Thr Thr His Thr Trp Asp Pro Gln Cys Ile Ser Met Glu
385                 390                 395                 400

Gly Lys Ile Pro Tyr Phe His Ala Gly Gly Ser Lys Cys Ser Thr Trp
                405                 410                 415

Pro Leu Pro Gln Pro Ser Gln His Asn Pro Arg Ser Ser Tyr His Asn
            420                 425                 430

Ile Thr Asp Val Cys Glu Leu Ala Val Gly Pro Ala Gly Ala Pro Ala
        435                 440                 445

Thr Leu Leu Asn Glu Ala Gly Lys Asp Ala Leu Lys Ser Ser Gln Thr
    450                 455                 460

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

Ser Phe His Ser Glu Thr Asp Gln Asp Thr Pro Trp Leu Leu Pro Gln
                485                 490                 495

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

His Lys Val Asn Lys Asp Gly Ala Leu Ser Leu Leu Pro Lys Gln Arg
        515                 520                 525

Glu Asn Ser Gly Lys Pro Lys Lys Pro Gly Thr Pro Glu Asn Asn Lys
    530                 535                 540

Glu Tyr Ala Lys Val Ser Gly Val Met Asp Asn Asn Ile Leu Val Leu
545                 550                 555                 560

Val Pro Asp Pro His Ala Lys Asn Val Ala Cys Phe Glu Glu Ser Ala
                565                 570                 575

Lys Glu Ala Pro Pro Ser Leu Glu Gln Asn Gln Ala Glu Lys Ala Leu
            580                 585                 590

Ala Asn Phe Thr Ala Thr Ser Ser Lys Cys Arg Leu Gln Leu Gly Gly
        595                 600                 605

Leu Asp Tyr Leu Asp Pro Ala Cys Phe Thr His Ser Phe His
    610                 615                 620
```

<210> 334
<211> 635
<212> PRT
<213> Homo sapiens

<400> 334

Met Pro Ser Trp Ala Leu Phe Met Val Thr Ser Cys Leu Leu Leu Ala
1 5 10 15

Pro Gln Asn Leu Ala Gln Val Ser Ser Gln Asp Val Ser Leu Leu Ala
20 25 30

Ser Asp Ser Glu Pro Leu Lys Cys Phe Ser Arg Thr Phe Glu Asp Leu
35 40 45

Thr Cys Phe Trp Asp Glu Glu Glu Ala Ala Pro Ser Gly Thr Tyr Gln
50 55 60

Leu Leu Tyr Ala Tyr Pro Arg Glu Lys Pro Arg Ala Cys Pro Leu Ser
65 70 75 80

Ser Gln Ser Met Pro His Phe Gly Thr Arg Tyr Val Cys Gln Phe Pro
85 90 95

Asp Gln Glu Glu Val Arg Leu Phe Phe Pro Leu His Leu Trp Val Lys
100 105 110

Asn Val Phe Leu Asn Gln Thr Arg Thr Gln Arg Val Leu Phe Val Asp
115 120 125

Ser Val Gly Leu Pro Ala Pro Pro Ser Ile Ile Lys Ala Met Gly Gly
130 135 140

Ser Gln Pro Gly Glu Leu Gln Ile Ser Trp Glu Glu Pro Ala Pro Glu
145 150 155 160

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

Lys Asn Ser Thr Gly Pro Thr Val Ile Gln Leu Ile Ala Thr Glu Thr
180 185 190

Cys Cys Pro Ala Leu Gln Arg Pro His Ser Ala Ser Ala Leu Asp Gln
195 200 205

Ser Pro Cys Ala Gln Pro Thr Met Pro Trp Gln Asp Gly Pro Lys Gln
210 215 220

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

```
Cys Leu Ile Ser Gly Leu Gln Pro Gly Asn Ser Tyr Trp Leu Gln Leu
                245                 250                 255

Arg Ser Glu Pro Asp Gly Ile Ser Leu Gly Gly Ser Trp Gly Ser Trp
            260                 265                 270

Ser Leu Pro Val Thr Val Asp Leu Pro Gly Asp Ala Val Ala Leu Gly
        275                 280                 285

Leu Gln Cys Phe Thr Leu Asp Leu Lys Asn Val Thr Cys Gln Trp Gln
    290                 295                 300

Gln Gln Asp His Ala Ser Ser Gln Gly Phe Phe Tyr His Ser Arg Ala
305                 310                 315                 320

Arg Cys Cys Pro Arg Asp Arg Tyr Pro Ile Trp Glu Asn Cys Glu Glu
                325                 330                 335

Glu Glu Lys Thr Asn Pro Gly Leu Gln Thr Pro Gln Phe Ser Arg Cys
            340                 345                 350

His Phe Lys Ser Arg Asn Asp Ser Ile Ile His Ile Leu Val Glu Val
        355                 360                 365

Thr Thr Ala Pro Gly Thr Val His Ser Tyr Leu Gly Ser Pro Phe Trp
    370                 375                 380

Ile His Gln Ala Val Arg Leu Pro Thr Pro Asn Leu His Trp Arg Glu
385                 390                 395                 400

Ile Ser Ser Gly His Leu Glu Leu Glu Trp Gln His Pro Ser Ser Trp
                405                 410                 415

Ala Ala Gln Glu Thr Cys Tyr Gln Leu Arg Tyr Thr Gly Glu Gly His
            420                 425                 430

Gln Asp Trp Lys Val Leu Glu Pro Pro Leu Gly Ala Arg Gly Gly Thr
        435                 440                 445

Leu Glu Leu Arg Pro Arg Ser Arg Tyr Arg Leu Gln Leu Arg Ala Arg
    450                 455                 460

Leu Asn Gly Pro Thr Tyr Gln Gly Pro Trp Ser Ser Trp Ser Asp Pro
465                 470                 475                 480

Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Ser Leu Val Thr
                485                 490                 495

Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu
            500                 505                 510
```

Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu
515 520 525

Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg
530 535 540

Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys
545 550 555 560

Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu
565 570 575

Arg Thr Pro Leu Pro Leu Cys Ser Ser Gln Ala Gln Met Asp Tyr Arg
580 585 590

Arg Leu Gln Pro Ser Cys Leu Gly Thr Met Pro Leu Ser Val Cys Pro
595 600 605

Pro Met Ala Glu Ser Gly Ser Cys Cys Thr Thr His Ile Ala Asn His
610 615 620

Ser Tyr Leu Pro Leu Ser Tyr Trp Gln Gln Pro
625 630 635

<210> 335
<211> 557
<212> PRT
<213> Homo sapiens

<400> 335

Met Met Val Val Leu Leu Gly Ala Thr Thr Leu Val Leu Val Ala Val
1 5 10 15

Ala Pro Trp Val Leu Ser Ala Ala Ala Gly Gly Lys Asn Leu Lys Ser
20 25 30

Pro Gln Lys Val Glu Val Asp Ile Ile Asp Asp Asn Phe Ile Leu Arg
35 40 45

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

Tyr Gln Lys Thr Gly Met Asp Asn Trp Ile Lys Leu Ser Gly Cys Gln
65 70 75 80

Asn Ile Thr Ser Thr Lys Cys Asn Phe Ser Ser Leu Lys Leu Asn Val
85 90 95

Tyr Glu Glu Ile Lys Leu Arg Ile Arg Ala Glu Lys Glu Asn Thr Ser
100 105 110

Ser Trp Tyr Glu Val Asp Ser Phe Thr Pro Phe Arg Lys Ala Gln Ile

115 120 125

Gly Pro Pro Glu Val His Leu Glu Ala Glu Asp Lys Ala Ile Val Ile
130 135 140

His Ile Ser Pro Gly Thr Lys Asp Ser Val Met Trp Ala Leu Asp Gly
145 150 155 160

Leu Ser Phe Thr Tyr Ser Leu Val Ile Trp Lys Asn Ser Ser Gly Val
165 170 175

Glu Glu Arg Ile Glu Asn Ile Tyr Ser Arg His Lys Ile Tyr Lys Leu
180 185 190

Ser Pro Glu Thr Thr Tyr Cys Leu Lys Val Lys Ala Ala Leu Leu Thr
195 200 205

Ser Trp Lys Ile Gly Val Tyr Ser Pro Val His Cys Ile Lys Thr Thr
210 215 220

Val Glu Asn Glu Leu Pro Pro Pro Glu Asn Ile Glu Val Ser Val Gln
225 230 235 240

Asn Gln Asn Tyr Val Leu Lys Trp Asp Tyr Thr Tyr Ala Asn Met Thr
245 250 255

Phe Gln Val Gln Trp Leu His Ala Phe Leu Lys Arg Asn Pro Gly Asn
260 265 270

His Leu Tyr Lys Trp Lys Gln Ile Pro Asp Cys Glu Asn Val Lys Thr
275 280 285

Thr Gln Cys Val Phe Pro Gln Asn Val Phe Gln Lys Gly Ile Tyr Leu
290 295 300

Leu Arg Val Gln Ala Ser Asp Gly Asn Asn Thr Ser Phe Trp Ser Glu
305 310 315 320

Glu Ile Lys Phe Asp Thr Glu Ile Gln Ala Phe Leu Leu Pro Pro Val
325 330 335

Phe Asn Ile Arg Ser Leu Ser Asp Ser Phe His Ile Tyr Ile Gly Ala
340 345 350

Pro Lys Gln Ser Gly Asn Thr Pro Val Ile Gln Asp Tyr Pro Leu Ile
355 360 365

Tyr Glu Ile Ile Phe Trp Glu Asn Thr Ser Asn Ala Glu Arg Lys Ile
370 375 380

Ile Glu Lys Lys Thr Asp Val Thr Val Pro Asn Leu Lys Pro Leu Thr

385 390 395 400

Val Tyr Cys Val Lys Ala Arg Ala His Thr Met Asp Glu Lys Leu Asn
405 410 415

Lys Ser Ser Val Phe Ser Asp Ala Val Cys Glu Lys Thr Lys Pro Gly
420 425 430

Asn Thr Ser Lys Ile Trp Leu Ile Val Gly Ile Cys Ile Ala Leu Phe
435 440 445

Ala Leu Pro Phe Val Ile Tyr Ala Ala Lys Val Phe Leu Arg Cys Ile
450 455 460

Asn Tyr Val Phe Phe Pro Ser Leu Lys Pro Ser Ser Ser Ile Asp Glu
465 470 475 480

Tyr Phe Ser Glu Gln Pro Leu Lys Asn Leu Leu Leu Ser Thr Ser Glu
485 490 495

Glu Gln Ile Glu Lys Cys Phe Ile Ile Glu Asn Ile Ser Thr Ile Ala
500 505 510

Thr Val Glu Glu Thr Asn Gln Thr Asp Glu Asp His Lys Lys Tyr Ser
515 520 525

Ser Gln Thr Ser Gln Asp Ser Gly Asn Tyr Ser Asn Glu Asp Glu Ser
530 535 540

Glu Ser Lys Thr Ser Glu Glu Leu Gln Gln Asp Phe Val
545 550 555

<210> 336
<211> 331
<212> PRT
<213> Homo sapiens

<400> 336

Met Leu Leu Ser Gln Asn Ala Phe Ile Phe Arg Ser Leu Asn Leu Val
1 5 10 15

Leu Met Val Tyr Ile Ser Leu Val Phe Gly Ile Ser Tyr Asp Ser Pro
20 25 30

Asp Tyr Thr Asp Glu Ser Cys Thr Phe Lys Ile Ser Leu Arg Asn Phe
35 40 45

Arg Ser Ile Leu Ser Trp Glu Leu Lys Asn His Ser Ile Val Pro Thr
50 55 60

His Tyr Thr Leu Leu Tyr Thr Ile Met Ser Lys Pro Glu Asp Leu Lys
65 70 75 80

```
Val Val Lys Asn Cys Ala Asn Thr Thr Arg Ser Phe Cys Asp Leu Thr
                85                  90                  95

Asp Glu Trp Arg Ser Thr His Glu Ala Tyr Val Thr Val Leu Glu Gly
            100                 105                 110

Phe Ser Gly Asn Thr Thr Leu Phe Ser Cys Ser His Asn Phe Trp Leu
        115                 120                 125

Ala Ile Asp Met Ser Phe Glu Pro Pro Glu Phe Glu Ile Val Gly Phe
    130                 135                 140

Thr Asn His Ile Asn Val Met Val Lys Phe Pro Ser Ile Val Glu Glu
145                 150                 155                 160

Glu Leu Gln Phe Asp Leu Ser Leu Val Ile Glu Glu Gln Ser Glu Gly
                165                 170                 175

Ile Val Lys Lys His Lys Pro Glu Ile Lys Gly Asn Met Ser Gly Asn
            180                 185                 190

Phe Thr Tyr Ile Ile Asp Lys Leu Ile Pro Asn Thr Asn Tyr Cys Val
        195                 200                 205

Ser Val Tyr Leu Glu His Ser Asp Glu Gln Ala Val Ile Lys Ser Pro
    210                 215                 220

Leu Lys Cys Thr Leu Leu Pro Pro Gly Gln Glu Ser Glu Ser Ala Glu
225                 230                 235                 240

Ser Ala Lys Ile Gly Gly Ile Ile Thr Val Phe Leu Ile Ala Leu Val
                245                 250                 255

Leu Thr Ser Thr Ile Val Thr Leu Lys Trp Ile Gly Tyr Ile Cys Leu
            260                 265                 270

Arg Asn Ser Leu Pro Lys Val Leu Arg Gln Gly Leu Ala Lys Gly Trp
        275                 280                 285

Asn Ala Val Ala Ile His Arg Cys Ser His Asn Ala Leu Gln Ser Glu
    290                 295                 300

Thr Pro Glu Leu Lys Gln Ser Ser Cys Leu Ser Phe Pro Ser Ser Trp
305                 310                 315                 320

Asp Tyr Lys Arg Ala Ser Leu Cys Pro Ser Asp
                325                 330
```

<210> 337
<211> 489

<212> PRT
<213> Homo sapiens

<400> 337

```
Met Ala Leu Leu Phe Leu Leu Pro Leu Val Met Gln Gly Val Ser Arg
1               5                  10                  15

Ala Glu Met Gly Thr Ala Asp Leu Gly Pro Ser Ser Val Pro Thr Pro
            20                  25                  30

Thr Asn Val Thr Ile Glu Ser Tyr Asn Met Asn Pro Ile Val Tyr Trp
        35                  40                  45

Glu Tyr Gln Ile Met Pro Gln Val Pro Val Phe Thr Val Glu Val Lys
    50                  55                  60

Asn Tyr Gly Val Lys Asn Ser Glu Trp Ile Asp Ala Cys Ile Asn Ile
65                  70                  75                  80

Ser His His Tyr Cys Asn Ile Ser Asp His Val Gly Asp Pro Ser Asn
                85                  90                  95

Ser Leu Trp Val Arg Val Lys Ala Arg Val Gly Gln Lys Glu Ser Ala
            100                 105                 110

Tyr Ala Lys Ser Glu Glu Phe Ala Val Cys Arg Asp Gly Lys Ile Gly
        115                 120                 125

Pro Pro Lys Leu Asp Ile Arg Lys Glu Glu Lys Gln Ile Met Ile Asp
    130                 135                 140

Ile Phe His Pro Ser Val Phe Val Asn Gly Asp Glu Gln Glu Val Asp
145                 150                 155                 160

Tyr Asp Pro Glu Thr Thr Cys Tyr Ile Arg Val Tyr Asn Val Tyr Val
                165                 170                 175

Arg Met Asn Gly Ser Glu Ile Gln Tyr Lys Ile Leu Thr Gln Lys Glu
            180                 185                 190

Asp Asp Cys Asp Glu Ile Gln Cys Gln Leu Ala Ile Pro Val Ser Ser
        195                 200                 205

Leu Asn Ser Gln Tyr Cys Val Ser Ala Glu Gly Val Leu His Val Trp
    210                 215                 220

Gly Val Thr Thr Glu Lys Ser Lys Glu Val Cys Ile Thr Ile Phe Asn
225                 230                 235                 240

Ser Ser Ile Lys Gly Ser Leu Trp Ile Pro Val Val Ala Ala Leu Leu
                245                 250                 255
```

```
Leu Phe Leu Val Leu Ser Leu Val Phe Ile Cys Phe Tyr Ile Lys Lys
            260                 265                 270

Ile Asn Pro Leu Lys Glu Lys Ser Ile Ile Leu Pro Lys Ser Leu Ile
        275                 280                 285

Ser Val Val Arg Ser Ala Thr Leu Glu Thr Lys Pro Glu Ser Lys Tyr
    290                 295                 300

Val Ser Leu Ile Thr Ser Tyr Gln Pro Phe Ser Leu Glu Lys Glu Val
305                 310                 315                 320

Val Cys Glu Glu Pro Leu Ser Pro Ala Thr Val Pro Gly Met His Thr
                325                 330                 335

Glu Asp Asn Pro Gly Lys Val Glu His Thr Glu Glu Leu Ser Ser Ile
            340                 345                 350

Thr Glu Val Val Thr Thr Glu Glu Asn Ile Pro Asp Val Val Pro Gly
        355                 360                 365

Ser His Leu Thr Pro Ile Glu Arg Glu Ser Ser Ser Pro Leu Ser Ser
    370                 375                 380

Asn Gln Ser Glu Pro Gly Ser Ile Ala Leu Asn Ser Tyr His Ser Arg
385                 390                 395                 400

Asn Cys Ser Glu Ser Asp His Ser Arg Asn Gly Phe Asp Thr Asp Ser
                405                 410                 415

Ser Cys Leu Glu Ser His Ser Ser Leu Ser Asp Ser Glu Phe Pro Pro
            420                 425                 430

Asn Asn Lys Gly Glu Ile Lys Thr Glu Gly Gln Glu Leu Ile Thr Val
        435                 440                 445

Ile Lys Ala Pro Thr Ser Phe Gly Tyr Asp Lys Pro His Val Leu Val
    450                 455                 460

Asp Leu Leu Val Asp Asp Ser Gly Lys Glu Ser Leu Ile Gly Tyr Arg
465                 470                 475                 480

Pro Thr Glu Asp Ser Lys Glu Phe Ser
                485
```

<210> 338
<211> 337
<212> PRT
<213> Homo sapiens

<400> 338

```
Met Arg Pro Thr Leu Leu Trp Ser Leu Leu Leu Leu Leu Gly Val Phe
1               5                  10                  15

Ala Ala Ala Ala Ala Ala Pro Pro Asp Pro Leu Ser Gln Leu Pro Ala
            20                  25                  30

Pro Gln His Pro Lys Ile Arg Leu Tyr Asn Ala Glu Gln Val Leu Ser
        35                  40                  45

Trp Glu Pro Val Ala Leu Ser Asn Ser Thr Arg Pro Val Val Tyr Gln
    50                  55                  60

Val Gln Phe Lys Tyr Thr Asp Ser Lys Trp Phe Thr Ala Asp Ile Met
65                  70                  75                  80

Ser Ile Gly Val Asn Cys Thr Gln Ile Thr Ala Thr Glu Cys Asp Phe
                85                  90                  95

Thr Ala Ala Ser Pro Ser Ala Gly Phe Pro Met Asp Phe Asn Val Thr
            100                 105                 110

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

Met Pro Trp Phe Gln His Tyr Arg Asn Val Thr Val Gly Pro Pro Glu
    130                 135                 140

Asn Ile Glu Val Thr Pro Gly Glu Gly Ser Leu Ile Ile Arg Phe Ser
145                 150                 155                 160

Ser Pro Phe Asp Ile Ala Asp Thr Ser Thr Ala Phe Phe Cys Tyr Tyr
                165                 170                 175

Val His Tyr Trp Glu Lys Gly Gly Ile Gln Gln Val Lys Gly Pro Phe
            180                 185                 190

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

Cys Leu Gln Val Gln Ala Gln Leu Leu Trp Asn Lys Ser Asn Ile Phe
    210                 215                 220

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

Ala Ser Thr Glu Leu Gln Gln Val Ile Leu Ile Ser Val Gly Thr Phe
                245                 250                 255

Ser Leu Leu Ser Val Leu Ala Gly Ala Cys Phe Phe Leu Val Leu Lys
            260                 265                 270
```

Tyr Arg Gly Leu Ile Lys Tyr Trp Phe His Thr Pro Pro Ser Ile Pro
275 280 285

Leu Gln Ile Glu Glu Tyr Leu Lys Asp Pro Thr Gln Pro Ile Leu Glu
290 295 300

Ala Leu Asp Lys Asp Ser Ser Pro Lys Asp Asp Val Trp Asp Ser Val
305 310 315 320

Ser Ile Ile Ser Phe Pro Glu Lys Glu Gln Glu Asp Val Leu Gln Thr
325 330 335

Leu

<210> 339
<211> 263
<212> PRT
<213> Homo sapiens

<400> 339

Met Met Pro Lys His Cys Phe Leu Gly Phe Leu Ile Ser Phe Phe Leu
1 5 10 15

Thr Gly Val Ala Gly Thr Gln Ser Thr His Glu Ser Leu Lys Pro Gln
20 25 30

Arg Val Gln Phe Gln Ser Arg Asn Phe His Asn Ile Leu Gln Trp Gln
35 40 45

Pro Gly Arg Ala Leu Thr Gly Asn Ser Ser Val Tyr Phe Val Gln Tyr
50 55 60

Lys Ile Met Phe Ser Cys Ser Met Lys Ser Ser His Gln Lys Pro Ser
65 70 75 80

Gly Cys Trp Gln His Ile Ser Cys Asn Phe Pro Gly Cys Arg Thr Leu
85 90 95

Ala Lys Tyr Gly Gln Arg Gln Trp Lys Asn Lys Glu Asp Cys Trp Gly
100 105 110

Thr Gln Glu Leu Ser Cys Asp Leu Thr Ser Glu Thr Ser Asp Ile Gln
115 120 125

Glu Pro Tyr Tyr Gly Arg Val Arg Ala Ala Ser Ala Gly Ser Tyr Ser
130 135 140

Glu Trp Ser Met Thr Pro Arg Phe Thr Pro Trp Trp Glu Thr Lys Ile
145 150 155 160

Asp Pro Pro Val Met Asn Ile Thr Gln Val Asn Gly Ser Leu Leu Val

165 170 175

Ile Leu His Ala Pro Asn Leu Pro Tyr Arg Tyr Gln Lys Glu Lys Asn
180 185 190

Val Ser Ile Glu Asp Tyr Tyr Glu Leu Leu Tyr Arg Val Phe Ile Ile
195 200 205

Asn Asn Ser Leu Glu Lys Glu Gln Lys Val Tyr Glu Gly Ala His Arg
210 215 220

Ala Val Glu Ile Glu Ala Leu Thr Pro His Ser Ser Tyr Cys Val Val
225 230 235 240

Ala Glu Ile Tyr Gln Pro Met Leu Asp Arg Arg Ser Gln Arg Ser Glu
245 250 255

Glu Arg Cys Val Glu Ile Pro
260

<210> 340
<211> 578
<212> PRT
<213> Homo sapiens

<400> 340

Met Leu Pro Cys Leu Val Val Leu Leu Ala Ala Leu Leu Ser Leu Arg
1 5 10 15

Leu Gly Ser Asp Ala His Gly Thr Glu Leu Pro Ser Pro Pro Ser Val
20 25 30

Trp Phe Glu Ala Glu Phe Phe His His Ile Leu His Trp Thr Pro Ile
35 40 45

Pro Asn Gln Ser Glu Ser Thr Cys Tyr Glu Val Ala Leu Leu Arg Tyr
50 55 60

Gly Ile Glu Ser Trp Asn Ser Ile Ser Asn Cys Ser Gln Thr Leu Ser
65 70 75 80

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

Arg Ala Arg Val Arg Ala Val Asp Gly Ser Arg His Ser Asn Trp Thr
100 105 110

Val Thr Asn Thr Arg Phe Ser Val Asp Glu Val Thr Leu Thr Val Gly
115 120 125

Ser Val Asn Leu Glu Ile His Asn Gly Phe Ile Leu Gly Lys Ile Gln
130 135 140

```
Leu Pro Arg Pro Lys Met Ala Pro Ala Asn Asp Thr Tyr Glu Ser Ile
145                 150                 155                 160

Phe Ser His Phe Arg Glu Tyr Glu Ile Ala Ile Arg Lys Val Pro Gly
                165                 170                 175

Asn Phe Thr Phe Thr His Lys Lys Val Lys His Glu Asn Phe Ser Leu
            180                 185                 190

Leu Thr Ser Gly Glu Val Gly Glu Phe Cys Val Gln Val Lys Pro Ser
        195                 200                 205

Val Ala Ser Arg Ser Asn Lys Gly Met Trp Ser Lys Glu Glu Cys Ile
    210                 215                 220

Ser Leu Thr Arg Gln Tyr Phe Thr Val Thr Asn Val Ile Ile Phe Phe
225                 230                 235                 240

Ala Phe Val Leu Leu Leu Ser Gly Ala Leu Ala Tyr Cys Leu Ala Leu
                245                 250                 255

Gln Leu Tyr Val Arg Arg Arg Lys Lys Leu Pro Ser Val Leu Leu Phe
            260                 265                 270

Lys Lys Pro Ser Pro Phe Ile Phe Ile Ser Gln Arg Pro Ser Pro Glu
        275                 280                 285

Thr Gln Asp Thr Ile His Pro Leu Asp Glu Glu Ala Phe Leu Lys Val
    290                 295                 300

Ser Pro Glu Leu Lys Asn Leu Asp Leu His Gly Ser Thr Asp Ser Gly
305                 310                 315                 320

Phe Gly Ser Thr Lys Pro Ser Leu Gln Thr Glu Glu Pro Gln Phe Leu
                325                 330                 335

Leu Pro Asp Pro His Pro Gln Ala Asp Arg Thr Leu Gly Asn Arg Glu
            340                 345                 350

Pro Pro Val Leu Gly Asp Ser Cys Ser Ser Gly Ser Ser Asn Ser Thr
        355                 360                 365

Asp Ser Gly Ile Cys Leu Gln Glu Pro Ser Leu Ser Pro Ser Thr Gly
    370                 375                 380

Pro Thr Trp Glu Gln Gln Val Gly Ser Asn Ser Arg Gly Gln Asp Asp
385                 390                 395                 400

Ser Gly Ile Asp Leu Val Gln Asn Ser Glu Gly Arg Ala Gly Asp Thr
                405                 410                 415
```

```
Gln Gly Gly Ser Ala Leu Gly His His Ser Pro Pro Glu Pro Glu Val
            420                 425                 430

Pro Gly Glu Glu Asp Pro Ala Ala Val Ala Phe Gln Gly Tyr Leu Arg
        435                 440                 445

Gln Thr Arg Cys Ala Glu Glu Lys Ala Thr Lys Thr Gly Cys Leu Glu
    450                 455                 460

Glu Glu Ser Pro Leu Thr Asp Gly Leu Gly Pro Lys Phe Gly Arg Cys
465                 470                 475                 480

Leu Val Asp Glu Ala Gly Leu His Pro Pro Ala Leu Ala Lys Gly Tyr
                485                 490                 495

Leu Lys Gln Asp Pro Leu Glu Met Thr Leu Ala Ser Ser Gly Ala Pro
            500                 505                 510

Thr Gly Gln Trp Asn Gln Pro Thr Glu Glu Trp Ser Leu Leu Ala Leu
        515                 520                 525

Ser Ser Cys Ser Asp Leu Gly Ile Ser Asp Trp Ser Phe Ala His Asp
    530                 535                 540

Leu Ala Pro Leu Gly Cys Val Ala Ala Pro Gly Gly Leu Leu Gly Ser
545                 550                 555                 560

Phe Asn Ser Asp Leu Val Thr Leu Pro Leu Ile Ser Ser Leu Gln Ser
                565                 570                 575

Ser Glu
```

<210> 341
<211> 325
<212> PRT
<213> Homo sapiens

<400> 341

```
Met Ala Trp Ser Leu Gly Ser Trp Leu Gly Gly Cys Leu Leu Val Ser
1               5                   10                  15

Ala Leu Gly Met Val Pro Pro Pro Glu Asn Val Arg Met Asn Ser Val
            20                  25                  30

Asn Phe Lys Asn Ile Leu Gln Trp Glu Ser Pro Ala Phe Ala Lys Gly
        35                  40                  45

Asn Leu Thr Phe Thr Ala Gln Tyr Leu Ser Tyr Arg Ile Phe Gln Asp
    50                  55                  60
```

```
Lys Cys Met Asn Thr Thr Leu Thr Glu Cys Asp Phe Ser Ser Leu Ser
65                  70                  75                  80

Lys Tyr Gly Asp His Thr Leu Arg Val Arg Ala Glu Phe Ala Asp Glu
                85                  90                  95

His Ser Asp Trp Val Asn Ile Thr Phe Cys Pro Val Asp Asp Thr Ile
            100                 105                 110

Ile Gly Pro Pro Gly Met Gln Val Glu Val Leu Ala Asp Ser Leu His
        115                 120                 125

Met Arg Phe Leu Ala Pro Lys Ile Glu Asn Glu Tyr Glu Thr Trp Thr
    130                 135                 140

Met Lys Asn Val Tyr Asn Ser Trp Thr Tyr Asn Val Gln Tyr Trp Lys
145                 150                 155                 160

Asn Gly Thr Asp Glu Lys Phe Gln Ile Thr Pro Gln Tyr Asp Phe Glu
                165                 170                 175

Val Leu Arg Asn Leu Glu Pro Trp Thr Thr Tyr Cys Val Gln Val Arg
            180                 185                 190

Gly Phe Leu Pro Asp Arg Asn Lys Ala Gly Glu Trp Ser Glu Pro Val
        195                 200                 205

Cys Glu Gln Thr Thr His Asp Glu Thr Val Pro Ser Trp Met Val Ala
    210                 215                 220

Val Ile Leu Met Ala Ser Val Phe Met Val Cys Leu Ala Leu Leu Gly
225                 230                 235                 240

Cys Phe Ala Leu Leu Trp Cys Val Tyr Lys Lys Thr Lys Tyr Ala Phe
                245                 250                 255

Ser Pro Arg Asn Ser Leu Pro Gln His Leu Lys Glu Phe Leu Gly His
            260                 265                 270

Pro His His Asn Thr Leu Leu Phe Phe Ser Phe Pro Leu Ser Asp Glu
        275                 280                 285

Asn Asp Val Phe Asp Lys Leu Ser Val Ile Ala Glu Asp Ser Glu Ser
    290                 295                 300

Gly Lys Gln Asn Pro Gly Asp Ser Cys Ser Leu Gly Thr Pro Pro Gly
305                 310                 315                 320

Gln Gly Pro Gln Ser
                325
```

<210> 342
<211> 504
<212> PRT
<213> Homo sapiens

<400> 342

Met Lys Asn Val Leu Gln Trp Thr Pro Pro Glu Gly Leu Gln Gly Val
1 5 10 15

Lys Val Thr Tyr Thr Val Gln Tyr Phe Ile Tyr Gly Gln Lys Lys Trp
20 25 30

Leu Asn Lys Ser Glu Cys Arg Asn Ile Asn Arg Thr Tyr Cys Asp Leu
35 40 45

Ser Ala Glu Thr Ser Asp Tyr Glu His Gln Tyr Tyr Ala Lys Val Lys
50 55 60

Ala Ile Trp Gly Thr Lys Cys Ser Lys Trp Ala Glu Ser Gly Arg Phe
65 70 75 80

Tyr Pro Phe Leu Glu Thr Gln Ile Gly Pro Pro Glu Val Ala Leu Thr
85 90 95

Thr Asp Glu Lys Ser Ile Ser Val Val Leu Thr Ala Pro Glu Lys Trp
100 105 110

Lys Arg Asn Pro Glu Asp Leu Pro Val Ser Met Gln Gln Ile Tyr Ser
115 120 125

Asn Leu Lys Tyr Asn Val Ser Val Leu Asn Thr Lys Ser Asn Arg Thr
130 135 140

Trp Ser Gln Cys Val Thr Asn His Thr Leu Val Leu Thr Trp Leu Glu
145 150 155 160

Pro Asn Thr Leu Tyr Cys Val His Val Glu Ser Phe Val Pro Gly Pro
165 170 175

Pro Arg Arg Ala Gln Pro Ser Glu Lys Gln Cys Ala Arg Thr Leu Lys
180 185 190

Asp Gln Ser Ser Glu Phe Lys Ala Lys Ile Ile Phe Trp Tyr Val Leu
195 200 205

Pro Ile Ser Ile Thr Val Phe Leu Phe Ser Val Met Gly Tyr Ser Ile
210 215 220

Tyr Arg Tyr Ile His Val Gly Lys Glu Lys His Pro Ala Asn Leu Ile
225 230 235 240

```
Leu Ile Tyr Gly Asn Glu Phe Asp Lys Arg Phe Phe Val Pro Ala Glu
                245                 250                 255

Lys Ile Val Ile Asn Phe Ile Thr Leu Asn Ile Ser Asp Asp Ser Lys
            260                 265                 270

Ile Ser His Gln Asp Met Ser Leu Leu Gly Lys Ser Ser Asp Val Ser
        275                 280                 285

Ser Leu Asn Asp Pro Gln Pro Ser Gly Asn Leu Arg Pro Pro Gln Glu
    290                 295                 300

Glu Glu Glu Val Lys His Leu Gly Tyr Ala Ser His Leu Met Glu Ile
305                 310                 315                 320

Phe Cys Asp Ser Glu Glu Asn Thr Glu Gly Thr Ser Leu Thr Gln Gln
                325                 330                 335

Glu Ser Leu Ser Arg Thr Ile Pro Pro Asp Lys Thr Val Ile Glu Tyr
            340                 345                 350

Glu Tyr Asp Val Arg Thr Thr Asp Ile Cys Ala Gly Pro Glu Glu Gln
        355                 360                 365

Glu Leu Ser Leu Gln Glu Glu Val Ser Thr Gln Gly Thr Leu Leu Glu
    370                 375                 380

Ser Gln Ala Ala Leu Ala Val Leu Gly Pro Gln Thr Leu Gln Tyr Ser
385                 390                 395                 400

Tyr Thr Pro Gln Leu Gln Asp Leu Asp Pro Leu Ala Gln Glu His Thr
                405                 410                 415

Asp Ser Glu Glu Gly Pro Glu Glu Glu Pro Ser Thr Thr Leu Val Asp
            420                 425                 430

Trp Asp Pro Gln Thr Gly Arg Leu Cys Ile Pro Ser Leu Ser Ser Phe
        435                 440                 445

Asp Gln Asp Ser Glu Gly Cys Glu Pro Ser Glu Gly Asp Gly Leu Gly
    450                 455                 460

Glu Glu Gly Leu Leu Ser Arg Leu Tyr Glu Glu Pro Ala Pro Asp Arg
465                 470                 475                 480

Pro Pro Gly Glu Asn Glu Thr Tyr Leu Met Gln Phe Met Glu Glu Trp
                485                 490                 495

Gly Leu Tyr Val Gln Met Glu Asn
            500
```

<210> 343
<211> 311
<212> PRT
<213> Homo sapiens

<400> 343

Met Gln Thr Phe Thr Met Val Leu Glu Glu Ile Trp Thr Ser Leu Phe
1 5 10 15

Met Trp Phe Phe Tyr Ala Leu Ile Pro Cys Leu Leu Thr Asp Glu Val
20 25 30

Ala Ile Leu Pro Ala Pro Gln Asn Leu Ser Val Leu Ser Thr Asn Met
35 40 45

Lys His Leu Leu Met Trp Ser Pro Val Ile Ala Pro Gly Glu Thr Val
50 55 60

Tyr Tyr Ser Val Glu Tyr Gln Gly Glu Tyr Glu Ser Leu Tyr Thr Ser
65 70 75 80

His Ile Trp Ile Pro Ser Ser Trp Cys Ser Leu Thr Glu Gly Pro Glu
85 90 95

Cys Asp Val Thr Asp Asp Ile Thr Ala Thr Val Pro Tyr Asn Leu Arg
100 105 110

Val Arg Ala Thr Leu Gly Ser Gln Thr Ser Ala Trp Ser Ile Leu Lys
115 120 125

His Pro Phe Asn Arg Asn Ser Thr Ile Leu Thr Arg Pro Gly Met Glu
130 135 140

Ile Thr Lys Asp Gly Phe His Leu Val Ile Glu Leu Glu Asp Leu Gly
145 150 155 160

Pro Gln Phe Glu Phe Leu Val Ala Tyr Trp Arg Arg Glu Pro Gly Ala
165 170 175

Glu Glu His Val Lys Met Val Arg Ser Gly Gly Ile Pro Val His Leu
180 185 190

Glu Thr Met Glu Pro Gly Ala Ala Tyr Cys Val Lys Ala Gln Thr Phe
195 200 205

Val Lys Ala Ile Gly Arg Tyr Ser Ala Phe Ser Gln Thr Glu Cys Val
210 215 220

Glu Val Gln Gly Glu Ala Ile Pro Leu Val Leu Ala Leu Phe Ala Phe
225 230 235 240

Val Gly Phe Met Leu Ile Leu Val Val Val Pro Leu Phe Val Trp Lys

245 250 255

Met Gly Arg Leu Leu Gln Tyr Ser Cys Cys Pro Val Val Val Leu Pro
260 265 270

Asp Thr Leu Lys Ile Thr Asn Ser Pro Gln Lys Leu Ile Ser Cys Arg
275 280 285

Arg Glu Glu Val Asp Ala Cys Ala Thr Ala Val Met Ser Pro Glu Glu
290 295 300

Leu Leu Arg Ala Trp Ile Ser
305 310

<210> 344
<211> 574
<212> PRT
<213> Homo sapiens

<400> 344

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

Ala Pro Glu Asp Pro Ser Asp Leu Leu Gln His Val Lys Phe Gln Ser
20 25 30

Ser Asn Phe Glu Asn Ile Leu Thr Trp Asp Ser Gly Pro Glu Gly Thr
35 40 45

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

Trp Val Ala Lys Lys Gly Cys Gln Arg Ile Thr Arg Lys Ser Cys Asn
65 70 75 80

Leu Thr Val Glu Thr Gly Asn Leu Thr Glu Leu Tyr Tyr Ala Arg Val
85 90 95

Thr Ala Val Ser Ala Gly Gly Arg Ser Ala Thr Lys Met Thr Asp Arg
100 105 110

Phe Ser Ser Leu Gln His Thr Thr Leu Lys Pro Pro Asp Val Thr Cys
115 120 125

Ile Ser Lys Val Arg Ser Ile Gln Met Ile Val His Pro Thr Pro Thr
130 135 140

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

His Asp Leu Phe Tyr His Leu Glu Leu Gln Val Asn Arg Thr Tyr Gln
165 170 175

```
Met His Leu Gly Gly Lys Gln Arg Glu Tyr Glu Phe Phe Gly Leu Thr
            180                 185                 190

Pro Asp Thr Glu Phe Leu Gly Thr Ile Met Ile Cys Val Pro Thr Trp
        195                 200                 205

Ala Lys Glu Ser Ala Pro Tyr Met Cys Arg Val Lys Thr Leu Pro Asp
    210                 215                 220

Arg Thr Trp Thr Tyr Ser Phe Ser Gly Ala Phe Leu Phe Ser Met Gly
225                 230                 235                 240

Phe Leu Val Ala Val Leu Cys Tyr Leu Ser Tyr Arg Tyr Val Thr Lys
                245                 250                 255

Pro Pro Ala Pro Pro Asn Ser Leu Asn Val Gln Arg Val Leu Thr Phe
            260                 265                 270

Gln Pro Leu Arg Phe Ile Gln Glu His Val Leu Ile Pro Val Phe Asp
        275                 280                 285

Leu Ser Gly Pro Ser Ser Leu Ala Gln Pro Val Gln Tyr Ser Gln Ile
    290                 295                 300

Arg Val Ser Gly Pro Arg Glu Pro Ala Gly Ala Pro Gln Arg His Ser
305                 310                 315                 320

Leu Ser Glu Ile Thr Tyr Leu Gly Gln Pro Asp Ile Ser Ile Leu Gln
                325                 330                 335

Pro Ser Asn Val Pro Pro Pro Gln Ile Leu Ser Pro Leu Ser Tyr Ala
            340                 345                 350

Pro Asn Ala Ala Pro Glu Val Gly Pro Pro Ser Tyr Ala Pro Gln Val
        355                 360                 365

Thr Pro Glu Ala Gln Phe Pro Phe Tyr Ala Pro Gln Ala Ile Ser Lys
    370                 375                 380

Val Gln Pro Ser Ser Tyr Ala Pro Gln Ala Thr Pro Asp Ser Trp Pro
385                 390                 395                 400

Pro Ser Tyr Gly Val Cys Met Glu Gly Ser Gly Lys Asp Ser Pro Thr
                405                 410                 415

Gly Thr Leu Ser Ser Pro Lys His Leu Arg Pro Lys Gly Gln Leu Gln
            420                 425                 430

Lys Glu Pro Pro Ala Gly Ser Cys Met Leu Gly Gly Leu Ser Leu Gln
        435                 440                 445
```

Glu Val Thr Ser Leu Ala Met Glu Glu Ser Gln Glu Ala Lys Ser Leu
450 455 460

His Gln Pro Leu Gly Ile Cys Thr Asp Arg Thr Ser Asp Pro Asn Val
465 470 475 480

Leu His Ser Gly Glu Glu Gly Thr Pro Gln Tyr Leu Lys Gly Gln Leu
485 490 495

Pro Leu Leu Ser Ser Val Gln Ile Glu Gly His Pro Met Ser Leu Pro
500 505 510

Leu Gln Pro Pro Ser Arg Pro Cys Ser Pro Ser Asp Gln Gly Pro Ser
515 520 525

Pro Trp Gly Leu Leu Glu Ser Leu Val Cys Pro Lys Asp Glu Ala Lys
530 535 540

Ser Pro Ala Pro Glu Thr Ser Asp Leu Glu Gln Pro Thr Glu Leu Asp
545 550 555 560

Ser Leu Phe Arg Gly Leu Ala Leu Thr Val Gln Trp Glu Ser
565 570

<210> 345
<211> 520
<212> PRT
<213> Homo sapiens

<400> 345

Met Ala Gly Pro Glu Arg Trp Gly Pro Leu Leu Leu Cys Leu Leu Gln
1 5 10 15

Ala Ala Pro Gly Arg Pro Arg Leu Ala Pro Pro Gln Asn Val Thr Leu
20 25 30

Leu Ser Gln Asn Phe Ser Val Tyr Leu Thr Trp Leu Pro Gly Leu Gly
35 40 45

Asn Pro Gln Asp Val Thr Tyr Phe Val Ala Tyr Gln Ser Ser Pro Thr
50 55 60

Arg Arg Arg Trp Arg Glu Val Glu Glu Cys Ala Gly Thr Lys Glu Leu
65 70 75 80

Leu Cys Ser Met Met Cys Leu Lys Lys Gln Asp Leu Tyr Asn Lys Phe
85 90 95

Lys Gly Arg Val Arg Thr Val Ser Pro Ser Ser Lys Ser Pro Trp Val
100 105 110

```
Glu Ser Glu Tyr Leu Asp Tyr Leu Phe Glu Val Glu Pro Ala Pro Pro
        115                 120                 125

Val Leu Val Leu Thr Gln Thr Glu Glu Ile Leu Ser Ala Asn Ala Thr
    130                 135                 140

Tyr Gln Leu Pro Pro Cys Met Pro Pro Leu Asp Leu Lys Tyr Glu Val
145                 150                 155                 160

Ala Phe Trp Lys Glu Gly Ala Gly Asn Lys Thr Leu Phe Pro Val Thr
                165                 170                 175

Pro His Gly Gln Pro Val Gln Ile Thr Leu Gln Pro Ala Ala Ser Glu
            180                 185                 190

His His Cys Leu Ser Ala Arg Thr Ile Tyr Thr Phe Ser Val Pro Lys
        195                 200                 205

Tyr Ser Lys Phe Ser Lys Pro Thr Cys Phe Leu Leu Glu Val Pro Glu
    210                 215                 220

Ala Asn Trp Ala Phe Leu Val Leu Pro Ser Leu Leu Ile Leu Leu Leu
225                 230                 235                 240

Val Ile Ala Ala Gly Gly Val Ile Trp Lys Thr Leu Met Gly Asn Pro
                245                 250                 255

Trp Phe Gln Arg Ala Lys Met Pro Arg Ala Leu Asp Phe Ser Gly His
            260                 265                 270

Thr His Pro Val Ala Thr Phe Gln Pro Ser Arg Pro Glu Ser Val Asn
        275                 280                 285

Asp Leu Phe Leu Cys Pro Gln Lys Glu Leu Thr Arg Gly Val Arg Pro
    290                 295                 300

Thr Pro Arg Val Arg Ala Pro Ala Thr Gln Gln Thr Arg Trp Lys Lys
305                 310                 315                 320

Asp Leu Ala Glu Asp Glu Glu Glu Glu Asp Glu Glu Asp Thr Glu Asp
                325                 330                 335

Gly Val Ser Phe Gln Pro Tyr Ile Glu Pro Pro Ser Phe Leu Gly Gln
            340                 345                 350

Glu His Gln Ala Pro Gly His Ser Glu Ala Gly Gly Val Asp Ser Gly
        355                 360                 365

Arg Pro Arg Ala Pro Leu Val Pro Ser Glu Gly Ser Ser Ala Trp Asp
    370                 375                 380
```

```
Ser Ser Asp Arg Ser Trp Ala Ser Thr Val Asp Ser Ser Trp Asp Arg
385                 390                 395                 400

Ala Gly Ser Ser Gly Tyr Leu Ala Glu Lys Gly Pro Gly Gln Gly Pro
                405                 410                 415

Gly Gly Asp Gly His Gln Glu Ser Leu Pro Pro Pro Glu Phe Ser Lys
            420                 425                 430

Asp Ser Gly Phe Leu Glu Glu Leu Pro Glu Asp Asn Leu Ser Ser Trp
        435                 440                 445

Ala Thr Trp Gly Thr Leu Pro Pro Glu Pro Asn Leu Val Pro Gly Gly
    450                 455                 460

Pro Pro Val Ser Leu Gln Thr Leu Thr Phe Cys Trp Glu Ser Ser Pro
465                 470                 475                 480

Glu Glu Glu Glu Glu Ala Arg Glu Ser Glu Ile Glu Asp Ser Asp Ala
                485                 490                 495

Gly Ser Trp Gly Ala Glu Ser Thr Gln Arg Thr Glu Asp Arg Gly Arg
            500                 505                 510

Thr Leu Gly His Tyr Met Ala Arg
        515                 520


<210>  346
<211>  832
<212>  PRT
<213>  Homo sapiens

<400>  346

Met Gly Ala Ala Arg Ser Pro Pro Ser Ala Val Pro Gly Pro Leu Leu
1               5                   10                  15

Gly Leu Leu Leu Leu Leu Leu Gly Val Leu Ala Pro Gly Gly Ala Ser
            20                  25                  30

Leu Arg Leu Leu Asp His Arg Ala Leu Val Cys Ser Gln Pro Gly Leu
        35                  40                  45

Asn Cys Thr Val Lys Asn Ser Thr Cys Leu Asp Asp Ser Trp Ile His
    50                  55                  60

Pro Arg Asn Leu Thr Pro Ser Ser Pro Lys Asp Leu Gln Ile Gln Leu
65                  70                  75                  80

His Phe Ala His Thr Gln Gln Gly Asp Leu Phe Pro Val Ala His Ile
                85                  90                  95
```

```
Glu Trp Thr Leu Gln Thr Asp Ala Ser Ile Leu Tyr Leu Glu Gly Ala
            100                 105                 110

Glu Leu Ser Val Leu Gln Leu Asn Thr Asn Glu Arg Leu Cys Val Arg
        115                 120                 125

Phe Glu Phe Leu Ser Lys Leu Arg His His His Arg Arg Trp Arg Phe
    130                 135                 140

Thr Phe Ser His Phe Val Val Asp Pro Asp Gln Glu Tyr Glu Val Thr
145                 150                 155                 160

Val His His Leu Pro Lys Pro Ile Pro Asp Gly Asp Pro Asn His Gln
                165                 170                 175

Ser Lys Asn Phe Leu Val Pro Asp Cys Glu His Ala Arg Met Lys Val
            180                 185                 190

Thr Thr Pro Cys Met Ser Ser Gly Ser Leu Trp Asp Pro Asn Ile Thr
        195                 200                 205

Val Glu Thr Leu Glu Ala His Gln Leu Arg Val Ser Phe Thr Leu Trp
    210                 215                 220

Asn Glu Ser Thr His Tyr Gln Ile Leu Leu Thr Ser Phe Pro His Met
225                 230                 235                 240

Glu Asn His Ser Cys Phe Glu His Met His His Ile Pro Ala Pro Arg
                245                 250                 255

Pro Glu Glu Phe His Gln Arg Ser Asn Val Thr Leu Thr Leu Arg Asn
            260                 265                 270

Leu Lys Gly Cys Cys Arg His Gln Val Gln Ile Gln Pro Phe Phe Ser
        275                 280                 285

Ser Cys Leu Asn Asp Cys Leu Arg His Ser Ala Thr Val Ser Cys Pro
    290                 295                 300

Glu Met Pro Asp Thr Pro Glu Pro Ile Pro Gly Pro Gly Ser Glu Lys
305                 310                 315                 320

Tyr Ser Asp Asp Thr Lys Tyr Thr Asp Gly Leu Pro Ala Ala Asp Leu
                325                 330                 335

Ile Pro Pro Pro Leu Lys Pro Arg Lys Val Trp Ile Ile Tyr Ser Ala
            340                 345                 350

Asp His Pro Leu Tyr Val Asp Val Val Leu Lys Phe Ala Gln Phe Leu
        355                 360                 365
```

```
Leu Thr Ala Cys Gly Thr Glu Val Ala Leu Asp Leu Leu Glu Glu Gln
    370                 375                 380

Ala Ile Ser Glu Ala Gly Val Met Thr Trp Val Gly Arg Gln Lys Gln
385                 390                 395                 400

Glu Met Val Glu Ser Asn Ser Lys Ile Ile Val Leu Cys Ser Arg Gly
                405                 410                 415

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

Leu Arg Cys Asp His Gly Lys Pro Val Gly Asp Leu Phe Thr Ala Ala
        435                 440                 445

Met Asn Met Ile Leu Pro Asp Phe Lys Arg Pro Ala Cys Phe Gly Thr
    450                 455                 460

Tyr Val Val Cys Tyr Phe Ser Glu Val Ser Cys Asp Gly Asp Val Pro
465                 470                 475                 480

Asp Leu Phe Gly Ala Ala Pro Arg Tyr Pro Leu Met Asp Arg Phe Glu
                485                 490                 495

Glu Val Tyr Phe Arg Ile Gln Asp Leu Glu Met Phe Gln Pro Gly Arg
            500                 505                 510

Met His Arg Val Gly Glu Leu Ser Gly Asp Asn Tyr Leu Arg Ser Pro
        515                 520                 525

Gly Gly Arg Gln Leu Arg Ala Ala Leu Asp Arg Phe Arg Asp Trp Gln
    530                 535                 540

Val Arg Cys Pro Asp Trp Phe Glu Cys Glu Asn Leu Tyr Ser Ala Asp
545                 550                 555                 560

Asp Gln Asp Ala Pro Ser Leu Asp Glu Glu Val Phe Glu Glu Pro Leu
                565                 570                 575

Leu Pro Pro Gly Thr Gly Ile Val Lys Arg Ala Pro Leu Val Arg Glu
            580                 585                 590

Pro Gly Ser Gln Ala Cys Leu Ala Ile Asp Pro Leu Val Gly Glu Glu
        595                 600                 605

Gly Gly Ala Ala Val Ala Lys Leu Glu Pro His Leu Gln Pro Arg Gly
    610                 615                 620

Gln Pro Ala Pro Gln Pro Leu His Thr Leu Val Leu Ala Ala Glu Glu
625                 630                 635                 640
```

```
Gly Ala Leu Val Ala Ala Val Glu Pro Gly Pro Leu Ala Asp Gly Ala
                645                 650                 655

Ala Val Arg Leu Ala Leu Ala Gly Glu Gly Glu Ala Cys Pro Leu Leu
            660                 665                 670

Gly Ser Pro Gly Ala Gly Arg Asn Ser Val Leu Phe Leu Pro Val Asp
        675                 680                 685

Pro Glu Asp Ser Pro Leu Gly Ser Ser Thr Pro Met Ala Ser Pro Asp
    690                 695                 700

Leu Leu Pro Glu Asp Val Arg Glu His Leu Glu Gly Leu Met Leu Ser
705                 710                 715                 720

Leu Phe Glu Gln Ser Leu Ser Cys Gln Ala Gln Gly Gly Cys Ser Arg
                725                 730                 735

Pro Ala Met Val Leu Thr Asp Pro His Thr Pro Tyr Glu Glu Glu Gln
            740                 745                 750

Arg Gln Ser Val Gln Ser Asp Gln Gly Tyr Ile Ser Arg Ser Ser Pro
        755                 760                 765

Gln Pro Pro Glu Gly Leu Thr Glu Met Glu Glu Glu Glu Glu Glu Glu
    770                 775                 780

Gln Asp Pro Gly Lys Pro Ala Leu Pro Leu Ser Pro Glu Asp Leu Glu
785                 790                 795                 800

Ser Leu Arg Ser Leu Gln Arg Gln Leu Leu Phe Arg Gln Leu Gln Lys
                805                 810                 815

Asn Ser Gly Trp Asp Thr Met Gly Ser Glu Ser Glu Gly Pro Ser Ala
            820                 825                 830


<210>  347
<211>  502
<212>  PRT
<213>  Homo sapiens

<400>  347

Met Ser Leu Val Leu Leu Ser Leu Ala Ala Leu Cys Arg Ser Ala Val
1               5                   10                  15

Pro Arg Glu Pro Thr Val Gln Cys Gly Ser Glu Thr Gly Pro Ser Pro
            20                  25                  30

Glu Trp Met Leu Gln His Asp Leu Ile Pro Gly Asp Leu Arg Asp Leu
        35                  40                  45

Arg Val Glu Pro Val Thr Thr Ser Val Ala Thr Gly Asp Tyr Ser Ile
```

50 55 60

Leu Met Asn Val Ser Trp Val Leu Arg Ala Asp Ala Ser Ile Arg Leu
65 70 75 80

Leu Lys Ala Thr Lys Ile Cys Val Thr Gly Lys Ser Asn Phe Gln Ser
85 90 95

Tyr Ser Cys Val Arg Cys Asn Tyr Thr Glu Ala Phe Gln Thr Gln Thr
100 105 110

Arg Pro Ser Gly Gly Lys Trp Thr Phe Ser Tyr Ile Gly Phe Pro Val
115 120 125

Glu Leu Asn Thr Val Tyr Phe Ile Gly Ala His Asn Ile Pro Asn Ala
130 135 140

Asn Met Asn Glu Asp Gly Pro Ser Met Ser Val Asn Phe Thr Ser Pro
145 150 155 160

Gly Cys Leu Asp His Ile Met Lys Tyr Lys Lys Lys Cys Val Lys Ala
165 170 175

Gly Ser Leu Trp Asp Pro Asn Ile Thr Ala Cys Lys Lys Asn Glu Glu
180 185 190

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

Ala Leu Ile Gln His Ser Thr Ile Ile Gly Phe Ser Gln Val Phe Glu
210 215 220

Pro His Gln Lys Lys Gln Thr Arg Ala Ser Val Val Ile Pro Val Thr
225 230 235 240

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

Cys Gly Ser Asp Cys Ile Arg His Lys Gly Thr Val Val Leu Cys Pro
260 265 270

Gln Thr Gly Val Pro Phe Pro Leu Asp Asn Asn Lys Ser Lys Pro Gly
275 280 285

Gly Trp Leu Pro Leu Leu Leu Leu Ser Leu Leu Val Ala Thr Trp Val
290 295 300

Leu Val Ala Gly Ile Tyr Leu Met Trp Arg His Glu Arg Ile Lys Lys
305 310 315 320

Thr Ser Phe Ser Thr Thr Thr Leu Leu Pro Pro Ile Lys Val Leu Val

325 330 335

Val Tyr Pro Ser Glu Ile Cys Phe His His Thr Ile Cys Tyr Phe Thr
340 345 350

Glu Phe Leu Gln Asn His Cys Arg Ser Glu Val Ile Leu Glu Lys Trp
355 360 365

Gln Lys Lys Lys Ile Ala Glu Met Gly Pro Val Gln Trp Leu Ala Thr
370 375 380

Gln Lys Lys Ala Ala Asp Lys Val Val Phe Leu Leu Ser Asn Asp Val
385 390 395 400

Asn Ser Val Cys Asp Gly Thr Cys Gly Lys Ser Glu Gly Ser Pro Ser
405 410 415

Glu Asn Ser Gln Asp Leu Phe Pro Leu Ala Phe Asn Leu Phe Cys Ser
420 425 430

Asp Leu Arg Ser Gln Ile His Leu His Lys Tyr Val Val Val Tyr Phe
435 440 445

Arg Glu Ile Asp Thr Lys Asp Asp Tyr Asn Ala Leu Ser Val Cys Pro
450 455 460

Lys Tyr His Leu Met Lys Asp Ala Thr Ala Phe Cys Ala Glu Leu Leu
465 470 475 480

His Val Lys Gln Gln Val Ser Ala Gly Lys Arg Ser Gln Ala Cys His
485 490 495

Asp Gly Cys Cys Ser Leu
500

<210> 348
<211> 707
<212> PRT
<213> Homo sapiens

<400> 348

Met Pro Val Pro Trp Phe Leu Leu Ser Leu Ala Leu Gly Arg Ser Pro
1 5 10 15

Val Val Leu Ser Leu Glu Arg Leu Val Gly Pro Gln Asp Ala Thr His
20 25 30

Cys Ser Pro Gly Leu Ser Cys Arg Leu Trp Asp Ser Asp Ile Leu Cys
35 40 45

Leu Pro Gly Asp Ile Val Pro Ala Pro Gly Pro Val Leu Ala Pro Thr
50 55 60

```
His Leu Gln Thr Glu Leu Val Leu Arg Cys Gln Lys Glu Thr Asp Cys
65                  70                  75                  80

Asp Leu Cys Leu Arg Val Ala Val His Leu Ala Val His Gly His Trp
                85                  90                  95

Glu Glu Pro Glu Asp Glu Glu Lys Phe Gly Gly Ala Ala Asp Ser Gly
            100                 105                 110

Val Glu Glu Pro Arg Asn Ala Ser Leu Gln Ala Gln Val Val Leu Ser
        115                 120                 125

Phe Gln Ala Tyr Pro Thr Ala Arg Cys Val Leu Leu Glu Val Gln Val
    130                 135                 140

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

Asp Cys Phe Glu Ala Ala Leu Gly Ser Glu Val Arg Ile Trp Ser Tyr
                165                 170                 175

Thr Gln Pro Arg Tyr Glu Lys Glu Leu Asn His Thr Gln Gln Leu Pro
            180                 185                 190

Asp Cys Arg Gly Leu Glu Val Trp Asn Ser Ile Pro Ser Cys Trp Ala
        195                 200                 205

Leu Pro Trp Leu Asn Val Ser Ala Asp Gly Asp Asn Val His Leu Val
    210                 215                 220

Leu Asn Val Ser Glu Glu Gln His Phe Gly Leu Ser Leu Tyr Trp Asn
225                 230                 235                 240

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

Pro Gln Ile Ile Thr Leu Asn His Thr Asp Leu Val Pro Cys Leu Cys
            260                 265                 270

Ile Gln Val Trp Pro Leu Glu Pro Asp Ser Val Arg Thr Asn Ile Cys
        275                 280                 285

Pro Phe Arg Glu Asp Pro Arg Ala His Gln Asn Leu Trp Gln Ala Ala
    290                 295                 300

Arg Leu Arg Leu Leu Thr Leu Gln Ser Trp Leu Leu Asp Ala Pro Cys
305                 310                 315                 320

Ser Leu Pro Ala Glu Ala Ala Leu Cys Trp Arg Ala Pro Gly Gly Asp
                325                 330                 335
```

```
Pro Cys Gln Pro Leu Val Pro Pro Leu Ser Trp Glu Asn Val Thr Val
            340                 345                 350

Asp Lys Val Leu Glu Phe Pro Leu Leu Lys Gly His Pro Asn Leu Cys
        355                 360                 365

Val Gln Val Asn Ser Ser Glu Lys Leu Gln Leu Gln Glu Cys Leu Trp
    370                 375                 380

Ala Asp Ser Leu Gly Pro Leu Lys Asp Asp Val Leu Leu Leu Glu Thr
385                 390                 395                 400

Arg Gly Pro Gln Asp Asn Arg Ser Leu Cys Ala Leu Glu Pro Ser Gly
                405                 410                 415

Cys Thr Ser Leu Pro Ser Lys Ala Ser Thr Arg Ala Ala Arg Leu Gly
            420                 425                 430

Glu Tyr Leu Leu Gln Asp Leu Gln Ser Gly Gln Cys Leu Gln Leu Trp
        435                 440                 445

Asp Asp Asp Leu Gly Ala Leu Trp Ala Cys Pro Met Asp Lys Tyr Ile
    450                 455                 460

His Lys Arg Trp Ala Leu Val Trp Leu Ala Cys Leu Leu Phe Ala Ala
465                 470                 475                 480

Ala Leu Ser Leu Ile Leu Leu Leu Lys Lys Asp His Ala Lys Ala Ala
                485                 490                 495

Ala Arg Gly Arg Ala Ala Leu Leu Leu Tyr Ser Ala Asp Asp Ser Gly
            500                 505                 510

Phe Glu Arg Leu Val Gly Ala Leu Ala Ser Ala Leu Cys Gln Leu Pro
        515                 520                 525

Leu Arg Val Ala Val Asp Leu Trp Ser Arg Arg Glu Leu Ser Ala Gln
    530                 535                 540

Gly Pro Val Ala Trp Phe His Ala Gln Arg Arg Gln Thr Leu Gln Glu
545                 550                 555                 560

Gly Gly Val Val Val Leu Leu Phe Ser Pro Gly Ala Val Ala Leu Cys
                565                 570                 575

Ser Glu Trp Leu Gln Asp Gly Val Ser Gly Pro Gly Ala His Gly Pro
            580                 585                 590

His Asp Ala Phe Arg Ala Ser Leu Ser Cys Val Leu Pro Asp Phe Leu
        595                 600                 605
```

Gln Gly Arg Ala Pro Gly Ser Tyr Val Gly Ala Cys Phe Asp Arg Leu
610 615 620

Leu His Pro Asp Ala Val Pro Ala Leu Phe Arg Thr Val Pro Val Phe
625 630 635 640

Thr Leu Pro Ser Gln Leu Pro Asp Phe Leu Gly Ala Leu Gln Gln Pro
645 650 655

Arg Ala Pro Arg Ser Gly Arg Leu Gln Glu Arg Ala Glu Gln Val Ser
660 665 670

Arg Ala Leu Gln Pro Ala Leu Asp Ser Tyr Phe His Pro Pro Gly Thr
675 680 685

Pro Ala Pro Gly Arg Gly Val Gly Pro Gly Ala Gly Pro Gly Ala Gly
690 695 700

Asp Gly Thr
705

<210> 349
<211> 595
<212> PRT
<213> Homo sapiens

<400> 349

Met Glu Ser Gln Pro Phe Leu Asn Met Lys Phe Glu Thr Asp Tyr Phe
1 5 10 15

Val Lys Val Val Pro Phe Pro Ser Ile Lys Asn Glu Ser Asn Tyr His
20 25 30

Pro Phe Phe Phe Arg Thr Arg Ala Cys Asp Leu Leu Leu Gln Pro Asp
35 40 45

Asn Leu Ala Cys Lys Pro Phe Trp Lys Pro Arg Asn Leu Asn Ile Ser
50 55 60

Gln His Gly Ser Asp Met Gln Val Ser Phe Asp His Ala Pro His Asn
65 70 75 80

Phe Gly Phe Arg Phe Phe Tyr Leu His Tyr Lys Leu Lys His Glu Gly
85 90 95

Pro Phe Lys Arg Lys Thr Cys Lys Gln Glu Gln Thr Thr Glu Thr Thr
100 105 110

Ser Cys Leu Leu Gln Asn Val Ser Pro Gly Asp Tyr Ile Ile Glu Leu
115 120 125

```
Val Asp Asp Thr Asn Thr Thr Arg Lys Val Met His Tyr Ala Leu Lys
    130                 135                 140

Pro Val His Ser Pro Trp Ala Gly Pro Ile Arg Ala Val Ala Ile Thr
145                 150                 155                 160

Val Pro Leu Val Val Ile Ser Ala Phe Ala Thr Leu Phe Thr Val Met
                165                 170                 175

Cys Arg Lys Lys Gln Gln Glu Asn Ile Tyr Ser His Leu Asp Glu Glu
            180                 185                 190

Ser Ser Glu Ser Ser Thr Tyr Thr Ala Ala Leu Pro Arg Glu Arg Leu
        195                 200                 205

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

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

Cys Gly Cys Glu Val Ala Leu Asp Leu Trp Glu Asp Phe Ser Leu Cys
                245                 250                 255

Arg Glu Gly Gln Arg Glu Trp Val Ile Gln Lys Ile His Glu Ser Gln
            260                 265                 270

Phe Ile Ile Val Val Cys Ser Lys Gly Met Lys Tyr Phe Val Asp Lys
        275                 280                 285

Lys Asn Tyr Lys His Lys Gly Gly Gly Arg Gly Ser Gly Lys Gly Glu
    290                 295                 300

Leu Phe Leu Val Ala Val Ser Ala Ile Ala Glu Lys Leu Arg Gln Ala
305                 310                 315                 320

Lys Gln Ser Ser Ser Ala Ala Leu Ser Lys Phe Ile Ala Val Tyr Phe
                325                 330                 335

Asp Tyr Ser Cys Glu Gly Asp Val Pro Gly Ile Leu Asp Leu Ser Thr
            340                 345                 350

Lys Tyr Arg Leu Met Asp Asn Leu Pro Gln Leu Cys Ser His Leu His
        355                 360                 365

Ser Arg Asp His Gly Leu Gln Glu Pro Gly Gln His Thr Arg Gln Gly
    370                 375                 380

Ser Arg Arg Asn Tyr Phe Arg Ser Lys Ser Gly Arg Ser Leu Tyr Val
385                 390                 395                 400
```

```
Ala Ile Cys Asn Met His Gln Phe Ile Asp Glu Glu Pro Asp Trp Phe
                405                 410                 415

Glu Lys Gln Phe Val Pro Phe His Pro Pro Pro Leu Arg Tyr Arg Glu
            420                 425                 430

Pro Val Leu Glu Lys Phe Asp Ser Gly Leu Val Leu Asn Asp Val Met
        435                 440                 445

Cys Lys Pro Gly Pro Glu Ser Asp Phe Cys Leu Lys Val Glu Ala Ala
    450                 455                 460

Val Leu Gly Ala Thr Gly Pro Ala Asp Ser Gln His Glu Ser Gln His
465                 470                 475                 480

Gly Gly Leu Asp Gln Asp Gly Glu Ala Arg Pro Ala Leu Asp Gly Ser
                485                 490                 495

Ala Ala Leu Gln Pro Leu Leu His Thr Val Lys Ala Gly Ser Pro Ser
            500                 505                 510

Asp Met Pro Arg Asp Ser Gly Ile Tyr Asp Ser Ser Val Pro Ser Ser
        515                 520                 525

Glu Leu Ser Leu Pro Leu Met Glu Gly Leu Ser Thr Asp Gln Thr Glu
    530                 535                 540

Thr Ser Ser Leu Thr Glu Ser Val Ser Ser Ser Ser Gly Leu Gly Glu
545                 550                 555                 560

Glu Glu Pro Pro Ala Leu Pro Ser Lys Leu Leu Ser Ser Gly Ser Cys
                565                 570                 575

Lys Ala Asp Leu Gly Cys Arg Ser Tyr Thr Asp Glu Leu His Ala Val
            580                 585                 590

Ala Pro Leu
        595


<210>  350
<211>  533
<212>  PRT
<213>  Homo sapiens

<400>  350

Met Gly Ser Ser Arg Leu Ala Ala Leu Leu Leu Pro Leu Leu Leu Ile
1               5                   10                  15

Val Ile Asp Leu Ser Asp Ser Ala Gly Ile Gly Phe Arg His Leu Pro
            20                  25                  30
```

```
His Trp Asn Thr Arg Cys Pro Leu Ala Ser His Thr Asp Asp Ser Phe
        35                  40                  45

Thr Gly Ser Ser Ala Tyr Ile Pro Cys Arg Thr Trp Trp Ala Leu Phe
    50                  55                  60

Ser Thr Lys Pro Trp Cys Val Arg Val Trp His Cys Ser Arg Cys Leu
65                  70                  75                  80

Cys Gln His Leu Leu Ser Gly Gly Ser Gly Leu Gln Arg Gly Leu Phe
                85                  90                  95

His Leu Leu Val Gln Lys Ser Lys Lys Ser Ser Thr Phe Lys Phe Tyr
            100                 105                 110

Arg Arg His Lys Met Pro Ala Pro Ala Gln Arg Lys Leu Leu Pro Arg
        115                 120                 125

Arg His Leu Ser Glu Lys Ser His His Ile Ser Ile Pro Ser Pro Asp
    130                 135                 140

Ile Ser His Lys Gly Leu Arg Ser Lys Arg Thr Gln Pro Ser Asp Pro
145                 150                 155                 160

Glu Thr Trp Glu Ser Leu Pro Arg Leu Asp Ser Gln Arg His Gly Gly
                165                 170                 175

Pro Glu Phe Ser Phe Asp Leu Leu Pro Glu Ala Arg Ala Ile Arg Val
            180                 185                 190

Thr Ile Ser Ser Gly Pro Glu Val Ser Val Arg Leu Cys His Gln Trp
        195                 200                 205

Ala Leu Glu Cys Glu Glu Leu Ser Ser Pro Tyr Asp Val Gln Lys Ile
    210                 215                 220

Val Ser Gly Gly His Thr Val Glu Leu Pro Tyr Glu Phe Leu Leu Pro
225                 230                 235                 240

Cys Leu Cys Ile Glu Ala Ser Tyr Leu Gln Glu Asp Thr Val Arg Arg
                245                 250                 255

Lys Lys Cys Pro Phe Gln Ser Trp Pro Glu Ala Tyr Gly Ser Asp Phe
            260                 265                 270

Trp Lys Ser Val His Phe Thr Asp Tyr Ser Gln His Thr Gln Met Val
        275                 280                 285

Met Ala Leu Thr Leu Arg Cys Pro Leu Lys Leu Glu Ala Ala Leu Cys
    290                 295                 300
```

```
Gln Arg His Asp Trp His Thr Leu Cys Lys Asp Leu Pro Asn Ala Thr
305                 310                 315                 320

Ala Arg Glu Ser Asp Gly Trp Tyr Val Leu Glu Lys Val Asp Leu His
                325                 330                 335

Pro Gln Leu Cys Phe Lys Phe Ser Phe Gly Asn Ser Ser His Val Glu
            340                 345                 350

Cys Pro His Gln Thr Gly Ser Leu Thr Ser Trp Asn Val Ser Met Asp
        355                 360                 365

Thr Gln Ala Gln Gln Leu Ile Leu His Phe Ser Ser Arg Met His Ala
    370                 375                 380

Thr Phe Ser Ala Ala Trp Ser Leu Pro Gly Leu Gly Gln Asp Thr Leu
385                 390                 395                 400

Val Pro Pro Val Tyr Thr Val Ser Gln Ala Arg Gly Ser Ser Pro Val
                405                 410                 415

Ser Leu Asp Leu Ile Ile Pro Phe Leu Arg Pro Gly Cys Cys Val Leu
            420                 425                 430

Leu His Ala Ser Leu Ser Ser Pro Gly Gly Glu Asp Ala Trp Leu Ile
        435                 440                 445

Gly Val Gly Gly Ser Val Pro Ser Gly Val Ala Val Arg Cys Pro Val
    450                 455                 460

Cys Leu Glu Ala Pro Leu Val Ser Gly Cys Leu Leu Gln Thr Pro Gly
465                 470                 475                 480

Ala Leu Asp Pro Gly Thr Ala Gly Pro Pro His Pro Thr Gly Cys Cys
                485                 490                 495

Ser Gly Pro His Leu Pro Ala Pro Thr Val Arg Pro Gly Pro Ser Ala
            500                 505                 510

Ala Ser Ala Pro Pro Ala Arg Gly Gly Leu Gly Gly Ala Ala Ala Pro
        515                 520                 525

Gly Gly Ser Ala Gly
    530
```

<210> 351
<211> 569
<212> PRT
<213> Homo sapiens

<400> 351

```
Met Lys Val Leu Leu Arg Leu Ile Cys Phe Ile Ala Leu Leu Ile Ser
```

```
1               5                  10                  15

Ser Leu Glu Ala Asp Lys Cys Lys Glu Arg Glu Glu Lys Ile Ile Leu
            20                  25                  30

Val Ser Ser Ala Asn Glu Ile Asp Val Arg Pro Cys Pro Leu Asn Pro
        35                  40                  45

Asn Glu His Lys Gly Thr Ile Thr Trp Tyr Lys Asp Asp Ser Lys Thr
    50                  55                  60

Pro Val Ser Thr Glu Gln Ala Ser Arg Ile His Gln His Lys Glu Lys
65                  70                  75                  80

Leu Trp Phe Val Pro Ala Lys Val Glu Asp Ser Gly His Tyr Tyr Cys
                85                  90                  95

Val Val Arg Asn Ser Ser Tyr Cys Leu Arg Ile Lys Ile Ser Ala Lys
            100                 105                 110

Phe Val Glu Asn Glu Pro Asn Leu Cys Tyr Asn Ala Gln Ala Ile Phe
        115                 120                 125

Lys Gln Lys Leu Pro Val Ala Gly Asp Gly Gly Leu Val Cys Pro Tyr
    130                 135                 140

Met Glu Phe Phe Lys Asn Glu Asn Asn Glu Leu Pro Lys Leu Gln Trp
145                 150                 155                 160

Tyr Lys Asp Cys Lys Pro Leu Leu Leu Asp Asn Ile His Phe Ser Gly
                165                 170                 175

Val Lys Asp Arg Leu Ile Val Met Asn Val Ala Glu Lys His Arg Gly
            180                 185                 190

Asn Tyr Thr Cys His Ala Ser Tyr Thr Tyr Leu Gly Lys Gln Tyr Pro
        195                 200                 205

Ile Thr Arg Val Ile Glu Phe Ile Thr Leu Glu Glu Asn Lys Pro Thr
    210                 215                 220

Arg Pro Val Ile Val Ser Pro Ala Asn Glu Thr Met Glu Val Asp Leu
225                 230                 235                 240

Gly Ser Gln Ile Gln Leu Ile Cys Asn Val Thr Gly Gln Leu Ser Asp
                245                 250                 255

Ile Ala Tyr Trp Lys Trp Asn Gly Ser Val Ile Asp Glu Asp Asp Pro
            260                 265                 270

Val Leu Gly Glu Asp Tyr Tyr Ser Val Glu Asn Pro Ala Asn Lys Arg
```

275 280 285

Arg Ser Thr Leu Ile Thr Val Leu Asn Ile Ser Glu Ile Glu Ser Arg
290 295 300

Phe Tyr Lys His Pro Phe Thr Cys Phe Ala Lys Asn Thr His Gly Ile
305 310 315 320

Asp Ala Ala Tyr Ile Gln Leu Ile Tyr Pro Val Thr Asn Phe Gln Lys
325 330 335

His Met Ile Gly Ile Cys Val Thr Leu Thr Val Ile Ile Val Cys Ser
340 345 350

Val Phe Ile Tyr Lys Ile Phe Lys Ile Asp Ile Val Leu Trp Tyr Arg
355 360 365

Asp Ser Cys Tyr Asp Phe Leu Pro Ile Lys Ala Ser Asp Gly Lys Thr
370 375 380

Tyr Asp Ala Tyr Ile Leu Tyr Pro Lys Thr Val Gly Glu Gly Ser Thr
385 390 395 400

Ser Asp Cys Asp Ile Phe Val Phe Lys Val Leu Pro Glu Val Leu Glu
405 410 415

Lys Gln Cys Gly Tyr Lys Leu Phe Ile Tyr Gly Arg Asp Asp Tyr Val
420 425 430

Gly Glu Asp Ile Val Glu Val Ile Asn Glu Asn Val Lys Lys Ser Arg
435 440 445

Arg Leu Ile Ile Ile Leu Val Arg Glu Thr Ser Gly Phe Ser Trp Leu
450 455 460

Gly Gly Ser Ser Glu Glu Gln Ile Ala Met Tyr Asn Ala Leu Val Gln
465 470 475 480

Asp Gly Ile Lys Val Val Leu Leu Glu Leu Glu Lys Ile Gln Asp Tyr
485 490 495

Glu Lys Met Pro Glu Ser Ile Lys Phe Ile Lys Gln Lys His Gly Ala
500 505 510

Ile Arg Trp Ser Gly Asp Phe Thr Gln Gly Pro Gln Ser Ala Lys Thr
515 520 525

Arg Phe Trp Lys Asn Val Arg Tyr His Met Pro Val Gln Arg Arg Ser
530 535 540

Pro Ser Ser Lys His Gln Leu Leu Ser Pro Ala Thr Lys Glu Lys Leu

545 550 555 560

Gln Arg Glu Ala His Val Pro Leu Gly
565

<210> 352
<211> 296
<212> PRT
<213> Homo sapiens

<400> 352

Met Leu Arg Leu Tyr Val Leu Val Met Gly Val Ser Ala Phe Thr Leu
1 5 10 15

Gln Pro Ala Ala His Thr Gly Ala Ala Arg Ser Cys Arg Phe Arg Gly
20 25 30

Arg His Tyr Lys Arg Glu Phe Arg Leu Glu Gly Glu Pro Val Ala Leu
35 40 45

Arg Cys Pro Gln Val Pro Tyr Trp Leu Trp Ala Ser Val Ser Pro Arg
50 55 60

Ile Asn Leu Thr Trp His Lys Asn Asp Ser Ala Arg Thr Val Pro Gly
65 70 75 80

Glu Glu Glu Thr Arg Met Trp Ala Gln Asp Gly Ala Leu Trp Leu Leu
85 90 95

Pro Ala Leu Gln Glu Asp Ser Gly Thr Tyr Val Cys Thr Thr Arg Asn
100 105 110

Ala Ser Tyr Cys Asp Lys Met Ser Ile Glu Leu Arg Val Phe Glu Asn
115 120 125

Thr Asp Ala Phe Leu Pro Phe Ile Ser Tyr Pro Gln Ile Leu Thr Leu
130 135 140

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

Asp Lys Thr Asp Val Lys Ile Gln Trp Tyr Lys Asp Ser Leu Leu Leu
165 170 175

Asp Lys Asp Asn Glu Lys Phe Leu Ser Val Arg Gly Thr Thr His Leu
180 185 190

Leu Val His Asp Val Ala Leu Glu Asp Ala Gly Tyr Tyr Arg Cys Val
195 200 205

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

Glu Leu Arg Ile Lys Lys Lys Glu Glu Thr Ile Pro Val Ile Ile
225 230 235 240

Ser Pro Leu Lys Thr Ile Ser Ala Ser Leu Gly Ser Arg Leu Thr Ile
245 250 255

Pro Cys Lys Val Phe Leu Gly Thr Gly Thr Pro Leu Thr Thr Met Leu
260 265 270

Trp Trp Thr Ala Asn Asp Thr His Ile Glu Ser Ala Tyr Pro Gly Gly
275 280 285

Arg Val Thr Glu Gly Pro Arg Gln
290 295

<210> 353
<211> 211
<212> PRT
<213> Homo sapiens

<400> 353

Met Tyr Ser Thr Val Ser Gly Ser Glu Lys Asn Ser Lys Ile Tyr Cys
1 5 10 15

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

Asn Cys Gln Ala Leu Gln Gly Ser Arg Tyr Arg Ala His Lys Ser Phe
35 40 45

Leu Val Ile Asp Asn Val Met Thr Glu Asp Ala Gly Asp Tyr Thr Cys
50 55 60

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

Arg Ser Phe Thr Val Lys Asp Glu Gln Gly Phe Ser Leu Phe Pro Val
85 90 95

Ile Gly Ala Pro Ala Gln Asn Glu Ile Lys Glu Val Glu Ile Gly Lys
100 105 110

Asn Ala Asn Leu Thr Cys Ser Ala Cys Phe Gly Lys Gly Thr Gln Phe
115 120 125

Leu Ala Ala Val Leu Trp Gln Leu Asn Gly Thr Lys Ile Thr Asp Phe
130 135 140

Gly Glu Pro Arg Ile Gln Gln Glu Glu Gly Gln Asn Gln Ser Phe Ser
145 150 155 160

```
Asn Gly Leu Ala Cys Leu Asp Met Val Leu Arg Ile Ala Asp Val Lys
                165                 170                 175

Glu Glu Asp Leu Leu Leu Gln Tyr Asp Cys Leu Ala Leu Asn Leu His
            180                 185                 190

Gly Leu Arg Arg His Thr Val Arg Leu Ser Arg Lys Asn Pro Ser Lys
        195                 200                 205

Glu Cys Phe
    210
```

<210> 354
<211> 575
<212> PRT
<213> Homo sapiens

<400> 354

```
Met Trp Ser Leu Leu Leu Cys Gly Leu Ser Ile Ala Leu Pro Leu Ser
1               5                   10                  15

Val Thr Ala Asp Gly Cys Lys Asp Ile Phe Met Lys Asn Glu Ile Leu
            20                  25                  30

Ser Ala Ser Gln Pro Phe Ala Phe Asn Cys Thr Phe Pro Pro Ile Thr
        35                  40                  45

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

Val Ser Lys Ile Ile Gln Ser Arg Ile His Gln Asp Glu Thr Trp Ile
65                  70                  75                  80

Leu Phe Leu Pro Met Glu Trp Gly Asp Ser Gly Val Tyr Gln Cys Val
                85                  90                  95

Ile Lys Gly Arg Asp Ser Cys His Arg Ile His Val Asn Leu Thr Val
            100                 105                 110

Phe Glu Lys His Trp Cys Asp Thr Ser Ile Gly Gly Leu Pro Asn Leu
        115                 120                 125

Ser Asp Glu Tyr Lys Gln Ile Leu His Leu Gly Lys Asp Asp Ser Leu
    130                 135                 140

Thr Cys His Leu His Phe Pro Lys Ser Cys Val Leu Gly Pro Ile Lys
145                 150                 155                 160

Trp Tyr Lys Asp Cys Asn Glu Ile Lys Gly Glu Arg Phe Thr Val Leu
                165                 170                 175
```

```
Glu Thr Arg Leu Leu Val Ser Asn Val Ser Ala Glu Asp Arg Gly Asn
            180                 185                 190

Tyr Ala Cys Gln Ala Ile Leu Thr His Ser Gly Lys Gln Tyr Glu Val
        195                 200                 205

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

Ser Val Pro Lys Ile Ile Tyr Pro Lys Asn His Ser Ile Glu Val Gln
225                 230                 235                 240

Leu Gly Thr Thr Leu Ile Val Asp Cys Asn Val Thr Asp Thr Lys Asp
                245                 250                 255

Asn Thr Asn Leu Arg Cys Trp Arg Val Asn Asn Thr Leu Val Asp Asp
            260                 265                 270

Tyr Tyr Asp Glu Ser Lys Arg Ile Arg Glu Gly Val Glu Thr His Val
        275                 280                 285

Ser Phe Arg Glu His Asn Leu Tyr Thr Val Asn Ile Thr Phe Leu Glu
    290                 295                 300

Val Lys Met Glu Asp Tyr Gly Leu Pro Phe Met Cys His Ala Gly Val
305                 310                 315                 320

Ser Thr Ala Tyr Ile Ile Leu Gln Leu Pro Ala Pro Asp Phe Arg Ala
                325                 330                 335

Tyr Leu Ile Gly Gly Leu Ile Ala Leu Val Ala Val Ala Val Ser Val
            340                 345                 350

Val Tyr Ile Tyr Asn Ile Phe Lys Ile Asp Ile Val Leu Trp Tyr Arg
        355                 360                 365

Ser Ala Phe His Ser Thr Glu Thr Ile Val Asp Gly Lys Leu Tyr Asp
    370                 375                 380

Ala Tyr Val Leu Tyr Pro Lys Pro His Lys Glu Ser Gln Arg His Ala
385                 390                 395                 400

Val Asp Ala Leu Val Leu Asn Ile Leu Pro Glu Val Leu Glu Arg Gln
                405                 410                 415

Cys Gly Tyr Lys Leu Phe Ile Phe Gly Arg Asp Glu Phe Pro Gly Gln
            420                 425                 430

Ala Val Ala Asn Val Ile Asp Glu Asn Val Lys Leu Cys Arg Arg Leu
        435                 440                 445
```

Ile Val Ile Val Val Pro Glu Ser Leu Gly Phe Gly Leu Leu Lys Asn
450 455 460

Leu Ser Glu Glu Gln Ile Ala Val Tyr Ser Ala Leu Ile Gln Asp Gly
465 470 475 480

Met Lys Val Ile Leu Ile Glu Leu Glu Lys Ile Glu Asp Tyr Thr Val
485 490 495

Met Pro Glu Ser Ile Gln Tyr Ile Lys Gln Lys His Gly Ala Ile Arg
500 505 510

Trp His Gly Asp Phe Thr Glu Gln Ser Gln Cys Met Lys Thr Lys Phe
515 520 525

Trp Lys Thr Val Arg Tyr His Met Pro Pro Arg Arg Cys Arg Pro Phe
530 535 540

Pro Pro Val Gln Leu Leu Gln His Thr Pro Cys Tyr Arg Thr Ala Gly
545 550 555 560

Pro Glu Leu Gly Ser Arg Arg Lys Lys Cys Thr Leu Thr Thr Gly
565 570 575

<210> 355
<211> 385
<212> PRT
<213> Homo sapiens

<400> 355

Met Asn Cys Lys Lys Leu Leu Leu Glu Asn Asn Lys Asn Pro Thr Ile
1 5 10 15

Lys Lys Asn Ala Glu Phe Glu Asp Gln Gly Tyr Tyr Ser Cys Val His
20 25 30

Phe Leu His His Asn Gly Lys Leu Phe Asn Ile Thr Lys Thr Phe Asn
35 40 45

Ile Thr Ile Val Glu Asp Arg Ser Asn Ile Val Pro Val Leu Leu Gly
50 55 60

Pro Lys Leu Asn His Val Ala Val Glu Leu Gly Lys Asn Val Arg Leu
65 70 75 80

Asn Cys Ser Ala Leu Leu Asn Glu Glu Asp Val Ile Tyr Trp Met Phe
85 90 95

Gly Glu Glu Asn Gly Ser Asp Pro Asn Ile His Glu Glu Lys Glu Met
100 105 110

Arg Ile Met Thr Pro Glu Gly Lys Trp His Ala Ser Lys Val Leu Arg

115 120 125

Ile Glu Asn Ile Gly Glu Ser Asn Leu Asn Val Leu Tyr Asn Cys Thr
130 135 140

Val Ala Ser Thr Gly Gly Thr Asp Thr Lys Ser Phe Ile Leu Val Arg
145 150 155 160

Lys Asp Met Ala Asp Ile Pro Gly His Val Phe Thr Arg Gly Met Ile
165 170 175

Ile Ala Val Leu Ile Leu Val Ala Val Val Cys Leu Val Thr Val Cys
180 185 190

Val Ile Tyr Arg Val Asp Leu Val Leu Phe Tyr Arg His Leu Thr Arg
195 200 205

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

Tyr Leu Lys Glu Cys Arg Pro Glu Asn Gly Glu Glu His Thr Phe Ala
225 230 235 240

Val Glu Ile Leu Pro Arg Val Leu Glu Lys His Phe Gly Tyr Lys Leu
245 250 255

Cys Ile Phe Glu Arg Asp Val Val Pro Gly Gly Ala Val Val Asp Glu
260 265 270

Ile His Ser Leu Ile Glu Lys Ser Arg Arg Leu Ile Ile Val Leu Ser
275 280 285

Lys Ser Tyr Met Ser Asn Glu Val Arg Tyr Glu Leu Glu Ser Gly Leu
290 295 300

His Glu Ala Leu Val Glu Arg Lys Ile Lys Ile Ile Leu Ile Glu Phe
305 310 315 320

Thr Pro Val Thr Asp Phe Thr Phe Leu Pro Gln Ser Leu Lys Leu Leu
325 330 335

Lys Ser His Arg Val Leu Lys Trp Lys Ala Asp Lys Ser Leu Ser Tyr
340 345 350

Asn Ser Arg Phe Trp Lys Asn Leu Leu Tyr Leu Met Pro Ala Lys Thr
355 360 365

Val Lys Pro Gly Arg Asp Glu Pro Glu Val Leu Pro Val Leu Ser Glu
370 375 380

Ser

385

<210> 356
<211> 570
<212> PRT
<213> Homo sapiens

<400> 356

Met Thr Leu Leu Trp Cys Val Val Ser Leu Tyr Phe Tyr Gly Ile Leu
1 5 10 15

Gln Ser Asp Ala Ser Glu Arg Cys Asp Asp Trp Gly Leu Asp Thr Met
20 25 30

Arg Gln Ile Gln Val Phe Glu Asp Glu Pro Ala Arg Ile Lys Cys Pro
35 40 45

Leu Phe Glu His Phe Leu Lys Phe Asn Tyr Ser Thr Ala His Ser Ala
50 55 60

Gly Leu Thr Leu Ile Trp Tyr Trp Thr Arg Gln Asp Arg Asp Leu Glu
65 70 75 80

Glu Pro Ile Asn Phe Arg Leu Pro Glu Asn Arg Ile Ser Lys Glu Lys
85 90 95

Asp Val Leu Trp Phe Arg Pro Thr Leu Leu Asn Asp Thr Gly Asn Tyr
100 105 110

Thr Cys Met Leu Arg Asn Thr Thr Tyr Cys Ser Lys Val Ala Phe Pro
115 120 125

Leu Glu Val Val Gln Lys Asp Ser Cys Phe Asn Ser Pro Met Lys Leu
130 135 140

Pro Val His Lys Leu Tyr Ile Glu Tyr Gly Ile Gln Arg Ile Thr Cys
145 150 155 160

Pro Asn Val Asp Gly Tyr Phe Pro Ser Ser Val Lys Pro Thr Ile Thr
165 170 175

Trp Tyr Met Gly Cys Tyr Lys Ile Gln Asn Phe Asn Asn Val Ile Pro
180 185 190

Glu Gly Met Asn Leu Ser Phe Leu Ile Ala Leu Ile Ser Asn Asn Gly
195 200 205

Asn Tyr Thr Cys Val Val Thr Tyr Pro Glu Asn Gly Arg Thr Phe His
210 215 220

Leu Thr Arg Thr Leu Thr Val Lys Val Val Gly Ser Pro Lys Asn Ala
225 230 235 240

```
Val Pro Pro Val Ile His Ser Pro Asn Asp His Val Val Tyr Glu Lys
                245                 250                 255

Glu Pro Gly Glu Glu Leu Leu Ile Pro Cys Thr Val Tyr Phe Ser Phe
            260                 265                 270

Leu Met Asp Ser Arg Asn Glu Val Trp Trp Thr Ile Asp Gly Lys Lys
        275                 280                 285

Pro Asp Asp Ile Thr Ile Asp Val Thr Ile Asn Glu Ser Ile Ser His
    290                 295                 300

Ser Arg Thr Glu Asp Glu Thr Arg Thr Gln Ile Leu Ser Ile Lys Lys
305                 310                 315                 320

Val Thr Ser Glu Asp Leu Lys Arg Ser Tyr Val Cys His Ala Arg Ser
                325                 330                 335

Ala Lys Gly Glu Val Ala Lys Ala Ala Lys Val Lys Gln Lys Val Pro
            340                 345                 350

Ala Pro Arg Tyr Thr Val Glu Leu Ala Cys Gly Phe Gly Ala Thr Val
        355                 360                 365

Leu Leu Val Val Ile Leu Ile Val Val Tyr His Val Tyr Trp Leu Glu
    370                 375                 380

Met Val Leu Phe Tyr Arg Ala His Phe Gly Thr Asp Glu Thr Ile Leu
385                 390                 395                 400

Asp Gly Lys Glu Tyr Asp Ile Tyr Val Ser Tyr Ala Arg Asn Ala Glu
                405                 410                 415

Glu Glu Glu Phe Val Leu Leu Thr Leu Arg Gly Val Leu Glu Asn Glu
            420                 425                 430

Phe Gly Tyr Lys Leu Cys Ile Phe Asp Arg Asp Ser Leu Pro Gly Gly
        435                 440                 445

Ile Val Thr Asp Glu Thr Leu Ser Phe Ile Gln Lys Ser Arg Arg Leu
    450                 455                 460

Leu Val Val Leu Ser Pro Asn Tyr Val Leu Gln Gly Thr Gln Ala Leu
465                 470                 475                 480

Leu Glu Leu Lys Ala Gly Leu Glu Asn Met Ala Ser Arg Gly Asn Ile
                485                 490                 495

Asn Val Ile Leu Val Gln Tyr Lys Ala Val Lys Glu Thr Lys Val Lys
            500                 505                 510
```

Glu Leu Lys Arg Ala Lys Thr Val Leu Thr Val Ile Lys Trp Lys Gly
515 520 525

Glu Lys Ser Lys Tyr Pro Gln Gly Arg Phe Trp Lys Gln Leu Gln Val
530 535 540

Ala Met Pro Val Lys Lys Ser Pro Arg Arg Ser Ser Ser Asp Glu Gln
545 550 555 560

Gly Leu Ser Tyr Ser Ser Leu Lys Asn Val
565 570

<210> 357
<211> 599
<212> PRT
<213> Homo sapiens

<400> 357

Met Leu Cys Leu Gly Trp Ile Phe Leu Trp Leu Val Ala Gly Glu Arg
1 5 10 15

Ile Lys Gly Phe Asn Ile Ser Gly Cys Ser Thr Lys Lys Leu Leu Trp
20 25 30

Thr Tyr Ser Thr Arg Ser Glu Glu Glu Phe Val Leu Phe Cys Asp Leu
35 40 45

Pro Glu Pro Gln Lys Ser His Phe Cys His Arg Asn Arg Leu Ser Pro
50 55 60

Lys Gln Val Pro Glu His Leu Pro Phe Met Gly Ser Asn Asp Leu Ser
65 70 75 80

Asp Val Gln Trp Tyr Gln Gln Pro Ser Asn Gly Asp Pro Leu Glu Asp
85 90 95

Ile Arg Lys Ser Tyr Pro His Ile Ile Gln Asp Lys Cys Thr Leu His
100 105 110

Phe Leu Thr Pro Gly Val Asn Asn Ser Gly Ser Tyr Ile Cys Arg Pro
115 120 125

Lys Met Ile Lys Ser Pro Tyr Asp Val Ala Cys Cys Val Lys Met Ile
130 135 140

Leu Glu Val Lys Pro Gln Thr Asn Ala Ser Cys Glu Tyr Ser Ala Ser
145 150 155 160

His Lys Gln Asp Leu Leu Leu Gly Ser Thr Gly Ser Ile Ser Cys Pro
165 170 175

```
Ser Leu Ser Cys Gln Ser Asp Ala Gln Ser Pro Ala Val Thr Trp Tyr
            180                 185                 190

Lys Asn Gly Lys Leu Leu Ser Val Glu Arg Ser Asn Arg Ile Val Val
        195                 200                 205

Asp Glu Val Tyr Asp Tyr His Gln Gly Thr Tyr Val Cys Asp Tyr Thr
    210                 215                 220

Gln Ser Asp Thr Val Ser Ser Trp Thr Val Arg Ala Val Val Gln Val
225                 230                 235                 240

Arg Thr Ile Val Gly Asp Thr Lys Leu Lys Pro Asp Ile Leu Asp Pro
                245                 250                 255

Val Glu Asp Thr Leu Glu Val Glu Leu Gly Lys Pro Leu Thr Ile Ser
            260                 265                 270

Cys Lys Ala Arg Phe Gly Phe Glu Arg Val Phe Asn Pro Val Ile Lys
        275                 280                 285

Trp Tyr Ile Lys Asp Ser Asp Leu Glu Trp Glu Val Ser Val Pro Glu
    290                 295                 300

Ala Lys Ser Ile Lys Ser Thr Leu Lys Asp Glu Ile Ile Glu Arg Asn
305                 310                 315                 320

Ile Ile Leu Glu Lys Val Thr Gln Arg Asp Leu Arg Arg Lys Phe Val
                325                 330                 335

Cys Phe Val Gln Asn Ser Ile Gly Asn Thr Thr Gln Ser Val Gln Leu
            340                 345                 350

Lys Glu Lys Arg Gly Val Val Leu Leu Tyr Ile Leu Leu Gly Thr Ile
        355                 360                 365

Gly Thr Leu Val Ala Val Leu Ala Ala Ser Ala Leu Leu Tyr Arg His
    370                 375                 380

Trp Ile Glu Ile Val Leu Leu Tyr Arg Thr Tyr Gln Ser Lys Asp Gln
385                 390                 395                 400

Thr Leu Gly Asp Lys Lys Asp Phe Asp Ala Phe Val Ser Tyr Ala Lys
                405                 410                 415

Trp Ser Ser Phe Pro Ser Glu Ala Thr Ser Ser Leu Ser Glu Glu His
            420                 425                 430

Leu Ala Leu Ser Leu Phe Pro Asp Val Leu Glu Asn Lys Tyr Gly Tyr
        435                 440                 445
```

```
Ser Leu Cys Leu Leu Glu Arg Asp Val Ala Pro Gly Gly Val Tyr Ala
    450                 455                 460

Glu Asp Ile Val Ser Ile Ile Lys Arg Ser Arg Arg Gly Ile Phe Ile
465                 470                 475                 480

Leu Ser Pro Asn Tyr Val Asn Gly Pro Ser Ile Phe Glu Leu Gln Ala
                485                 490                 495

Ala Val Asn Leu Ala Leu Asp Asp Gln Thr Leu Lys Leu Ile Leu Ile
            500                 505                 510

Lys Phe Cys Tyr Phe Gln Glu Pro Glu Ser Leu Pro His Leu Val Lys
        515                 520                 525

Lys Ala Leu Arg Val Leu Pro Thr Val Thr Trp Arg Gly Leu Lys Ser
    530                 535                 540

Val Pro Pro Asn Ser Arg Phe Trp Ala Lys Met Arg Tyr His Met Pro
545                 550                 555                 560

Val Lys Asn Ser Gln Gly Phe Thr Trp Asn Gln Leu Arg Ile Thr Ser
                565                 570                 575

Arg Ile Phe Gln Trp Lys Gly Leu Ser Arg Thr Glu Thr Thr Gly Arg
            580                 585                 590

Ser Ser Gln Pro Lys Glu Trp
        595
```

<210> 358
<211> 1089
<212> PRT
<213> Homo sapiens

<400> 358

```
Met Gly Thr Ser His Pro Ala Phe Leu Val Leu Gly Cys Leu Leu Thr
1               5                   10                  15

Gly Leu Ser Leu Ile Leu Cys Gln Leu Ser Leu Pro Ser Ile Leu Pro
            20                  25                  30

Asn Glu Asn Glu Lys Val Val Gln Leu Asn Ser Ser Phe Ser Leu Arg
        35                  40                  45

Cys Phe Gly Glu Ser Glu Val Ser Trp Gln Tyr Pro Met Ser Glu Glu
    50                  55                  60

Glu Ser Ser Asp Val Glu Ile Arg Asn Glu Glu Asn Asn Ser Gly Leu
65                  70                  75                  80
```

```
Phe Val Thr Val Leu Glu Val Ser Ser Ala Ser Ala Ala His Thr Gly
                85                  90                  95

Leu Tyr Thr Cys Tyr Tyr Asn His Thr Gln Thr Glu Glu Asn Glu Leu
            100                 105                 110

Glu Gly Arg His Ile Tyr Ile Tyr Val Pro Asp Pro Asp Val Ala Phe
        115                 120                 125

Val Pro Leu Gly Met Thr Asp Tyr Leu Val Ile Val Glu Asp Asp Asp
    130                 135                 140

Ser Ala Ile Ile Pro Cys Arg Thr Thr Asp Pro Glu Thr Pro Val Thr
145                 150                 155                 160

Leu His Asn Ser Glu Gly Val Val Pro Ala Ser Tyr Asp Ser Arg Gln
                165                 170                 175

Gly Phe Asn Gly Thr Phe Thr Val Gly Pro Tyr Ile Cys Glu Ala Thr
            180                 185                 190

Val Lys Gly Lys Lys Phe Gln Thr Ile Pro Phe Asn Val Tyr Ala Leu
        195                 200                 205

Lys Ala Thr Ser Glu Leu Asp Leu Glu Met Glu Ala Leu Lys Thr Val
    210                 215                 220

Tyr Lys Ser Gly Glu Thr Ile Val Val Thr Cys Ala Val Phe Asn Asn
225                 230                 235                 240

Glu Val Val Asp Leu Gln Trp Thr Tyr Pro Gly Glu Val Lys Gly Lys
                245                 250                 255

Gly Ile Thr Met Leu Glu Glu Ile Lys Val Pro Ser Ile Lys Leu Val
            260                 265                 270

Tyr Thr Leu Thr Val Pro Glu Ala Thr Val Lys Asp Ser Gly Asp Tyr
        275                 280                 285

Glu Cys Ala Ala Arg Gln Ala Thr Arg Glu Val Lys Glu Met Lys Lys
    290                 295                 300

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

Phe Ser Gln Leu Glu Ala Val Asn Leu His Glu Val Lys His Phe Val
                325                 330                 335

Val Glu Val Arg Ala Tyr Pro Pro Pro Arg Ile Ser Trp Leu Lys Asn
            340                 345                 350
```

```
Asn Leu Thr Leu Ile Glu Asn Leu Thr Glu Ile Thr Thr Asp Val Glu
        355                 360                 365

Lys Ile Gln Glu Ile Arg Tyr Arg Ser Lys Leu Lys Leu Ile Arg Ala
    370                 375                 380

Lys Glu Glu Asp Ser Gly His Tyr Thr Ile Val Ala Gln Asn Glu Asp
385                 390                 395                 400

Ala Val Lys Ser Tyr Thr Phe Glu Leu Leu Thr Gln Val Pro Ser Ser
                405                 410                 415

Ile Leu Asp Leu Val Asp Asp His His Gly Ser Thr Gly Gly Gln Thr
            420                 425                 430

Val Arg Cys Thr Ala Glu Gly Thr Pro Leu Pro Asp Ile Glu Trp Met
        435                 440                 445

Ile Cys Lys Asp Ile Lys Lys Cys Asn Asn Glu Thr Ser Trp Thr Ile
    450                 455                 460

Leu Ala Asn Asn Val Ser Asn Ile Ile Thr Glu Ile His Ser Arg Asp
465                 470                 475                 480

Arg Ser Thr Val Glu Gly Arg Val Thr Phe Ala Lys Val Glu Glu Thr
                485                 490                 495

Ile Ala Val Arg Cys Leu Ala Lys Asn Leu Leu Gly Ala Glu Asn Arg
            500                 505                 510

Glu Leu Lys Leu Val Ala Pro Thr Leu Arg Ser Glu Leu Thr Val Ala
        515                 520                 525

Ala Ala Val Leu Val Leu Leu Val Ile Val Ile Ile Ser Leu Ile Val
    530                 535                 540

Leu Val Val Ile Trp Lys Gln Lys Pro Arg Tyr Glu Ile Arg Trp Arg
545                 550                 555                 560

Val Ile Glu Ser Ile Ser Pro Asp Gly His Glu Tyr Ile Tyr Val Asp
                565                 570                 575

Pro Met Gln Leu Pro Tyr Asp Ser Arg Trp Glu Phe Pro Arg Asp Gly
            580                 585                 590

Leu Val Leu Gly Arg Val Leu Gly Ser Gly Ala Phe Gly Lys Val Val
        595                 600                 605

Glu Gly Thr Ala Tyr Gly Leu Ser Arg Ser Gln Pro Val Met Lys Val
    610                 615                 620
```

```
Ala Val Lys Met Leu Lys Pro Thr Ala Arg Ser Ser Glu Lys Gln Ala
625                 630                 635                 640

Leu Met Ser Glu Leu Lys Ile Met Thr His Leu Gly Pro His Leu Asn
                645                 650                 655

Ile Val Asn Leu Leu Gly Ala Cys Thr Lys Ser Gly Pro Ile Tyr Ile
            660                 665                 670

Ile Thr Glu Tyr Cys Phe Tyr Gly Asp Leu Val Asn Tyr Leu His Lys
        675                 680                 685

Asn Arg Asp Ser Phe Leu Ser His His Pro Glu Lys Pro Lys Lys Glu
    690                 695                 700

Leu Asp Ile Phe Gly Leu Asn Pro Ala Asp Glu Ser Thr Arg Ser Tyr
705                 710                 715                 720

Val Ile Leu Ser Phe Glu Asn Asn Gly Asp Tyr Met Asp Met Lys Gln
                725                 730                 735

Ala Asp Thr Thr Gln Tyr Val Pro Met Leu Glu Arg Lys Glu Val Ser
            740                 745                 750

Lys Tyr Ser Asp Ile Gln Arg Ser Leu Tyr Asp Arg Pro Ala Ser Tyr
        755                 760                 765

Lys Lys Lys Ser Met Leu Asp Ser Glu Val Lys Asn Leu Leu Ser Asp
    770                 775                 780

Asp Asn Ser Glu Gly Leu Thr Leu Leu Asp Leu Leu Ser Phe Thr Tyr
785                 790                 795                 800

Gln Val Ala Arg Gly Met Glu Phe Leu Ala Ser Lys Asn Cys Val His
                805                 810                 815

Arg Asp Leu Ala Ala Arg Asn Val Leu Leu Ala Gln Gly Lys Ile Val
            820                 825                 830

Lys Ile Cys Asp Phe Gly Leu Ala Arg Asp Ile Met His Asp Ser Asn
        835                 840                 845

Tyr Val Ser Lys Gly Ser Thr Phe Leu Pro Val Lys Trp Met Ala Pro
    850                 855                 860

Glu Ser Ile Phe Asp Asn Leu Tyr Thr Thr Leu Ser Asp Val Trp Ser
865                 870                 875                 880

Tyr Gly Ile Leu Leu Trp Glu Ile Phe Ser Leu Gly Gly Thr Pro Tyr
                885                 890                 895
```

```
Pro Gly Met Met Val Asp Ser Thr Phe Tyr Asn Lys Ile Lys Ser Gly
            900                 905                 910

Tyr Arg Met Ala Lys Pro Asp His Ala Thr Ser Glu Val Tyr Glu Ile
        915                 920                 925

Met Val Lys Cys Trp Asn Ser Glu Pro Glu Lys Arg Pro Ser Phe Tyr
    930                 935                 940

His Leu Ser Glu Ile Val Glu Asn Leu Leu Pro Gly Gln Tyr Lys Lys
945                 950                 955                 960

Ser Tyr Glu Lys Ile His Leu Asp Phe Leu Lys Ser Asp His Pro Ala
                965                 970                 975

Val Ala Arg Met Arg Val Asp Ser Asp Asn Ala Tyr Ile Gly Val Thr
            980                 985                 990

Tyr Lys Asn Glu Glu Asp Lys Leu  Lys Asp Trp Glu Gly  Gly Leu Asp
        995                 1000                1005

Glu Gln  Arg Leu Ser Ala Asp  Ser Gly Tyr Ile Ile  Pro Leu Pro
    1010                1015                1020

Asp Ile  Asp Pro Val Pro Glu  Glu Glu Asp Leu Gly  Lys Arg Asn
    1025                1030                1035

Arg His  Ser Ser Gln Thr Ser  Glu Glu Ser Ala Ile  Glu Thr Gly
    1040                1045                1050

Ser Ser  Ser Ser Thr Phe Ile  Lys Arg Glu Asp Glu  Thr Ile Glu
    1055                1060                1065

Asp Ile  Asp Met Met Asp Asp  Ile Gly Ile Asp Ser  Ser Asp Leu
    1070                1075                1080

Val Glu  Asp Ser Phe Leu
    1085
```

<210> 359
<211> 1106
<212> PRT
<213> Homo sapiens

<400> 359

```
Met Arg Leu Pro Gly Ala Met Pro Ala Leu Ala Leu Lys Gly Glu Leu
1               5                   10                  15

Leu Leu Leu Ser Leu Leu Leu Leu Leu Glu Pro Gln Ile Ser Gln Gly
            20                  25                  30

Leu Val Val Thr Pro Pro Gly Pro Glu Leu Val Leu Asn Val Ser Ser
```

35 40 45

Thr Phe Val Leu Thr Cys Ser Gly Ser Ala Pro Val Val Trp Glu Arg
50 55 60

Met Ser Gln Glu Pro Pro Gln Glu Met Ala Lys Ala Gln Asp Gly Thr
65 70 75 80

Phe Ser Ser Val Leu Thr Leu Thr Asn Leu Thr Gly Leu Asp Thr Gly
85 90 95

Glu Tyr Phe Cys Thr His Asn Asp Ser Arg Gly Leu Glu Thr Asp Glu
100 105 110

Arg Lys Arg Leu Tyr Ile Phe Val Pro Asp Pro Thr Val Gly Phe Leu
115 120 125

Pro Asn Asp Ala Glu Glu Leu Phe Ile Phe Leu Thr Glu Ile Thr Glu
130 135 140

Ile Thr Ile Pro Cys Arg Val Thr Asp Pro Gln Leu Val Val Thr Leu
145 150 155 160

His Glu Lys Lys Gly Asp Val Ala Leu Pro Val Pro Tyr Asp His Gln
165 170 175

Arg Gly Phe Ser Gly Ile Phe Glu Asp Arg Ser Tyr Ile Cys Lys Thr
180 185 190

Thr Ile Gly Asp Arg Glu Val Asp Ser Asp Ala Tyr Tyr Val Tyr Arg
195 200 205

Leu Gln Val Ser Ser Ile Asn Val Ser Val Asn Ala Val Gln Thr Val
210 215 220

Val Arg Gln Gly Glu Asn Ile Thr Leu Met Cys Ile Val Ile Gly Asn
225 230 235 240

Glu Val Val Asn Phe Glu Trp Thr Tyr Pro Arg Lys Glu Ser Gly Arg
245 250 255

Leu Val Glu Pro Val Thr Asp Phe Leu Leu Asp Met Pro Tyr His Ile
260 265 270

Arg Ser Ile Leu His Ile Pro Ser Ala Glu Leu Glu Asp Ser Gly Thr
275 280 285

Tyr Thr Cys Asn Val Thr Glu Ser Val Asn Asp His Gln Asp Glu Lys
290 295 300

Ala Ile Asn Ile Thr Val Val Glu Ser Gly Tyr Val Arg Leu Leu Gly

305 310 315 320

Glu Val Gly Thr Leu Gln Phe Ala Glu Leu His Arg Ser Arg Thr Leu
325 330 335

Gln Val Val Phe Glu Ala Tyr Pro Pro Pro Thr Val Leu Trp Phe Lys
340 345 350

Asp Asn Arg Thr Leu Gly Asp Ser Ser Ala Gly Glu Ile Ala Leu Ser
355 360 365

Thr Arg Asn Val Ser Glu Thr Arg Tyr Val Ser Glu Leu Thr Leu Val
370 375 380

Arg Val Lys Val Ala Glu Ala Gly His Tyr Thr Met Arg Ala Phe His
385 390 395 400

Glu Asp Ala Glu Val Gln Leu Ser Phe Gln Leu Gln Ile Asn Val Pro
405 410 415

Val Arg Val Leu Glu Leu Ser Glu Ser His Pro Asp Ser Gly Glu Gln
420 425 430

Thr Val Arg Cys Arg Gly Arg Gly Met Pro Gln Pro Asn Ile Ile Trp
435 440 445

Ser Ala Cys Arg Asp Leu Lys Arg Cys Pro Arg Glu Leu Pro Pro Thr
450 455 460

Leu Leu Gly Asn Ser Ser Glu Glu Glu Ser Gln Leu Glu Thr Asn Val
465 470 475 480

Thr Tyr Trp Glu Glu Glu Gln Glu Phe Glu Val Val Ser Thr Leu Arg
485 490 495

Leu Gln His Val Asp Arg Pro Leu Ser Val Arg Cys Thr Leu Arg Asn
500 505 510

Ala Val Gly Gln Asp Thr Gln Glu Val Ile Val Val Pro His Ser Leu
515 520 525

Pro Phe Lys Val Val Val Ile Ser Ala Ile Leu Ala Leu Val Val Leu
530 535 540

Thr Ile Ile Ser Leu Ile Ile Leu Ile Met Leu Trp Gln Lys Lys Pro
545 550 555 560

Arg Tyr Glu Ile Arg Trp Lys Val Ile Glu Ser Val Ser Ser Asp Gly
565 570 575

His Glu Tyr Ile Tyr Val Asp Pro Met Gln Leu Pro Tyr Asp Ser Thr

580 585 590

Trp Glu Leu Pro Arg Asp Gln Leu Val Leu Gly Arg Thr Leu Gly Ser
595 600 605

Gly Ala Phe Gly Gln Val Val Glu Ala Thr Ala His Gly Leu Ser His
610 615 620

Ser Gln Ala Thr Met Lys Val Ala Val Lys Met Leu Lys Ser Thr Ala
625 630 635 640

Arg Ser Ser Glu Lys Gln Ala Leu Met Ser Glu Leu Lys Ile Met Ser
645 650 655

His Leu Gly Pro His Leu Asn Val Val Asn Leu Leu Gly Ala Cys Thr
660 665 670

Lys Gly Gly Pro Ile Tyr Ile Ile Thr Glu Tyr Cys Arg Tyr Gly Asp
675 680 685

Leu Val Asp Tyr Leu His Arg Asn Lys His Thr Phe Leu Gln His His
690 695 700

Ser Asp Lys Arg Arg Pro Pro Ser Ala Glu Leu Tyr Ser Asn Ala Leu
705 710 715 720

Pro Val Gly Leu Pro Leu Pro Ser His Val Ser Leu Thr Gly Glu Ser
725 730 735

Asp Gly Gly Tyr Met Asp Met Ser Lys Asp Glu Ser Val Asp Tyr Val
740 745 750

Pro Met Leu Asp Met Lys Gly Asp Val Lys Tyr Ala Asp Ile Glu Ser
755 760 765

Ser Asn Tyr Met Ala Pro Tyr Asp Asn Tyr Val Pro Ser Ala Pro Glu
770 775 780

Arg Thr Cys Arg Ala Thr Leu Ile Asn Glu Ser Pro Val Leu Ser Tyr
785 790 795 800

Met Asp Leu Val Gly Phe Ser Tyr Gln Val Ala Asn Gly Met Glu Phe
805 810 815

Leu Ala Ser Lys Asn Cys Val His Arg Asp Leu Ala Ala Arg Asn Val
820 825 830

Leu Ile Cys Glu Gly Lys Leu Val Lys Ile Cys Asp Phe Gly Leu Ala
835 840 845

Arg Asp Ile Met Arg Asp Ser Asn Tyr Ile Ser Lys Gly Ser Thr Phe

850 855 860

Leu Pro Leu Lys Trp Met Ala Pro Glu Ser Ile Phe Asn Ser Leu Tyr
865 870 875 880

Thr Thr Leu Ser Asp Val Trp Ser Phe Gly Ile Leu Leu Trp Glu Ile
885 890 895

Phe Thr Leu Gly Gly Thr Pro Tyr Pro Glu Leu Pro Met Asn Glu Gln
900 905 910

Phe Tyr Asn Ala Ile Lys Arg Gly Tyr Arg Met Ala Gln Pro Ala His
915 920 925

Ala Ser Asp Glu Ile Tyr Glu Ile Met Gln Lys Cys Trp Glu Glu Lys
930 935 940

Phe Glu Ile Arg Pro Pro Phe Ser Gln Leu Val Leu Leu Leu Glu Arg
945 950 955 960

Leu Leu Gly Glu Gly Tyr Lys Lys Lys Tyr Gln Gln Val Asp Glu Glu
965 970 975

Phe Leu Arg Ser Asp His Pro Ala Ile Leu Arg Ser Gln Ala Arg Leu
980 985 990

Pro Gly Phe His Gly Leu Arg Ser Pro Leu Asp Thr Ser Ser Val Leu
995 1000 1005

Tyr Thr Ala Val Gln Pro Asn Glu Gly Asp Asn Asp Tyr Ile Ile
1010 1015 1020

Pro Leu Pro Asp Pro Lys Pro Glu Val Ala Asp Glu Gly Pro Leu
1025 1030 1035

Glu Gly Ser Pro Ser Leu Ala Ser Ser Thr Leu Asn Glu Val Asn
1040 1045 1050

Thr Ser Ser Thr Ile Ser Cys Asp Ser Pro Leu Glu Pro Gln Asp
1055 1060 1065

Glu Pro Glu Pro Glu Pro Gln Leu Glu Leu Gln Val Glu Pro Glu
1070 1075 1080

Pro Glu Leu Glu Gln Leu Pro Asp Ser Gly Cys Pro Ala Pro Arg
1085 1090 1095

Ala Glu Ala Glu Asp Ser Phe Leu
1100 1105

<210> 360

<211> 976
<212> PRT
<213> Homo sapiens

<400> 360

Met Arg Gly Ala Arg Gly Ala Trp Asp Phe Leu Cys Val Leu Leu Leu
1 5 10 15

Leu Leu Arg Val Gln Thr Gly Ser Ser Gln Pro Ser Val Ser Pro Gly
20 25 30

Glu Pro Ser Pro Pro Ser Ile His Pro Gly Lys Ser Asp Leu Ile Val
35 40 45

Arg Val Gly Asp Glu Ile Arg Leu Leu Cys Thr Asp Pro Gly Phe Val
50 55 60

Lys Trp Thr Phe Glu Ile Leu Asp Glu Thr Asn Glu Asn Lys Gln Asn
65 70 75 80

Glu Trp Ile Thr Glu Lys Ala Glu Ala Thr Asn Thr Gly Lys Tyr Thr
85 90 95

Cys Thr Asn Lys His Gly Leu Ser Asn Ser Ile Tyr Val Phe Val Arg
100 105 110

Asp Pro Ala Lys Leu Phe Leu Val Asp Arg Ser Leu Tyr Gly Lys Glu
115 120 125

Asp Asn Asp Thr Leu Val Arg Cys Pro Leu Thr Asp Pro Glu Val Thr
130 135 140

Asn Tyr Ser Leu Lys Gly Cys Gln Gly Lys Pro Leu Pro Lys Asp Leu
145 150 155 160

Arg Phe Ile Pro Asp Pro Lys Ala Gly Ile Met Ile Lys Ser Val Lys
165 170 175

Arg Ala Tyr His Arg Leu Cys Leu His Cys Ser Val Asp Gln Glu Gly
180 185 190

Lys Ser Val Leu Ser Glu Lys Phe Ile Leu Lys Val Arg Pro Ala Phe
195 200 205

Lys Ala Val Pro Val Val Ser Val Ser Lys Ala Ser Tyr Leu Leu Arg
210 215 220

Glu Gly Glu Glu Phe Thr Val Thr Cys Thr Ile Lys Asp Val Ser Ser
225 230 235 240

Ser Val Tyr Ser Thr Trp Lys Arg Glu Asn Ser Gln Thr Lys Leu Gln
245 250 255

```
Glu Lys Tyr Asn Ser Trp His His Gly Asp Phe Asn Tyr Glu Arg Gln
            260                 265                 270

Ala Thr Leu Thr Ile Ser Ser Ala Arg Val Asn Asp Ser Gly Val Phe
        275                 280                 285

Met Cys Tyr Ala Asn Asn Thr Phe Gly Ser Ala Asn Val Thr Thr Thr
    290                 295                 300

Leu Glu Val Val Asp Lys Gly Phe Ile Asn Ile Phe Pro Met Ile Asn
305                 310                 315                 320

Thr Thr Val Phe Val Asn Asp Gly Glu Asn Val Asp Leu Ile Val Glu
                325                 330                 335

Tyr Glu Ala Phe Pro Lys Pro Glu His Gln Gln Trp Ile Tyr Met Asn
            340                 345                 350

Arg Thr Phe Thr Asp Lys Trp Glu Asp Tyr Pro Lys Ser Glu Asn Glu
        355                 360                 365

Ser Asn Ile Arg Tyr Val Ser Glu Leu His Leu Thr Arg Leu Lys Gly
    370                 375                 380

Thr Glu Gly Gly Thr Tyr Thr Phe Leu Val Ser Asn Ser Asp Val Asn
385                 390                 395                 400

Ala Ala Ile Ala Phe Asn Val Tyr Val Asn Thr Lys Pro Glu Ile Leu
                405                 410                 415

Thr Tyr Asp Arg Leu Val Asn Gly Met Leu Gln Cys Val Ala Ala Gly
            420                 425                 430

Phe Pro Glu Pro Thr Ile Asp Trp Tyr Phe Cys Pro Gly Thr Glu Gln
        435                 440                 445

Arg Cys Ser Ala Ser Val Leu Pro Val Asp Val Gln Thr Leu Asn Ser
    450                 455                 460

Ser Gly Pro Pro Phe Gly Lys Leu Val Val Gln Ser Ser Ile Asp Ser
465                 470                 475                 480

Ser Ala Phe Lys His Asn Gly Thr Val Glu Cys Lys Ala Tyr Asn Asp
                485                 490                 495

Val Gly Lys Thr Ser Ala Tyr Phe Asn Phe Ala Phe Lys Gly Asn Asn
            500                 505                 510

Lys Glu Gln Ile His Pro His Thr Leu Phe Thr Pro Leu Leu Ile Gly
        515                 520                 525
```

```
Phe Val Ile Val Ala Gly Met Met Cys Ile Ile Val Met Ile Leu Thr
    530                 535                 540

Tyr Lys Tyr Leu Gln Lys Pro Met Tyr Glu Val Gln Trp Lys Val Val
545                 550                 555                 560

Glu Glu Ile Asn Gly Asn Asn Tyr Val Tyr Ile Asp Pro Thr Gln Leu
                565                 570                 575

Pro Tyr Asp His Lys Trp Glu Phe Pro Arg Asn Arg Leu Ser Phe Gly
            580                 585                 590

Lys Thr Leu Gly Ala Gly Ala Phe Gly Lys Val Val Glu Ala Thr Ala
        595                 600                 605

Tyr Gly Leu Ile Lys Ser Asp Ala Ala Met Thr Val Ala Val Lys Met
    610                 615                 620

Leu Lys Pro Ser Ala His Leu Thr Glu Arg Glu Ala Leu Met Ser Glu
625                 630                 635                 640

Leu Lys Val Leu Ser Tyr Leu Gly Asn His Met Asn Ile Val Asn Leu
                645                 650                 655

Leu Gly Ala Cys Thr Ile Gly Gly Pro Thr Leu Val Ile Thr Glu Tyr
            660                 665                 670

Cys Cys Tyr Gly Asp Leu Leu Asn Phe Leu Arg Arg Lys Arg Asp Ser
        675                 680                 685

Phe Ile Cys Ser Lys Gln Glu Asp His Ala Glu Ala Ala Leu Tyr Lys
    690                 695                 700

Asn Leu Leu His Ser Lys Glu Ser Ser Cys Ser Asp Ser Thr Asn Glu
705                 710                 715                 720

Tyr Met Asp Met Lys Pro Gly Val Ser Tyr Val Val Pro Thr Lys Ala
                725                 730                 735

Asp Lys Arg Arg Ser Val Arg Ile Gly Ser Tyr Ile Glu Arg Asp Val
            740                 745                 750

Thr Pro Ala Ile Met Glu Asp Asp Glu Leu Ala Leu Asp Leu Glu Asp
        755                 760                 765

Leu Leu Ser Phe Ser Tyr Gln Val Ala Lys Gly Met Ala Phe Leu Ala
    770                 775                 780

Ser Lys Asn Cys Ile His Arg Asp Leu Ala Ala Arg Asn Ile Leu Leu
785                 790                 795                 800
```

```
Thr His Gly Arg Ile Thr Lys Ile Cys Asp Phe Gly Leu Ala Arg Asp
                805                 810                 815

Ile Lys Asn Asp Ser Asn Tyr Val Val Lys Gly Asn Ala Arg Leu Pro
            820                 825                 830

Val Lys Trp Met Ala Pro Glu Ser Ile Phe Asn Cys Val Tyr Thr Phe
        835                 840                 845

Glu Ser Asp Val Trp Ser Tyr Gly Ile Phe Leu Trp Glu Leu Phe Ser
    850                 855                 860

Leu Gly Ser Ser Pro Tyr Pro Gly Met Pro Val Asp Ser Lys Phe Tyr
865                 870                 875                 880

Lys Met Ile Lys Glu Gly Phe Arg Met Leu Ser Pro Glu His Ala Pro
                885                 890                 895

Ala Glu Met Tyr Asp Ile Met Lys Thr Cys Trp Asp Ala Asp Pro Leu
            900                 905                 910

Lys Arg Pro Thr Phe Lys Gln Ile Val Gln Leu Ile Glu Lys Gln Ile
        915                 920                 925

Ser Glu Ser Thr Asn His Ile Tyr Ser Asn Leu Ala Asn Cys Ser Pro
    930                 935                 940

Asn Arg Gln Lys Pro Val Val Asp His Ser Val Arg Ile Asn Ser Val
945                 950                 955                 960

Gly Ser Thr Ala Ser Ser Ser Gln Pro Leu Leu Val His Asp Asp Val
                965                 970                 975


<210>  361
<211>  972
<212>  PRT
<213>  Homo sapiens

<400>  361

Met Gly Pro Gly Val Leu Leu Leu Leu Leu Val Ala Thr Ala Trp His
1               5                   10                  15

Gly Gln Gly Ile Pro Val Ile Glu Pro Ser Val Pro Glu Leu Val Val
            20                  25                  30

Lys Pro Gly Ala Thr Val Thr Leu Arg Cys Val Gly Asn Gly Ser Val
        35                  40                  45

Glu Trp Asp Gly Pro Pro Ser Pro His Trp Thr Leu Tyr Ser Asp Gly
    50                  55                  60
```

```
Ser Ser Ser Ile Leu Ser Thr Asn Asn Ala Thr Phe Gln Asn Thr Gly
65                  70                  75                  80

Thr Tyr Arg Cys Thr Glu Pro Gly Asp Pro Leu Gly Gly Ser Ala Ala
                85                  90                  95

Ile His Leu Tyr Val Lys Asp Pro Ala Arg Pro Trp Asn Val Leu Ala
            100                 105                 110

Gln Glu Val Val Val Phe Glu Asp Gln Asp Ala Leu Leu Pro Cys Leu
        115                 120                 125

Leu Thr Asp Pro Val Leu Glu Ala Gly Val Ser Leu Val Arg Val Arg
    130                 135                 140

Gly Arg Pro Leu Met Arg His Thr Asn Tyr Ser Phe Ser Pro Trp His
145                 150                 155                 160

Gly Phe Thr Ile His Arg Ala Lys Phe Ile Gln Ser Gln Asp Tyr Gln
                165                 170                 175

Cys Ser Ala Leu Met Gly Gly Arg Lys Val Met Ser Ile Ser Ile Arg
            180                 185                 190

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

Pro Ala Glu Leu Val Arg Ile Arg Gly Glu Ala Ala Gln Ile Val Cys
    210                 215                 220

Ser Ala Ser Ser Val Asp Val Asn Phe Asp Val Phe Leu Gln His Asn
225                 230                 235                 240

Asn Thr Lys Leu Ala Ile Pro Gln Gln Ser Asp Phe His Asn Asn Arg
                245                 250                 255

Tyr Gln Lys Val Leu Thr Leu Asn Leu Asp Gln Val Asp Phe Gln His
            260                 265                 270

Ala Gly Asn Tyr Ser Cys Val Ala Ser Asn Val Gln Gly Lys His Ser
        275                 280                 285

Thr Ser Met Phe Phe Arg Val Val Glu Ser Ala Tyr Leu Asn Leu Ser
    290                 295                 300

Ser Glu Gln Asn Leu Ile Gln Glu Val Thr Val Gly Glu Gly Leu Asn
305                 310                 315                 320

Leu Lys Val Met Val Glu Ala Tyr Pro Gly Leu Gln Gly Phe Asn Trp
                325                 330                 335
```

```
Thr Tyr Leu Gly Pro Phe Ser Asp His Gln Pro Glu Pro Lys Leu Ala
            340                 345                 350

Asn Ala Thr Thr Lys Asp Thr Tyr Arg His Thr Phe Thr Leu Ser Leu
        355                 360                 365

Pro Arg Leu Lys Pro Ser Glu Ala Gly Arg Tyr Ser Phe Leu Ala Arg
    370                 375                 380

Asn Pro Gly Gly Trp Arg Ala Leu Thr Phe Glu Leu Thr Leu Arg Tyr
385                 390                 395                 400

Pro Pro Glu Val Ser Val Ile Trp Thr Phe Ile Asn Gly Ser Gly Thr
                405                 410                 415

Leu Leu Cys Ala Ala Ser Gly Tyr Pro Gln Pro Asn Val Thr Trp Leu
            420                 425                 430

Gln Cys Ser Gly His Thr Asp Arg Cys Asp Glu Ala Gln Val Leu Gln
        435                 440                 445

Val Trp Asp Asp Pro Tyr Pro Glu Val Leu Ser Gln Glu Pro Phe His
    450                 455                 460

Lys Val Thr Val Gln Ser Leu Leu Thr Val Glu Thr Leu Glu His Asn
465                 470                 475                 480

Gln Thr Tyr Glu Cys Arg Ala His Asn Ser Val Gly Ser Gly Ser Trp
                485                 490                 495

Ala Phe Ile Pro Ile Ser Ala Gly Ala His Thr His Pro Pro Asp Glu
            500                 505                 510

Phe Leu Phe Thr Pro Val Val Val Ala Cys Met Ser Ile Met Ala Leu
        515                 520                 525

Leu Leu Leu Leu Leu Leu Leu Leu Leu Tyr Lys Tyr Lys Gln Lys Pro
    530                 535                 540

Lys Tyr Gln Val Arg Trp Lys Ile Ile Glu Ser Tyr Glu Gly Asn Ser
545                 550                 555                 560

Tyr Thr Phe Ile Asp Pro Thr Gln Leu Pro Tyr Asn Glu Lys Trp Glu
                565                 570                 575

Phe Pro Arg Asn Asn Leu Gln Phe Gly Lys Thr Leu Gly Ala Gly Ala
            580                 585                 590

Phe Gly Lys Val Val Glu Ala Thr Ala Phe Gly Leu Gly Lys Glu Asp
        595                 600                 605
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Ala Val Leu Lys Val Ala Val Lys Met Leu Lys Ser Thr Ala His Ala
    610                 615                 620

Asp Glu Lys Glu Ala Leu Met Ser Glu Leu Lys Ile Met Ser His Leu
625                 630                 635                 640

Gly Gln His Glu Asn Ile Val Asn Leu Leu Gly Ala Cys Thr His Gly
                645                 650                 655

Gly Pro Val Leu Val Ile Thr Glu Tyr Cys Cys Tyr Gly Asp Leu Leu
            660                 665                 670

Asn Phe Leu Arg Arg Lys Ala Glu Ala Met Leu Gly Pro Ser Leu Ser
        675                 680                 685

Pro Gly Gln Asp Pro Glu Gly Gly Val Asp Tyr Lys Asn Ile His Leu
    690                 695                 700

Glu Lys Lys Tyr Val Arg Arg Asp Ser Gly Phe Ser Ser Gln Gly Val
705                 710                 715                 720

Asp Thr Tyr Val Glu Met Arg Pro Val Ser Thr Ser Ser Asn Asp Ser
                725                 730                 735

Phe Ser Glu Gln Asp Leu Asp Lys Glu Asp Gly Arg Pro Leu Glu Leu
            740                 745                 750

Arg Asp Leu Leu His Phe Ser Ser Gln Val Ala Gln Gly Met Ala Phe
        755                 760                 765

Leu Ala Ser Lys Asn Cys Ile His Arg Asp Val Ala Ala Arg Asn Val
    770                 775                 780

Leu Leu Thr Asn Gly His Val Ala Lys Ile Gly Asp Phe Gly Leu Ala
785                 790                 795                 800

Arg Asp Ile Met Asn Asp Ser Asn Tyr Ile Val Lys Gly Asn Ala Arg
                805                 810                 815

Leu Pro Val Lys Trp Met Ala Pro Glu Ser Ile Phe Asp Cys Val Tyr
            820                 825                 830

Thr Val Gln Ser Asp Val Trp Ser Tyr Gly Ile Leu Leu Trp Glu Ile
        835                 840                 845

Phe Ser Leu Gly Leu Asn Pro Tyr Pro Gly Ile Leu Val Asn Ser Lys
    850                 855                 860

Phe Tyr Lys Leu Val Lys Asp Gly Tyr Gln Met Ala Gln Pro Ala Phe
865                 870                 875                 880
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```
Ala Pro Lys Asn Ile Tyr Ser Ile Met Gln Ala Cys Trp Ala Leu Glu
                885                 890                 895

Pro Thr His Arg Pro Thr Phe Gln Gln Ile Cys Ser Phe Leu Gln Glu
            900                 905                 910

Gln Ala Gln Glu Asp Arg Arg Glu Arg Asp Tyr Thr Asn Leu Pro Ser
        915                 920                 925

Ser Ser Arg Ser Gly Gly Ser Gly Ser Ser Ser Ser Glu Leu Glu Glu
    930                 935                 940

Glu Ser Ser Ser Glu His Leu Thr Cys Cys Glu Gln Gly Asp Ile Ala
945                 950                 955                 960

Gln Pro Leu Leu Gln Pro Asn Asn Tyr Gln Phe Cys
                965                 970


<210>  362
<211>  455
<212>  PRT
<213>  Homo sapiens

<400>  362

Met Gly Leu Ser Thr Val Pro Asp Leu Leu Leu Pro Leu Val Leu Leu
1               5                   10                  15

Glu Leu Leu Val Gly Ile Tyr Pro Ser Gly Val Ile Gly Leu Val Pro
            20                  25                  30

His Leu Gly Asp Arg Glu Lys Arg Asp Ser Val Cys Pro Gln Gly Lys
        35                  40                  45

Tyr Ile His Pro Gln Asn Asn Ser Ile Cys Cys Thr Lys Cys His Lys
    50                  55                  60

Gly Thr Tyr Leu Tyr Asn Asp Cys Pro Gly Pro Gly Gln Asp Thr Asp
65                  70                  75                  80

Cys Arg Glu Cys Glu Ser Gly Ser Phe Thr Ala Ser Glu Asn His Leu
                85                  90                  95

Arg His Cys Leu Ser Cys Ser Lys Cys Arg Lys Glu Met Gly Gln Val
            100                 105                 110

Glu Ile Ser Ser Cys Thr Val Asp Arg Asp Thr Val Cys Gly Cys Arg
        115                 120                 125

Lys Asn Gln Tyr Arg His Tyr Trp Ser Glu Asn Leu Phe Gln Cys Phe
    130                 135                 140
```

```
Asn Cys Ser Leu Cys Leu Asn Gly Thr Val His Leu Ser Cys Gln Glu
145                 150                 155                 160

Lys Gln Asn Thr Val Cys Thr Cys His Ala Gly Phe Phe Leu Arg Glu
                165                 170                 175

Asn Glu Cys Val Ser Cys Ser Asn Cys Lys Lys Ser Leu Glu Cys Thr
            180                 185                 190

Lys Leu Cys Leu Pro Gln Ile Glu Asn Val Lys Gly Thr Glu Asp Ser
        195                 200                 205

Gly Thr Thr Val Leu Leu Pro Leu Val Ile Phe Phe Gly Leu Cys Leu
    210                 215                 220

Leu Ser Leu Leu Phe Ile Gly Leu Met Tyr Arg Tyr Gln Arg Trp Lys
225                 230                 235                 240

Ser Lys Leu Tyr Ser Ile Val Cys Gly Lys Ser Thr Pro Glu Lys Glu
                245                 250                 255

Gly Glu Leu Glu Gly Thr Thr Thr Lys Pro Leu Ala Pro Asn Pro Ser
            260                 265                 270

Phe Ser Pro Thr Pro Gly Phe Thr Pro Thr Leu Gly Phe Ser Pro Val
        275                 280                 285

Pro Ser Ser Thr Phe Thr Ser Ser Ser Thr Tyr Thr Pro Gly Asp Cys
    290                 295                 300

Pro Asn Phe Ala Ala Pro Arg Arg Glu Val Ala Pro Pro Tyr Gln Gly
305                 310                 315                 320

Ala Asp Pro Ile Leu Ala Thr Ala Leu Ala Ser Asp Pro Ile Pro Asn
                325                 330                 335

Pro Leu Gln Lys Trp Glu Asp Ser Ala His Lys Pro Gln Ser Leu Asp
            340                 345                 350

Thr Asp Asp Pro Ala Thr Leu Tyr Ala Val Val Glu Asn Val Pro Pro
        355                 360                 365

Leu Arg Trp Lys Glu Phe Val Arg Arg Leu Gly Leu Ser Asp His Glu
    370                 375                 380

Ile Asp Arg Leu Glu Leu Gln Asn Gly Arg Cys Leu Arg Glu Ala Gln
385                 390                 395                 400

Tyr Ser Met Leu Ala Thr Trp Arg Arg Arg Thr Pro Arg Arg Glu Ala
                405                 410                 415
```

Thr Leu Glu Leu Leu Gly Arg Val Leu Arg Asp Met Asp Leu Leu Gly
420 425 430

Cys Leu Glu Asp Ile Glu Glu Ala Leu Cys Gly Pro Ala Ala Leu Pro
435 440 445

Pro Ala Pro Ser Leu Leu Arg
450 455

<210> 363
<211> 461
<212> PRT
<213> Homo sapiens

<400> 363

Met Ala Pro Val Ala Val Trp Ala Ala Leu Ala Val Gly Leu Glu Leu
1 5 10 15

Trp Ala Ala Ala His Ala Leu Pro Ala Gln Val Ala Phe Thr Pro Tyr
20 25 30

Ala Pro Glu Pro Gly Ser Thr Cys Arg Leu Arg Glu Tyr Tyr Asp Gln
35 40 45

Thr Ala Gln Met Cys Cys Ser Lys Cys Ser Pro Gly Gln His Ala Lys
50 55 60

Val Phe Cys Thr Lys Thr Ser Asp Thr Val Cys Asp Ser Cys Glu Asp
65 70 75 80

Ser Thr Tyr Thr Gln Leu Trp Asn Trp Val Pro Glu Cys Leu Ser Cys
85 90 95

Gly Ser Arg Cys Ser Ser Asp Gln Val Glu Thr Gln Ala Cys Thr Arg
100 105 110

Glu Gln Asn Arg Ile Cys Thr Cys Arg Pro Gly Trp Tyr Cys Ala Leu
115 120 125

Ser Lys Gln Glu Gly Cys Arg Leu Cys Ala Pro Leu Arg Lys Cys Arg
130 135 140

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

Cys Lys Pro Cys Ala Pro Gly Thr Phe Ser Asn Thr Thr Ser Ser Thr
165 170 175

Asp Ile Cys Arg Pro His Gln Ile Cys Asn Val Val Ala Ile Pro Gly
180 185 190

Asn Ala Ser Met Asp Ala Val Cys Thr Ser Thr Ser Pro Thr Arg Ser

195 200 205

Met Ala Pro Gly Ala Val His Leu Pro Gln Pro Val Ser Thr Arg Ser
210 215 220

Gln His Thr Gln Pro Thr Pro Glu Pro Ser Thr Ala Pro Ser Thr Ser
225 230 235 240

Phe Leu Leu Pro Met Gly Pro Ser Pro Pro Ala Glu Gly Ser Thr Gly
245 250 255

Asp Phe Ala Leu Pro Val Gly Leu Ile Val Gly Val Thr Ala Leu Gly
260 265 270

Leu Leu Ile Ile Gly Val Val Asn Cys Val Ile Met Thr Gln Val Lys
275 280 285

Lys Lys Pro Leu Cys Leu Gln Arg Glu Ala Lys Val Pro His Leu Pro
290 295 300

Ala Asp Lys Ala Arg Gly Thr Gln Gly Pro Glu Gln Gln His Leu Leu
305 310 315 320

Ile Thr Ala Pro Ser Ser Ser Ser Ser Ser Leu Glu Ser Ser Ala Ser
325 330 335

Ala Leu Asp Arg Arg Ala Pro Thr Arg Asn Gln Pro Gln Ala Pro Gly
340 345 350

Val Glu Ala Ser Gly Ala Gly Glu Ala Arg Ala Ser Thr Gly Ser Ser
355 360 365

Asp Ser Ser Pro Gly Gly His Gly Thr Gln Val Asn Val Thr Cys Ile
370 375 380

Val Asn Val Cys Ser Ser Ser Asp His Ser Ser Gln Cys Ser Ser Gln
385 390 395 400

Ala Ser Ser Thr Met Gly Asp Thr Asp Ser Ser Pro Ser Glu Ser Pro
405 410 415

Lys Asp Glu Gln Val Pro Phe Ser Lys Glu Glu Cys Ala Phe Arg Ser
420 425 430

Gln Leu Glu Thr Pro Glu Thr Leu Leu Gly Ser Thr Glu Glu Lys Pro
435 440 445

Leu Pro Leu Gly Val Pro Asp Ala Gly Met Lys Pro Ser
450 455 460

<210> 364

<211> 416
<212> PRT
<213> Homo sapiens

<400> 364

Met Glu Ala Thr Gly Ile Ser Leu Ala Ser Gln Leu Lys Val Pro Pro
1 5 10 15

Tyr Ala Ser Glu Asn Gln Thr Cys Arg Asp Gln Glu Lys Glu Tyr Tyr
20 25 30

Glu Pro Gln His Arg Ile Cys Cys Ser Arg Cys Pro Pro Gly Thr Tyr
35 40 45

Val Ser Ala Lys Cys Ser Arg Ile Arg Asp Thr Val Cys Ala Thr Cys
50 55 60

Ala Glu Asn Ser Tyr Asn Glu His Trp Asn Tyr Leu Thr Ile Cys Gln
65 70 75 80

Leu Cys Arg Pro Cys Asp Pro Val Met Gly Leu Glu Glu Ile Ala Pro
85 90 95

Cys Thr Ser Lys Arg Lys Thr Gln Cys Arg Cys Gln Pro Gly Met Phe
100 105 110

Cys Ala Ala Trp Ala Leu Glu Cys Thr His Cys Glu Leu Leu Ser Asp
115 120 125

Cys Pro Pro Gly Thr Glu Ala Glu Leu Lys Asp Glu Val Gly Lys Gly
130 135 140

Asn Asn His Cys Val Pro Cys Lys Ala Gly His Phe Gln Asn Thr Ser
145 150 155 160

Ser Pro Ser Ala Arg Cys Gln Pro His Thr Arg Cys Glu Asn Gln Gly
165 170 175

Leu Val Glu Ala Ala Pro Gly Thr Ala Gln Ser Asp Thr Thr Cys Lys
180 185 190

Asn Pro Leu Glu Pro Leu Pro Pro Glu Met Ser Gly Thr Met Leu Met
195 200 205

Leu Ala Val Leu Leu Pro Leu Ala Phe Phe Leu Leu Leu Ala Thr Val
210 215 220

Phe Ser Cys Ile Trp Lys Ser His Pro Ser Leu Cys Arg Lys Leu Gly
225 230 235 240

Ser Leu Leu Lys Arg Arg Pro Gln Gly Glu Gly Pro Asn Pro Val Ala
245 250 255

```
Gly Ser Trp Glu Pro Pro Lys Ala His Pro Tyr Phe Pro Asp Leu Val
            260                 265                 270

Gln Pro Leu Leu Pro Ile Ser Gly Asp Val Ser Pro Val Ser Thr Gly
        275                 280                 285

Leu Pro Ala Ala Pro Val Leu Glu Ala Gly Val Pro Gln Gln Gln Ser
    290                 295                 300

Pro Leu Asp Leu Thr Arg Glu Pro Gln Leu Glu Pro Gly Glu Gln Ser
305                 310                 315                 320

Gln Val Ala His Gly Thr Asn Gly Ile His Val Thr Gly Gly Ser Met
                325                 330                 335

Thr Ile Thr Gly Asn Ile Tyr Ile Tyr Asn Gly Pro Val Leu Gly Gly
            340                 345                 350

Pro Pro Gly Pro Gly Asp Leu Pro Ala Thr Pro Glu Pro Pro Tyr Pro
        355                 360                 365

Ile Pro Glu Glu Gly Asp Pro Gly Pro Pro Gly Leu Ser Thr Pro His
    370                 375                 380

Gln Glu Asp Gly Lys Ala Trp His Leu Ala Glu Thr Glu His Cys Gly
385                 390                 395                 400

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


<210>  365
<211>  277
<212>  PRT
<213>  Homo sapiens

<400>  365

Met Cys Val Gly Ala Arg Arg Leu Gly Arg Gly Pro Cys Ala Ala Leu
1               5                   10                  15

Leu Leu Leu Gly Leu Gly Leu Ser Thr Val Thr Gly Leu His Cys Val
            20                  25                  30

Gly Asp Thr Tyr Pro Ser Asn Asp Arg Cys Cys His Glu Cys Arg Pro
        35                  40                  45

Gly Asn Gly Met Val Ser Arg Cys Ser Arg Ser Gln Asn Thr Val Cys
    50                  55                  60

Arg Pro Cys Gly Pro Gly Phe Tyr Asn Asp Val Val Ser Ser Lys Pro
65                  70                  75                  80
```

```
Cys Lys Pro Cys Thr Trp Cys Asn Leu Arg Ser Gly Ser Glu Arg Lys
                85                  90                  95

Gln Leu Cys Thr Ala Thr Gln Asp Thr Val Cys Arg Cys Arg Ala Gly
            100                 105                 110

Thr Gln Pro Leu Asp Ser Tyr Lys Pro Gly Val Asp Cys Ala Pro Cys
        115                 120                 125

Pro Pro Gly His Phe Ser Pro Gly Asp Asn Gln Ala Cys Lys Pro Trp
    130                 135                 140

Thr Asn Cys Thr Leu Ala Gly Lys His Thr Leu Gln Pro Ala Ser Asn
145                 150                 155                 160

Ser Ser Asp Ala Ile Cys Glu Asp Arg Asp Pro Pro Ala Thr Gln Pro
                165                 170                 175

Gln Glu Thr Gln Gly Pro Pro Ala Arg Pro Ile Thr Val Gln Pro Thr
            180                 185                 190

Glu Ala Trp Pro Arg Thr Ser Gln Gly Pro Ser Thr Arg Pro Val Glu
        195                 200                 205

Val Pro Gly Gly Arg Ala Val Ala Ala Ile Leu Gly Leu Gly Leu Val
    210                 215                 220

Leu Gly Leu Leu Gly Pro Leu Ala Ile Leu Leu Ala Leu Tyr Leu Leu
225                 230                 235                 240

Arg Arg Asp Gln Arg Leu Pro Pro Asp Ala His Lys Pro Pro Gly Gly
                245                 250                 255

Gly Ser Phe Arg Thr Pro Ile Gln Glu Glu Gln Ala Asp Ala His Ser
            260                 265                 270

Thr Leu Ala Lys Ile
        275


<210>  366
<211>  277
<212>  PRT
<213>  Homo sapiens

<400>  366

Met Val Arg Leu Pro Leu Gln Cys Val Leu Trp Gly Cys Leu Leu Thr
1               5                   10                  15

Ala Val His Pro Glu Pro Pro Thr Ala Cys Arg Glu Lys Gln Tyr Leu
            20                  25                  30
```

```
Ile Asn Ser Gln Cys Cys Ser Leu Cys Gln Pro Gly Gln Lys Leu Val
        35                  40                  45

Ser Asp Cys Thr Glu Phe Thr Glu Thr Glu Cys Leu Pro Cys Gly Glu
    50                  55                  60

Ser Glu Phe Leu Asp Thr Trp Asn Arg Glu Thr His Cys His Gln His
65                  70                  75                  80

Lys Tyr Cys Asp Pro Asn Leu Gly Leu Arg Val Gln Gln Lys Gly Thr
                85                  90                  95

Ser Glu Thr Asp Thr Ile Cys Thr Cys Glu Glu Gly Trp His Cys Thr
            100                 105                 110

Ser Glu Ala Cys Glu Ser Cys Val Leu His Arg Ser Cys Ser Pro Gly
        115                 120                 125

Phe Gly Val Lys Gln Ile Ala Thr Gly Val Ser Asp Thr Ile Cys Glu
    130                 135                 140

Pro Cys Pro Val Gly Phe Phe Ser Asn Val Ser Ser Ala Phe Glu Lys
145                 150                 155                 160

Cys His Pro Trp Thr Ser Cys Glu Thr Lys Asp Leu Val Val Gln Gln
                165                 170                 175

Ala Gly Thr Asn Lys Thr Asp Val Val Cys Gly Pro Gln Asp Arg Leu
            180                 185                 190

Arg Ala Leu Val Val Ile Pro Ile Ile Phe Gly Ile Leu Phe Ala Ile
        195                 200                 205

Leu Leu Val Leu Val Phe Ile Lys Lys Val Ala Lys Lys Pro Thr Asn
    210                 215                 220

Lys Ala Pro His Pro Lys Gln Glu Pro Gln Glu Ile Asn Phe Pro Asp
225                 230                 235                 240

Asp Leu Pro Gly Ser Asn Thr Ala Ala Pro Val Gln Glu Thr Leu His
                245                 250                 255

Gly Cys Gln Pro Val Thr Gln Glu Asp Gly Lys Glu Ser Arg Ile Ser
            260                 265                 270

Val Gln Glu Arg Gln
        275
```

<210> 367
<211> 335
<212> PRT
<213> Homo sapiens

<400> 367

Met Leu Gly Ile Trp Thr Leu Leu Pro Leu Val Leu Thr Ser Val Ala
1 5 10 15

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

Lys Gly Leu Glu Leu Arg Lys Thr Val Thr Thr Val Glu Thr Gln Asn
35 40 45

Leu Glu Gly Leu His His Asp Gly Gln Phe Cys His Lys Pro Cys Pro
50 55 60

Pro Gly Glu Arg Lys Ala Arg Asp Cys Thr Val Asn Gly Asp Glu Pro
65 70 75 80

Asp Cys Val Pro Cys Gln Glu Gly Lys Glu Tyr Thr Asp Lys Ala His
85 90 95

Phe Ser Ser Lys Cys Arg Arg Cys Arg Leu Cys Asp Glu Gly His Gly
100 105 110

Leu Glu Val Glu Ile Asn Cys Thr Arg Thr Gln Asn Thr Lys Cys Arg
115 120 125

Cys Lys Pro Asn Phe Phe Cys Asn Ser Thr Val Cys Glu His Cys Asp
130 135 140

Pro Cys Thr Lys Cys Glu His Gly Ile Ile Lys Glu Cys Thr Leu Thr
145 150 155 160

Ser Asn Thr Lys Cys Lys Glu Glu Gly Ser Arg Ser Asn Leu Gly Trp
165 170 175

Leu Cys Leu Leu Leu Leu Pro Ile Pro Leu Ile Val Trp Val Lys Arg
180 185 190

Lys Glu Val Gln Lys Thr Cys Arg Lys His Arg Lys Glu Asn Gln Gly
195 200 205

Ser His Glu Ser Pro Thr Leu Asn Pro Glu Thr Val Ala Ile Asn Leu
210 215 220

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

Thr Leu Ser Gln Val Lys Gly Phe Val Arg Lys Asn Gly Val Asn Glu
245 250 255

Ala Lys Ile Asp Glu Ile Lys Asn Asp Asn Val Gln Asp Thr Ala Glu

260 265 270

Gln Lys Val Gln Leu Leu Arg Asn Trp His Gln Leu His Gly Lys Lys
275 280 285

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

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

Asp Ser Glu Asn Ser Asn Phe Arg Asn Glu Ile Gln Ser Leu Val
325 330 335

<210> 368
<211> 300
<212> PRT
<213> Homo sapiens

<400> 368

Met Arg Ala Leu Glu Gly Pro Gly Leu Ser Leu Leu Cys Leu Val Leu
1 5 10 15

Ala Leu Pro Ala Leu Leu Pro Val Pro Ala Val Arg Gly Val Ala Glu
20 25 30

Thr Pro Thr Tyr Pro Trp Arg Asp Ala Glu Thr Gly Glu Arg Leu Val
35 40 45

Cys Ala Gln Cys Pro Pro Gly Thr Phe Val Gln Arg Pro Cys Arg Arg
50 55 60

Asp Ser Pro Thr Thr Cys Gly Pro Cys Pro Pro Arg His Tyr Thr Gln
65 70 75 80

Phe Trp Asn Tyr Leu Glu Arg Cys Arg Tyr Cys Asn Val Leu Cys Gly
85 90 95

Glu Arg Glu Glu Glu Ala Arg Ala Cys His Ala Thr His Asn Arg Ala
100 105 110

Cys Arg Cys Arg Thr Gly Phe Phe Ala His Ala Gly Phe Cys Leu Glu
115 120 125

His Ala Ser Cys Pro Pro Gly Ala Gly Val Ile Ala Pro Gly Thr Pro
130 135 140

Ser Gln Asn Thr Gln Cys Gln Pro Cys Pro Pro Gly Thr Phe Ser Ala
145 150 155 160

Ser Ser Ser Ser Ser Glu Gln Cys Gln Pro His Arg Asn Cys Thr Ala
165 170 175

```
Leu Gly Leu Ala Leu Asn Val Pro Gly Ser Ser Ser His Asp Thr Leu
            180                 185                 190

Cys Thr Ser Cys Thr Gly Phe Pro Leu Ser Thr Arg Val Pro Gly Ala
        195                 200                 205

Glu Glu Cys Glu Arg Ala Val Ile Asp Phe Val Ala Phe Gln Asp Ile
    210                 215                 220

Ser Ile Lys Arg Leu Gln Arg Leu Leu Gln Ala Leu Glu Ala Pro Glu
225                 230                 235                 240

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

Leu Arg Arg Arg Leu Thr Glu Leu Leu Gly Ala Gln Asp Gly Ala Leu
            260                 265                 270

Leu Val Arg Leu Leu Gln Ala Leu Arg Val Ala Arg Met Pro Gly Leu
        275                 280                 285

Glu Arg Ser Val Arg Glu Arg Phe Leu Pro Val His
    290                 295                 300


<210>  369
<211>  260
<212>  PRT
<213>  Homo sapiens

<400>  369

Met Ala Arg Pro His Pro Trp Trp Leu Cys Val Leu Gly Thr Leu Val
1               5                   10                  15

Gly Leu Ser Ala Thr Pro Ala Pro Lys Ser Cys Pro Glu Arg His Tyr
            20                  25                  30

Trp Ala Gln Gly Lys Leu Cys Cys Gln Met Cys Glu Pro Gly Thr Phe
        35                  40                  45

Leu Val Lys Asp Cys Asp Gln His Arg Lys Ala Ala Gln Cys Asp Pro
    50                  55                  60

Cys Ile Pro Gly Val Ser Phe Ser Pro Asp His His Thr Arg Pro His
65                  70                  75                  80

Cys Glu Ser Cys Arg His Cys Asn Ser Gly Leu Leu Val Arg Asn Cys
                85                  90                  95

Thr Ile Thr Ala Asn Ala Glu Cys Ala Cys Arg Asn Gly Trp Gln Cys
            100                 105                 110
```

```
Arg Asp Lys Glu Cys Thr Glu Cys Asp Pro Leu Pro Asn Pro Ser Leu
        115                 120                 125

Thr Ala Arg Ser Ser Gln Ala Leu Ser Pro His Pro Gln Pro Thr His
    130                 135                 140

Leu Pro Tyr Val Ser Glu Met Leu Glu Ala Arg Thr Ala Gly His Met
145                 150                 155                 160

Gln Thr Leu Ala Asp Phe Arg Gln Leu Pro Ala Arg Thr Leu Ser Thr
                165                 170                 175

His Trp Pro Pro Gln Arg Ser Leu Cys Ser Ser Asp Phe Ile Arg Ile
            180                 185                 190

Leu Val Ile Phe Ser Gly Met Phe Leu Val Phe Thr Leu Ala Gly Ala
        195                 200                 205

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

Pro Val Glu Pro Ala Glu Pro Cys Arg Tyr Ser Cys Pro Arg Glu Glu
225                 230                 235                 240

Glu Gly Ser Thr Ile Pro Ile Gln Glu Asp Tyr Arg Lys Pro Glu Pro
                245                 250                 255

Ala Cys Ser Pro
            260


<210>  370
<211>  595
<212>  PRT
<213>  Homo sapiens

<400>  370

Met Arg Val Leu Leu Ala Ala Leu Gly Leu Leu Phe Leu Gly Ala Leu
1               5                   10                  15

Arg Ala Phe Pro Gln Asp Arg Pro Phe Glu Asp Thr Cys His Gly Asn
            20                  25                  30

Pro Ser His Tyr Tyr Asp Lys Ala Val Arg Arg Cys Cys Tyr Arg Cys
        35                  40                  45

Pro Met Gly Leu Phe Pro Thr Gln Gln Cys Pro Gln Arg Pro Thr Asp
    50                  55                  60

Cys Arg Lys Gln Cys Glu Pro Asp Tyr Tyr Leu Asp Glu Ala Asp Arg
65                  70                  75                  80
```

```
Cys Thr Ala Cys Val Thr Cys Ser Arg Asp Asp Leu Val Glu Lys Thr
                85                  90                  95

Pro Cys Ala Trp Asn Ser Ser Arg Val Cys Glu Cys Arg Pro Gly Met
            100                 105                 110

Phe Cys Ser Thr Ser Ala Val Asn Ser Cys Ala Arg Cys Phe Phe His
        115                 120                 125

Ser Val Cys Pro Ala Gly Met Ile Val Lys Phe Pro Gly Thr Ala Gln
    130                 135                 140

Lys Asn Thr Val Cys Glu Pro Ala Ser Pro Gly Val Ser Pro Ala Cys
145                 150                 155                 160

Ala Ser Pro Glu Asn Cys Lys Glu Pro Ser Ser Gly Thr Ile Pro Gln
                165                 170                 175

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

Pro Val Arg Gly Gly Thr Arg Leu Ala Gln Glu Ala Ala Ser Lys Leu
        195                 200                 205

Thr Arg Ala Pro Asp Ser Pro Ser Ser Val Gly Arg Pro Ser Ser Asp
    210                 215                 220

Pro Gly Leu Ser Pro Thr Gln Pro Cys Pro Glu Gly Ser Gly Asp Cys
225                 230                 235                 240

Arg Lys Gln Cys Glu Pro Asp Tyr Tyr Leu Asp Glu Ala Gly Arg Cys
                245                 250                 255

Thr Ala Cys Val Ser Cys Ser Arg Asp Asp Leu Val Glu Lys Thr Pro
            260                 265                 270

Cys Ala Trp Asn Ser Ser Arg Thr Cys Glu Cys Arg Pro Gly Met Ile
        275                 280                 285

Cys Ala Thr Ser Ala Thr Asn Ser Cys Ala Arg Cys Val Pro Tyr Pro
    290                 295                 300

Ile Cys Ala Ala Glu Thr Val Thr Lys Pro Gln Asp Met Ala Glu Lys
305                 310                 315                 320

Asp Thr Thr Phe Glu Ala Pro Pro Leu Gly Thr Gln Pro Asp Cys Asn
                325                 330                 335

Pro Thr Pro Glu Asn Gly Glu Ala Pro Ala Ser Thr Ser Pro Thr Gln
            340                 345                 350
```

Ser Leu Leu Val Asp Ser Gln Ala Ser Lys Thr Leu Pro Ile Pro Thr
355 360 365

Ser Ala Pro Val Ala Leu Ser Ser Thr Gly Lys Pro Val Leu Asp Ala
370 375 380

Gly Pro Val Leu Phe Trp Val Ile Leu Val Leu Val Val Val Val Gly
385 390 395 400

Ser Ser Ala Phe Leu Leu Cys His Arg Arg Ala Cys Arg Lys Arg Ile
405 410 415

Arg Gln Lys Leu His Leu Cys Tyr Pro Val Gln Thr Ser Gln Pro Lys
420 425 430

Leu Glu Leu Val Asp Ser Arg Pro Arg Arg Ser Ser Thr Gln Leu Arg
435 440 445

Ser Gly Ala Ser Val Thr Glu Pro Val Ala Glu Glu Arg Gly Leu Met
450 455 460

Ser Gln Pro Leu Met Glu Thr Cys His Ser Val Gly Ala Ala Tyr Leu
465 470 475 480

Glu Ser Leu Pro Leu Gln Asp Ala Ser Pro Ala Gly Gly Pro Ser Ser
485 490 495

Pro Arg Asp Leu Pro Glu Pro Arg Val Ser Thr Glu His Thr Asn Asn
500 505 510

Lys Ile Glu Lys Ile Tyr Ile Met Lys Ala Asp Thr Val Ile Val Gly
515 520 525

Thr Val Lys Ala Glu Leu Pro Glu Gly Arg Gly Leu Ala Gly Pro Ala
530 535 540

Glu Pro Glu Leu Glu Glu Glu Leu Glu Ala Asp His Thr Pro His Tyr
545 550 555 560

Pro Glu Gln Glu Thr Glu Pro Pro Leu Gly Ser Cys Ser Asp Val Met
565 570 575

Leu Ser Val Glu Glu Glu Gly Lys Glu Asp Pro Leu Pro Thr Ala Ala
580 585 590

Ser Gly Lys
595

<210> 371
<211> 255
<212> PRT
<213> Homo sapiens

<400> 371

```
Met Gly Asn Ser Cys Tyr Asn Ile Val Ala Thr Leu Leu Leu Val Leu
1               5                  10                  15

Asn Phe Glu Arg Thr Arg Ser Leu Gln Asp Pro Cys Ser Asn Cys Pro
            20                  25                  30

Ala Gly Thr Phe Cys Asp Asn Asn Arg Asn Gln Ile Cys Ser Pro Cys
        35                  40                  45

Pro Pro Asn Ser Phe Ser Ser Ala Gly Gly Gln Arg Thr Cys Asp Ile
    50                  55                  60

Cys Arg Gln Cys Lys Gly Val Phe Arg Thr Arg Lys Glu Cys Ser Ser
65                  70                  75                  80

Thr Ser Asn Ala Glu Cys Asp Cys Thr Pro Gly Phe His Cys Leu Gly
                85                  90                  95

Ala Gly Cys Ser Met Cys Glu Gln Asp Cys Lys Gln Gly Gln Glu Leu
            100                 105                 110

Thr Lys Lys Gly Cys Lys Asp Cys Cys Phe Gly Thr Phe Asn Asp Gln
        115                 120                 125

Lys Arg Gly Ile Cys Arg Pro Trp Thr Asn Cys Ser Leu Asp Gly Lys
    130                 135                 140

Ser Val Leu Val Asn Gly Thr Lys Glu Arg Asp Val Val Cys Gly Pro
145                 150                 155                 160

Ser Pro Ala Asp Leu Ser Pro Gly Ala Ser Ser Val Thr Pro Pro Ala
                165                 170                 175

Pro Ala Arg Glu Pro Gly His Ser Pro Gln Ile Ile Ser Phe Phe Leu
            180                 185                 190

Ala Leu Thr Ser Thr Ala Leu Leu Phe Leu Leu Phe Phe Leu Thr Leu
        195                 200                 205

Arg Phe Ser Val Val Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe
    210                 215                 220

Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly
225                 230                 235                 240

Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu
                245                 250                 255
```

<210> 372

<211> 468
<212> PRT
<213> Homo sapiens

<400> 372

Met Ala Pro Pro Pro Ala Arg Val His Leu Gly Ala Phe Leu Ala Val
1 5 10 15

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

Thr Pro Ser Lys Val Trp Gly Ser Ser Ala Gly Arg Ile Glu Pro Arg
35 40 45

Gly Gly Gly Arg Gly Ala Leu Pro Thr Ser Met Gly Gln His Gly Pro
50 55 60

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

Glu Ala Ser Pro Arg Leu Arg Val His Lys Thr Phe Lys Phe Val Val
85 90 95

Val Gly Val Leu Leu Gln Val Val Pro Ser Ser Ala Ala Thr Ile Lys
100 105 110

Leu His Asp Gln Ser Ile Gly Thr Gln Gln Trp Glu His Ser Pro Leu
115 120 125

Gly Glu Leu Cys Pro Pro Gly Ser His Arg Ser Glu His Pro Gly Ala
130 135 140

Cys Asn Arg Cys Thr Glu Gly Val Gly Tyr Thr Asn Ala Ser Asn Asn
145 150 155 160

Leu Phe Ala Cys Leu Pro Cys Thr Ala Cys Lys Ser Asp Glu Glu Glu
165 170 175

Arg Ser Pro Cys Thr Thr Thr Arg Asn Thr Ala Cys Gln Cys Lys Pro
180 185 190

Gly Thr Phe Arg Asn Asp Asn Ser Ala Glu Met Cys Arg Lys Cys Ser
195 200 205

Arg Gly Cys Pro Arg Gly Met Val Lys Val Lys Asp Cys Thr Pro Trp
210 215 220

Ser Asp Ile Glu Cys Val His Lys Glu Ser Gly Asn Gly His Asn Ile
225 230 235 240

Trp Val Ile Leu Val Val Thr Leu Val Val Pro Leu Leu Leu Val Ala
245 250 255

```
Val Leu Ile Val Cys Cys Cys Ile Gly Ser Gly Cys Gly Gly Asp Pro
            260                 265                 270

Lys Cys Met Asp Arg Val Cys Phe Trp Arg Leu Gly Leu Leu Arg Gly
        275                 280                 285

Pro Gly Ala Glu Asp Asn Ala His Asn Glu Ile Leu Ser Asn Ala Asp
    290                 295                 300

Ser Leu Ser Thr Phe Val Ser Glu Gln Gln Met Glu Ser Gln Glu Pro
305                 310                 315                 320

Ala Asp Leu Thr Gly Val Thr Val Gln Ser Pro Gly Glu Ala Gln Cys
                325                 330                 335

Leu Leu Gly Pro Ala Glu Ala Glu Gly Ser Gln Arg Arg Arg Leu Leu
            340                 345                 350

Val Pro Ala Asn Gly Ala Asp Pro Thr Glu Thr Leu Met Leu Phe Phe
        355                 360                 365

Asp Lys Phe Ala Asn Ile Val Pro Phe Asp Ser Trp Asp Gln Leu Met
    370                 375                 380

Arg Gln Leu Asp Leu Thr Lys Asn Glu Ile Asp Val Val Arg Ala Gly
385                 390                 395                 400

Thr Ala Gly Pro Gly Asp Ala Leu Tyr Ala Met Leu Met Lys Trp Val
                405                 410                 415

Asn Lys Thr Gly Arg Asn Ala Ser Ile His Thr Leu Leu Asp Ala Leu
            420                 425                 430

Glu Arg Met Glu Glu Arg His Ala Arg Glu Lys Ile Gln Asp Leu Leu
        435                 440                 445

Val Asp Ser Gly Lys Phe Ile Tyr Leu Glu Asp Gly Thr Gly Ser Ala
    450                 455                 460

Val Ser Leu Glu
465


<210>  373
<211>  440
<212>  PRT
<213>  Homo sapiens

<400>  373

Met Glu Gln Arg Gly Gln Asn Ala Pro Ala Ala Ser Gly Ala Arg Lys
1               5                   10                  15
```

```
Arg His Gly Pro Gly Pro Arg Glu Ala Arg Gly Ala Arg Pro Gly Pro
            20                  25                  30

Arg Val Pro Lys Thr Leu Val Leu Val Val Ala Ala Val Leu Leu Leu
        35                  40                  45

Val Ser Ala Glu Ser Ala Leu Ile Thr Gln Gln Asp Leu Ala Pro Gln
    50                  55                  60

Gln Arg Ala Ala Pro Gln Gln Lys Arg Ser Ser Pro Ser Glu Gly Leu
65                  70                  75                  80

Cys Pro Pro Gly His His Ile Ser Glu Asp Gly Arg Asp Cys Ile Ser
                85                  90                  95

Cys Lys Tyr Gly Gln Asp Tyr Ser Thr His Trp Asn Asp Leu Leu Phe
            100                 105                 110

Cys Leu Arg Cys Thr Arg Cys Asp Ser Gly Glu Val Glu Leu Ser Pro
        115                 120                 125

Cys Thr Thr Thr Arg Asn Thr Val Cys Gln Cys Glu Glu Gly Thr Phe
    130                 135                 140

Arg Glu Glu Asp Ser Pro Glu Met Cys Arg Lys Cys Arg Thr Gly Cys
145                 150                 155                 160

Pro Arg Gly Met Val Lys Val Gly Asp Cys Thr Pro Trp Ser Asp Ile
                165                 170                 175

Glu Cys Val His Lys Glu Ser Gly Thr Lys His Ser Gly Glu Val Pro
            180                 185                 190

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

Cys Ser Leu Ser Gly Ile Ile Ile Gly Val Thr Val Ala Ala Val Val
    210                 215                 220

Leu Ile Val Ala Val Phe Val Cys Lys Ser Leu Leu Trp Lys Lys Val
225                 230                 235                 240

Leu Pro Tyr Leu Lys Gly Ile Cys Ser Gly Gly Gly Gly Asp Pro Glu
                245                 250                 255

Arg Val Asp Arg Ser Ser Gln Arg Pro Gly Ala Glu Asp Asn Val Leu
            260                 265                 270

Asn Glu Ile Val Ser Ile Leu Gln Pro Thr Gln Val Pro Glu Gln Glu
        275                 280                 285
```

```
Met Glu Val Gln Glu Pro Ala Glu Pro Thr Gly Val Asn Met Leu Ser
    290                 295                 300

Pro Gly Glu Ser Glu His Leu Leu Glu Pro Ala Glu Ala Glu Arg Ser
305                 310                 315                 320

Gln Arg Arg Arg Leu Leu Val Pro Ala Asn Glu Gly Asp Pro Thr Glu
                325                 330                 335

Thr Leu Arg Gln Cys Phe Asp Asp Phe Ala Asp Leu Val Pro Phe Asp
            340                 345                 350

Ser Trp Glu Pro Leu Met Arg Lys Leu Gly Leu Met Asp Asn Glu Ile
        355                 360                 365

Lys Val Ala Lys Ala Glu Ala Ala Gly His Arg Asp Thr Leu Tyr Thr
    370                 375                 380

Met Leu Ile Lys Trp Val Asn Lys Thr Gly Arg Asp Ala Ser Val His
385                 390                 395                 400

Thr Leu Leu Asp Ala Leu Glu Thr Leu Gly Glu Arg Leu Ala Lys Gln
                405                 410                 415

Lys Ile Glu Asp His Leu Leu Ser Ser Gly Lys Phe Met Tyr Leu Glu
            420                 425                 430

Gly Asn Ala Asp Ser Ala Met Ser
        435                 440
```

<210> 374
<211> 259
<212> PRT
<213> Homo sapiens

<400> 374

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

Val Leu Leu Pro Val Leu Ala Tyr Ser Ala Thr Thr Ala Arg Gln Glu
            20                  25                  30

Glu Val Pro Gln Gln Thr Val Ala Pro Gln Gln Gln Arg His Ser Phe
        35                  40                  45

Lys Gly Glu Glu Cys Pro Ala Gly Ser His Arg Ser Glu His Thr Gly
    50                  55                  60

Ala Cys Asn Pro Cys Thr Glu Gly Val Asp Tyr Thr Asn Ala Ser Asn
65                  70                  75                  80
```

```
Asn Glu Pro Ser Cys Phe Pro Cys Thr Val Cys Lys Ser Asp Gln Lys
                85                  90                  95

His Lys Ser Ser Cys Thr Met Thr Arg Asp Thr Val Cys Gln Cys Lys
            100                 105                 110

Glu Gly Thr Phe Arg Asn Glu Asn Ser Pro Glu Met Cys Arg Lys Cys
        115                 120                 125

Ser Arg Cys Pro Ser Gly Glu Val Gln Val Ser Asn Cys Thr Ser Trp
    130                 135                 140

Asp Asp Ile Gln Cys Val Glu Glu Phe Gly Ala Asn Ala Thr Val Glu
145                 150                 155                 160

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

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

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

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

Glu Glu Thr Met Thr Thr Ser Pro Gly Thr Pro Ala Ser Ser His Tyr
225                 230                 235                 240

Leu Ser Cys Thr Ile Val Gly Ile Ile Val Leu Ile Val Leu Leu Ile
                245                 250                 255

Val Phe Val
```

<210> 375
<211> 386
<212> PRT
<213> Homo sapiens

<400> 375

```
Met Gly Leu Trp Gly Gln Ser Val Pro Thr Ala Ser Ser Ala Arg Ala
1               5                   10                  15

Gly Arg Tyr Pro Gly Ala Arg Thr Ala Ser Gly Thr Arg Pro Trp Leu
            20                  25                  30

Leu Asp Pro Lys Ile Leu Lys Phe Val Val Phe Ile Val Ala Val Leu
        35                  40                  45

Leu Pro Val Arg Val Asp Ser Ala Thr Ile Pro Arg Gln Asp Glu Val
```

50 55 60

Pro Gln Gln Thr Val Ala Pro Gln Gln Gln Arg Arg Ser Leu Lys Glu
65 70 75 80

Glu Glu Cys Pro Ala Gly Ser His Arg Ser Glu Tyr Thr Gly Ala Cys
85 90 95

Asn Pro Cys Thr Glu Gly Val Asp Tyr Thr Ile Ala Ser Asn Asn Leu
100 105 110

Pro Ser Cys Leu Leu Cys Thr Val Cys Lys Ser Gly Gln Thr Asn Lys
115 120 125

Ser Ser Cys Thr Thr Thr Arg Asp Thr Val Cys Gln Cys Glu Lys Gly
130 135 140

Ser Phe Gln Asp Lys Asn Ser Pro Glu Met Cys Arg Thr Cys Arg Thr
145 150 155 160

Gly Cys Pro Arg Gly Met Val Lys Val Ser Asn Cys Thr Pro Arg Ser
165 170 175

Asp Ile Lys Cys Lys Asn Glu Ser Ala Ala Ser Ser Thr Gly Lys Thr
180 185 190

Pro Ala Ala Glu Glu Thr Val Thr Thr Ile Leu Gly Met Leu Ala Ser
195 200 205

Pro Tyr His Tyr Leu Ile Ile Ile Val Val Leu Val Ile Ile Leu Ala
210 215 220

Val Val Val Val Gly Phe Ser Cys Arg Lys Lys Phe Ile Ser Tyr Leu
225 230 235 240

Lys Gly Ile Cys Ser Gly Gly Gly Gly Gly Pro Glu Arg Val His Arg
245 250 255

Val Leu Phe Arg Arg Arg Ser Cys Pro Ser Arg Val Pro Gly Ala Glu
260 265 270

Asp Asn Ala Arg Asn Glu Thr Leu Ser Asn Arg Tyr Leu Gln Pro Thr
275 280 285

Gln Val Ser Glu Gln Glu Ile Gln Gly Gln Glu Leu Ala Glu Leu Thr
290 295 300

Gly Val Thr Val Glu Leu Pro Glu Glu Pro Gln Arg Leu Leu Glu Gln
305 310 315 320

Ala Glu Ala Glu Gly Cys Gln Arg Arg Arg Leu Leu Val Pro Val Asn

325 330 335

Asp Ala Asp Ser Ala Asp Ile Ser Thr Leu Leu Asp Ala Ser Ala Thr
340 345 350

Leu Glu Glu Gly His Ala Lys Glu Thr Ile Gln Asp Gln Leu Val Gly
355 360 365

Ser Glu Lys Leu Phe Tyr Glu Glu Asp Glu Ala Gly Ser Ala Thr Ser
370 375 380

Cys Leu
385

<210> 376
<211> 263
<212> PRT
<213> Homo sapiens

<400> 376

Met Ala Pro Arg Ala Arg Arg Arg Arg Pro Leu Phe Ala Leu Leu Leu
1 5 10 15

Leu Cys Ala Leu Leu Ala Arg Leu Gln Val Ala Leu Gln Ile Ala Pro
20 25 30

Pro Cys Thr Ser Glu Lys His Tyr Glu His Leu Gly Arg Cys Cys Asn
35 40 45

Lys Cys Glu Pro Gly Lys Tyr Met Ser Ser Lys Cys Thr Thr Thr Ser
50 55 60

Asp Ser Val Cys Leu Pro Cys Gly Pro Asp Glu Tyr Leu Asp Ser Trp
65 70 75 80

Asn Glu Glu Asp Lys Cys Leu Leu His Lys Val Cys Asp Thr Gly Lys
85 90 95

Ala Leu Val Ala Val Val Ala Gly Asn Ser Thr Thr Pro Arg Arg Cys
100 105 110

Ala Cys Thr Ala Gly Tyr His Trp Ser Gln Asp Cys Glu Cys Cys Arg
115 120 125

Arg Asn Thr Glu Cys Ala Pro Gly Leu Gly Ala Gln His Pro Leu Gln
130 135 140

Leu Asn Lys Asp Thr Val Cys Lys Pro Cys Leu Ala Gly Tyr Phe Ser
145 150 155 160

Asp Ala Phe Ser Ser Thr Asp Lys Cys Arg Pro Trp Thr Asn Cys Thr
165 170 175

```
Phe Leu Gly Lys Arg Val Glu His His Gly Thr Glu Lys Ser Asp Ala
            180                 185                 190

Val Cys Ser Ser Ser Leu Pro Ala Arg Lys Pro Pro Asn Glu Pro His
        195                 200                 205

Val Tyr Leu Pro Gly Leu Ile Ile Leu Leu Leu Phe Ala Ser Val Ala
    210                 215                 220

Leu Val Ala Ala Ile Ile Phe Gly Val Cys Tyr Arg Lys Lys Gly Lys
225                 230                 235                 240

Ala Leu Thr Ala Asn Leu Trp His Trp Ile Asn Glu Ala Cys Gly Arg
                245                 250                 255

Leu Ser Gly Asp Lys Glu Met
            260
```

<210> 377
<211> 401
<212> PRT
<213> Homo sapiens

<400> 377

```
Met Asn Asn Leu Leu Cys Cys Ala Leu Val Phe Leu Asp Ile Ser Ile
1               5                   10                  15

Lys Trp Thr Thr Gln Glu Thr Phe Pro Pro Lys Tyr Leu His Tyr Asp
            20                  25                  30

Glu Glu Thr Ser His Gln Leu Leu Cys Asp Lys Cys Pro Pro Gly Thr
        35                  40                  45

Tyr Leu Lys Gln His Cys Thr Ala Lys Trp Lys Thr Val Cys Ala Pro
    50                  55                  60

Cys Pro Asp His Tyr Tyr Thr Asp Ser Trp His Thr Ser Asp Glu Cys
65                  70                  75                  80

Leu Tyr Cys Ser Pro Val Cys Lys Glu Leu Gln Tyr Val Lys Gln Glu
                85                  90                  95

Cys Asn Arg Thr His Asn Arg Val Cys Glu Cys Lys Glu Gly Arg Tyr
            100                 105                 110

Leu Glu Ile Glu Phe Cys Leu Lys His Arg Ser Cys Pro Pro Gly Phe
        115                 120                 125

Gly Val Val Gln Ala Gly Thr Pro Glu Arg Asn Thr Val Cys Lys Arg
    130                 135                 140
```

```
Cys Pro Asp Gly Phe Phe Ser Asn Glu Thr Ser Ser Lys Ala Pro Cys
145                 150                 155                 160

Arg Lys His Thr Asn Cys Ser Val Phe Gly Leu Leu Leu Thr Gln Lys
                165                 170                 175

Gly Asn Ala Thr His Asp Asn Ile Cys Ser Gly Asn Ser Glu Ser Thr
            180                 185                 190

Gln Lys Cys Gly Ile Asp Val Thr Leu Cys Glu Glu Ala Phe Phe Arg
        195                 200                 205

Phe Ala Val Pro Thr Lys Phe Thr Pro Asn Trp Leu Ser Val Leu Val
    210                 215                 220

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

Lys Arg Gln His Ser Ser Gln Glu Gln Thr Phe Gln Leu Leu Lys Leu
                245                 250                 255

Trp Lys His Gln Asn Lys Asp Gln Asp Ile Val Lys Lys Ile Ile Gln
            260                 265                 270

Asp Ile Asp Leu Cys Glu Asn Ser Val Gln Arg His Ile Gly His Ala
        275                 280                 285

Asn Leu Thr Phe Glu Gln Leu Arg Ser Leu Met Glu Ser Leu Pro Gly
    290                 295                 300

Lys Lys Val Gly Ala Glu Asp Ile Glu Lys Thr Ile Lys Ala Cys Lys
305                 310                 315                 320

Pro Ser Asp Gln Ile Leu Lys Leu Leu Ser Leu Trp Arg Ile Lys Asn
                325                 330                 335

Gly Asp Gln Asp Thr Leu Lys Gly Leu Met His Ala Leu Lys His Ser
            340                 345                 350

Lys Thr Tyr His Phe Pro Lys Thr Val Thr Gln Ser Leu Lys Lys Thr
        355                 360                 365

Ile Arg Phe Leu His Ser Phe Thr Met Tyr Lys Leu Tyr Gln Lys Leu
    370                 375                 380

Phe Leu Glu Met Ile Gly Asn Gln Val Gln Ser Val Lys Ile Ser Cys
385                 390                 395                 400

Leu
```

<210> 378
<211> 181
<212> PRT
<213> Homo sapiens

<400> 378

Met Glu Gln Arg Pro Arg Gly Cys Ala Ala Val Ala Ala Ala Leu Leu
1 5 10 15

Leu Val Leu Leu Gly Ala Arg Ala Gln Gly Gly Thr Arg Ser Pro Arg
20 25 30

Cys Asp Cys Ala Gly Asp Phe His Lys Lys Ile Gly Leu Phe Cys Cys
35 40 45

Arg Gly Cys Pro Ala Gly His Tyr Leu Lys Ala Pro Cys Thr Glu Pro
50 55 60

Cys Gly Asn Ser Thr Cys Leu Val Cys Pro Gln Asp Thr Phe Leu Ala
65 70 75 80

Trp Glu Asn His His Asn Ser Glu Cys Ala Arg Cys Gln Ala Cys Asp
85 90 95

Glu Gln Ala Ser Gln Val Ala Leu Glu Asn Cys Ser Ala Val Ala Asp
100 105 110

Thr Arg Cys Gly Cys Lys Pro Gly Trp Phe Val Glu Cys Gln Val Ser
115 120 125

Gln Cys Val Ser Ser Ser Pro Phe Tyr Cys Gln Pro Cys Leu Asp Cys
130 135 140

Gly Ala Leu His Arg His Thr Arg Leu Leu Cys Ser Arg Arg Asp Thr
145 150 155 160

Asp Cys Gly Thr Cys Leu Pro Gly Phe Tyr Glu His Gly Asp Gly Cys
165 170 175

Val Ser Cys Pro Thr
180

<210> 379
<211> 129
<212> PRT
<213> Homo sapiens

<400> 379

Met Ala Arg Gly Ser Leu Arg Arg Leu Leu Arg Leu Leu Val Leu Gly
1 5 10 15

Leu Trp Leu Ala Leu Leu Arg Ser Val Ala Gly Glu Gln Ala Pro Gly

20 25 30

Thr Ala Pro Cys Ser Arg Gly Ser Ser Trp Ser Ala Asp Leu Asp Lys
35 40 45

Cys Met Asp Cys Ala Ser Cys Arg Ala Arg Pro His Ser Asp Phe Cys
50 55 60

Leu Gly Cys Ala Ala Ala Pro Pro Ala Pro Phe Arg Leu Leu Trp Pro
65 70 75 80

Ile Leu Gly Gly Ala Leu Ser Leu Thr Phe Val Leu Gly Leu Leu Ser
85 90 95

Gly Phe Leu Val Trp Arg Arg Cys Arg Arg Arg Glu Lys Phe Thr Thr
100 105 110

Pro Ile Glu Glu Thr Gly Gly Glu Gly Cys Pro Ala Val Ala Leu Ile
115 120 125

Gln

<210> 380
<211> 293
<212> PRT
<213> Homo sapiens

<400> 380

Met Ser Gly Leu Gly Arg Ser Arg Arg Gly Gly Arg Ser Arg Val Asp
1 5 10 15

Gln Glu Glu Arg Phe Pro Gln Gly Leu Trp Thr Gly Val Ala Met Arg
20 25 30

Ser Cys Pro Glu Glu Gln Tyr Trp Asp Pro Leu Leu Gly Thr Cys Met
35 40 45

Ser Cys Lys Thr Ile Cys Asn His Gln Ser Gln Arg Thr Cys Ala Ala
50 55 60

Phe Cys Arg Ser Leu Ser Cys Arg Lys Glu Gln Gly Lys Phe Tyr Asp
65 70 75 80

His Leu Leu Arg Asp Cys Ile Ser Cys Ala Ser Ile Cys Gly Gln His
85 90 95

Pro Lys Gln Cys Ala Tyr Phe Cys Glu Asn Lys Leu Arg Ser Pro Val
100 105 110

Asn Leu Pro Pro Glu Leu Arg Arg Gln Arg Ser Gly Glu Val Glu Asn
115 120 125

```
Asn Ser Asp Asn Ser Gly Arg Tyr Gln Gly Leu Glu His Arg Gly Ser
    130                 135                 140

Glu Ala Ser Pro Ala Leu Pro Gly Leu Lys Leu Ser Ala Asp Gln Val
145                 150                 155                 160

Ala Leu Val Tyr Ser Thr Leu Gly Leu Cys Leu Cys Ala Val Leu Cys
                165                 170                 175

Cys Phe Leu Val Ala Val Ala Cys Phe Leu Lys Lys Arg Gly Asp Pro
            180                 185                 190

Cys Ser Cys Gln Pro Arg Ser Arg Pro Arg Gln Ser Pro Ala Lys Ser
        195                 200                 205

Ser Gln Asp His Ala Met Glu Ala Gly Ser Pro Val Ser Thr Ser Pro
    210                 215                 220

Glu Pro Val Glu Thr Cys Ser Phe Cys Phe Pro Glu Cys Arg Ala Pro
225                 230                 235                 240

Thr Gln Glu Ser Ala Val Thr Pro Gly Thr Pro Asp Pro Thr Cys Ala
                245                 250                 255

Gly Arg Trp Gly Cys His Thr Arg Thr Thr Val Leu Gln Pro Cys Pro
            260                 265                 270

His Ile Pro Asp Ser Gly Leu Gly Ile Val Cys Val Pro Ala Gln Glu
        275                 280                 285

Gly Gly Pro Gly Ala
    290
```

<210> 381
<211> 184
<212> PRT
<213> Homo sapiens

<400> 381

```
Met Arg Arg Gly Pro Arg Ser Leu Arg Gly Arg Asp Ala Pro Ala Pro
1               5                   10                  15

Thr Pro Cys Val Pro Ala Glu Cys Phe Asp Leu Leu Val Arg His Cys
            20                  25                  30

Val Ala Cys Gly Leu Leu Arg Thr Pro Arg Pro Lys Pro Ala Gly Ala
        35                  40                  45

Ser Ser Pro Ala Pro Arg Thr Ala Leu Gln Pro Gln Glu Ser Val Gly
    50                  55                  60
```

Ala Gly Ala Gly Glu Ala Ala Leu Pro Leu Pro Gly Leu Leu Phe Gly
65 70 75 80

Ala Pro Ala Leu Leu Gly Leu Ala Leu Val Leu Ala Leu Val Leu Val
85 90 95

Gly Leu Val Ser Trp Arg Arg Arg Gln Arg Arg Leu Arg Gly Ala Ser
100 105 110

Ser Ala Glu Ala Pro Asp Gly Asp Lys Asp Ala Pro Glu Pro Leu Asp
115 120 125

Lys Val Ile Ile Leu Ser Pro Gly Ile Ser Asp Ala Thr Ala Pro Ala
130 135 140

Trp Pro Pro Pro Gly Glu Asp Pro Gly Thr Thr Pro Pro Gly His Ser
145 150 155 160

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

Lys Thr Ala Gly Pro Glu Gln Gln
180

<210> 382
<211> 283
<212> PRT
<213> Homo sapiens

<400> 382

Met Glu Pro Pro Gly Asp Trp Gly Pro Pro Pro Trp Arg Ser Thr Pro
1 5 10 15

Lys Thr Asp Val Leu Arg Leu Val Leu Tyr Leu Thr Phe Leu Gly Ala
20 25 30

Pro Cys Tyr Ala Pro Ala Leu Pro Ser Cys Lys Glu Asp Glu Tyr Pro
35 40 45

Val Gly Ser Glu Cys Cys Pro Lys Cys Ser Pro Gly Tyr Arg Val Lys
50 55 60

Glu Ala Cys Gly Glu Leu Thr Gly Thr Val Cys Glu Pro Cys Pro Pro
65 70 75 80

Gly Thr Tyr Ile Ala His Leu Asn Gly Leu Ser Lys Cys Leu Gln Cys
85 90 95

Gln Met Cys Asp Pro Ala Met Gly Leu Arg Ala Ser Arg Asn Cys Ser
100 105 110

```
Arg Thr Glu Asn Ala Val Cys Gly Cys Ser Pro Gly His Phe Cys Ile
        115                 120                 125

Val Gln Asp Gly Asp His Cys Ala Ala Cys Arg Ala Tyr Ala Thr Ser
    130                 135                 140

Ser Pro Gly Gln Arg Val Gln Lys Gly Gly Thr Glu Ser Gln Asp Thr
145                 150                 155                 160

Leu Cys Gln Asn Cys Pro Pro Gly Thr Phe Ser Pro Asn Gly Thr Leu
                165                 170                 175

Glu Glu Cys Gln His Gln Thr Lys Cys Ser Trp Leu Val Thr Lys Ala
            180                 185                 190

Gly Ala Gly Thr Ser Ser Ser His Trp Val Trp Trp Phe Leu Ser Gly
        195                 200                 205

Ser Leu Val Ile Val Ile Val Cys Ser Thr Val Gly Leu Ile Ile Cys
    210                 215                 220

Val Lys Arg Arg Lys Pro Arg Gly Asp Val Val Lys Val Ile Val Ser
225                 230                 235                 240

Val Gln Arg Lys Arg Gln Glu Ala Glu Gly Glu Ala Thr Val Ile Glu
                245                 250                 255

Ala Leu Gln Ala Pro Pro Asp Val Thr Thr Val Ala Val Glu Glu Thr
            260                 265                 270

Ile Pro Ser Phe Thr Gly Arg Ser Pro Asn His
        275                 280


<210>  383
<211>  427
<212>  PRT
<213>  Homo sapiens

<400>  383

Met Gly Ala Gly Ala Thr Gly Arg Ala Met Asp Gly Pro Arg Leu Leu
1               5                   10                  15

Leu Leu Leu Leu Leu Gly Val Ser Leu Gly Gly Ala Lys Glu Ala Cys
            20                  25                  30

Pro Thr Gly Leu Tyr Thr His Ser Gly Glu Cys Cys Lys Ala Cys Asn
        35                  40                  45

Leu Gly Glu Gly Val Ala Gln Pro Cys Gly Ala Asn Gln Thr Val Cys
    50                  55                  60

Glu Pro Cys Leu Asp Ser Val Thr Phe Ser Asp Val Val Ser Ala Thr
```

65 70 75 80

Glu Pro Cys Lys Pro Cys Thr Glu Cys Val Gly Leu Gln Ser Met Ser
85 90 95

Ala Pro Cys Val Glu Ala Asp Asp Ala Val Cys Arg Cys Ala Tyr Gly
100 105 110

Tyr Tyr Gln Asp Glu Thr Thr Gly Arg Cys Glu Ala Cys Arg Val Cys
115 120 125

Glu Ala Gly Ser Gly Leu Val Phe Ser Cys Gln Asp Lys Gln Asn Thr
130 135 140

Val Cys Glu Glu Cys Pro Asp Gly Thr Tyr Ser Asp Glu Ala Asn His
145 150 155 160

Val Asp Pro Cys Leu Pro Cys Thr Val Cys Glu Asp Thr Glu Arg Gln
165 170 175

Leu Arg Glu Cys Thr Arg Trp Ala Asp Ala Glu Cys Glu Glu Ile Pro
180 185 190

Gly Arg Trp Ile Thr Arg Ser Thr Pro Pro Glu Gly Ser Asp Ser Thr
195 200 205

Ala Pro Ser Thr Gln Glu Pro Glu Ala Pro Pro Glu Gln Asp Leu Ile
210 215 220

Ala Ser Thr Val Ala Gly Val Val Thr Thr Val Met Gly Ser Ser Gln
225 230 235 240

Pro Val Val Thr Arg Gly Thr Thr Asp Asn Leu Ile Pro Val Tyr Cys
245 250 255

Ser Ile Leu Ala Ala Val Val Val Gly Leu Val Ala Tyr Ile Ala Phe
260 265 270

Lys Arg Trp Asn Ser Cys Lys Gln Asn Lys Gln Gly Ala Asn Ser Arg
275 280 285

Pro Val Asn Gln Thr Pro Pro Pro Glu Gly Glu Lys Leu His Ser Asp
290 295 300

Ser Gly Ile Ser Val Asp Ser Gln Ser Leu His Asp Gln Gln Pro His
305 310 315 320

Thr Gln Thr Ala Ser Gly Gln Ala Leu Lys Gly Asp Gly Gly Leu Tyr
325 330 335

Ser Ser Leu Pro Pro Ala Lys Arg Glu Glu Val Glu Lys Leu Leu Asn

340 345 350

Gly Ser Ala Gly Asp Thr Trp Arg His Leu Ala Gly Glu Leu Gly Tyr
355 360 365

Gln Pro Glu His Ile Asp Ser Phe Thr His Glu Ala Cys Pro Val Arg
370 375 380

Ala Leu Leu Ala Ser Trp Ala Thr Gln Asp Ser Ala Thr Leu Asp Ala
385 390 395 400

Leu Leu Ala Ala Leu Arg Arg Ile Gln Arg Ala Asp Leu Val Glu Ser
405 410 415

Leu Cys Ser Glu Ser Thr Ala Thr Ser Pro Val
420 425

<210> 384
<211> 184
<212> PRT
<213> Homo sapiens

<400> 384

Met Leu Gln Met Ala Gly Gln Cys Ser Gln Asn Glu Tyr Phe Asp Ser
1 5 10 15

Leu Leu His Ala Cys Ile Pro Cys Gln Leu Arg Cys Ser Ser Asn Thr
20 25 30

Pro Pro Leu Thr Cys Gln Arg Tyr Cys Asn Ala Ser Val Thr Asn Ser
35 40 45

Val Lys Gly Thr Asn Ala Ile Leu Trp Thr Cys Leu Gly Leu Ser Leu
50 55 60

Ile Ile Ser Leu Ala Val Phe Val Leu Met Phe Leu Leu Arg Lys Ile
65 70 75 80

Asn Ser Glu Pro Leu Lys Asp Glu Phe Lys Asn Thr Gly Ser Gly Leu
85 90 95

Leu Gly Met Ala Asn Ile Asp Leu Glu Lys Ser Arg Thr Gly Asp Glu
100 105 110

Ile Ile Leu Pro Arg Gly Leu Glu Tyr Thr Val Glu Glu Cys Thr Cys
115 120 125

Glu Asp Cys Ile Lys Ser Lys Pro Lys Val Asp Ser Asp His Cys Phe
130 135 140

Pro Leu Pro Ala Met Glu Glu Gly Ala Thr Ile Leu Val Thr Thr Lys
145 150 155 160

```
Thr Asn Asp Tyr Cys Lys Ser Leu Pro Ala Ala Leu Ser Ala Thr Glu
                165                 170                 175

Ile Glu Lys Ser Ile Ser Ala Arg
            180
```

<210> 385
<211> 241
<212> PRT
<213> Homo sapiens

<400> 385

```
Met Ala Gln His Gly Ala Met Gly Ala Phe Arg Ala Leu Cys Gly Leu
1               5                   10                  15

Ala Leu Leu Cys Ala Leu Ser Leu Gly Gln Arg Pro Thr Gly Gly Pro
            20                  25                  30

Gly Cys Gly Pro Gly Arg Leu Leu Leu Gly Thr Gly Thr Asp Ala Arg
        35                  40                  45

Cys Cys Arg Val His Thr Thr Arg Cys Cys Arg Asp Tyr Pro Gly Glu
    50                  55                  60

Glu Cys Cys Ser Glu Trp Asp Cys Met Cys Val Gln Pro Glu Phe His
65                  70                  75                  80

Cys Gly Asp Pro Cys Cys Thr Thr Cys Arg His His Pro Cys Pro Pro
                85                  90                  95

Gly Gln Gly Val Gln Ser Gln Gly Lys Phe Ser Phe Gly Phe Gln Cys
            100                 105                 110

Ile Asp Cys Ala Ser Gly Thr Phe Ser Gly Gly His Glu Gly His Cys
        115                 120                 125

Lys Pro Trp Thr Asp Cys Thr Gln Phe Gly Phe Leu Thr Val Phe Pro
    130                 135                 140

Gly Asn Lys Thr His Asn Ala Val Cys Val Pro Gly Ser Pro Pro Ala
145                 150                 155                 160

Glu Pro Leu Gly Trp Leu Thr Val Val Leu Leu Ala Val Ala Ala Cys
                165                 170                 175

Val Leu Leu Leu Thr Ser Ala Gln Leu Gly Leu His Ile Trp Gln Leu
            180                 185                 190

Arg Ser Gln Cys Met Trp Pro Arg Glu Thr Gln Leu Leu Leu Glu Val
        195                 200                 205
```

Pro Pro Ser Thr Glu Asp Ala Arg Ser Cys Gln Phe Pro Glu Glu Glu
210 215 220

Arg Gly Glu Arg Ser Ala Glu Glu Lys Gly Arg Leu Gly Asp Leu Trp
225 230 235 240

Val

<210> 386
<211> 417
<212> PRT
<213> Homo sapiens

<400> 386

Met Ala Leu Lys Val Leu Leu Glu Gln Glu Lys Thr Phe Phe Thr Leu
1 5 10 15

Leu Val Leu Leu Gly Tyr Leu Ser Cys Lys Val Thr Cys Glu Ser Gly
20 25 30

Asp Cys Arg Gln Gln Glu Phe Arg Asp Arg Ser Gly Asn Cys Val Pro
35 40 45

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

Gly Tyr Gly Glu Asp Ala Gln Cys Val Thr Cys Arg Leu His Arg Phe
65 70 75 80

Lys Glu Asp Trp Gly Phe Gln Lys Cys Lys Pro Cys Leu Asp Cys Ala
85 90 95

Val Val Asn Arg Phe Gln Lys Ala Asn Cys Ser Ala Thr Ser Asp Ala
100 105 110

Ile Cys Gly Asp Cys Leu Pro Gly Phe Tyr Arg Lys Thr Lys Leu Val
115 120 125

Gly Phe Gln Asp Met Glu Cys Val Pro Cys Gly Asp Pro Pro Pro Pro
130 135 140

Tyr Glu Pro His Cys Ala Ser Lys Val Asn Leu Val Lys Ile Ala Ser
145 150 155 160

Thr Ala Ser Ser Pro Arg Asp Thr Ala Leu Ala Ala Val Ile Cys Ser
165 170 175

Ala Leu Ala Thr Val Leu Leu Ala Leu Leu Ile Leu Cys Val Ile Tyr
180 185 190

```
Cys Lys Arg Gln Phe Met Glu Lys Lys Pro Ser Trp Ser Leu Arg Ser
        195                 200                 205

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

Gln Leu His Glu Tyr Ala His Arg Ala Cys Cys Gln Cys Arg Arg Asp
225                 230                 235                 240

Ser Val Gln Thr Cys Gly Pro Val Arg Leu Leu Pro Ser Met Cys Cys
                245                 250                 255

Glu Glu Ala Cys Ser Pro Asn Pro Ala Thr Leu Gly Cys Gly Val His
            260                 265                 270

Ser Ala Ala Ser Leu Gln Ala Arg Asn Ala Gly Pro Ala Gly Glu Met
        275                 280                 285

Val Pro Thr Phe Phe Gly Ser Leu Thr Gln Ser Ile Cys Gly Glu Phe
    290                 295                 300

Ser Asp Ala Trp Pro Leu Met Gln Asn Pro Met Gly Gly Asp Asn Ile
305                 310                 315                 320

Ser Phe Cys Asp Ser Tyr Pro Glu Leu Thr Gly Glu Asp Ile His Ser
                325                 330                 335

Leu Asn Pro Glu Leu Glu Ser Ser Thr Ser Leu Asp Ser Asn Ser Ser
            340                 345                 350

Gln Asp Leu Val Gly Gly Ala Val Pro Val Gln Ser His Ser Glu Asn
        355                 360                 365

Phe Thr Ala Ala Thr Asp Leu Ser Arg Tyr Asn Asn Thr Leu Val Glu
    370                 375                 380

Ser Ala Ser Thr Gln Asp Ala Leu Thr Met Arg Ser Gln Leu Asp Gln
385                 390                 395                 400

Glu Ser Gly Ala Val Ile His Pro Ala Thr Gln Thr Ser Leu Gln Glu
                405                 410                 415

Ala
```

<210> 387
<211> 430
<212> PRT
<213> Homo sapiens

<400> 387

```
Met Lys Pro Ser Leu Leu Cys Arg Pro Leu Ser Cys Phe Leu Met Leu
```

1 5 10 15

Leu Pro Trp Pro Leu Ala Thr Leu Thr Ser Thr Thr Leu Trp Gln Cys
20 25 30

Pro Pro Gly Glu Glu Pro Asp Leu Asp Pro Gly Gln Gly Thr Leu Cys
35 40 45

Arg Pro Cys Pro Pro Gly Thr Phe Ser Ala Ala Trp Gly Ser Ser Pro
50 55 60

Cys Gln Pro His Ala Arg Cys Ser Leu Trp Arg Arg Leu Glu Ala Gln
65 70 75 80

Val Gly Met Ala Thr Arg Asp Thr Leu Cys Gly Asp Cys Trp Pro Gly
85 90 95

Trp Phe Gly Pro Trp Gly Val Pro Arg Val Pro Cys Gln Pro Cys Ser
100 105 110

Trp Ala Pro Leu Gly Thr His Gly Cys Asp Glu Trp Gly Arg Arg Ala
115 120 125

Arg Arg Gly Val Glu Val Ala Ala Gly Ala Ser Ser Gly Gly Glu Thr
130 135 140

Arg Gln Pro Gly Asn Gly Thr Arg Ala Gly Gly Pro Glu Glu Thr Ala
145 150 155 160

Ala Gln Tyr Ala Val Ile Ala Ile Val Pro Val Phe Cys Leu Met Gly
165 170 175

Leu Leu Gly Ile Leu Val Cys Asn Leu Leu Lys Arg Lys Gly Tyr His
180 185 190

Cys Thr Ala His Lys Glu Val Gly Pro Gly Pro Gly Gly Gly Gly Ser
195 200 205

Gly Ile Asn Pro Ala Tyr Arg Thr Glu Asp Ala Asn Glu Asp Thr Ile
210 215 220

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

Leu Glu Glu Leu Leu Lys Glu Tyr His Ser Lys Gln Leu Val Gln Thr
245 250 255

Ser His Arg Pro Val Ser Lys Leu Pro Pro Ala Pro Pro Asn Val Pro
260 265 270

His Ile Cys Pro His Arg His His Leu His Thr Val Gln Gly Leu Ala

275 280 285

Ser Leu Ser Gly Pro Cys Cys Ser Arg Cys Ser Gln Lys Lys Trp Pro
290 295 300

Glu Val Leu Leu Ser Pro Glu Ala Val Ala Ala Thr Thr Pro Val Pro
305 310 315 320

Ser Leu Leu Pro Asn Pro Thr Arg Val Pro Lys Ala Gly Ala Lys Ala
325 330 335

Gly Arg Gln Gly Glu Ile Thr Ile Leu Ser Val Gly Arg Phe Arg Val
340 345 350

Ala Arg Ile Pro Glu Gln Arg Thr Ser Ser Met Val Ser Glu Val Lys
355 360 365

Thr Ile Thr Glu Ala Gly Pro Ser Trp Gly Asp Leu Pro Asp Ser Pro
370 375 380

Gln Pro Gly Leu Pro Pro Glu Gln Gln Ala Leu Leu Gly Ser Gly Gly
385 390 395 400

Ser Arg Thr Lys Trp Leu Lys Pro Pro Ala Glu Asn Lys Ala Glu Glu
405 410 415

Asn Arg Tyr Val Val Arg Leu Ser Glu Ser Asn Leu Val Ile
420 425 430

<210> 388
<211> 655
<212> PRT
<213> Homo sapiens

<400> 388

Met Gly Thr Ser Pro Ser Ser Ser Thr Ala Leu Ala Ser Cys Ser Arg
1 5 10 15

Ile Ala Arg Arg Ala Thr Ala Thr Met Ile Ala Gly Ser Leu Leu Leu
20 25 30

Leu Gly Phe Leu Ser Thr Thr Thr Ala Gln Pro Glu Gln Lys Ala Ser
35 40 45

Asn Leu Ile Gly Thr Tyr Arg His Val Asp Arg Ala Thr Gly Gln Val
50 55 60

Leu Thr Cys Asp Lys Cys Pro Ala Gly Thr Tyr Val Ser Glu His Cys
65 70 75 80

Thr Asn Thr Ser Leu Arg Val Cys Ser Ser Cys Pro Val Gly Thr Phe
85 90 95

```
Thr Arg His Glu Asn Gly Ile Glu Lys Cys His Asp Cys Ser Gln Pro
            100                 105                 110

Cys Pro Trp Pro Met Ile Glu Lys Leu Pro Cys Ala Ala Leu Thr Asp
        115                 120                 125

Arg Glu Cys Thr Cys Pro Pro Gly Met Phe Gln Ser Asn Ala Thr Cys
    130                 135                 140

Ala Pro His Thr Val Cys Pro Val Gly Trp Gly Val Arg Lys Lys Gly
145                 150                 155                 160

Thr Glu Thr Glu Asp Val Arg Cys Lys Gln Cys Ala Arg Gly Thr Phe
                165                 170                 175

Ser Asp Val Pro Ser Ser Val Met Lys Cys Lys Ala Tyr Thr Asp Cys
            180                 185                 190

Leu Ser Gln Asn Leu Val Val Ile Lys Pro Gly Thr Lys Glu Thr Asp
        195                 200                 205

Asn Val Cys Gly Thr Leu Pro Ser Phe Ser Ser Ser Thr Ser Pro Ser
    210                 215                 220

Pro Gly Thr Ala Ile Phe Pro Arg Pro Glu His Met Glu Thr His Glu
225                 230                 235                 240

Val Pro Ser Ser Thr Tyr Val Pro Lys Gly Met Asn Ser Thr Glu Ser
                245                 250                 255

Asn Ser Ser Ala Ser Val Arg Pro Lys Val Leu Ser Ser Ile Gln Glu
            260                 265                 270

Gly Thr Val Pro Asp Asn Thr Ser Ser Ala Arg Gly Lys Glu Asp Val
        275                 280                 285

Asn Lys Thr Leu Pro Asn Leu Gln Val Val Asn His Gln Gln Gly Pro
    290                 295                 300

His His Arg His Ile Leu Lys Leu Leu Pro Ser Met Glu Ala Thr Gly
305                 310                 315                 320

Gly Glu Lys Ser Ser Thr Pro Ile Lys Gly Pro Lys Arg Gly His Pro
                325                 330                 335

Arg Gln Asn Leu His Lys His Phe Asp Ile Asn Glu His Leu Pro Trp
            340                 345                 350

Met Ile Val Leu Phe Leu Leu Leu Val Leu Val Val Ile Val Val Cys
        355                 360                 365
```

```
Ser Ile Arg Lys Ser Ser Arg Thr Leu Lys Lys Gly Pro Arg Gln Asp
    370                 375                 380

Pro Ser Ala Ile Val Glu Lys Ala Gly Leu Lys Lys Ser Met Thr Pro
385                 390                 395                 400

Thr Gln Asn Arg Glu Lys Trp Ile Tyr Tyr Cys Asn Gly His Gly Ile
                405                 410                 415

Asp Ile Leu Lys Leu Val Ala Ala Gln Val Gly Ser Gln Trp Lys Asp
            420                 425                 430

Ile Tyr Gln Phe Leu Cys Asn Ala Ser Glu Arg Glu Val Ala Ala Phe
        435                 440                 445

Ser Asn Gly Tyr Thr Ala Asp His Glu Arg Ala Tyr Ala Ala Leu Gln
    450                 455                 460

His Trp Thr Ile Arg Gly Pro Glu Ala Ser Leu Ala Gln Leu Ile Ser
465                 470                 475                 480

Ala Leu Arg Gln His Arg Arg Asn Asp Val Val Glu Lys Ile Arg Gly
                485                 490                 495

Leu Met Glu Asp Thr Thr Gln Leu Glu Thr Asp Lys Leu Ala Leu Pro
            500                 505                 510

Met Ser Pro Ser Pro Leu Ser Pro Ser Pro Ile Pro Ser Pro Asn Ala
        515                 520                 525

Lys Leu Glu Asn Ser Ala Leu Leu Thr Val Glu Pro Ser Pro Gln Asp
    530                 535                 540

Lys Asn Lys Gly Phe Phe Val Asp Glu Ser Glu Pro Leu Leu Arg Cys
545                 550                 555                 560

Asp Ser Thr Ser Ser Gly Ser Ser Ala Leu Ser Arg Asn Gly Ser Phe
                565                 570                 575

Ile Thr Lys Glu Lys Lys Asp Thr Val Leu Arg Gln Val Arg Leu Asp
            580                 585                 590

Pro Cys Asp Leu Gln Pro Ile Phe Asp Asp Met Leu His Phe Leu Asn
        595                 600                 605

Pro Glu Glu Leu Arg Val Ile Glu Glu Ile Pro Gln Ala Glu Asp Lys
    610                 615                 620

Leu Asp Arg Leu Phe Glu Ile Ile Gly Val Lys Ser Gln Glu Ala Ser
625                 630                 635                 640
```

Gln Thr Leu Leu Asp Ser Val Tyr Ser His Leu Pro Asp Leu Leu
645 650 655

<210> 389
<211> 198
<212> PRT
<213> Homo sapiens

<400> 389

Met Phe Gly Phe Phe Cys Ser Leu Val Ser Ser Leu Ser Arg Trp Phe
1 5 10 15

Leu Trp Arg Arg Leu Leu Leu Leu Leu Leu Leu Leu Leu Leu Asn Leu
20 25 30

Pro Leu Gln Val Lys Phe Ala Met Leu Glu Leu His Ser Phe Lys Cys
35 40 45

Pro Ala Gly Glu Tyr Trp Ser Lys Asp Val Cys Cys Lys Asn Cys Ser
50 55 60

Ala Gly Thr Phe Val Lys Ala Pro Cys Glu Ile Pro His Thr Gln Gly
65 70 75 80

Gln Cys Glu Lys Cys His Pro Gly Thr Phe Thr Glu Lys Asp Asn Tyr
85 90 95

Leu Asp Ala Cys Ile Leu Cys Ser Thr Cys Asp Lys Asp Gln Glu Met
100 105 110

Val Ala Asp Cys Ser Ala Thr Ser Asp Arg Lys Cys Gln Cys Arg Thr
115 120 125

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

Thr Lys Cys Pro Gln Gly Ile Pro Val Leu Gln Glu Cys Asn Ser Thr
145 150 155 160

Ala Asn Thr Val Cys Ser Ser Ser Val Ser Asn Pro Arg Asn Arg Leu
165 170 175

Phe Leu Leu Leu Ser Pro Leu Ser Val Leu Ile Val Ser Val Val Val
180 185 190

Phe Arg Ile Ile Arg Arg
195

<210> 390
<211> 176
<212> PRT

<213> Homo sapiens

<400> 390

```
Met Val Thr Phe Ser His Val Ser Ser Leu Ser His Trp Phe Leu Leu
1               5                   10                  15

Leu Leu Leu Leu Asn Leu Phe Leu Pro Val Ile Phe Ala Met Pro Glu
            20                  25                  30

Ser Tyr Ser Phe Asn Cys Pro Asp Gly Glu Tyr Gln Ser Asn Asp Val
        35                  40                  45

Cys Cys Lys Thr Cys Pro Ser Gly Thr Phe Val Lys Ala Pro Cys Lys
    50                  55                  60

Ile Pro His Thr Gln Gly Gln Cys Glu Lys Cys His Pro Gly Thr Phe
65                  70                  75                  80

Thr Gly Lys Asp Asn Gly Leu His Asp Cys Glu Leu Cys Ser Thr Cys
                85                  90                  95

Asp Lys Asp Gln Asn Met Val Ala Asp Cys Ser Ala Thr Ser Asp Arg
            100                 105                 110

Lys Cys Glu Cys Gln Ile Gly Leu Tyr Tyr Tyr Asp Pro Lys Phe Pro
        115                 120                 125

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

Gln Glu Cys Asn Ser Thr Ala Asn Thr Val Cys Ser Ser Ser Val Ser
145                 150                 155                 160

Asn Pro Arg Asn Trp Leu Phe Leu Leu Met Leu Ile Val Phe Cys Ile
                165                 170                 175
```

<210> 391
<211> 297
<212> PRT
<213> Homo sapiens

<400> 391

```
Met Asp Cys Gln Glu Asn Glu Tyr Trp Asp Gln Trp Gly Arg Cys Val
1               5                   10                  15

Thr Cys Gln Arg Cys Gly Pro Gly Gln Glu Leu Ser Lys Asp Cys Gly
            20                  25                  30

Tyr Gly Glu Gly Gly Asp Ala Tyr Cys Thr Ala Cys Pro Pro Arg Arg
        35                  40                  45

Tyr Lys Ser Ser Trp Gly His His Arg Cys Gln Ser Cys Ile Thr Cys
```

50 55 60

Ala Val Ile Asn Arg Val Gln Lys Val Asn Cys Thr Ala Thr Ser Asn
65 70 75 80

Ala Val Cys Gly Asp Cys Leu Pro Arg Phe Tyr Arg Lys Thr Arg Ile
85 90 95

Gly Gly Leu Gln Asp Gln Glu Cys Ile Pro Cys Thr Lys Gln Thr Pro
100 105 110

Thr Ser Glu Val Gln Cys Ala Phe Gln Leu Ser Leu Val Glu Ala Asp
115 120 125

Ala Pro Thr Val Pro Pro Gln Glu Ala Thr Leu Val Ala Leu Val Ser
130 135 140

Ser Leu Leu Val Val Phe Thr Leu Ala Phe Leu Gly Leu Phe Phe Leu
145 150 155 160

Tyr Cys Lys Gln Phe Phe Asn Arg His Cys Gln Arg Gly Gly Leu Leu
165 170 175

Gln Phe Glu Ala Asp Lys Thr Ala Lys Glu Glu Ser Leu Phe Pro Val
180 185 190

Pro Pro Ser Lys Glu Thr Ser Ala Glu Ser Gln Val Ser Glu Asn Ile
195 200 205

Phe Gln Thr Gln Pro Leu Asn Pro Ile Leu Glu Asp Asp Cys Ser Ser
210 215 220

Thr Ser Gly Phe Pro Thr Gln Glu Ser Phe Thr Met Ala Ser Cys Thr
225 230 235 240

Ser Glu Ser His Ser His Trp Val His Ser Pro Ile Glu Cys Thr Glu
245 250 255

Leu Asp Leu Gln Lys Phe Ser Ser Ser Ala Ser Tyr Thr Gly Ala Glu
260 265 270

Thr Leu Gly Gly Asn Thr Val Glu Ser Thr Gly Asp Arg Leu Glu Leu
275 280 285

Asn Val Pro Phe Glu Val Pro Ser Pro
290 295

<210> 392
<211> 448
<212> PRT
<213> Homo sapiens

<400> 392

```
Met Ala His Val Gly Asp Cys Thr Gln Thr Pro Trp Leu Pro Val Leu
1               5                  10                  15

Val Val Ser Leu Met Cys Ser Ala Arg Ala Glu Tyr Ser Asn Cys Gly
            20                  25                  30

Glu Asn Glu Tyr Tyr Asn Gln Thr Thr Gly Leu Cys Gln Glu Cys Pro
        35                  40                  45

Pro Cys Gly Pro Gly Glu Glu Pro Tyr Leu Ser Cys Gly Tyr Gly Thr
    50                  55                  60

Lys Asp Glu Asp Tyr Gly Cys Val Pro Cys Pro Ala Glu Lys Phe Ser
65                  70                  75                  80

Lys Gly Gly Tyr Gln Ile Cys Arg Arg His Lys Asp Cys Glu Gly Phe
                85                  90                  95

Phe Arg Ala Thr Val Leu Thr Pro Gly Asp Met Glu Asn Asp Ala Glu
            100                 105                 110

Cys Gly Pro Cys Leu Pro Gly Tyr Tyr Met Leu Glu Asn Arg Pro Arg
        115                 120                 125

Asn Ile Tyr Gly Met Val Cys Tyr Ser Cys Leu Leu Ala Pro Pro Asn
    130                 135                 140

Thr Lys Glu Cys Val Gly Ala Thr Ser Gly Ala Ser Ala Asn Phe Pro
145                 150                 155                 160

Gly Thr Ser Gly Ser Ser Thr Leu Ser Pro Phe Gln His Ala His Lys
                165                 170                 175

Glu Leu Ser Gly Gln Gly His Leu Ala Thr Ala Leu Ile Ile Ala Met
            180                 185                 190

Ser Thr Ile Phe Ile Met Ala Ile Ala Ile Val Leu Ile Ile Met Phe
        195                 200                 205

Tyr Ile Leu Lys Thr Lys Pro Ser Ala Pro Ala Cys Cys Thr Ser His
    210                 215                 220

Pro Gly Lys Ser Val Glu Ala Gln Val Ser Lys Asp Glu Glu Lys Lys
225                 230                 235                 240

Glu Ala Pro Asp Asn Val Val Met Phe Ser Glu Lys Asp Glu Phe Glu
                245                 250                 255

Lys Leu Thr Ala Thr Pro Ala Lys Pro Thr Lys Ser Glu Asn Asp Ala
            260                 265                 270
```

Ser Ser Glu Asn Glu Gln Leu Leu Ser Arg Ser Val Asp Ser Asp Glu
275 280 285

Glu Pro Ala Pro Asp Lys Gln Gly Ser Pro Glu Leu Cys Leu Leu Ser
290 295 300

Leu Val His Leu Ala Arg Glu Lys Ser Ala Thr Ser Asn Lys Ser Ala
305 310 315 320

Gly Ile Gln Ser Arg Arg Lys Lys Ile Leu Asp Val Tyr Ala Asn Val
325 330 335

Cys Gly Val Val Glu Gly Leu Ser Pro Thr Glu Leu Pro Phe Asp Cys
340 345 350

Leu Glu Lys Thr Ser Arg Met Leu Ser Ser Thr Tyr Asn Ser Glu Lys
355 360 365

Ala Val Val Lys Thr Trp Arg His Leu Ala Glu Ser Phe Gly Leu Lys
370 375 380

Arg Asp Glu Ile Gly Gly Met Thr Asp Gly Met Gln Leu Phe Asp Arg
385 390 395 400

Ile Ser Thr Ala Gly Tyr Ser Ile Pro Glu Leu Leu Thr Lys Leu Val
405 410 415

Gln Ile Glu Arg Leu Asp Ala Val Glu Ser Leu Cys Ala Asp Ile Leu
420 425 430

Glu Trp Ala Gly Val Val Pro Pro Ala Ser Gln Pro His Ala Ala Ser
435 440 445

<210> 393
<211> 355
<212> PRT
<213> Homo sapiens

<400> 393

Met Glu Thr Pro Asn Thr Thr Glu Asp Tyr Asp Thr Thr Thr Glu Phe
1 5 10 15

Asp Tyr Gly Asp Ala Thr Pro Cys Gln Lys Val Asn Glu Arg Ala Phe
20 25 30

Gly Ala Gln Leu Leu Pro Pro Leu Tyr Ser Leu Val Phe Val Ile Gly
35 40 45

Leu Val Gly Asn Ile Leu Val Val Leu Val Leu Val Gln Tyr Lys Arg
50 55 60

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

Leu Leu Phe Leu Phe Thr Leu Pro Phe Trp Ile Asp Tyr Lys Leu Lys
                85                  90                  95

Asp Asp Trp Val Phe Gly Asp Ala Met Cys Lys Ile Leu Ser Gly Phe
            100                 105                 110

Tyr Tyr Thr Gly Leu Tyr Ser Glu Ile Phe Phe Ile Ile Leu Leu Thr
        115                 120                 125

Ile Asp Arg Tyr Leu Ala Ile Val His Ala Val Phe Ala Leu Arg Ala
    130                 135                 140

Arg Thr Val Thr Phe Gly Val Ile Thr Ser Ile Ile Ile Trp Ala Leu
145                 150                 155                 160

Ala Ile Leu Ala Ser Met Pro Gly Leu Tyr Phe Ser Lys Thr Gln Trp
                165                 170                 175

Glu Phe Thr His His Thr Cys Ser Leu His Phe Pro His Glu Ser Leu
            180                 185                 190

Arg Glu Trp Lys Leu Phe Gln Ala Leu Lys Leu Asn Leu Phe Gly Leu
        195                 200                 205

Val Leu Pro Leu Leu Val Met Ile Ile Cys Tyr Thr Gly Ile Ile Lys
    210                 215                 220

Ile Leu Leu Arg Arg Pro Asn Glu Lys Lys Ser Lys Ala Val Arg Leu
225                 230                 235                 240

Ile Phe Val Ile Met Ile Ile Phe Phe Leu Phe Trp Thr Pro Tyr Asn
                245                 250                 255

Leu Thr Ile Leu Ile Ser Val Phe Gln Asp Phe Leu Phe Thr His Glu
            260                 265                 270

Cys Glu Gln Ser Arg His Leu Asp Leu Ala Val Gln Val Thr Glu Val
        275                 280                 285

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

Gly Glu Arg Phe Arg Lys Tyr Leu Arg Gln Leu Phe His Arg Arg Val
305                 310                 315                 320

Ala Val His Leu Val Lys Trp Leu Pro Phe Leu Ser Val Asp Arg Leu
                325                 330                 335
```

Glu Arg Val Ser Ser Thr Ser Pro Ser Thr Gly Glu His Glu Leu Ser
340 345 350

Ala Gly Phe
355

<210> 394
<211> 374
<212> PRT
<213> Homo sapiens

<400> 394

Met Leu Ser Thr Ser Arg Ser Arg Phe Ile Arg Asn Thr Asn Glu Ser
1 5 10 15

Gly Glu Glu Val Thr Thr Phe Phe Asp Tyr Asp Tyr Gly Ala Pro Cys
20 25 30

His Lys Phe Asp Val Lys Gln Ile Gly Ala Gln Leu Leu Pro Pro Leu
35 40 45

Tyr Ser Leu Val Phe Ile Phe Gly Phe Val Gly Asn Met Leu Val Val
50 55 60

Leu Ile Leu Ile Asn Cys Lys Lys Leu Lys Cys Leu Thr Asp Ile Tyr
65 70 75 80

Leu Leu Asn Leu Ala Ile Ser Asp Leu Leu Phe Leu Ile Thr Leu Pro
85 90 95

Leu Trp Ala His Ser Ala Ala Asn Glu Trp Val Phe Gly Asn Ala Met
100 105 110

Cys Lys Leu Phe Thr Gly Leu Tyr His Ile Gly Tyr Phe Gly Gly Ile
115 120 125

Phe Phe Ile Ile Leu Leu Thr Ile Asp Arg Tyr Leu Ala Ile Val His
130 135 140

Ala Val Phe Ala Leu Lys Ala Arg Thr Val Thr Phe Gly Val Val Thr
145 150 155 160

Ser Val Ile Thr Trp Leu Val Ala Val Phe Ala Ser Val Pro Gly Ile
165 170 175

Ile Phe Thr Lys Cys Gln Lys Glu Asp Ser Val Tyr Val Cys Gly Pro
180 185 190

Tyr Phe Pro Arg Gly Trp Asn Asn Phe His Thr Ile Met Arg Asn Ile
195 200 205

Leu Gly Leu Val Leu Pro Leu Leu Ile Met Val Ile Cys Tyr Ser Gly
210 215 220

Ile Leu Lys Thr Leu Leu Arg Cys Arg Asn Glu Lys Lys Arg His Arg
225 230 235 240

Ala Val Arg Val Ile Phe Thr Ile Met Ile Val Tyr Phe Leu Phe Trp
245 250 255

Thr Pro Tyr Asn Ile Val Ile Leu Leu Asn Thr Phe Gln Glu Phe Phe
260 265 270

Gly Leu Ser Asn Cys Glu Ser Thr Ser Gln Leu Asp Gln Ala Thr Gln
275 280 285

Val Thr Glu Thr Leu Gly Met Thr His Cys Cys Ile Asn Pro Ile Ile
290 295 300

Tyr Ala Phe Val Gly Glu Lys Phe Arg Ser Leu Phe His Ile Ala Leu
305 310 315 320

Gly Cys Arg Ile Ala Pro Leu Gln Lys Pro Val Cys Gly Gly Pro Gly
325 330 335

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

Gly Arg Gly Lys Gly Lys Ser Ile Gly Arg Ala Pro Glu Ala Ser Leu
355 360 365

Gln Asp Lys Glu Gly Ala
370

<210> 395
<211> 355
<212> PRT
<213> Homo sapiens

<400> 395

Met Thr Thr Ser Leu Asp Thr Val Glu Thr Phe Gly Thr Thr Ser Tyr
1 5 10 15

Tyr Asp Asp Val Gly Leu Leu Cys Glu Lys Ala Asp Thr Arg Ala Leu
20 25 30

Met Ala Gln Phe Val Pro Pro Leu Tyr Ser Leu Val Phe Thr Val Gly
35 40 45

Leu Leu Gly Asn Val Val Val Val Met Ile Leu Ile Lys Tyr Arg Arg
50 55 60

Leu Arg Ile Met Thr Asn Ile Tyr Leu Leu Asn Leu Ala Ile Ser Asp

65 70 75 80

Leu Leu Phe Leu Val Thr Leu Pro Phe Trp Ile His Tyr Val Arg Gly
85 90 95

His Asn Trp Val Phe Gly His Gly Met Cys Lys Leu Leu Ser Gly Phe
100 105 110

Tyr His Thr Gly Leu Tyr Ser Glu Ile Phe Phe Ile Ile Leu Leu Thr
115 120 125

Ile Asp Arg Tyr Leu Ala Ile Val His Ala Val Phe Ala Leu Arg Ala
130 135 140

Arg Thr Val Thr Phe Gly Val Ile Thr Ser Ile Val Thr Trp Gly Leu
145 150 155 160

Ala Val Leu Ala Ala Leu Pro Glu Phe Ile Phe Tyr Glu Thr Glu Glu
165 170 175

Leu Phe Glu Glu Thr Leu Cys Ser Ala Leu Tyr Pro Glu Asp Thr Val
180 185 190

Tyr Ser Trp Arg His Phe His Thr Leu Arg Met Thr Ile Phe Cys Leu
195 200 205

Val Leu Pro Leu Leu Val Met Ala Ile Cys Tyr Thr Gly Ile Ile Lys
210 215 220

Thr Leu Leu Arg Cys Pro Ser Lys Lys Lys Tyr Lys Ala Ile Arg Leu
225 230 235 240

Ile Phe Val Ile Met Ala Val Phe Phe Ile Phe Trp Thr Pro Tyr Asn
245 250 255

Val Ala Ile Leu Leu Ser Ser Tyr Gln Ser Ile Leu Phe Gly Asn Asp
260 265 270

Cys Glu Arg Ser Lys His Leu Asp Leu Val Met Leu Val Thr Glu Val
275 280 285

Ile Ala Tyr Ser His Cys Cys Met Asn Pro Val Ile Tyr Ala Phe Val
290 295 300

Gly Glu Arg Phe Arg Lys Tyr Leu Arg His Phe Phe His Arg His Leu
305 310 315 320

Leu Met His Leu Gly Arg Tyr Ile Pro Phe Leu Pro Ser Glu Lys Leu
325 330 335

Glu Arg Thr Ser Ser Val Ser Pro Ser Thr Ala Glu Pro Glu Leu Ser

340 345 350

Ile Val Phe
355

<210> 396
<211> 360
<212> PRT
<213> Homo sapiens

<400> 396

Met Asn Pro Thr Asp Ile Ala Asp Thr Thr Leu Asp Glu Ser Ile Tyr
1 5 10 15

Ser Asn Tyr Tyr Leu Tyr Glu Ser Ile Pro Lys Pro Cys Thr Lys Glu
20 25 30

Gly Ile Lys Ala Phe Gly Glu Leu Phe Leu Pro Pro Leu Tyr Ser Leu
35 40 45

Val Phe Val Phe Gly Leu Leu Gly Asn Ser Val Val Val Leu Val Leu
50 55 60

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

Leu Ala Ile Ser Asp Leu Leu Phe Val Phe Ser Leu Pro Phe Trp Gly
85 90 95

Tyr Tyr Ala Ala Asp Gln Trp Val Phe Gly Leu Gly Leu Cys Lys Met
100 105 110

Ile Ser Trp Met Tyr Leu Val Gly Phe Tyr Ser Gly Ile Phe Phe Val
115 120 125

Met Leu Met Ser Ile Asp Arg Tyr Leu Ala Ile Val His Ala Val Phe
130 135 140

Ser Leu Arg Ala Arg Thr Leu Thr Tyr Gly Val Ile Thr Ser Leu Ala
145 150 155 160

Thr Trp Ser Val Ala Val Phe Ala Ser Leu Pro Gly Phe Leu Phe Ser
165 170 175

Thr Cys Tyr Thr Glu Arg Asn His Thr Tyr Cys Lys Thr Lys Tyr Ser
180 185 190

Leu Asn Ser Thr Thr Trp Lys Val Leu Ser Ser Leu Glu Ile Asn Ile
195 200 205

Leu Gly Leu Val Ile Pro Leu Gly Ile Met Leu Phe Cys Tyr Ser Met
210 215 220

```
Ile Ile Arg Thr Leu Gln His Cys Lys Asn Glu Lys Lys Asn Lys Ala
225                 230                 235                 240

Val Lys Met Ile Phe Ala Val Val Val Leu Phe Leu Gly Phe Trp Thr
                245                 250                 255

Pro Tyr Asn Ile Val Leu Phe Leu Glu Thr Leu Val Glu Leu Glu Val
            260                 265                 270

Leu Gln Asp Cys Thr Phe Glu Arg Tyr Leu Asp Tyr Ala Ile Gln Ala
        275                 280                 285

Thr Glu Thr Leu Ala Phe Val His Cys Cys Leu Asn Pro Ile Ile Tyr
    290                 295                 300

Phe Phe Leu Gly Glu Lys Phe Arg Lys Tyr Ile Leu Gln Leu Phe Lys
305                 310                 315                 320

Thr Cys Arg Gly Leu Phe Val Leu Cys Gln Tyr Cys Gly Leu Leu Gln
                325                 330                 335

Ile Tyr Ser Ala Asp Thr Pro Ser Ser Ser Tyr Thr Gln Ser Thr Met
            340                 345                 350

Asp His Asp Leu His Asp Ala Leu
        355                 360


<210>  397
<211>  352
<212>  PRT
<213>  Homo sapiens

<400>  397

Met Asp Tyr Gln Val Ser Ser Pro Ile Tyr Asp Ile Asn Tyr Tyr Thr
1               5                   10                  15

Ser Glu Pro Cys Gln Lys Ile Asn Val Lys Gln Ile Ala Ala Arg Leu
            20                  25                  30

Leu Pro Pro Leu Tyr Ser Leu Val Phe Ile Phe Gly Phe Val Gly Asn
        35                  40                  45

Met Leu Val Ile Leu Ile Leu Ile Asn Cys Lys Arg Leu Lys Ser Met
    50                  55                  60

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

Leu Thr Val Pro Phe Trp Ala His Tyr Ala Ala Ala Gln Trp Asp Phe
                85                  90                  95
```

```
Gly Asn Thr Met Cys Gln Leu Leu Thr Gly Leu Tyr Phe Ile Gly Phe
            100                 105                 110

Phe Ser Gly Ile Phe Phe Ile Ile Leu Leu Thr Ile Asp Arg Tyr Leu
        115                 120                 125

Ala Val Val His Ala Val Phe Ala Leu Lys Ala Arg Thr Val Thr Phe
    130                 135                 140

Gly Val Val Thr Ser Val Ile Thr Trp Val Val Ala Val Phe Ala Ser
145                 150                 155                 160

Leu Pro Gly Ile Ile Phe Thr Arg Ser Gln Lys Glu Gly Leu His Tyr
                165                 170                 175

Thr Cys Ser Ser His Phe Pro Tyr Ser Gln Tyr Gln Phe Trp Lys Asn
            180                 185                 190

Phe Gln Thr Leu Lys Ile Val Ile Leu Gly Leu Val Leu Pro Leu Leu
        195                 200                 205

Val Met Val Ile Cys Tyr Ser Gly Ile Leu Lys Thr Leu Leu Arg Cys
    210                 215                 220

Arg Asn Glu Lys Lys Arg His Arg Ala Val Arg Leu Ile Phe Thr Ile
225                 230                 235                 240

Met Ile Val Tyr Phe Leu Phe Trp Ala Pro Tyr Asn Ile Val Leu Leu
                245                 250                 255

Leu Asn Thr Phe Gln Glu Phe Phe Gly Leu Asn Asn Cys Ser Ser Ser
            260                 265                 270

Asn Arg Leu Asp Gln Ala Met Gln Val Thr Glu Thr Leu Gly Met Thr
        275                 280                 285

His Cys Cys Ile Asn Pro Ile Ile Tyr Ala Phe Val Gly Glu Lys Phe
    290                 295                 300

Arg Asn Tyr Leu Leu Val Phe Phe Gln Lys His Ile Ala Lys Arg Phe
305                 310                 315                 320

Cys Lys Cys Cys Ser Ile Phe Gln Gln Glu Ala Pro Glu Arg Ala Ser
                325                 330                 335

Ser Val Tyr Thr Arg Ser Thr Gly Glu Gln Glu Ile Ser Val Gly Leu
            340                 345                 350
```

<210> 398
<211> 374
<212> PRT

<213> Homo sapiens

<400> 398

```
Met Ser Gly Glu Ser Met Asn Phe Ser Asp Val Phe Asp Ser Ser Glu
1               5                  10                  15

Asp Tyr Phe Val Ser Val Asn Thr Ser Tyr Tyr Ser Val Asp Ser Glu
            20                  25                  30

Met Leu Leu Cys Ser Leu Gln Glu Val Arg Gln Phe Ser Arg Leu Phe
        35                  40                  45

Val Pro Ile Ala Tyr Ser Leu Ile Cys Val Phe Gly Leu Leu Gly Asn
    50                  55                  60

Ile Leu Val Val Ile Thr Phe Ala Phe Tyr Lys Lys Ala Arg Ser Met
65                  70                  75                  80

Thr Asp Val Tyr Leu Leu Asn Met Ala Ile Ala Asp Ile Leu Phe Val
                85                  90                  95

Leu Thr Leu Pro Phe Trp Ala Val Ser His Ala Thr Gly Ala Trp Val
            100                 105                 110

Phe Ser Asn Ala Thr Cys Lys Leu Leu Lys Gly Ile Tyr Ala Ile Asn
        115                 120                 125

Phe Asn Cys Gly Met Leu Leu Leu Thr Cys Ile Ser Met Asp Arg Tyr
    130                 135                 140

Ile Ala Ile Val Gln Ala Thr Lys Ser Phe Arg Leu Arg Ser Arg Thr
145                 150                 155                 160

Leu Pro Arg Ser Lys Ile Ile Cys Leu Val Val Trp Gly Leu Ser Val
                165                 170                 175

Ile Ile Ser Ser Ser Thr Phe Val Phe Asn Gln Lys Tyr Asn Thr Gln
            180                 185                 190

Gly Ser Asp Val Cys Glu Pro Lys Tyr Gln Thr Val Ser Glu Pro Ile
        195                 200                 205

Arg Trp Lys Leu Leu Met Leu Gly Leu Glu Leu Leu Phe Gly Phe Phe
    210                 215                 220

Ile Pro Leu Met Phe Met Ile Phe Cys Tyr Thr Phe Ile Val Lys Thr
225                 230                 235                 240

Leu Val Gln Ala Gln Asn Ser Lys Arg His Lys Ala Ile Arg Val Ile
                245                 250                 255
```

Ile Ala Val Val Leu Val Phe Leu Ala Cys Gln Ile Pro His Asn Met
260 265 270

Val Leu Leu Val Thr Ala Ala Asn Leu Gly Lys Met Asn Arg Ser Cys
275 280 285

Gln Ser Glu Lys Leu Ile Gly Tyr Thr Lys Thr Val Thr Glu Val Leu
290 295 300

Ala Phe Leu His Cys Cys Leu Asn Pro Val Leu Tyr Ala Phe Ile Gly
305 310 315 320

Gln Lys Phe Arg Asn Tyr Phe Leu Lys Ile Leu Lys Asp Leu Trp Cys
325 330 335

Val Arg Arg Lys Tyr Lys Ser Ser Gly Phe Ser Cys Ala Gly Arg Tyr
340 345 350

Ser Glu Asn Ile Ser Arg Gln Thr Ser Glu Thr Ala Asp Asn Asp Asn
355 360 365

Ala Ser Ser Phe Thr Met
370

<210> 399
<211> 315
<212> PRT
<213> Homo sapiens

<400> 399

Met Tyr Ser Ile Ile Cys Phe Val Gly Leu Leu Gly Asn Gly Leu Val
1 5 10 15

Val Leu Thr Tyr Ile Tyr Phe Lys Arg Leu Lys Thr Met Thr Asp Thr
20 25 30

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

Pro Phe Trp Ala Tyr Ser Ala Ala Lys Ser Trp Val Phe Gly Val His
50 55 60

Phe Cys Lys Leu Ile Phe Ala Ile Tyr Lys Met Ser Phe Phe Ser Gly
65 70 75 80

Met Leu Leu Leu Leu Cys Ile Ser Ile Asp Arg Tyr Val Ala Ile Val
85 90 95

Gln Ala Val Ser Ala His Arg His Arg Ala Arg Val Leu Leu Ile Ser
100 105 110

Lys Leu Ser Cys Val Gly Ile Trp Ile Leu Ala Thr Val Leu Ser Ile

115 120 125

Pro Glu Leu Leu Tyr Ser Asp Leu Gln Arg Ser Ser Ser Glu Gln Ala
130 135 140

Met Arg Cys Ser Leu Ile Thr Glu His Val Glu Ala Phe Ile Thr Ile
145 150 155 160

Gln Val Ala Gln Met Val Ile Gly Phe Leu Val Pro Leu Leu Ala Met
165 170 175

Ser Phe Cys Tyr Leu Val Ile Ile Arg Thr Leu Leu Gln Ala Arg Asn
180 185 190

Phe Glu Arg Asn Lys Ala Ile Lys Val Ile Ile Ala Val Val Val Val
195 200 205

Phe Ile Val Phe Gln Leu Pro Tyr Asn Gly Val Val Leu Ala Gln Thr
210 215 220

Val Ala Asn Phe Asn Ile Thr Ser Ser Thr Cys Glu Leu Ser Lys Gln
225 230 235 240

Leu Asn Ile Ala Tyr Asp Val Thr Tyr Ser Leu Ala Cys Val Arg Cys
245 250 255

Cys Val Asn Pro Phe Leu Tyr Ala Phe Ile Gly Val Lys Phe Arg Asn
260 265 270

Asp Leu Phe Lys Leu Phe Lys Asp Leu Gly Cys Leu Ser Gln Glu Gln
275 280 285

Leu Arg Gln Trp Ser Ser Cys Arg His Ile Arg Arg Ser Ser Met Ser
290 295 300

Val Glu Ala Glu Thr Thr Thr Thr Phe Ser Pro
305 310 315

<210> 400
<211> 355
<212> PRT
<213> Homo sapiens

<400> 400

Met Asp Tyr Thr Leu Asp Leu Ser Val Thr Thr Val Thr Asp Tyr Tyr
1 5 10 15

Tyr Pro Asp Ile Phe Ser Ser Pro Cys Asp Ala Glu Leu Ile Gln Thr
20 25 30

Asn Gly Lys Leu Leu Leu Ala Val Phe Tyr Cys Leu Leu Phe Val Phe
35 40 45

```
Ser Leu Leu Gly Asn Ser Leu Val Ile Leu Val Leu Val Val Cys Lys
    50                  55                  60

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

Asp Leu Leu Phe Val Phe Ser Phe Pro Phe Gln Thr Tyr Tyr Leu Leu
                85                  90                  95

Asp Gln Trp Val Phe Gly Thr Val Met Cys Lys Val Val Ser Gly Phe
            100                 105                 110

Tyr Tyr Ile Gly Phe Tyr Ser Ser Met Phe Phe Ile Thr Leu Met Ser
        115                 120                 125

Val Asp Arg Tyr Leu Ala Val Val His Ala Val Tyr Ala Leu Lys Val
    130                 135                 140

Arg Thr Ile Arg Met Gly Thr Thr Leu Cys Leu Ala Val Trp Leu Thr
145                 150                 155                 160

Ala Ile Met Ala Thr Ile Pro Leu Leu Val Phe Tyr Gln Val Ala Ser
                165                 170                 175

Glu Asp Gly Val Leu Gln Cys Tyr Ser Phe Tyr Asn Gln Gln Thr Leu
            180                 185                 190

Lys Trp Lys Ile Phe Thr Asn Phe Lys Met Asn Ile Leu Gly Leu Leu
        195                 200                 205

Ile Pro Phe Thr Ile Phe Met Phe Cys Tyr Ile Lys Ile Leu His Gln
    210                 215                 220

Leu Lys Arg Cys Gln Asn His Asn Lys Thr Lys Ala Ile Arg Leu Val
225                 230                 235                 240

Leu Ile Val Val Ile Ala Ser Leu Leu Phe Trp Val Pro Phe Asn Val
                245                 250                 255

Val Leu Phe Leu Thr Ser Leu His Ser Met His Ile Leu Asp Gly Cys
            260                 265                 270

Ser Ile Ser Gln Gln Leu Thr Tyr Ala Thr His Val Thr Glu Ile Ile
        275                 280                 285

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

Glu Lys Phe Lys Lys His Leu Ser Glu Ile Phe Gln Lys Ser Cys Ser
305                 310                 315                 320
```

Gln Ile Phe Asn Tyr Leu Gly Arg Gln Met Pro Arg Glu Ser Cys Glu
325 330 335

Lys Ser Ser Ser Cys Gln Gln His Ser Ser Arg Ser Ser Ser Val Asp
340 345 350

Tyr Ile Leu
355

<210> 401
<211> 357
<212> PRT
<213> Homo sapiens

<400> 401

Met Ala Asp Asp Tyr Gly Ser Glu Ser Thr Ser Ser Met Glu Asp Tyr
1 5 10 15

Val Asn Phe Asn Phe Thr Asp Phe Tyr Cys Glu Lys Asn Asn Val Arg
20 25 30

Gln Phe Ala Ser His Phe Leu Pro Pro Leu Tyr Trp Leu Val Phe Ile
35 40 45

Val Gly Ala Leu Gly Asn Ser Leu Val Ile Leu Val Tyr Trp Tyr Cys
50 55 60

Thr Arg Val Lys Thr Met Thr Asp Met Phe Leu Leu Asn Leu Ala Ile
65 70 75 80

Ala Asp Leu Leu Phe Leu Val Thr Leu Pro Phe Trp Ala Ile Ala Ala
85 90 95

Ala Asp Gln Trp Lys Phe Gln Thr Phe Met Cys Lys Val Val Asn Ser
100 105 110

Met Tyr Lys Met Asn Phe Tyr Ser Cys Val Leu Leu Ile Met Cys Ile
115 120 125

Ser Val Asp Arg Tyr Ile Ala Ile Ala Gln Ala Met Arg Ala His Thr
130 135 140

Trp Arg Glu Lys Arg Leu Leu Tyr Ser Lys Met Val Cys Phe Thr Ile
145 150 155 160

Trp Val Leu Ala Ala Ala Leu Cys Ile Pro Glu Ile Leu Tyr Ser Gln
165 170 175

Ile Lys Glu Glu Ser Gly Ile Ala Ile Cys Thr Met Val Tyr Pro Ser
180 185 190

```
Asp Glu Ser Thr Lys Leu Lys Ser Ala Val Leu Thr Leu Lys Val Ile
        195                 200                 205

Leu Gly Phe Phe Leu Pro Phe Val Val Met Ala Cys Cys Tyr Thr Ile
    210                 215                 220

Ile Ile His Thr Leu Ile Gln Ala Lys Lys Ser Ser Lys His Lys Ala
225                 230                 235                 240

Leu Lys Val Thr Ile Thr Val Leu Thr Val Phe Val Leu Ser Gln Phe
                245                 250                 255

Pro Tyr Asn Cys Ile Leu Leu Val Gln Thr Ile Asp Ala Tyr Ala Met
            260                 265                 270

Phe Ile Ser Asn Cys Ala Val Ser Thr Asn Ile Asp Ile Cys Phe Gln
        275                 280                 285

Val Thr Gln Thr Ile Ala Phe Phe His Ser Cys Leu Asn Pro Val Leu
    290                 295                 300

Tyr Val Phe Val Gly Glu Arg Phe Arg Arg Asp Leu Val Lys Thr Leu
305                 310                 315                 320

Lys Asn Leu Gly Cys Ile Ser Gln Ala Gln Trp Val Ser Phe Thr Arg
                325                 330                 335

Arg Glu Gly Ser Leu Lys Leu Ser Ser Met Leu Leu Glu Thr Thr Ser
            340                 345                 350

Gly Ala Leu Ser Leu
        355


<210>  402
<211>  362
<212>  PRT
<213>  Homo sapiens

<400>  402

Met Gly Thr Glu Ala Thr Glu Gln Val Ser Trp Gly His Tyr Ser Gly
1               5                   10                  15

Asp Glu Glu Asp Ala Tyr Ser Ala Glu Pro Leu Pro Glu Leu Cys Tyr
            20                  25                  30

Lys Ala Asp Val Gln Ala Phe Ser Arg Ala Phe Gln Pro Ser Val Ser
        35                  40                  45

Leu Thr Val Ala Ala Leu Gly Leu Ala Gly Asn Gly Leu Val Leu Ala
    50                  55                  60
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Thr His Leu Ala Ala Arg Arg Ala Ala Arg Ser Pro Thr Ser Ala His
65                  70                  75                  80

Leu Leu Gln Leu Ala Leu Ala Asp Leu Leu Leu Ala Leu Thr Leu Pro
                85                  90                  95

Phe Ala Ala Ala Gly Ala Leu Gln Gly Trp Ser Leu Gly Ser Ala Thr
            100                 105                 110

Cys Arg Thr Ile Ser Gly Leu Tyr Ser Ala Ser Phe His Ala Gly Phe
        115                 120                 125

Leu Phe Leu Ala Cys Ile Ser Ala Asp Arg Tyr Val Ala Ile Ala Arg
    130                 135                 140

Ala Leu Pro Ala Gly Pro Arg Pro Ser Thr Pro Gly Arg Ala His Leu
145                 150                 155                 160

Val Ser Val Ile Val Trp Leu Leu Ser Leu Leu Leu Ala Leu Pro Ala
                165                 170                 175

Leu Leu Phe Ser Gln Asp Gly Gln Arg Glu Gly Gln Arg Arg Cys Arg
            180                 185                 190

Leu Ile Phe Pro Glu Gly Leu Thr Gln Thr Val Lys Gly Ala Ser Ala
        195                 200                 205

Val Ala Gln Val Ala Leu Gly Phe Ala Leu Pro Leu Gly Val Met Val
    210                 215                 220

Ala Cys Tyr Ala Leu Leu Gly Arg Thr Leu Leu Ala Ala Arg Gly Pro
225                 230                 235                 240

Glu Arg Arg Arg Ala Leu Arg Val Val Val Ala Leu Val Ala Ala Phe
                245                 250                 255

Val Val Leu Gln Leu Pro Tyr Ser Leu Ala Leu Leu Leu Asp Thr Ala
            260                 265                 270

Asp Leu Leu Ala Ala Arg Glu Arg Ser Cys Pro Ala Ser Lys Arg Lys
        275                 280                 285

Asp Val Ala Leu Leu Val Thr Ser Gly Leu Ala Leu Ala Arg Cys Gly
    290                 295                 300

Leu Asn Pro Val Leu Tyr Ala Phe Leu Gly Leu Arg Phe Arg Gln Asp
305                 310                 315                 320

Leu Arg Arg Leu Leu Arg Gly Gly Ser Cys Pro Ser Gly Pro Gln Pro
                325                 330                 335
```

Arg Arg Gly Cys Pro Arg Arg Pro Arg Leu Ser Ser Cys Ser Ala Pro
340 345 350

Thr Glu Thr His Ser Leu Ser Trp Asp Asn
355 360

<210> 403
<211> 350
<212> PRT
<213> Homo sapiens

<400> 403

Met Ser Asn Ile Thr Asp Pro Gln Met Trp Asp Phe Asp Asp Leu Asn
1 5 10 15

Phe Thr Gly Met Pro Pro Ala Asp Glu Asp Tyr Ser Pro Cys Met Leu
20 25 30

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

Val Phe Leu Leu Ser Leu Leu Gly Asn Ser Leu Val Met Leu Val Ile
50 55 60

Leu Tyr Ser Arg Val Gly Arg Ser Val Thr Asp Val Tyr Leu Leu Asn
65 70 75 80

Leu Ala Leu Ala Asp Leu Leu Phe Ala Leu Thr Leu Pro Ile Trp Ala
85 90 95

Ala Ser Lys Val Asn Gly Trp Ile Phe Gly Thr Phe Leu Cys Lys Val
100 105 110

Val Ser Leu Leu Lys Glu Val Asn Phe Tyr Ser Gly Ile Leu Leu Leu
115 120 125

Ala Cys Ile Ser Val Asp Arg Tyr Leu Ala Ile Val His Ala Thr Arg
130 135 140

Thr Leu Thr Gln Lys Arg His Leu Val Lys Phe Val Cys Leu Gly Cys
145 150 155 160

Trp Gly Leu Ser Met Asn Leu Ser Leu Pro Phe Phe Leu Phe Arg Gln
165 170 175

Ala Tyr His Pro Asn Asn Ser Ser Pro Val Cys Tyr Glu Val Leu Gly
180 185 190

Asn Asp Thr Ala Lys Trp Arg Met Val Leu Arg Ile Leu Pro His Thr
195 200 205

Phe Gly Phe Ile Val Pro Leu Phe Val Met Leu Phe Cys Tyr Gly Phe

210 215 220

Thr Leu Arg Thr Leu Phe Lys Ala His Met Gly Gln Lys His Arg Ala
225 230 235 240

Met Arg Val Ile Phe Ala Val Val Leu Ile Phe Leu Leu Cys Trp Leu
245 250 255

Pro Tyr Asn Leu Val Leu Leu Ala Asp Thr Leu Met Arg Thr Gln Val
260 265 270

Ile Gln Glu Ser Cys Glu Arg Arg Asn Asn Ile Gly Arg Ala Leu Asp
275 280 285

Ala Thr Glu Ile Leu Gly Phe Leu His Ser Cys Leu Asn Pro Ile Ile
290 295 300

Tyr Ala Phe Ile Gly Gln Asn Phe Arg His Gly Phe Leu Lys Ile Leu
305 310 315 320

Ala Met His Gly Leu Val Ser Lys Glu Phe Leu Ala Arg His Arg Val
325 330 335

Thr Ser Tyr Thr Ser Ser Ser Val Asn Val Ser Ser Asn Leu
340 345 350

<210> 404
<211> 360
<212> PRT
<213> Homo sapiens

<400> 404

Met Glu Asp Phe Asn Met Glu Ser Asp Ser Phe Glu Asp Phe Trp Lys
1 5 10 15

Gly Glu Asp Leu Ser Asn Tyr Ser Tyr Ser Ser Thr Leu Pro Pro Phe
20 25 30

Leu Leu Asp Ala Ala Pro Cys Glu Pro Glu Ser Leu Glu Ile Asn Lys
35 40 45

Tyr Phe Val Val Ile Ile Tyr Ala Leu Val Phe Leu Leu Ser Leu Leu
50 55 60

Gly Asn Ser Leu Val Met Leu Val Ile Leu Tyr Ser Arg Val Gly Arg
65 70 75 80

Ser Val Thr Asp Val Tyr Leu Leu Asn Leu Ala Leu Ala Asp Leu Leu
85 90 95

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

Ile Phe Gly Thr Phe Leu Cys Lys Val Val Ser Leu Leu Lys Glu Val
115 120 125

Asn Phe Tyr Ser Gly Ile Leu Leu Leu Ala Cys Ile Ser Val Asp Arg
130 135 140

Tyr Leu Ala Ile Val His Ala Thr Arg Thr Leu Thr Gln Lys Arg Tyr
145 150 155 160

Leu Val Lys Phe Ile Cys Leu Ser Ile Trp Gly Leu Ser Leu Leu Leu
165 170 175

Ala Leu Pro Val Leu Leu Phe Arg Arg Thr Val Tyr Ser Ser Asn Val
180 185 190

Ser Pro Ala Cys Tyr Glu Asp Met Gly Asn Asn Thr Ala Asn Trp Arg
195 200 205

Met Leu Leu Arg Ile Leu Pro Gln Ser Phe Gly Phe Ile Val Pro Leu
210 215 220

Leu Ile Met Leu Phe Cys Tyr Gly Phe Thr Leu Arg Thr Leu Phe Lys
225 230 235 240

Ala His Met Gly Gln Lys His Arg Ala Met Arg Val Ile Phe Ala Val
245 250 255

Val Leu Ile Phe Leu Leu Cys Trp Leu Pro Tyr Asn Leu Val Leu Leu
260 265 270

Ala Asp Thr Leu Met Arg Thr Gln Val Ile Gln Glu Thr Cys Glu Arg
275 280 285

Arg Asn His Ile Asp Arg Ala Leu Asp Ala Thr Glu Ile Leu Gly Ile
290 295 300

Leu His Ser Cys Leu Asn Pro Leu Ile Tyr Ala Phe Ile Gly Gln Lys
305 310 315 320

Phe Arg His Gly Leu Leu Lys Ile Leu Ala Ile His Gly Leu Ile Ser
325 330 335

Lys Asp Ser Leu Pro Lys Asp Ser Arg Pro Ser Phe Val Gly Ser Ser
340 345 350

Ser Gly His Thr Ser Thr Thr Leu
355 360

<210> 405
<211> 415

<212> PRT
<213> Homo sapiens

<400> 405

```
Met Glu Leu Arg Lys Tyr Gly Pro Gly Arg Leu Ala Gly Thr Val Ile
1               5                  10                  15

Gly Gly Ala Ala Gln Ser Lys Ser Gln Thr Lys Ser Asp Ser Ile Thr
            20                  25                  30

Lys Glu Phe Leu Pro Gly Leu Tyr Thr Ala Pro Ser Ser Pro Phe Pro
        35                  40                  45

Pro Ser Gln Val Ser Asp His Gln Val Leu Asn Asp Ala Glu Val Ala
    50                  55                  60

Ala Leu Leu Glu Asn Phe Ser Ser Ser Tyr Asp Tyr Gly Glu Asn Glu
65                  70                  75                  80

Ser Asp Ser Cys Cys Thr Ser Pro Pro Cys Pro Gln Asp Phe Ser Leu
                85                  90                  95

Asn Phe Asp Arg Ala Phe Leu Pro Ala Leu Tyr Ser Leu Leu Phe Leu
            100                 105                 110

Leu Gly Leu Leu Gly Asn Gly Ala Val Ala Ala Val Leu Leu Ser Arg
        115                 120                 125

Arg Thr Ala Leu Ser Ser Thr Asp Thr Phe Leu Leu His Leu Ala Val
    130                 135                 140

Ala Asp Thr Leu Leu Val Leu Thr Leu Pro Leu Trp Ala Val Asp Ala
145                 150                 155                 160

Ala Val Gln Trp Val Phe Gly Ser Gly Leu Cys Lys Val Ala Gly Ala
                165                 170                 175

Leu Phe Asn Ile Asn Phe Tyr Ala Gly Ala Leu Leu Leu Ala Cys Ile
            180                 185                 190

Ser Phe Asp Arg Tyr Leu Asn Ile Val His Ala Thr Gln Leu Tyr Arg
        195                 200                 205

Arg Gly Pro Pro Ala Arg Val Thr Leu Thr Cys Leu Ala Val Trp Gly
    210                 215                 220

Leu Cys Leu Leu Phe Ala Leu Pro Asp Phe Ile Phe Leu Ser Ala His
225                 230                 235                 240

His Asp Glu Arg Leu Asn Ala Thr His Cys Gln Tyr Asn Phe Pro Gln
                245                 250                 255
```

Val Gly Arg Thr Ala Leu Arg Val Leu Gln Leu Val Ala Gly Phe Leu
260 265 270

Leu Pro Leu Leu Val Met Ala Tyr Cys Tyr Ala His Ile Leu Ala Val
275 280 285

Leu Leu Val Ser Arg Gly Gln Arg Arg Leu Arg Ala Met Arg Leu Val
290 295 300

Val Val Val Val Val Ala Phe Ala Leu Cys Trp Thr Pro Tyr His Leu
305 310 315 320

Val Val Leu Val Asp Ile Leu Met Asp Leu Gly Ala Leu Ala Arg Asn
325 330 335

Cys Gly Arg Glu Ser Arg Val Asp Val Ala Lys Ser Val Thr Ser Gly
340 345 350

Leu Gly Tyr Met His Cys Cys Leu Asn Pro Leu Leu Tyr Ala Phe Val
355 360 365

Gly Val Lys Phe Arg Glu Arg Met Trp Met Leu Leu Leu Arg Leu Gly
370 375 380

Cys Pro Asn Gln Arg Gly Leu Gln Arg Gln Pro Ser Ser Ser Arg Arg
385 390 395 400

Asp Ser Ser Trp Ser Glu Thr Ser Glu Ala Ser Tyr Ser Gly Leu
405 410 415

<210> 406
<211> 356
<212> PRT
<213> Homo sapiens

<400> 406

Met Ser Ile Pro Leu Pro Leu Leu Gln Ile Tyr Thr Ser Asp Asn Tyr
1 5 10 15

Thr Glu Glu Met Gly Ser Gly Asp Tyr Asp Ser Met Lys Glu Pro Cys
20 25 30

Phe Arg Glu Glu Asn Ala Asn Phe Asn Lys Ile Phe Leu Pro Thr Ile
35 40 45

Tyr Ser Ile Ile Phe Leu Thr Gly Ile Val Gly Asn Gly Leu Val Ile
50 55 60

Leu Val Met Gly Tyr Gln Lys Lys Leu Arg Ser Met Thr Asp Lys Tyr
65 70 75 80

```
Arg Leu His Leu Ser Val Ala Asp Leu Leu Phe Val Ile Thr Leu Pro
                85                  90                  95

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

Cys Lys Ala Val His Val Ile Tyr Thr Val Asn Leu Tyr Ser Ser Val
        115                 120                 125

Leu Ile Leu Ala Phe Ile Ser Leu Asp Arg Tyr Leu Ala Ile Val His
    130                 135                 140

Ala Thr Asn Ser Gln Arg Pro Arg Lys Leu Leu Ala Glu Lys Val Val
145                 150                 155                 160

Tyr Val Gly Val Trp Ile Pro Ala Leu Leu Leu Thr Ile Pro Asp Phe
                165                 170                 175

Ile Phe Ala Asn Val Ser Glu Ala Asp Asp Arg Tyr Ile Cys Asp Arg
            180                 185                 190

Phe Tyr Pro Asn Asp Leu Trp Val Val Val Phe Gln Phe Gln His Ile
        195                 200                 205

Met Val Gly Leu Ile Leu Pro Gly Ile Val Ile Leu Ser Cys Tyr Cys
    210                 215                 220

Ile Ile Ile Ser Lys Leu Ser His Ser Lys Gly His Gln Lys Arg Lys
225                 230                 235                 240

Ala Leu Lys Thr Thr Val Ile Leu Ile Leu Ala Phe Phe Ala Cys Trp
                245                 250                 255

Leu Pro Tyr Tyr Ile Gly Ile Ser Ile Asp Ser Phe Ile Leu Leu Glu
            260                 265                 270

Ile Ile Lys Gln Gly Cys Glu Phe Glu Asn Thr Val His Lys Trp Ile
        275                 280                 285

Ser Ile Thr Glu Ala Leu Ala Phe Phe His Cys Cys Leu Asn Pro Ile
    290                 295                 300

Leu Tyr Ala Phe Leu Gly Ala Lys Phe Lys Thr Ser Ala Gln His Ala
305                 310                 315                 320

Leu Thr Ser Val Ser Arg Gly Ser Ser Leu Lys Ile Leu Ser Lys Gly
                325                 330                 335

Lys Arg Gly Gly His Ser Ser Val Ser Thr Glu Ser Glu Ser Ser Ser
            340                 345                 350
```

Phe His Ser Ser
355

<210> 407
<211> 372
<212> PRT
<213> Homo sapiens

<400> 407

Met Asn Tyr Pro Leu Thr Leu Glu Met Asp Leu Glu Asn Leu Glu Asp
1 5 10 15

Leu Phe Trp Glu Leu Asp Arg Leu Asp Asn Tyr Asn Asp Thr Ser Leu
20 25 30

Val Glu Asn His Leu Cys Pro Ala Thr Glu Gly Pro Leu Met Ala Ser
35 40 45

Phe Lys Ala Val Phe Val Pro Val Ala Tyr Ser Leu Ile Phe Leu Leu
50 55 60

Gly Val Ile Gly Asn Val Leu Val Leu Val Ile Leu Glu Arg His Arg
65 70 75 80

Gln Thr Arg Ser Ser Thr Glu Thr Phe Leu Phe His Leu Ala Val Ala
85 90 95

Asp Leu Leu Leu Val Phe Ile Leu Pro Phe Ala Val Ala Glu Gly Ser
100 105 110

Val Gly Trp Val Leu Gly Thr Phe Leu Cys Lys Thr Val Ile Ala Leu
115 120 125

His Lys Val Asn Phe Tyr Cys Ser Ser Leu Leu Leu Ala Cys Ile Ala
130 135 140

Val Asp Arg Tyr Leu Ala Ile Val His Ala Val His Ala Tyr Arg His
145 150 155 160

Arg Arg Leu Leu Ser Ile His Ile Thr Cys Gly Thr Ile Trp Leu Val
165 170 175

Gly Phe Leu Leu Ala Leu Pro Glu Ile Leu Phe Ala Lys Val Ser Gln
180 185 190

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

Gln Ala Glu Thr His Ala Trp Phe Thr Ser Arg Phe Leu Tyr His Val
210 215 220

Ala Gly Phe Leu Leu Pro Met Leu Val Met Gly Trp Cys Tyr Val Gly

225 230 235 240

Val Val His Arg Leu Arg Gln Ala Gln Arg Arg Pro Gln Arg Gln Lys
245 250 255

Ala Val Arg Val Ala Ile Leu Val Thr Ser Ile Phe Phe Leu Cys Trp
260 265 270

Ser Pro Tyr His Ile Val Ile Phe Leu Asp Thr Leu Ala Arg Leu Lys
275 280 285

Ala Val Asp Asn Thr Cys Lys Leu Asn Gly Ser Leu Pro Val Ala Ile
290 295 300

Thr Met Cys Glu Phe Leu Gly Leu Ala His Cys Cys Leu Asn Pro Met
305 310 315 320

Leu Tyr Thr Phe Ala Gly Val Lys Phe Arg Ser Asp Leu Ser Arg Leu
325 330 335

Leu Thr Lys Leu Gly Cys Thr Gly Pro Ala Ser Leu Cys Gln Leu Phe
340 345 350

Pro Ser Trp Arg Arg Ser Ser Leu Ser Glu Ser Glu Asn Ala Thr Ser
355 360 365

Leu Thr Thr Phe
370

<210> 408
<211> 342
<212> PRT
<213> Homo sapiens

<400> 408

Met Ala Glu His Asp Tyr His Glu Asp Tyr Gly Phe Ser Ser Phe Asn
1 5 10 15

Asp Ser Ser Gln Glu Glu His Gln Asp Phe Leu Gln Phe Ser Lys Val
20 25 30

Phe Leu Pro Cys Met Tyr Leu Val Val Phe Val Cys Gly Leu Val Gly
35 40 45

Asn Ser Leu Val Leu Val Ile Ser Ile Phe Tyr His Lys Leu Gln Ser
50 55 60

Leu Thr Asp Val Phe Leu Val Asn Leu Pro Leu Ala Asp Leu Val Phe
65 70 75 80

Val Cys Thr Leu Pro Phe Trp Ala Tyr Ala Gly Ile His Glu Trp Val
85 90 95

```
Phe Gly Gln Val Met Cys Lys Ser Leu Leu Gly Ile Tyr Thr Ile Asn
            100                 105                 110

Phe Tyr Thr Ser Met Leu Ile Leu Thr Cys Ile Thr Val Asp Arg Phe
        115                 120                 125

Ile Val Val Val Lys Ala Thr Lys Ala Tyr Asn Gln Gln Ala Lys Arg
    130                 135                 140

Met Thr Trp Gly Lys Val Thr Ser Leu Leu Ile Trp Val Ile Ser Leu
145                 150                 155                 160

Leu Val Ser Leu Pro Gln Ile Ile Tyr Gly Asn Val Phe Asn Leu Asp
                165                 170                 175

Lys Leu Ile Cys Gly Tyr His Asp Glu Ala Ile Ser Thr Val Val Leu
            180                 185                 190

Ala Thr Gln Met Thr Leu Gly Phe Phe Leu Pro Leu Leu Thr Met Ile
        195                 200                 205

Val Cys Tyr Ser Val Ile Ile Lys Thr Leu Leu His Ala Gly Gly Phe
    210                 215                 220

Gln Lys His Arg Ser Leu Lys Ile Ile Phe Leu Val Met Ala Val Phe
225                 230                 235                 240

Leu Leu Thr Gln Met Pro Phe Asn Leu Met Lys Phe Ile Arg Ser Thr
                245                 250                 255

His Trp Glu Tyr Tyr Ala Met Thr Ser Phe His Tyr Thr Ile Met Val
            260                 265                 270

Thr Glu Ala Ile Ala Tyr Leu Arg Ala Cys Leu Asn Pro Val Leu Tyr
        275                 280                 285

Ala Phe Val Ser Leu Lys Phe Arg Lys Asn Phe Trp Lys Leu Val Lys
    290                 295                 300

Asp Ile Gly Cys Leu Pro Tyr Leu Gly Val Ser His Gln Trp Lys Ser
305                 310                 315                 320

Ser Glu Asp Asn Ser Lys Thr Phe Ser Ala Ser His Asn Val Glu Ala
                325                 330                 335

Thr Ser Met Phe Gln Leu
            340
```

<210> 409
<211> 355

<212> PRT
<213> Homo sapiens

<400> 409

```
Met Asp Gln Phe Pro Glu Ser Val Thr Glu Asn Phe Glu Tyr Asp Asp
1               5                  10                  15

Leu Ala Glu Ala Cys Tyr Ile Gly Asp Ile Val Val Phe Gly Thr Val
            20                  25                  30

Phe Leu Ser Ile Phe Tyr Ser Val Ile Phe Ala Ile Gly Leu Val Gly
        35                  40                  45

Asn Leu Leu Val Val Phe Ala Leu Thr Asn Ser Lys Lys Pro Lys Ser
    50                  55                  60

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

Val Ala Thr Leu Pro Phe Trp Thr His Tyr Leu Ile Asn Glu Lys Gly
                85                  90                  95

Leu His Asn Ala Met Cys Lys Phe Thr Thr Ala Phe Phe Phe Ile Gly
            100                 105                 110

Phe Phe Gly Ser Ile Phe Phe Ile Thr Val Ile Ser Ile Asp Arg Tyr
        115                 120                 125

Leu Ala Ile Val Leu Ala Ala Asn Ser Met Asn Asn Arg Thr Val Gln
    130                 135                 140

His Gly Val Thr Ile Ser Leu Gly Val Trp Ala Ala Ala Ile Leu Val
145                 150                 155                 160

Ala Ala Pro Gln Phe Met Phe Thr Lys Gln Lys Glu Asn Glu Cys Leu
                165                 170                 175

Gly Asp Tyr Pro Glu Val Leu Gln Glu Ile Trp Pro Val Leu Arg Asn
            180                 185                 190

Val Glu Thr Asn Phe Leu Gly Phe Leu Leu Pro Leu Leu Ile Met Ser
        195                 200                 205

Tyr Cys Tyr Phe Arg Ile Ile Gln Thr Leu Phe Ser Cys Lys Asn His
    210                 215                 220

Lys Lys Ala Lys Ala Ile Lys Leu Ile Leu Leu Val Val Ile Val Phe
225                 230                 235                 240

Phe Leu Phe Trp Thr Pro Tyr Asn Val Met Ile Phe Leu Glu Thr Leu
                245                 250                 255
```

Lys Leu Tyr Asp Phe Phe Pro Ser Cys Asp Met Arg Lys Asp Leu Arg
260 265 270

Leu Ala Leu Ser Val Thr Glu Thr Val Ala Phe Ser His Cys Cys Leu
275 280 285

Asn Pro Leu Ile Tyr Ala Phe Ala Gly Glu Lys Phe Arg Arg Tyr Leu
290 295 300

Tyr His Leu Tyr Gly Lys Cys Leu Ala Val Leu Cys Gly Arg Ser Val
305 310 315 320

His Val Asp Phe Ser Ser Ser Glu Ser Gln Arg Ser Arg His Gly Ser
325 330 335

Val Leu Ser Ser Asn Phe Thr Tyr His Thr Ser Asp Gly Asp Ala Leu
340 345 350

Leu Leu Leu
355

<210> 410
<211> 503
<212> PRT
<213> Homo sapiens

<400> 410

Met Glu Ala Ala Val Ala Ala Pro Arg Pro Arg Leu Leu Leu Leu Val
1 5 10 15

Leu Ala Ala Ala Ala Ala Ala Ala Ala Ala Leu Leu Pro Gly Ala Thr
20 25 30

Ala Leu Gln Cys Phe Cys His Leu Cys Thr Lys Asp Asn Phe Thr Cys
35 40 45

Val Thr Asp Gly Leu Cys Phe Val Ser Val Thr Glu Thr Thr Asp Lys
50 55 60

Val Ile His Asn Ser Met Cys Ile Ala Glu Ile Asp Leu Ile Pro Arg
65 70 75 80

Asp Arg Pro Phe Val Cys Ala Pro Ser Ser Lys Thr Gly Ser Val Thr
85 90 95

Thr Thr Tyr Cys Cys Asn Gln Asp His Cys Asn Lys Ile Glu Leu Pro
100 105 110

Thr Thr Val Lys Ser Ser Pro Gly Leu Gly Pro Val Glu Leu Ala Ala
115 120 125

```
Val Ile Ala Gly Pro Val Cys Phe Val Cys Ile Ser Leu Met Leu Met
    130                 135                 140

Val Tyr Ile Cys His Asn Arg Thr Val Ile His His Arg Val Pro Asn
145                 150                 155                 160

Glu Glu Asp Pro Ser Leu Asp Arg Pro Phe Ile Ser Glu Gly Thr Thr
                165                 170                 175

Leu Lys Asp Leu Ile Tyr Asp Met Thr Thr Ser Gly Ser Gly Ser Gly
            180                 185                 190

Leu Pro Leu Leu Val Gln Arg Thr Ile Ala Arg Thr Ile Val Leu Gln
        195                 200                 205

Glu Ser Ile Gly Lys Gly Arg Phe Gly Glu Val Trp Arg Gly Lys Trp
    210                 215                 220

Arg Gly Glu Glu Val Ala Val Lys Ile Phe Ser Ser Arg Glu Glu Arg
225                 230                 235                 240

Ser Trp Phe Arg Glu Ala Glu Ile Tyr Gln Thr Val Met Leu Arg His
                245                 250                 255

Glu Asn Ile Leu Gly Phe Ile Ala Ala Asp Asn Lys Asp Asn Gly Thr
            260                 265                 270

Trp Thr Gln Leu Trp Leu Val Ser Asp Tyr His Glu His Gly Ser Leu
        275                 280                 285

Phe Asp Tyr Leu Asn Arg Tyr Thr Val Thr Val Glu Gly Met Ile Lys
    290                 295                 300

Leu Ala Leu Ser Thr Ala Ser Gly Leu Ala His Leu His Met Glu Ile
305                 310                 315                 320

Val Gly Thr Gln Gly Lys Pro Ala Ile Ala His Arg Asp Leu Lys Ser
                325                 330                 335

Lys Asn Ile Leu Val Lys Lys Asn Gly Thr Cys Cys Ile Ala Asp Leu
            340                 345                 350

Gly Leu Ala Val Arg His Asp Ser Ala Thr Asp Thr Ile Asp Ile Ala
        355                 360                 365

Pro Asn His Arg Val Gly Thr Lys Arg Tyr Met Ala Pro Glu Val Leu
    370                 375                 380

Asp Asp Ser Ile Asn Met Lys His Phe Glu Ser Phe Lys Arg Ala Asp
385                 390                 395                 400
```

Ile Tyr Ala Met Gly Leu Val Phe Trp Glu Ile Ala Arg Arg Cys Ser
405 410 415

Ile Gly Gly Ile His Glu Asp Tyr Gln Leu Pro Tyr Tyr Asp Leu Val
420 425 430

Pro Ser Asp Pro Ser Val Glu Glu Met Arg Lys Val Val Cys Glu Gln
435 440 445

Lys Leu Arg Pro Asn Ile Pro Asn Arg Trp Gln Ser Cys Glu Ala Leu
450 455 460

Arg Val Met Ala Lys Ile Met Arg Glu Cys Trp Tyr Ala Asn Gly Ala
465 470 475 480

Ala Arg Leu Thr Ala Leu Arg Ile Lys Lys Thr Leu Ser Gln Leu Ser
485 490 495

Gln Gln Glu Gly Ile Lys Met
500

<210> 411
<211> 567
<212> PRT
<213> Homo sapiens

<400> 411

Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro Leu His Ile Val Leu
1 5 10 15

Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His Val Gln Lys Ser Val
20 25 30

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

Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser Thr Cys Asp Asn Gln
50 55 60

Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser Ile Cys Glu Lys Pro
65 70 75 80

Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn Asp Glu Asn Ile Thr
85 90 95

Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro Tyr His Asp Phe Ile
100 105 110

Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met Lys Glu Lys Lys Lys
115 120 125

Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser Ser Asp Glu Cys Asn

130 135 140

Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr Ser Asn Pro Asp Leu
145 150 155 160

Leu Leu Val Ile Phe Gln Val Thr Gly Ile Ser Leu Leu Pro Pro Leu
165 170 175

Gly Val Ala Ile Ser Val Ile Ile Ile Phe Tyr Cys Tyr Arg Val Asn
180 185 190

Arg Gln Gln Lys Leu Ser Ser Thr Trp Glu Thr Gly Lys Thr Arg Lys
195 200 205

Leu Met Glu Phe Ser Glu His Cys Ala Ile Ile Leu Glu Asp Asp Arg
210 215 220

Ser Asp Ile Ser Ser Thr Cys Ala Asn Asn Ile Asn His Asn Thr Glu
225 230 235 240

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

Glu Val Tyr Lys Ala Lys Leu Lys Gln Asn Thr Ser Glu Gln Phe Glu
260 265 270

Thr Val Ala Val Lys Ile Phe Pro Tyr Glu Glu Tyr Ala Ser Trp Lys
275 280 285

Thr Glu Lys Asp Ile Phe Ser Asp Ile Asn Leu Lys His Glu Asn Ile
290 295 300

Leu Gln Phe Leu Thr Ala Glu Glu Arg Lys Thr Glu Leu Gly Lys Gln
305 310 315 320

Tyr Trp Leu Ile Thr Ala Phe His Ala Lys Gly Asn Leu Gln Glu Tyr
325 330 335

Leu Thr Arg His Val Ile Ser Trp Glu Asp Leu Arg Lys Leu Gly Ser
340 345 350

Ser Leu Ala Arg Gly Ile Ala His Leu His Ser Asp His Thr Pro Cys
355 360 365

Gly Arg Pro Lys Met Pro Ile Val His Arg Asp Leu Lys Ser Ser Asn
370 375 380

Ile Leu Val Lys Asn Asp Leu Thr Cys Cys Leu Cys Asp Phe Gly Leu
385 390 395 400

Ser Leu Arg Leu Asp Pro Thr Leu Ser Val Asp Asp Leu Ala Asn Ser

405 410 415

Gly Gln Val Gly Thr Ala Arg Tyr Met Ala Pro Glu Val Leu Glu Ser
420 425 430

Arg Met Asn Leu Glu Asn Val Glu Ser Phe Lys Gln Thr Asp Val Tyr
435 440 445

Ser Met Ala Leu Val Leu Trp Glu Met Thr Ser Arg Cys Asn Ala Val
450 455 460

Gly Glu Val Lys Asp Tyr Glu Pro Pro Phe Gly Ser Lys Val Arg Glu
465 470 475 480

His Pro Cys Val Glu Ser Met Lys Asp Asn Val Leu Arg Asp Arg Gly
485 490 495

Arg Pro Glu Ile Pro Ser Phe Trp Leu Asn His Gln Gly Ile Gln Met
500 505 510

Val Cys Glu Thr Leu Thr Glu Cys Trp Asp His Asp Pro Glu Ala Arg
515 520 525

Leu Thr Ala Gln Cys Val Ala Glu Arg Phe Ser Glu Leu Glu His Leu
530 535 540

Asp Arg Leu Ser Gly Arg Ser Cys Ser Glu Glu Lys Ile Pro Glu Asp
545 550 555 560

Gly Ser Leu Asn Thr Thr Lys
565

<210> 412
<211> 851
<212> PRT
<213> Homo sapiens

<400> 412

Met Thr Ser His Tyr Val Ile Ala Ile Phe Ala Leu Met Ser Ser Cys
1 5 10 15

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

Val Ser Ala Ser His Pro Val Gln Ala Leu Met Glu Ser Phe Thr Val
35 40 45

Leu Ser Gly Cys Ala Ser Arg Gly Thr Thr Gly Leu Pro Gln Glu Val
50 55 60

His Val Leu Asn Leu Arg Thr Ala Gly Gln Gly Pro Gly Gln Leu Gln
65 70 75 80

```
Arg Glu Val Thr Leu His Leu Asn Pro Ile Ser Ser Val His Ile His
                85                  90                  95

His Lys Ser Val Val Phe Leu Leu Asn Ser Pro His Pro Leu Val Trp
            100                 105                 110

His Leu Lys Thr Glu Arg Leu Ala Thr Gly Val Ser Arg Leu Phe Leu
        115                 120                 125

Val Ser Glu Gly Ser Val Val Gln Phe Ser Ser Ala Asn Phe Ser Leu
    130                 135                 140

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

Leu Asn Trp Ala Arg Lys Glu Tyr Gly Ala Val Thr Ser Phe Thr Glu
                165                 170                 175

Leu Lys Ile Ala Arg Asn Ile Tyr Ile Lys Val Gly Glu Asp Gln Val
            180                 185                 190

Phe Pro Pro Lys Cys Asn Ile Gly Lys Asn Phe Leu Ser Leu Asn Tyr
        195                 200                 205

Leu Ala Glu Tyr Leu Gln Pro Lys Ala Ala Glu Gly Cys Val Met Ser
    210                 215                 220

Ser Gln Pro Gln Asn Glu Glu Val His Ile Ile Glu Leu Ile Thr Pro
225                 230                 235                 240

Asn Ser Asn Pro Tyr Ser Ala Phe Gln Val Asp Ile Thr Ile Asp Ile
                245                 250                 255

Arg Pro Ser Gln Glu Asp Leu Glu Val Val Lys Asn Leu Ile Leu Ile
            260                 265                 270

Leu Lys Cys Lys Lys Ser Val Asn Trp Val Ile Lys Ser Phe Asp Val
        275                 280                 285

Lys Gly Ser Leu Lys Ile Ile Ala Pro Asn Ser Ile Gly Phe Gly Lys
    290                 295                 300

Glu Ser Glu Arg Ser Met Thr Met Thr Lys Ser Ile Arg Asp Asp Ile
305                 310                 315                 320

Pro Ser Thr Gln Gly Asn Leu Val Lys Trp Ala Leu Asp Asn Gly Tyr
                325                 330                 335

Ser Pro Ile Thr Ser Tyr Thr Met Ala Pro Val Ala Asn Arg Phe His
            340                 345                 350
```

```
Leu Arg Leu Glu Asn Asn Ala Glu Glu Met Gly Asp Glu Glu Val His
        355                 360                 365

Thr Ile Pro Pro Glu Leu Arg Ile Leu Leu Asp Pro Gly Ala Leu Pro
    370                 375                 380

Ala Leu Gln Asn Pro Pro Ile Arg Gly Gly Glu Gly Gln Asn Gly Gly
385                 390                 395                 400

Leu Pro Phe Pro Phe Pro Asp Ile Ser Arg Arg Val Trp Asn Glu Glu
                405                 410                 415

Gly Glu Asp Gly Leu Pro Arg Pro Lys Asp Pro Val Ile Pro Ser Ile
            420                 425                 430

Gln Leu Phe Pro Gly Leu Arg Glu Pro Glu Glu Val Gln Gly Ser Val
        435                 440                 445

Asp Ile Ala Leu Ser Val Lys Cys Asp Asn Glu Lys Met Ile Val Ala
    450                 455                 460

Val Glu Lys Asp Ser Phe Gln Ala Ser Gly Tyr Ser Gly Met Asp Val
465                 470                 475                 480

Thr Leu Leu Asp Pro Thr Cys Lys Ala Lys Met Asn Gly Thr His Phe
                485                 490                 495

Val Leu Glu Ser Pro Leu Asn Gly Cys Gly Thr Arg Pro Arg Trp Ser
            500                 505                 510

Ala Leu Asp Gly Val Val Tyr Tyr Asn Ser Ile Val Ile Gln Val Pro
        515                 520                 525

Ala Leu Gly Asp Ser Ser Gly Trp Pro Asp Gly Tyr Glu Asp Leu Glu
    530                 535                 540

Ser Gly Asp Asn Gly Phe Pro Gly Asp Met Asp Glu Gly Asp Ala Ser
545                 550                 555                 560

Leu Phe Thr Arg Pro Glu Ile Val Val Phe Asn Cys Ser Leu Gln Gln
                565                 570                 575

Val Arg Asn Pro Ser Ser Phe Gln Glu Gln Pro His Gly Asn Ile Thr
            580                 585                 590

Phe Asn Met Glu Leu Tyr Asn Thr Asp Leu Phe Leu Val Pro Ser Gln
        595                 600                 605

Gly Val Phe Ser Val Pro Glu Asn Gly His Val Tyr Val Glu Val Ser
    610                 615                 620
```

Val Thr Lys Ala Glu Gln Glu Leu Gly Phe Ala Ile Gln Thr Cys Phe
625 630 635 640

Ile Ser Pro Tyr Ser Asn Pro Asp Arg Met Ser His Tyr Thr Ile Ile
645 650 655

Glu Asn Ile Cys Pro Lys Asp Glu Ser Val Lys Phe Tyr Ser Pro Lys
660 665 670

Arg Val His Phe Pro Ile Pro Gln Ala Asp Met Asp Lys Lys Arg Phe
675 680 685

Ser Phe Val Phe Lys Pro Val Phe Asn Thr Ser Leu Leu Phe Leu Gln
690 695 700

Cys Glu Leu Thr Leu Cys Thr Lys Met Glu Lys His Pro Gln Lys Leu
705 710 715 720

Pro Lys Cys Val Pro Pro Asp Glu Ala Cys Thr Ser Leu Asp Ala Ser
725 730 735

Ile Ile Trp Ala Met Met Gln Asn Lys Lys Thr Phe Thr Lys Pro Leu
740 745 750

Ala Val Ile His His Glu Ala Glu Ser Lys Glu Lys Gly Pro Ser Met
755 760 765

Lys Glu Pro Asn Pro Ile Ser Pro Pro Ile Phe His Gly Leu Asp Thr
770 775 780

Leu Thr Val Met Gly Ile Ala Phe Ala Ala Phe Val Ile Gly Ala Leu
785 790 795 800

Leu Thr Gly Ala Leu Trp Tyr Ile Tyr Ser His Thr Gly Glu Thr Ala
805 810 815

Gly Arg Gln Gln Val Pro Thr Ser Pro Pro Ala Ser Glu Asn Ser Ser
820 825 830

Ala Ala His Ser Ile Gly Ser Thr Gln Ser Thr Pro Cys Ser Ser Ser
835 840 845

Ser Thr Ala
850

<210> 413
<211> 999
<212> PRT
<213> Homo sapiens

<400> 413

```
Met Gly Pro Ala Pro Leu Pro Leu Leu Leu Gly Leu Phe Leu Pro Ala
1               5                  10                  15

Leu Trp Arg Arg Ala Ile Thr Glu Ala Arg Glu Glu Ala Lys Pro Tyr
            20                  25                  30

Pro Leu Phe Pro Gly Pro Phe Pro Gly Ser Leu Gln Thr Asp His Thr
        35                  40                  45

Pro Leu Leu Ser Leu Pro His Ala Ser Gly Tyr Gln Pro Ala Leu Met
    50                  55                  60

Phe Ser Pro Thr Gln Pro Gly Arg Pro His Thr Gly Asn Val Ala Ile
65                  70                  75                  80

Pro Gln Val Thr Ser Val Glu Ser Lys Pro Leu Pro Pro Leu Ala Phe
                85                  90                  95

Lys His Thr Val Gly His Ile Ile Leu Ser Glu His Lys Gly Val Lys
            100                 105                 110

Phe Asn Cys Ser Ile Ser Val Pro Asn Ile Tyr Gln Asp Thr Thr Ile
        115                 120                 125

Ser Trp Trp Lys Asp Gly Lys Glu Leu Leu Gly Ala His His Ala Ile
    130                 135                 140

Thr Gln Phe Tyr Pro Asp Asp Glu Val Thr Ala Ile Ile Ala Ser Phe
145                 150                 155                 160

Ser Ile Thr Ser Val Gln Arg Ser Asp Asn Gly Ser Tyr Ile Cys Lys
                165                 170                 175

Met Lys Ile Asn Asn Glu Glu Ile Val Ser Asp Pro Ile Tyr Ile Glu
            180                 185                 190

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

Thr Arg Asn Thr Ala Phe Asn Leu Thr Cys Gln Ala Val Gly Pro Pro
    210                 215                 220

Glu Pro Val Asn Ile Phe Trp Val Gln Asn Ser Ser Arg Val Asn Glu
225                 230                 235                 240

Gln Pro Glu Lys Ser Pro Ser Val Leu Thr Val Pro Gly Leu Thr Glu
                245                 250                 255

Met Ala Val Phe Ser Cys Glu Ala His Asn Asp Lys Gly Leu Thr Val
            260                 265                 270
```

```
Ser Lys Gly Val Gln Ile Asn Ile Lys Ala Ile Pro Ser Pro Pro Thr
        275                 280                 285

Glu Val Ser Ile Arg Asn Ser Thr Ala His Ser Ile Leu Ile Ser Trp
    290                 295                 300

Val Pro Gly Phe Asp Gly Tyr Ser Pro Phe Arg Asn Cys Ser Ile Gln
305                 310                 315                 320

Val Lys Glu Ala Asp Pro Leu Ser Asn Gly Ser Val Met Ile Phe Asn
                325                 330                 335

Thr Ser Ala Leu Pro His Leu Tyr Gln Ile Lys Gln Leu Gln Ala Leu
            340                 345                 350

Ala Asn Tyr Ser Ile Gly Val Ser Cys Met Asn Glu Ile Gly Trp Ser
        355                 360                 365

Ala Val Ser Pro Trp Ile Leu Ala Ser Thr Thr Glu Gly Ala Pro Ser
    370                 375                 380

Val Ala Pro Leu Asn Val Thr Val Phe Leu Asn Glu Ser Ser Asp Asn
385                 390                 395                 400

Val Asp Ile Arg Trp Met Lys Pro Pro Thr Lys Gln Gln Asp Gly Glu
                405                 410                 415

Leu Val Gly Tyr Arg Ile Ser His Val Trp Gln Ser Ala Gly Ile Ser
            420                 425                 430

Lys Glu Leu Leu Glu Glu Val Gly Gln Asn Gly Ser Arg Ala Arg Ile
        435                 440                 445

Ser Val Gln Val His Asn Ala Thr Cys Thr Val Arg Ile Ala Ala Val
    450                 455                 460

Thr Arg Gly Gly Val Gly Pro Phe Ser Asp Pro Val Lys Ile Phe Ile
465                 470                 475                 480

Pro Ala His Gly Trp Val Asp Tyr Ala Pro Ser Ser Thr Pro Ala Pro
                485                 490                 495

Gly Asn Ala Asp Pro Val Leu Ile Ile Phe Gly Cys Phe Cys Gly Phe
            500                 505                 510

Ile Leu Ile Gly Leu Ile Leu Tyr Ile Ser Leu Ala Ile Arg Lys Arg
        515                 520                 525

Val Gln Glu Thr Lys Phe Gly Asn Ala Phe Thr Glu Glu Asp Ser Glu
    530                 535                 540
```

```
Leu Val Val Asn Tyr Ile Ala Lys Lys Ser Phe Cys Arg Arg Ala Ile
545                 550                 555                 560

Glu Leu Thr Leu His Ser Leu Gly Val Ser Glu Glu Leu Gln Asn Lys
                565                 570                 575

Leu Glu Asp Val Val Ile Asp Arg Asn Leu Leu Ile Leu Gly Lys Ile
            580                 585                 590

Leu Gly Glu Gly Glu Phe Gly Ser Val Met Glu Gly Asn Leu Lys Gln
        595                 600                 605

Glu Asp Gly Thr Ser Leu Lys Val Ala Val Lys Thr Met Lys Leu Asp
    610                 615                 620

Asn Ser Ser Gln Arg Glu Ile Glu Glu Phe Leu Ser Glu Ala Ala Cys
625                 630                 635                 640

Met Lys Asp Phe Ser His Pro Asn Val Ile Arg Leu Leu Gly Val Cys
                645                 650                 655

Ile Glu Met Ser Ser Gln Gly Ile Pro Lys Pro Met Val Ile Leu Pro
            660                 665                 670

Phe Met Lys Tyr Gly Asp Leu His Thr Tyr Leu Leu Tyr Ser Arg Leu
        675                 680                 685

Glu Thr Gly Pro Lys His Ile Pro Leu Gln Thr Leu Leu Lys Phe Met
    690                 695                 700

Val Asp Ile Ala Leu Gly Met Glu Tyr Leu Ser Asn Arg Asn Phe Leu
705                 710                 715                 720

His Arg Asp Leu Ala Ala Arg Asn Cys Met Leu Arg Asp Asp Met Thr
                725                 730                 735

Val Cys Val Ala Asp Phe Gly Leu Ser Lys Lys Ile Tyr Ser Gly Asp
            740                 745                 750

Tyr Tyr Arg Gln Gly Arg Ile Ala Lys Met Pro Val Lys Trp Ile Ala
        755                 760                 765

Ile Glu Ser Leu Ala Asp Arg Val Tyr Thr Ser Lys Ser Asp Val Trp
    770                 775                 780

Ala Phe Gly Val Thr Met Trp Glu Ile Ala Thr Arg Gly Met Thr Pro
785                 790                 795                 800

Tyr Pro Gly Val Gln Asn His Glu Met Tyr Asp Tyr Leu Leu His Gly
                805                 810                 815
```

```
His Arg Leu Lys Gln Pro Glu Asp Cys Leu Asp Glu Leu Tyr Glu Ile
            820                 825                 830

Met Tyr Ser Cys Trp Arg Thr Asp Pro Leu Asp Arg Pro Thr Phe Ser
        835                 840                 845

Val Leu Arg Leu Gln Leu Glu Lys Leu Leu Glu Ser Leu Pro Asp Val
    850                 855                 860

Arg Asn Gln Ala Asp Val Ile Tyr Val Asn Thr Gln Leu Leu Glu Ser
865                 870                 875                 880

Ser Glu Gly Leu Ala Gln Gly Ser Thr Leu Ala Pro Leu Asp Leu Asn
                885                 890                 895

Ile Asp Pro Asp Ser Ile Ile Ala Ser Cys Thr Pro Arg Ala Ala Ile
            900                 905                 910

Ser Val Val Thr Ala Glu Val His Asp Ser Lys Pro His Glu Gly Arg
        915                 920                 925

Tyr Ile Leu Asn Gly Gly Ser Glu Glu Trp Glu Asp Leu Thr Ser Ala
    930                 935                 940

Pro Ser Ala Ala Val Thr Ala Glu Lys Asn Ser Val Leu Pro Gly Glu
945                 950                 955                 960

Arg Leu Val Arg Asn Gly Val Ser Trp Ser His Ser Ser Met Leu Pro
                965                 970                 975

Leu Gly Ser Ser Leu Pro Asp Glu Leu Leu Phe Ala Asp Asp Ser Ser
            980                 985                 990

Glu Gly Ser Glu Val Leu Met
        995


<210>  414
<211>  1489
<212>  PRT
<213>  Homo sapiens

<400>  414

Met Arg Gln Val Leu Trp Leu Cys Asn Val Cys Val Thr Ala Arg Glu
1               5                   10                  15

Thr Arg His His Leu His Leu Pro Ala Ile Leu Asp Lys Met Pro Ala
            20                  25                  30

Pro Gly Ala Leu Ile Leu Leu Ala Ala Val Ser Ala Ser Gly Cys Leu
        35                  40                  45
```

```
Ala Ser Pro Ala His Pro Asp Gly Phe Ala Leu Gly Arg Ala Pro Leu
    50                  55                  60

Ala Pro Pro Tyr Ala Val Val Leu Ile Ser Cys Ser Gly Leu Leu Ala
65                  70                  75                  80

Phe Ile Phe Leu Leu Leu Thr Cys Leu Cys Cys Lys Arg Gly Asp Val
                85                  90                  95

Gly Phe Lys Glu Phe Glu Asn Pro Glu Gly Glu Asp Cys Ser Gly Glu
            100                 105                 110

Tyr Thr Pro Pro Ala Glu Glu Thr Ser Ser Ser Gln Ser Leu Pro Asp
        115                 120                 125

Val Tyr Ile Leu Pro Leu Ala Glu Val Ser Leu Pro Met Pro Ala Pro
    130                 135                 140

Gln Pro Ser His Ser Asp Met Thr Thr Pro Leu Gly Leu Ser Arg Gln
145                 150                 155                 160

His Leu Ser Tyr Leu Gln Glu Ile Gly Ser Gly Trp Phe Gly Lys Val
                165                 170                 175

Ile Leu Gly Glu Ile Phe Ser Asp Tyr Thr Pro Ala Gln Val Val Val
            180                 185                 190

Lys Glu Leu Arg Ala Ser Ala Gly Pro Leu Glu Gln Arg Lys Phe Ile
        195                 200                 205

Ser Glu Ala Gln Pro Tyr Arg Ser Leu Gln His Pro Asn Val Leu Gln
    210                 215                 220

Cys Leu Gly Leu Cys Val Glu Thr Leu Pro Phe Leu Leu Ile Met Glu
225                 230                 235                 240

Phe Cys Gln Leu Gly Asp Leu Lys Arg Tyr Leu Arg Ala Gln Arg Pro
                245                 250                 255

Pro Glu Gly Leu Ser Pro Glu Leu Pro Pro Arg Asp Leu Arg Thr Leu
            260                 265                 270

Gln Arg Met Gly Leu Glu Ile Ala Arg Gly Leu Ala His Leu His Ser
        275                 280                 285

His Asn Tyr Val His Ser Asp Leu Ala Leu Arg Asn Cys Leu Leu Thr
    290                 295                 300

Ser Asp Leu Thr Val Arg Ile Gly Asp Tyr Gly Leu Ala His Ser Asn
305                 310                 315                 320
```

```
Tyr Lys Glu Asp Tyr Tyr Leu Thr Pro Glu Arg Leu Trp Ile Pro Leu
                325                 330                 335

Arg Trp Ala Ala Pro Glu Leu Leu Gly Glu Leu His Gly Thr Phe Met
            340                 345                 350

Val Val Asp Gln Ser Arg Glu Ser Asn Ile Trp Ser Leu Gly Val Thr
        355                 360                 365

Leu Trp Glu Leu Phe Glu Phe Gly Ala Gln Pro Tyr Arg His Leu Ser
    370                 375                 380

Asp Glu Glu Val Leu Ala Phe Val Val Arg Gln Gln His Val Lys Leu
385                 390                 395                 400

Ala Arg Pro Arg Leu Lys Leu Pro Tyr Ala Asp Tyr Trp Tyr Asp Ile
                405                 410                 415

Leu Gln Ser Cys Trp Arg Pro Pro Ala Gln Arg Pro Ser Ala Ser Asp
            420                 425                 430

Leu Gln Leu Gln Leu Thr Tyr Leu Leu Ser Glu Arg Pro Pro Arg Pro
        435                 440                 445

Pro Pro Pro Pro Pro Pro Pro Arg Asp Gly Pro Phe Pro Trp Pro Trp
    450                 455                 460

Pro Pro Ala His Ser Ala Pro Arg Pro Gly Thr Leu Ser Ser Pro Phe
465                 470                 475                 480

Pro Leu Leu Asp Gly Phe Pro Gly Ala Asp Pro Asp Asp Val Leu Thr
                485                 490                 495

Val Thr Glu Ser Ser Arg Gly Leu Asn Leu Glu Cys Leu Trp Glu Lys
            500                 505                 510

Ala Arg Arg Gly Ala Gly Arg Gly Gly Gly Ala Pro Ala Trp Gln Pro
        515                 520                 525

Ala Ser Ala Pro Pro Ala Pro His Ala Asn Pro Ser Asn Pro Phe Tyr
    530                 535                 540

Glu Ala Leu Ser Thr Pro Ser Val Leu Pro Val Ile Ser Ala Arg Ser
545                 550                 555                 560

Pro Ser Val Ser Ser Glu Tyr Tyr Ile Arg Leu Glu Glu His Gly Ser
                565                 570                 575

Pro Pro Glu Pro Leu Phe Pro Asn Asp Trp Asp Pro Leu Asp Pro Gly
            580                 585                 590
```

```
Val Pro Ala Pro Gln Ala Pro Gln Ala Pro Ser Glu Val Pro Gln Leu
        595                 600                 605

Val Ser Glu Thr Trp Ala Ser Pro Leu Phe Pro Ala Pro Arg Pro Phe
    610                 615                 620

Pro Ala Gln Ser Ser Ala Ser Gly Ser Phe Leu Leu Ser Gly Trp Asp
625                 630                 635                 640

Pro Glu Gly Arg Gly Ala Gly Glu Thr Leu Ala Gly Asp Pro Ala Glu
                645                 650                 655

Val Leu Gly Glu Arg Gly Thr Ala Pro Trp Val Glu Glu Glu Glu Glu
            660                 665                 670

Glu Glu Glu Gly Ser Ser Pro Gly Glu Asp Ser Ser Ser Leu Gly Gly
        675                 680                 685

Gly Pro Ser Arg Arg Gly Pro Leu Pro Cys Pro Leu Cys Ser Arg Glu
    690                 695                 700

Gly Ala Cys Ser Cys Leu Pro Leu Glu Arg Gly Asp Ala Val Ala Gly
705                 710                 715                 720

Trp Gly Gly His Pro Ala Leu Gly Cys Pro His Pro Pro Glu Asp Asp
                725                 730                 735

Ser Ser Leu Arg Ala Glu Arg Gly Ser Leu Ala Asp Leu Pro Met Ala
            740                 745                 750

Pro Pro Ala Ser Ala Pro Pro Glu Phe Leu Asp Pro Leu Met Gly Ala
        755                 760                 765

Ala Ala Pro Gln Tyr Pro Gly Arg Gly Pro Pro Pro Ala Pro Pro Pro
    770                 775                 780

Pro Pro Pro Pro Pro Arg Ala Pro Ala Asp Pro Ala Ala Ser Pro Asp
785                 790                 795                 800

Pro Pro Ser Ala Val Ala Ser Pro Gly Ser Gly Leu Ser Ser Pro Gly
                805                 810                 815

Pro Lys Pro Gly Asp Ser Gly Tyr Glu Thr Glu Thr Pro Phe Ser Pro
            820                 825                 830

Glu Gly Ala Phe Pro Gly Gly Gly Ala Ala Glu Glu Glu Gly Val Pro
        835                 840                 845

Arg Pro Arg Ala Pro Pro Glu Pro Pro Asp Pro Gly Ala Pro Arg Pro
    850                 855                 860
```

```
Pro Pro Asp Pro Gly Pro Leu Pro Leu Pro Gly Pro Arg Glu Lys Pro
865                 870                 875                 880

Thr Phe Val Val Gln Val Ser Thr Glu Gln Leu Leu Met Ser Leu Arg
                885                 890                 895

Glu Asp Val Thr Arg Asn Leu Leu Gly Glu Lys Gly Ala Thr Ala Arg
            900                 905                 910

Glu Thr Gly Pro Arg Lys Ala Gly Arg Gly Pro Gly Asn Arg Glu Lys
        915                 920                 925

Val Pro Gly Leu Asn Arg Asp Pro Thr Val Leu Gly Asn Gly Lys Gln
    930                 935                 940

Ala Pro Ser Leu Ser Leu Pro Val Asn Gly Val Thr Val Leu Glu Asn
945                 950                 955                 960

Gly Asp Gln Arg Ala Pro Gly Ile Glu Glu Lys Ala Ala Glu Asn Gly
                965                 970                 975

Ala Leu Gly Ser Pro Glu Arg Glu Glu Lys Val Leu Glu Asn Gly Glu
            980                 985                 990

Leu Thr Pro Pro Arg Arg Glu Glu  Lys Ala Leu Glu Asn  Gly Glu Leu
        995                 1000                1005

Arg Ser  Pro Glu Ala Gly Glu  Lys Val Leu Val Asn  Gly Gly Leu
    1010                1015                1020

Thr Pro  Pro Lys Ser Glu Asp  Lys Val Ser Glu Asn  Gly Gly Leu
    1025                1030                1035

Arg Phe  Pro Arg Asn Thr Glu  Arg Pro Pro Glu Thr  Gly Pro Trp
    1040                1045                1050

Arg Ala  Pro Gly Pro Trp Glu  Lys Thr Pro Glu Ser  Trp Gly Pro
    1055                1060                1065

Ala Pro  Thr Ile Gly Glu Pro  Ala Pro Glu Thr Ser  Leu Glu Arg
    1070                1075                1080

Ala Pro  Ala Pro Ser Ala Val  Val Ser Ser Arg Asn  Gly Gly Glu
    1085                1090                1095

Thr Ala  Pro Gly Pro Leu Gly  Pro Ala Pro Lys Asn  Gly Thr Leu
    1100                1105                1110

Glu Pro  Gly Thr Glu Arg Arg  Ala Pro Glu Thr Gly  Gly Ala Pro
    1115                1120                1125
```

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Arg Ala  Pro Gly Ala Gly Arg  Leu Asp Leu Gly Ser  Gly Gly Arg
    1130                 1135                 1140

Ala Pro  Val Gly Thr Gly Thr  Ala Pro Gly Gly Gly  Pro Gly Ser
    1145                 1150                 1155

Gly Val  Asp Ala Lys Ala Gly  Trp Val Asp Asn Thr  Arg Pro Gln
    1160                 1165                 1170

Pro Pro  Pro Pro Pro Leu Pro  Pro Pro Pro Glu Ala  Gln Pro Arg
    1175                 1180                 1185

Arg Leu  Glu Pro Ala Pro Pro  Arg Ala Arg Pro Glu  Val Ala Pro
    1190                 1195                 1200

Glu Gly  Glu Pro Gly Ala Pro  Asp Ser Arg Ala Gly  Gly Asp Thr
    1205                 1210                 1215

Ala Leu  Ser Gly Asp Gly Asp  Pro Pro Lys Pro Glu  Arg Lys Gly
    1220                 1225                 1230

Pro Glu  Met Pro Arg Leu Phe  Leu Asp Leu Gly Pro  Pro Gln Gly
    1235                 1240                 1245

Asn Ser  Glu Gln Ile Lys Ala  Arg Leu Ser Arg Leu  Ser Leu Ala
    1250                 1255                 1260

Leu Pro  Pro Leu Thr Leu Thr  Pro Phe Pro Gly Pro  Gly Pro Arg
    1265                 1270                 1275

Arg Pro  Pro Trp Glu Gly Ala  Asp Ala Gly Ala Ala  Gly Gly Glu
    1280                 1285                 1290

Ala Gly  Gly Ala Gly Ala Pro  Gly Pro Ala Glu Glu  Asp Gly Glu
    1295                 1300                 1305

Asp Glu  Asp Glu Asp Glu Glu  Glu Asp Glu Glu Ala  Ala Ala Pro
    1310                 1315                 1320

Gly Ala  Ala Ala Gly Pro Arg  Gly Pro Gly Arg Ala  Arg Ala Ala
    1325                 1330                 1335

Pro Val  Pro Val Val Val Ser  Ser Ala Asp Ala Asp  Ala Ala Arg
    1340                 1345                 1350

Pro Leu  Arg Gly Leu Leu Lys  Ser Pro Arg Gly Ala  Asp Glu Pro
    1355                 1360                 1365

Glu Asp  Ser Glu Leu Glu Arg  Lys Arg Lys Met Val  Ser Phe His
    1370                 1375                 1380
```

Gly Asp Val Thr Val Tyr Leu Phe Asp Gln Glu Thr Pro Thr Asn
1385 1390 1395

Glu Leu Ser Val Gln Ala Pro Pro Glu Gly Asp Thr Asp Pro Ser
1400 1405 1410

Thr Pro Pro Ala Pro Pro Thr Pro Pro His Pro Ala Thr Pro Gly
1415 1420 1425

Asp Gly Phe Pro Ser Asn Asp Ser Gly Phe Gly Gly Ser Phe Glu
1430 1435 1440

Trp Ala Glu Asp Phe Pro Leu Leu Pro Pro Pro Gly Pro Pro Leu
1445 1450 1455

Cys Phe Ser Arg Phe Ser Val Ser Pro Ala Leu Glu Thr Pro Gly
1460 1465 1470

Pro Pro Ala Arg Ala Pro Asp Ala Arg Pro Ala Gly Pro Val Glu
1475 1480 1485

Asn

<210> 415
<211> 972
<212> PRT
<213> Homo sapiens

<400> 415

Met Gly Pro Gly Val Leu Leu Leu Leu Leu Val Ala Thr Ala Trp His
1 5 10 15

Gly Gln Gly Ile Pro Val Ile Glu Pro Ser Val Pro Glu Leu Val Val
20 25 30

Lys Pro Gly Ala Thr Val Thr Leu Arg Cys Val Gly Asn Gly Ser Val
35 40 45

Glu Trp Asp Gly Pro Pro Ser Pro His Trp Thr Leu Tyr Ser Asp Gly
50 55 60

Ser Ser Ser Ile Leu Ser Thr Asn Asn Ala Thr Phe Gln Asn Thr Gly
65 70 75 80

Thr Tyr Arg Cys Thr Glu Pro Gly Asp Pro Leu Gly Gly Ser Ala Ala
85 90 95

Ile His Leu Tyr Val Lys Asp Pro Ala Arg Pro Trp Asn Val Leu Ala
100 105 110

Gln Glu Val Val Val Phe Glu Asp Gln Asp Ala Leu Leu Pro Cys Leu

115 120 125

Leu Thr Asp Pro Val Leu Glu Ala Gly Val Ser Leu Val Arg Val Arg
130 135 140

Gly Arg Pro Leu Met Arg His Thr Asn Tyr Ser Phe Ser Pro Trp His
145 150 155 160

Gly Phe Thr Ile His Arg Ala Lys Phe Ile Gln Ser Gln Asp Tyr Gln
165 170 175

Cys Ser Ala Leu Met Gly Gly Arg Lys Val Met Ser Ile Ser Ile Arg
180 185 190

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

Pro Ala Glu Leu Val Arg Ile Arg Gly Glu Ala Ala Gln Ile Val Cys
210 215 220

Ser Ala Ser Ser Val Asp Val Asn Phe Asp Val Phe Leu Gln His Asn
225 230 235 240

Asn Thr Lys Leu Ala Ile Pro Gln Gln Ser Asp Phe His Asn Asn Arg
245 250 255

Tyr Gln Lys Val Leu Thr Leu Asn Leu Asp Gln Val Asp Phe Gln His
260 265 270

Ala Gly Asn Tyr Ser Cys Val Ala Ser Asn Val Gln Gly Lys His Ser
275 280 285

Thr Ser Met Phe Phe Arg Val Val Glu Ser Ala Tyr Leu Asn Leu Ser
290 295 300

Ser Glu Gln Asn Leu Ile Gln Glu Val Thr Val Gly Glu Gly Leu Asn
305 310 315 320

Leu Lys Val Met Val Glu Ala Tyr Pro Gly Leu Gln Gly Phe Asn Trp
325 330 335

Thr Tyr Leu Gly Pro Phe Ser Asp His Gln Pro Glu Pro Lys Leu Ala
340 345 350

Asn Ala Thr Thr Lys Asp Thr Tyr Arg His Thr Phe Thr Leu Ser Leu
355 360 365

Pro Arg Leu Lys Pro Ser Glu Ala Gly Arg Tyr Ser Phe Leu Ala Arg
370 375 380

Asn Pro Gly Gly Trp Arg Ala Leu Thr Phe Glu Leu Thr Leu Arg Tyr

385 390 395 400

Pro Pro Glu Val Ser Val Ile Trp Thr Phe Ile Asn Gly Ser Gly Thr
405 410 415

Leu Leu Cys Ala Ala Ser Gly Tyr Pro Gln Pro Asn Val Thr Trp Leu
420 425 430

Gln Cys Ser Gly His Thr Asp Arg Cys Asp Glu Ala Gln Val Leu Gln
435 440 445

Val Trp Asp Asp Pro Tyr Pro Glu Val Leu Ser Gln Glu Pro Phe His
450 455 460

Lys Val Thr Val Gln Ser Leu Leu Thr Val Glu Thr Leu Glu His Asn
465 470 475 480

Gln Thr Tyr Glu Cys Arg Ala His Asn Ser Val Gly Ser Gly Ser Trp
485 490 495

Ala Phe Ile Pro Ile Ser Ala Gly Ala His Thr His Pro Pro Asp Glu
500 505 510

Phe Leu Phe Thr Pro Val Val Val Ala Cys Met Ser Ile Met Ala Leu
515 520 525

Leu Leu Leu Leu Leu Leu Leu Leu Leu Tyr Lys Tyr Lys Gln Lys Pro
530 535 540

Lys Tyr Gln Val Arg Trp Lys Ile Ile Glu Ser Tyr Glu Gly Asn Ser
545 550 555 560

Tyr Thr Phe Ile Asp Pro Thr Gln Leu Pro Tyr Asn Glu Lys Trp Glu
565 570 575

Phe Pro Arg Asn Asn Leu Gln Phe Gly Lys Thr Leu Gly Ala Gly Ala
580 585 590

Phe Gly Lys Val Val Glu Ala Thr Ala Phe Gly Leu Gly Lys Glu Asp
595 600 605

Ala Val Leu Lys Val Ala Val Lys Met Leu Lys Ser Thr Ala His Ala
610 615 620

Asp Glu Lys Glu Ala Leu Met Ser Glu Leu Lys Ile Met Ser His Leu
625 630 635 640

Gly Gln His Glu Asn Ile Val Asn Leu Leu Gly Ala Cys Thr His Gly
645 650 655

Gly Pro Val Leu Val Ile Thr Glu Tyr Cys Cys Tyr Gly Asp Leu Leu

660 665 670

Asn Phe Leu Arg Arg Lys Ala Glu Ala Met Leu Gly Pro Ser Leu Ser
675 680 685

Pro Gly Gln Asp Pro Glu Gly Gly Val Asp Tyr Lys Asn Ile His Leu
690 695 700

Glu Lys Lys Tyr Val Arg Arg Asp Ser Gly Phe Ser Ser Gln Gly Val
705 710 715 720

Asp Thr Tyr Val Glu Met Arg Pro Val Ser Thr Ser Ser Asn Asp Ser
725 730 735

Phe Ser Glu Gln Asp Leu Asp Lys Glu Asp Gly Arg Pro Leu Glu Leu
740 745 750

Arg Asp Leu Leu His Phe Ser Ser Gln Val Ala Gln Gly Met Ala Phe
755 760 765

Leu Ala Ser Lys Asn Cys Ile His Arg Asp Val Ala Ala Arg Asn Val
770 775 780

Leu Leu Thr Asn Gly His Val Ala Lys Ile Gly Asp Phe Gly Leu Ala
785 790 795 800

Arg Asp Ile Met Asn Asp Ser Asn Tyr Ile Val Lys Gly Asn Ala Arg
805 810 815

Leu Pro Val Lys Trp Met Ala Pro Glu Ser Ile Phe Asp Cys Val Tyr
820 825 830

Thr Val Gln Ser Asp Val Trp Ser Tyr Gly Ile Leu Leu Trp Glu Ile
835 840 845

Phe Ser Leu Gly Leu Asn Pro Tyr Pro Gly Ile Leu Val Asn Ser Lys
850 855 860

Phe Tyr Lys Leu Val Lys Asp Gly Tyr Gln Met Ala Gln Pro Ala Phe
865 870 875 880

Ala Pro Lys Asn Ile Tyr Ser Ile Met Gln Ala Cys Trp Ala Leu Glu
885 890 895

Pro Thr His Arg Pro Thr Phe Gln Gln Ile Cys Ser Phe Leu Gln Glu
900 905 910

Gln Ala Gln Glu Asp Arg Arg Glu Arg Asp Tyr Thr Asn Leu Pro Ser
915 920 925

Ser Ser Arg Ser Gly Gly Ser Gly Ser Ser Ser Ser Glu Leu Glu Glu

930 935 940

Glu Ser Ser Ser Glu His Leu Thr Cys Cys Glu Gln Gly Asp Ile Ala
945 950 955 960

Gln Pro Leu Leu Gln Pro Asn Asn Tyr Gln Phe Cys
965 970

<210> 416
<211> 1210
<212> PRT
<213> Homo sapiens

<400> 416

Met Arg Pro Ser Gly Thr Ala Gly Ala Ala Leu Leu Ala Leu Leu Ala
1 5 10 15

Ala Leu Cys Pro Ala Ser Arg Ala Leu Glu Glu Lys Lys Val Cys Gln
20 25 30

Gly Thr Ser Asn Lys Leu Thr Gln Leu Gly Thr Phe Glu Asp His Phe
35 40 45

Leu Ser Leu Gln Arg Met Phe Asn Asn Cys Glu Val Val Leu Gly Asn
50 55 60

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

Thr Ile Gln Glu Val Ala Gly Tyr Val Leu Ile Ala Leu Asn Thr Val
85 90 95

Glu Arg Ile Pro Leu Glu Asn Leu Gln Ile Ile Arg Gly Asn Met Tyr
100 105 110

Tyr Glu Asn Ser Tyr Ala Leu Ala Val Leu Ser Asn Tyr Asp Ala Asn
115 120 125

Lys Thr Gly Leu Lys Glu Leu Pro Met Arg Asn Leu Gln Glu Ile Leu
130 135 140

His Gly Ala Val Arg Phe Ser Asn Asn Pro Ala Leu Cys Asn Val Glu
145 150 155 160

Ser Ile Gln Trp Arg Asp Ile Val Ser Ser Asp Phe Leu Ser Asn Met
165 170 175

Ser Met Asp Phe Gln Asn His Leu Gly Ser Cys Gln Lys Cys Asp Pro
180 185 190

Ser Cys Pro Asn Gly Ser Cys Trp Gly Ala Gly Glu Glu Asn Cys Gln
195 200 205

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Lys Leu Thr Lys Ile Ile Cys Ala Gln Gln Cys Ser Gly Arg Cys Arg
    210                 215                 220

Gly Lys Ser Pro Ser Asp Cys Cys His Asn Gln Cys Ala Ala Gly Cys
225                 230                 235                 240

Thr Gly Pro Arg Glu Ser Asp Cys Leu Val Cys Arg Lys Phe Arg Asp
                245                 250                 255

Glu Ala Thr Cys Lys Asp Thr Cys Pro Pro Leu Met Leu Tyr Asn Pro
            260                 265                 270

Thr Thr Tyr Gln Met Asp Val Asn Pro Glu Gly Lys Tyr Ser Phe Gly
        275                 280                 285

Ala Thr Cys Val Lys Lys Cys Pro Arg Asn Tyr Val Val Thr Asp His
    290                 295                 300

Gly Ser Cys Val Arg Ala Cys Gly Ala Asp Ser Tyr Glu Met Glu Glu
305                 310                 315                 320

Asp Gly Val Arg Lys Cys Lys Lys Cys Glu Gly Pro Cys Arg Lys Val
                325                 330                 335

Cys Asn Gly Ile Gly Ile Gly Glu Phe Lys Asp Ser Leu Ser Ile Asn
            340                 345                 350

Ala Thr Asn Ile Lys His Phe Lys Asn Cys Thr Ser Ile Ser Gly Asp
        355                 360                 365

Leu His Ile Leu Pro Val Ala Phe Arg Gly Asp Ser Phe Thr His Thr
    370                 375                 380

Pro Pro Leu Asp Pro Gln Glu Leu Asp Ile Leu Lys Thr Val Lys Glu
385                 390                 395                 400

Ile Thr Gly Phe Leu Leu Ile Gln Ala Trp Pro Glu Asn Arg Thr Asp
                405                 410                 415

Leu His Ala Phe Glu Asn Leu Glu Ile Ile Arg Gly Arg Thr Lys Gln
            420                 425                 430

His Gly Gln Phe Ser Leu Ala Val Val Ser Leu Asn Ile Thr Ser Leu
        435                 440                 445

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

Gly Asn Lys Asn Leu Cys Tyr Ala Asn Thr Ile Asn Trp Lys Lys Leu
465                 470                 475                 480
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```
Phe Gly Thr Ser Gly Gln Lys Thr Lys Ile Ile Ser Asn Arg Gly Glu
                485                 490                 495

Asn Ser Cys Lys Ala Thr Gly Gln Val Cys His Ala Leu Cys Ser Pro
            500                 505                 510

Glu Gly Cys Trp Gly Pro Glu Pro Arg Asp Cys Val Ser Cys Arg Asn
        515                 520                 525

Val Ser Arg Gly Arg Glu Cys Val Asp Lys Cys Asn Leu Leu Glu Gly
    530                 535                 540

Glu Pro Arg Glu Phe Val Glu Asn Ser Glu Cys Ile Gln Cys His Pro
545                 550                 555                 560

Glu Cys Leu Pro Gln Ala Met Asn Ile Thr Cys Thr Gly Arg Gly Pro
                565                 570                 575

Asp Asn Cys Ile Gln Cys Ala His Tyr Ile Asp Gly Pro His Cys Val
            580                 585                 590

Lys Thr Cys Pro Ala Gly Val Met Gly Glu Asn Asn Thr Leu Val Trp
        595                 600                 605

Lys Tyr Ala Asp Ala Gly His Val Cys His Leu Cys His Pro Asn Cys
    610                 615                 620

Thr Tyr Gly Cys Thr Gly Pro Gly Leu Glu Gly Cys Pro Thr Asn Gly
625                 630                 635                 640

Pro Lys Ile Pro Ser Ile Ala Thr Gly Met Val Gly Ala Leu Leu Leu
                645                 650                 655

Leu Leu Val Val Ala Leu Gly Ile Gly Leu Phe Met Arg Arg Arg His
            660                 665                 670

Ile Val Arg Lys Arg Thr Leu Arg Arg Leu Leu Gln Glu Arg Glu Leu
        675                 680                 685

Val Glu Pro Leu Thr Pro Ser Gly Glu Ala Pro Asn Gln Ala Leu Leu
    690                 695                 700

Arg Ile Leu Lys Glu Thr Glu Phe Lys Lys Ile Lys Val Leu Gly Ser
705                 710                 715                 720

Gly Ala Phe Gly Thr Val Tyr Lys Gly Leu Trp Ile Pro Glu Gly Glu
                725                 730                 735

Lys Val Lys Ile Pro Val Ala Ile Lys Glu Leu Arg Glu Ala Thr Ser
            740                 745                 750
```

```
Pro Lys Ala Asn Lys Glu Ile Leu Asp Glu Ala Tyr Val Met Ala Ser
        755                 760                 765

Val Asp Asn Pro His Val Cys Arg Leu Leu Gly Ile Cys Leu Thr Ser
    770                 775                 780

Thr Val Gln Leu Ile Thr Gln Leu Met Pro Phe Gly Cys Leu Leu Asp
785                 790                 795                 800

Tyr Val Arg Glu His Lys Asp Asn Ile Gly Ser Gln Tyr Leu Leu Asn
                805                 810                 815

Trp Cys Val Gln Ile Ala Lys Gly Met Asn Tyr Leu Glu Asp Arg Arg
            820                 825                 830

Leu Val His Arg Asp Leu Ala Ala Arg Asn Val Leu Val Lys Thr Pro
        835                 840                 845

Gln His Val Lys Ile Thr Asp Phe Gly Leu Ala Lys Leu Leu Gly Ala
    850                 855                 860

Glu Glu Lys Glu Tyr His Ala Glu Gly Gly Lys Val Pro Ile Lys Trp
865                 870                 875                 880

Met Ala Leu Glu Ser Ile Leu His Arg Ile Tyr Thr His Gln Ser Asp
                885                 890                 895

Val Trp Ser Tyr Gly Val Thr Val Trp Glu Leu Met Thr Phe Gly Ser
            900                 905                 910

Lys Pro Tyr Asp Gly Ile Pro Ala Ser Glu Ile Ser Ser Ile Leu Glu
        915                 920                 925

Lys Gly Glu Arg Leu Pro Gln Pro Pro Ile Cys Thr Ile Asp Val Tyr
    930                 935                 940

Met Ile Met Val Lys Cys Trp Met Ile Asp Ala Asp Ser Arg Pro Lys
945                 950                 955                 960

Phe Arg Glu Leu Ile Ile Glu Phe Ser Lys Met Ala Arg Asp Pro Gln
                965                 970                 975

Arg Tyr Leu Val Ile Gln Gly Asp Glu Arg Met His Leu Pro Ser Pro
            980                 985                 990

Thr Asp Ser Asn Phe Tyr Arg Ala  Leu Met Asp Glu Glu  Asp Met Asp
        995                 1000                1005

Asp Val  Val Asp Ala Asp Glu  Tyr Leu Ile Pro Gln  Gln Gly Phe
    1010                1015                1020
```

```
Phe Ser  Ser Pro Ser Thr Ser  Arg Thr Pro Leu Leu  Ser Ser Leu
    1025                 1030                 1035

Ser Ala  Thr Ser Asn Asn Ser  Thr Val Ala Cys Ile  Asp Arg Asn
    1040                 1045                 1050

Gly Leu  Gln Ser Cys Pro Ile  Lys Glu Asp Ser Phe  Leu Gln Arg
    1055                 1060                 1065

Tyr Ser  Ser Asp Pro Thr Gly  Ala Leu Thr Glu Asp  Ser Ile Asp
    1070                 1075                 1080

Asp Thr  Phe Leu Pro Val Pro  Glu Tyr Ile Asn Gln  Ser Val Pro
    1085                 1090                 1095

Lys Arg  Pro Ala Gly Ser Val  Gln Asn Pro Val Tyr  His Asn Gln
    1100                 1105                 1110

Pro Leu  Asn Pro Ala Pro Ser  Arg Asp Pro His Tyr  Gln Asp Pro
    1115                 1120                 1125

His Ser  Thr Ala Val Gly Asn  Pro Glu Tyr Leu Asn  Thr Val Gln
    1130                 1135                 1140

Pro Thr  Cys Val Asn Ser Thr  Phe Asp Ser Pro Ala  His Trp Ala
    1145                 1150                 1155

Gln Lys  Gly Ser His Gln Ile  Ser Leu Asp Asn Pro  Asp Tyr Gln
    1160                 1165                 1170

Gln Asp  Phe Phe Pro Lys Glu  Ala Lys Pro Asn Gly  Ile Phe Lys
    1175                 1180                 1185

Gly Ser  Thr Ala Glu Asn Ala  Glu Tyr Leu Arg Val  Ala Pro Gln
    1190                 1195                 1200

Ser Ser  Glu Phe Ile Gly Ala
    1205                 1210


<210>  417
<211>  976
<212>  PRT
<213>  Homo sapiens

<400>  417

Met Glu Leu Gln Ala Ala Arg Ala Cys Phe Ala Leu Leu Trp Gly Cys
1               5                  10                  15

Ala Leu Ala Ala Ala Ala Ala Ala Gln Gly Lys Glu Val Val Leu Leu
            20                  25                  30
```

```
Asp Phe Ala Ala Ala Gly Gly Glu Leu Gly Trp Leu Thr His Pro Tyr
        35                  40                  45

Gly Lys Gly Trp Asp Leu Met Gln Asn Ile Met Asn Asp Met Pro Ile
    50                  55                  60

Tyr Met Tyr Ser Val Cys Asn Val Met Ser Gly Asp Gln Asp Asn Trp
65                  70                  75                  80

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

Glu Leu Lys Phe Thr Val Arg Asp Cys Asn Ser Phe Pro Gly Gly Ala
            100                 105                 110

Ser Ser Cys Lys Glu Thr Phe Asn Leu Tyr Tyr Ala Glu Ser Asp Leu
        115                 120                 125

Asp Tyr Gly Thr Asn Phe Gln Lys Arg Leu Phe Thr Lys Ile Asp Thr
    130                 135                 140

Ile Ala Pro Asp Glu Ile Thr Val Ser Ser Asp Phe Glu Ala Arg His
145                 150                 155                 160

Val Lys Leu Asn Val Glu Glu Arg Ser Val Gly Pro Leu Thr Arg Lys
                165                 170                 175

Gly Phe Tyr Leu Ala Phe Gln Asp Ile Gly Ala Cys Val Ala Leu Leu
            180                 185                 190

Ser Val Arg Val Tyr Tyr Lys Lys Cys Pro Glu Leu Leu Gln Gly Leu
        195                 200                 205

Ala His Phe Pro Glu Thr Ile Ala Gly Ser Asp Ala Pro Ser Leu Ala
    210                 215                 220

Thr Val Ala Gly Thr Cys Val Asp His Ala Val Val Pro Pro Gly Gly
225                 230                 235                 240

Glu Glu Pro Arg Met His Cys Ala Val Asp Gly Glu Trp Leu Val Pro
                245                 250                 255

Ile Gly Gln Cys Leu Cys Gln Ala Gly Tyr Glu Lys Val Glu Asp Ala
            260                 265                 270

Cys Gln Ala Cys Ser Pro Gly Phe Phe Lys Phe Glu Ala Ser Glu Ser
        275                 280                 285

Pro Cys Leu Glu Cys Pro Glu His Thr Leu Pro Ser Pro Glu Gly Ala
    290                 295                 300
```

```
Thr Ser Cys Glu Cys Glu Glu Gly Phe Phe Arg Ala Pro Gln Asp Pro
305                 310                 315                 320

Ala Ser Met Pro Cys Thr Arg Pro Pro Ser Ala Pro His Tyr Leu Thr
                325                 330                 335

Ala Val Gly Met Gly Ala Lys Val Glu Leu Arg Trp Thr Pro Pro Gln
            340                 345                 350

Asp Ser Gly Gly Arg Glu Asp Ile Val Tyr Ser Val Thr Cys Glu Gln
        355                 360                 365

Cys Trp Pro Glu Ser Gly Glu Cys Gly Pro Cys Glu Ala Ser Val Arg
    370                 375                 380

Tyr Ser Glu Pro Pro His Gly Leu Thr Arg Thr Ser Val Thr Val Ser
385                 390                 395                 400

Asp Leu Glu Pro His Met Asn Tyr Thr Phe Thr Val Glu Ala Arg Asn
                405                 410                 415

Gly Val Ser Gly Leu Val Thr Ser Arg Ser Phe Arg Thr Ala Ser Val
            420                 425                 430

Ser Ile Asn Gln Thr Glu Pro Pro Lys Val Arg Leu Glu Gly Arg Ser
        435                 440                 445

Thr Thr Ser Leu Ser Val Ser Trp Ser Ile Pro Pro Pro Gln Gln Ser
    450                 455                 460

Arg Val Trp Lys Tyr Glu Val Thr Tyr Arg Lys Lys Gly Asp Ser Asn
465                 470                 475                 480

Ser Tyr Asn Val Arg Arg Thr Glu Gly Phe Ser Val Thr Leu Asp Asp
                485                 490                 495

Leu Ala Pro Asp Thr Thr Tyr Leu Val Gln Val Gln Ala Leu Thr Gln
            500                 505                 510

Glu Gly Gln Gly Ala Gly Ser Lys Val His Glu Phe Gln Thr Leu Ser
        515                 520                 525

Pro Glu Gly Ser Gly Asn Leu Ala Val Ile Gly Gly Val Ala Val Gly
    530                 535                 540

Val Val Leu Leu Leu Val Leu Ala Gly Val Gly Phe Phe Ile His Arg
545                 550                 555                 560

Arg Arg Lys Asn Gln Arg Ala Arg Gln Ser Pro Glu Asp Val Tyr Phe
                565                 570                 575
```

```
Ser Lys Ser Glu Gln Leu Lys Pro Leu Lys Thr Tyr Val Asp Pro His
            580                 585                 590

Thr Tyr Glu Asp Pro Asn Gln Ala Val Leu Lys Phe Thr Thr Glu Ile
        595                 600                 605

His Pro Ser Cys Val Thr Arg Gln Lys Val Ile Gly Ala Gly Glu Phe
    610                 615                 620

Gly Glu Val Tyr Lys Gly Met Leu Lys Thr Ser Ser Gly Lys Lys Glu
625                 630                 635                 640

Val Pro Val Ala Ile Lys Thr Leu Lys Ala Gly Tyr Thr Glu Lys Gln
                645                 650                 655

Arg Val Asp Phe Leu Gly Glu Ala Gly Ile Met Gly Gln Phe Ser His
            660                 665                 670

His Asn Ile Ile Arg Leu Glu Gly Val Ile Ser Lys Tyr Lys Pro Met
        675                 680                 685

Met Ile Ile Thr Glu Tyr Met Glu Asn Gly Ala Leu Asp Lys Phe Leu
    690                 695                 700

Arg Glu Lys Asp Gly Glu Phe Ser Val Leu Gln Leu Val Gly Met Leu
705                 710                 715                 720

Arg Gly Ile Ala Ala Gly Met Lys Tyr Leu Ala Asn Met Asn Tyr Val
                725                 730                 735

His Arg Asp Leu Ala Ala Arg Asn Ile Leu Val Asn Ser Asn Leu Val
            740                 745                 750

Cys Lys Val Ser Asp Phe Gly Leu Ser Arg Val Leu Glu Asp Asp Pro
        755                 760                 765

Glu Ala Thr Tyr Thr Thr Ser Gly Gly Lys Ile Pro Ile Arg Trp Thr
    770                 775                 780

Ala Pro Glu Ala Ile Ser Tyr Arg Lys Phe Thr Ser Ala Ser Asp Val
785                 790                 795                 800

Trp Ser Phe Gly Ile Val Met Trp Glu Val Met Thr Tyr Gly Glu Arg
                805                 810                 815

Pro Tyr Trp Glu Leu Ser Asn His Glu Val Met Lys Ala Ile Asn Asp
            820                 825                 830

Gly Phe Arg Leu Pro Thr Pro Met Asp Cys Pro Ser Ala Ile Tyr Gln
        835                 840                 845
```

Leu Met Met Gln Cys Trp Gln Gln Glu Arg Ala Arg Arg Pro Lys Phe
850 855 860

Ala Asp Ile Val Ser Ile Leu Asp Lys Leu Ile Arg Ala Pro Asp Ser
865 870 875 880

Leu Lys Thr Leu Ala Asp Phe Asp Pro Arg Val Ser Ile Arg Leu Pro
885 890 895

Ser Thr Ser Gly Ser Glu Gly Val Pro Phe Arg Thr Val Ser Glu Trp
900 905 910

Leu Glu Ser Ile Lys Met Gln Gln Tyr Thr Glu His Phe Met Ala Ala
915 920 925

Gly Tyr Thr Ala Ile Glu Lys Val Val Gln Met Thr Asn Asp Asp Ile
930 935 940

Lys Arg Ile Gly Val Arg Leu Pro Gly His Gln Lys Arg Ile Ala Tyr
945 950 955 960

Ser Leu Leu Gly Leu Lys Asp Gln Val Asn Thr Val Gly Ile Pro Ile
965 970 975

<210> 418
<211> 976
<212> PRT
<213> Homo sapiens

<400> 418

Met Glu Arg Arg Trp Pro Leu Gly Leu Gly Leu Val Leu Leu Leu Cys
1 5 10 15

Ala Pro Leu Pro Pro Gly Ala Arg Ala Lys Glu Val Thr Leu Met Asp
20 25 30

Thr Ser Lys Ala Gln Gly Glu Leu Gly Trp Leu Leu Asp Pro Pro Lys
35 40 45

Asp Gly Trp Ser Glu Gln Gln Gln Ile Leu Asn Gly Thr Pro Leu Tyr
50 55 60

Met Tyr Gln Asp Cys Pro Met Gln Gly Arg Arg Asp Thr Asp His Trp
65 70 75 80

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

Val Glu Leu Gln Phe Thr Val Arg Asp Cys Lys Ser Phe Pro Gly Gly
100 105 110

```
Ala Gly Pro Leu Gly Cys Lys Glu Thr Phe Asn Leu Leu Tyr Met Glu
        115                 120                 125

Ser Asp Gln Asp Val Gly Ile Gln Leu Arg Arg Pro Leu Phe Gln Lys
    130                 135                 140

Val Thr Thr Val Ala Ala Asp Gln Ser Phe Thr Ile Arg Asp Leu Val
145                 150                 155                 160

Ser Gly Ser Val Lys Leu Asn Val Glu Arg Cys Ser Leu Gly Arg Leu
                165                 170                 175

Thr Arg Arg Gly Leu Tyr Leu Ala Phe His Asn Pro Gly Ala Cys Val
            180                 185                 190

Ala Leu Val Ser Val Arg Val Phe Tyr Gln Arg Cys Pro Glu Thr Leu
        195                 200                 205

Asn Gly Leu Ala Gln Phe Pro Asp Thr Leu Pro Gly Pro Ala Gly Leu
    210                 215                 220

Val Glu Val Ala Gly Thr Cys Leu Pro His Ala Arg Ala Ser Pro Arg
225                 230                 235                 240

Pro Ser Gly Ala Pro Arg Met His Cys Ser Pro Asp Gly Glu Trp Leu
                245                 250                 255

Val Pro Val Gly Arg Cys His Cys Glu Pro Gly Tyr Glu Glu Gly Gly
            260                 265                 270

Ser Gly Glu Ala Cys Val Ala Cys Pro Ser Gly Ser Tyr Arg Met Asp
        275                 280                 285

Met Asp Thr Pro His Cys Leu Thr Cys Pro Gln Gln Ser Thr Ala Glu
    290                 295                 300

Ser Glu Gly Ala Thr Ile Cys Thr Cys Glu Ser Gly His Tyr Arg Ala
305                 310                 315                 320

Pro Gly Glu Gly Pro Gln Val Ala Cys Thr Gly Pro Pro Ser Ala Pro
                325                 330                 335

Arg Asn Leu Ser Phe Ser Ala Ser Gly Thr Gln Leu Ser Leu Arg Trp
            340                 345                 350

Glu Pro Pro Ala Asp Thr Gly Gly Arg Gln Asp Val Arg Tyr Ser Val
        355                 360                 365

Arg Cys Ser Gln Cys Gln Gly Thr Ala Gln Asp Gly Gly Pro Cys Gln
    370                 375                 380
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Pro Cys Gly Val Gly Val His Phe Ser Pro Gly Ala Arg Gly Leu Thr
385                 390                 395                 400

Thr Pro Ala Val His Val Asn Gly Leu Glu Pro Tyr Ala Asn Tyr Thr
                405                 410                 415

Phe Asn Val Glu Ala Gln Asn Gly Val Ser Gly Leu Gly Ser Ser Gly
            420                 425                 430

His Ala Ser Thr Ser Val Ser Ile Ser Met Gly His Ala Glu Ser Leu
        435                 440                 445

Ser Gly Leu Ser Leu Arg Leu Val Lys Lys Glu Pro Arg Gln Leu Glu
    450                 455                 460

Leu Thr Trp Ala Gly Ser Arg Pro Arg Ser Pro Gly Ala Asn Leu Thr
465                 470                 475                 480

Tyr Glu Leu His Val Leu Asn Gln Asp Glu Glu Arg Tyr Gln Met Val
                485                 490                 495

Leu Glu Pro Arg Val Leu Leu Thr Glu Leu Gln Pro Asp Thr Thr Tyr
            500                 505                 510

Ile Val Arg Val Arg Met Leu Thr Pro Leu Gly Pro Gly Pro Phe Ser
        515                 520                 525

Pro Asp His Glu Phe Arg Thr Ser Pro Pro Val Ser Arg Gly Leu Thr
    530                 535                 540

Gly Gly Glu Ile Val Ala Val Ile Phe Gly Leu Leu Leu Gly Ala Ala
545                 550                 555                 560

Leu Leu Leu Gly Ile Leu Val Phe Arg Ser Arg Arg Ala Gln Arg Gln
                565                 570                 575

Arg Gln Gln Arg Gln Arg Asp Arg Ala Thr Asp Val Asp Arg Glu Asp
            580                 585                 590

Lys Leu Trp Leu Lys Pro Tyr Val Asp Leu Gln Ala Tyr Glu Asp Pro
        595                 600                 605

Ala Gln Gly Ala Leu Asp Phe Thr Arg Glu Leu Asp Pro Ala Trp Leu
    610                 615                 620

Met Val Asp Thr Val Ile Gly Glu Gly Glu Phe Gly Glu Val Tyr Arg
625                 630                 635                 640

Gly Thr Leu Arg Leu Pro Ser Gln Asp Cys Lys Thr Val Ala Ile Lys
                645                 650                 655
```

```
Thr Leu Lys Asp Thr Ser Pro Gly Gly Gln Trp Trp Asn Phe Leu Arg
            660                 665                 670

Glu Ala Thr Ile Met Gly Gln Phe Ser His Pro His Ile Leu His Leu
        675                 680                 685

Glu Gly Val Val Thr Lys Arg Lys Pro Ile Met Ile Ile Thr Glu Phe
    690                 695                 700

Met Glu Asn Gly Ala Leu Asp Ala Phe Leu Arg Glu Arg Glu Asp Gln
705                 710                 715                 720

Leu Val Pro Gly Gln Leu Val Ala Met Leu Gln Gly Ile Ala Ser Gly
                725                 730                 735

Met Asn Tyr Leu Ser Asn His Asn Tyr Val His Arg Asp Leu Ala Ala
            740                 745                 750

Arg Asn Ile Leu Val Asn Gln Asn Leu Cys Cys Lys Val Ser Asp Phe
        755                 760                 765

Gly Leu Thr Arg Leu Leu Asp Asp Phe Asp Gly Thr Tyr Glu Thr Gln
    770                 775                 780

Gly Gly Lys Ile Pro Ile Arg Trp Thr Ala Pro Glu Ala Ile Ala His
785                 790                 795                 800

Arg Ile Phe Thr Thr Ala Ser Asp Val Trp Ser Phe Gly Ile Val Met
                805                 810                 815

Trp Glu Val Leu Ser Phe Gly Asp Lys Pro Tyr Gly Glu Met Ser Asn
            820                 825                 830

Gln Glu Val Met Lys Ser Ile Glu Asp Gly Tyr Arg Leu Pro Pro Pro
        835                 840                 845

Val Asp Cys Pro Ala Pro Leu Tyr Glu Leu Met Lys Asn Cys Trp Ala
    850                 855                 860

Tyr Asp Arg Ala Arg Arg Pro His Phe Gln Lys Leu Gln Ala His Leu
865                 870                 875                 880

Glu Gln Leu Leu Ala Asn Pro His Ser Leu Arg Thr Ile Ala Asn Phe
                885                 890                 895

Asp Pro Arg Met Thr Leu Arg Leu Pro Ser Leu Ser Gly Ser Asp Gly
            900                 905                 910

Ile Pro Tyr Arg Thr Val Ser Glu Trp Leu Glu Ser Ile Arg Met Lys
        915                 920                 925
```

Arg Tyr Ile Leu His Phe His Ser Ala Gly Leu Asp Thr Met Glu Cys
930 935 940

Val Leu Glu Leu Thr Ala Glu Asp Leu Thr Gln Met Gly Ile Thr Leu
945 950 955 960

Pro Gly His Gln Lys Arg Ile Leu Cys Ser Ile Gln Gly Phe Lys Asp
965 970 975

<210> 419
<211> 983
<212> PRT
<213> Homo sapiens

<400> 419

Met Asp Cys Gln Leu Ser Ile Leu Leu Leu Leu Ser Cys Ser Val Leu
1 5 10 15

Asp Ser Phe Gly Glu Leu Ile Pro Gln Pro Ser Asn Glu Val Asn Leu
20 25 30

Leu Asp Ser Lys Thr Ile Gln Gly Glu Leu Gly Trp Ile Ser Tyr Pro
35 40 45

Ser His Gly Trp Glu Glu Ile Ser Gly Val Asp Glu His Tyr Thr Pro
50 55 60

Ile Arg Thr Tyr Gln Val Cys Asn Val Met Asp His Ser Gln Asn Asn
65 70 75 80

Trp Leu Arg Thr Asn Trp Val Pro Arg Asn Ser Ala Gln Lys Ile Tyr
85 90 95

Val Glu Leu Lys Phe Thr Leu Arg Asp Cys Asn Ser Ile Pro Leu Val
100 105 110

Leu Gly Thr Cys Lys Glu Thr Phe Asn Leu Tyr Tyr Met Glu Ser Asp
115 120 125

Asp Asp His Gly Val Lys Phe Arg Glu His Gln Phe Thr Lys Ile Asp
130 135 140

Thr Ile Ala Ala Asp Glu Ser Phe Thr Gln Met Asp Leu Gly Asp Arg
145 150 155 160

Ile Leu Lys Leu Asn Thr Glu Ile Arg Glu Val Gly Pro Val Asn Lys
165 170 175

Lys Gly Phe Tyr Leu Ala Phe Gln Asp Val Gly Ala Cys Val Ala Leu
180 185 190

Val Ser Val Arg Val Tyr Phe Lys Lys Cys Pro Phe Thr Val Lys Asn

195 200 205

Leu Ala Met Phe Pro Asp Thr Val Pro Met Asp Ser Gln Ser Leu Val
210 215 220

Glu Val Arg Gly Ser Cys Val Asn Asn Ser Lys Glu Glu Asp Pro Pro
225 230 235 240

Arg Met Tyr Cys Ser Thr Glu Gly Glu Trp Leu Val Pro Ile Gly Lys
245 250 255

Cys Ser Cys Asn Ala Gly Tyr Glu Glu Arg Gly Phe Met Cys Gln Ala
260 265 270

Cys Arg Pro Gly Phe Tyr Lys Ala Leu Asp Gly Asn Met Lys Cys Ala
275 280 285

Lys Cys Pro Pro His Ser Ser Thr Gln Glu Asp Gly Ser Met Asn Cys
290 295 300

Arg Cys Glu Asn Asn Tyr Phe Arg Ala Asp Lys Asp Pro Pro Ser Met
305 310 315 320

Ala Cys Thr Arg Pro Pro Ser Ser Pro Arg Asn Val Ile Ser Asn Ile
325 330 335

Asn Glu Thr Ser Val Ile Leu Asp Trp Ser Trp Pro Leu Asp Thr Gly
340 345 350

Gly Arg Lys Asp Val Thr Phe Asn Ile Ile Cys Lys Lys Cys Gly Trp
355 360 365

Asn Ile Lys Gln Cys Glu Pro Cys Ser Pro Asn Val Arg Phe Leu Pro
370 375 380

Arg Gln Phe Gly Leu Thr Asn Thr Thr Val Thr Val Thr Asp Leu Leu
385 390 395 400

Ala His Thr Asn Tyr Thr Phe Glu Ile Asp Ala Val Asn Gly Val Ser
405 410 415

Glu Leu Ser Ser Pro Pro Arg Gln Phe Ala Ala Val Ser Ile Thr Thr
420 425 430

Asn Gln Ala Ala Pro Ser Pro Val Leu Thr Ile Lys Lys Asp Arg Thr
435 440 445

Ser Arg Asn Ser Ile Ser Leu Ser Trp Gln Glu Pro Glu His Pro Asn
450 455 460

Gly Ile Ile Leu Asp Tyr Glu Val Lys Tyr Tyr Glu Lys Gln Glu Gln

465 470 475 480

Glu Thr Ser Tyr Thr Ile Leu Arg Ala Arg Gly Thr Asn Val Thr Ile
485 490 495

Ser Ser Leu Lys Pro Asp Thr Ile Tyr Val Phe Gln Ile Arg Ala Arg
500 505 510

Thr Ala Ala Gly Tyr Gly Thr Asn Ser Arg Lys Phe Glu Phe Glu Thr
515 520 525

Ser Pro Asp Ser Phe Ser Ile Ser Gly Glu Ser Ser Gln Val Val Met
530 535 540

Ile Ala Ile Ser Ala Ala Val Ala Ile Ile Leu Leu Thr Val Val Ile
545 550 555 560

Tyr Val Leu Ile Gly Arg Phe Cys Gly Tyr Lys Ser Lys His Gly Ala
565 570 575

Asp Glu Lys Arg Leu His Phe Gly Asn Gly His Leu Lys Leu Pro Gly
580 585 590

Leu Arg Thr Tyr Val Asp Pro His Thr Tyr Glu Asp Pro Thr Gln Ala
595 600 605

Val His Glu Phe Ala Lys Glu Leu Asp Ala Thr Asn Ile Ser Ile Asp
610 615 620

Lys Val Val Gly Ala Gly Glu Phe Gly Glu Val Cys Ser Gly Arg Leu
625 630 635 640

Lys Leu Pro Ser Lys Lys Glu Ile Ser Val Ala Ile Lys Thr Leu Lys
645 650 655

Val Gly Tyr Thr Glu Lys Gln Arg Arg Asp Phe Leu Gly Glu Ala Ser
660 665 670

Ile Met Gly Gln Phe Asp His Pro Asn Ile Ile Arg Leu Glu Gly Val
675 680 685

Val Thr Lys Ser Lys Pro Val Met Ile Val Thr Glu Tyr Met Glu Asn
690 695 700

Gly Ser Leu Asp Ser Phe Leu Arg Lys His Asp Ala Gln Phe Thr Val
705 710 715 720

Ile Gln Leu Val Gly Met Leu Arg Gly Ile Ala Ser Gly Met Lys Tyr
725 730 735

Leu Ser Asp Met Gly Tyr Val His Arg Asp Leu Ala Ala Arg Asn Ile

740 745 750

Leu Ile Asn Ser Asn Leu Val Cys Lys Val Ser Asp Phe Gly Leu Ser
755 760 765

Arg Val Leu Glu Asp Asp Pro Glu Ala Ala Tyr Thr Thr Arg Gly Gly
770 775 780

Lys Ile Pro Ile Arg Trp Thr Ser Pro Glu Ala Ile Ala Tyr Arg Lys
785 790 795 800

Phe Thr Ser Ala Ser Asp Val Trp Ser Tyr Gly Ile Val Leu Trp Glu
805 810 815

Val Met Ser Tyr Gly Glu Arg Pro Tyr Trp Glu Met Ser Asn Gln Asp
820 825 830

Val Ile Lys Ala Val Asp Glu Gly Tyr Arg Leu Pro Pro Pro Met Asp
835 840 845

Cys Pro Ala Ala Leu Tyr Gln Leu Met Leu Asp Cys Trp Gln Lys Asp
850 855 860

Arg Asn Asn Arg Pro Lys Phe Glu Gln Ile Val Ser Ile Leu Asp Lys
865 870 875 880

Leu Ile Arg Asn Pro Gly Ser Leu Lys Ile Ile Thr Ser Ala Ala Ala
885 890 895

Arg Pro Ser Asn Leu Leu Leu Asp Gln Ser Asn Val Asp Ile Thr Thr
900 905 910

Phe Arg Thr Thr Gly Asp Trp Leu Asn Gly Val Trp Thr Ala His Cys
915 920 925

Lys Glu Ile Phe Thr Gly Val Glu Tyr Ser Ser Cys Asp Thr Ile Ala
930 935 940

Lys Ile Ser Thr Asp Asp Met Lys Lys Val Gly Val Thr Val Val Gly
945 950 955 960

Pro Gln Lys Lys Ile Ile Ser Ser Ile Lys Ala Leu Glu Thr Gln Ser
965 970 975

Lys Asn Gly Pro Val Pro Val
980

<210> 420
<211> 986
<212> PRT
<213> Homo sapiens

<400> 420

Met Ala Gly Ile Phe Tyr Phe Ala Leu Phe Ser Cys Leu Phe Gly Ile
1 5 10 15

Cys Asp Ala Val Thr Gly Ser Arg Val Tyr Pro Ala Asn Glu Val Thr
20 25 30

Leu Leu Asp Ser Arg Ser Val Gln Gly Glu Leu Gly Trp Ile Ala Ser
35 40 45

Pro Leu Glu Gly Gly Trp Glu Glu Val Ser Ile Met Asp Glu Lys Asn
50 55 60

Thr Pro Ile Arg Thr Tyr Gln Val Cys Asn Val Met Glu Pro Ser Gln
65 70 75 80

Asn Asn Trp Leu Arg Thr Asp Trp Ile Thr Arg Glu Gly Ala Gln Arg
85 90 95

Val Tyr Ile Glu Ile Lys Phe Thr Leu Arg Asp Cys Asn Ser Leu Pro
100 105 110

Gly Val Met Gly Thr Cys Lys Glu Thr Phe Asn Leu Tyr Tyr Tyr Glu
115 120 125

Ser Asp Asn Asp Lys Glu Arg Phe Ile Arg Glu Asn Gln Phe Val Lys
130 135 140

Ile Asp Thr Ile Ala Ala Asp Glu Ser Phe Thr Gln Val Asp Ile Gly
145 150 155 160

Asp Arg Ile Met Lys Leu Asn Thr Glu Ile Arg Asp Val Gly Pro Leu
165 170 175

Ser Lys Lys Gly Phe Tyr Leu Ala Phe Gln Asp Val Gly Ala Cys Ile
180 185 190

Ala Leu Val Ser Val Arg Val Phe Tyr Lys Lys Cys Pro Leu Thr Val
195 200 205

Arg Asn Leu Ala Gln Phe Pro Asp Thr Ile Thr Gly Ala Asp Thr Ser
210 215 220

Ser Leu Val Glu Val Arg Gly Ser Cys Val Asn Asn Ser Glu Glu Lys
225 230 235 240

Asp Val Pro Lys Met Tyr Cys Gly Ala Asp Gly Glu Trp Leu Val Pro
245 250 255

Ile Gly Asn Cys Leu Cys Asn Ala Gly His Glu Glu Arg Ser Gly Glu
260 265 270

```
Cys Gln Ala Cys Lys Ile Gly Tyr Tyr Lys Ala Leu Ser Thr Asp Ala
        275                 280                 285

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

Thr Ser Cys Thr Cys Asp Arg Gly Phe Phe Arg Ala Asp Asn Asp Ala
305                 310                 315                 320

Ala Ser Met Pro Cys Thr Arg Pro Pro Ser Ala Pro Leu Asn Leu Ile
                325                 330                 335

Ser Asn Val Asn Glu Thr Ser Val Asn Leu Glu Trp Ser Ser Pro Gln
            340                 345                 350

Asn Thr Gly Gly Arg Gln Asp Ile Ser Tyr Asn Val Val Cys Lys Lys
        355                 360                 365

Cys Gly Ala Gly Asp Pro Ser Lys Cys Arg Pro Cys Gly Ser Gly Val
    370                 375                 380

His Tyr Thr Pro Gln Gln Asn Gly Leu Lys Thr Thr Lys Val Ser Ile
385                 390                 395                 400

Thr Asp Leu Leu Ala His Thr Asn Tyr Thr Phe Glu Ile Trp Ala Val
                405                 410                 415

Asn Gly Val Ser Lys Tyr Asn Pro Asn Pro Asp Gln Ser Val Ser Val
            420                 425                 430

Thr Val Thr Thr Asn Gln Ala Ala Pro Ser Ser Ile Ala Leu Val Gln
        435                 440                 445

Ala Lys Glu Val Thr Arg Tyr Ser Val Ala Leu Ala Trp Leu Glu Pro
    450                 455                 460

Asp Arg Pro Asn Gly Val Ile Leu Glu Tyr Glu Val Lys Tyr Tyr Glu
465                 470                 475                 480

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

Asn Thr Asp Ile Lys Gly Leu Asn Pro Leu Thr Ser Tyr Val Phe His
            500                 505                 510

Val Arg Ala Arg Thr Ala Ala Gly Tyr Gly Asp Phe Ser Glu Pro Leu
        515                 520                 525

Glu Val Thr Thr Asn Thr Val Pro Ser Arg Ile Ile Gly Asp Gly Ala
    530                 535                 540
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```
Asn Ser Thr Val Leu Leu Val Ser Val Ser Gly Ser Val Val Leu Val
545                 550                 555                 560

Val Ile Leu Ile Ala Ala Phe Val Ile Ser Arg Arg Arg Ser Lys Tyr
                565                 570                 575

Ser Lys Ala Lys Gln Glu Ala Asp Glu Glu Lys His Leu Asn Gln Gly
            580                 585                 590

Val Arg Thr Tyr Val Asp Pro Phe Thr Tyr Glu Asp Pro Asn Gln Ala
        595                 600                 605

Val Arg Glu Phe Ala Lys Glu Ile Asp Ala Ser Cys Ile Lys Ile Glu
    610                 615                 620

Lys Val Ile Gly Val Gly Glu Phe Gly Glu Val Cys Ser Gly Arg Leu
625                 630                 635                 640

Lys Val Pro Gly Lys Arg Glu Ile Cys Val Ala Ile Lys Thr Leu Lys
                645                 650                 655

Ala Gly Tyr Thr Asp Lys Gln Arg Arg Asp Phe Leu Ser Glu Ala Ser
            660                 665                 670

Ile Met Gly Gln Phe Asp His Pro Asn Ile Ile His Leu Glu Gly Val
        675                 680                 685

Val Thr Lys Cys Lys Pro Val Met Ile Ile Thr Glu Tyr Met Glu Asn
    690                 695                 700

Gly Ser Leu Asp Ala Phe Leu Arg Lys Asn Asp Gly Arg Phe Thr Val
705                 710                 715                 720

Ile Gln Leu Val Gly Met Leu Arg Gly Ile Gly Ser Gly Met Lys Tyr
                725                 730                 735

Leu Ser Asp Met Ser Tyr Val His Arg Asp Leu Ala Ala Arg Asn Ile
            740                 745                 750

Leu Val Asn Ser Asn Leu Val Cys Lys Val Ser Asp Phe Gly Met Ser
        755                 760                 765

Arg Val Leu Glu Asp Asp Pro Glu Ala Ala Tyr Thr Thr Arg Gly Gly
    770                 775                 780

Lys Ile Pro Ile Arg Trp Thr Ala Pro Glu Ala Ile Ala Tyr Arg Lys
785                 790                 795                 800

Phe Thr Ser Ala Ser Asp Val Trp Ser Tyr Gly Ile Val Met Trp Glu
                805                 810                 815
```

```
Val Met Ser Tyr Gly Glu Arg Pro Tyr Trp Asp Met Ser Asn Gln Asp
            820                 825                 830

Val Ile Lys Ala Ile Glu Glu Gly Tyr Arg Leu Pro Pro Pro Met Asp
        835                 840                 845

Cys Pro Ile Ala Leu His Gln Leu Met Leu Asp Cys Trp Gln Lys Glu
    850                 855                 860

Arg Ser Asp Arg Pro Lys Phe Gly Gln Ile Val Asn Met Leu Asp Lys
865                 870                 875                 880

Leu Ile Arg Asn Pro Asn Ser Leu Lys Arg Thr Gly Thr Glu Ser Ser
                885                 890                 895

Arg Pro Asn Thr Ala Leu Leu Asp Pro Ser Ser Pro Glu Phe Ser Ala
            900                 905                 910

Val Val Ser Val Gly Asp Trp Leu Gln Ala Ile Lys Met Asp Arg Tyr
        915                 920                 925

Lys Asp Asn Phe Thr Ala Ala Gly Tyr Thr Thr Leu Glu Ala Val Val
    930                 935                 940

His Val Asn Gln Glu Asp Leu Ala Arg Ile Gly Ile Thr Ala Ile Thr
945                 950                 955                 960

His Gln Asn Lys Ile Leu Ser Ser Val Gln Ala Met Arg Thr Gln Met
                965                 970                 975

Gln Gln Met His Gly Arg Met Val Pro Val
            980                 985


<210>  421
<211>  1037
<212>  PRT
<213>  Homo sapiens

<400>  421

Met Arg Gly Ser Gly Pro Arg Gly Ala Gly Arg Arg Arg Pro Pro Ser
1               5                   10                  15

Gly Gly Gly Asp Thr Pro Ile Thr Pro Ala Ser Leu Ala Gly Cys Tyr
            20                  25                  30

Ser Ala Pro Arg Arg Ala Pro Leu Trp Thr Cys Leu Leu Leu Cys Ala
        35                  40                  45

Ala Leu Arg Thr Leu Leu Ala Ser Pro Ser Asn Glu Val Asn Leu Leu
    50                  55                  60
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```
Asp Ser Arg Thr Val Met Gly Asp Leu Gly Trp Ile Ala Phe Pro Lys
65                  70                  75                  80

Asn Gly Trp Glu Glu Ile Gly Glu Val Asp Glu Asn Tyr Ala Pro Ile
                85                  90                  95

His Thr Tyr Gln Val Cys Lys Val Met Glu Gln Asn Gln Asn Asn Trp
            100                 105                 110

Leu Leu Thr Ser Trp Ile Ser Asn Glu Gly Ala Ser Arg Ile Phe Ile
        115                 120                 125

Glu Leu Lys Phe Thr Leu Arg Asp Cys Asn Ser Leu Pro Gly Gly Leu
    130                 135                 140

Gly Thr Cys Lys Glu Thr Phe Asn Met Tyr Tyr Phe Glu Ser Asp Asp
145                 150                 155                 160

Gln Asn Gly Arg Asn Ile Lys Glu Asn Gln Tyr Ile Lys Ile Asp Thr
                165                 170                 175

Ile Ala Ala Asp Glu Ser Phe Thr Glu Leu Asp Leu Gly Asp Arg Val
            180                 185                 190

Met Lys Leu Asn Thr Glu Val Arg Asp Val Gly Pro Leu Ser Lys Lys
        195                 200                 205

Gly Phe Tyr Leu Ala Phe Gln Asp Val Gly Ala Cys Ile Ala Leu Val
    210                 215                 220

Ser Val Arg Val Tyr Tyr Lys Lys Cys Pro Ser Val Val Arg His Leu
225                 230                 235                 240

Ala Val Phe Pro Asp Thr Ile Thr Gly Ala Asp Ser Ser Gln Leu Leu
                245                 250                 255

Glu Val Ser Gly Ser Cys Val Asn His Ser Val Thr Asp Glu Pro Pro
            260                 265                 270

Lys Met His Cys Ser Ala Glu Gly Glu Trp Leu Val Pro Ile Gly Lys
        275                 280                 285

Cys Met Cys Lys Ala Gly Tyr Glu Glu Lys Asn Gly Thr Cys Gln Val
    290                 295                 300

Cys Arg Pro Gly Phe Phe Lys Ala Ser Pro His Ile Gln Ser Cys Gly
305                 310                 315                 320

Lys Cys Pro Pro His Ser Tyr Thr His Glu Glu Ala Ser Thr Ser Cys
                325                 330                 335
```

```
Val Cys Glu Lys Asp Tyr Phe Arg Arg Glu Ser Asp Pro Pro Thr Met
            340                 345                 350

Ala Cys Thr Arg Pro Pro Ser Ala Pro Arg Asn Ala Ile Ser Asn Val
        355                 360                 365

Asn Glu Thr Ser Val Phe Leu Glu Trp Ile Pro Pro Ala Asp Thr Gly
    370                 375                 380

Gly Arg Lys Asp Val Ser Tyr Tyr Ile Ala Cys Lys Lys Cys Asn Ser
385                 390                 395                 400

His Ala Gly Val Cys Glu Glu Cys Gly Gly His Val Arg Tyr Leu Pro
                405                 410                 415

Arg Gln Ser Gly Leu Lys Asn Thr Ser Val Met Met Val Asp Leu Leu
            420                 425                 430

Ala His Thr Asn Tyr Thr Phe Glu Ile Glu Ala Val Asn Gly Val Ser
        435                 440                 445

Asp Leu Ser Pro Gly Ala Arg Gln Tyr Val Ser Val Asn Val Thr Thr
    450                 455                 460

Asn Gln Ala Ala Pro Ser Pro Val Thr Asn Val Lys Lys Gly Lys Ile
465                 470                 475                 480

Ala Lys Asn Ser Ile Ser Leu Ser Trp Gln Glu Pro Asp Arg Pro Asn
                485                 490                 495

Gly Ile Ile Leu Glu Tyr Glu Ile Lys Tyr Phe Glu Lys Asp Gln Glu
            500                 505                 510

Thr Ser Tyr Thr Ile Ile Lys Ser Lys Glu Thr Thr Ile Thr Ala Glu
        515                 520                 525

Gly Leu Lys Pro Ala Ser Val Tyr Val Phe Gln Ile Arg Ala Arg Thr
    530                 535                 540

Ala Ala Gly Tyr Gly Val Phe Ser Arg Arg Phe Glu Phe Glu Thr Thr
545                 550                 555                 560

Pro Val Phe Ala Ala Ser Ser Asp Gln Ser Gln Ile Pro Val Ile Ala
                565                 570                 575

Val Ser Val Thr Val Gly Val Ile Leu Leu Ala Val Val Ile Gly Val
            580                 585                 590

Leu Leu Ser Gly Ser Cys Cys Glu Cys Gly Cys Gly Arg Ala Ser Ser
        595                 600                 605
```

```
Leu Cys Ala Val Ala His Pro Ser Leu Ile Trp Arg Cys Gly Tyr Ser
    610                 615                 620

Lys Ala Lys Gln Asp Pro Glu Glu Glu Lys Met His Phe His Asn Gly
625                 630                 635                 640

His Ile Lys Leu Pro Gly Val Arg Thr Tyr Ile Asp Pro His Thr Tyr
                645                 650                 655

Glu Asp Pro Asn Gln Ala Val His Glu Phe Ala Lys Glu Ile Glu Ala
            660                 665                 670

Ser Cys Ile Thr Ile Glu Arg Val Ile Gly Ala Gly Glu Phe Gly Glu
        675                 680                 685

Val Cys Ser Gly Arg Leu Lys Leu Pro Gly Lys Arg Glu Leu Pro Val
    690                 695                 700

Ala Ile Lys Thr Leu Lys Val Gly Tyr Thr Glu Lys Gln Arg Arg Asp
705                 710                 715                 720

Phe Leu Gly Glu Ala Ser Ile Met Gly Gln Phe Asp His Pro Asn Ile
                725                 730                 735

Ile His Leu Glu Gly Val Val Thr Lys Ser Lys Pro Val Met Ile Val
            740                 745                 750

Thr Glu Tyr Met Glu Asn Gly Ser Leu Asp Thr Phe Leu Lys Lys Asn
        755                 760                 765

Asp Gly Gln Phe Thr Val Ile Gln Leu Val Gly Met Leu Arg Gly Ile
    770                 775                 780

Ser Ala Gly Met Lys Tyr Leu Ser Asp Met Gly Tyr Val His Arg Asp
785                 790                 795                 800

Leu Ala Ala Arg Asn Ile Leu Ile Asn Ser Asn Leu Val Cys Lys Val
                805                 810                 815

Ser Asp Phe Gly Leu Ser Arg Val Leu Glu Asp Asp Pro Glu Ala Ala
            820                 825                 830

Tyr Thr Thr Arg Gly Gly Lys Ile Pro Ile Arg Trp Thr Ala Pro Glu
        835                 840                 845

Ala Ile Ala Phe Arg Lys Phe Thr Ser Ala Ser Asp Val Trp Ser Tyr
    850                 855                 860

Gly Ile Val Met Trp Glu Val Val Ser Tyr Gly Glu Arg Pro Tyr Trp
865                 870                 875                 880
```

```
Glu Met Thr Asn Gln Asp Val Ile Lys Ala Val Glu Glu Gly Tyr Arg
                885                 890                 895


Leu Pro Ser Pro Met Asp Cys Pro Ala Ala Leu Tyr Gln Leu Met Leu
            900                 905                 910


Asp Cys Trp Gln Lys Glu Arg Asn Ser Arg Pro Lys Phe Asp Glu Ile
        915                 920                 925


Val Asn Met Leu Asp Lys Leu Ile Arg Asn Pro Ser Ser Leu Lys Thr
    930                 935                 940


Leu Val Asn Ala Ser Cys Arg Val Ser Asn Leu Leu Ala Glu His Ser
945                 950                 955                 960


Pro Leu Gly Ser Gly Ala Tyr Arg Ser Val Gly Glu Trp Leu Glu Ala
                965                 970                 975


Ile Lys Met Gly Arg Tyr Thr Glu Ile Phe Met Glu Asn Gly Tyr Ser
            980                 985                 990


Ser Met Asp Ala Val Ala Gln Val  Thr Leu Glu Asp Leu  Arg Arg Leu
        995                 1000                1005


Gly Val  Thr Leu Val Gly His  Gln Lys Lys Ile Met  Asn Ser Leu
    1010                1015                1020


Gln Glu  Met Lys Val Gln Leu  Val Asn Gly Met Val  Pro Leu
    1025                1030                1035


<210>  422
<211>  998
<212>  PRT
<213>  Homo sapiens

<400>  422

Met Val Phe Gln Thr Arg Tyr Pro Ser Trp Ile Ile Leu Cys Tyr Ile
1               5                   10                  15


Trp Leu Leu Arg Phe Ala His Thr Gly Glu Ala Gln Ala Ala Lys Glu
            20                  25                  30


Val Leu Leu Leu Asp Ser Lys Ala Gln Gln Thr Glu Leu Glu Trp Ile
        35                  40                  45


Ser Ser Pro Pro Asn Gly Trp Glu Glu Ile Ser Gly Leu Asp Glu Asn
    50                  55                  60


Tyr Thr Pro Ile Arg Thr Tyr Gln Val Cys Gln Val Met Glu Pro Asn
65                  70                  75                  80
```

```
Gln Asn Asn Trp Leu Arg Thr Asn Trp Ile Ser Lys Gly Asn Ala Gln
                85                  90                  95

Arg Ile Phe Val Glu Leu Lys Phe Thr Leu Arg Asp Cys Asn Ser Leu
            100                 105                 110

Pro Gly Val Leu Gly Thr Cys Lys Glu Thr Phe Asn Leu Tyr Tyr Tyr
        115                 120                 125

Glu Thr Asp Tyr Asp Thr Gly Arg Asn Ile Arg Glu Asn Leu Tyr Val
    130                 135                 140

Lys Ile Asp Thr Ile Ala Ala Asp Glu Ser Phe Thr Gln Gly Asp Leu
145                 150                 155                 160

Gly Glu Arg Lys Met Lys Leu Asn Thr Glu Val Arg Glu Ile Gly Pro
                165                 170                 175

Leu Ser Lys Lys Gly Phe Tyr Leu Ala Phe Gln Asp Val Gly Ala Cys
            180                 185                 190

Ile Ala Leu Val Ser Val Lys Val Tyr Tyr Lys Lys Cys Trp Ser Ile
        195                 200                 205

Ile Glu Asn Leu Ala Ile Phe Pro Asp Thr Val Thr Gly Ser Glu Phe
    210                 215                 220

Ser Ser Leu Val Glu Val Arg Gly Thr Cys Val Ser Ser Ala Glu Glu
225                 230                 235                 240

Glu Ala Glu Asn Ala Pro Arg Met His Cys Ser Ala Glu Gly Glu Trp
                245                 250                 255

Leu Val Pro Ile Gly Lys Cys Ile Cys Lys Ala Gly Tyr Gln Gln Lys
            260                 265                 270

Gly Asp Thr Cys Glu Pro Cys Gly Arg Gly Phe Tyr Lys Ser Ser Ser
        275                 280                 285

Gln Asp Leu Gln Cys Ser Arg Cys Pro Thr His Ser Phe Ser Asp Lys
    290                 295                 300

Glu Gly Ser Ser Arg Cys Glu Cys Glu Asp Gly Tyr Tyr Arg Ala Pro
305                 310                 315                 320

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

Asn Leu Ile Phe Asn Ile Asn Gln Thr Thr Val Ser Leu Glu Trp Ser
            340                 345                 350
```

```
Pro Pro Ala Asp Asn Gly Gly Arg Asn Asp Val Thr Tyr Arg Ile Leu
        355                 360                 365

Cys Lys Arg Cys Ser Trp Glu Gln Gly Glu Cys Val Pro Cys Gly Ser
    370                 375                 380

Asn Ile Gly Tyr Met Pro Gln Gln Thr Gly Leu Glu Asp Asn Tyr Val
385                 390                 395                 400

Thr Val Met Asp Leu Leu Ala His Ala Asn Tyr Thr Phe Glu Val Glu
                405                 410                 415

Ala Val Asn Gly Val Ser Asp Leu Ser Arg Ser Gln Arg Leu Phe Ala
            420                 425                 430

Ala Val Ser Ile Thr Thr Gly Gln Ala Ala Pro Ser Gln Val Ser Gly
        435                 440                 445

Val Met Lys Glu Arg Val Leu Gln Arg Ser Val Glu Leu Ser Trp Gln
    450                 455                 460

Glu Pro Glu His Pro Asn Gly Val Ile Thr Glu Tyr Glu Ile Lys Tyr
465                 470                 475                 480

Tyr Glu Lys Asp Gln Arg Glu Arg Thr Tyr Ser Thr Val Lys Thr Lys
                485                 490                 495

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

Phe Gln Ile Arg Ala Phe Thr Ala Ala Gly Tyr Gly Asn Tyr Ser Pro
        515                 520                 525

Arg Leu Asp Val Ala Thr Leu Glu Glu Ala Thr Gly Lys Met Phe Glu
    530                 535                 540

Ala Thr Ala Val Ser Ser Glu Gln Asn Pro Val Ile Ile Ile Ala Val
545                 550                 555                 560

Val Ala Val Ala Gly Thr Ile Ile Leu Val Phe Met Val Phe Gly Phe
                565                 570                 575

Ile Ile Gly Arg Arg His Cys Gly Tyr Ser Lys Ala Asp Gln Glu Gly
            580                 585                 590

Asp Glu Glu Leu Tyr Phe His Phe Lys Phe Pro Gly Thr Lys Thr Tyr
        595                 600                 605

Ile Asp Pro Glu Thr Tyr Glu Asp Pro Asn Arg Ala Val His Gln Phe
    610                 615                 620
```

```
Ala Lys Glu Leu Asp Ala Ser Cys Ile Lys Ile Glu Arg Val Ile Gly
625                 630                 635                 640

Ala Gly Glu Phe Gly Glu Val Cys Ser Gly Arg Leu Lys Leu Pro Gly
                645                 650                 655

Lys Arg Asp Val Ala Val Ala Ile Lys Thr Leu Lys Val Gly Tyr Thr
            660                 665                 670

Glu Lys Gln Arg Arg Asp Phe Leu Cys Glu Ala Ser Ile Met Gly Gln
        675                 680                 685

Phe Asp His Pro Asn Val Val His Leu Glu Gly Val Val Thr Arg Gly
    690                 695                 700

Lys Pro Val Met Ile Val Ile Glu Phe Met Glu Asn Gly Ala Leu Asp
705                 710                 715                 720

Ala Phe Leu Arg Lys His Asp Gly Gln Phe Thr Val Ile Gln Leu Val
                725                 730                 735

Gly Met Leu Arg Gly Ile Ala Ala Gly Met Arg Tyr Leu Ala Asp Met
            740                 745                 750

Gly Tyr Val His Arg Asp Leu Ala Ala Arg Asn Ile Leu Val Asn Ser
        755                 760                 765

Asn Leu Val Cys Lys Val Ser Asp Phe Gly Leu Ser Arg Val Ile Glu
    770                 775                 780

Asp Asp Pro Glu Ala Val Tyr Thr Thr Thr Gly Gly Lys Ile Pro Val
785                 790                 795                 800

Arg Trp Thr Ala Pro Glu Ala Ile Gln Tyr Arg Lys Phe Thr Ser Ala
                805                 810                 815

Ser Asp Val Trp Ser Tyr Gly Ile Val Met Trp Glu Val Met Ser Tyr
            820                 825                 830

Gly Glu Arg Pro Tyr Trp Asp Met Ser Asn Gln Asp Val Ile Lys Ala
        835                 840                 845

Ile Glu Glu Gly Tyr Arg Leu Pro Ala Pro Met Asp Cys Pro Ala Gly
    850                 855                 860

Leu His Gln Leu Met Leu Asp Cys Trp Gln Lys Glu Arg Ala Glu Arg
865                 870                 875                 880

Pro Lys Phe Glu Gln Ile Val Gly Ile Leu Asp Lys Met Ile Arg Asn
                885                 890                 895
```

Pro Asn Ser Leu Lys Thr Pro Leu Gly Thr Cys Ser Arg Pro Ile Ser
900 905 910

Pro Leu Leu Asp Gln Asn Thr Pro Asp Phe Thr Thr Phe Cys Ser Val
915 920 925

Gly Glu Trp Leu Gln Ala Ile Lys Met Glu Arg Tyr Lys Asp Asn Phe
930 935 940

Thr Ala Ala Gly Tyr Asn Ser Leu Glu Ser Val Ala Arg Met Thr Ile
945 950 955 960

Glu Asp Val Met Ser Leu Gly Ile Thr Leu Val Gly His Gln Lys Lys
965 970 975

Ile Met Ser Ser Ile Gln Thr Met Arg Ala Gln Met Leu His Leu His
980 985 990

Gly Thr Gly Ile Gln Val
995

<210> 423
<211> 1005
<212> PRT
<213> Homo sapiens

<400> 423

Met Ala Pro Ala Arg Gly Arg Leu Pro Pro Ala Leu Trp Val Val Thr
1 5 10 15

Ala Ala Ala Ala Ala Ala Thr Cys Val Ser Ala Ala Arg Gly Glu Val
20 25 30

Asn Leu Leu Asp Thr Ser Thr Ile His Gly Asp Trp Gly Trp Leu Thr
35 40 45

Tyr Pro Ala His Gly Trp Asp Ser Ile Asn Glu Val Asp Glu Ser Phe
50 55 60

Gln Pro Ile His Thr Tyr Gln Val Cys Asn Val Met Ser Pro Asn Gln
65 70 75 80

Asn Asn Trp Leu Arg Thr Ser Trp Val Pro Arg Asp Gly Ala Arg Arg
85 90 95

Val Tyr Ala Glu Ile Lys Phe Thr Leu Arg Asp Cys Asn Ser Met Pro
100 105 110

Gly Val Leu Gly Thr Cys Lys Glu Thr Phe Asn Leu Tyr Tyr Leu Glu
115 120 125

Ser Asp Arg Asp Leu Gly Ala Ser Thr Gln Glu Ser Gln Phe Leu Lys

130 135 140

Ile Asp Thr Ile Ala Ala Asp Glu Ser Phe Thr Gly Ala Asp Leu Gly
145 150 155 160

Val Arg Arg Leu Lys Leu Asn Thr Glu Val Arg Ser Val Gly Pro Leu
165 170 175

Ser Lys Arg Gly Phe Tyr Leu Ala Phe Gln Asp Ile Gly Ala Cys Leu
180 185 190

Ala Ile Leu Ser Leu Arg Ile Tyr Tyr Lys Lys Cys Pro Ala Met Val
195 200 205

Arg Asn Leu Ala Ala Phe Ser Glu Ala Val Thr Gly Ala Asp Ser Ser
210 215 220

Ser Leu Val Glu Val Arg Gly Gln Cys Val Arg His Ser Glu Glu Arg
225 230 235 240

Asp Thr Pro Lys Met Tyr Cys Ser Ala Glu Gly Glu Trp Leu Val Pro
245 250 255

Ile Gly Lys Cys Val Cys Ser Ala Gly Tyr Glu Glu Arg Arg Asp Ala
260 265 270

Cys Val Ala Cys Glu Leu Gly Phe Tyr Lys Ser Ala Pro Gly Asp Gln
275 280 285

Leu Cys Ala Arg Cys Pro Pro His Ser His Ser Ala Ala Pro Ala Ala
290 295 300

Gln Ala Cys His Cys Asp Leu Ser Tyr Tyr Arg Ala Ala Leu Asp Pro
305 310 315 320

Pro Ser Ser Ala Cys Thr Arg Pro Pro Ser Ala Pro Val Asn Leu Ile
325 330 335

Ser Ser Val Asn Gly Thr Ser Val Thr Leu Glu Trp Ala Pro Pro Leu
340 345 350

Asp Pro Gly Gly Arg Ser Asp Ile Thr Tyr Asn Ala Val Cys Arg Arg
355 360 365

Cys Pro Trp Ala Leu Ser Arg Cys Glu Ala Cys Gly Ser Gly Thr Arg
370 375 380

Phe Val Pro Gln Gln Thr Ser Leu Val Gln Ala Ser Leu Leu Val Ala
385 390 395 400

Asn Leu Leu Ala His Met Asn Tyr Ser Phe Trp Ile Glu Ala Val Asn

405 410 415

Gly Val Ser Asp Leu Ser Pro Glu Pro Arg Arg Ala Ala Val Val Asn
420 425 430

Ile Thr Thr Asn Gln Ala Ala Pro Ser Gln Val Val Val Ile Arg Gln
435 440 445

Glu Arg Ala Gly Gln Thr Ser Val Ser Leu Leu Trp Gln Glu Pro Glu
450 455 460

Gln Pro Asn Gly Ile Ile Leu Glu Tyr Glu Ile Lys Tyr Tyr Glu Lys
465 470 475 480

Asp Lys Glu Met Gln Ser Tyr Ser Thr Leu Lys Ala Val Thr Thr Arg
485 490 495

Ala Thr Val Ser Gly Leu Lys Pro Gly Thr Arg Tyr Val Phe Gln Val
500 505 510

Arg Ala Arg Thr Ser Ala Gly Cys Gly Arg Phe Ser Gln Ala Met Glu
515 520 525

Val Glu Thr Gly Lys Pro Arg Pro Arg Tyr Asp Thr Arg Thr Ile Val
530 535 540

Trp Ile Cys Leu Thr Leu Ile Thr Gly Leu Val Val Leu Leu Leu Leu
545 550 555 560

Leu Ile Cys Lys Lys Arg His Cys Gly Tyr Ser Lys Ala Phe Gln Asp
565 570 575

Ser Asp Glu Glu Lys Met His Tyr Gln Asn Gly Gln Ala Pro Pro Pro
580 585 590

Val Phe Leu Pro Leu His His Pro Pro Gly Lys Leu Pro Glu Pro Gln
595 600 605

Phe Tyr Ala Glu Pro His Thr Tyr Glu Glu Pro Gly Arg Ala Gly Arg
610 615 620

Ser Phe Thr Arg Glu Ile Glu Ala Ser Arg Ile His Ile Glu Lys Ile
625 630 635 640

Ile Gly Ser Gly Asp Ser Gly Glu Val Cys Tyr Gly Arg Leu Arg Val
645 650 655

Pro Gly Gln Arg Asp Val Pro Val Ala Ile Lys Ala Leu Lys Ala Gly
660 665 670

Tyr Thr Glu Arg Gln Arg Arg Asp Phe Leu Ser Glu Ala Ser Ile Met

675 680 685

Gly Gln Phe Asp His Pro Asn Ile Ile Arg Leu Glu Gly Val Val Thr
690 695 700

Arg Gly Arg Leu Ala Met Ile Val Thr Glu Tyr Met Glu Asn Gly Ser
705 710 715 720

Leu Asp Thr Phe Leu Arg Thr His Asp Gly Gln Phe Thr Ile Met Gln
725 730 735

Leu Val Gly Met Leu Arg Gly Val Gly Ala Gly Met Arg Tyr Leu Ser
740 745 750

Asp Leu Gly Tyr Val His Arg Asp Leu Ala Ala Arg Asn Val Leu Val
755 760 765

Asp Ser Asn Leu Val Cys Lys Val Ser Asp Phe Gly Leu Ser Arg Val
770 775 780

Leu Glu Asp Asp Pro Asp Ala Ala Tyr Thr Thr Thr Gly Gly Lys Ile
785 790 795 800

Pro Ile Arg Trp Thr Ala Pro Glu Ala Ile Ala Phe Arg Thr Phe Ser
805 810 815

Ser Ala Ser Asp Val Trp Ser Phe Gly Val Val Met Trp Glu Val Leu
820 825 830

Ala Tyr Gly Glu Arg Pro Tyr Trp Asn Met Thr Asn Arg Asp Val Ile
835 840 845

Ser Ser Val Glu Glu Gly Tyr Arg Leu Pro Ala Pro Met Gly Cys Pro
850 855 860

His Ala Leu His Gln Leu Met Leu Asp Cys Trp His Lys Asp Arg Ala
865 870 875 880

Gln Arg Pro Arg Phe Ser Gln Ile Val Ser Val Leu Asp Ala Leu Ile
885 890 895

Arg Ser Pro Glu Ser Leu Arg Ala Thr Ala Thr Val Ser Arg Cys Pro
900 905 910

Pro Pro Ala Phe Val Arg Ser Cys Phe Asp Leu Arg Gly Gly Ser Gly
915 920 925

Gly Gly Gly Gly Leu Thr Val Gly Asp Trp Leu Asp Ser Ile Arg Met
930 935 940

Gly Arg Tyr Arg Asp His Phe Ala Ala Gly Gly Tyr Ser Ser Leu Gly

945 950 955 960

Met Val Leu Arg Met Asn Ala Gln Asp Val Arg Ala Leu Gly Ile Thr
965 970 975

Leu Met Gly His Gln Lys Lys Ile Leu Gly Ser Ile Gln Thr Met Arg
980 985 990

Ala Gln Leu Thr Ser Thr Gln Gly Pro Arg Arg His Leu
995 1000 1005

<210> 424
<211> 984
<212> PRT
<213> Homo sapiens

<400> 424

Met Ala Leu Asp Tyr Leu Leu Leu Leu Leu Leu Ala Ser Ala Val Ala
1 5 10 15

Ala Met Glu Glu Thr Leu Met Asp Thr Arg Thr Ala Thr Ala Glu Leu
20 25 30

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

Asp Glu Asn Leu Asn Thr Ile Arg Thr Tyr Gln Val Cys Asn Val Phe
50 55 60

Glu Pro Asn Gln Asn Asn Trp Leu Leu Thr Thr Phe Ile Asn Arg Arg
65 70 75 80

Gly Ala His Arg Ile Tyr Thr Glu Met Arg Phe Thr Val Arg Asp Cys
85 90 95

Ser Ser Leu Pro Asn Val Pro Gly Ser Cys Lys Glu Thr Phe Asn Leu
100 105 110

Tyr Tyr Tyr Glu Thr Asp Ser Val Ile Ala Thr Lys Lys Ser Ala Phe
115 120 125

Trp Ser Glu Ala Pro Tyr Leu Lys Val Asp Thr Ile Ala Ala Asp Glu
130 135 140

Ser Phe Ser Gln Val Asp Phe Gly Gly Arg Leu Met Lys Val Asn Thr
145 150 155 160

Glu Val Arg Ser Phe Gly Pro Leu Thr Arg Asn Gly Phe Tyr Leu Ala
165 170 175

Phe Gln Asp Tyr Gly Ala Cys Met Ser Leu Leu Ser Val Arg Val Phe
180 185 190

```
Phe Lys Lys Cys Pro Ser Ile Val Gln Asn Phe Ala Val Phe Pro Glu
        195                 200                 205

Thr Met Thr Gly Ala Glu Ser Thr Ser Leu Val Ile Ala Arg Gly Thr
    210                 215                 220

Cys Ile Pro Asn Ala Glu Glu Val Asp Val Pro Ile Lys Leu Tyr Cys
225                 230                 235                 240

Asn Gly Asp Gly Glu Trp Met Val Pro Ile Gly Arg Cys Thr Cys Lys
                245                 250                 255

Pro Gly Tyr Glu Pro Glu Asn Ser Val Ala Cys Lys Ala Cys Pro Ala
            260                 265                 270

Gly Thr Phe Lys Ala Ser Gln Glu Ala Glu Gly Cys Ser His Cys Pro
        275                 280                 285

Ser Asn Ser Arg Ser Pro Ala Glu Ala Ser Pro Ile Cys Thr Cys Arg
    290                 295                 300

Thr Gly Tyr Tyr Arg Ala Asp Phe Asp Pro Pro Glu Val Ala Cys Thr
305                 310                 315                 320

Ser Val Pro Ser Gly Pro Arg Asn Val Ile Ser Ile Val Asn Glu Thr
                325                 330                 335

Ser Ile Ile Leu Glu Trp His Pro Pro Arg Glu Thr Gly Gly Arg Asp
            340                 345                 350

Asp Val Thr Tyr Asn Ile Ile Cys Lys Lys Cys Arg Ala Asp Arg Arg
        355                 360                 365

Ser Cys Ser Arg Cys Asp Asp Asn Val Glu Phe Val Pro Arg Gln Leu
    370                 375                 380

Gly Leu Thr Glu Cys Arg Val Ser Ile Ser Ser Leu Trp Ala His Thr
385                 390                 395                 400

Pro Tyr Thr Phe Asp Ile Gln Ala Ile Asn Gly Val Ser Ser Lys Ser
                405                 410                 415

Pro Phe Pro Pro Gln His Val Ser Val Asn Ile Thr Thr Asn Gln Ala
            420                 425                 430

Ala Pro Ser Thr Val Pro Ile Met His Gln Val Ser Ala Thr Met Arg
        435                 440                 445

Ser Ile Thr Leu Ser Trp Pro Gln Pro Glu Gln Pro Asn Gly Ile Ile
    450                 455                 460
```

```
Leu Asp Tyr Glu Ile Arg Tyr Tyr Glu Lys Glu His Asn Glu Phe Asn
465                 470                 475                 480

Ser Ser Met Ala Arg Ser Gln Thr Asn Thr Ala Arg Ile Asp Gly Leu
                485                 490                 495

Arg Pro Gly Met Val Tyr Val Val Gln Val Arg Ala Arg Thr Val Ala
            500                 505                 510

Gly Tyr Gly Lys Phe Ser Gly Lys Met Cys Phe Gln Thr Leu Thr Asp
        515                 520                 525

Asp Asp Tyr Lys Ser Glu Leu Arg Glu Gln Leu Pro Leu Ile Ala Gly
    530                 535                 540

Ser Ala Ala Ala Gly Val Val Phe Val Val Ser Leu Val Ala Ile Ser
545                 550                 555                 560

Ile Val Cys Ser Arg Lys Arg Ala Tyr Ser Lys Glu Ala Val Tyr Ser
                565                 570                 575

Asp Lys Leu Gln His Tyr Ser Thr Gly Arg Gly Ser Pro Gly Met Lys
            580                 585                 590

Ile Tyr Ile Asp Pro Phe Thr Tyr Glu Asp Pro Asn Glu Ala Val Arg
        595                 600                 605

Glu Phe Ala Lys Glu Ile Asp Val Ser Phe Val Lys Ile Glu Glu Val
    610                 615                 620

Ile Gly Ala Gly Glu Phe Gly Glu Val Tyr Lys Gly Arg Leu Lys Leu
625                 630                 635                 640

Pro Gly Lys Arg Glu Ile Tyr Val Ala Ile Lys Thr Leu Lys Ala Gly
                645                 650                 655

Tyr Ser Glu Lys Gln Arg Arg Asp Phe Leu Ser Glu Ala Ser Ile Met
            660                 665                 670

Gly Gln Phe Asp His Pro Asn Ile Ile Arg Leu Glu Gly Val Val Thr
        675                 680                 685

Lys Ser Arg Pro Val Met Ile Ile Thr Glu Phe Met Glu Asn Gly Ala
    690                 695                 700

Leu Asp Ser Phe Leu Arg Gln Asn Asp Gly Gln Phe Thr Val Ile Gln
705                 710                 715                 720

Leu Val Gly Met Leu Arg Gly Ile Ala Ala Gly Met Lys Tyr Leu Ala
                725                 730                 735
```

```
Glu Met Asn Tyr Val His Arg Asp Leu Ala Ala Arg Asn Ile Leu Val
            740                 745                 750

Asn Ser Asn Leu Val Cys Lys Val Ser Asp Phe Gly Leu Ser Arg Tyr
        755                 760                 765

Leu Gln Asp Asp Thr Ser Asp Pro Thr Tyr Thr Ser Ser Leu Gly Gly
    770                 775                 780

Lys Ile Pro Val Arg Trp Thr Ala Pro Glu Ala Ile Ala Tyr Arg Lys
785                 790                 795                 800

Phe Thr Ser Ala Ser Asp Val Trp Ser Tyr Gly Ile Val Met Trp Glu
                805                 810                 815

Val Met Ser Phe Gly Glu Arg Pro Tyr Trp Asp Met Ser Asn Gln Asp
            820                 825                 830

Val Ile Asn Ala Ile Glu Gln Asp Tyr Arg Leu Pro Pro Pro Met Asp
        835                 840                 845

Cys Pro Ala Ala Leu His Gln Leu Met Leu Asp Cys Trp Gln Lys Asp
    850                 855                 860

Arg Asn Ser Arg Pro Arg Phe Ala Glu Ile Val Asn Thr Leu Asp Lys
865                 870                 875                 880

Met Ile Arg Asn Pro Ala Ser Leu Lys Thr Val Ala Thr Ile Thr Ala
                885                 890                 895

Val Pro Ser Gln Pro Leu Leu Asp Arg Ser Ile Pro Asp Phe Thr Ala
            900                 905                 910

Phe Thr Thr Val Asp Asp Trp Leu Ser Ala Ile Lys Met Val Gln Tyr
        915                 920                 925

Arg Asp Ser Phe Leu Thr Ala Gly Phe Thr Ser Leu Gln Leu Val Thr
    930                 935                 940

Gln Met Thr Ser Glu Asp Leu Leu Arg Ile Gly Ile Thr Leu Ala Gly
945                 950                 955                 960

His Gln Lys Lys Ile Leu Asn Ser Ile His Ser Met Arg Val Gln Ile
                965                 970                 975

Ser Gln Ser Pro Thr Ala Met Ala
            980
```

<210> 425
<211> 1055

<212> PRT
<213> Homo sapiens

<400> 425

```
Met Ala Leu Arg Arg Leu Gly Ala Ala Leu Leu Leu Leu Pro Leu Leu
1               5                  10                  15

Ala Ala Val Glu Glu Thr Leu Met Asp Ser Thr Thr Ala Thr Ala Glu
            20                  25                  30

Leu Gly Trp Met Val His Pro Pro Ser Gly Trp Glu Glu Val Ser Gly
        35                  40                  45

Tyr Asp Glu Asn Met Asn Thr Ile Arg Thr Tyr Gln Val Cys Asn Val
    50                  55                  60

Phe Glu Ser Ser Gln Asn Asn Trp Leu Arg Thr Lys Phe Ile Arg Arg
65                  70                  75                  80

Arg Gly Ala His Arg Ile His Val Glu Met Lys Phe Ser Val Arg Asp
                85                  90                  95

Cys Ser Ser Ile Pro Ser Val Pro Gly Ser Cys Lys Glu Thr Phe Asn
            100                 105                 110

Leu Tyr Tyr Tyr Glu Ala Asp Phe Asp Ser Ala Thr Lys Thr Phe Pro
        115                 120                 125

Asn Trp Met Glu Asn Pro Trp Val Lys Val Asp Thr Ile Ala Ala Asp
    130                 135                 140

Glu Ser Phe Ser Gln Val Asp Leu Gly Gly Arg Val Met Lys Ile Asn
145                 150                 155                 160

Thr Glu Val Arg Ser Phe Gly Pro Val Ser Arg Ser Gly Phe Tyr Leu
                165                 170                 175

Ala Phe Gln Asp Tyr Gly Gly Cys Met Ser Leu Ile Ala Val Arg Val
            180                 185                 190

Phe Tyr Arg Lys Cys Pro Arg Ile Ile Gln Asn Gly Ala Ile Phe Gln
        195                 200                 205

Glu Thr Leu Ser Gly Ala Glu Ser Thr Ser Leu Val Ala Ala Arg Gly
    210                 215                 220

Ser Cys Ile Ala Asn Ala Glu Glu Val Asp Val Pro Ile Lys Leu Tyr
225                 230                 235                 240

Cys Asn Gly Asp Gly Glu Trp Leu Val Pro Ile Gly Arg Cys Met Cys
                245                 250                 255
```

```
Lys Ala Gly Phe Glu Ala Val Glu Asn Gly Thr Val Cys Arg Gly Cys
            260                 265                 270

Pro Ser Gly Thr Phe Lys Ala Asn Gln Gly Asp Glu Ala Cys Thr His
        275                 280                 285

Cys Pro Ile Asn Ser Arg Thr Thr Ser Glu Gly Ala Thr Asn Cys Val
    290                 295                 300

Cys Arg Asn Gly Tyr Tyr Arg Ala Asp Leu Asp Pro Leu Asp Met Pro
305                 310                 315                 320

Cys Thr Thr Ile Pro Ser Ala Pro Gln Ala Val Ile Ser Ser Val Asn
                325                 330                 335

Glu Thr Ser Leu Met Leu Glu Trp Thr Pro Pro Arg Asp Ser Gly Gly
            340                 345                 350

Arg Glu Asp Leu Val Tyr Asn Ile Ile Cys Lys Ser Cys Gly Ser Gly
        355                 360                 365

Arg Gly Ala Cys Thr Arg Cys Gly Asp Asn Val Gln Tyr Ala Pro Arg
    370                 375                 380

Gln Leu Gly Leu Thr Glu Pro Arg Ile Tyr Ile Ser Asp Leu Leu Ala
385                 390                 395                 400

His Thr Gln Tyr Thr Phe Glu Ile Gln Ala Val Asn Gly Val Thr Asp
                405                 410                 415

Gln Ser Pro Phe Ser Pro Gln Phe Ala Ser Val Asn Ile Thr Thr Asn
            420                 425                 430

Gln Ala Ala Pro Ser Ala Val Ser Ile Met His Gln Val Ser Arg Thr
        435                 440                 445

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

Val Ile Leu Asp Tyr Glu Leu Gln Tyr Tyr Glu Lys Glu Leu Ser Glu
465                 470                 475                 480

Tyr Asn Ala Thr Ala Ile Lys Ser Pro Thr Asn Thr Val Thr Val Gln
                485                 490                 495

Gly Leu Lys Ala Gly Ala Ile Tyr Val Phe Gln Val Arg Ala Arg Thr
            500                 505                 510

Val Ala Gly Tyr Gly Arg Tyr Ser Gly Lys Met Tyr Phe Gln Thr Met
        515                 520                 525
```

```
Thr Glu Ala Glu Tyr Gln Thr Ser Ile Gln Glu Lys Leu Pro Leu Ile
    530                 535                 540

Ile Gly Ser Ser Ala Ala Gly Leu Val Phe Leu Ile Ala Val Val Val
545                 550                 555                 560

Ile Ala Ile Val Cys Asn Arg Arg Gly Phe Glu Arg Ala Asp Ser Glu
                565                 570                 575

Tyr Thr Asp Lys Leu Gln His Tyr Thr Ser Gly His Met Thr Pro Gly
            580                 585                 590

Met Lys Ile Tyr Ile Asp Pro Phe Thr Tyr Glu Asp Pro Asn Glu Ala
        595                 600                 605

Val Arg Glu Phe Ala Lys Glu Ile Asp Ile Ser Cys Val Lys Ile Glu
    610                 615                 620

Gln Val Ile Gly Ala Gly Glu Phe Gly Glu Val Cys Ser Gly His Leu
625                 630                 635                 640

Lys Leu Pro Gly Lys Arg Glu Ile Phe Val Ala Ile Lys Thr Leu Lys
                645                 650                 655

Ser Gly Tyr Thr Glu Lys Gln Arg Arg Asp Phe Leu Ser Glu Ala Ser
            660                 665                 670

Ile Met Gly Gln Phe Asp His Pro Asn Val Ile His Leu Glu Gly Val
        675                 680                 685

Val Thr Lys Ser Thr Pro Val Met Ile Ile Thr Glu Phe Met Glu Asn
    690                 695                 700

Gly Ser Leu Asp Ser Phe Leu Arg Gln Asn Asp Gly Gln Phe Thr Val
705                 710                 715                 720

Ile Gln Leu Val Gly Met Leu Arg Gly Ile Ala Ala Gly Met Lys Tyr
                725                 730                 735

Leu Ala Asp Met Asn Tyr Val His Arg Asp Leu Ala Ala Arg Asn Ile
            740                 745                 750

Leu Val Asn Ser Asn Leu Val Cys Lys Val Ser Asp Phe Gly Leu Ser
        755                 760                 765

Arg Phe Leu Glu Asp Asp Thr Ser Asp Pro Thr Tyr Thr Ser Ala Leu
    770                 775                 780

Gly Gly Lys Ile Pro Ile Arg Trp Thr Ala Pro Glu Ala Ile Gln Tyr
785                 790                 795                 800
```

```
Arg Lys Phe Thr Ser Ala Ser Asp Val Trp Ser Tyr Gly Ile Val Met
                805                 810                 815

Trp Glu Val Met Ser Tyr Gly Glu Arg Pro Tyr Trp Asp Met Thr Asn
            820                 825                 830

Gln Asp Val Ile Asn Ala Ile Glu Gln Asp Tyr Arg Leu Pro Pro Pro
        835                 840                 845

Met Asp Cys Pro Ser Ala Leu His Gln Leu Met Leu Asp Cys Trp Gln
    850                 855                 860

Lys Asp Arg Asn His Arg Pro Lys Phe Gly Gln Ile Val Asn Thr Leu
865                 870                 875                 880

Asp Lys Met Ile Arg Asn Pro Asn Ser Leu Lys Ala Met Ala Pro Leu
                885                 890                 895

Ser Ser Gly Ile Asn Leu Pro Leu Leu Asp Arg Thr Ile Pro Asp Tyr
            900                 905                 910

Thr Ser Phe Asn Thr Val Asp Glu Trp Leu Glu Ala Ile Lys Met Gly
        915                 920                 925

Gln Tyr Lys Glu Ser Phe Ala Asn Ala Gly Phe Thr Ser Phe Asp Val
    930                 935                 940

Val Ser Gln Met Met Met Glu Asp Ile Leu Arg Val Gly Val Thr Leu
945                 950                 955                 960

Ala Gly His Gln Lys Lys Ile Leu Asn Ser Ile Gln Val Met Arg Ala
                965                 970                 975

Gln Met Asn Gln Ile Gln Ser Val Glu Gly Gln Pro Leu Ala Arg Arg
            980                 985                 990

Pro Arg Ala Thr Gly Arg Thr Lys  Arg Cys Gln Pro Arg  Asp Val Thr
        995                 1000                1005

Lys Lys  Thr Cys Asn Ser Asn  Asp Gly Lys Lys Lys  Gly Met Gly
    1010                1015                1020

Lys Lys  Lys Thr Asp Pro Gly  Arg Gly Arg Glu Ile  Gln Gly Ile
    1025                1030                1035

Phe Phe  Lys Glu Asp Ser His  Lys Glu Ser Asn Asp  Cys Ser Cys
    1040                1045                1050

Gly Gly
    1055
```

<210> 426
<211> 998
<212> PRT
<213> Homo sapiens

<400> 426

```
Met Ala Arg Ala Arg Pro Pro Pro Pro Pro Ser Pro Pro Pro Gly Leu
1               5                   10                  15

Leu Pro Leu Leu Pro Pro Leu Leu Leu Leu Pro Leu Leu Leu Leu Pro
            20                  25                  30

Ala Gly Cys Arg Ala Leu Glu Glu Thr Leu Met Asp Thr Lys Trp Val
        35                  40                  45

Thr Ser Glu Leu Ala Trp Thr Ser His Pro Glu Ser Gly Trp Glu Glu
    50                  55                  60

Val Ser Gly Tyr Asp Glu Ala Met Asn Pro Ile Arg Thr Tyr Gln Val
65                  70                  75                  80

Cys Asn Val Arg Glu Ser Ser Gln Asn Asn Trp Leu Arg Thr Gly Phe
                85                  90                  95

Ile Trp Arg Arg Asp Val Gln Arg Val Tyr Val Glu Leu Lys Phe Thr
            100                 105                 110

Val Arg Asp Cys Asn Ser Ile Pro Asn Ile Pro Gly Ser Cys Lys Glu
        115                 120                 125

Thr Phe Asn Leu Phe Tyr Tyr Glu Ala Asp Ser Asp Val Ala Ser Ala
    130                 135                 140

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

Ala Pro Asp Glu Ser Phe Ser Arg Leu Asp Ala Gly Arg Val Asn Thr
                165                 170                 175

Lys Val Arg Ser Phe Gly Pro Leu Ser Lys Ala Gly Phe Tyr Leu Ala
            180                 185                 190

Phe Gln Asp Gln Gly Ala Cys Met Ser Leu Ile Ser Val Arg Ala Phe
        195                 200                 205

Tyr Lys Lys Cys Ala Ser Thr Thr Ala Gly Phe Ala Leu Phe Pro Glu
    210                 215                 220

Thr Leu Thr Gly Ala Glu Pro Thr Ser Leu Val Ile Ala Pro Gly Thr
225                 230                 235                 240
```

```
Cys Ile Pro Asn Ala Val Glu Val Ser Val Pro Leu Lys Leu Tyr Cys
                245                 250                 255

Asn Gly Asp Gly Glu Trp Met Val Pro Val Gly Ala Cys Thr Cys Ala
            260                 265                 270

Thr Gly His Glu Pro Ala Ala Lys Glu Ser Gln Cys Arg Pro Cys Pro
        275                 280                 285

Pro Gly Ser Tyr Lys Ala Lys Gln Gly Glu Gly Pro Cys Leu Pro Cys
    290                 295                 300

Pro Pro Asn Ser Arg Thr Thr Ser Pro Ala Ala Ser Ile Cys Thr Cys
305                 310                 315                 320

His Asn Asn Phe Tyr Arg Ala Asp Ser Asp Ser Ala Asp Ser Ala Cys
                325                 330                 335

Thr Thr Val Pro Ser Pro Pro Arg Gly Val Ile Ser Asn Val Asn Glu
            340                 345                 350

Thr Ser Leu Ile Leu Glu Trp Ser Glu Pro Arg Asp Leu Gly Gly Arg
        355                 360                 365

Asp Asp Leu Leu Tyr Asn Val Ile Cys Lys Lys Cys His Gly Ala Gly
    370                 375                 380

Gly Ala Ser Ala Cys Ser Arg Cys Asp Asp Asn Val Glu Phe Val Pro
385                 390                 395                 400

Arg Gln Leu Gly Leu Thr Glu Arg Arg Val His Ile Ser His Leu Leu
                405                 410                 415

Ala His Thr Arg Tyr Thr Phe Glu Val Gln Ala Val Asn Gly Val Ser
            420                 425                 430

Gly Lys Ser Pro Leu Pro Pro Arg Tyr Ala Ala Val Asn Ile Thr Thr
        435                 440                 445

Asn Gln Ala Ala Pro Ser Glu Val Pro Thr Leu Arg Leu His Ser Ser
    450                 455                 460

Ser Gly Ser Ser Leu Thr Leu Ser Trp Ala Pro Pro Glu Arg Pro Asn
465                 470                 475                 480

Gly Val Ile Leu Asp Tyr Glu Met Lys Tyr Phe Glu Lys Ser Glu Gly
                485                 490                 495

Ile Ala Ser Thr Val Thr Ser Gln Met Asn Ser Val Gln Leu Asp Gly
            500                 505                 510
```

```
Leu Arg Pro Asp Ala Arg Tyr Val Val Gln Val Arg Ala Arg Thr Val
        515                 520                 525

Ala Gly Tyr Gly Gln Tyr Ser Arg Pro Ala Glu Phe Glu Thr Thr Ser
    530                 535                 540

Glu Arg Gly Ser Gly Ala Gln Gln Leu Gln Glu Gln Leu Pro Leu Ile
545                 550                 555                 560

Val Gly Ser Ala Thr Ala Gly Leu Val Phe Val Val Ala Val Val Val
                565                 570                 575

Ile Ala Ile Val Cys Leu Arg Lys Gln Arg His Gly Ser Asp Ser Glu
            580                 585                 590

Tyr Thr Glu Lys Leu Gln Gln Tyr Ile Ala Pro Gly Met Lys Val Tyr
        595                 600                 605

Ile Asp Pro Phe Thr Tyr Glu Asp Pro Asn Glu Ala Val Arg Glu Phe
    610                 615                 620

Ala Lys Glu Ile Asp Val Ser Cys Val Lys Ile Glu Glu Val Ile Gly
625                 630                 635                 640

Ala Gly Glu Phe Gly Glu Val Cys Arg Gly Arg Leu Lys Gln Pro Gly
                645                 650                 655

Arg Arg Glu Val Phe Val Ala Ile Lys Thr Leu Lys Val Gly Tyr Thr
            660                 665                 670

Glu Arg Gln Arg Arg Asp Phe Leu Ser Glu Ala Ser Ile Met Gly Gln
        675                 680                 685

Phe Asp His Pro Asn Ile Ile Arg Leu Glu Gly Val Val Thr Lys Ser
    690                 695                 700

Arg Pro Val Met Ile Leu Thr Glu Phe Met Glu Asn Cys Ala Leu Asp
705                 710                 715                 720

Ser Phe Leu Arg Leu Asn Asp Gly Gln Phe Thr Val Ile Gln Leu Val
                725                 730                 735

Gly Met Leu Arg Gly Ile Ala Ala Gly Met Lys Tyr Leu Ser Glu Met
            740                 745                 750

Asn Tyr Val His Arg Asp Leu Ala Ala Arg Asn Ile Leu Val Asn Ser
        755                 760                 765

Asn Leu Val Cys Lys Val Ser Asp Phe Gly Leu Ser Arg Phe Leu Glu
    770                 775                 780
```

```
Asp Asp Pro Ser Asp Pro Thr Tyr Thr Ser Ser Leu Gly Gly Lys Ile
785                 790                 795                 800

Pro Ile Arg Trp Thr Ala Pro Glu Ala Ile Ala Tyr Arg Lys Phe Thr
                805                 810                 815

Ser Ala Ser Asp Val Trp Ser Tyr Gly Ile Val Met Trp Glu Val Met
            820                 825                 830

Ser Tyr Gly Glu Arg Pro Tyr Trp Asp Met Ser Asn Gln Asp Val Ile
        835                 840                 845

Asn Ala Val Glu Gln Asp Tyr Arg Leu Pro Pro Pro Met Asp Cys Pro
    850                 855                 860

Thr Ala Leu His Gln Leu Met Leu Asp Cys Trp Val Arg Asp Arg Asn
865                 870                 875                 880

Leu Arg Pro Lys Phe Ser Gln Ile Val Asn Thr Leu Asp Lys Leu Ile
                885                 890                 895

Arg Asn Ala Ala Ser Leu Lys Val Ile Ala Ser Ala Gln Ser Gly Met
            900                 905                 910

Ser Gln Pro Leu Leu Asp Arg Thr Val Pro Asp Tyr Thr Thr Phe Thr
        915                 920                 925

Thr Val Gly Asp Trp Leu Asp Ala Ile Lys Met Gly Arg Tyr Lys Glu
    930                 935                 940

Ser Phe Val Ser Ala Gly Phe Ala Ser Phe Asp Leu Val Ala Gln Met
945                 950                 955                 960

Thr Ala Glu Asp Leu Leu Arg Ile Gly Val Thr Leu Ala Gly His Gln
                965                 970                 975

Lys Lys Ile Leu Ser Ser Ile Gln Asp Met Arg Leu Gln Met Asn Gln
            980                 985                 990

Thr Leu Pro Val Gln Val
        995


<210>  427
<211>  987
<212>  PRT
<213>  Homo sapiens

<400>  427

Met Glu Leu Arg Val Leu Leu Cys Trp Ala Ser Leu Ala Ala Ala Leu
1               5                   10                  15

Glu Glu Thr Leu Leu Asn Thr Lys Leu Glu Thr Ala Asp Leu Lys Trp
```

20 25 30

Val Thr Phe Pro Gln Val Asp Gly Gln Trp Glu Glu Leu Ser Gly Leu
35 40 45

Asp Glu Glu Gln His Ser Val Arg Thr Tyr Glu Val Cys Asp Val Gln
50 55 60

Arg Ala Pro Gly Gln Ala His Trp Leu Arg Thr Gly Trp Val Pro Arg
65 70 75 80

Arg Gly Ala Val His Val Tyr Ala Thr Leu Arg Phe Thr Met Leu Glu
85 90 95

Cys Leu Ser Leu Pro Arg Ala Gly Arg Ser Cys Lys Glu Thr Phe Thr
100 105 110

Val Phe Tyr Tyr Glu Ser Asp Ala Asp Thr Ala Thr Ala Leu Thr Pro
115 120 125

Ala Trp Met Glu Asn Pro Tyr Ile Lys Val Asp Thr Val Ala Ala Glu
130 135 140

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

Val Lys Thr Leu Arg Leu Gly Pro Leu Ser Lys Ala Gly Phe Tyr Leu
165 170 175

Ala Phe Gln Asp Gln Gly Ala Cys Met Ala Leu Leu Ser Leu His Leu
180 185 190

Phe Tyr Lys Lys Cys Ala Gln Leu Thr Val Asn Leu Thr Arg Phe Pro
195 200 205

Glu Thr Val Pro Arg Glu Leu Val Val Pro Val Ala Gly Ser Cys Val
210 215 220

Val Asp Ala Val Pro Ala Pro Gly Pro Ser Pro Ser Leu Tyr Cys Arg
225 230 235 240

Glu Asp Gly Gln Trp Ala Glu Gln Pro Val Thr Gly Cys Ser Cys Ala
245 250 255

Pro Gly Phe Glu Ala Ala Glu Gly Asn Thr Lys Cys Arg Ala Cys Ala
260 265 270

Gln Gly Thr Phe Lys Pro Leu Ser Gly Glu Gly Ser Cys Gln Pro Cys
275 280 285

Pro Ala Asn Ser His Ser Asn Thr Ile Gly Ser Ala Val Cys Gln Cys

290 295 300

Arg Val Gly Tyr Phe Arg Ala Arg Thr Asp Pro Arg Gly Ala Pro Cys
305 310 315 320

Thr Thr Pro Pro Ser Ala Pro Arg Ser Val Val Ser Arg Leu Asn Gly
325 330 335

Ser Ser Leu His Leu Glu Trp Ser Ala Pro Leu Glu Ser Gly Gly Arg
340 345 350

Glu Asp Leu Thr Tyr Ala Leu Arg Cys Arg Glu Cys Arg Pro Gly Gly
355 360 365

Ser Cys Ala Pro Cys Gly Gly Asp Leu Thr Phe Asp Pro Gly Pro Arg
370 375 380

Asp Leu Val Glu Pro Trp Val Val Val Arg Gly Leu Arg Pro Asp Phe
385 390 395 400

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

Thr Gly Pro Val Pro Phe Glu Pro Val Asn Val Thr Thr Asp Arg Glu
420 425 430

Val Pro Pro Ala Val Ser Asp Ile Arg Val Thr Arg Ser Ser Pro Ser
435 440 445

Ser Leu Ser Leu Ala Trp Ala Val Pro Arg Ala Pro Ser Gly Ala Val
450 455 460

Leu Asp Tyr Glu Val Lys Tyr His Glu Lys Gly Ala Glu Gly Pro Ser
465 470 475 480

Ser Val Arg Phe Leu Lys Thr Ser Glu Asn Arg Ala Glu Leu Arg Gly
485 490 495

Leu Lys Arg Gly Ala Ser Tyr Leu Val Gln Val Arg Ala Arg Ser Glu
500 505 510

Ala Gly Tyr Gly Pro Phe Gly Gln Glu His His Ser Gln Thr Gln Leu
515 520 525

Asp Glu Ser Glu Gly Trp Arg Glu Gln Leu Ala Leu Ile Ala Gly Thr
530 535 540

Ala Val Val Gly Val Val Leu Val Leu Val Val Ile Val Val Ala Val
545 550 555 560

Leu Cys Leu Arg Lys Gln Ser Asn Gly Arg Glu Ala Glu Tyr Ser Asp

565 570 575

Lys His Gly Gln Tyr Leu Ile Gly His Gly Thr Lys Val Tyr Ile Asp
580 585 590

Pro Phe Thr Tyr Glu Asp Pro Asn Glu Ala Val Arg Glu Phe Ala Lys
595 600 605

Glu Ile Asp Val Ser Tyr Val Lys Ile Glu Glu Val Ile Gly Ala Gly
610 615 620

Glu Phe Gly Glu Val Cys Arg Gly Arg Leu Lys Ala Pro Gly Lys Lys
625 630 635 640

Glu Ser Cys Val Ala Ile Lys Thr Leu Lys Gly Gly Tyr Thr Glu Arg
645 650 655

Gln Arg Arg Glu Phe Leu Ser Glu Ala Ser Ile Met Gly Gln Phe Glu
660 665 670

His Pro Asn Ile Ile Arg Leu Glu Gly Val Val Thr Asn Ser Met Pro
675 680 685

Val Met Ile Leu Thr Glu Phe Met Glu Asn Gly Ala Leu Asp Ser Phe
690 695 700

Leu Arg Leu Asn Asp Gly Gln Phe Thr Val Ile Gln Leu Val Gly Met
705 710 715 720

Leu Arg Gly Ile Ala Ser Gly Met Arg Tyr Leu Ala Glu Met Ser Tyr
725 730 735

Val His Arg Asp Leu Ala Ala Arg Asn Ile Leu Val Asn Ser Asn Leu
740 745 750

Val Cys Lys Val Ser Asp Phe Gly Leu Ser Arg Phe Leu Glu Glu Asn
755 760 765

Ser Ser Asp Pro Thr Tyr Thr Ser Ser Leu Gly Gly Lys Ile Pro Ile
770 775 780

Arg Trp Thr Ala Pro Glu Ala Ile Ala Phe Arg Lys Phe Thr Ser Ala
785 790 795 800

Ser Asp Ala Trp Ser Tyr Gly Ile Val Met Trp Glu Val Met Ser Phe
805 810 815

Gly Glu Arg Pro Tyr Trp Asp Met Ser Asn Gln Asp Val Ile Asn Ala
820 825 830

Ile Glu Gln Asp Tyr Arg Leu Pro Pro Pro Pro Asp Cys Pro Thr Ser

835 840 845

Leu His Gln Leu Met Leu Asp Cys Trp Gln Lys Asp Arg Asn Ala Arg
850 855 860

Pro Arg Phe Pro Gln Val Val Ser Ala Leu Asp Lys Met Ile Arg Asn
865 870 875 880

Pro Ala Ser Leu Lys Ile Val Ala Arg Glu Asn Gly Gly Ala Ser His
885 890 895

Pro Leu Leu Asp Gln Arg Gln Pro His Tyr Ser Ala Phe Gly Ser Val
900 905 910

Gly Glu Trp Leu Arg Ala Ile Lys Met Gly Arg Tyr Glu Glu Ser Phe
915 920 925

Ala Ala Ala Gly Phe Gly Ser Phe Glu Leu Val Ser Gln Ile Ser Ala
930 935 940

Glu Asp Leu Leu Arg Ile Gly Val Thr Leu Ala Gly His Gln Lys Lys
945 950 955 960

Ile Leu Ala Ser Val Gln His Met Lys Ser Gln Ala Lys Pro Gly Thr
965 970 975

Pro Gly Gly Thr Gly Gly Pro Ala Pro Gln Tyr
980 985

<210> 428
<211> 1022
<212> PRT
<213> Homo sapiens

<400> 428

Met Ala Thr Glu Gly Ala Ala Gln Leu Gly Asn Arg Val Ala Gly Met
1 5 10 15

Val Cys Ser Leu Trp Val Leu Leu Leu Val Ser Ser Val Leu Ala Leu
20 25 30

Glu Glu Val Leu Leu Asp Thr Thr Gly Glu Thr Ser Glu Ile Gly Trp
35 40 45

Leu Thr Tyr Pro Pro Gly Gly Trp Asp Glu Val Ser Val Leu Asp Asp
50 55 60

Gln Arg Arg Leu Thr Arg Thr Phe Glu Ala Cys His Val Ala Gly Ala
65 70 75 80

Pro Pro Gly Thr Gly Gln Asp Asn Trp Leu Gln Thr His Phe Val Glu
85 90 95

```
Arg Arg Gly Ala Gln Arg Ala His Ile Arg Leu His Phe Ser Val Arg
            100                 105                 110

Ala Cys Ser Ser Leu Gly Val Ser Gly Gly Thr Cys Arg Glu Thr Phe
        115                 120                 125

Thr Leu Tyr Tyr Arg Gln Ala Glu Glu Pro Asp Ser Pro Asp Ser Val
    130                 135                 140

Ser Ser Trp His Leu Lys Arg Trp Thr Lys Val Asp Thr Ile Ala Ala
145                 150                 155                 160

Asp Glu Ser Phe Pro Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser
                165                 170                 175

Ser Ala Ala Trp Ala Val Gly Pro His Gly Ala Gly Gln Arg Ala Gly
            180                 185                 190

Leu Gln Leu Asn Val Lys Glu Arg Ser Phe Gly Pro Leu Thr Gln Arg
        195                 200                 205

Gly Phe Tyr Val Ala Phe Gln Asp Thr Gly Ala Cys Leu Ala Leu Val
    210                 215                 220

Ala Val Arg Leu Phe Ser Tyr Thr Cys Pro Ala Val Leu Arg Ser Phe
225                 230                 235                 240

Ala Ser Phe Pro Glu Thr Gln Ala Ser Gly Ala Gly Gly Ala Ser Leu
                245                 250                 255

Val Ala Ala Val Gly Thr Cys Val Ala His Ala Glu Pro Glu Glu Asp
            260                 265                 270

Gly Val Gly Gly Gln Ala Gly Gly Ser Pro Pro Arg Leu His Cys Asn
        275                 280                 285

Gly Glu Gly Lys Trp Met Val Ala Val Gly Gly Cys Arg Cys Gln Pro
    290                 295                 300

Gly Tyr Gln Pro Ala Arg Gly Asp Lys Ala Cys Gln Ala Cys Pro Arg
305                 310                 315                 320

Gly Leu Tyr Lys Ala Ser Ala Gly Asn Ala Pro Cys Ser Pro Cys Pro
                325                 330                 335

Ala Arg Ser His Ala Pro Asn Pro Ala Ala Pro Val Cys Pro Cys Leu
            340                 345                 350

Glu Gly Phe Tyr Arg Ala Ser Ser Asp Pro Pro Glu Ala Pro Cys Thr
        355                 360                 365
```

```
Gly Pro Pro Ser Ala Pro Gln Glu Leu Trp Phe Glu Val Gln Gly Ser
    370                 375                 380

Ala Leu Met Leu His Trp Arg Leu Pro Arg Glu Leu Gly Gly Arg Gly
385                 390                 395                 400

Asp Leu Leu Phe Asn Val Val Cys Lys Glu Cys Glu Gly Arg Gln Glu
                405                 410                 415

Pro Ala Ser Gly Gly Gly Gly Thr Cys His Arg Cys Arg Asp Glu Val
            420                 425                 430

His Phe Asp Pro Arg Gln Arg Gly Leu Thr Glu Ser Arg Val Leu Val
        435                 440                 445

Gly Gly Leu Arg Ala His Val Pro Tyr Ile Leu Glu Val Gln Ala Val
    450                 455                 460

Asn Gly Val Ser Glu Leu Ser Pro Asp Pro Pro Gln Ala Ala Ala Ile
465                 470                 475                 480

Asn Val Ser Thr Ser His Glu Val Pro Ser Ala Val Pro Val Val His
                485                 490                 495

Gln Val Ser Arg Ala Ser Asn Ser Ile Thr Val Ser Trp Pro Gln Pro
            500                 505                 510

Asp Gln Thr Asn Gly Asn Ile Leu Asp Tyr Gln Leu Arg Tyr Tyr Asp
        515                 520                 525

Gln Ala Glu Asp Glu Ser His Ser Phe Thr Leu Thr Ser Glu Thr Asn
    530                 535                 540

Thr Ala Thr Val Thr Gln Leu Ser Pro Gly His Ile Tyr Gly Phe Gln
545                 550                 555                 560

Val Arg Ala Arg Thr Ala Ala Gly His Gly Pro Tyr Gly Gly Lys Val
                565                 570                 575

Tyr Phe Gln Thr Leu Pro Gln Gly Glu Leu Ser Ser Gln Leu Pro Glu
            580                 585                 590

Arg Leu Ser Leu Val Ile Gly Ser Ile Leu Gly Ala Leu Ala Phe Leu
        595                 600                 605

Leu Leu Ala Ala Ile Thr Val Leu Ala Val Val Phe Gln Arg Lys Arg
    610                 615                 620

Arg Gly Thr Gly Tyr Thr Glu Gln Leu Gln Gln Tyr Ser Ser Pro Gly
625                 630                 635                 640
```

```
Leu Gly Val Lys Tyr Tyr Ile Asp Pro Ser Thr Tyr Glu Asp Pro Cys
                645                 650                 655

Gln Ala Ile Arg Glu Leu Ala Arg Glu Val Asp Pro Ala Tyr Ile Lys
            660                 665                 670

Ile Glu Glu Val Ile Gly Thr Gly Ser Phe Gly Glu Val Arg Gln Gly
        675                 680                 685

Arg Leu Gln Pro Arg Gly Arg Arg Glu Gln Thr Val Ala Ile Gln Ala
    690                 695                 700

Leu Trp Ala Gly Gly Ala Glu Ser Leu Gln Met Thr Phe Leu Gly Arg
705                 710                 715                 720

Ala Ala Val Leu Gly Gln Phe Gln His Pro Asn Ile Leu Arg Leu Glu
                725                 730                 735

Gly Val Val Thr Lys Ser Arg Pro Leu Met Val Leu Thr Glu Phe Met
            740                 745                 750

Glu Leu Gly Pro Leu Asp Ser Phe Leu Arg Gln Arg Glu Gly Gln Phe
        755                 760                 765

Ser Ser Leu Gln Leu Val Ala Met Gln Arg Gly Val Ala Ala Ala Met
    770                 775                 780

Gln Tyr Leu Ser Ser Phe Ala Phe Val His Arg Ser Leu Ser Ala His
785                 790                 795                 800

Ser Val Leu Val Asn Ser His Leu Val Cys Lys Val Ala Arg Leu Gly
                805                 810                 815

His Ser Pro Gln Gly Pro Ser Cys Leu Leu Arg Trp Ala Ala Pro Glu
            820                 825                 830

Val Ile Ala His Gly Lys His Thr Thr Ser Ser Asp Val Trp Ser Phe
        835                 840                 845

Gly Ile Leu Met Trp Glu Val Met Ser Tyr Gly Glu Arg Pro Tyr Trp
    850                 855                 860

Asp Met Ser Glu Gln Glu Val Leu Asn Ala Ile Glu Gln Glu Phe Arg
865                 870                 875                 880

Leu Pro Pro Pro Pro Gly Cys Pro Pro Gly Leu His Leu Leu Met Leu
                885                 890                 895

Asp Thr Trp Gln Lys Asp Arg Ala Arg Arg Pro His Phe Asp Gln Leu
            900                 905                 910
```

Val Ala Ala Phe Asp Lys Met Ile Arg Lys Pro Asp Thr Leu Gln Ala
915 920 925

Gly Gly Asp Pro Gly Glu Arg Pro Ser Gln Ala Leu Leu Thr Pro Val
930 935 940

Ala Leu Asp Phe Pro Cys Leu Asp Ser Pro Gln Ala Trp Leu Ser Ala
945 950 955 960

Ile Gly Leu Glu Cys Tyr Gln Asp Asn Phe Ser Lys Phe Gly Leu Cys
965 970 975

Thr Phe Ser Asp Val Ala Gln Leu Ser Leu Glu Asp Leu Pro Ala Leu
980 985 990

Gly Ile Thr Leu Ala Gly His Gln Lys Lys Leu Leu His His Ile Gln
995 1000 1005

Leu Leu Gln Gln His Leu Arg Gln Gln Gly Ser Val Glu Val
1010 1015 1020

<210> 429
<211> 1255
<212> PRT
<213> Homo sapiens

<400> 429

Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Leu Ala Leu Leu
1 5 10 15

Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys
20 25 30

Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
35 40 45

Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
50 55 60

Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
65 70 75 80

Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu
85 90 95

Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr
100 105 110

Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro
115 120 125

```
Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser
    130                 135                 140

Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln
145                 150                 155                 160

Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn
                165                 170                 175

Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys
            180                 185                 190

His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser
        195                 200                 205

Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys
    210                 215                 220

Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys
225                 230                 235                 240

Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu
                245                 250                 255

His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val
            260                 265                 270

Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg
        275                 280                 285

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

Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln
305                 310                 315                 320

Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys
                325                 330                 335

Pro Cys Ala Arg Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg Glu
            340                 345                 350

Val Arg Ala Val Thr Ser Ala Asn Ile Gln Glu Phe Ala Gly Cys Lys
        355                 360                 365

Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser Phe Asp Gly Asp
    370                 375                 380

Pro Ala Ser Asn Thr Ala Pro Leu Gln Pro Glu Gln Leu Gln Val Phe
385                 390                 395                 400
```

```
Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro
                405                 410                 415

Asp Ser Leu Pro Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg
            420                 425                 430

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

Gly Ile Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly
    450                 455                 460

Leu Ala Leu Ile His His Asn Thr His Leu Cys Phe Val His Thr Val
465                 470                 475                 480

Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His Thr
                485                 490                 495

Ala Asn Arg Pro Glu Asp Glu Cys Val Gly Glu Gly Leu Ala Cys His
            500                 505                 510

Gln Leu Cys Ala Arg Gly His Cys Trp Gly Pro Gly Pro Thr Gln Cys
        515                 520                 525

Val Asn Cys Ser Gln Phe Leu Arg Gly Gln Glu Cys Val Glu Glu Cys
    530                 535                 540

Arg Val Leu Gln Gly Leu Pro Arg Glu Tyr Val Asn Ala Arg His Cys
545                 550                 555                 560

Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Gly Ser Val Thr Cys
                565                 570                 575

Phe Gly Pro Glu Ala Asp Gln Cys Val Ala Cys Ala His Tyr Lys Asp
            580                 585                 590

Pro Pro Phe Cys Val Ala Arg Cys Pro Ser Gly Val Lys Pro Asp Leu
        595                 600                 605

Ser Tyr Met Pro Ile Trp Lys Phe Pro Asp Glu Glu Gly Ala Cys Gln
    610                 615                 620

Pro Cys Pro Ile Asn Cys Thr His Ser Cys Val Asp Leu Asp Asp Lys
625                 630                 635                 640

Gly Cys Pro Ala Glu Gln Arg Ala Ser Pro Leu Thr Ser Ile Ile Ser
                645                 650                 655

Ala Val Val Gly Ile Leu Leu Val Val Val Leu Gly Val Val Phe Gly
            660                 665                 670
```

```
Ile Leu Ile Lys Arg Arg Gln Gln Lys Ile Arg Lys Tyr Thr Met Arg
        675                 680                 685

Arg Leu Leu Gln Glu Thr Glu Leu Val Glu Pro Leu Thr Pro Ser Gly
    690                 695                 700

Ala Met Pro Asn Gln Ala Gln Met Arg Ile Leu Lys Glu Thr Glu Leu
705                 710                 715                 720

Arg Lys Val Lys Val Leu Gly Ser Gly Ala Phe Gly Thr Val Tyr Lys
                725                 730                 735

Gly Ile Trp Ile Pro Asp Gly Glu Asn Val Lys Ile Pro Val Ala Ile
            740                 745                 750

Lys Val Leu Arg Glu Asn Thr Ser Pro Lys Ala Asn Lys Glu Ile Leu
        755                 760                 765

Asp Glu Ala Tyr Val Met Ala Gly Val Gly Ser Pro Tyr Val Ser Arg
    770                 775                 780

Leu Leu Gly Ile Cys Leu Thr Ser Thr Val Gln Leu Val Thr Gln Leu
785                 790                 795                 800

Met Pro Tyr Gly Cys Leu Leu Asp His Val Arg Glu Asn Arg Gly Arg
                805                 810                 815

Leu Gly Ser Gln Asp Leu Leu Asn Trp Cys Met Gln Ile Ala Lys Gly
            820                 825                 830

Met Ser Tyr Leu Glu Asp Val Arg Leu Val His Arg Asp Leu Ala Ala
        835                 840                 845

Arg Asn Val Leu Val Lys Ser Pro Asn His Val Lys Ile Thr Asp Phe
    850                 855                 860

Gly Leu Ala Arg Leu Leu Asp Ile Asp Glu Thr Glu Tyr His Ala Asp
865                 870                 875                 880

Gly Gly Lys Val Pro Ile Lys Trp Met Ala Leu Glu Ser Ile Leu Arg
                885                 890                 895

Arg Arg Phe Thr His Gln Ser Asp Val Trp Ser Tyr Gly Val Thr Val
            900                 905                 910

Trp Glu Leu Met Thr Phe Gly Ala Lys Pro Tyr Asp Gly Ile Pro Ala
        915                 920                 925

Arg Glu Ile Pro Asp Leu Leu Glu Lys Gly Glu Arg Leu Pro Gln Pro
    930                 935                 940
```

```
Pro Ile Cys Thr Ile Asp Val Tyr Met Ile Met Val Lys Cys Trp Met
945                 950                 955                 960

Ile Asp Ser Glu Cys Arg Pro Arg Phe Arg Glu Leu Val Ser Glu Phe
                965                 970                 975

Ser Arg Met Ala Arg Asp Pro Gln Arg Phe Val Val Ile Gln Asn Glu
            980                 985                 990

Asp Leu Gly Pro Ala Ser Pro Leu  Asp Ser Thr Phe Tyr  Arg Ser Leu
        995                 1000                1005

Leu Glu  Asp Asp Asp Met Gly  Asp Leu Val Asp Ala  Glu Glu Tyr
    1010                1015                1020

Leu Val  Pro Gln Gln Gly Phe  Phe Cys Pro Asp Pro  Ala Pro Gly
    1025                1030                1035

Ala Gly  Gly Met Val His His  Arg His Arg Ser Ser  Ser Thr Arg
    1040                1045                1050

Ser Gly  Gly Gly Asp Leu Thr  Leu Gly Leu Glu Pro  Ser Glu Glu
    1055                1060                1065

Glu Ala  Pro Arg Ser Pro Leu  Ala Pro Ser Glu Gly  Ala Gly Ser
    1070                1075                1080

Asp Val  Phe Asp Gly Asp Leu  Gly Met Gly Ala Ala  Lys Gly Leu
    1085                1090                1095

Gln Ser  Leu Pro Thr His Asp  Pro Ser Pro Leu Gln  Arg Tyr Ser
    1100                1105                1110

Glu Asp  Pro Thr Val Pro Leu  Pro Ser Glu Thr Asp  Gly Tyr Val
    1115                1120                1125

Ala Pro  Leu Thr Cys Ser Pro  Gln Pro Glu Tyr Val  Asn Gln Pro
    1130                1135                1140

Asp Val  Arg Pro Gln Pro Pro  Ser Pro Arg Glu Gly  Pro Leu Pro
    1145                1150                1155

Ala Ala  Arg Pro Ala Gly Ala  Thr Leu Glu Arg Pro  Lys Thr Leu
    1160                1165                1170

Ser Pro  Gly Lys Asn Gly Val  Val Lys Asp Val Phe  Ala Phe Gly
    1175                1180                1185

Gly Ala  Val Glu Asn Pro Glu  Tyr Leu Thr Pro Gln  Gly Gly Ala
    1190                1195                1200
```

```
Ala Pro  Gln Pro His Pro Pro  Pro Ala Phe Ser Pro  Ala Phe Asp
    1205                1210                1215


Asn Leu  Tyr Tyr Trp Asp Gln  Asp Pro Pro Glu Arg  Gly Ala Pro
    1220                1225                1230


Pro Ser  Thr Phe Lys Gly Thr  Pro Thr Ala Glu Asn  Pro Glu Tyr
    1235                1240                1245


Leu Gly  Leu Asp Val Pro Val
    1250                1255
```

<210> 430
<211> 1342
<212> PRT
<213> Homo sapiens

<400> 430

```
Met Arg Ala Asn Asp Ala Leu Gln Val Leu Gly Leu Leu Phe Ser Leu
1               5                   10                  15


Ala Arg Gly Ser Glu Val Gly Asn Ser Gln Ala Val Cys Pro Gly Thr
            20                  25                  30


Leu Asn Gly Leu Ser Val Thr Gly Asp Ala Glu Asn Gln Tyr Gln Thr
        35                  40                  45


Leu Tyr Lys Leu Tyr Glu Arg Cys Glu Val Val Met Gly Asn Leu Glu
    50                  55                  60


Ile Val Leu Thr Gly His Asn Ala Asp Leu Ser Phe Leu Gln Trp Ile
65                  70                  75                  80


Arg Glu Val Thr Gly Tyr Val Leu Val Ala Met Asn Glu Phe Ser Thr
                85                  90                  95


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


Gly Lys Phe Ala Ile Phe Val Met Leu Asn Tyr Asn Thr Asn Ser Ser
        115                 120                 125


His Ala Leu Arg Gln Leu Arg Leu Thr Gln Leu Thr Glu Ile Leu Ser
    130                 135                 140


Gly Gly Val Tyr Ile Glu Lys Asn Asp Lys Leu Cys His Met Asp Thr
145                 150                 155                 160


Ile Asp Trp Arg Asp Ile Val Arg Asp Arg Asp Ala Glu Ile Val Val
                165                 170                 175
```

```
Lys Asp Asn Gly Arg Ser Cys Pro Pro Cys His Glu Val Cys Lys Gly
            180                 185                 190

Arg Cys Trp Gly Pro Gly Ser Glu Asp Cys Gln Thr Leu Thr Lys Thr
        195                 200                 205

Ile Cys Ala Pro Gln Cys Asn Gly His Cys Phe Gly Pro Asn Pro Asn
    210                 215                 220

Gln Cys Cys His Asp Glu Cys Ala Gly Gly Cys Ser Gly Pro Gln Asp
225                 230                 235                 240

Thr Asp Cys Phe Ala Cys Arg His Phe Asn Asp Ser Gly Ala Cys Val
                245                 250                 255

Pro Arg Cys Pro Gln Pro Leu Val Tyr Asn Lys Leu Thr Phe Gln Leu
            260                 265                 270

Glu Pro Asn Pro His Thr Lys Tyr Gln Tyr Gly Gly Val Cys Val Ala
        275                 280                 285

Ser Cys Pro His Asn Phe Val Val Asp Gln Thr Ser Cys Val Arg Ala
    290                 295                 300

Cys Pro Pro Asp Lys Met Glu Val Asp Lys Asn Gly Leu Lys Met Cys
305                 310                 315                 320

Glu Pro Cys Gly Gly Leu Cys Pro Lys Ala Cys Glu Gly Thr Gly Ser
                325                 330                 335

Gly Ser Arg Phe Gln Thr Val Asp Ser Ser Asn Ile Asp Gly Phe Val
            340                 345                 350

Asn Cys Thr Lys Ile Leu Gly Asn Leu Asp Phe Leu Ile Thr Gly Leu
        355                 360                 365

Asn Gly Asp Pro Trp His Lys Ile Pro Ala Leu Asp Pro Glu Lys Leu
    370                 375                 380

Asn Val Phe Arg Thr Val Arg Glu Ile Thr Gly Tyr Leu Asn Ile Gln
385                 390                 395                 400

Ser Trp Pro Pro His Met His Asn Phe Ser Val Phe Ser Asn Leu Thr
                405                 410                 415

Thr Ile Gly Gly Arg Ser Leu Tyr Asn Arg Gly Phe Ser Leu Leu Ile
            420                 425                 430

Met Lys Asn Leu Asn Val Thr Ser Leu Gly Phe Arg Ser Leu Lys Glu
        435                 440                 445
```

```
Ile Ser Ala Gly Arg Ile Tyr Ile Ser Ala Asn Arg Gln Leu Cys Tyr
    450                 455                 460

His His Ser Leu Asn Trp Thr Lys Val Leu Arg Gly Pro Thr Glu Glu
465                 470                 475                 480

Arg Leu Asp Ile Lys His Asn Arg Pro Arg Arg Asp Cys Val Ala Glu
                485                 490                 495

Gly Lys Val Cys Asp Pro Leu Cys Ser Ser Gly Gly Cys Trp Gly Pro
            500                 505                 510

Gly Pro Gly Gln Cys Leu Ser Cys Arg Asn Tyr Ser Arg Gly Gly Val
        515                 520                 525

Cys Val Thr His Cys Asn Phe Leu Asn Gly Glu Pro Arg Glu Phe Ala
    530                 535                 540

His Glu Ala Glu Cys Phe Ser Cys His Pro Glu Cys Gln Pro Met Glu
545                 550                 555                 560

Gly Thr Ala Thr Cys Asn Gly Ser Gly Ser Asp Thr Cys Ala Gln Cys
                565                 570                 575

Ala His Phe Arg Asp Gly Pro His Cys Val Ser Ser Cys Pro His Gly
            580                 585                 590

Val Leu Gly Ala Lys Gly Pro Ile Tyr Lys Tyr Pro Asp Val Gln Asn
        595                 600                 605

Glu Cys Arg Pro Cys His Glu Asn Cys Thr Gln Gly Cys Lys Gly Pro
    610                 615                 620

Glu Leu Gln Asp Cys Leu Gly Gln Thr Leu Val Leu Ile Gly Lys Thr
625                 630                 635                 640

His Leu Thr Met Ala Leu Thr Val Ile Ala Gly Leu Val Val Ile Phe
                645                 650                 655

Met Met Leu Gly Gly Thr Phe Leu Tyr Trp Arg Gly Arg Arg Ile Gln
            660                 665                 670

Asn Lys Arg Ala Met Arg Arg Tyr Leu Glu Arg Gly Glu Ser Ile Glu
        675                 680                 685

Pro Leu Asp Pro Ser Glu Lys Ala Asn Lys Val Leu Ala Arg Ile Phe
    690                 695                 700

Lys Glu Thr Glu Leu Arg Lys Leu Lys Val Leu Gly Ser Gly Val Phe
705                 710                 715                 720
```

```
Gly Thr Val His Lys Gly Val Trp Ile Pro Glu Gly Glu Ser Ile Lys
                725                 730                 735

Ile Pro Val Cys Ile Lys Val Ile Glu Asp Lys Ser Gly Arg Gln Ser
            740                 745                 750

Phe Gln Ala Val Thr Asp His Met Leu Ala Ile Gly Ser Leu Asp His
        755                 760                 765

Ala His Ile Val Arg Leu Leu Gly Leu Cys Pro Gly Ser Ser Leu Gln
    770                 775                 780

Leu Val Thr Gln Tyr Leu Pro Leu Gly Ser Leu Leu Asp His Val Arg
785                 790                 795                 800

Gln His Arg Gly Ala Leu Gly Pro Gln Leu Leu Leu Asn Trp Gly Val
                805                 810                 815

Gln Ile Ala Lys Gly Met Tyr Tyr Leu Glu Glu His Gly Met Val His
            820                 825                 830

Arg Asn Leu Ala Ala Arg Asn Val Leu Leu Lys Ser Pro Ser Gln Val
        835                 840                 845

Gln Val Ala Asp Phe Gly Val Ala Asp Leu Leu Pro Pro Asp Asp Lys
    850                 855                 860

Gln Leu Leu Tyr Ser Glu Ala Lys Thr Pro Ile Lys Trp Met Ala Leu
865                 870                 875                 880

Glu Ser Ile His Phe Gly Lys Tyr Thr His Gln Ser Asp Val Trp Ser
                885                 890                 895

Tyr Gly Val Thr Val Trp Glu Leu Met Thr Phe Gly Ala Glu Pro Tyr
            900                 905                 910

Ala Gly Leu Arg Leu Ala Glu Val Pro Asp Leu Leu Glu Lys Gly Glu
        915                 920                 925

Arg Leu Ala Gln Pro Gln Ile Cys Thr Ile Asp Val Tyr Met Val Met
    930                 935                 940

Val Lys Cys Trp Met Ile Asp Glu Asn Ile Arg Pro Thr Phe Lys Glu
945                 950                 955                 960

Leu Ala Asn Glu Phe Thr Arg Met Ala Arg Asp Pro Pro Arg Tyr Leu
                965                 970                 975

Val Ile Lys Arg Glu Ser Gly Pro Gly Ile Ala Pro Gly Pro Glu Pro
            980                 985                 990
```

```
His Gly Leu Thr Asn Lys Lys Leu  Glu Glu Val Glu Leu  Glu Pro Glu
        995                 1000                1005

Leu Asp  Leu Asp Leu Asp Leu  Glu Ala Glu Glu Asp  Asn Leu Ala
    1010                1015                1020

Thr Thr  Thr Leu Gly Ser Ala  Leu Ser Leu Pro Val  Gly Thr Leu
    1025                1030                1035

Asn Arg  Pro Arg Gly Ser Gln  Ser Leu Leu Ser Pro  Ser Ser Gly
    1040                1045                1050

Tyr Met  Pro Met Asn Gln Gly  Asn Leu Gly Glu Ser  Cys Gln Glu
    1055                1060                1065

Ser Ala  Val Ser Gly Ser Ser  Glu Arg Cys Pro Arg  Pro Val Ser
    1070                1075                1080

Leu His  Pro Met Pro Arg Gly  Cys Leu Ala Ser Glu  Ser Ser Glu
    1085                1090                1095

Gly His  Val Thr Gly Ser Glu  Ala Glu Leu Gln Glu  Lys Val Ser
    1100                1105                1110

Met Cys  Arg Ser Arg Ser Arg  Ser Arg Ser Pro Arg  Pro Arg Gly
    1115                1120                1125

Asp Ser  Ala Tyr His Ser Gln  Arg His Ser Leu Leu  Thr Pro Val
    1130                1135                1140

Thr Pro  Leu Ser Pro Pro Gly  Leu Glu Glu Glu Asp  Val Asn Gly
    1145                1150                1155

Tyr Val  Met Pro Asp Thr His  Leu Lys Gly Thr Pro  Ser Ser Arg
    1160                1165                1170

Glu Gly  Thr Leu Ser Ser Val  Gly Leu Ser Ser Val  Leu Gly Thr
    1175                1180                1185

Glu Glu  Glu Asp Glu Asp Glu  Glu Tyr Glu Tyr Met  Asn Arg Arg
    1190                1195                1200

Arg Arg  His Ser Pro Pro His  Pro Pro Arg Pro Ser  Ser Leu Glu
    1205                1210                1215

Glu Leu  Gly Tyr Glu Tyr Met  Asp Val Gly Ser Asp  Leu Ser Ala
    1220                1225                1230

Ser Leu  Gly Ser Thr Gln Ser  Cys Pro Leu His Pro  Val Pro Ile
    1235                1240                1245
```

Met Pro Thr Ala Gly Thr Thr Pro Asp Glu Asp Tyr Glu Tyr Met
1250 1255 1260

Asn Arg Gln Arg Asp Gly Gly Gly Pro Gly Gly Asp Tyr Ala Ala
1265 1270 1275

Met Gly Ala Cys Pro Ala Ser Glu Gln Gly Tyr Glu Glu Met Arg
1280 1285 1290

Ala Phe Gln Gly Pro Gly His Gln Ala Pro His Val His Tyr Ala
1295 1300 1305

Arg Leu Lys Thr Leu Arg Ser Leu Glu Ala Thr Asp Ser Ala Phe
1310 1315 1320

Asp Asn Pro Asp Tyr Trp His Ser Arg Leu Phe Pro Lys Ala Asn
1325 1330 1335

Ala Gln Arg Thr
1340

<210> 431
<211> 1308
<212> PRT
<213> Homo sapiens

<400> 431

Met Lys Pro Ala Thr Gly Leu Trp Val Trp Val Ser Leu Leu Val Ala
1 5 10 15

Ala Gly Thr Val Gln Pro Ser Asp Ser Gln Ser Val Cys Ala Gly Thr
20 25 30

Glu Asn Lys Leu Ser Ser Leu Ser Asp Leu Glu Gln Gln Tyr Arg Ala
35 40 45

Leu Arg Lys Tyr Tyr Glu Asn Cys Glu Val Val Met Gly Asn Leu Glu
50 55 60

Ile Thr Ser Ile Glu His Asn Arg Asp Leu Ser Phe Leu Arg Ser Val
65 70 75 80

Arg Glu Val Thr Gly Tyr Val Leu Val Ala Leu Asn Gln Phe Arg Tyr
85 90 95

Leu Pro Leu Glu Asn Leu Arg Ile Ile Arg Gly Thr Lys Leu Tyr Glu
100 105 110

Asp Arg Tyr Ala Leu Ala Ile Phe Leu Asn Tyr Arg Lys Asp Gly Asn
115 120 125

Phe Gly Leu Gln Glu Leu Gly Leu Lys Asn Leu Thr Glu Ile Leu Asn

130 135 140

Gly Gly Val Tyr Val Asp Gln Asn Lys Phe Leu Cys Tyr Ala Asp Thr
145 150 155 160

Ile His Trp Gln Asp Ile Val Arg Asn Pro Trp Pro Ser Asn Leu Thr
165 170 175

Leu Val Ser Thr Asn Gly Ser Ser Gly Cys Gly Arg Cys His Lys Ser
180 185 190

Cys Thr Gly Arg Cys Trp Gly Pro Thr Glu Asn His Cys Gln Thr Leu
195 200 205

Thr Arg Thr Val Cys Ala Glu Gln Cys Asp Gly Arg Cys Tyr Gly Pro
210 215 220

Tyr Val Ser Asp Cys Cys His Arg Glu Cys Ala Gly Gly Cys Ser Gly
225 230 235 240

Pro Lys Asp Thr Asp Cys Phe Ala Cys Met Asn Phe Asn Asp Ser Gly
245 250 255

Ala Cys Val Thr Gln Cys Pro Gln Thr Phe Val Tyr Asn Pro Thr Thr
260 265 270

Phe Gln Leu Glu His Asn Phe Asn Ala Lys Tyr Thr Tyr Gly Ala Phe
275 280 285

Cys Val Lys Lys Cys Pro His Asn Phe Val Val Asp Ser Ser Ser Cys
290 295 300

Val Arg Ala Cys Pro Ser Ser Lys Met Glu Val Glu Glu Asn Gly Ile
305 310 315 320

Lys Met Cys Lys Pro Cys Thr Asp Ile Cys Pro Lys Ala Cys Asp Gly
325 330 335

Ile Gly Thr Gly Ser Leu Met Ser Ala Gln Thr Val Asp Ser Ser Asn
340 345 350

Ile Asp Lys Phe Ile Asn Cys Thr Lys Ile Asn Gly Asn Leu Ile Phe
355 360 365

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

Asp Pro Glu Lys Leu Asn Val Phe Arg Thr Val Arg Glu Ile Thr Gly
385 390 395 400

Phe Leu Asn Ile Gln Ser Trp Pro Pro Asn Met Thr Asp Phe Ser Val

405 410 415

Phe Ser Asn Leu Val Thr Ile Gly Gly Arg Val Leu Tyr Ser Gly Leu
420 425 430

Ser Leu Leu Ile Leu Lys Gln Gln Gly Ile Thr Ser Leu Gln Phe Gln
435 440 445

Ser Leu Lys Glu Ile Ser Ala Gly Asn Ile Tyr Ile Thr Asp Asn Ser
450 455 460

Asn Leu Cys Tyr Tyr His Thr Ile Asn Trp Thr Thr Leu Phe Ser Thr
465 470 475 480

Ile Asn Gln Arg Ile Val Ile Arg Asp Asn Arg Lys Ala Glu Asn Cys
485 490 495

Thr Ala Glu Gly Met Val Cys Asn His Leu Cys Ser Ser Asp Gly Cys
500 505 510

Trp Gly Pro Gly Pro Asp Gln Cys Leu Ser Cys Arg Arg Phe Ser Arg
515 520 525

Gly Arg Ile Cys Ile Glu Ser Cys Asn Leu Tyr Asp Gly Glu Phe Arg
530 535 540

Glu Phe Glu Asn Gly Ser Ile Cys Val Glu Cys Asp Pro Gln Cys Glu
545 550 555 560

Lys Met Glu Asp Gly Leu Leu Thr Cys His Gly Pro Gly Pro Asp Asn
565 570 575

Cys Thr Lys Cys Ser His Phe Lys Asp Gly Pro Asn Cys Val Glu Lys
580 585 590

Cys Pro Asp Gly Leu Gln Gly Ala Asn Ser Phe Ile Phe Lys Tyr Ala
595 600 605

Asp Pro Asp Arg Glu Cys His Pro Cys His Pro Asn Cys Thr Gln Gly
610 615 620

Cys Asn Gly Pro Thr Ser His Asp Cys Ile Tyr Tyr Pro Trp Thr Gly
625 630 635 640

His Ser Thr Leu Pro Gln His Ala Arg Thr Pro Leu Ile Ala Ala Gly
645 650 655

Val Ile Gly Gly Leu Phe Ile Leu Val Ile Val Gly Leu Thr Phe Ala
660 665 670

Val Tyr Val Arg Arg Lys Ser Ile Lys Lys Lys Arg Ala Leu Arg Arg

675 680 685

Phe Leu Glu Thr Glu Leu Val Glu Pro Leu Thr Pro Ser Gly Thr Ala
690 695 700

Pro Asn Gln Ala Gln Leu Arg Ile Leu Lys Glu Thr Glu Leu Lys Arg
705 710 715 720

Val Lys Val Leu Gly Ser Gly Ala Phe Gly Thr Val Tyr Lys Gly Ile
725 730 735

Trp Val Pro Glu Gly Glu Thr Val Lys Ile Pro Val Ala Ile Lys Ile
740 745 750

Leu Asn Glu Thr Thr Gly Pro Lys Ala Asn Val Glu Phe Met Asp Glu
755 760 765

Ala Leu Ile Met Ala Ser Met Asp His Pro His Leu Val Arg Leu Leu
770 775 780

Gly Val Cys Leu Ser Pro Thr Ile Gln Leu Val Thr Gln Leu Met Pro
785 790 795 800

His Gly Cys Leu Leu Glu Tyr Val His Glu His Lys Asp Asn Ile Gly
805 810 815

Ser Gln Leu Leu Leu Asn Trp Cys Val Gln Ile Ala Lys Gly Met Met
820 825 830

Tyr Leu Glu Glu Arg Arg Leu Val His Arg Asp Leu Ala Ala Arg Asn
835 840 845

Val Leu Val Lys Ser Pro Asn His Val Lys Ile Thr Asp Phe Gly Leu
850 855 860

Ala Arg Leu Leu Glu Gly Asp Glu Lys Glu Tyr Asn Ala Asp Gly Gly
865 870 875 880

Lys Met Pro Ile Lys Trp Met Ala Leu Glu Cys Ile His Tyr Arg Lys
885 890 895

Phe Thr His Gln Ser Asp Val Trp Ser Tyr Gly Val Thr Ile Trp Glu
900 905 910

Leu Met Thr Phe Gly Gly Lys Pro Tyr Asp Gly Ile Pro Thr Arg Glu
915 920 925

Ile Pro Asp Leu Leu Glu Lys Gly Glu Arg Leu Pro Gln Pro Pro Ile
930 935 940

Cys Thr Ile Asp Val Tyr Met Val Met Val Lys Cys Trp Met Ile Asp

945 950 955 960

Ala Asp Ser Arg Pro Lys Phe Lys Glu Leu Ala Ala Glu Phe Ser Arg
965 970 975

Met Ala Arg Asp Pro Gln Arg Tyr Leu Val Ile Gln Gly Asp Asp Arg
980 985 990

Met Lys Leu Pro Ser Pro Asn Asp Ser Lys Phe Phe Gln Asn Leu Leu
995 1000 1005

Asp Glu Glu Asp Leu Glu Asp Met Met Asp Ala Glu Glu Tyr Leu
1010 1015 1020

Val Pro Gln Ala Phe Asn Ile Pro Pro Pro Ile Tyr Thr Ser Arg
1025 1030 1035

Ala Arg Ile Asp Ser Asn Arg Ser Glu Ile Gly His Ser Pro Pro
1040 1045 1050

Pro Ala Tyr Thr Pro Met Ser Gly Asn Gln Phe Val Tyr Arg Asp
1055 1060 1065

Gly Gly Phe Ala Ala Glu Gln Gly Val Ser Val Pro Tyr Arg Ala
1070 1075 1080

Pro Thr Ser Thr Ile Pro Glu Ala Pro Val Ala Gln Gly Ala Thr
1085 1090 1095

Ala Glu Ile Phe Asp Asp Ser Cys Cys Asn Gly Thr Leu Arg Lys
1100 1105 1110

Pro Val Ala Pro His Val Gln Glu Asp Ser Ser Thr Gln Arg Tyr
1115 1120 1125

Ser Ala Asp Pro Thr Val Phe Ala Pro Glu Arg Ser Pro Arg Gly
1130 1135 1140

Glu Leu Asp Glu Glu Gly Tyr Met Thr Pro Met Arg Asp Lys Pro
1145 1150 1155

Lys Gln Glu Tyr Leu Asn Pro Val Glu Glu Asn Pro Phe Val Ser
1160 1165 1170

Arg Arg Lys Asn Gly Asp Leu Gln Ala Leu Asp Asn Pro Glu Tyr
1175 1180 1185

His Asn Ala Ser Asn Gly Pro Pro Lys Ala Glu Asp Glu Tyr Val
1190 1195 1200

Asn Glu Pro Leu Tyr Leu Asn Thr Phe Ala Asn Thr Leu Gly Lys

1205 1210 1215

Ala Glu Tyr Leu Lys Asn Asn Ile Leu Ser Met Pro Glu Lys Ala
1220 1225 1230

Lys Lys Ala Phe Asp Asn Pro Asp Tyr Trp Asn His Ser Leu Pro
1235 1240 1245

Pro Arg Ser Thr Leu Gln His Pro Asp Tyr Leu Gln Glu Tyr Ser
1250 1255 1260

Thr Lys Tyr Phe Tyr Lys Gln Asn Gly Arg Ile Arg Pro Ile Val
1265 1270 1275

Ala Glu Asn Pro Glu Tyr Leu Ser Glu Phe Ser Leu Lys Pro Gly
1280 1285 1290

Thr Val Leu Pro Pro Pro Pro Tyr Arg His Arg Asn Thr Val Val
1295 1300 1305

<210> 432
<211> 822
<212> PRT
<213> Homo sapiens

<400> 432

Met Trp Ser Trp Lys Cys Leu Leu Phe Trp Ala Val Leu Val Thr Ala
1 5 10 15

Thr Leu Cys Thr Ala Arg Pro Ser Pro Thr Leu Pro Glu Gln Ala Gln
20 25 30

Pro Trp Gly Ala Pro Val Glu Val Glu Ser Phe Leu Val His Pro Gly
35 40 45

Asp Leu Leu Gln Leu Arg Cys Arg Leu Arg Asp Asp Val Gln Ser Ile
50 55 60

Asn Trp Leu Arg Asp Gly Val Gln Leu Ala Glu Ser Asn Arg Thr Arg
65 70 75 80

Ile Thr Gly Glu Glu Val Glu Val Gln Asp Ser Val Pro Ala Asp Ser
85 90 95

Gly Leu Tyr Ala Cys Val Thr Ser Ser Pro Ser Gly Ser Asp Thr Thr
100 105 110

Tyr Phe Ser Val Asn Val Ser Asp Ala Leu Pro Ser Ser Glu Asp Asp
115 120 125

Asp Asp Asp Asp Asp Ser Ser Ser Glu Glu Lys Glu Thr Asp Asn Thr
130 135 140

```
Lys Pro Asn Arg Met Pro Val Ala Pro Tyr Trp Thr Ser Pro Glu Lys
145                 150                 155                 160

Met Glu Lys Lys Leu His Ala Val Pro Ala Ala Lys Thr Val Lys Phe
                165                 170                 175

Lys Cys Pro Ser Ser Gly Thr Pro Asn Pro Thr Leu Arg Trp Leu Lys
            180                 185                 190

Asn Gly Lys Glu Phe Lys Pro Asp His Arg Ile Gly Gly Tyr Lys Val
        195                 200                 205

Arg Tyr Ala Thr Trp Ser Ile Ile Met Asp Ser Val Val Pro Ser Asp
    210                 215                 220

Lys Gly Asn Tyr Thr Cys Ile Val Glu Asn Glu Tyr Gly Ser Ile Asn
225                 230                 235                 240

His Thr Tyr Gln Leu Asp Val Val Glu Arg Ser Pro His Arg Pro Ile
                245                 250                 255

Leu Gln Ala Gly Leu Pro Ala Asn Lys Thr Val Ala Leu Gly Ser Asn
            260                 265                 270

Val Glu Phe Met Cys Lys Val Tyr Ser Asp Pro Gln Pro His Ile Gln
        275                 280                 285

Trp Leu Lys His Ile Glu Val Asn Gly Ser Lys Ile Gly Pro Asp Asn
    290                 295                 300

Leu Pro Tyr Val Gln Ile Leu Lys Thr Ala Gly Val Asn Thr Thr Asp
305                 310                 315                 320

Lys Glu Met Glu Val Leu His Leu Arg Asn Val Ser Phe Glu Asp Ala
                325                 330                 335

Gly Glu Tyr Thr Cys Leu Ala Gly Asn Ser Ile Gly Leu Ser His His
            340                 345                 350

Ser Ala Trp Leu Thr Val Leu Glu Ala Leu Glu Glu Arg Pro Ala Val
        355                 360                 365

Met Thr Ser Pro Leu Tyr Leu Glu Ile Ile Ile Tyr Cys Thr Gly Ala
    370                 375                 380

Phe Leu Ile Ser Cys Met Val Gly Ser Val Ile Val Tyr Lys Met Lys
385                 390                 395                 400

Ser Gly Thr Lys Lys Ser Asp Phe His Ser Gln Met Ala Val His Lys
                405                 410                 415
```

```
Leu Ala Lys Ser Ile Pro Leu Arg Arg Gln Val Thr Val Ser Ala Asp
            420                 425                 430

Ser Ser Ala Ser Met Asn Ser Gly Val Leu Leu Val Arg Pro Ser Arg
        435                 440                 445

Leu Ser Ser Ser Gly Thr Pro Met Leu Ala Gly Val Ser Glu Tyr Glu
    450                 455                 460

Leu Pro Glu Asp Pro Arg Trp Glu Leu Pro Arg Asp Arg Leu Val Leu
465                 470                 475                 480

Gly Lys Pro Leu Gly Glu Gly Cys Phe Gly Gln Val Val Leu Ala Glu
                485                 490                 495

Ala Ile Gly Leu Asp Lys Asp Lys Pro Asn Arg Val Thr Lys Val Ala
            500                 505                 510

Val Lys Met Leu Lys Ser Asp Ala Thr Glu Lys Asp Leu Ser Asp Leu
        515                 520                 525

Ile Ser Glu Met Glu Met Met Lys Met Ile Gly Lys His Lys Asn Ile
    530                 535                 540

Ile Asn Leu Leu Gly Ala Cys Thr Gln Asp Gly Pro Leu Tyr Val Ile
545                 550                 555                 560

Val Glu Tyr Ala Ser Lys Gly Asn Leu Arg Glu Tyr Leu Gln Ala Arg
                565                 570                 575

Arg Pro Pro Gly Leu Glu Tyr Cys Tyr Asn Pro Ser His Asn Pro Glu
            580                 585                 590

Glu Gln Leu Ser Ser Lys Asp Leu Val Ser Cys Ala Tyr Gln Val Ala
        595                 600                 605

Arg Gly Met Glu Tyr Leu Ala Ser Lys Lys Cys Ile His Arg Asp Leu
    610                 615                 620

Ala Ala Arg Asn Val Leu Val Thr Glu Asp Asn Val Met Lys Ile Ala
625                 630                 635                 640

Asp Phe Gly Leu Ala Arg Asp Ile His His Ile Asp Tyr Tyr Lys Lys
                645                 650                 655

Thr Thr Asn Gly Arg Leu Pro Val Lys Trp Met Ala Pro Glu Ala Leu
            660                 665                 670

Phe Asp Arg Ile Tyr Thr His Gln Ser Asp Val Trp Ser Phe Gly Val
        675                 680                 685
```

```
Leu Leu Trp Glu Ile Phe Thr Leu Gly Gly Ser Pro Tyr Pro Gly Val
    690                 695                 700

Pro Val Glu Glu Leu Phe Lys Leu Leu Lys Glu Gly His Arg Met Asp
705                 710                 715                 720

Lys Pro Ser Asn Cys Thr Asn Glu Leu Tyr Met Met Met Arg Asp Cys
                725                 730                 735

Trp His Ala Val Pro Ser Gln Arg Pro Thr Phe Lys Gln Leu Val Glu
            740                 745                 750

Asp Leu Asp Arg Ile Val Ala Leu Thr Ser Asn Gln Glu Tyr Leu Asp
        755                 760                 765

Leu Ser Met Pro Leu Asp Gln Tyr Ser Pro Ser Phe Pro Asp Thr Arg
    770                 775                 780

Ser Ser Thr Cys Ser Ser Gly Glu Asp Ser Val Phe Ser His Glu Pro
785                 790                 795                 800

Leu Pro Glu Glu Pro Cys Leu Pro Arg His Pro Ala Gln Leu Ala Asn
                805                 810                 815

Gly Gly Leu Lys Arg Arg
            820
```

<210> 433
<211> 806
<212> PRT
<213> Homo sapiens

<400> 433

```
Met Gly Ala Pro Ala Cys Ala Leu Ala Leu Cys Val Ala Val Ala Ile
1               5                   10                  15

Val Ala Gly Ala Ser Ser Glu Ser Leu Gly Thr Glu Gln Arg Val Val
            20                  25                  30

Gly Arg Ala Ala Glu Val Pro Gly Pro Glu Pro Gly Gln Gln Glu Gln
        35                  40                  45

Leu Val Phe Gly Ser Gly Asp Ala Val Glu Leu Ser Cys Pro Pro Pro
    50                  55                  60

Gly Gly Gly Pro Met Gly Pro Thr Val Trp Val Lys Asp Gly Thr Gly
65                  70                  75                  80

Leu Val Pro Ser Glu Arg Val Leu Val Gly Pro Gln Arg Leu Gln Val
                85                  90                  95
```

```
Leu Asn Ala Ser His Glu Asp Ser Gly Ala Tyr Ser Cys Arg Gln Arg
            100                 105                 110

Leu Thr Gln Arg Val Leu Cys His Phe Ser Val Arg Val Thr Asp Ala
        115                 120                 125

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

Gly Val Asp Thr Gly Ala Pro Tyr Trp Thr Arg Pro Glu Arg Met Asp
145                 150                 155                 160

Lys Lys Leu Leu Ala Val Pro Ala Ala Asn Thr Val Arg Phe Arg Cys
                165                 170                 175

Pro Ala Ala Gly Asn Pro Thr Pro Ser Ile Ser Trp Leu Lys Asn Gly
            180                 185                 190

Arg Glu Phe Arg Gly Glu His Arg Ile Gly Gly Ile Lys Leu Arg His
        195                 200                 205

Gln Gln Trp Ser Leu Val Met Glu Ser Val Val Pro Ser Asp Arg Gly
    210                 215                 220

Asn Tyr Thr Cys Val Val Glu Asn Lys Phe Gly Ser Ile Arg Gln Thr
225                 230                 235                 240

Tyr Thr Leu Asp Val Leu Glu Arg Ser Pro His Arg Pro Ile Leu Gln
                245                 250                 255

Ala Gly Leu Pro Ala Asn Gln Thr Ala Val Leu Gly Ser Asp Val Glu
            260                 265                 270

Phe His Cys Lys Val Tyr Ser Asp Ala Gln Pro His Ile Gln Trp Leu
        275                 280                 285

Lys His Val Glu Val Asn Gly Ser Lys Val Gly Pro Asp Gly Thr Pro
    290                 295                 300

Tyr Val Thr Val Leu Lys Thr Ala Gly Ala Asn Thr Thr Asp Lys Glu
305                 310                 315                 320

Leu Glu Val Leu Ser Leu His Asn Val Thr Phe Glu Asp Ala Gly Glu
                325                 330                 335

Tyr Thr Cys Leu Ala Gly Asn Ser Ile Gly Phe Ser His His Ser Ala
            340                 345                 350

Trp Leu Val Val Leu Pro Ala Glu Glu Glu Leu Val Glu Ala Asp Glu
        355                 360                 365
```

```
Ala Gly Ser Val Tyr Ala Gly Ile Leu Ser Tyr Gly Val Gly Phe Phe
    370                 375                 380

Leu Phe Ile Leu Val Val Ala Ala Val Thr Leu Cys Arg Leu Arg Ser
385                 390                 395                 400

Pro Pro Lys Lys Gly Leu Gly Ser Pro Thr Val His Lys Ile Ser Arg
                405                 410                 415

Phe Pro Leu Lys Arg Gln Val Ser Leu Glu Ser Asn Ala Ser Met Ser
            420                 425                 430

Ser Asn Thr Pro Leu Val Arg Ile Ala Arg Leu Ser Ser Gly Glu Gly
        435                 440                 445

Pro Thr Leu Ala Asn Val Ser Glu Leu Glu Leu Pro Ala Asp Pro Lys
    450                 455                 460

Trp Glu Leu Ser Arg Ala Arg Leu Thr Leu Gly Lys Pro Leu Gly Glu
465                 470                 475                 480

Gly Cys Phe Gly Gln Val Val Met Ala Glu Ala Ile Gly Ile Asp Lys
                485                 490                 495

Asp Arg Ala Ala Lys Pro Val Thr Val Ala Val Lys Met Leu Lys Asp
            500                 505                 510

Asp Ala Thr Asp Lys Asp Leu Ser Asp Leu Val Ser Glu Met Glu Met
        515                 520                 525

Met Lys Met Ile Gly Lys His Lys Asn Ile Ile Asn Leu Leu Gly Ala
    530                 535                 540

Cys Thr Gln Gly Gly Pro Leu Tyr Val Leu Val Glu Tyr Ala Ala Lys
545                 550                 555                 560

Gly Asn Leu Arg Glu Phe Leu Arg Ala Arg Arg Pro Pro Gly Leu Asp
                565                 570                 575

Tyr Ser Phe Asp Thr Cys Lys Pro Pro Glu Glu Gln Leu Thr Phe Lys
            580                 585                 590

Asp Leu Val Ser Cys Ala Tyr Gln Val Ala Arg Gly Met Glu Tyr Leu
        595                 600                 605

Ala Ser Gln Lys Cys Ile His Arg Asp Leu Ala Ala Arg Asn Val Leu
    610                 615                 620

Val Thr Glu Asp Asn Val Met Lys Ile Ala Asp Phe Gly Leu Ala Arg
625                 630                 635                 640
```

```
Asp Val His Asn Leu Asp Tyr Tyr Lys Lys Thr Thr Asn Gly Arg Leu
                645                 650                 655

Pro Val Lys Trp Met Ala Pro Glu Ala Leu Phe Asp Arg Val Tyr Thr
            660                 665                 670

His Gln Ser Asp Val Trp Ser Phe Gly Val Leu Leu Trp Glu Ile Phe
        675                 680                 685

Thr Leu Gly Gly Ser Pro Tyr Pro Gly Ile Pro Val Glu Glu Leu Phe
    690                 695                 700

Lys Leu Leu Lys Glu Gly His Arg Met Asp Lys Pro Ala Asn Cys Thr
705                 710                 715                 720

His Asp Leu Tyr Met Ile Met Arg Glu Cys Trp His Ala Ala Pro Ser
                725                 730                 735

Gln Arg Pro Thr Phe Lys Gln Leu Val Glu Asp Leu Asp Arg Val Leu
            740                 745                 750

Thr Val Thr Ser Thr Asp Glu Tyr Leu Asp Leu Ser Ala Pro Phe Glu
        755                 760                 765

Gln Tyr Ser Pro Gly Gly Gln Asp Thr Pro Ser Ser Ser Ser Ser Gly
    770                 775                 780

Asp Asp Ser Val Phe Ala His Asp Leu Leu Pro Pro Ala Pro Pro Ser
785                 790                 795                 800

Ser Gly Gly Ser Arg Thr
                805
```

<210> 434
<211> 821
<212> PRT
<213> Homo sapiens

<400> 434

```
Met Val Ser Trp Gly Arg Phe Ile Cys Leu Val Val Val Thr Met Ala
1               5                   10                  15

Thr Leu Ser Leu Ala Arg Pro Ser Phe Ser Leu Val Glu Asp Thr Thr
            20                  25                  30

Leu Glu Pro Glu Glu Pro Pro Thr Lys Tyr Gln Ile Ser Gln Pro Glu
        35                  40                  45

Val Tyr Val Ala Ala Pro Gly Glu Ser Leu Glu Val Arg Cys Leu Leu
    50                  55                  60
```

```
Lys Asp Ala Ala Val Ile Ser Trp Thr Lys Asp Gly Val His Leu Gly
65                  70                  75                  80

Pro Asn Asn Arg Thr Val Leu Ile Gly Glu Tyr Leu Gln Ile Lys Gly
                85                  90                  95

Ala Thr Pro Arg Asp Ser Gly Leu Tyr Ala Cys Thr Ala Ser Arg Thr
            100                 105                 110

Val Asp Ser Glu Thr Trp Tyr Phe Met Val Asn Val Thr Asp Ala Ile
        115                 120                 125

Ser Ser Gly Asp Asp Glu Asp Asp Thr Asp Gly Ala Glu Asp Phe Val
    130                 135                 140

Ser Glu Asn Ser Asn Asn Lys Arg Ala Pro Tyr Trp Thr Asn Thr Glu
145                 150                 155                 160

Lys Met Glu Lys Arg Leu His Ala Val Pro Ala Ala Asn Thr Val Lys
                165                 170                 175

Phe Arg Cys Pro Ala Gly Gly Asn Pro Met Pro Thr Met Arg Trp Leu
            180                 185                 190

Lys Asn Gly Lys Glu Phe Lys Gln Glu His Arg Ile Gly Gly Tyr Lys
        195                 200                 205

Val Arg Asn Gln His Trp Ser Leu Ile Met Glu Ser Val Val Pro Ser
    210                 215                 220

Asp Lys Gly Asn Tyr Thr Cys Val Val Glu Asn Glu Tyr Gly Ser Ile
225                 230                 235                 240

Asn His Thr Tyr His Leu Asp Val Val Glu Arg Ser Pro His Arg Pro
                245                 250                 255

Ile Leu Gln Ala Gly Leu Pro Ala Asn Ala Ser Thr Val Val Gly Gly
            260                 265                 270

Asp Val Glu Phe Val Cys Lys Val Tyr Ser Asp Ala Gln Pro His Ile
        275                 280                 285

Gln Trp Ile Lys His Val Glu Lys Asn Gly Ser Lys Tyr Gly Pro Asp
    290                 295                 300

Gly Leu Pro Tyr Leu Lys Val Leu Lys Ala Ala Gly Val Asn Thr Thr
305                 310                 315                 320

Asp Lys Glu Ile Glu Val Leu Tyr Ile Arg Asn Val Thr Phe Glu Asp
                325                 330                 335
```

```
Ala Gly Glu Tyr Thr Cys Leu Ala Gly Asn Ser Ile Gly Ile Ser Phe
            340                 345                 350

His Ser Ala Trp Leu Thr Val Leu Pro Ala Pro Gly Arg Glu Lys Glu
        355                 360                 365

Ile Thr Ala Ser Pro Asp Tyr Leu Glu Ile Ala Ile Tyr Cys Ile Gly
    370                 375                 380

Val Phe Leu Ile Ala Cys Met Val Val Thr Val Ile Leu Cys Arg Met
385                 390                 395                 400

Lys Asn Thr Thr Lys Lys Pro Asp Phe Ser Ser Gln Pro Ala Val His
                405                 410                 415

Lys Leu Thr Lys Arg Ile Pro Leu Arg Arg Gln Val Thr Val Ser Ala
            420                 425                 430

Glu Ser Ser Ser Ser Met Asn Ser Asn Thr Pro Leu Val Arg Ile Thr
        435                 440                 445

Thr Arg Leu Ser Ser Thr Ala Asp Thr Pro Met Leu Ala Gly Val Ser
    450                 455                 460

Glu Tyr Glu Leu Pro Glu Asp Pro Lys Trp Glu Phe Pro Arg Asp Lys
465                 470                 475                 480

Leu Thr Leu Gly Lys Pro Leu Gly Glu Gly Cys Phe Gly Gln Val Val
                485                 490                 495

Met Ala Glu Ala Val Gly Ile Asp Lys Asp Lys Pro Lys Glu Ala Val
            500                 505                 510

Thr Val Ala Val Lys Met Leu Lys Asp Asp Ala Thr Glu Lys Asp Leu
        515                 520                 525

Ser Asp Leu Val Ser Glu Met Glu Met Met Lys Met Ile Gly Lys His
    530                 535                 540

Lys Asn Ile Ile Asn Leu Leu Gly Ala Cys Thr Gln Asp Gly Pro Leu
545                 550                 555                 560

Tyr Val Ile Val Glu Tyr Ala Ser Lys Gly Asn Leu Arg Glu Tyr Leu
                565                 570                 575

Arg Ala Arg Arg Pro Pro Gly Met Glu Tyr Ser Tyr Asp Ile Asn Arg
            580                 585                 590

Val Pro Glu Glu Gln Met Thr Phe Lys Asp Leu Val Ser Cys Thr Tyr
        595                 600                 605
```

Gln Leu Ala Arg Gly Met Glu Tyr Leu Ala Ser Gln Lys Cys Ile His
610 615 620

Arg Asp Leu Ala Ala Arg Asn Val Leu Val Thr Glu Asn Asn Val Met
625 630 635 640

Lys Ile Ala Asp Phe Gly Leu Ala Arg Asp Ile Asn Asn Ile Asp Tyr
645 650 655

Tyr Lys Lys Thr Thr Asn Gly Arg Leu Pro Val Lys Trp Met Ala Pro
660 665 670

Glu Ala Leu Phe Asp Arg Val Tyr Thr His Gln Ser Asp Val Trp Ser
675 680 685

Phe Gly Val Leu Met Trp Glu Ile Phe Thr Leu Gly Gly Ser Pro Tyr
690 695 700

Pro Gly Ile Pro Val Glu Glu Leu Phe Lys Leu Leu Lys Glu Gly His
705 710 715 720

Arg Met Asp Lys Pro Ala Asn Cys Thr Asn Glu Leu Tyr Met Met Met
725 730 735

Arg Asp Cys Trp His Ala Val Pro Ser Gln Arg Pro Thr Phe Lys Gln
740 745 750

Leu Val Glu Asp Leu Asp Arg Ile Leu Thr Leu Thr Thr Asn Glu Glu
755 760 765

Tyr Leu Asp Leu Ser Gln Pro Leu Glu Gln Tyr Ser Pro Ser Tyr Pro
770 775 780

Asp Thr Arg Ser Ser Cys Ser Ser Gly Asp Asp Ser Val Phe Ser Pro
785 790 795 800

Asp Pro Met Pro Tyr Glu Pro Cys Leu Pro Gln Tyr Pro His Ile Asn
805 810 815

Gly Ser Val Lys Thr
820

<210> 435
<211> 802
<212> PRT
<213> Homo sapiens

<400> 435

Met Arg Leu Leu Leu Ala Leu Leu Gly Val Leu Leu Ser Val Pro Gly
1 5 10 15

Pro Pro Val Leu Ser Leu Glu Ala Ser Glu Glu Val Glu Leu Glu Pro

```
            20                  25                  30

Cys Leu Ala Pro Ser Leu Glu Gln Gln Glu Gln Glu Leu Thr Val Ala
        35                  40                  45

Leu Gly Gln Pro Val Arg Leu Cys Cys Gly Arg Ala Glu Arg Gly Gly
    50                  55                  60

His Trp Tyr Lys Glu Gly Ser Arg Leu Ala Pro Ala Gly Arg Val Arg
65                  70                  75                  80

Gly Trp Arg Gly Arg Leu Glu Ile Ala Ser Phe Leu Pro Glu Asp Ala
                85                  90                  95

Gly Arg Tyr Leu Cys Leu Ala Arg Gly Ser Met Ile Val Leu Gln Asn
            100                 105                 110

Leu Thr Leu Ile Thr Gly Asp Ser Leu Thr Ser Ser Asn Asp Asp Glu
        115                 120                 125

Asp Pro Lys Ser His Arg Asp Pro Ser Asn Arg His Ser Tyr Pro Gln
    130                 135                 140

Gln Ala Pro Tyr Trp Thr His Pro Gln Arg Met Glu Lys Lys Leu His
145                 150                 155                 160

Ala Val Pro Ala Gly Asn Thr Val Lys Phe Arg Cys Pro Ala Ala Gly
                165                 170                 175

Asn Pro Thr Pro Thr Ile Arg Trp Leu Lys Asp Gly Gln Ala Phe His
            180                 185                 190

Gly Glu Asn Arg Ile Gly Gly Ile Arg Leu Arg His Gln His Trp Ser
        195                 200                 205

Leu Val Met Glu Ser Val Val Pro Ser Asp Arg Gly Thr Tyr Thr Cys
    210                 215                 220

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

Val Leu Glu Arg Ser Pro His Arg Pro Ile Leu Gln Ala Gly Leu Pro
                245                 250                 255

Ala Asn Thr Thr Ala Val Val Gly Ser Asp Val Glu Leu Leu Cys Lys
            260                 265                 270

Val Tyr Ser Asp Ala Gln Pro His Ile Gln Trp Leu Lys His Ile Val
        275                 280                 285

Ile Asn Gly Ser Ser Phe Gly Ala Asp Gly Phe Pro Tyr Val Gln Val
```

290 295 300

Leu Lys Thr Ala Asp Ile Asn Ser Ser Glu Val Glu Val Leu Tyr Leu
305 310 315 320

Arg Asn Val Ser Ala Glu Asp Ala Gly Glu Tyr Thr Cys Leu Ala Gly
325 330 335

Asn Ser Ile Gly Leu Ser Tyr Gln Ser Ala Trp Leu Thr Val Leu Pro
340 345 350

Glu Glu Asp Pro Thr Trp Thr Ala Ala Ala Pro Glu Ala Arg Tyr Thr
355 360 365

Asp Ile Ile Leu Tyr Ala Ser Gly Ser Leu Ala Leu Ala Val Leu Leu
370 375 380

Leu Leu Ala Gly Leu Tyr Arg Gly Gln Ala Leu His Gly Arg His Pro
385 390 395 400

Arg Pro Pro Ala Thr Val Gln Lys Leu Ser Arg Phe Pro Leu Ala Arg
405 410 415

Gln Phe Ser Leu Glu Ser Gly Ser Ser Gly Lys Ser Ser Ser Ser Leu
420 425 430

Val Arg Gly Val Arg Leu Ser Ser Ser Gly Pro Ala Leu Leu Ala Gly
435 440 445

Leu Val Ser Leu Asp Leu Pro Leu Asp Pro Leu Trp Glu Phe Pro Arg
450 455 460

Asp Arg Leu Val Leu Gly Lys Pro Leu Gly Glu Gly Cys Phe Gly Gln
465 470 475 480

Val Val Arg Ala Glu Ala Phe Gly Met Asp Pro Ala Arg Pro Asp Gln
485 490 495

Ala Ser Thr Val Ala Val Lys Met Leu Lys Asp Asn Ala Ser Asp Lys
500 505 510

Asp Leu Ala Asp Leu Val Ser Glu Met Glu Val Met Lys Leu Ile Gly
515 520 525

Arg His Lys Asn Ile Ile Asn Leu Leu Gly Val Cys Thr Gln Glu Gly
530 535 540

Pro Leu Tyr Val Ile Val Glu Cys Ala Ala Lys Gly Asn Leu Arg Glu
545 550 555 560

Phe Leu Arg Ala Arg Arg Pro Pro Gly Pro Asp Leu Ser Pro Asp Gly

565 570 575

Pro Arg Ser Ser Glu Gly Pro Leu Ser Phe Pro Val Leu Val Ser Cys
580 585 590

Ala Tyr Gln Val Ala Arg Gly Met Gln Tyr Leu Glu Ser Arg Lys Cys
595 600 605

Ile His Arg Asp Leu Ala Ala Arg Asn Val Leu Val Thr Glu Asp Asn
610 615 620

Val Met Lys Ile Ala Asp Phe Gly Leu Ala Arg Gly Val His His Ile
625 630 635 640

Asp Tyr Tyr Lys Lys Thr Ser Asn Gly Arg Leu Pro Val Lys Trp Met
645 650 655

Ala Pro Glu Ala Leu Phe Asp Arg Val Tyr Thr His Gln Ser Asp Val
660 665 670

Trp Ser Phe Gly Ile Leu Leu Trp Glu Ile Phe Thr Leu Gly Gly Ser
675 680 685

Pro Tyr Pro Gly Ile Pro Val Glu Glu Leu Phe Ser Leu Leu Arg Glu
690 695 700

Gly His Arg Met Asp Arg Pro Pro His Cys Pro Pro Glu Leu Tyr Gly
705 710 715 720

Leu Met Arg Glu Cys Trp His Ala Ala Pro Ser Gln Arg Pro Thr Phe
725 730 735

Lys Gln Leu Val Glu Ala Leu Asp Lys Val Leu Leu Ala Val Ser Glu
740 745 750

Glu Tyr Leu Asp Leu Arg Leu Thr Phe Gly Pro Tyr Ser Pro Ser Gly
755 760 765

Gly Asp Ala Ser Ser Thr Cys Ser Ser Ser Asp Ser Val Phe Ser His
770 775 780

Asp Pro Leu Pro Leu Gly Ser Ser Ser Phe Pro Phe Gly Ser Gly Val
785 790 795 800

Gln Thr

<210> 436
<211> 1503
<212> PRT
<213> Homo sapiens

<400> 436

Met Pro Gly Pro Pro Ala Leu Arg Arg Arg Leu Leu Leu Leu Leu Leu
1 5 10 15

Val Leu Leu Ile Ala Gly Ser Ala Gly Ala Ala Pro Leu Pro Gln Thr
20 25 30

Gly Ala Gly Glu Ala Pro Pro Ala Ala Glu Val Ser Ser Ser Phe Val
35 40 45

Ile Leu Cys Val Cys Ser Leu Ile Ile Leu Ile Val Leu Ile Ala Asn
50 55 60

Cys Val Ser Cys Cys Lys Asp Pro Glu Ile Asp Phe Lys Glu Phe Glu
65 70 75 80

Asp Asn Phe Asp Asp Glu Ile Asp Phe Thr Pro Pro Ala Glu Asp Thr
85 90 95

Pro Ser Val Gln Ser Pro Ala Glu Val Phe Thr Leu Ser Val Pro Asn
100 105 110

Ile Ser Leu Pro Ala Pro Ser Gln Phe Gln Pro Ser Val Glu Gly Leu
115 120 125

Lys Ser Gln Val Ala Arg His Ser Leu Asn Tyr Ile Gln Glu Ile Gly
130 135 140

Asn Gly Trp Phe Gly Lys Val Leu Leu Gly Glu Ile Tyr Thr Gly Thr
145 150 155 160

Ser Val Ala Arg Val Ile Val Lys Glu Leu Lys Ala Ser Ala Asn Pro
165 170 175

Lys Glu Gln Asp Thr Phe Leu Lys Asn Gly Glu Pro Tyr Tyr Ile Leu
180 185 190

Gln His Pro Asn Ile Leu Gln Cys Val Gly Gln Cys Val Glu Ala Ile
195 200 205

Pro Tyr Leu Leu Val Phe Glu Phe Cys Asp Leu Gly Asp Leu Lys Ala
210 215 220

Tyr Leu Arg Ser Glu Gln Glu His Met Arg Gly Asp Ser Gln Thr Met
225 230 235 240

Leu Leu Gln Arg Met Ala Cys Glu Val Ala Ala Gly Leu Ala Ala Met
245 250 255

His Lys Leu His Phe Leu His Ser Asp Leu Ala Leu Arg Asn Cys Phe
260 265 270

```
Leu Thr Ser Asp Leu Asn Val Lys Val Gly Asp Tyr Gly Ile Gly Phe
        275                 280                 285

Ser Arg Tyr Lys Glu Asp Tyr Ile Glu Thr Asp Asp Lys Lys Val Phe
    290                 295                 300

Pro Leu Arg Trp Thr Ala Pro Glu Leu Val Thr Ser Phe Gln Asp Arg
305                 310                 315                 320

Leu Leu Thr Ala Asp Gln Thr Lys Tyr Ser Asn Ile Trp Ser Leu Gly
                325                 330                 335

Val Thr Leu Trp Glu Leu Phe Asp Asn Ala Ala Gln Pro Tyr Ser Asn
            340                 345                 350

Leu Ser Asn Leu Asp Val Leu Asn Gln Val Ile Arg Glu Arg Asp Thr
        355                 360                 365

Lys Leu Pro Lys Pro Gln Leu Glu Gln Pro Tyr Ser Asp Arg Trp Tyr
    370                 375                 380

Glu Val Leu Gln Phe Cys Trp Leu Ser Pro Glu Lys Arg Pro Ala Ala
385                 390                 395                 400

Glu Asp Val His Arg Leu Leu Thr Tyr Leu Arg Leu Gln Ser Gln Arg
                405                 410                 415

Asp Ser Glu Val Asp Phe Glu Gln Gln Trp Asn Ala Leu Lys Pro Asn
            420                 425                 430

Thr Asn Ser Arg Asp Ser Ser Asn Asn Ala Ala Phe Pro Ile Leu Asp
        435                 440                 445

His Phe Ala Arg Asp Arg Leu Gly Arg Glu Met Glu Glu Val Leu Thr
    450                 455                 460

Val Thr Glu Thr Ser Gln Gly Leu Ser Phe Glu Tyr Val Trp Glu Ala
465                 470                 475                 480

Ala Lys His Asp His Phe Asp Glu Arg Ser Arg Gly His Leu Asp Glu
                485                 490                 495

Gly Leu Ser Tyr Thr Ser Ile Phe Tyr Pro Val Glu Val Phe Glu Ser
            500                 505                 510

Ser Leu Ser Asp Pro Gly Pro Gly Lys Gln Asp Asp Ser Gly Gln Asp
        515                 520                 525

Val Pro Leu Arg Val Pro Gly Val Val Pro Val Phe Asp Ala His Asn
    530                 535                 540
```

```
Leu Ser Val Gly Ser Asp Tyr Tyr Ile Gln Leu Glu Glu Lys Ser Gly
545                 550                 555                 560

Ser Asn Leu Glu Leu Asp Tyr Pro Pro Ala Leu Leu Thr Thr Asp Met
                565                 570                 575

Asp Asn Pro Glu Arg Thr Gly Pro Glu Leu Ser Gln Leu Thr Ala Leu
            580                 585                 590

Arg Ser Val Glu Leu Glu Glu Ser Ser Thr Asp Glu Asp Phe Phe Gln
        595                 600                 605

Ser Ser Thr Asp Pro Lys Asp Ser Ser Leu Pro Gly Asp Leu His Val
    610                 615                 620

Thr Ser Gly Pro Glu Ser Pro Phe Asn Asn Ile Phe Asn Asp Val Asp
625                 630                 635                 640

Lys Ser Glu Asp Leu Pro Ser His Gln Lys Ile Phe Asp Leu Met Glu
                645                 650                 655

Leu Asn Gly Val Gln Ala Asp Phe Lys Pro Ala Thr Leu Ser Ser Ser
            660                 665                 670

Leu Asp Asn Pro Lys Glu Ser Val Ile Thr Gly His Phe Glu Lys Glu
        675                 680                 685

Lys Pro Arg Lys Ile Phe Asp Ser Glu Pro Leu Cys Leu Ser Asp Asn
    690                 695                 700

Leu Met His Gln Asp Asn Phe Asp Pro Leu Asn Val Gln Glu Leu Ser
705                 710                 715                 720

Glu Asn Phe Leu Phe Leu Gln Glu Lys Asn Leu Leu Lys Gly Ser Leu
                725                 730                 735

Ser Ser Lys Glu His Ile Asn Asp Leu Gln Thr Glu Leu Lys Asn Ala
            740                 745                 750

Gly Phe Thr Glu Ala Met Leu Glu Thr Ser Cys Arg Asn Ser Leu Asp
        755                 760                 765

Thr Glu Leu Gln Phe Ala Glu Asn Lys Pro Gly Leu Ser Leu Leu Gln
    770                 775                 780

Glu Asn Val Ser Thr Lys Gly Asp Asp Thr Asp Val Met Leu Thr Gly
785                 790                 795                 800

Asp Thr Leu Ser Thr Ser Leu Gln Ser Ser Pro Glu Val Gln Val Pro
                805                 810                 815
```

```
Pro Thr Ser Phe Glu Thr Glu Glu Thr Pro Arg Arg Val Pro Pro Asp
            820                 825                 830

Ser Leu Pro Thr Gln Gly Glu Thr Gln Pro Thr Cys Leu Asp Val Ile
        835                 840                 845

Val Pro Glu Asp Cys Leu His Gln Asp Ile Ser Pro Asp Ala Val Thr
    850                 855                 860

Val Pro Val Glu Ile Leu Ser Thr Asp Ala Arg Thr His Ser Leu Asp
865                 870                 875                 880

Asn Arg Ser Gln Asp Ser Pro Gly Glu Ser Glu Glu Thr Leu Arg Leu
                885                 890                 895

Thr Glu Ser Asp Ser Val Leu Ala Asp Asp Ile Leu Ala Ser Arg Val
            900                 905                 910

Ser Val Gly Ser Ser Leu Pro Glu Leu Gly Gln Glu Leu His Asn Lys
        915                 920                 925

Pro Phe Ser Glu Asp His His Ser His Arg Arg Leu Glu Lys Asn Leu
    930                 935                 940

Glu Ala Val Glu Thr Leu Asn Gln Leu Asn Ser Lys Asp Ala Ala Lys
945                 950                 955                 960

Glu Ala Gly Leu Val Ser Ala Leu Ser Ser Asp Ser Thr Ser Gln Asp
                965                 970                 975

Ser Leu Leu Glu Asp Ser Leu Ser Ala Pro Phe Pro Ala Ser Glu Pro
            980                 985                 990

Ser Leu Glu Thr Pro Asp Ser Leu  Glu Ser Val Asp Val  His Glu Ala
        995                 1000                1005

Leu Leu  Asp Ser Leu Gly Ser  His Thr Pro Gln Lys  Leu Val Pro
    1010                1015                1020

Pro Asp  Lys Pro Ala Asp Ser  Gly Tyr Glu Thr Glu  Asn Leu Glu
    1025                1030                1035

Ser Pro  Glu Trp Thr Leu His  Pro Ala Pro Glu Gly  Thr Ala Asp
    1040                1045                1050

Ser Glu  Pro Ala Thr Thr Gly  Asp Gly Gly His Ser  Gly Leu Pro
    1055                1060                1065

Pro Asn  Pro Val Ile Val Ile  Ser Asp Ala Gly Asp  Gly His Arg
    1070                1075                1080
```

```
Gly Thr  Glu Val Thr Pro Glu  Thr Phe Thr Ala Gly  Ser Gln Gly
    1085                1090                1095

Ser Tyr  Arg Asp Ser Ala Tyr  Phe Ser Asp Asn Asp  Ser Glu Pro
    1100                1105                1110

Glu Lys  Arg Ser Glu Glu Val  Pro Gly Thr Ser Pro  Ser Ala Leu
    1115                1120                1125

Val Leu  Val Gln Glu Gln Pro  Leu Pro Glu Pro Val  Leu Pro Glu
    1130                1135                1140

Gln Ser  Pro Ala Ala Gln Asp  Ser Cys Leu Glu Ala  Arg Lys Ser
    1145                1150                1155

Gln Pro  Asp Glu Ser Cys Leu  Ser Ala Leu His Asn  Ser Ser Asp
    1160                1165                1170

Leu Glu  Leu Arg Ala Thr Pro  Glu Pro Ala Gln Thr  Gly Val Pro
    1175                1180                1185

Gln Gln  Val His Pro Thr Glu  Asp Glu Ala Ser Ser  Pro Trp Ser
    1190                1195                1200

Val Leu  Asn Ala Glu Leu Ser  Ser Gly Asp Asp Phe  Glu Thr Gln
    1205                1210                1215

Asp Asp  Arg Pro Cys Thr Leu  Ala Ser Thr Gly Thr  Asn Thr Asn
    1220                1225                1230

Glu Leu  Leu Ala Tyr Thr Asn  Ser Ala Leu Asp Lys  Ser Leu Ser
    1235                1240                1245

Ser His  Ser Glu Gly Pro Lys  Leu Lys Glu Pro Asp  Ile Glu Gly
    1250                1255                1260

Lys Tyr  Leu Gly Lys Leu Gly  Val Ser Gly Met Leu  Asp Leu Ser
    1265                1270                1275

Glu Asp  Gly Met Asp Ala Asp  Glu Glu Asp Glu Asn  Ser Asp Asp
    1280                1285                1290

Ser Asp  Glu Asp Leu Arg Ala  Phe Asn Leu His Ser  Leu Ser Ser
    1295                1300                1305

Glu Ser  Glu Asp Glu Thr Glu  His Pro Val Pro Ile  Ile Leu Ser
    1310                1315                1320

Asn Glu  Asp Gly Arg His Leu  Arg Ser Leu Leu Lys  Pro Thr Ala
    1325                1330                1335
```

```
Ala Asn  Ala Pro Asp Pro Leu  Pro Glu Asp Trp Lys  Lys Glu Lys
    1340                1345                1350

Lys Ala  Val Thr Phe Phe Asp  Asp Val Thr Val Tyr  Leu Phe Asp
    1355                1360                1365

Gln Glu  Thr Pro Thr Lys Glu  Leu Gly Pro Cys Gly  Gly Glu Ala
    1370                1375                1380

Cys Gly  Pro Asp Leu Ser Gly  Pro Ala Pro Ala Ser  Gly Ser Pro
    1385                1390                1395

Tyr Leu  Ser Arg Cys Ile Asn  Ser Glu Ser Ser Thr  Asp Glu Glu
    1400                1405                1410

Gly Gly  Gly Phe Glu Trp Asp  Asp Asp Phe Ser Pro  Asp Pro Phe
    1415                1420                1425

Met Ser  Lys Thr Thr Ser Asn  Leu Leu Ser Ser Lys  Pro Ser Leu
    1430                1435                1440

Gln Thr  Ser Lys Tyr Phe Ser  Pro Pro Pro Pro Ala  Arg Ser Thr
    1445                1450                1455

Glu Gln  Ser Trp Pro His Ser  Ala Pro Tyr Ser Arg  Phe Ser Ile
    1460                1465                1470

Ser Pro  Ala Asn Ile Ala Ser  Phe Ser Leu Thr His  Leu Thr Asp
    1475                1480                1485

Ser Asp  Ile Glu Gln Gly Gly  Ser Ser Glu Asp Gly  Glu Lys Asp
    1490                1495                1500


<210>  437
<211>  1338
<212>  PRT
<213>  Homo sapiens

<400>  437

Met Val Ser Tyr Trp Asp Thr Gly Val Leu Leu Cys Ala Leu Leu Ser
1               5                  10                  15

Cys Leu Leu Leu Thr Gly Ser Ser Ser Gly Ser Lys Leu Lys Asp Pro
            20                  25                  30

Glu Leu Ser Leu Lys Gly Thr Gln His Ile Met Gln Ala Gly Gln Thr
        35                  40                  45

Leu His Leu Gln Cys Arg Gly Glu Ala Ala His Lys Trp Ser Leu Pro
    50                  55                  60
```

```
Glu Met Val Ser Lys Glu Ser Glu Arg Leu Ser Ile Thr Lys Ser Ala
65                  70                  75                  80

Cys Gly Arg Asn Gly Lys Gln Phe Cys Ser Thr Leu Thr Leu Asn Thr
                85                  90                  95

Ala Gln Ala Asn His Thr Gly Phe Tyr Ser Cys Lys Tyr Leu Ala Val
            100                 105                 110

Pro Thr Ser Lys Lys Lys Glu Thr Glu Ser Ala Ile Tyr Ile Phe Ile
        115                 120                 125

Ser Asp Thr Gly Arg Pro Phe Val Glu Met Tyr Ser Glu Ile Pro Glu
    130                 135                 140

Ile Ile His Met Thr Glu Gly Arg Glu Leu Val Ile Pro Cys Arg Val
145                 150                 155                 160

Thr Ser Pro Asn Ile Thr Val Thr Leu Lys Lys Phe Pro Leu Asp Thr
                165                 170                 175

Leu Ile Pro Asp Gly Lys Arg Ile Ile Trp Asp Ser Arg Lys Gly Phe
            180                 185                 190

Ile Ile Ser Asn Ala Thr Tyr Lys Glu Ile Gly Leu Leu Thr Cys Glu
        195                 200                 205

Ala Thr Val Asn Gly His Leu Tyr Lys Thr Asn Tyr Leu Thr His Arg
    210                 215                 220

Gln Thr Asn Thr Ile Ile Asp Val Gln Ile Ser Thr Pro Arg Pro Val
225                 230                 235                 240

Lys Leu Leu Arg Gly His Thr Leu Val Leu Asn Cys Thr Ala Thr Thr
                245                 250                 255

Pro Leu Asn Thr Arg Val Gln Met Thr Trp Ser Tyr Pro Asp Glu Lys
            260                 265                 270

Asn Lys Arg Ala Ser Val Arg Arg Arg Ile Asp Gln Ser Asn Ser His
        275                 280                 285

Ala Asn Ile Phe Tyr Ser Val Leu Thr Ile Asp Lys Met Gln Asn Lys
    290                 295                 300

Asp Lys Gly Leu Tyr Thr Cys Arg Val Arg Ser Gly Pro Ser Phe Lys
305                 310                 315                 320

Ser Val Asn Thr Ser Val His Ile Tyr Asp Lys Ala Phe Ile Thr Val
                325                 330                 335
```

```
Lys His Arg Lys Gln Gln Val Leu Glu Thr Val Ala Gly Lys Arg Ser
            340                 345                 350

Tyr Arg Leu Ser Met Lys Val Lys Ala Phe Pro Ser Pro Glu Val Val
        355                 360                 365

Trp Leu Lys Asp Gly Leu Pro Ala Thr Glu Lys Ser Ala Arg Tyr Leu
    370                 375                 380

Thr Arg Gly Tyr Ser Leu Ile Ile Lys Asp Val Thr Glu Glu Asp Ala
385                 390                 395                 400

Gly Asn Tyr Thr Ile Leu Leu Ser Ile Lys Gln Ser Asn Val Phe Lys
                405                 410                 415

Asn Leu Thr Ala Thr Leu Ile Val Asn Val Lys Pro Gln Ile Tyr Glu
            420                 425                 430

Lys Ala Val Ser Ser Phe Pro Asp Pro Ala Leu Tyr Pro Leu Gly Ser
        435                 440                 445

Arg Gln Ile Leu Thr Cys Thr Ala Tyr Gly Ile Pro Gln Pro Thr Ile
    450                 455                 460

Lys Trp Phe Trp His Pro Cys Asn His Asn His Ser Glu Ala Arg Cys
465                 470                 475                 480

Asp Phe Cys Ser Asn Asn Glu Glu Ser Phe Ile Leu Asp Ala Asp Ser
                485                 490                 495

Asn Met Gly Asn Arg Ile Glu Ser Ile Thr Gln Arg Met Ala Ile Ile
            500                 505                 510

Glu Gly Lys Asn Lys Met Ala Ser Thr Leu Val Val Ala Asp Ser Arg
        515                 520                 525

Ile Ser Gly Ile Tyr Ile Cys Ile Ala Ser Asn Lys Val Gly Thr Val
    530                 535                 540

Gly Arg Asn Ile Ser Phe Tyr Ile Thr Asp Val Pro Asn Gly Phe His
545                 550                 555                 560

Val Asn Leu Glu Lys Met Pro Thr Glu Gly Glu Asp Leu Lys Leu Ser
                565                 570                 575

Cys Thr Val Asn Lys Phe Leu Tyr Arg Asp Val Thr Trp Ile Leu Leu
            580                 585                 590

Arg Thr Val Asn Asn Arg Thr Met His Tyr Ser Ile Ser Lys Gln Lys
        595                 600                 605
```

```
Met Ala Ile Thr Lys Glu His Ser Ile Thr Leu Asn Leu Thr Ile Met
    610                 615                 620

Asn Val Ser Leu Gln Asp Ser Gly Thr Tyr Ala Cys Arg Ala Arg Asn
625                 630                 635                 640

Val Tyr Thr Gly Glu Glu Ile Leu Gln Lys Lys Glu Ile Thr Ile Arg
                645                 650                 655

Asp Gln Glu Ala Pro Tyr Leu Leu Arg Asn Leu Ser Asp His Thr Val
            660                 665                 670

Ala Ile Ser Ser Ser Thr Thr Leu Asp Cys His Ala Asn Gly Val Pro
        675                 680                 685

Glu Pro Gln Ile Thr Trp Phe Lys Asn Asn His Lys Ile Gln Gln Glu
    690                 695                 700

Pro Gly Ile Ile Leu Gly Pro Gly Ser Ser Thr Leu Phe Ile Glu Arg
705                 710                 715                 720

Val Thr Glu Glu Asp Glu Gly Val Tyr His Cys Lys Ala Thr Asn Gln
                725                 730                 735

Lys Gly Ser Val Glu Ser Ser Ala Tyr Leu Thr Val Gln Gly Thr Ser
            740                 745                 750

Asp Lys Ser Asn Leu Glu Leu Ile Thr Leu Thr Cys Thr Cys Val Ala
        755                 760                 765

Ala Thr Leu Phe Trp Leu Leu Leu Thr Leu Phe Ile Arg Lys Met Lys
    770                 775                 780

Arg Ser Ser Ser Glu Ile Lys Thr Asp Tyr Leu Ser Ile Ile Met Asp
785                 790                 795                 800

Pro Asp Glu Val Pro Leu Asp Glu Gln Cys Glu Arg Leu Pro Tyr Asp
                805                 810                 815

Ala Ser Lys Trp Glu Phe Ala Arg Glu Arg Leu Lys Leu Gly Lys Ser
            820                 825                 830

Leu Gly Arg Gly Ala Phe Gly Lys Val Val Gln Ala Ser Ala Phe Gly
        835                 840                 845

Ile Lys Lys Ser Pro Thr Cys Arg Thr Val Ala Val Lys Met Leu Lys
    850                 855                 860

Glu Gly Ala Thr Ala Ser Glu Tyr Lys Ala Leu Met Thr Glu Leu Lys
865                 870                 875                 880
```

```
Ile Leu Thr His Ile Gly His His Leu Asn Val Val Asn Leu Leu Gly
                885                 890                 895

Ala Cys Thr Lys Gln Gly Gly Pro Leu Met Val Ile Val Glu Tyr Cys
            900                 905                 910

Lys Tyr Gly Asn Leu Ser Asn Tyr Leu Lys Ser Lys Arg Asp Leu Phe
        915                 920                 925

Phe Leu Asn Lys Asp Ala Ala Leu His Met Glu Pro Lys Lys Glu Lys
    930                 935                 940

Met Glu Pro Gly Leu Glu Gln Gly Lys Lys Pro Arg Leu Asp Ser Val
945                 950                 955                 960

Thr Ser Ser Glu Ser Phe Ala Ser Ser Gly Phe Gln Glu Asp Lys Ser
                965                 970                 975

Leu Ser Asp Val Glu Glu Glu Glu Asp Ser Asp Gly Phe Tyr Lys Glu
            980                 985                 990

Pro Ile Thr Met Glu Asp Leu Ile  Ser Tyr Ser Phe Gln  Val Ala Arg
        995                 1000                1005

Gly Met  Glu Phe Leu Ser Ser  Arg Lys Cys Ile His  Arg Asp Leu
    1010                1015                1020

Ala Ala  Arg Asn Ile Leu Leu  Ser Glu Asn Asn Val  Val Lys Ile
    1025                1030                1035

Cys Asp  Phe Gly Leu Ala Arg  Asp Ile Tyr Lys Asn  Pro Asp Tyr
    1040                1045                1050

Val Arg  Lys Gly Asp Thr Arg  Leu Pro Leu Lys Trp  Met Ala Pro
    1055                1060                1065

Glu Ser  Ile Phe Asp Lys Ile  Tyr Ser Thr Lys Ser  Asp Val Trp
    1070                1075                1080

Ser Tyr  Gly Val Leu Leu Trp  Glu Ile Phe Ser Leu  Gly Gly Ser
    1085                1090                1095

Pro Tyr  Pro Gly Val Gln Met  Asp Glu Asp Phe Cys  Ser Arg Leu
    1100                1105                1110

Arg Glu  Gly Met Arg Met Arg  Ala Pro Glu Tyr Ser  Thr Pro Glu
    1115                1120                1125

Ile Tyr  Gln Ile Met Leu Asp  Cys Trp His Arg Asp  Pro Lys Glu
    1130                1135                1140
```

```
Arg Pro  Arg Phe Ala Glu Leu  Val Glu Lys Leu Gly  Asp Leu Leu
    1145                1150                1155


Gln Ala  Asn Val Gln Gln Asp  Gly Lys Asp Tyr Ile  Pro Ile Asn
    1160                1165                1170


Ala Ile  Leu Thr Gly Asn Ser  Gly Phe Thr Tyr Ser  Thr Pro Ala
    1175                1180                1185


Phe Ser  Glu Asp Phe Phe Lys  Glu Ser Ile Ser Ala  Pro Lys Phe
    1190                1195                1200


Asn Ser  Gly Ser Ser Asp Asp  Val Arg Tyr Val Asn  Ala Phe Lys
    1205                1210                1215


Phe Met  Ser Leu Glu Arg Ile  Lys Thr Phe Glu Glu  Leu Leu Pro
    1220                1225                1230


Asn Ala  Thr Ser Met Phe Asp  Asp Tyr Gln Gly Asp  Ser Ser Thr
    1235                1240                1245


Leu Leu  Ala Ser Pro Met Leu  Lys Arg Phe Thr Trp  Thr Asp Ser
    1250                1255                1260


Lys Pro  Lys Ala Ser Leu Lys  Ile Asp Leu Arg Val  Thr Ser Lys
    1265                1270                1275


Ser Lys  Glu Ser Gly Leu Ser  Asp Val Ser Arg Pro  Ser Phe Cys
    1280                1285                1290


His Ser  Ser Cys Gly His Val  Ser Glu Gly Lys Arg  Arg Phe Thr
    1295                1300                1305


Tyr Asp  His Ala Glu Leu Glu  Arg Lys Ile Ala Cys  Cys Ser Pro
    1310                1315                1320


Pro Pro  Asp Tyr Asn Ser Val  Val Leu Tyr Ser Thr  Pro Pro Ile
    1325                1330                1335


<210>  438
<211>  993
<212>  PRT
<213>  Homo sapiens

<400>  438

Met Pro Ala Leu Ala Arg Asp Gly Gly Gln Leu Pro Leu Leu Val Val
1               5                  10                  15


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

```
Ile Lys Cys Val Leu Ile Asn His Lys Asn Asn Asp Ser Ser Val Gly
        35                  40                  45

Lys Ser Ser Ser Tyr Pro Met Val Ser Glu Ser Pro Glu Asp Leu Gly
    50                  55                  60

Cys Ala Leu Arg Pro Gln Ser Ser Gly Thr Val Tyr Glu Ala Ala Ala
65                  70                  75                  80

Val Glu Val Asp Val Ser Ala Ser Ile Thr Leu Gln Val Leu Val Asp
                85                  90                  95

Ala Pro Gly Asn Ile Ser Cys Leu Trp Val Phe Lys His Ser Ser Leu
            100                 105                 110

Asn Cys Gln Pro His Phe Asp Leu Gln Asn Arg Gly Val Val Ser Met
        115                 120                 125

Val Ile Leu Lys Met Thr Glu Thr Gln Ala Gly Glu Tyr Leu Leu Phe
    130                 135                 140

Ile Gln Ser Glu Ala Thr Asn Tyr Thr Ile Leu Phe Thr Val Ser Ile
145                 150                 155                 160

Arg Asn Thr Leu Leu Tyr Thr Leu Arg Arg Pro Tyr Phe Arg Lys Met
                165                 170                 175

Glu Asn Gln Asp Ala Leu Val Cys Ile Ser Glu Ser Val Pro Glu Pro
            180                 185                 190

Ile Val Glu Trp Val Leu Cys Asp Ser Gln Gly Glu Ser Cys Lys Glu
        195                 200                 205

Glu Ser Pro Ala Val Val Lys Lys Glu Glu Lys Val Leu His Glu Leu
    210                 215                 220

Phe Gly Thr Asp Ile Arg Cys Cys Ala Arg Asn Glu Leu Gly Arg Glu
225                 230                 235                 240

Cys Thr Arg Leu Phe Thr Ile Asp Leu Asn Gln Thr Pro Gln Thr Thr
                245                 250                 255

Leu Pro Gln Leu Phe Leu Lys Val Gly Glu Pro Leu Trp Ile Arg Cys
            260                 265                 270

Lys Ala Val His Val Asn His Gly Phe Gly Leu Thr Trp Glu Leu Glu
        275                 280                 285

Asn Lys Ala Leu Glu Glu Gly Asn Tyr Phe Glu Met Ser Thr Tyr Ser
    290                 295                 300
```

```
Thr Asn Arg Thr Met Ile Arg Ile Leu Phe Ala Phe Val Ser Ser Val
305                 310                 315                 320

Ala Arg Asn Asp Thr Gly Tyr Tyr Thr Cys Ser Ser Ser Lys His Pro
                325                 330                 335

Ser Gln Ser Ala Leu Val Thr Ile Val Glu Lys Gly Phe Ile Asn Ala
            340                 345                 350

Thr Asn Ser Ser Glu Asp Tyr Glu Ile Asp Gln Tyr Glu Glu Phe Cys
        355                 360                 365

Phe Ser Val Arg Phe Lys Ala Tyr Pro Gln Ile Arg Cys Thr Trp Thr
    370                 375                 380

Phe Ser Arg Lys Ser Phe Pro Cys Glu Gln Lys Gly Leu Asp Asn Gly
385                 390                 395                 400

Tyr Ser Ile Ser Lys Phe Cys Asn His Lys His Gln Pro Gly Glu Tyr
                405                 410                 415

Ile Phe His Ala Glu Asn Asp Asp Ala Gln Phe Thr Lys Met Phe Thr
            420                 425                 430

Leu Asn Ile Arg Arg Lys Pro Gln Val Leu Ala Glu Ala Ser Ala Ser
        435                 440                 445

Gln Ala Ser Cys Phe Ser Asp Gly Tyr Pro Leu Pro Ser Trp Thr Trp
    450                 455                 460

Lys Lys Cys Ser Asp Lys Ser Pro Asn Cys Thr Glu Glu Ile Thr Glu
465                 470                 475                 480

Gly Val Trp Asn Arg Lys Ala Asn Arg Lys Val Phe Gly Gln Trp Val
                485                 490                 495

Ser Ser Ser Thr Leu Asn Met Ser Glu Ala Ile Lys Gly Phe Leu Val
            500                 505                 510

Lys Cys Cys Ala Tyr Asn Ser Leu Gly Thr Ser Cys Glu Thr Ile Leu
        515                 520                 525

Leu Asn Ser Pro Gly Pro Phe Pro Phe Ile Gln Asp Asn Ile Ser Phe
    530                 535                 540

Tyr Ala Thr Ile Gly Val Cys Leu Leu Phe Ile Val Val Leu Thr Leu
545                 550                 555                 560

Leu Ile Cys His Lys Tyr Lys Lys Gln Phe Arg Tyr Glu Ser Gln Leu
                565                 570                 575
```

```
Gln Met Val Gln Val Thr Gly Ser Ser Asp Asn Glu Tyr Phe Tyr Val
            580                 585                 590

Asp Phe Arg Glu Tyr Glu Tyr Asp Leu Lys Trp Glu Phe Pro Arg Glu
        595                 600                 605

Asn Leu Glu Phe Gly Lys Val Leu Gly Ser Gly Ala Phe Gly Lys Val
    610                 615                 620

Met Asn Ala Thr Ala Tyr Gly Ile Ser Lys Thr Gly Val Ser Ile Gln
625                 630                 635                 640

Val Ala Val Lys Met Leu Lys Glu Lys Ala Asp Ser Ser Glu Arg Glu
                645                 650                 655

Ala Leu Met Ser Glu Leu Lys Met Met Thr Gln Leu Gly Ser His Glu
            660                 665                 670

Asn Ile Val Asn Leu Leu Gly Ala Cys Thr Leu Ser Gly Pro Ile Tyr
        675                 680                 685

Leu Ile Phe Glu Tyr Cys Cys Tyr Gly Asp Leu Leu Asn Tyr Leu Arg
    690                 695                 700

Ser Lys Arg Glu Lys Phe His Arg Thr Trp Thr Glu Ile Phe Lys Glu
705                 710                 715                 720

His Asn Phe Ser Phe Tyr Pro Thr Phe Gln Ser His Pro Asn Ser Ser
                725                 730                 735

Met Pro Gly Ser Arg Glu Val Gln Ile His Pro Asp Ser Asp Gln Ile
            740                 745                 750

Ser Gly Leu His Gly Asn Ser Phe His Ser Glu Asp Glu Ile Glu Tyr
        755                 760                 765

Glu Asn Gln Lys Arg Leu Glu Glu Glu Glu Asp Leu Asn Val Leu Thr
    770                 775                 780

Phe Glu Asp Leu Leu Cys Phe Ala Tyr Gln Val Ala Lys Gly Met Glu
785                 790                 795                 800

Phe Leu Glu Phe Lys Ser Cys Val His Arg Asp Leu Ala Ala Arg Asn
                805                 810                 815

Val Leu Val Thr His Gly Lys Val Val Lys Ile Cys Asp Phe Gly Leu
            820                 825                 830

Ala Arg Asp Ile Met Ser Asp Ser Asn Tyr Val Val Arg Gly Asn Ala
        835                 840                 845
```

Arg Leu Pro Val Lys Trp Met Ala Pro Glu Ser Leu Phe Glu Gly Ile
850 855 860

Tyr Thr Ile Lys Ser Asp Val Trp Ser Tyr Gly Ile Leu Leu Trp Glu
865 870 875 880

Ile Phe Ser Leu Gly Val Asn Pro Tyr Pro Gly Ile Pro Val Asp Ala
885 890 895

Asn Phe Tyr Lys Leu Ile Gln Asn Gly Phe Lys Met Asp Gln Pro Phe
900 905 910

Tyr Ala Thr Glu Glu Ile Tyr Ile Ile Met Gln Ser Cys Trp Ala Phe
915 920 925

Asp Ser Arg Lys Arg Pro Ser Phe Pro Asn Leu Thr Ser Phe Leu Gly
930 935 940

Cys Gln Leu Ala Asp Ala Glu Glu Ala Met Tyr Gln Asn Val Asp Gly
945 950 955 960

Arg Val Ser Glu Cys Pro His Thr Tyr Gln Asn Arg Arg Pro Phe Ser
965 970 975

Arg Glu Met Asp Leu Gly Leu Leu Ser Pro Gln Ala Gln Val Glu Asp
980 985 990

Ser

<210> 439
<211> 1363
<212> PRT
<213> Homo sapiens

<400> 439

Met Gln Arg Gly Ala Ala Leu Cys Leu Arg Leu Trp Leu Cys Leu Gly
1 5 10 15

Leu Leu Asp Gly Leu Val Ser Gly Tyr Ser Met Thr Pro Pro Thr Leu
20 25 30

Asn Ile Thr Glu Glu Ser His Val Ile Asp Thr Gly Asp Ser Leu Ser
35 40 45

Ile Ser Cys Arg Gly Gln His Pro Leu Glu Trp Ala Trp Pro Gly Ala
50 55 60

Gln Glu Ala Pro Ala Thr Gly Asp Lys Asp Ser Glu Asp Thr Gly Val
65 70 75 80

Val Arg Asp Cys Glu Gly Thr Asp Ala Arg Pro Tyr Cys Lys Val Leu

85 90 95

Leu Leu His Glu Val His Ala Asn Asp Thr Gly Ser Tyr Val Cys Tyr
100 105 110

Tyr Lys Tyr Ile Lys Ala Arg Ile Glu Gly Thr Thr Ala Ala Ser Ser
115 120 125

Tyr Val Phe Val Arg Asp Phe Glu Gln Pro Phe Ile Asn Lys Pro Asp
130 135 140

Thr Leu Leu Val Asn Arg Lys Asp Ala Met Trp Val Pro Cys Leu Val
145 150 155 160

Ser Ile Pro Gly Leu Asn Val Thr Leu Arg Ser Gln Ser Ser Val Leu
165 170 175

Trp Pro Asp Gly Gln Glu Val Val Trp Asp Asp Arg Arg Gly Met Leu
180 185 190

Val Ser Thr Pro Leu Leu His Asp Ala Leu Tyr Leu Gln Cys Glu Thr
195 200 205

Thr Trp Gly Asp Gln Asp Phe Leu Ser Asn Pro Phe Leu Val His Ile
210 215 220

Thr Gly Asn Glu Leu Tyr Asp Ile Gln Leu Leu Pro Arg Lys Ser Leu
225 230 235 240

Glu Leu Leu Val Gly Glu Lys Leu Val Leu Asn Cys Thr Val Trp Ala
245 250 255

Glu Phe Asn Ser Gly Val Thr Phe Asp Trp Asp Tyr Pro Gly Lys Gln
260 265 270

Ala Glu Arg Gly Lys Trp Val Pro Glu Arg Arg Ser Gln Gln Thr His
275 280 285

Thr Glu Leu Ser Ser Ile Leu Thr Ile His Asn Val Ser Gln His Asp
290 295 300

Leu Gly Ser Tyr Val Cys Lys Ala Asn Asn Gly Ile Gln Arg Phe Arg
305 310 315 320

Glu Ser Thr Glu Val Ile Val His Glu Asn Pro Phe Ile Ser Val Glu
325 330 335

Trp Leu Lys Gly Pro Ile Leu Glu Ala Thr Ala Gly Asp Glu Leu Val
340 345 350

Lys Leu Pro Val Lys Leu Ala Ala Tyr Pro Pro Pro Glu Phe Gln Trp

```
        355                 360                 365

Tyr Lys Asp Gly Lys Ala Leu Ser Gly Arg His Ser Pro His Ala Leu
    370                 375                 380

Val Leu Lys Glu Val Thr Glu Ala Ser Thr Gly Thr Tyr Thr Leu Ala
385                 390                 395                 400

Leu Trp Asn Ser Ala Ala Gly Leu Arg Arg Asn Ile Ser Leu Glu Leu
                405                 410                 415

Val Val Asn Val Pro Pro Gln Ile His Glu Lys Glu Ala Ser Ser Pro
            420                 425                 430

Ser Ile Tyr Ser Arg His Ser Arg Gln Ala Leu Thr Cys Thr Ala Tyr
        435                 440                 445

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

Pro Cys Lys Met Phe Ala Gln Arg Ser Leu Arg Arg Arg Gln Gln Gln
465                 470                 475                 480

Asp Leu Met Pro Gln Cys Arg Asp Trp Arg Ala Val Thr Thr Gln Asp
                485                 490                 495

Ala Val Asn Pro Ile Glu Ser Leu Asp Thr Trp Thr Glu Phe Val Glu
            500                 505                 510

Gly Lys Asn Lys Thr Val Ser Lys Leu Val Ile Gln Asn Ala Asn Val
        515                 520                 525

Ser Ala Met Tyr Lys Cys Val Val Ser Asn Lys Val Gly Gln Asp Glu
    530                 535                 540

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

Glu Ser Lys Pro Ser Glu Glu Leu Leu Glu Gly Gln Pro Val Leu Leu
                565                 570                 575

Ser Cys Gln Ala Asp Ser Tyr Lys Tyr Glu His Leu Arg Trp Tyr Arg
            580                 585                 590

Leu Asn Leu Ser Thr Leu His Asp Ala His Gly Asn Pro Leu Leu Leu
        595                 600                 605

Asp Cys Lys Asn Val His Leu Phe Ala Thr Pro Leu Ala Ala Ser Leu
    610                 615                 620

Glu Glu Val Ala Pro Gly Ala Arg His Ala Thr Leu Ser Leu Ser Ile
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625 630 635 640

Pro Arg Val Ala Pro Glu His Glu Gly His Tyr Val Cys Glu Val Gln
645 650 655

Asp Arg Arg Ser His Asp Lys His Cys His Lys Lys Tyr Leu Ser Val
660 665 670

Gln Ala Leu Glu Ala Pro Arg Leu Thr Gln Asn Leu Thr Asp Leu Leu
675 680 685

Val Asn Val Ser Asp Ser Leu Glu Met Gln Cys Leu Val Ala Gly Ala
690 695 700

His Ala Pro Ser Ile Val Trp Tyr Lys Asp Glu Arg Leu Leu Glu Glu
705 710 715 720

Lys Ser Gly Val Asp Leu Ala Asp Ser Asn Gln Lys Leu Ser Ile Gln
725 730 735

Arg Val Arg Glu Glu Asp Ala Gly Arg Tyr Leu Cys Ser Val Cys Asn
740 745 750

Ala Lys Gly Cys Val Asn Ser Ser Ala Ser Val Ala Val Glu Gly Ser
755 760 765

Glu Asp Lys Gly Ser Met Glu Ile Val Ile Leu Val Gly Thr Gly Val
770 775 780

Ile Ala Val Phe Phe Trp Val Leu Leu Leu Leu Ile Phe Cys Asn Met
785 790 795 800

Arg Arg Pro Ala His Ala Asp Ile Lys Thr Gly Tyr Leu Ser Ile Ile
805 810 815

Met Asp Pro Gly Glu Val Pro Leu Glu Glu Gln Cys Glu Tyr Leu Ser
820 825 830

Tyr Asp Ala Ser Gln Trp Glu Phe Pro Arg Glu Arg Leu His Leu Gly
835 840 845

Arg Val Leu Gly Tyr Gly Ala Phe Gly Lys Val Val Glu Ala Ser Ala
850 855 860

Phe Gly Ile His Lys Gly Ser Ser Cys Asp Thr Val Ala Val Lys Met
865 870 875 880

Leu Lys Glu Gly Ala Thr Ala Ser Glu His Arg Ala Leu Met Ser Glu
885 890 895

Leu Lys Ile Leu Ile His Ile Gly Asn His Leu Asn Val Val Asn Leu

900 905 910

Leu Gly Ala Cys Thr Lys Pro Gln Gly Pro Leu Met Val Ile Val Glu
915 920 925

Phe Cys Lys Tyr Gly Asn Leu Ser Asn Phe Leu Arg Ala Lys Arg Asp
930 935 940

Ala Phe Ser Pro Cys Ala Glu Lys Ser Pro Glu Gln Arg Gly Arg Phe
945 950 955 960

Arg Ala Met Val Glu Leu Ala Arg Leu Asp Arg Arg Arg Pro Gly Ser
965 970 975

Ser Asp Arg Val Leu Phe Ala Arg Phe Ser Lys Thr Glu Gly Gly Ala
980 985 990

Arg Arg Ala Ser Pro Asp Gln Glu Ala Glu Asp Leu Trp Leu Ser Pro
995 1000 1005

Leu Thr Met Glu Asp Leu Val Cys Tyr Ser Phe Gln Val Ala Arg
1010 1015 1020

Gly Met Glu Phe Leu Ala Ser Arg Lys Cys Ile His Arg Asp Leu
1025 1030 1035

Ala Ala Arg Asn Ile Leu Leu Ser Glu Ser Asp Val Val Lys Ile
1040 1045 1050

Cys Asp Phe Gly Leu Ala Arg Asp Ile Tyr Lys Asp Pro Asp Tyr
1055 1060 1065

Val Arg Lys Gly Ser Ala Arg Leu Pro Leu Lys Trp Met Ala Pro
1070 1075 1080

Glu Ser Ile Phe Asp Lys Val Tyr Thr Thr Gln Ser Asp Val Trp
1085 1090 1095

Ser Phe Gly Val Leu Leu Trp Glu Ile Phe Ser Leu Gly Ala Ser
1100 1105 1110

Pro Tyr Pro Gly Val Gln Ile Asn Glu Glu Phe Cys Gln Arg Leu
1115 1120 1125

Arg Asp Gly Thr Arg Met Arg Ala Pro Glu Leu Ala Thr Pro Ala
1130 1135 1140

Ile Arg Arg Ile Met Leu Asn Cys Trp Ser Gly Asp Pro Lys Ala
1145 1150 1155

Arg Pro Ala Phe Ser Glu Leu Val Glu Ile Leu Gly Asp Leu Leu

1160 1165 1170

Gln Gly Arg Gly Leu Gln Glu Glu Glu Glu Val Cys Met Ala Pro
1175 1180 1185

Arg Ser Ser Gln Ser Ser Glu Glu Gly Ser Phe Ser Gln Val Ser
1190 1195 1200

Thr Met Ala Leu His Ile Ala Gln Ala Asp Ala Glu Asp Ser Pro
1205 1210 1215

Pro Ser Leu Gln Arg His Ser Leu Ala Ala Arg Tyr Tyr Asn Trp
1220 1225 1230

Val Ser Phe Pro Gly Cys Leu Ala Arg Gly Ala Glu Thr Arg Gly
1235 1240 1245

Ser Ser Arg Met Lys Thr Phe Glu Glu Phe Pro Met Thr Pro Thr
1250 1255 1260

Thr Tyr Lys Gly Ser Val Asp Asn Gln Thr Asp Ser Gly Met Val
1265 1270 1275

Leu Ala Ser Glu Glu Phe Glu Gln Ile Glu Ser Arg His Arg Gln
1280 1285 1290

Glu Ser Gly Phe Ser Cys Lys Gly Pro Gly Gln Asn Val Ala Val
1295 1300 1305

Thr Arg Ala His Pro Asp Ser Gln Gly Arg Arg Arg Arg Pro Glu
1310 1315 1320

Arg Gly Ala Arg Gly Gly Gln Val Phe Tyr Asn Ser Glu Tyr Gly
1325 1330 1335

Glu Leu Ser Glu Pro Ser Glu Glu Asp His Cys Ser Pro Ser Ala
1340 1345 1350

Arg Val Thr Phe Phe Thr Asp Asn Ser Tyr
1355 1360

<210> 440
<211> 1620
<212> PRT
<213> Homo sapiens

<400> 440

Met Gly Ala Ile Gly Leu Leu Trp Leu Leu Pro Leu Leu Leu Ser Thr
1 5 10 15

Ala Ala Val Gly Ser Gly Met Gly Thr Gly Gln Arg Ala Gly Ser Pro
20 25 30

```
Ala Ala Gly Pro Pro Leu Gln Pro Arg Glu Pro Leu Ser Tyr Ser Arg
        35                  40                  45

Leu Gln Arg Lys Ser Leu Ala Val Asp Phe Val Val Pro Ser Leu Phe
    50                  55                  60

Arg Val Tyr Ala Arg Asp Leu Leu Leu Pro Pro Ser Ser Ser Glu Leu
65                  70                  75                  80

Lys Ala Gly Arg Pro Glu Ala Arg Gly Ser Leu Ala Leu Asp Cys Ala
                85                  90                  95

Pro Leu Leu Arg Leu Leu Gly Pro Ala Pro Gly Val Ser Trp Thr Ala
            100                 105                 110

Gly Ser Pro Ala Pro Ala Glu Ala Arg Thr Leu Ser Arg Val Leu Lys
        115                 120                 125

Gly Gly Ser Val Arg Lys Leu Arg Arg Ala Lys Gln Leu Val Leu Glu
    130                 135                 140

Leu Gly Glu Glu Ala Ile Leu Glu Gly Cys Val Gly Pro Pro Gly Glu
145                 150                 155                 160

Ala Ala Val Gly Leu Leu Gln Phe Asn Leu Ser Glu Leu Phe Ser Trp
                165                 170                 175

Trp Ile Arg Gln Gly Glu Gly Arg Leu Arg Ile Arg Leu Met Pro Glu
            180                 185                 190

Lys Lys Ala Ser Glu Val Gly Arg Glu Gly Arg Leu Ser Ala Ala Ile
        195                 200                 205

Arg Ala Ser Gln Pro Arg Leu Leu Phe Gln Ile Phe Gly Thr Gly His
    210                 215                 220

Ser Ser Leu Glu Ser Pro Thr Asn Met Pro Ser Pro Ser Pro Asp Tyr
225                 230                 235                 240

Phe Thr Trp Asn Leu Thr Trp Ile Met Lys Asp Ser Phe Pro Phe Leu
                245                 250                 255

Ser His Arg Ser Arg Tyr Gly Leu Glu Cys Ser Phe Asp Phe Pro Cys
            260                 265                 270

Glu Leu Glu Tyr Ser Pro Pro Leu His Asp Leu Arg Asn Gln Ser Trp
        275                 280                 285

Ser Trp Arg Arg Ile Pro Ser Glu Glu Ala Ser Gln Met Asp Leu Leu
    290                 295                 300
```

```
Asp Gly Pro Gly Ala Glu Arg Ser Lys Glu Met Pro Arg Gly Ser Phe
305                 310                 315                 320

Leu Leu Leu Asn Thr Ser Ala Asp Ser Lys His Thr Ile Leu Ser Pro
                325                 330                 335

Trp Met Arg Ser Ser Ser Glu His Cys Thr Leu Ala Val Ser Val His
            340                 345                 350

Arg His Leu Gln Pro Ser Gly Arg Tyr Ile Ala Gln Leu Leu Pro His
        355                 360                 365

Asn Glu Ala Ala Arg Glu Ile Leu Leu Met Pro Thr Pro Gly Lys His
    370                 375                 380

Gly Trp Thr Val Leu Gln Gly Arg Ile Gly Arg Pro Asp Asn Pro Phe
385                 390                 395                 400

Arg Val Ala Leu Glu Tyr Ile Ser Ser Gly Asn Arg Ser Leu Ser Ala
                405                 410                 415

Val Asp Phe Phe Ala Leu Lys Asn Cys Ser Glu Gly Thr Ser Pro Gly
            420                 425                 430

Ser Lys Met Ala Leu Gln Ser Ser Phe Thr Cys Trp Asn Gly Thr Val
        435                 440                 445

Leu Gln Leu Gly Gln Ala Cys Asp Phe His Gln Asp Cys Ala Gln Gly
    450                 455                 460

Glu Asp Glu Ser Gln Met Cys Arg Lys Leu Pro Val Gly Phe Tyr Cys
465                 470                 475                 480

Asn Phe Glu Asp Gly Phe Cys Gly Trp Thr Gln Gly Thr Leu Ser Pro
                485                 490                 495

His Thr Pro Gln Trp Gln Val Arg Thr Leu Lys Asp Ala Arg Phe Gln
            500                 505                 510

Asp His Gln Asp His Ala Leu Leu Leu Ser Thr Thr Asp Val Pro Ala
        515                 520                 525

Ser Glu Ser Ala Thr Val Thr Ser Ala Thr Phe Pro Ala Pro Ile Lys
    530                 535                 540

Ser Ser Pro Cys Glu Leu Arg Met Ser Trp Leu Ile Arg Gly Val Leu
545                 550                 555                 560

Arg Gly Asn Val Ser Leu Val Leu Val Glu Asn Lys Thr Gly Lys Glu
                565                 570                 575
```

```
Gln Gly Arg Met Val Trp His Val Ala Ala Tyr Glu Gly Leu Ser Leu
            580                 585                 590

Trp Gln Trp Met Val Leu Pro Leu Leu Asp Val Ser Asp Arg Phe Trp
        595                 600                 605

Leu Gln Met Val Ala Trp Trp Gly Gln Gly Ser Arg Ala Ile Val Ala
    610                 615                 620

Phe Asp Asn Ile Ser Ile Ser Leu Asp Cys Tyr Leu Thr Ile Ser Gly
625                 630                 635                 640

Glu Asp Lys Ile Leu Gln Asn Thr Ala Pro Lys Ser Arg Asn Leu Phe
                645                 650                 655

Glu Arg Asn Pro Asn Lys Glu Leu Lys Pro Gly Glu Asn Ser Pro Arg
            660                 665                 670

Gln Thr Pro Ile Phe Asp Pro Thr Val His Trp Leu Phe Thr Thr Cys
        675                 680                 685

Gly Ala Ser Gly Pro His Gly Pro Thr Gln Ala Gln Cys Asn Asn Ala
    690                 695                 700

Tyr Gln Asn Ser Asn Leu Ser Val Glu Val Gly Ser Glu Gly Pro Leu
705                 710                 715                 720

Lys Gly Ile Gln Ile Trp Lys Val Pro Ala Thr Asp Thr Tyr Ser Ile
                725                 730                 735

Ser Gly Tyr Gly Ala Ala Gly Gly Lys Gly Gly Lys Asn Thr Met Met
            740                 745                 750

Arg Ser His Gly Val Ser Val Leu Gly Ile Phe Asn Leu Glu Lys Asp
        755                 760                 765

Asp Met Leu Tyr Ile Leu Val Gly Gln Gln Gly Glu Asp Ala Cys Pro
    770                 775                 780

Ser Thr Asn Gln Leu Ile Gln Lys Val Cys Ile Gly Glu Asn Asn Val
785                 790                 795                 800

Ile Glu Glu Glu Ile Arg Val Asn Arg Ser Val His Glu Trp Ala Gly
                805                 810                 815

Gly Gly Gly Gly Gly Gly Gly Ala Thr Tyr Val Phe Lys Met Lys Asp
            820                 825                 830

Gly Val Pro Val Pro Leu Ile Ile Ala Ala Gly Gly Gly Gly Arg Ala
        835                 840                 845
```

```
Tyr Gly Ala Lys Thr Asp Thr Phe His Pro Glu Arg Leu Glu Asn Asn
    850                 855                 860

Ser Ser Val Leu Gly Leu Asn Gly Asn Ser Gly Ala Ala Gly Gly Gly
865                 870                 875                 880

Gly Gly Trp Asn Asp Asn Thr Ser Leu Leu Trp Ala Gly Lys Ser Leu
                885                 890                 895

Gln Glu Gly Ala Thr Gly Gly His Ser Cys Pro Gln Ala Met Lys Lys
            900                 905                 910

Trp Gly Trp Glu Thr Arg Gly Gly Phe Gly Gly Gly Gly Gly Gly Cys
        915                 920                 925

Ser Ser Gly Gly Gly Gly Gly Gly Tyr Ile Gly Gly Asn Ala Ala Ser
    930                 935                 940

Asn Asn Asp Pro Glu Met Asp Gly Glu Asp Gly Val Ser Phe Ile Ser
945                 950                 955                 960

Pro Leu Gly Ile Leu Tyr Thr Pro Ala Leu Lys Val Met Glu Gly His
                965                 970                 975

Gly Glu Val Asn Ile Lys His Tyr Leu Asn Cys Ser His Cys Glu Val
            980                 985                 990

Asp Glu Cys His Met Asp Pro Glu  Ser His Lys Val Ile  Cys Phe Cys
        995                 1000                1005

Asp His  Gly Thr Val Leu Ala  Glu Asp Gly Val Ser  Cys Ile Val
    1010                1015                1020

Ser Pro  Thr Pro Glu Pro His  Leu Pro Leu Ser Leu  Ile Leu Ser
    1025                1030                1035

Val Val  Thr Ser Ala Leu Val  Ala Ala Leu Val Leu  Ala Phe Ser
    1040                1045                1050

Gly Ile  Met Ile Val Tyr Arg  Arg Lys His Gln Glu  Leu Gln Ala
    1055                1060                1065

Met Gln  Met Glu Leu Gln Ser  Pro Glu Tyr Lys Leu  Ser Lys Leu
    1070                1075                1080

Arg Thr  Ser Thr Ile Met Thr  Asp Tyr Asn Pro Asn  Tyr Cys Phe
    1085                1090                1095

Ala Gly  Lys Thr Ser Ser Ile  Ser Asp Leu Lys Glu  Val Pro Arg
    1100                1105                1110
```

Lys Asn Ile Thr Leu Ile Arg Gly Leu Gly His Gly Ala Phe Gly
1115 1120 1125

Glu Val Tyr Glu Gly Gln Val Ser Gly Met Pro Asn Asp Pro Ser
1130 1135 1140

Pro Leu Gln Val Ala Val Lys Thr Leu Pro Glu Val Cys Ser Glu
1145 1150 1155

Gln Asp Glu Leu Asp Phe Leu Met Glu Ala Leu Ile Ile Ser Lys
1160 1165 1170

Phe Asn His Gln Asn Ile Val Arg Cys Ile Gly Val Ser Leu Gln
1175 1180 1185

Ser Leu Pro Arg Phe Ile Leu Leu Glu Leu Met Ala Gly Gly Asp
1190 1195 1200

Leu Lys Ser Phe Leu Arg Glu Thr Arg Pro Arg Pro Ser Gln Pro
1205 1210 1215

Ser Ser Leu Ala Met Leu Asp Leu Leu His Val Ala Arg Asp Ile
1220 1225 1230

Ala Cys Gly Cys Gln Tyr Leu Glu Glu Asn His Phe Ile His Arg
1235 1240 1245

Asp Ile Ala Ala Arg Asn Cys Leu Leu Thr Cys Pro Gly Pro Gly
1250 1255 1260

Arg Val Ala Lys Ile Gly Asp Phe Gly Met Ala Arg Asp Ile Tyr
1265 1270 1275

Arg Ala Ser Tyr Tyr Arg Lys Gly Gly Cys Ala Met Leu Pro Val
1280 1285 1290

Lys Trp Met Pro Pro Glu Ala Phe Met Glu Gly Ile Phe Thr Ser
1295 1300 1305

Lys Thr Asp Thr Trp Ser Phe Gly Val Leu Leu Trp Glu Ile Phe
1310 1315 1320

Ser Leu Gly Tyr Met Pro Tyr Pro Ser Lys Ser Asn Gln Glu Val
1325 1330 1335

Leu Glu Phe Val Thr Ser Gly Gly Arg Met Asp Pro Pro Lys Asn
1340 1345 1350

Cys Pro Gly Pro Val Tyr Arg Ile Met Thr Gln Cys Trp Gln His
1355 1360 1365

```
Gln Pro  Glu Asp Arg Pro Asn  Phe Ala Ile Ile Leu  Glu Arg Ile
    1370                1375                1380

Glu Tyr  Cys Thr Gln Asp Pro  Asp Val Ile Asn Thr  Ala Leu Pro
    1385                1390                1395

Ile Glu  Tyr Gly Pro Leu Val  Glu Glu Glu Glu Lys  Val Pro Val
    1400                1405                1410

Arg Pro  Lys Asp Pro Glu Gly  Val Pro Pro Leu Leu  Val Ser Gln
    1415                1420                1425

Gln Ala  Lys Arg Glu Glu Glu  Arg Ser Pro Ala Ala  Pro Pro Pro
    1430                1435                1440

Leu Pro  Thr Thr Ser Ser Gly  Lys Ala Ala Lys Lys  Pro Thr Ala
    1445                1450                1455

Ala Glu  Ile Ser Val Arg Val  Pro Arg Gly Pro Ala  Val Glu Gly
    1460                1465                1470

Gly His  Val Asn Met Ala Phe  Ser Gln Ser Asn Pro  Pro Ser Glu
    1475                1480                1485

Leu His  Lys Val His Gly Ser  Arg Asn Lys Pro Thr  Ser Leu Trp
    1490                1495                1500

Asn Pro  Thr Tyr Gly Ser Trp  Phe Thr Glu Lys Pro  Thr Lys Lys
    1505                1510                1515

Asn Asn  Pro Ile Ala Lys Lys  Glu Pro His Asp Arg  Gly Asn Leu
    1520                1525                1530

Gly Leu  Glu Gly Ser Cys Thr  Val Pro Pro Asn Val  Ala Thr Gly
    1535                1540                1545

Arg Leu  Pro Gly Ala Ser Leu  Leu Leu Glu Pro Ser  Ser Leu Thr
    1550                1555                1560

Ala Asn  Met Lys Glu Val Pro  Leu Phe Arg Leu Arg  His Phe Pro
    1565                1570                1575

Cys Gly  Asn Val Asn Tyr Gly  Tyr Gln Gln Gln Gly  Leu Pro Leu
    1580                1585                1590

Glu Ala  Ala Thr Ala Pro Gly  Ala Gly His Tyr Glu  Asp Thr Ile
    1595                1600                1605

Leu Lys  Ser Lys Asn Ser Met  Asn Gln Pro Gly Pro
    1610                1615                1620
```

<210> 441
<211> 1008
<212> PRT
<213> Homo sapiens

<400> 441

Met Glu Thr Cys Ala Gly Pro His Pro Leu Arg Leu Phe Leu Cys Arg
1 5 10 15

Met Gln Leu Cys Leu Ala Leu Leu Leu Gly Pro Trp Arg Pro Gly Thr
20 25 30

Ala Glu Glu Val Ile Leu Leu Asp Ser Lys Ala Ser Gln Ala Glu Leu
35 40 45

Gly Trp Thr Ala Leu Pro Ser Asn Gly Trp Glu Glu Ile Ser Gly Val
50 55 60

Asp Glu His Asp Arg Pro Ile Arg Thr Tyr Gln Val Cys Asn Val Leu
65 70 75 80

Glu Pro Asn Gln Asp Asn Trp Leu Gln Thr Gly Trp Ile Ser Arg Gly
85 90 95

Arg Gly Gln Arg Ile Phe Val Glu Leu Gln Phe Thr Leu Arg Asp Cys
100 105 110

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

Tyr Tyr Leu Glu Thr Glu Ala Asp Leu Gly Arg Gly Arg Pro Arg Leu
130 135 140

Gly Gly Ser Arg Pro Arg Lys Ile Asp Thr Ile Ala Ala Asp Glu Ser
145 150 155 160

Phe Thr Gln Gly Asp Leu Gly Glu Arg Lys Met Lys Leu Asn Thr Glu
165 170 175

Val Arg Glu Ile Gly Pro Leu Ser Arg Arg Gly Phe His Leu Ala Phe
180 185 190

Gln Asp Val Gly Ala Cys Val Ala Leu Val Ser Val Arg Val Tyr Tyr
195 200 205

Lys Gln Cys Arg Ala Thr Val Arg Gly Leu Ala Thr Phe Pro Ala Thr
210 215 220

Ala Ala Glu Ser Ala Phe Ser Thr Leu Val Glu Val Ala Gly Thr Cys
225 230 235 240

```
Val Ala His Ser Glu Gly Glu Pro Gly Ser Pro Pro Arg Met His Cys
                245                 250                 255

Gly Ala Asp Gly Glu Trp Leu Val Pro Val Gly Arg Cys Ser Cys Ser
            260                 265                 270

Ala Gly Phe Gln Glu Arg Gly Asp Phe Cys Glu Ala Cys Pro Pro Gly
        275                 280                 285

Phe Tyr Lys Val Ser Pro Arg Arg Pro Leu Cys Ser Pro Cys Pro Glu
    290                 295                 300

His Ser Arg Ala Leu Glu Asn Ala Ser Thr Phe Cys Val Cys Gln Asp
305                 310                 315                 320

Ser Tyr Ala Arg Ser Pro Thr Asp Pro Pro Ser Ala Ser Cys Thr Arg
                325                 330                 335

Pro Pro Ser Ala Pro Arg Asp Leu Gln Tyr Ser Leu Ser Arg Ser Pro
            340                 345                 350

Leu Val Leu Arg Leu Arg Trp Leu Pro Pro Ala Asp Ser Gly Gly Arg
        355                 360                 365

Ser Asp Val Thr Tyr Ser Leu Leu Cys Leu Arg Cys Gly Arg Glu Gly
    370                 375                 380

Pro Ala Gly Ala Cys Glu Pro Cys Gly Pro Arg Val Ala Phe Leu Pro
385                 390                 395                 400

Arg Gln Ala Gly Leu Arg Glu Arg Ala Ala Thr Leu Leu His Leu Arg
                405                 410                 415

Pro Gly Ala Arg Tyr Thr Val Arg Val Ala Ala Leu Asn Gly Val Ser
            420                 425                 430

Gly Pro Ala Ala Ala Ala Gly Thr Thr Tyr Ala Gln Val Thr Val Ser
        435                 440                 445

Thr Gly Pro Gly Ala Pro Trp Glu Glu Asp Glu Ile Arg Arg Asp Arg
    450                 455                 460

Val Glu Pro Gln Ser Val Ser Leu Ser Trp Arg Glu Pro Ile Pro Ala
465                 470                 475                 480

Gly Ala Pro Gly Ala Asn Asp Thr Glu Tyr Glu Ile Arg Tyr Tyr Glu
                485                 490                 495

Lys Gly Gln Ser Glu Gln Thr Tyr Ser Met Val Lys Thr Gly Ala Pro
            500                 505                 510
```

```
Thr Val Thr Val Thr Asn Leu Lys Pro Ala Thr Arg Tyr Val Phe Gln
        515                 520                 525

Ile Arg Ala Ala Ser Pro Gly Pro Ser Trp Glu Ala Gln Ser Phe Asn
    530                 535                 540

Pro Ser Ile Glu Val Gln Thr Leu Gly Glu Ala Ala Ser Gly Ser Arg
545                 550                 555                 560

Asp Gln Ser Pro Ala Ile Val Val Thr Val Val Thr Ile Ser Ala Leu
                565                 570                 575

Leu Val Leu Gly Ser Val Met Ser Val Leu Ala Ile Trp Arg Arg Pro
            580                 585                 590

Cys Ser Tyr Gly Lys Gly Gly Gly Asp Ala His Asp Glu Glu Glu Leu
        595                 600                 605

Tyr Phe His Phe Lys Val Pro Thr Arg Arg Thr Phe Leu Asp Pro Gln
    610                 615                 620

Ser Cys Gly Asp Leu Leu Gln Ala Val His Leu Phe Ala Lys Glu Leu
625                 630                 635                 640

Asp Ala Lys Ser Val Thr Leu Glu Arg Ser Leu Gly Gly Gly Arg Phe
                645                 650                 655

Gly Glu Leu Cys Cys Gly Cys Leu Gln Leu Pro Gly Arg Gln Glu Leu
            660                 665                 670

Leu Val Ala Val His Met Leu Arg Asp Ser Ala Ser Asp Ser Gln Arg
        675                 680                 685

Leu Gly Phe Leu Ala Glu Ala Leu Thr Leu Gly Gln Phe Asp His Ser
    690                 695                 700

His Ile Val Arg Leu Glu Gly Val Val Thr Arg Gly Ser Thr Leu Met
705                 710                 715                 720

Ile Val Thr Glu Tyr Met Ser His Gly Ala Leu Asp Gly Phe Leu Arg
                725                 730                 735

Arg His Glu Gly Gln Leu Val Ala Gly Gln Leu Met Gly Leu Leu Pro
            740                 745                 750

Gly Leu Ala Ser Ala Met Lys Tyr Leu Ser Glu Met Gly Tyr Val His
        755                 760                 765

Arg Gly Leu Ala Ala Arg His Val Leu Val Ser Ser Asp Leu Val Cys
    770                 775                 780
```

```
Lys Ile Ser Gly Phe Gly Arg Gly Pro Arg Asp Arg Ser Glu Ala Val
785                 790                 795                 800

Tyr Thr Thr Met Ser Gly Arg Ser Pro Ala Leu Trp Ala Ala Pro Glu
                805                 810                 815

Thr Leu Gln Phe Gly His Phe Ser Ser Ala Ser Asp Val Trp Ser Phe
            820                 825                 830

Gly Ile Ile Met Trp Glu Val Met Ala Phe Gly Glu Arg Pro Tyr Trp
        835                 840                 845

Asp Met Ser Gly Gln Asp Val Ile Lys Ala Val Glu Asp Gly Phe Arg
    850                 855                 860

Leu Pro Pro Pro Arg Asn Cys Pro Asn Leu Leu His Arg Leu Met Leu
865                 870                 875                 880

Asp Cys Trp Gln Lys Asp Pro Gly Glu Arg Pro Arg Phe Ser Gln Ile
                885                 890                 895

His Ser Ile Leu Ser Lys Met Val Gln Asp Pro Glu Pro Pro Lys Cys
            900                 905                 910

Ala Leu Thr Thr Cys Pro Arg Pro Pro Thr Pro Leu Ala Asp Arg Ala
        915                 920                 925

Phe Ser Thr Phe Pro Ser Phe Gly Ser Val Gly Ala Trp Leu Glu Ala
    930                 935                 940

Leu Asp Leu Cys Arg Tyr Lys Asp Ser Phe Ala Ala Ala Gly Tyr Gly
945                 950                 955                 960

Ser Leu Glu Ala Val Ala Glu Met Thr Ala Gln Asp Leu Val Ser Leu
                965                 970                 975

Gly Ile Ser Leu Ala Glu His Arg Glu Ala Leu Leu Ser Gly Ile Ser
            980                 985                 990

Ala Leu Gln Ala Arg Val Leu Gln  Leu Gln Gly Gln Gly  Val Gln Val
        995                 1000                1005


<210>  442
<211>  398
<212>  PRT
<213>  Homo sapiens

<400>  442

Met Lys Asp Ser Pro Phe Gln Val Thr Lys Leu Tyr Trp Leu Asn Glu
1               5                   10                  15
```

```
Lys Trp Asp Phe Ile Ala Ser Ala Ser Asp Met Ala Ala Glu Gln Gly
            20                  25                  30

Gln Ile Leu Val Ile Ala Thr Ala Ala Val Gly Gly Phe Thr Leu Leu
        35                  40                  45

Val Ile Leu Thr Leu Phe Phe Leu Ile Thr Gly Arg Cys Gln Trp Tyr
    50                  55                  60

Ile Lys Ala Lys Met Lys Ser Glu Glu Lys Arg Arg Asn His Leu Gln
65                  70                  75                  80

Asn Gly His Leu Arg Phe Pro Gly Ile Lys Thr Tyr Ile Asp Pro Asp
                85                  90                  95

Thr Tyr Glu Asp Pro Ser Leu Ala Val His Glu Phe Ala Lys Glu Ile
            100                 105                 110

Asp Pro Ser Arg Ile Arg Ile Glu Arg Val Ile Gly Ala Gly Glu Phe
        115                 120                 125

Gly Glu Val Cys Ser Gly Arg Leu Lys Thr Pro Gly Lys Arg Glu Ile
    130                 135                 140

Pro Val Ala Ile Lys Thr Leu Lys Gly Gly His Met Asp Arg Gln Arg
145                 150                 155                 160

Arg Asp Phe Leu Arg Glu Ala Ser Ile Met Gly Gln Phe Asp His Pro
                165                 170                 175

Asn Ile Ile Arg Leu Glu Gly Val Val Thr Lys Arg Ser Phe Pro Ala
            180                 185                 190

Ile Gly Val Glu Ala Phe Cys Pro Ser Phe Leu Arg Ala Gly Phe Leu
        195                 200                 205

Asn Ser Ile Gln Ala Pro His Pro Val Pro Gly Gly Gly Ser Leu Pro
    210                 215                 220

Pro Arg Ile Pro Ala Gly Arg Pro Val Met Ile Val Val Glu Tyr Met
225                 230                 235                 240

Glu Asn Gly Ser Leu Asp Ser Phe Leu Arg Lys His Asp Gly His Phe
                245                 250                 255

Thr Val Ile Gln Leu Val Gly Met Leu Arg Gly Ile Ala Ser Gly Met
            260                 265                 270

Lys Tyr Leu Ser Asp Met Gly Tyr Val His Arg Asp Leu Ala Ala Arg
        275                 280                 285
```

Asn Ile Leu Val Asn Ser Asn Leu Val Cys Lys Val Ser Asp Phe Gly
290 295 300

Leu Ser Arg Val Leu Glu Asp Asp Pro Glu Ala Ala Tyr Thr Thr Thr
305 310 315 320

Arg Pro Thr Asn His Asn Lys Glu Gln Ser Glu Leu Val Lys Glu Asp
325 330 335

Gly Leu Glu Ser Leu Cys Glu Gln Cys Glu Ser Ser Ser Gly Tyr Gly
340 345 350

Thr Gly Leu Val Leu Met Trp Lys Arg Asn Arg Arg Ala Met Gly Ala
355 360 365

Ser Gly Gln Thr Arg Lys Gln Cys Asp Lys Arg Asp Asn Pro Pro Thr
370 375 380

Asp Leu Phe Gln Thr Leu Thr Leu Asn Leu Cys Tyr Ser Ala
385 390 395

<210> 443
<211> 1367
<212> PRT
<213> Homo sapiens

<400> 443

Met Lys Ser Gly Ser Gly Gly Gly Ser Pro Thr Ser Leu Trp Gly Leu
1 5 10 15

Leu Phe Leu Ser Ala Ala Leu Ser Leu Trp Pro Thr Ser Gly Glu Ile
20 25 30

Cys Gly Pro Gly Ile Asp Ile Arg Asn Asp Tyr Gln Gln Leu Lys Arg
35 40 45

Leu Glu Asn Cys Thr Val Ile Glu Gly Tyr Leu His Ile Leu Leu Ile
50 55 60

Ser Lys Ala Glu Asp Tyr Arg Ser Tyr Arg Phe Pro Lys Leu Thr Val
65 70 75 80

Ile Thr Glu Tyr Leu Leu Leu Phe Arg Val Ala Gly Leu Glu Ser Leu
85 90 95

Gly Asp Leu Phe Pro Asn Leu Thr Val Ile Arg Gly Trp Lys Leu Phe
100 105 110

Tyr Asn Tyr Ala Leu Val Ile Phe Glu Met Thr Asn Leu Lys Asp Ile
115 120 125

Gly Leu Tyr Asn Leu Arg Asn Ile Thr Arg Gly Ala Ile Arg Ile Glu

130 135 140

Lys Asn Ala Asp Leu Cys Tyr Leu Ser Thr Val Asp Trp Ser Leu Ile
145 150 155 160

Leu Asp Ala Val Ser Asn Asn Tyr Ile Val Gly Asn Lys Pro Pro Lys
165 170 175

Glu Cys Gly Asp Leu Cys Pro Gly Thr Met Glu Glu Lys Pro Met Cys
180 185 190

Glu Lys Thr Thr Ile Asn Asn Glu Tyr Asn Tyr Arg Cys Trp Thr Thr
195 200 205

Asn Arg Cys Gln Lys Met Cys Pro Ser Thr Cys Gly Lys Arg Ala Cys
210 215 220

Thr Glu Asn Asn Glu Cys Cys His Pro Glu Cys Leu Gly Ser Cys Ser
225 230 235 240

Ala Pro Asp Asn Asp Thr Ala Cys Val Ala Cys Arg His Tyr Tyr Tyr
245 250 255

Ala Gly Val Cys Val Pro Ala Cys Pro Pro Asn Thr Tyr Arg Phe Glu
260 265 270

Gly Trp Arg Cys Val Asp Arg Asp Phe Cys Ala Asn Ile Leu Ser Ala
275 280 285

Glu Ser Ser Asp Ser Glu Gly Phe Val Ile His Asp Gly Glu Cys Met
290 295 300

Gln Glu Cys Pro Ser Gly Phe Ile Arg Asn Gly Ser Gln Ser Met Tyr
305 310 315 320

Cys Ile Pro Cys Glu Gly Pro Cys Pro Lys Val Cys Glu Glu Glu Lys
325 330 335

Lys Thr Lys Thr Ile Asp Ser Val Thr Ser Ala Gln Met Leu Gln Gly
340 345 350

Cys Thr Ile Phe Lys Gly Asn Leu Leu Ile Asn Ile Arg Arg Gly Asn
355 360 365

Asn Ile Ala Ser Glu Leu Glu Asn Phe Met Gly Leu Ile Glu Val Val
370 375 380

Thr Gly Tyr Val Lys Ile Arg His Ser His Ala Leu Val Ser Leu Ser
385 390 395 400

Phe Leu Lys Asn Leu Arg Leu Ile Leu Gly Glu Glu Gln Leu Glu Gly

405 410 415

Asn Tyr Ser Phe Tyr Val Leu Asp Asn Gln Asn Leu Gln Gln Leu Trp
420 425 430

Asp Trp Asp His Arg Asn Leu Thr Ile Lys Ala Gly Lys Met Tyr Phe
435 440 445

Ala Phe Asn Pro Lys Leu Cys Val Ser Glu Ile Tyr Arg Met Glu Glu
450 455 460

Val Thr Gly Thr Lys Gly Arg Gln Ser Lys Gly Asp Ile Asn Thr Arg
465 470 475 480

Asn Asn Gly Glu Arg Ala Ser Cys Glu Ser Asp Val Leu His Phe Thr
485 490 495

Ser Thr Thr Thr Ser Lys Asn Arg Ile Ile Ile Thr Trp His Arg Tyr
500 505 510

Arg Pro Pro Asp Tyr Arg Asp Leu Ile Ser Phe Thr Val Tyr Tyr Lys
515 520 525

Glu Ala Pro Phe Lys Asn Val Thr Glu Tyr Asp Gly Gln Asp Ala Cys
530 535 540

Gly Ser Asn Ser Trp Asn Met Val Asp Val Asp Leu Pro Pro Asn Lys
545 550 555 560

Asp Val Glu Pro Gly Ile Leu Leu His Gly Leu Lys Pro Trp Thr Gln
565 570 575

Tyr Ala Val Tyr Val Lys Ala Val Thr Leu Thr Met Val Glu Asn Asp
580 585 590

His Ile Arg Gly Ala Lys Ser Glu Ile Leu Tyr Ile Arg Thr Asn Ala
595 600 605

Ser Val Pro Ser Ile Pro Leu Asp Val Leu Ser Ala Ser Asn Ser Ser
610 615 620

Ser Gln Leu Ile Val Lys Trp Asn Pro Pro Ser Leu Pro Asn Gly Asn
625 630 635 640

Leu Ser Tyr Tyr Ile Val Arg Trp Gln Arg Gln Pro Gln Asp Gly Tyr
645 650 655

Leu Tyr Arg His Asn Tyr Cys Ser Lys Asp Lys Ile Pro Ile Arg Lys
660 665 670

Tyr Ala Asp Gly Thr Ile Asp Ile Glu Glu Val Thr Glu Asn Pro Lys

675 680 685

Thr Glu Val Cys Gly Gly Glu Lys Gly Pro Cys Cys Ala Cys Pro Lys
690 695 700

Thr Glu Ala Glu Lys Gln Ala Glu Lys Glu Glu Ala Glu Tyr Arg Lys
705 710 715 720

Val Phe Glu Asn Phe Leu His Asn Ser Ile Phe Val Pro Arg Pro Glu
725 730 735

Arg Lys Arg Arg Asp Val Met Gln Val Ala Asn Thr Thr Met Ser Ser
740 745 750

Arg Ser Arg Asn Thr Thr Ala Ala Asp Thr Tyr Asn Ile Thr Asp Pro
755 760 765

Glu Glu Leu Glu Thr Glu Tyr Pro Phe Phe Glu Ser Arg Val Asp Asn
770 775 780

Lys Glu Arg Thr Val Ile Ser Asn Leu Arg Pro Phe Thr Leu Tyr Arg
785 790 795 800

Ile Asp Ile His Ser Cys Asn His Glu Ala Glu Lys Leu Gly Cys Ser
805 810 815

Ala Ser Asn Phe Val Phe Ala Arg Thr Met Pro Ala Glu Gly Ala Asp
820 825 830

Asp Ile Pro Gly Pro Val Thr Trp Glu Pro Arg Pro Glu Asn Ser Ile
835 840 845

Phe Leu Lys Trp Pro Glu Pro Glu Asn Pro Asn Gly Leu Ile Leu Met
850 855 860

Tyr Glu Ile Lys Tyr Gly Ser Gln Val Glu Asp Gln Arg Glu Cys Val
865 870 875 880

Ser Arg Gln Glu Tyr Arg Lys Tyr Gly Gly Ala Lys Leu Asn Arg Leu
885 890 895

Asn Pro Gly Asn Tyr Thr Ala Arg Ile Gln Ala Thr Ser Leu Ser Gly
900 905 910

Asn Gly Ser Trp Thr Asp Pro Val Phe Phe Tyr Val Gln Ala Lys Thr
915 920 925

Gly Tyr Glu Asn Phe Ile His Leu Ile Ile Ala Leu Pro Val Ala Val
930 935 940

Leu Leu Ile Val Gly Gly Leu Val Ile Met Leu Tyr Val Phe His Arg

945 950 955 960

Lys Arg Asn Asn Ser Arg Leu Gly Asn Gly Val Leu Tyr Ala Ser Val
965 970 975

Asn Pro Glu Tyr Phe Ser Ala Ala Asp Val Tyr Val Pro Asp Glu Trp
980 985 990

Glu Val Ala Arg Glu Lys Ile Thr Met Ser Arg Glu Leu Gly Gln Gly
995 1000 1005

Ser Phe Gly Met Val Tyr Glu Gly Val Ala Lys Gly Val Val Lys
1010 1015 1020

Asp Glu Pro Glu Thr Arg Val Ala Ile Lys Thr Val Asn Glu Ala
1025 1030 1035

Ala Ser Met Arg Glu Arg Ile Glu Phe Leu Asn Glu Ala Ser Val
1040 1045 1050

Met Lys Glu Phe Asn Cys His His Val Val Arg Leu Leu Gly Val
1055 1060 1065

Val Ser Gln Gly Gln Pro Thr Leu Val Ile Met Glu Leu Met Thr
1070 1075 1080

Arg Gly Asp Leu Lys Ser Tyr Leu Arg Ser Leu Arg Pro Glu Met
1085 1090 1095

Glu Asn Asn Pro Val Leu Ala Pro Pro Ser Leu Ser Lys Met Ile
1100 1105 1110

Gln Met Ala Gly Glu Ile Ala Asp Gly Met Ala Tyr Leu Asn Ala
1115 1120 1125

Asn Lys Phe Val His Arg Asp Leu Ala Ala Arg Asn Cys Met Val
1130 1135 1140

Ala Glu Asp Phe Thr Val Lys Ile Gly Asp Phe Gly Met Thr Arg
1145 1150 1155

Asp Ile Tyr Glu Thr Asp Tyr Tyr Arg Lys Gly Gly Lys Gly Leu
1160 1165 1170

Leu Pro Val Arg Trp Met Ser Pro Glu Ser Leu Lys Asp Gly Val
1175 1180 1185

Phe Thr Thr Tyr Ser Asp Val Trp Ser Phe Gly Val Val Leu Trp
1190 1195 1200

Glu Ile Ala Thr Leu Ala Glu Gln Pro Tyr Gln Gly Leu Ser Asn

1205 1210 1215

Glu Gln Val Leu Arg Phe Val Met Glu Gly Gly Leu Leu Asp Lys
1220 1225 1230

Pro Asp Asn Cys Pro Asp Met Leu Phe Glu Leu Met Arg Met Cys
1235 1240 1245

Trp Gln Tyr Asn Pro Lys Met Arg Pro Ser Phe Leu Glu Ile Ile
1250 1255 1260

Ser Ser Ile Lys Glu Glu Met Glu Pro Gly Phe Arg Glu Val Ser
1265 1270 1275

Phe Tyr Tyr Ser Glu Glu Asn Lys Leu Pro Glu Pro Glu Glu Leu
1280 1285 1290

Asp Leu Glu Pro Glu Asn Met Glu Ser Val Pro Leu Asp Pro Ser
1295 1300 1305

Ala Ser Ser Ser Ser Leu Pro Leu Pro Asp Arg His Ser Gly His
1310 1315 1320

Lys Ala Glu Asn Gly Pro Gly Pro Gly Val Leu Val Leu Arg Ala
1325 1330 1335

Ser Phe Asp Glu Arg Gln Pro Tyr Ala His Met Asn Gly Gly Arg
1340 1345 1350

Lys Asn Glu Arg Ala Leu Pro Leu Pro Gln Ser Ser Thr Cys
1355 1360 1365

<210> 444
<211> 1382
<212> PRT
<213> Homo sapiens

<400> 444

Met Ala Thr Gly Gly Arg Arg Gly Ala Ala Ala Ala Pro Leu Leu Val
1 5 10 15

Ala Val Ala Ala Leu Leu Leu Gly Ala Ala Gly His Leu Tyr Pro Gly
20 25 30

Glu Val Cys Pro Gly Met Asp Ile Arg Asn Asn Leu Thr Arg Leu His
35 40 45

Glu Leu Glu Asn Cys Ser Val Ile Glu Gly His Leu Gln Ile Leu Leu
50 55 60

Met Phe Lys Thr Arg Pro Glu Asp Phe Arg Asp Leu Ser Phe Pro Lys
65 70 75 80

```
Leu Ile Met Ile Thr Asp Tyr Leu Leu Leu Phe Arg Val Tyr Gly Leu
                85                  90                  95

Glu Ser Leu Lys Asp Leu Phe Pro Asn Leu Thr Val Ile Arg Gly Ser
            100                 105                 110

Arg Leu Phe Phe Asn Tyr Ala Leu Val Ile Phe Glu Met Val His Leu
        115                 120                 125

Lys Glu Leu Gly Leu Tyr Asn Leu Met Asn Ile Thr Arg Gly Ser Val
    130                 135                 140

Arg Ile Glu Lys Asn Asn Glu Leu Cys Tyr Leu Ala Thr Ile Asp Trp
145                 150                 155                 160

Ser Arg Ile Leu Asp Ser Val Glu Asp Asn Tyr Ile Val Leu Asn Lys
                165                 170                 175

Asp Asp Asn Glu Glu Cys Gly Asp Ile Cys Pro Gly Thr Ala Lys Gly
            180                 185                 190

Lys Thr Asn Cys Pro Ala Thr Val Ile Asn Gly Gln Phe Val Glu Arg
        195                 200                 205

Cys Trp Thr His Ser His Cys Gln Lys Val Cys Pro Thr Ile Cys Lys
    210                 215                 220

Ser His Gly Cys Thr Ala Glu Gly Leu Cys Cys His Ser Glu Cys Leu
225                 230                 235                 240

Gly Asn Cys Ser Gln Pro Asp Asp Pro Thr Lys Cys Val Ala Cys Arg
                245                 250                 255

Asn Phe Tyr Leu Asp Gly Arg Cys Val Glu Thr Cys Pro Pro Pro Tyr
            260                 265                 270

Tyr His Phe Gln Asp Trp Arg Cys Val Asn Phe Ser Phe Cys Gln Asp
        275                 280                 285

Leu His His Lys Cys Lys Asn Ser Arg Arg Gln Gly Cys His Gln Tyr
    290                 295                 300

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

Met Asn Ser Ser Asn Leu Leu Cys Thr Pro Cys Leu Gly Pro Cys Pro
                325                 330                 335

Lys Val Cys His Leu Leu Glu Gly Glu Lys Thr Ile Asp Ser Val Thr
            340                 345                 350
```

```
Ser Ala Gln Glu Leu Arg Gly Cys Thr Val Ile Asn Gly Ser Leu Ile
        355                 360                 365

Ile Asn Ile Arg Gly Gly Asn Asn Leu Ala Ala Glu Leu Glu Ala Asn
    370                 375                 380

Leu Gly Leu Ile Glu Glu Ile Ser Gly Tyr Leu Lys Ile Arg Arg Ser
385                 390                 395                 400

Tyr Ala Leu Val Ser Leu Ser Phe Phe Arg Lys Leu Arg Leu Ile Arg
                405                 410                 415

Gly Glu Thr Leu Glu Ile Gly Asn Tyr Ser Phe Tyr Ala Leu Asp Asn
            420                 425                 430

Gln Asn Leu Arg Gln Leu Trp Asp Trp Ser Lys His Asn Leu Thr Ile
        435                 440                 445

Thr Gln Gly Lys Leu Phe Phe His Tyr Asn Pro Lys Leu Cys Leu Ser
    450                 455                 460

Glu Ile His Lys Met Glu Glu Val Ser Gly Thr Lys Gly Arg Gln Glu
465                 470                 475                 480

Arg Asn Asp Ile Ala Leu Lys Thr Asn Gly Asp Gln Ala Ser Cys Glu
                485                 490                 495

Asn Glu Leu Leu Lys Phe Ser Tyr Ile Arg Thr Ser Phe Asp Lys Ile
            500                 505                 510

Leu Leu Arg Trp Glu Pro Tyr Trp Pro Pro Asp Phe Arg Asp Leu Leu
        515                 520                 525

Gly Phe Met Leu Phe Tyr Lys Glu Ala Pro Tyr Gln Asn Val Thr Glu
    530                 535                 540

Phe Asp Gly Gln Asp Ala Cys Gly Ser Asn Ser Trp Thr Val Val Asp
545                 550                 555                 560

Ile Asp Pro Pro Leu Arg Ser Asn Asp Pro Lys Ser Gln Asn His Pro
                565                 570                 575

Gly Trp Leu Met Arg Gly Leu Lys Pro Trp Thr Gln Tyr Ala Ile Phe
            580                 585                 590

Val Lys Thr Leu Val Thr Phe Ser Asp Glu Arg Arg Thr Tyr Gly Ala
        595                 600                 605

Lys Ser Asp Ile Ile Tyr Val Gln Thr Asp Ala Thr Asn Pro Ser Val
    610                 615                 620
```

```
Pro Leu Asp Pro Ile Ser Val Ser Asn Ser Ser Ser Gln Ile Ile Leu
625                 630                 635                 640

Lys Trp Lys Pro Pro Ser Asp Pro Asn Gly Asn Ile Thr His Tyr Leu
                645                 650                 655

Val Phe Trp Glu Arg Gln Ala Glu Asp Ser Glu Leu Phe Glu Leu Asp
            660                 665                 670

Tyr Cys Leu Lys Gly Leu Lys Leu Pro Ser Arg Thr Trp Ser Pro Pro
        675                 680                 685

Phe Glu Ser Glu Asp Ser Gln Lys His Asn Gln Ser Glu Tyr Glu Asp
    690                 695                 700

Ser Ala Gly Glu Cys Cys Ser Cys Pro Lys Thr Asp Ser Gln Ile Leu
705                 710                 715                 720

Lys Glu Leu Glu Glu Ser Ser Phe Arg Lys Thr Phe Glu Asp Tyr Leu
                725                 730                 735

His Asn Val Val Phe Val Pro Arg Lys Thr Ser Ser Gly Thr Gly Ala
            740                 745                 750

Glu Asp Pro Arg Pro Ser Arg Lys Arg Arg Ser Leu Gly Asp Val Gly
        755                 760                 765

Asn Val Thr Val Ala Val Pro Thr Val Ala Ala Phe Pro Asn Thr Ser
    770                 775                 780

Ser Thr Ser Val Pro Thr Ser Pro Glu Glu His Arg Pro Phe Glu Lys
785                 790                 795                 800

Val Val Asn Lys Glu Ser Leu Val Ile Ser Gly Leu Arg His Phe Thr
                805                 810                 815

Gly Tyr Arg Ile Glu Leu Gln Ala Cys Asn Gln Asp Thr Pro Glu Glu
            820                 825                 830

Arg Cys Ser Val Ala Ala Tyr Val Ser Ala Arg Thr Met Pro Glu Ala
        835                 840                 845

Lys Ala Asp Asp Ile Val Gly Pro Val Thr His Glu Ile Phe Glu Asn
    850                 855                 860

Asn Val Val His Leu Met Trp Gln Glu Pro Lys Glu Pro Asn Gly Leu
865                 870                 875                 880

Ile Val Leu Tyr Glu Val Ser Tyr Arg Arg Tyr Gly Asp Glu Glu Leu
                885                 890                 895
```

```
His Leu Cys Val Ser Arg Lys His Phe Ala Leu Glu Arg Gly Cys Arg
            900                 905                 910

Leu Arg Gly Leu Ser Pro Gly Asn Tyr Ser Val Arg Ile Arg Ala Thr
        915                 920                 925

Ser Leu Ala Gly Asn Gly Ser Trp Thr Glu Pro Thr Tyr Phe Tyr Val
    930                 935                 940

Thr Asp Tyr Leu Asp Val Pro Ser Asn Ile Ala Lys Ile Ile Ile Gly
945                 950                 955                 960

Pro Leu Ile Phe Val Phe Leu Phe Ser Val Val Ile Gly Ser Ile Tyr
                965                 970                 975

Leu Phe Leu Arg Lys Arg Gln Pro Asp Gly Pro Leu Gly Pro Leu Tyr
            980                 985                 990

Ala Ser Ser Asn Pro Glu Tyr Leu  Ser Ala Ser Asp Val  Phe Pro Cys
        995                 1000                1005

Ser Val  Tyr Val Pro Asp Glu  Trp Glu Val Ser Arg  Glu Lys Ile
    1010                1015                1020

Thr Leu  Leu Arg Glu Leu Gly  Gln Gly Ser Phe Gly  Met Val Tyr
    1025                1030                1035

Glu Gly  Asn Ala Arg Asp Ile  Ile Lys Gly Glu Ala  Glu Thr Arg
    1040                1045                1050

Val Ala  Val Lys Thr Val Asn  Glu Ser Ala Ser Leu  Arg Glu Arg
    1055                1060                1065

Ile Glu  Phe Leu Asn Glu Ala  Ser Val Met Lys Gly  Phe Thr Cys
    1070                1075                1080

His His  Val Val Arg Leu Leu  Gly Val Val Ser Lys  Gly Gln Pro
    1085                1090                1095

Thr Leu  Val Val Met Glu Leu  Met Ala His Gly Asp  Leu Lys Ser
    1100                1105                1110

Tyr Leu  Arg Ser Leu Arg Pro  Glu Ala Glu Asn Asn  Pro Gly Arg
    1115                1120                1125

Pro Pro  Pro Thr Leu Gln Glu  Met Ile Gln Met Ala  Ala Glu Ile
    1130                1135                1140

Ala Asp  Gly Met Ala Tyr Leu  Asn Ala Lys Lys Phe  Val His Arg
    1145                1150                1155
```

```
Asp Leu  Ala Ala Arg Asn Cys  Met Val Ala His Asp  Phe Thr Val
    1160                1165                1170

Lys Ile  Gly Asp Phe Gly Met  Thr Arg Asp Ile Tyr  Glu Thr Asp
    1175                1180                1185

Tyr Tyr  Arg Lys Gly Gly Lys  Gly Leu Leu Pro Val  Arg Trp Met
    1190                1195                1200

Ala Pro  Glu Ser Leu Lys Asp  Gly Val Phe Thr Thr  Ser Ser Asp
    1205                1210                1215

Met Trp  Ser Phe Gly Val Val  Leu Trp Glu Ile Thr  Ser Leu Ala
    1220                1225                1230

Glu Gln  Pro Tyr Gln Gly Leu  Ser Asn Glu Gln Val  Leu Lys Phe
    1235                1240                1245

Val Met  Asp Gly Gly Tyr Leu  Asp Gln Pro Asp Asn  Cys Pro Glu
    1250                1255                1260

Arg Val  Thr Asp Leu Met Arg  Met Cys Trp Gln Phe  Asn Pro Lys
    1265                1270                1275

Met Arg  Pro Thr Phe Leu Glu  Ile Val Asn Leu Leu  Lys Asp Asp
    1280                1285                1290

Leu His  Pro Ser Phe Pro Glu  Val Ser Phe Phe His  Ser Glu Glu
    1295                1300                1305

Asn Lys  Ala Pro Glu Ser Glu  Glu Leu Glu Met Glu  Phe Glu Asp
    1310                1315                1320

Met Glu  Asn Val Pro Leu Asp  Arg Ser Ser His Cys  Gln Arg Glu
    1325                1330                1335

Glu Ala  Gly Gly Arg Asp Gly  Gly Ser Ser Leu Gly  Phe Lys Arg
    1340                1345                1350

Ser Tyr  Glu Glu His Ile Pro  Tyr Thr His Met Asn  Gly Gly Lys
    1355                1360                1365

Lys Asn  Gly Arg Ile Leu Thr  Leu Pro Arg Ser Asn  Pro Ser
    1370                1375                1380
```

<210> 445
<211> 1297
<212> PRT
<213> Homo sapiens

<400> 445

```
Met Ala Val Pro Ser Leu Trp Pro Trp Gly Ala Cys Leu Pro Val Ile
1               5                  10                  15

Phe Leu Ser Leu Gly Phe Gly Leu Asp Thr Val Glu Val Cys Pro Ser
            20                  25                  30

Leu Asp Ile Arg Ser Glu Val Ala Glu Leu Arg Gln Leu Glu Asn Cys
        35                  40                  45

Ser Val Val Glu Gly His Leu Gln Ile Leu Leu Met Phe Thr Ala Thr
    50                  55                  60

Gly Glu Asp Phe Arg Gly Leu Ser Phe Pro Arg Leu Thr Gln Val Thr
65                  70                  75                  80

Asp Tyr Leu Leu Leu Phe Arg Val Tyr Gly Leu Glu Ser Leu Arg Asp
                85                  90                  95

Leu Phe Pro Asn Leu Ala Val Ile Arg Gly Thr Arg Leu Phe Leu Gly
            100                 105                 110

Tyr Ala Leu Val Ile Phe Glu Met Pro His Leu Arg Asp Val Ala Leu
        115                 120                 125

Pro Ala Leu Gly Ala Val Leu Arg Gly Ala Val Arg Val Glu Lys Asn
    130                 135                 140

Gln Glu Leu Cys His Leu Ser Thr Ile Asp Trp Gly Leu Leu Gln Pro
145                 150                 155                 160

Ala Pro Gly Ala Asn His Ile Val Gly Asn Lys Leu Gly Glu Glu Cys
                165                 170                 175

Ala Asp Val Cys Pro Gly Val Leu Gly Ala Ala Gly Glu Pro Cys Ala
            180                 185                 190

Lys Thr Thr Phe Ser Gly His Thr Asp Tyr Arg Cys Trp Thr Ser Ser
        195                 200                 205

His Cys Gln Arg Val Cys Pro Cys Pro His Gly Met Ala Cys Thr Ala
    210                 215                 220

Arg Gly Glu Cys Cys His Thr Glu Cys Leu Gly Gly Cys Ser Gln Pro
225                 230                 235                 240

Glu Asp Pro Arg Ala Cys Val Ala Cys Arg His Leu Tyr Phe Gln Gly
                245                 250                 255

Ala Cys Leu Trp Ala Cys Pro Pro Gly Thr Tyr Gln Tyr Glu Ser Trp
            260                 265                 270
```

```
Arg Cys Val Thr Ala Glu Arg Cys Ala Ser Leu His Ser Val Pro Gly
        275                 280                 285

Arg Ala Ser Thr Phe Gly Ile His Gln Gly Ser Cys Leu Ala Gln Cys
    290                 295                 300

Pro Ser Gly Phe Thr Arg Asn Ser Ser Ser Ile Phe Cys His Lys Cys
305                 310                 315                 320

Glu Gly Leu Cys Pro Lys Glu Cys Lys Val Gly Thr Lys Thr Ile Asp
                325                 330                 335

Ser Ile Gln Ala Ala Gln Asp Leu Val Gly Cys Thr His Val Glu Gly
            340                 345                 350

Ser Leu Ile Leu Asn Leu Arg Gln Gly Tyr Asn Leu Glu Pro Gln Leu
        355                 360                 365

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

Lys His Ser Phe Ala Leu Val Ser Leu Gly Phe Phe Lys Asn Leu Lys
385                 390                 395                 400

Leu Ile Arg Gly Asp Ala Met Val Asp Gly Asn Tyr Thr Leu Tyr Val
                405                 410                 415

Leu Asp Asn Gln Asn Leu Gln Gln Leu Gly Ser Trp Val Ala Ala Gly
            420                 425                 430

Leu Thr Ile Pro Val Gly Lys Ile Tyr Phe Ala Phe Asn Pro Arg Leu
        435                 440                 445

Cys Leu Glu His Ile Tyr Arg Leu Glu Glu Val Thr Gly Thr Arg Gly
    450                 455                 460

Arg Gln Asn Lys Ala Glu Ile Asn Pro Arg Thr Asn Gly Asp Arg Ala
465                 470                 475                 480

Ala Cys Gln Thr Arg Thr Leu Arg Phe Val Ser Asn Val Thr Glu Ala
                485                 490                 495

Asp Arg Ile Leu Leu Arg Trp Glu Arg Tyr Glu Pro Leu Glu Ala Arg
            500                 505                 510

Asp Leu Leu Ser Phe Ile Val Tyr Tyr Lys Glu Ser Pro Phe Gln Asn
        515                 520                 525

Ala Thr Glu His Val Gly Pro Asp Ala Cys Gly Thr Gln Ser Trp Asn
    530                 535                 540
```

```
Leu Leu Asp Val Glu Leu Pro Leu Ser Arg Thr Gln Glu Pro Gly Val
545                 550                 555                 560

Thr Leu Ala Ser Leu Lys Pro Trp Thr Gln Tyr Ala Val Phe Val Arg
                565                 570                 575

Ala Ile Thr Leu Thr Thr Glu Glu Asp Ser Pro His Gln Gly Ala Gln
            580                 585                 590

Ser Pro Ile Val Tyr Leu Arg Thr Leu Pro Ala Ala Pro Thr Val Pro
        595                 600                 605

Gln Asp Val Ile Ser Thr Ser Asn Ser Ser Ser His Leu Leu Val Arg
    610                 615                 620

Trp Lys Pro Pro Thr Gln Arg Asn Gly Asn Leu Thr Tyr Tyr Leu Val
625                 630                 635                 640

Leu Trp Gln Arg Leu Ala Glu Asp Gly Asp Leu Tyr Leu Asn Asp Tyr
                645                 650                 655

Cys His Arg Gly Leu Arg Leu Pro Thr Ser Asn Asn Asp Pro Arg Phe
            660                 665                 670

Asp Gly Glu Asp Gly Asp Pro Glu Ala Glu Met Glu Ser Asp Cys Cys
        675                 680                 685

Pro Cys Gln His Pro Pro Pro Gly Gln Val Leu Pro Pro Leu Glu Ala
    690                 695                 700

Gln Glu Ala Ser Phe Gln Lys Lys Phe Glu Asn Phe Leu His Asn Ala
705                 710                 715                 720

Ile Thr Ile Pro Ile Ser Pro Trp Lys Val Thr Ser Ile Asn Lys Ser
                725                 730                 735

Pro Gln Arg Asp Ser Gly Arg His Arg Arg Ala Ala Gly Pro Leu Arg
            740                 745                 750

Leu Gly Gly Asn Ser Ser Asp Phe Glu Ile Gln Glu Asp Lys Val Pro
        755                 760                 765

Arg Glu Arg Ala Val Leu Ser Gly Leu Arg His Phe Thr Glu Tyr Arg
    770                 775                 780

Ile Asp Ile His Ala Cys Asn His Ala Ala His Thr Val Gly Cys Ser
785                 790                 795                 800

Ala Ala Thr Phe Val Phe Ala Arg Thr Met Pro His Arg Glu Ala Asp
                805                 810                 815
```

```
Gly Ile Pro Gly Lys Val Ala Trp Glu Ala Ser Ser Lys Asn Ser Val
            820                 825                 830

Leu Leu Arg Trp Leu Glu Pro Pro Asp Pro Asn Gly Leu Ile Leu Lys
        835                 840                 845

Tyr Glu Ile Lys Tyr Arg Arg Leu Gly Glu Glu Ala Thr Val Leu Cys
    850                 855                 860

Val Ser Arg Leu Arg Tyr Ala Lys Phe Gly Gly Val His Leu Ala Leu
865                 870                 875                 880

Leu Pro Pro Gly Asn Tyr Ser Ala Arg Val Arg Ala Thr Ser Leu Ala
                885                 890                 895

Gly Asn Gly Ser Trp Thr Asp Ser Val Ala Phe Tyr Ile Leu Gly Pro
            900                 905                 910

Glu Glu Glu Asp Ala Gly Gly Leu His Val Leu Leu Thr Ala Thr Pro
        915                 920                 925

Val Gly Leu Thr Leu Leu Ile Val Leu Ala Ala Leu Gly Phe Phe Tyr
    930                 935                 940

Gly Lys Lys Arg Asn Arg Thr Leu Tyr Ala Ser Val Asn Pro Glu Tyr
945                 950                 955                 960

Phe Ser Ala Ser Asp Met Tyr Val Pro Asp Glu Trp Glu Val Pro Arg
                965                 970                 975

Glu Gln Ile Ser Ile Ile Arg Glu Leu Gly Gln Gly Ser Phe Gly Met
            980                 985                 990

Val Tyr Glu Gly Leu Ala Arg Gly  Leu Glu Ala Gly Glu  Glu Ser Thr
        995                 1000                1005

Pro Val  Ala Leu Lys Thr Val  Asn Glu Leu Ala Ser  Pro Arg Glu
    1010                1015                1020

Cys Ile  Glu Phe Leu Lys Glu  Ala Ser Val Met Lys  Ala Phe Lys
    1025                1030                1035

Cys His  His Val Val Arg Leu  Leu Gly Val Val Ser  Gln Gly Gln
    1040                1045                1050

Pro Thr  Leu Val Ile Met Glu  Leu Met Thr Arg Gly  Asp Leu Lys
    1055                1060                1065

Ser His  Leu Arg Ser Leu Arg  Pro Glu Ala Glu Asn  Asn Pro Gly
    1070                1075                1080
```

Leu Pro Gln Pro Ala Leu Gly Glu Met Ile Gln Met Ala Gly Glu
1085 1090 1095

Ile Ala Asp Gly Met Ala Tyr Leu Ala Ala Asn Lys Phe Val His
1100 1105 1110

Arg Asp Leu Ala Ala Arg Asn Cys Met Val Ser Gln Asp Phe Thr
1115 1120 1125

Val Lys Ile Gly Asp Phe Gly Met Thr Arg Asp Val Tyr Glu Thr
1130 1135 1140

Asp Tyr Tyr Arg Lys Gly Gly Lys Gly Leu Leu Pro Val Arg Trp
1145 1150 1155

Met Ala Pro Glu Ser Leu Lys Asp Gly Ile Phe Thr Thr His Ser
1160 1165 1170

Asp Val Trp Ser Phe Gly Val Val Leu Trp Glu Ile Val Thr Leu
1175 1180 1185

Ala Glu Gln Pro Tyr Gln Gly Leu Ser Asn Glu Gln Val Leu Lys
1190 1195 1200

Phe Val Met Asp Gly Gly Val Leu Glu Glu Leu Glu Gly Cys Pro
1205 1210 1215

Leu Gln Leu Gln Glu Leu Met Ser Arg Cys Trp Gln Pro Asn Pro
1220 1225 1230

Arg Leu Arg Pro Ser Phe Thr His Ile Leu Asp Ser Ile Gln Glu
1235 1240 1245

Glu Leu Arg Pro Ser Phe Arg Leu Leu Ser Phe Tyr Tyr Ser Pro
1250 1255 1260

Glu Cys Arg Gly Ala Arg Gly Ser Leu Pro Thr Thr Asp Ala Glu
1265 1270 1275

Pro Asp Ser Ser Pro Thr Pro Arg Asp Cys Ser Pro Gln Asn Gly
1280 1285 1290

Gly Pro Gly His
1295

<210> 446
<211> 1356
<212> PRT
<213> Homo sapiens

<400> 446

```
Met Gln Ser Lys Val Leu Leu Ala Val Ala Leu Trp Leu Cys Val Glu
1               5                  10                  15

Thr Arg Ala Ala Ser Val Gly Leu Pro Ser Val Ser Leu Asp Leu Pro
            20                  25                  30

Arg Leu Ser Ile Gln Lys Asp Ile Leu Thr Ile Lys Ala Asn Thr Thr
        35                  40                  45

Leu Gln Ile Thr Cys Arg Gly Gln Arg Asp Leu Asp Trp Leu Trp Pro
    50                  55                  60

Asn Asn Gln Ser Gly Ser Glu Gln Arg Val Glu Val Thr Glu Cys Ser
65                  70                  75                  80

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

Asp Thr Gly Ala Tyr Lys Cys Phe Tyr Arg Glu Thr Asp Leu Ala Ser
            100                 105                 110

Val Ile Tyr Val Tyr Val Gln Asp Tyr Arg Ser Pro Phe Ile Ala Ser
        115                 120                 125

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

Thr Val Val Ile Pro Cys Leu Gly Ser Ile Ser Asn Leu Asn Val Ser
145                 150                 155                 160

Leu Cys Ala Arg Tyr Pro Glu Lys Arg Phe Val Pro Asp Gly Asn Arg
                165                 170                 175

Ile Ser Trp Asp Ser Lys Lys Gly Phe Thr Ile Pro Ser Tyr Met Ile
            180                 185                 190

Ser Tyr Ala Gly Met Val Phe Cys Glu Ala Lys Ile Asn Asp Glu Ser
        195                 200                 205

Tyr Gln Ser Ile Met Tyr Ile Val Val Val Val Gly Tyr Arg Ile Tyr
    210                 215                 220

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

Lys Leu Val Leu Asn Cys Thr Ala Arg Thr Glu Leu Asn Val Gly Ile
                245                 250                 255

Asp Phe Asn Trp Glu Tyr Pro Ser Ser Lys His Gln His Lys Lys Leu
            260                 265                 270
```

```
Val Asn Arg Asp Leu Lys Thr Gln Ser Gly Ser Glu Met Lys Lys Phe
        275                 280                 285

Leu Ser Thr Leu Thr Ile Asp Gly Val Thr Arg Ser Asp Gln Gly Leu
    290                 295                 300

Tyr Thr Cys Ala Ala Ser Ser Gly Leu Met Thr Lys Lys Asn Ser Thr
305                 310                 315                 320

Phe Val Arg Val His Glu Lys Pro Phe Val Ala Phe Gly Ser Gly Met
                325                 330                 335

Glu Ser Leu Val Glu Ala Thr Val Gly Glu Arg Val Arg Ile Pro Ala
            340                 345                 350

Lys Tyr Leu Gly Tyr Pro Pro Pro Glu Ile Lys Trp Tyr Lys Asn Gly
        355                 360                 365

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

Ile Met Glu Val Ser Glu Arg Asp Thr Gly Asn Tyr Thr Val Ile Leu
385                 390                 395                 400

Thr Asn Pro Ile Ser Lys Glu Lys Gln Ser His Val Val Ser Leu Val
                405                 410                 415

Val Tyr Val Pro Pro Gln Ile Gly Glu Lys Ser Leu Ile Ser Pro Val
            420                 425                 430

Asp Ser Tyr Gln Tyr Gly Thr Thr Gln Thr Leu Thr Cys Thr Val Tyr
        435                 440                 445

Ala Ile Pro Pro Pro His His Ile His Trp Tyr Trp Gln Leu Glu Glu
    450                 455                 460

Glu Cys Ala Asn Glu Pro Ser Gln Ala Val Ser Val Thr Asn Pro Tyr
465                 470                 475                 480

Pro Cys Glu Glu Trp Arg Ser Val Glu Asp Phe Gln Gly Gly Asn Lys
                485                 490                 495

Ile Glu Val Asn Lys Asn Gln Phe Ala Leu Ile Glu Gly Lys Asn Lys
            500                 505                 510

Thr Val Ser Thr Leu Val Ile Gln Ala Ala Asn Val Ser Ala Leu Tyr
        515                 520                 525

Lys Cys Glu Ala Val Asn Lys Val Gly Arg Gly Glu Arg Val Ile Ser
    530                 535                 540
```

```
Phe His Val Thr Arg Gly Pro Glu Ile Thr Leu Gln Pro Asp Met Gln
545                 550                 555                 560

Pro Thr Glu Gln Glu Ser Val Ser Leu Trp Cys Thr Ala Asp Arg Ser
                565                 570                 575

Thr Phe Glu Asn Leu Thr Trp Tyr Lys Leu Gly Pro Gln Pro Leu Pro
            580                 585                 590

Ile His Val Gly Glu Leu Pro Thr Pro Val Cys Lys Asn Leu Asp Thr
        595                 600                 605

Leu Trp Lys Leu Asn Ala Thr Met Phe Ser Asn Ser Thr Asn Asp Ile
    610                 615                 620

Leu Ile Met Glu Leu Lys Asn Ala Ser Leu Gln Asp Gln Gly Asp Tyr
625                 630                 635                 640

Val Cys Leu Ala Gln Asp Arg Lys Thr Lys Lys Arg His Cys Val Val
                645                 650                 655

Arg Gln Leu Thr Val Leu Glu Arg Val Ala Pro Thr Ile Thr Gly Asn
            660                 665                 670

Leu Glu Asn Gln Thr Thr Ser Ile Gly Glu Ser Ile Glu Val Ser Cys
        675                 680                 685

Thr Ala Ser Gly Asn Pro Pro Pro Gln Ile Met Trp Phe Lys Asp Asn
    690                 695                 700

Glu Thr Leu Val Glu Asp Ser Gly Ile Val Leu Lys Asp Gly Asn Arg
705                 710                 715                 720

Asn Leu Thr Ile Arg Arg Val Arg Lys Glu Asp Glu Gly Leu Tyr Thr
                725                 730                 735

Cys Gln Ala Cys Ser Val Leu Gly Cys Ala Lys Val Glu Ala Phe Phe
            740                 745                 750

Ile Ile Glu Gly Ala Gln Glu Lys Thr Asn Leu Glu Ile Ile Ile Leu
        755                 760                 765

Val Gly Thr Ala Val Ile Ala Met Phe Phe Trp Leu Leu Leu Val Ile
    770                 775                 780

Ile Leu Arg Thr Val Lys Arg Ala Asn Gly Gly Glu Leu Lys Thr Gly
785                 790                 795                 800

Tyr Leu Ser Ile Val Met Asp Pro Asp Glu Leu Pro Leu Asp Glu His
                805                 810                 815
```

```
Cys Glu Arg Leu Pro Tyr Asp Ala Ser Lys Trp Glu Phe Pro Arg Asp
            820                 825                 830

Arg Leu Lys Leu Gly Lys Pro Leu Gly Arg Gly Ala Phe Gly Gln Val
        835                 840                 845

Ile Glu Ala Asp Ala Phe Gly Ile Asp Lys Thr Ala Thr Cys Arg Thr
    850                 855                 860

Val Ala Val Lys Met Leu Lys Glu Gly Ala Thr His Ser Glu His Arg
865                 870                 875                 880

Ala Leu Met Ser Glu Leu Lys Ile Leu Ile His Ile Gly His His Leu
                885                 890                 895

Asn Val Val Asn Leu Leu Gly Ala Cys Thr Lys Pro Gly Gly Pro Leu
            900                 905                 910

Met Val Ile Val Glu Phe Cys Lys Phe Gly Asn Leu Ser Thr Tyr Leu
        915                 920                 925

Arg Ser Lys Arg Asn Glu Phe Val Pro Tyr Lys Thr Lys Gly Ala Arg
    930                 935                 940

Phe Arg Gln Gly Lys Asp Tyr Val Gly Ala Ile Pro Val Asp Leu Lys
945                 950                 955                 960

Arg Arg Leu Asp Ser Ile Thr Ser Ser Gln Ser Ser Ala Ser Ser Gly
                965                 970                 975

Phe Val Glu Glu Lys Ser Leu Ser Asp Val Glu Glu Glu Glu Ala Pro
            980                 985                 990

Glu Asp Leu Tyr Lys Asp Phe Leu  Thr Leu Glu His Leu  Ile Cys Tyr
        995                 1000                1005

Ser Phe  Gln Val Ala Lys Gly  Met Glu Phe Leu Ala  Ser Arg Lys
    1010                1015                1020

Cys Ile  His Arg Asp Leu Ala  Ala Arg Asn Ile Leu  Leu Ser Glu
    1025                1030                1035

Lys Asn  Val Val Lys Ile Cys  Asp Phe Gly Leu Ala  Arg Asp Ile
    1040                1045                1050

Tyr Lys  Asp Pro Asp Tyr Val  Arg Lys Gly Asp Ala  Arg Leu Pro
    1055                1060                1065

Leu Lys  Trp Met Ala Pro Glu  Thr Ile Phe Asp Arg  Val Tyr Thr
    1070                1075                1080
```

```
Ile Gln  Ser Asp Val Trp Ser  Phe Gly Val Leu Leu  Trp Glu Ile
    1085                1090                1095

Phe Ser  Leu Gly Ala Ser Pro  Tyr Pro Gly Val Lys  Ile Asp Glu
    1100                1105                1110

Glu Phe  Cys Arg Arg Leu Lys  Glu Gly Thr Arg Met  Arg Ala Pro
    1115                1120                1125

Asp Tyr  Thr Thr Pro Glu Met  Tyr Gln Thr Met Leu  Asp Cys Trp
    1130                1135                1140

His Gly  Glu Pro Ser Gln Arg  Pro Thr Phe Ser Glu  Leu Val Glu
    1145                1150                1155

His Leu  Gly Asn Leu Leu Gln  Ala Asn Ala Gln Gln  Asp Gly Lys
    1160                1165                1170

Asp Tyr  Ile Val Leu Pro Ile  Ser Glu Thr Leu Ser  Met Glu Glu
    1175                1180                1185

Asp Ser  Gly Leu Ser Leu Pro  Thr Ser Pro Val Ser  Cys Met Glu
    1190                1195                1200

Glu Glu  Glu Val Cys Asp Pro  Lys Phe His Tyr Asp  Asn Thr Ala
    1205                1210                1215

Gly Ile  Ser Gln Tyr Leu Gln  Asn Ser Lys Arg Lys  Ser Arg Pro
    1220                1225                1230

Val Ser  Val Lys Thr Phe Glu  Asp Ile Pro Leu Glu  Glu Pro Glu
    1235                1240                1245

Val Lys  Val Ile Pro Asp Asp  Asn Gln Thr Asp Ser  Gly Met Val
    1250                1255                1260

Leu Ala  Ser Glu Glu Leu Lys  Thr Leu Glu Asp Arg  Thr Lys Leu
    1265                1270                1275

Ser Pro  Ser Phe Gly Gly Met  Val Pro Ser Lys Ser  Arg Glu Ser
    1280                1285                1290

Val Ala  Ser Glu Gly Ser Asn  Gln Thr Ser Gly Tyr  Gln Ser Gly
    1295                1300                1305

Tyr His  Ser Asp Asp Thr Asp  Thr Thr Val Tyr Ser  Ser Glu Glu
    1310                1315                1320

Ala Glu  Leu Leu Lys Leu Ile  Glu Ile Gly Val Gln  Thr Gly Ser
    1325                1330                1335
```

Thr Ala Gln Ile Leu Gln Pro Asp Ser Gly Thr Thr Leu Ser Ser
1340 1345 1350

Pro Pro Val
1355

<210> 447
<211> 976
<212> PRT
<213> Homo sapiens

<400> 447

Met Arg Gly Ala Arg Gly Ala Trp Asp Phe Leu Cys Val Leu Leu Leu
1 5 10 15

Leu Leu Arg Val Gln Thr Gly Ser Ser Gln Pro Ser Val Ser Pro Gly
20 25 30

Glu Pro Ser Pro Pro Ser Ile His Pro Gly Lys Ser Asp Leu Ile Val
35 40 45

Arg Val Gly Asp Glu Ile Arg Leu Leu Cys Thr Asp Pro Gly Phe Val
50 55 60

Lys Trp Thr Phe Glu Ile Leu Asp Glu Thr Asn Glu Asn Lys Gln Asn
65 70 75 80

Glu Trp Ile Thr Glu Lys Ala Glu Ala Thr Asn Thr Gly Lys Tyr Thr
85 90 95

Cys Thr Asn Lys His Gly Leu Ser Asn Ser Ile Tyr Val Phe Val Arg
100 105 110

Asp Pro Ala Lys Leu Phe Leu Val Asp Arg Ser Leu Tyr Gly Lys Glu
115 120 125

Asp Asn Asp Thr Leu Val Arg Cys Pro Leu Thr Asp Pro Glu Val Thr
130 135 140

Asn Tyr Ser Leu Lys Gly Cys Gln Gly Lys Pro Leu Pro Lys Asp Leu
145 150 155 160

Arg Phe Ile Pro Asp Pro Lys Ala Gly Ile Met Ile Lys Ser Val Lys
165 170 175

Arg Ala Tyr His Arg Leu Cys Leu His Cys Ser Val Asp Gln Glu Gly
180 185 190

Lys Ser Val Leu Ser Glu Lys Phe Ile Leu Lys Val Arg Pro Ala Phe
195 200 205

Lys Ala Val Pro Val Val Ser Val Ser Lys Ala Ser Tyr Leu Leu Arg

210 215 220

Glu Gly Glu Glu Phe Thr Val Thr Cys Thr Ile Lys Asp Val Ser Ser
225 230 235 240

Ser Val Tyr Ser Thr Trp Lys Arg Glu Asn Ser Gln Thr Lys Leu Gln
245 250 255

Glu Lys Tyr Asn Ser Trp His His Gly Asp Phe Asn Tyr Glu Arg Gln
260 265 270

Ala Thr Leu Thr Ile Ser Ser Ala Arg Val Asn Asp Ser Gly Val Phe
275 280 285

Met Cys Tyr Ala Asn Asn Thr Phe Gly Ser Ala Asn Val Thr Thr Thr
290 295 300

Leu Glu Val Val Asp Lys Gly Phe Ile Asn Ile Phe Pro Met Ile Asn
305 310 315 320

Thr Thr Val Phe Val Asn Asp Gly Glu Asn Val Asp Leu Ile Val Glu
325 330 335

Tyr Glu Ala Phe Pro Lys Pro Glu His Gln Gln Trp Ile Tyr Met Asn
340 345 350

Arg Thr Phe Thr Asp Lys Trp Glu Asp Tyr Pro Lys Ser Glu Asn Glu
355 360 365

Ser Asn Ile Arg Tyr Val Ser Glu Leu His Leu Thr Arg Leu Lys Gly
370 375 380

Thr Glu Gly Gly Thr Tyr Thr Phe Leu Val Ser Asn Ser Asp Val Asn
385 390 395 400

Ala Ala Ile Ala Phe Asn Val Tyr Val Asn Thr Lys Pro Glu Ile Leu
405 410 415

Thr Tyr Asp Arg Leu Val Asn Gly Met Leu Gln Cys Val Ala Ala Gly
420 425 430

Phe Pro Glu Pro Thr Ile Asp Trp Tyr Phe Cys Pro Gly Thr Glu Gln
435 440 445

Arg Cys Ser Ala Ser Val Leu Pro Val Asp Val Gln Thr Leu Asn Ser
450 455 460

Ser Gly Pro Pro Phe Gly Lys Leu Val Val Gln Ser Ser Ile Asp Ser
465 470 475 480

Ser Ala Phe Lys His Asn Gly Thr Val Glu Cys Lys Ala Tyr Asn Asp

485 490 495

Val Gly Lys Thr Ser Ala Tyr Phe Asn Phe Ala Phe Lys Gly Asn Asn
500 505 510

Lys Glu Gln Ile His Pro His Thr Leu Phe Thr Pro Leu Leu Ile Gly
515 520 525

Phe Val Ile Val Ala Gly Met Met Cys Ile Ile Val Met Ile Leu Thr
530 535 540

Tyr Lys Tyr Leu Gln Lys Pro Met Tyr Glu Val Gln Trp Lys Val Val
545 550 555 560

Glu Glu Ile Asn Gly Asn Asn Tyr Val Tyr Ile Asp Pro Thr Gln Leu
565 570 575

Pro Tyr Asp His Lys Trp Glu Phe Pro Arg Asn Arg Leu Ser Phe Gly
580 585 590

Lys Thr Leu Gly Ala Gly Ala Phe Gly Lys Val Val Glu Ala Thr Ala
595 600 605

Tyr Gly Leu Ile Lys Ser Asp Ala Ala Met Thr Val Ala Val Lys Met
610 615 620

Leu Lys Pro Ser Ala His Leu Thr Glu Arg Glu Ala Leu Met Ser Glu
625 630 635 640

Leu Lys Val Leu Ser Tyr Leu Gly Asn His Met Asn Ile Val Asn Leu
645 650 655

Leu Gly Ala Cys Thr Ile Gly Gly Pro Thr Leu Val Ile Thr Glu Tyr
660 665 670

Cys Cys Tyr Gly Asp Leu Leu Asn Phe Leu Arg Arg Lys Arg Asp Ser
675 680 685

Phe Ile Cys Ser Lys Gln Glu Asp His Ala Glu Ala Ala Leu Tyr Lys
690 695 700

Asn Leu Leu His Ser Lys Glu Ser Ser Cys Ser Asp Ser Thr Asn Glu
705 710 715 720

Tyr Met Asp Met Lys Pro Gly Val Ser Tyr Val Val Pro Thr Lys Ala
725 730 735

Asp Lys Arg Arg Ser Val Arg Ile Gly Ser Tyr Ile Glu Arg Asp Val
740 745 750

Thr Pro Ala Ile Met Glu Asp Asp Glu Leu Ala Leu Asp Leu Glu Asp

```
        755                 760                 765

Leu Leu Ser Phe Ser Tyr Gln Val Ala Lys Gly Met Ala Phe Leu Ala
    770                 775                 780

Ser Lys Asn Cys Ile His Arg Asp Leu Ala Ala Arg Asn Ile Leu Leu
785                 790                 795                 800

Thr His Gly Arg Ile Thr Lys Ile Cys Asp Phe Gly Leu Ala Arg Asp
                805                 810                 815

Ile Lys Asn Asp Ser Asn Tyr Val Val Lys Gly Asn Ala Arg Leu Pro
            820                 825                 830

Val Lys Trp Met Ala Pro Glu Ser Ile Phe Asn Cys Val Tyr Thr Phe
        835                 840                 845

Glu Ser Asp Val Trp Ser Tyr Gly Ile Phe Leu Trp Glu Leu Phe Ser
    850                 855                 860

Leu Gly Ser Ser Pro Tyr Pro Gly Met Pro Val Asp Ser Lys Phe Tyr
865                 870                 875                 880

Lys Met Ile Lys Glu Gly Phe Arg Met Leu Ser Pro Glu His Ala Pro
                885                 890                 895

Ala Glu Met Tyr Asp Ile Met Lys Thr Cys Trp Asp Ala Asp Pro Leu
            900                 905                 910

Lys Arg Pro Thr Phe Lys Gln Ile Val Gln Leu Ile Glu Lys Gln Ile
        915                 920                 925

Ser Glu Ser Thr Asn His Ile Tyr Ser Asn Leu Ala Asn Cys Ser Pro
    930                 935                 940

Asn Arg Gln Lys Pro Val Val Asp His Ser Val Arg Ile Asn Ser Val
945                 950                 955                 960

Gly Ser Thr Ala Ser Ser Ser Gln Pro Leu Leu Val His Asp Asp Val
                965                 970                 975


<210>  448
<211>  864
<212>  PRT
<213>  Homo sapiens

<400>  448

Met Gly Cys Trp Gly Gln Leu Leu Val Trp Phe Gly Ala Ala Gly Ala
1               5                   10                  15

Ile Leu Cys Ser Ser Pro Gly Ser Gln Glu Thr Phe Leu Arg Ser Ser
            20                  25                  30
```

```
Pro Leu Pro Leu Ala Ser Pro Ser Pro Arg Asp Pro Lys Val Ser Ala
        35                  40                  45

Pro Pro Ser Ile Leu Glu Pro Ala Ser Pro Leu Asn Ser Pro Gly Thr
    50                  55                  60

Glu Gly Ser Trp Leu Phe Ser Thr Cys Gly Ala Ser Gly Arg His Gly
65                  70                  75                  80

Pro Thr Gln Thr Gln Cys Asp Gly Ala Tyr Ala Gly Thr Ser Val Val
                85                  90                  95

Val Thr Val Gly Ala Ala Gly Gln Leu Arg Gly Val Gln Leu Trp Arg
            100                 105                 110

Val Pro Gly Pro Gly Gln Tyr Leu Ile Ser Ala Tyr Gly Ala Ala Gly
        115                 120                 125

Gly Lys Gly Ala Lys Asn His Leu Ser Arg Ala His Gly Val Phe Val
    130                 135                 140

Ser Ala Ile Phe Ser Leu Gly Leu Gly Glu Ser Leu Tyr Ile Leu Val
145                 150                 155                 160

Gly Gln Gln Gly Glu Asp Ala Cys Pro Gly Gly Ser Pro Glu Ser Gln
                165                 170                 175

Leu Val Cys Leu Gly Glu Ser Arg Ala Val Glu Glu His Ala Ala Met
            180                 185                 190

Asp Gly Ser Glu Gly Val Pro Gly Ser Arg Arg Trp Ala Gly Gly Gly
        195                 200                 205

Gly Gly Gly Gly Gly Ala Thr Tyr Val Phe Arg Val Arg Ala Gly Glu
    210                 215                 220

Leu Glu Pro Leu Leu Val Ala Ala Gly Gly Gly Gly Arg Ala Tyr Leu
225                 230                 235                 240

Arg Pro Arg Asp Arg Gly Arg Thr Gln Ala Ser Pro Glu Lys Leu Glu
                245                 250                 255

Asn Arg Ser Glu Ala Pro Gly Ser Gly Gly Arg Gly Gly Ala Ala Gly
            260                 265                 270

Gly Gly Gly Gly Trp Thr Ser Arg Ala Pro Ser Pro Gln Ala Gly Arg
        275                 280                 285

Ser Leu Gln Glu Gly Ala Glu Gly Gly Gln Gly Cys Ser Glu Ala Trp
    290                 295                 300
```

```
Ala Thr Leu Gly Trp Ala Ala Ala Gly Gly Phe Gly Gly Gly Gly Gly
305                 310                 315                 320

Ala Cys Thr Ala Gly Gly Gly Gly Gly Gly Tyr Arg Gly Gly Asp Ala
                325                 330                 335

Ser Glu Thr Asp Asn Leu Trp Ala Asp Gly Glu Asp Gly Val Ser Phe
            340                 345                 350

Ile His Pro Ser Ser Glu Leu Phe Leu Gln Pro Leu Ala Val Thr Glu
        355                 360                 365

Asn His Gly Glu Val Glu Ile Arg Arg His Leu Asn Cys Ser His Cys
    370                 375                 380

Pro Leu Arg Asp Cys Gln Trp Gln Ala Glu Leu Gln Leu Ala Glu Cys
385                 390                 395                 400

Leu Cys Pro Glu Gly Met Glu Leu Ala Val Asp Asn Val Thr Cys Met
                405                 410                 415

Asp Leu His Lys Pro Pro Gly Pro Leu Val Leu Met Val Ala Val Val
            420                 425                 430

Ala Thr Ser Thr Leu Ser Leu Leu Met Val Cys Gly Val Leu Ile Leu
        435                 440                 445

Val Lys Gln Lys Lys Trp Gln Gly Leu Gln Glu Met Arg Leu Pro Ser
    450                 455                 460

Pro Glu Leu Glu Leu Ser Lys Leu Arg Thr Ser Ala Ile Arg Thr Ala
465                 470                 475                 480

Pro Asn Pro Tyr Tyr Cys Gln Val Gly Leu Gly Pro Ala Gln Ser Trp
                485                 490                 495

Pro Leu Pro Pro Gly Val Thr Glu Val Ser Pro Ala Asn Val Thr Leu
            500                 505                 510

Leu Arg Ala Leu Gly His Gly Ala Phe Gly Glu Val Tyr Glu Gly Leu
        515                 520                 525

Val Ile Gly Leu Pro Gly Asp Ser Ser Pro Leu Gln Val Ala Ile Lys
    530                 535                 540

Thr Leu Pro Glu Leu Cys Ser Pro Gln Asp Glu Leu Asp Phe Leu Met
545                 550                 555                 560

Glu Ala Leu Ile Ile Ser Lys Phe Arg His Gln Asn Ile Val Arg Cys
                565                 570                 575
```

```
Val Gly Leu Ser Leu Arg Ala Thr Pro Arg Leu Ile Leu Leu Glu Leu
            580                 585                 590

Met Ser Gly Gly Asp Met Lys Ser Phe Leu Arg His Ser Arg Pro His
        595                 600                 605

Leu Gly Gln Pro Ser Pro Leu Val Met Arg Asp Leu Leu Gln Leu Ala
    610                 615                 620

Gln Asp Ile Ala Gln Gly Cys His Tyr Leu Glu Glu Asn His Phe Ile
625                 630                 635                 640

His Arg Asp Ile Ala Ala Arg Asn Cys Leu Leu Ser Cys Ala Gly Pro
                645                 650                 655

Ser Arg Val Ala Lys Ile Gly Asp Phe Gly Met Ala Arg Asp Ile Tyr
            660                 665                 670

Arg Ala Ser Tyr Tyr Arg Arg Gly Asp Arg Ala Leu Leu Pro Val Lys
        675                 680                 685

Trp Met Pro Pro Glu Ala Phe Leu Glu Gly Ile Phe Thr Ser Lys Thr
    690                 695                 700

Asp Ser Trp Ser Phe Gly Val Leu Leu Trp Glu Ile Phe Ser Leu Gly
705                 710                 715                 720

Tyr Met Pro Tyr Pro Gly Arg Thr Asn Gln Glu Val Leu Asp Phe Val
                725                 730                 735

Val Gly Gly Gly Arg Met Asp Pro Pro Arg Gly Cys Pro Gly Pro Val
            740                 745                 750

Tyr Arg Ile Met Thr Gln Cys Trp Gln His Glu Pro Glu Leu Arg Pro
        755                 760                 765

Ser Phe Ala Ser Ile Leu Glu Arg Leu Gln Tyr Cys Thr Gln Asp Pro
    770                 775                 780

Asp Val Leu Asn Ser Leu Leu Pro Met Glu Leu Gly Pro Thr Pro Glu
785                 790                 795                 800

Glu Glu Gly Thr Ser Gly Leu Gly Asn Arg Ser Leu Glu Cys Leu Arg
                805                 810                 815

Pro Pro Gln Pro Gln Glu Leu Ser Pro Glu Lys Leu Lys Ser Trp Gly
            820                 825                 830

Gly Ser Pro Leu Gly Pro Trp Leu Ser Ser Gly Leu Lys Pro Leu Lys
        835                 840                 845
```

Ser Arg Gly Leu Gln Pro Gln Asn Leu Trp Asn Pro Thr Tyr Arg Ser
850 855 860

<210> 449
<211> 1390
<212> PRT
<213> Homo sapiens

<400> 449

Met Lys Ala Pro Ala Val Leu Ala Pro Gly Ile Leu Val Leu Leu Phe
1 5 10 15

Thr Leu Val Gln Arg Ser Asn Gly Glu Cys Lys Glu Ala Leu Ala Lys
20 25 30

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

Glu Thr Pro Ile Gln Asn Val Ile Leu His Glu His His Ile Phe Leu
50 55 60

Gly Ala Thr Asn Tyr Ile Tyr Val Leu Asn Glu Glu Asp Leu Gln Lys
65 70 75 80

Val Ala Glu Tyr Lys Thr Gly Pro Val Leu Glu His Pro Asp Cys Phe
85 90 95

Pro Cys Gln Asp Cys Ser Ser Lys Ala Asn Leu Ser Gly Gly Val Trp
100 105 110

Lys Asp Asn Ile Asn Met Ala Leu Val Val Asp Thr Tyr Tyr Asp Asp
115 120 125

Gln Leu Ile Ser Cys Gly Ser Val Asn Arg Gly Thr Cys Gln Arg His
130 135 140

Val Phe Pro His Asn His Thr Ala Asp Ile Gln Ser Glu Val His Cys
145 150 155 160

Ile Phe Ser Pro Gln Ile Glu Glu Pro Ser Gln Cys Pro Asp Cys Val
165 170 175

Val Ser Ala Leu Gly Ala Lys Val Leu Ser Ser Val Lys Asp Arg Phe
180 185 190

Ile Asn Phe Phe Val Gly Asn Thr Ile Asn Ser Ser Tyr Phe Pro Asp
195 200 205

His Pro Leu His Ser Ile Ser Val Arg Arg Leu Lys Glu Thr Lys Asp
210 215 220

```
Gly Phe Met Phe Leu Thr Asp Gln Ser Tyr Ile Asp Val Leu Pro Glu
225                 230                 235                 240

Phe Arg Asp Ser Tyr Pro Ile Lys Tyr Val His Ala Phe Glu Ser Asn
                245                 250                 255

Asn Phe Ile Tyr Phe Leu Thr Val Gln Arg Glu Thr Leu Asp Ala Gln
            260                 265                 270

Thr Phe His Thr Arg Ile Ile Arg Phe Cys Ser Ile Asn Ser Gly Leu
        275                 280                 285

His Ser Tyr Met Glu Met Pro Leu Glu Cys Ile Leu Thr Glu Lys Arg
    290                 295                 300

Lys Lys Arg Ser Thr Lys Lys Glu Val Phe Asn Ile Leu Gln Ala Ala
305                 310                 315                 320

Tyr Val Ser Lys Pro Gly Ala Gln Leu Ala Arg Gln Ile Gly Ala Ser
                325                 330                 335

Leu Asn Asp Asp Ile Leu Phe Gly Val Phe Ala Gln Ser Lys Pro Asp
            340                 345                 350

Ser Ala Glu Pro Met Asp Arg Ser Ala Met Cys Ala Phe Pro Ile Lys
        355                 360                 365

Tyr Val Asn Asp Phe Phe Asn Lys Ile Val Asn Lys Asn Asn Val Arg
    370                 375                 380

Cys Leu Gln His Phe Tyr Gly Pro Asn His Glu His Cys Phe Asn Arg
385                 390                 395                 400

Thr Leu Leu Arg Asn Ser Ser Gly Cys Glu Ala Arg Arg Asp Glu Tyr
                405                 410                 415

Arg Thr Glu Phe Thr Thr Ala Leu Gln Arg Val Asp Leu Phe Met Gly
            420                 425                 430

Gln Phe Ser Glu Val Leu Leu Thr Ser Ile Ser Thr Phe Ile Lys Gly
        435                 440                 445

Asp Leu Thr Ile Ala Asn Leu Gly Thr Ser Glu Gly Arg Phe Met Gln
    450                 455                 460

Val Val Val Ser Arg Ser Gly Pro Ser Thr Pro His Val Asn Phe Leu
465                 470                 475                 480

Leu Asp Ser His Pro Val Ser Pro Glu Val Ile Val Glu His Thr Leu
                485                 490                 495
```

```
Asn Gln Asn Gly Tyr Thr Leu Val Ile Thr Gly Lys Lys Ile Thr Lys
            500                 505                 510

Ile Pro Leu Asn Gly Leu Gly Cys Arg His Phe Gln Ser Cys Ser Gln
        515                 520                 525

Cys Leu Ser Ala Pro Pro Phe Val Gln Cys Gly Trp Cys His Asp Lys
    530                 535                 540

Cys Val Arg Ser Glu Glu Cys Leu Ser Gly Thr Trp Thr Gln Gln Ile
545                 550                 555                 560

Cys Leu Pro Ala Ile Tyr Lys Val Phe Pro Asn Ser Ala Pro Leu Glu
                565                 570                 575

Gly Gly Thr Arg Leu Thr Ile Cys Gly Trp Asp Phe Gly Phe Arg Arg
            580                 585                 590

Asn Asn Lys Phe Asp Leu Lys Lys Thr Arg Val Leu Leu Gly Asn Glu
        595                 600                 605

Ser Cys Thr Leu Thr Leu Ser Glu Ser Thr Met Asn Thr Leu Lys Cys
    610                 615                 620

Thr Val Gly Pro Ala Met Asn Lys His Phe Asn Met Ser Ile Ile Ile
625                 630                 635                 640

Ser Asn Gly His Gly Thr Thr Gln Tyr Ser Thr Phe Ser Tyr Val Asp
                645                 650                 655

Pro Val Ile Thr Ser Ile Ser Pro Lys Tyr Gly Pro Met Ala Gly Gly
            660                 665                 670

Thr Leu Leu Thr Leu Thr Gly Asn Tyr Leu Asn Ser Gly Asn Ser Arg
        675                 680                 685

His Ile Ser Ile Gly Gly Lys Thr Cys Thr Leu Lys Ser Val Ser Asn
    690                 695                 700

Ser Ile Leu Glu Cys Tyr Thr Pro Ala Gln Thr Ile Ser Thr Glu Phe
705                 710                 715                 720

Ala Val Lys Leu Lys Ile Asp Leu Ala Asn Arg Glu Thr Ser Ile Phe
                725                 730                 735

Ser Tyr Arg Glu Asp Pro Ile Val Tyr Glu Ile His Pro Thr Lys Ser
            740                 745                 750

Phe Ile Ser Gly Gly Ser Thr Ile Thr Gly Val Gly Lys Asn Leu Asn
        755                 760                 765
```

```
Ser Val Ser Val Pro Arg Met Val Ile Asn Val His Glu Ala Gly Arg
    770                 775                 780

Asn Phe Thr Val Ala Cys Gln His Arg Ser Asn Ser Glu Ile Ile Cys
785                 790                 795                 800

Cys Thr Thr Pro Ser Leu Gln Gln Leu Asn Leu Gln Leu Pro Leu Lys
                805                 810                 815

Thr Lys Ala Phe Phe Met Leu Asp Gly Ile Leu Ser Lys Tyr Phe Asp
            820                 825                 830

Leu Ile Tyr Val His Asn Pro Val Phe Lys Pro Phe Glu Lys Pro Val
        835                 840                 845

Met Ile Ser Met Gly Asn Glu Asn Val Leu Glu Ile Lys Gly Asn Asp
    850                 855                 860

Ile Asp Pro Glu Ala Val Lys Gly Glu Val Leu Lys Val Gly Asn Lys
865                 870                 875                 880

Ser Cys Glu Asn Ile His Leu His Ser Glu Ala Val Leu Cys Thr Val
                885                 890                 895

Pro Asn Asp Leu Leu Lys Leu Asn Ser Glu Leu Asn Ile Glu Trp Lys
            900                 905                 910

Gln Ala Ile Ser Ser Thr Val Leu Gly Lys Val Ile Val Gln Pro Asp
        915                 920                 925

Gln Asn Phe Thr Gly Leu Ile Ala Gly Val Val Ser Ile Ser Thr Ala
    930                 935                 940

Leu Leu Leu Leu Leu Gly Phe Phe Leu Trp Leu Lys Lys Arg Lys Gln
945                 950                 955                 960

Ile Lys Asp Leu Gly Ser Glu Leu Val Arg Tyr Asp Ala Arg Val His
                965                 970                 975

Thr Pro His Leu Asp Arg Leu Val Ser Ala Arg Ser Val Ser Pro Thr
            980                 985                 990

Thr Glu Met Val Ser Asn Glu Ser  Val Asp Tyr Arg Ala  Thr Phe Pro
        995                 1000                1005

Glu Asp  Gln Phe Pro Asn Ser  Ser Gln Asn Gly Ser  Cys Arg Gln
    1010                1015                1020

Val Gln  Tyr Pro Leu Thr Asp  Met Ser Pro Ile Leu  Thr Ser Gly
    1025                1030                1035
```

```
Asp Ser  Asp Ile Ser Ser Pro  Leu Leu Gln Asn Thr  Val His Ile
    1040                1045                1050

Asp Leu  Ser Ala Leu Asn Pro  Glu Leu Val Gln Ala  Val Gln His
    1055                1060                1065

Val Val  Ile Gly Pro Ser Ser  Leu Ile Val His Phe  Asn Glu Val
    1070                1075                1080

Ile Gly  Arg Gly His Phe Gly  Cys Val Tyr His Gly  Thr Leu Leu
    1085                1090                1095

Asp Asn  Asp Gly Lys Lys Ile  His Cys Ala Val Lys  Ser Leu Asn
    1100                1105                1110

Arg Ile  Thr Asp Ile Gly Glu  Val Ser Gln Phe Leu  Thr Glu Gly
    1115                1120                1125

Ile Ile  Met Lys Asp Phe Ser  His Pro Asn Val Leu  Ser Leu Leu
    1130                1135                1140

Gly Ile  Cys Leu Arg Ser Glu  Gly Ser Pro Leu Val  Val Leu Pro
    1145                1150                1155

Tyr Met  Lys His Gly Asp Leu  Arg Asn Phe Ile Arg  Asn Glu Thr
    1160                1165                1170

His Asn  Pro Thr Val Lys Asp  Leu Ile Gly Phe Gly  Leu Gln Val
    1175                1180                1185

Ala Lys  Gly Met Lys Tyr Leu  Ala Ser Lys Lys Phe  Val His Arg
    1190                1195                1200

Asp Leu  Ala Ala Arg Asn Cys  Met Leu Asp Glu Lys  Phe Thr Val
    1205                1210                1215

Lys Val  Ala Asp Phe Gly Leu  Ala Arg Asp Met Tyr  Asp Lys Glu
    1220                1225                1230

Tyr Tyr  Ser Val His Asn Lys  Thr Gly Ala Lys Leu  Pro Val Lys
    1235                1240                1245

Trp Met  Ala Leu Glu Ser Leu  Gln Thr Gln Lys Phe  Thr Thr Lys
    1250                1255                1260

Ser Asp  Val Trp Ser Phe Gly  Val Leu Leu Trp Glu  Leu Met Thr
    1265                1270                1275

Arg Gly  Ala Pro Pro Tyr Pro  Asp Val Asn Thr Phe  Asp Ile Thr
    1280                1285                1290
```

```
Val Tyr  Leu Leu Gln Gly Arg  Arg Leu Leu Gln Pro  Glu Tyr Cys
    1295                 1300                 1305

Pro Asp  Pro Leu Tyr Glu Val  Met Leu Lys Cys Trp  His Pro Lys
    1310                 1315                 1320

Ala Glu  Met Arg Pro Ser Phe  Ser Glu Leu Val Ser  Arg Ile Ser
    1325                 1330                 1335

Ala Ile  Phe Ser Thr Phe Ile  Gly Glu His Tyr Val  His Val Asn
    1340                 1345                 1350

Ala Thr  Tyr Val Asn Val Lys  Cys Val Ala Pro Tyr  Pro Ser Leu
    1355                 1360                 1365

Leu Ser  Ser Glu Asp Asn Ala  Asp Asp Glu Val Asp  Thr Arg Pro
    1370                 1375                 1380

Ala Ser  Phe Trp Glu Thr Ser
    1385                 1390


<210>  450
<211>  1400
<212>  PRT
<213>  Homo sapiens

<400>  450

Met Glu Leu Leu Pro Pro Leu Pro Gln Ser Phe Leu Leu Leu Leu Leu
1               5                  10                  15

Leu Pro Ala Lys Pro Ala Ala Gly Glu Asp Trp Gln Cys Pro Arg Thr
            20                  25                  30

Pro Tyr Ala Ala Ser Arg Asp Phe Asp Val Lys Tyr Val Val Pro Ser
        35                  40                  45

Phe Ser Ala Gly Gly Leu Val Gln Ala Met Val Thr Tyr Glu Gly Asp
    50                  55                  60

Arg Asn Glu Ser Ala Val Phe Val Ala Ile Arg Asn Arg Leu His Val
65                  70                  75                  80

Leu Gly Pro Asp Leu Lys Ser Val Gln Ser Leu Ala Thr Gly Pro Ala
                85                  90                  95

Gly Asp Pro Gly Cys Gln Thr Cys Ala Ala Cys Gly Pro Gly Pro His
            100                 105                 110

Gly Pro Pro Gly Asp Thr Asp Thr Lys Val Leu Val Leu Asp Pro Ala
        115                 120                 125
```

```
Leu Pro Ala Leu Val Ser Cys Gly Ser Ser Leu Gln Gly Arg Cys Phe
    130                 135                 140

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

Ala Cys Leu Phe Ser Ala His His Asn Arg Pro Asp Asp Cys Pro Asp
                165                 170                 175

Cys Val Ala Ser Pro Leu Gly Thr Arg Val Thr Val Val Glu Gln Gly
            180                 185                 190

Gln Ala Ser Tyr Phe Tyr Val Ala Ser Ser Leu Asp Ala Ala Val Ala
        195                 200                 205

Ala Ser Phe Ser Pro Arg Ser Val Ser Ile Arg Arg Leu Lys Ala Asp
    210                 215                 220

Ala Ser Gly Phe Ala Pro Gly Phe Val Ala Leu Ser Val Leu Pro Lys
225                 230                 235                 240

His Leu Val Ser Tyr Ser Ile Glu Tyr Val His Ser Phe His Thr Gly
                245                 250                 255

Ala Phe Val Tyr Phe Leu Thr Val Gln Pro Ala Ser Val Thr Asp Asp
            260                 265                 270

Pro Ser Ala Leu His Thr Arg Leu Ala Arg Leu Ser Ala Thr Glu Pro
        275                 280                 285

Glu Leu Gly Asp Tyr Arg Glu Leu Val Leu Asp Cys Arg Phe Ala Pro
    290                 295                 300

Lys Arg Arg Arg Arg Gly Ala Pro Glu Gly Gly Gln Pro Tyr Pro Val
305                 310                 315                 320

Leu Arg Val Ala His Ser Ala Pro Val Gly Ala Gln Leu Ala Thr Glu
                325                 330                 335

Leu Ser Ile Ala Glu Gly Gln Glu Val Leu Phe Gly Val Phe Val Thr
            340                 345                 350

Gly Lys Asp Gly Gly Pro Gly Val Gly Pro Asn Ser Val Val Cys Ala
        355                 360                 365

Phe Pro Ile Asp Leu Leu Asp Thr Leu Ile Asp Glu Gly Val Glu Arg
    370                 375                 380

Cys Cys Glu Ser Pro Val His Pro Gly Leu Arg Arg Gly Leu Asp Phe
385                 390                 395                 400
```

```
Phe Gln Ser Pro Ser Phe Cys Pro Asn Pro Pro Gly Leu Glu Ala Leu
                405                 410                 415

Ser Pro Asn Thr Ser Cys Arg His Phe Pro Leu Leu Val Ser Ser Ser
            420                 425                 430

Phe Ser Arg Val Asp Leu Phe Asn Gly Leu Leu Gly Pro Val Gln Val
        435                 440                 445

Thr Ala Leu Tyr Val Thr Arg Leu Asp Asn Val Thr Val Ala His Met
    450                 455                 460

Gly Thr Met Asp Gly Arg Ile Leu Gln Val Glu Leu Val Arg Ser Leu
465                 470                 475                 480

Asn Tyr Leu Leu Tyr Val Ser Asn Phe Ser Leu Gly Asp Ser Gly Gln
                485                 490                 495

Pro Val Gln Arg Asp Val Ser Arg Leu Gly Asp His Leu Leu Phe Ala
            500                 505                 510

Ser Gly Asp Gln Val Phe Gln Val Pro Ile Gln Gly Pro Gly Cys Arg
        515                 520                 525

His Phe Leu Thr Cys Gly Arg Cys Leu Arg Ala Trp His Phe Met Gly
    530                 535                 540

Cys Gly Trp Cys Gly Asn Met Cys Gly Gln Gln Lys Glu Cys Pro Gly
545                 550                 555                 560

Ser Trp Gln Gln Asp His Cys Pro Pro Lys Leu Thr Glu Phe His Pro
                565                 570                 575

His Ser Gly Pro Leu Arg Gly Ser Thr Arg Leu Thr Leu Cys Gly Ser
            580                 585                 590

Asn Phe Tyr Leu His Pro Ser Gly Leu Val Pro Glu Gly Thr His Gln
        595                 600                 605

Val Thr Val Gly Gln Ser Pro Cys Arg Pro Leu Pro Lys Asp Ser Ser
    610                 615                 620

Lys Leu Arg Pro Val Pro Arg Lys Asp Phe Val Glu Glu Phe Glu Cys
625                 630                 635                 640

Glu Leu Glu Pro Leu Gly Thr Gln Ala Val Gly Pro Thr Asn Val Ser
                645                 650                 655

Leu Thr Val Thr Asn Met Pro Pro Gly Lys His Phe Arg Val Asp Gly
            660                 665                 670
```

```
Thr Ser Val Leu Arg Gly Phe Ser Phe Met Glu Pro Val Leu Ile Ala
        675                 680                 685

Val Gln Pro Leu Phe Gly Pro Arg Ala Gly Gly Thr Cys Leu Thr Leu
    690                 695                 700

Glu Gly Gln Ser Leu Ser Val Gly Thr Ser Arg Ala Val Leu Val Asn
705                 710                 715                 720

Gly Thr Glu Cys Leu Leu Ala Arg Val Ser Glu Gly Gln Leu Leu Cys
                725                 730                 735

Ala Thr Pro Pro Gly Ala Thr Val Ala Ser Val Pro Leu Ser Leu Gln
            740                 745                 750

Val Gly Gly Ala Gln Val Pro Gly Ser Trp Thr Phe Gln Tyr Arg Glu
        755                 760                 765

Asp Pro Val Val Leu Ser Ile Ser Pro Asn Cys Gly Tyr Ile Asn Ser
    770                 775                 780

His Ile Thr Ile Cys Gly Gln His Leu Thr Ser Ala Trp His Leu Val
785                 790                 795                 800

Leu Ser Phe His Asp Gly Leu Arg Ala Val Glu Ser Arg Cys Glu Arg
                805                 810                 815

Gln Leu Pro Glu Gln Gln Leu Cys Arg Leu Pro Glu Tyr Val Val Arg
            820                 825                 830

Asp Pro Gln Gly Trp Val Ala Gly Asn Leu Ser Ala Arg Gly Asp Gly
        835                 840                 845

Ala Ala Gly Phe Thr Leu Pro Gly Phe Arg Phe Leu Pro Pro Pro His
    850                 855                 860

Pro Pro Ser Ala Asn Leu Val Pro Leu Lys Pro Glu Glu His Ala Ile
865                 870                 875                 880

Lys Phe Glu Tyr Ile Gly Leu Gly Ala Val Ala Asp Cys Val Gly Ile
                885                 890                 895

Asn Val Thr Val Gly Gly Glu Ser Cys Gln His Glu Phe Arg Gly Asp
            900                 905                 910

Met Val Val Cys Pro Leu Pro Pro Ser Leu Gln Leu Gly Gln Asp Gly
        915                 920                 925

Ala Pro Leu Gln Val Cys Val Asp Gly Glu Cys His Ile Leu Gly Arg
    930                 935                 940
```

```
Val Val Arg Pro Gly Pro Asp Gly Val Pro Gln Ser Thr Leu Leu Gly
945                 950                 955                 960

Ile Leu Leu Pro Leu Leu Leu Leu Val Ala Ala Leu Ala Thr Ala Leu
                965                 970                 975

Val Phe Ser Tyr Trp Trp Arg Arg Lys Gln Leu Val Leu Pro Pro Asn
            980                 985                 990

Leu Asn Asp Leu Ala Ser Leu Asp  Gln Thr Ala Gly Ala  Thr Pro Leu
        995                 1000                1005

Pro Ile  Leu Tyr Ser Gly Ser  Asp Tyr Arg Ser Gly  Leu Ala Leu
    1010                1015                1020

Pro Ala  Ile Asp Gly Leu Asp  Ser Thr Thr Cys Val  His Gly Ala
    1025                1030                1035

Ser Phe  Ser Asp Ser Glu Asp  Glu Ser Cys Val Pro  Leu Leu Arg
    1040                1045                1050

Lys Glu  Ser Ile Gln Leu Arg  Asp Leu Asp Ser Ala  Leu Leu Ala
    1055                1060                1065

Glu Val  Lys Asp Val Leu Ile  Pro His Glu Arg Val  Val Thr His
    1070                1075                1080

Ser Asp  Arg Val Ile Gly Lys  Gly His Phe Gly Val  Val Tyr His
    1085                1090                1095

Gly Glu  Tyr Ile Asp Gln Ala  Gln Asn Arg Ile Gln  Cys Ala Ile
    1100                1105                1110

Lys Ser  Leu Ser Arg Ile Thr  Glu Met Gln Gln Val  Glu Ala Phe
    1115                1120                1125

Leu Arg  Glu Gly Leu Leu Met  Arg Gly Leu Asn His  Pro Asn Val
    1130                1135                1140

Leu Ala  Leu Ile Gly Ile Met  Leu Pro Pro Glu Gly  Leu Pro His
    1145                1150                1155

Val Leu  Leu Pro Tyr Met Cys  His Gly Asp Leu Leu  Gln Phe Ile
    1160                1165                1170

Arg Ser  Pro Gln Arg Asn Pro  Thr Val Lys Asp Leu  Ile Ser Phe
    1175                1180                1185

Gly Leu  Gln Val Ala Arg Gly  Met Glu Tyr Leu Ala  Glu Gln Lys
    1190                1195                1200
```

Phe Val His Arg Asp Leu Ala Ala Arg Asn Cys Met Leu Asp Glu
1205 1210 1215

Ser Phe Thr Val Lys Val Ala Asp Phe Gly Leu Ala Arg Asp Ile
1220 1225 1230

Leu Asp Arg Glu Tyr Tyr Ser Val Gln Gln His Arg His Ala Arg
1235 1240 1245

Leu Pro Val Lys Trp Met Ala Leu Glu Ser Leu Gln Thr Tyr Arg
1250 1255 1260

Phe Thr Thr Lys Ser Asp Val Trp Ser Phe Gly Val Leu Leu Trp
1265 1270 1275

Glu Leu Leu Thr Arg Gly Ala Pro Pro Tyr Arg His Ile Asp Pro
1280 1285 1290

Phe Asp Leu Thr His Phe Leu Ala Gln Gly Arg Arg Leu Pro Gln
1295 1300 1305

Pro Glu Tyr Cys Pro Asp Ser Leu Tyr Gln Val Met Gln Gln Cys
1310 1315 1320

Trp Glu Ala Asp Pro Ala Val Arg Pro Thr Phe Arg Val Leu Val
1325 1330 1335

Gly Glu Val Glu Gln Ile Val Ser Ala Leu Leu Gly Asp His Tyr
1340 1345 1350

Val Gln Leu Pro Ala Thr Tyr Met Asn Leu Gly Pro Ser Thr Ser
1355 1360 1365

His Glu Met Asn Val Arg Pro Glu Gln Pro Gln Phe Ser Pro Met
1370 1375 1380

Pro Gly Asn Val Arg Arg Pro Arg Pro Leu Ser Glu Pro Pro Arg
1385 1390 1395

Pro Thr
1400

<210> 451
<211> 869
<212> PRT
<213> Homo sapiens

<400> 451

Met Arg Glu Leu Val Asn Ile Pro Leu Val His Ile Leu Thr Leu Val
1 5 10 15

Ala Phe Ser Gly Thr Glu Lys Leu Pro Lys Ala Pro Val Ile Thr Thr

```
            20                  25                  30

Pro Leu Glu Thr Val Asp Ala Leu Val Glu Glu Val Ala Thr Phe Met
        35                  40                  45

Cys Ala Val Glu Ser Tyr Pro Gln Pro Glu Ile Ser Trp Thr Arg Asn
    50                  55                  60

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

Gly Gln Leu Leu Thr Ile Leu Ser Val Glu Asp Ser Asp Asp Gly Ile
                85                  90                  95

Tyr Cys Cys Thr Ala Asn Asn Gly Val Gly Gly Ala Val Glu Ser Cys
            100                 105                 110

Gly Ala Leu Gln Val Lys Met Lys Pro Lys Ile Thr Arg Pro Pro Ile
        115                 120                 125

Asn Val Lys Ile Ile Glu Gly Leu Lys Ala Val Leu Pro Cys Thr Thr
    130                 135                 140

Met Gly Asn Pro Lys Pro Ser Val Ser Trp Ile Lys Gly Asp Ser Pro
145                 150                 155                 160

Leu Arg Glu Asn Ser Arg Ile Ala Val Leu Glu Ser Gly Ser Leu Arg
                165                 170                 175

Ile His Asn Val Gln Lys Glu Asp Ala Gly Gln Tyr Arg Cys Val Ala
            180                 185                 190

Lys Asn Ser Leu Gly Thr Ala Tyr Ser Lys Val Val Lys Leu Glu Val
        195                 200                 205

Glu Val Phe Ala Arg Ile Leu Arg Ala Pro Glu Ser His Asn Val Thr
    210                 215                 220

Phe Gly Ser Phe Val Thr Leu His Cys Thr Ala Thr Gly Ile Pro Val
225                 230                 235                 240

Pro Thr Ile Thr Trp Ile Glu Asn Gly Asn Ala Val Ser Ser Gly Ser
                245                 250                 255

Ile Gln Glu Ser Val Lys Asp Arg Val Ile Asp Ser Arg Leu Gln Leu
            260                 265                 270

Phe Ile Thr Lys Pro Gly Leu Tyr Thr Cys Ile Ala Thr Asn Lys His
        275                 280                 285

Gly Glu Lys Phe Ser Thr Ala Lys Ala Ala Ala Thr Ile Ser Ile Ala
```

290 295 300

Glu Trp Ser Lys Pro Gln Lys Asp Asn Lys Gly Tyr Cys Ala Gln Tyr
305 310 315 320

Arg Gly Glu Val Cys Asn Ala Val Leu Ala Lys Asp Ala Leu Val Phe
325 330 335

Leu Asn Thr Ser Tyr Ala Asp Pro Glu Glu Ala Gln Glu Leu Leu Val
340 345 350

His Thr Ala Trp Asn Glu Leu Lys Val Val Ser Pro Val Cys Arg Pro
355 360 365

Ala Ala Glu Ala Leu Leu Cys Asn His Ile Phe Gln Glu Cys Ser Pro
370 375 380

Gly Val Val Pro Thr Pro Ile Pro Ile Cys Arg Glu Tyr Cys Leu Ala
385 390 395 400

Val Lys Glu Leu Phe Cys Ala Lys Glu Trp Leu Val Met Glu Glu Lys
405 410 415

Thr His Arg Gly Leu Tyr Arg Ser Glu Met His Leu Leu Ser Val Pro
420 425 430

Glu Cys Ser Lys Leu Pro Ser Met His Trp Asp Pro Thr Ala Cys Ala
435 440 445

Arg Leu Pro His Leu Asp Tyr Asn Lys Glu Asn Leu Lys Thr Phe Pro
450 455 460

Pro Met Thr Ser Ser Lys Pro Ser Val Asp Ile Pro Asn Leu Pro Ser
465 470 475 480

Ser Ser Ser Ser Ser Phe Ser Val Ser Pro Thr Tyr Ser Met Thr Val
485 490 495

Ile Ile Ser Ile Met Ser Ser Phe Ala Ile Phe Val Leu Leu Thr Ile
500 505 510

Thr Thr Leu Tyr Cys Cys Arg Arg Arg Lys Gln Trp Lys Asn Lys Lys
515 520 525

Arg Glu Ser Ala Ala Val Thr Leu Thr Thr Leu Pro Ser Glu Leu Leu
530 535 540

Leu Asp Arg Leu His Pro Asn Pro Met Tyr Gln Arg Met Pro Leu Leu
545 550 555 560

Leu Asn Pro Lys Leu Leu Ser Leu Glu Tyr Pro Arg Asn Asn Ile Glu

565 570 575

Tyr Val Arg Asp Ile Gly Glu Gly Ala Phe Gly Arg Val Phe Gln Ala
580 585 590

Arg Ala Pro Gly Leu Leu Pro Tyr Glu Pro Phe Thr Met Val Ala Val
595 600 605

Lys Met Leu Lys Glu Glu Ala Ser Ala Asp Met Gln Ala Asp Phe Gln
610 615 620

Arg Glu Ala Ala Leu Met Ala Glu Phe Asp Asn Pro Asn Ile Val Lys
625 630 635 640

Leu Leu Gly Val Cys Ala Val Gly Lys Pro Met Cys Leu Leu Phe Glu
645 650 655

Tyr Met Ala Tyr Gly Asp Leu Asn Glu Phe Leu Arg Ser Met Ser Pro
660 665 670

His Thr Val Cys Ser Leu Ser His Ser Asp Leu Ser Met Arg Ala Gln
675 680 685

Val Ser Ser Pro Gly Pro Pro Pro Leu Ser Cys Ala Glu Gln Leu Cys
690 695 700

Ile Ala Arg Gln Val Ala Ala Gly Met Ala Tyr Leu Ser Glu Arg Lys
705 710 715 720

Phe Val His Arg Asp Leu Ala Thr Arg Asn Cys Leu Val Gly Glu Asn
725 730 735

Met Val Val Lys Ile Ala Asp Phe Gly Leu Ser Arg Asn Ile Tyr Ser
740 745 750

Ala Asp Tyr Tyr Lys Ala Asn Glu Asn Asp Ala Ile Pro Ile Arg Trp
755 760 765

Met Pro Pro Glu Ser Ile Phe Tyr Asn Arg Tyr Thr Thr Glu Ser Asp
770 775 780

Val Trp Ala Tyr Gly Val Val Leu Trp Glu Ile Phe Ser Tyr Gly Leu
785 790 795 800

Gln Pro Tyr Tyr Gly Met Ala His Glu Glu Val Ile Tyr Tyr Val Arg
805 810 815

Asp Gly Asn Ile Leu Ser Cys Pro Glu Asn Cys Pro Val Glu Leu Tyr
820 825 830

Asn Leu Met Arg Leu Cys Trp Ser Lys Leu Pro Ala Asp Arg Pro Ser

835 840 845

Phe Thr Ser Ile His Arg Ile Leu Glu Arg Met Cys Glu Arg Ala Glu
850 855 860

Gly Thr Val Ser Val
865

<210> 452
<211> 796
<212> PRT
<213> Homo sapiens

<400> 452

Met Leu Arg Gly Gly Arg Arg Gly Gln Leu Gly Trp His Ser Trp Ala
1 5 10 15

Ala Gly Pro Gly Ser Leu Leu Ala Trp Leu Ile Leu Ala Ser Ala Gly
20 25 30

Ala Ala Pro Cys Pro Asp Ala Cys Cys Pro His Gly Ser Ser Gly Leu
35 40 45

Arg Cys Thr Arg Asp Gly Ala Leu Asp Ser Leu His His Leu Pro Gly
50 55 60

Ala Glu Asn Leu Thr Glu Leu Tyr Ile Glu Asn Gln Gln His Leu Gln
65 70 75 80

His Leu Glu Leu Arg Asp Leu Arg Gly Leu Gly Glu Leu Arg Asn Leu
85 90 95

Thr Ile Val Lys Ser Gly Leu Arg Phe Val Ala Pro Asp Ala Phe His
100 105 110

Phe Thr Pro Arg Leu Ser Arg Leu Asn Leu Ser Phe Asn Ala Leu Glu
115 120 125

Ser Leu Ser Trp Lys Thr Val Gln Gly Leu Ser Leu Gln Glu Leu Val
130 135 140

Leu Ser Gly Asn Pro Leu His Cys Ser Cys Ala Leu Arg Trp Leu Gln
145 150 155 160

Arg Trp Glu Glu Glu Gly Leu Gly Gly Val Pro Glu Gln Lys Leu Gln
165 170 175

Cys His Gly Gln Gly Pro Leu Ala His Met Pro Asn Ala Ser Cys Gly
180 185 190

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

```
Asp Asp Val Leu Leu Arg Cys Gln Val Glu Gly Arg Gly Leu Glu Gln
    210                 215                 220

Ala Gly Trp Ile Leu Thr Glu Leu Glu Gln Ser Ala Thr Val Met Lys
225                 230                 235                 240

Ser Gly Gly Leu Pro Ser Leu Gly Leu Thr Leu Ala Asn Val Thr Ser
                245                 250                 255

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

Arg Ala Glu Val Ser Val Gln Val Asn Val Ser Phe Pro Ala Ser Val
        275                 280                 285

Gln Leu His Thr Ala Val Glu Met His His Trp Cys Ile Pro Phe Ser
    290                 295                 300

Val Asp Gly Gln Pro Ala Pro Ser Leu Arg Trp Leu Phe Asn Gly Ser
305                 310                 315                 320

Val Leu Asn Glu Thr Ser Phe Ile Phe Thr Glu Phe Leu Glu Pro Ala
                325                 330                 335

Ala Asn Glu Thr Val Arg His Gly Cys Leu Arg Leu Asn Gln Pro Thr
            340                 345                 350

His Val Asn Asn Gly Asn Tyr Thr Leu Leu Ala Ala Asn Pro Phe Gly
        355                 360                 365

Gln Ala Ser Ala Ser Ile Met Ala Ala Phe Met Asp Asn Pro Phe Glu
    370                 375                 380

Phe Asn Pro Glu Asp Pro Ile Pro Val Ser Phe Ser Pro Val Asp Thr
385                 390                 395                 400

Asn Ser Thr Ser Gly Asp Pro Val Glu Lys Lys Asp Glu Thr Pro Phe
                405                 410                 415

Gly Val Ser Val Ala Val Gly Leu Ala Val Phe Ala Cys Leu Phe Leu
            420                 425                 430

Ser Thr Leu Leu Leu Val Leu Asn Lys Cys Gly Arg Arg Asn Lys Phe
        435                 440                 445

Gly Ile Asn Arg Pro Ala Val Leu Ala Pro Glu Asp Gly Leu Ala Met
    450                 455                 460

Ser Leu His Phe Met Thr Leu Gly Gly Ser Ser Leu Ser Pro Thr Glu
465                 470                 475                 480
```

```
Gly Lys Gly Ser Gly Leu Gln Gly His Ile Ile Glu Asn Pro Gln Tyr
                485                 490                 495

Phe Ser Asp Ala Cys Val His His Ile Lys Arg Arg Asp Ile Val Leu
            500                 505                 510

Lys Trp Glu Leu Gly Glu Gly Ala Phe Gly Lys Val Phe Leu Ala Glu
        515                 520                 525

Cys His Asn Leu Leu Pro Glu Gln Asp Lys Met Leu Val Ala Val Lys
    530                 535                 540

Ala Leu Lys Glu Ala Ser Glu Ser Ala Arg Gln Asp Phe Gln Arg Glu
545                 550                 555                 560

Ala Glu Leu Leu Thr Met Leu Gln His Gln His Ile Val Arg Phe Phe
                565                 570                 575

Gly Val Cys Thr Glu Gly Arg Pro Leu Leu Met Val Phe Glu Tyr Met
            580                 585                 590

Arg His Gly Asp Leu Asn Arg Phe Leu Arg Ser His Gly Pro Asp Ala
        595                 600                 605

Lys Leu Leu Ala Gly Gly Glu Asp Val Ala Pro Gly Pro Leu Gly Leu
    610                 615                 620

Gly Gln Leu Leu Ala Val Ala Ser Gln Val Ala Ala Gly Met Val Tyr
625                 630                 635                 640

Leu Ala Gly Leu His Phe Val His Arg Asp Leu Ala Thr Arg Asn Cys
                645                 650                 655

Leu Val Gly Gln Gly Leu Val Val Lys Ile Gly Asp Phe Gly Met Ser
            660                 665                 670

Arg Asp Ile Tyr Ser Thr Asp Tyr Tyr Arg Val Gly Gly Arg Thr Met
        675                 680                 685

Leu Pro Ile Arg Trp Met Pro Pro Glu Ser Ile Leu Tyr Arg Lys Phe
    690                 695                 700

Thr Thr Glu Ser Asp Val Trp Ser Phe Gly Val Val Leu Trp Glu Ile
705                 710                 715                 720

Phe Thr Tyr Gly Lys Gln Pro Trp Tyr Gln Leu Ser Asn Thr Glu Ala
                725                 730                 735

Ile Asp Cys Ile Thr Gln Gly Arg Glu Leu Glu Arg Pro Arg Ala Cys
            740                 745                 750
```

Pro Pro Glu Val Tyr Ala Ile Met Arg Gly Cys Trp Gln Arg Glu Pro
755 760 765

Gln Gln Arg His Ser Ile Lys Asp Val His Ala Arg Leu Gln Ala Leu
770 775 780

Ala Gln Ala Pro Pro Val Tyr Leu Asp Val Leu Gly
785 790 795

<210> 453
<211> 822
<212> PRT
<213> Homo sapiens

<400> 453

Met Ser Ser Trp Ile Arg Trp His Gly Pro Ala Met Ala Arg Leu Trp
1 5 10 15

Gly Phe Cys Trp Leu Val Val Gly Phe Trp Arg Ala Ala Phe Ala Cys
20 25 30

Pro Thr Ser Cys Lys Cys Ser Ala Ser Arg Ile Trp Cys Ser Asp Pro
35 40 45

Ser Pro Gly Ile Val Ala Phe Pro Arg Leu Glu Pro Asn Ser Val Asp
50 55 60

Pro Glu Asn Ile Thr Glu Ile Phe Ile Ala Asn Gln Lys Arg Leu Glu
65 70 75 80

Ile Ile Asn Glu Asp Asp Val Glu Ala Tyr Val Gly Leu Arg Asn Leu
85 90 95

Thr Ile Val Asp Ser Gly Leu Lys Phe Val Ala His Lys Ala Phe Leu
100 105 110

Lys Asn Ser Asn Leu Gln His Ile Asn Phe Thr Arg Asn Lys Leu Thr
115 120 125

Ser Leu Ser Arg Lys His Phe Arg His Leu Asp Leu Ser Glu Leu Ile
130 135 140

Leu Val Gly Asn Pro Phe Thr Cys Ser Cys Asp Ile Met Trp Ile Lys
145 150 155 160

Thr Leu Gln Glu Ala Lys Ser Ser Pro Asp Thr Gln Asp Leu Tyr Cys
165 170 175

Leu Asn Glu Ser Ser Lys Asn Ile Pro Leu Ala Asn Leu Gln Ile Pro
180 185 190

```
Asn Cys Gly Leu Pro Ser Ala Asn Leu Ala Ala Pro Asn Leu Thr Val
        195                 200                 205

Glu Glu Gly Lys Ser Ile Thr Leu Ser Cys Ser Val Ala Gly Asp Pro
    210                 215                 220

Val Pro Asn Met Tyr Trp Asp Val Gly Asn Leu Val Ser Lys His Met
225                 230                 235                 240

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

Ser Asp Asp Ser Gly Lys Gln Ile Ser Cys Val Ala Glu Asn Leu Val
            260                 265                 270

Gly Glu Asp Gln Asp Ser Val Asn Leu Thr Val His Phe Ala Pro Thr
        275                 280                 285

Ile Thr Phe Leu Glu Ser Pro Thr Ser Asp His His Trp Cys Ile Pro
    290                 295                 300

Phe Thr Val Lys Gly Asn Pro Lys Pro Ala Leu Gln Trp Phe Tyr Asn
305                 310                 315                 320

Gly Ala Ile Leu Asn Glu Ser Lys Tyr Ile Cys Thr Lys Ile His Val
                325                 330                 335

Thr Asn His Thr Glu Tyr His Gly Cys Leu Gln Leu Asp Asn Pro Thr
            340                 345                 350

His Met Asn Asn Gly Asp Tyr Thr Leu Ile Ala Lys Asn Glu Tyr Gly
        355                 360                 365

Lys Asp Glu Lys Gln Ile Ser Ala His Phe Met Gly Trp Pro Gly Ile
    370                 375                 380

Asp Asp Gly Ala Asn Pro Asn Tyr Pro Asp Val Ile Tyr Glu Asp Tyr
385                 390                 395                 400

Gly Thr Ala Ala Asn Asp Ile Gly Asp Thr Thr Asn Arg Ser Asn Glu
                405                 410                 415

Ile Pro Ser Thr Asp Val Thr Asp Lys Thr Gly Arg Glu His Leu Ser
            420                 425                 430

Val Tyr Ala Val Val Val Ile Ala Ser Val Val Gly Phe Cys Leu Leu
        435                 440                 445

Val Met Leu Phe Leu Leu Lys Leu Ala Arg His Ser Lys Phe Gly Met
    450                 455                 460
```

```
Lys Gly Pro Ala Ser Val Ile Ser Asn Asp Asp Ser Ala Ser Pro
465                 470                 475                 480

Leu His His Ile Ser Asn Gly Ser Asn Thr Pro Ser Ser Ser Glu Gly
                485                 490                 495

Gly Pro Asp Ala Val Ile Ile Gly Met Thr Lys Ile Pro Val Ile Glu
            500                 505                 510

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

Phe Val Gln His Ile Lys Arg His Asn Ile Val Leu Lys Arg Glu Leu
    530                 535                 540

Gly Glu Gly Ala Phe Gly Lys Val Phe Leu Ala Glu Cys Tyr Asn Leu
545                 550                 555                 560

Cys Pro Glu Gln Asp Lys Ile Leu Val Ala Val Lys Thr Leu Lys Asp
                565                 570                 575

Ala Ser Asp Asn Ala Arg Lys Asp Phe His Arg Glu Ala Glu Leu Leu
            580                 585                 590

Thr Asn Leu Gln His Glu His Ile Val Lys Phe Tyr Gly Val Cys Val
        595                 600                 605

Glu Gly Asp Pro Leu Ile Met Val Phe Glu Tyr Met Lys His Gly Asp
    610                 615                 620

Leu Asn Lys Phe Leu Arg Ala His Gly Pro Asp Ala Val Leu Met Ala
625                 630                 635                 640

Glu Gly Asn Pro Pro Thr Glu Leu Thr Gln Ser Gln Met Leu His Ile
                645                 650                 655

Ala Gln Gln Ile Ala Ala Gly Met Val Tyr Leu Ala Ser Gln His Phe
            660                 665                 670

Val His Arg Asp Leu Ala Thr Arg Asn Cys Leu Val Gly Glu Asn Leu
        675                 680                 685

Leu Val Lys Ile Gly Asp Phe Gly Met Ser Arg Asp Val Tyr Ser Thr
    690                 695                 700

Asp Tyr Tyr Arg Val Gly Gly His Thr Met Leu Pro Ile Arg Trp Met
705                 710                 715                 720

Pro Pro Glu Ser Ile Met Tyr Arg Lys Phe Thr Thr Glu Ser Asp Val
                725                 730                 735
```

```
Trp Ser Leu Gly Val Val Leu Trp Glu Ile Phe Thr Tyr Gly Lys Gln
            740                 745                 750

Pro Trp Tyr Gln Leu Ser Asn Asn Glu Val Ile Glu Cys Ile Thr Gln
        755                 760                 765

Gly Arg Val Leu Gln Arg Pro Arg Thr Cys Pro Gln Glu Val Tyr Glu
    770                 775                 780

Leu Met Leu Gly Cys Trp Gln Arg Glu Pro His Met Arg Lys Asn Ile
785                 790                 795                 800

Lys Gly Ile His Thr Leu Leu Gln Asn Leu Ala Lys Ala Ser Pro Val
                805                 810                 815

Tyr Leu Asp Ile Leu Gly
            820
```

<210> 454
<211> 839
<212> PRT
<213> Homo sapiens

<400> 454

```
Met Asp Val Ser Leu Cys Pro Ala Lys Cys Ser Phe Trp Arg Ile Phe
1               5                   10                  15

Leu Leu Gly Ser Val Trp Leu Asp Tyr Val Gly Ser Val Leu Ala Cys
            20                  25                  30

Pro Ala Asn Cys Val Cys Ser Lys Thr Glu Ile Asn Cys Arg Arg Pro
        35                  40                  45

Asp Asp Gly Asn Leu Phe Pro Leu Leu Glu Gly Gln Asp Ser Gly Asn
    50                  55                  60

Ser Asn Gly Asn Ala Ser Ile Asn Ile Thr Asp Ile Ser Arg Asn Ile
65                  70                  75                  80

Thr Ser Ile His Ile Glu Asn Trp Arg Ser Leu His Thr Leu Asn Ala
                85                  90                  95

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

Ser Gly Leu Arg Ser Ile Gln Pro Arg Ala Phe Ala Lys Asn Pro His
        115                 120                 125

Leu Arg Tyr Ile Asn Leu Ser Ser Asn Arg Leu Thr Thr Leu Ser Trp
    130                 135                 140
```

```
Gln Leu Phe Gln Thr Leu Ser Leu Arg Glu Leu Gln Leu Glu Gln Asn
145                 150                 155                 160

Phe Phe Asn Cys Ser Cys Asp Ile Arg Trp Met Gln Leu Trp Gln Glu
                165                 170                 175

Gln Gly Glu Ala Lys Leu Asn Ser Gln Asn Leu Tyr Cys Ile Asn Ala
            180                 185                 190

Asp Gly Ser Gln Leu Pro Leu Phe Arg Met Asn Ile Ser Gln Cys Asp
        195                 200                 205

Leu Pro Glu Ile Ser Val Ser His Val Asn Leu Thr Val Arg Glu Gly
    210                 215                 220

Asp Asn Ala Val Ile Thr Cys Asn Gly Ser Gly Ser Pro Leu Pro Asp
225                 230                 235                 240

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

Asn Leu Asn Trp Thr Asn Val His Ala Ile Asn Leu Thr Leu Val Asn
            260                 265                 270

Val Thr Ser Glu Asp Asn Gly Phe Thr Leu Thr Cys Ile Ala Glu Asn
        275                 280                 285

Val Val Gly Met Ser Asn Ala Ser Val Ala Leu Thr Val Tyr Tyr Pro
    290                 295                 300

Pro Arg Val Val Ser Leu Glu Glu Pro Glu Leu Arg Leu Glu His Cys
305                 310                 315                 320

Ile Glu Phe Val Val Arg Gly Asn Pro Pro Pro Thr Leu His Trp Leu
                325                 330                 335

His Asn Gly Gln Pro Leu Arg Glu Ser Lys Ile Ile His Val Glu Tyr
            340                 345                 350

Tyr Gln Glu Gly Glu Ile Ser Glu Gly Cys Leu Leu Phe Asn Lys Pro
        355                 360                 365

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

Gly Thr Ala Asn Gln Thr Ile Asn Gly His Phe Leu Lys Glu Pro Phe
385                 390                 395                 400

Pro Glu Ser Thr Asp Asn Phe Ile Leu Phe Asp Glu Val Ser Pro Thr
                405                 410                 415
```

```
Pro Pro Ile Thr Val Thr His Lys Pro Glu Glu Asp Thr Phe Gly Val
            420                 425                 430

Ser Ile Ala Val Gly Leu Ala Ala Phe Ala Cys Val Leu Leu Val Val
        435                 440                 445

Leu Phe Val Met Ile Asn Lys Tyr Gly Arg Arg Ser Lys Phe Gly Met
    450                 455                 460

Lys Gly Pro Val Ala Val Ile Ser Gly Glu Glu Asp Ser Ala Ser Pro
465                 470                 475                 480

Leu His His Ile Asn His Gly Ile Thr Thr Pro Ser Ser Leu Asp Ala
                485                 490                 495

Gly Pro Asp Thr Val Val Ile Gly Met Thr Arg Ile Pro Val Ile Glu
            500                 505                 510

Asn Pro Gln Tyr Phe Arg Gln Gly His Asn Cys His Lys Pro Asp Thr
        515                 520                 525

Tyr Val Gln His Ile Lys Arg Arg Asp Ile Val Leu Lys Arg Glu Leu
    530                 535                 540

Gly Glu Gly Ala Phe Gly Lys Val Phe Leu Ala Glu Cys Tyr Asn Leu
545                 550                 555                 560

Ser Pro Thr Lys Asp Lys Met Leu Val Ala Val Lys Ala Leu Lys Asp
                565                 570                 575

Pro Thr Leu Ala Ala Arg Lys Asp Phe Gln Arg Glu Ala Glu Leu Leu
            580                 585                 590

Thr Asn Leu Gln His Glu His Ile Val Lys Phe Tyr Gly Val Cys Gly
        595                 600                 605

Asp Gly Asp Pro Leu Ile Met Val Phe Glu Tyr Met Lys His Gly Asp
    610                 615                 620

Leu Asn Lys Phe Leu Arg Ala His Gly Pro Asp Ala Met Ile Leu Val
625                 630                 635                 640

Asp Gly Gln Pro Arg Gln Ala Lys Gly Glu Leu Gly Leu Ser Gln Met
                645                 650                 655

Leu His Ile Ala Ser Gln Ile Ala Ser Gly Met Val Tyr Leu Ala Ser
            660                 665                 670

Gln His Phe Val His Arg Asp Leu Ala Thr Arg Asn Cys Leu Val Gly
        675                 680                 685
```

Ala Asn Leu Leu Val Lys Ile Gly Asp Phe Gly Met Ser Arg Asp Val
690 695 700

Tyr Ser Thr Asp Tyr Tyr Arg Leu Phe Asn Pro Ser Gly Asn Asp Phe
705 710 715 720

Cys Ile Trp Cys Glu Val Gly Gly His Thr Met Leu Pro Ile Arg Trp
725 730 735

Met Pro Pro Glu Ser Ile Met Tyr Arg Lys Phe Thr Thr Glu Ser Asp
740 745 750

Val Trp Ser Phe Gly Val Ile Leu Trp Glu Ile Phe Thr Tyr Gly Lys
755 760 765

Gln Pro Trp Phe Gln Leu Ser Asn Thr Glu Val Ile Glu Cys Ile Thr
770 775 780

Gln Gly Arg Val Leu Glu Arg Pro Arg Val Cys Pro Lys Glu Val Tyr
785 790 795 800

Asp Val Met Leu Gly Cys Trp Gln Arg Glu Pro Gln Gln Arg Leu Asn
805 810 815

Ile Lys Glu Ile Tyr Lys Ile Leu His Ala Leu Gly Lys Ala Thr Pro
820 825 830

Ile Tyr Leu Asp Ile Leu Gly
835

<210> 455
<211> 937
<212> PRT
<213> Homo sapiens

<400> 455

Met His Arg Pro Arg Arg Arg Gly Thr Arg Pro Pro Leu Leu Ala Leu
1 5 10 15

Leu Ala Ala Leu Leu Leu Ala Ala Arg Gly Ala Ala Ala Gln Glu Thr
20 25 30

Glu Leu Ser Val Ser Ala Glu Leu Val Pro Thr Ser Ser Trp Asn Ile
35 40 45

Ser Ser Glu Leu Asn Lys Asp Ser Tyr Leu Thr Leu Asp Glu Pro Met
50 55 60

Asn Asn Ile Thr Thr Ser Leu Gly Gln Thr Ala Glu Leu His Cys Lys
65 70 75 80

Val Ser Gly Asn Pro Pro Pro Thr Ile Arg Trp Phe Lys Asn Asp Ala

85 90 95

Pro Val Val Gln Glu Pro Arg Arg Leu Ser Phe Arg Ser Thr Ile Tyr
100 105 110

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

Phe Gln Cys Val Ala Thr Asn Gly Lys Glu Val Val Ser Ser Thr Gly
130 135 140

Val Leu Phe Val Lys Phe Gly Pro Pro Pro Thr Ala Ser Pro Gly Tyr
145 150 155 160

Ser Asp Glu Tyr Glu Glu Asp Gly Phe Cys Gln Pro Tyr Arg Gly Ile
165 170 175

Ala Cys Ala Arg Phe Ile Gly Asn Arg Thr Val Tyr Met Glu Ser Leu
180 185 190

His Met Gln Gly Glu Ile Glu Asn Gln Ile Thr Ala Ala Phe Thr Met
195 200 205

Ile Gly Thr Ser Ser His Leu Ser Asp Lys Cys Ser Gln Phe Ala Ile
210 215 220

Pro Ser Leu Cys His Tyr Ala Phe Pro Tyr Cys Asp Glu Thr Ser Ser
225 230 235 240

Val Pro Lys Pro Arg Asp Leu Cys Arg Asp Glu Cys Glu Ile Leu Glu
245 250 255

Asn Val Leu Cys Gln Thr Glu Tyr Ile Phe Ala Arg Ser Asn Pro Met
260 265 270

Ile Leu Met Arg Leu Lys Leu Pro Asn Cys Glu Asp Leu Pro Gln Pro
275 280 285

Glu Ser Pro Glu Ala Ala Asn Cys Ile Arg Ile Gly Ile Pro Met Ala
290 295 300

Asp Pro Ile Asn Lys Asn His Lys Cys Tyr Asn Ser Thr Gly Val Asp
305 310 315 320

Tyr Arg Gly Thr Val Ser Val Thr Lys Ser Gly Arg Gln Cys Gln Pro
325 330 335

Trp Asn Ser Gln Tyr Pro His Thr His Thr Phe Thr Ala Leu Arg Phe
340 345 350

Pro Glu Leu Asn Gly Gly His Ser Tyr Cys Arg Asn Pro Gly Asn Gln

355 360 365

Lys Glu Ala Pro Trp Cys Phe Thr Leu Asp Glu Asn Phe Lys Ser Asp
370 375 380

Leu Cys Asp Ile Pro Ala Cys Asp Ser Lys Asp Ser Lys Glu Lys Asn
385 390 395 400

Lys Met Glu Ile Leu Tyr Ile Leu Val Pro Ser Val Ala Ile Pro Leu
405 410 415

Ala Ile Ala Leu Leu Phe Phe Phe Ile Cys Val Cys Arg Asn Asn Gln
420 425 430

Lys Ser Ser Ser Ala Pro Val Gln Arg Gln Pro Lys His Val Arg Gly
435 440 445

Gln Asn Val Glu Met Ser Met Leu Asn Ala Tyr Lys Pro Lys Ser Lys
450 455 460

Ala Lys Glu Leu Pro Leu Ser Ala Val Arg Phe Met Glu Glu Leu Gly
465 470 475 480

Glu Cys Ala Phe Gly Lys Ile Tyr Lys Gly His Leu Tyr Leu Pro Gly
485 490 495

Met Asp His Ala Gln Leu Val Ala Ile Lys Thr Leu Lys Asp Tyr Asn
500 505 510

Asn Pro Gln Gln Trp Thr Glu Phe Gln Gln Glu Ala Ser Leu Met Ala
515 520 525

Glu Leu His His Pro Asn Ile Val Cys Leu Leu Gly Ala Val Thr Gln
530 535 540

Glu Gln Pro Val Cys Met Leu Phe Glu Tyr Ile Asn Gln Gly Asp Leu
545 550 555 560

His Glu Phe Leu Ile Met Arg Ser Pro His Ser Asp Val Gly Cys Ser
565 570 575

Ser Asp Glu Asp Gly Thr Val Lys Ser Ser Leu Asp His Gly Asp Phe
580 585 590

Leu His Ile Ala Ile Gln Ile Ala Ala Gly Met Glu Tyr Leu Ser Ser
595 600 605

His Phe Phe Val His Lys Asp Leu Ala Ala Arg Asn Ile Leu Ile Gly
610 615 620

Glu Gln Leu His Val Lys Ile Ser Asp Leu Gly Leu Ser Arg Glu Ile

625 630 635 640

Tyr Ser Ala Asp Tyr Tyr Arg Val Gln Ser Lys Ser Leu Leu Pro Ile
645 650 655

Arg Trp Met Pro Pro Glu Ala Ile Met Tyr Gly Lys Phe Ser Ser Asp
660 665 670

Ser Asp Ile Trp Ser Phe Gly Val Val Leu Trp Glu Ile Phe Ser Phe
675 680 685

Gly Leu Gln Pro Tyr Tyr Gly Phe Ser Asn Gln Glu Val Ile Glu Met
690 695 700

Val Arg Lys Arg Gln Leu Leu Pro Cys Ser Glu Asp Cys Pro Pro Arg
705 710 715 720

Met Tyr Ser Leu Met Thr Glu Cys Trp Asn Glu Ile Pro Ser Arg Arg
725 730 735

Pro Arg Phe Lys Asp Ile His Val Arg Leu Arg Ser Trp Glu Gly Leu
740 745 750

Ser Ser His Thr Ser Ser Thr Thr Pro Ser Gly Gly Asn Ala Thr Thr
755 760 765

Gln Thr Thr Ser Leu Ser Ala Ser Pro Val Ser Asn Leu Ser Asn Pro
770 775 780

Arg Tyr Pro Asn Tyr Met Phe Pro Ser Gln Gly Ile Thr Pro Gln Gly
785 790 795 800

Gln Ile Ala Gly Phe Ile Gly Pro Pro Ile Pro Gln Asn Gln Arg Phe
805 810 815

Ile Pro Ile Asn Gly Tyr Pro Ile Pro Pro Gly Tyr Ala Ala Phe Pro
820 825 830

Ala Ala His Tyr Gln Pro Thr Gly Pro Pro Arg Val Ile Gln His Cys
835 840 845

Pro Pro Pro Lys Ser Arg Ser Pro Ser Ser Ala Ser Gly Ser Thr Ser
850 855 860

Thr Gly His Val Thr Ser Leu Pro Ser Ser Gly Ser Asn Gln Glu Ala
865 870 875 880

Asn Ile Pro Leu Leu Pro His Met Ser Ile Pro Asn His Pro Gly Gly
885 890 895

Met Gly Ile Thr Val Phe Gly Asn Lys Ser Gln Lys Pro Tyr Lys Ile

900 905 910

Asp Ser Lys Gln Ala Ser Leu Leu Gly Asp Ala Asn Ile His Gly His
915 920 925

Thr Glu Ser Met Ile Ser Ala Glu Leu
930 935

<210> 456
<211> 943
<212> PRT
<213> Homo sapiens

<400> 456

Met Ala Arg Gly Ser Ala Leu Pro Arg Arg Pro Leu Leu Cys Ile Pro
1 5 10 15

Ala Val Trp Ala Ala Ala Ala Leu Leu Leu Ser Val Ser Arg Thr Ser
20 25 30

Gly Glu Val Glu Val Leu Asp Pro Asn Asp Pro Leu Gly Pro Leu Asp
35 40 45

Gly Gln Asp Gly Pro Ile Pro Thr Leu Lys Gly Tyr Phe Leu Asn Phe
50 55 60

Leu Glu Pro Val Asn Asn Ile Thr Ile Val Gln Gly Gln Thr Ala Ile
65 70 75 80

Leu His Cys Lys Val Ala Gly Asn Pro Pro Pro Asn Val Arg Trp Leu
85 90 95

Lys Asn Asp Ala Pro Val Val Gln Glu Pro Arg Arg Ile Ile Ile Arg
100 105 110

Lys Thr Glu Tyr Gly Ser Arg Leu Arg Ile Gln Asp Leu Asp Thr Thr
115 120 125

Asp Thr Gly Tyr Tyr Gln Cys Val Ala Thr Asn Gly Met Lys Thr Ile
130 135 140

Thr Ala Thr Gly Val Leu Phe Val Arg Leu Gly Pro Thr His Ser Pro
145 150 155 160

Asn His Asn Phe Gln Asp Asp Tyr His Glu Asp Gly Phe Cys Gln Pro
165 170 175

Tyr Arg Gly Ile Ala Cys Ala Arg Phe Ile Gly Asn Arg Thr Ile Tyr
180 185 190

Val Asp Ser Leu Gln Met Gln Gly Glu Ile Glu Asn Arg Ile Thr Ala
195 200 205

```
Ala Phe Thr Met Ile Gly Thr Ser Thr His Leu Ser Asp Gln Cys Ser
    210                 215                 220

Gln Phe Ala Ile Pro Ser Phe Cys His Phe Val Phe Pro Leu Cys Asp
225                 230                 235                 240

Ala Arg Ser Arg Thr Pro Lys Pro Arg Glu Leu Cys Arg Asp Glu Cys
                245                 250                 255

Glu Val Leu Glu Ser Asp Leu Cys Arg Gln Glu Tyr Thr Ile Ala Arg
            260                 265                 270

Ser Asn Pro Leu Ile Leu Met Arg Leu Gln Leu Pro Lys Cys Glu Ala
        275                 280                 285

Leu Pro Met Pro Glu Ser Pro Asp Ala Ala Asn Cys Met Arg Ile Gly
    290                 295                 300

Ile Pro Ala Glu Arg Leu Gly Arg Tyr His Gln Cys Tyr Asn Gly Ser
305                 310                 315                 320

Gly Met Asp Tyr Arg Gly Thr Ala Ser Thr Thr Lys Ser Gly His Gln
                325                 330                 335

Cys Gln Pro Trp Ala Leu Gln His Pro His Ser His His Leu Ser Ser
            340                 345                 350

Thr Asp Phe Pro Glu Leu Gly Gly Gly His Ala Tyr Cys Arg Asn Pro
        355                 360                 365

Gly Gly Gln Met Glu Gly Pro Trp Cys Phe Thr Gln Asn Lys Asn Val
    370                 375                 380

Arg Met Glu Leu Cys Asp Val Pro Ser Cys Ser Pro Arg Asp Ser Ser
385                 390                 395                 400

Lys Met Gly Ile Leu Tyr Ile Leu Val Pro Ser Ile Ala Ile Pro Leu
                405                 410                 415

Val Ile Ala Cys Leu Phe Phe Leu Val Cys Met Cys Arg Asn Lys Gln
            420                 425                 430

Lys Ala Ser Ala Ser Thr Pro Gln Arg Arg Gln Leu Met Ala Ser Pro
        435                 440                 445

Ser Gln Asp Met Glu Met Pro Leu Ile Asn Gln His Lys Gln Ala Lys
    450                 455                 460

Leu Lys Glu Ile Ser Leu Ser Ala Val Arg Phe Met Glu Glu Leu Gly
465                 470                 475                 480
```

```
Glu Asp Arg Phe Gly Lys Val Tyr Lys Gly His Leu Phe Gly Pro Ala
                485                 490                 495

Pro Gly Glu Gln Thr Gln Ala Val Ala Ile Lys Thr Leu Lys Asp Lys
            500                 505                 510

Ala Glu Gly Pro Leu Arg Glu Glu Phe Arg His Glu Ala Met Leu Arg
        515                 520                 525

Ala Arg Leu Gln His Pro Asn Val Val Cys Leu Leu Gly Val Val Thr
    530                 535                 540

Lys Asp Gln Pro Leu Ser Met Ile Phe Ser Tyr Cys Ser His Gly Asp
545                 550                 555                 560

Leu His Glu Phe Leu Val Met Arg Ser Pro His Ser Asp Val Gly Ser
                565                 570                 575

Thr Asp Asp Asp Arg Thr Val Lys Ser Ala Leu Glu Pro Pro Asp Phe
            580                 585                 590

Val His Leu Val Ala Gln Ile Ala Ala Gly Met Glu Tyr Leu Ser Ser
        595                 600                 605

His His Val Val His Lys Asp Leu Ala Thr Arg Asn Val Leu Val Tyr
    610                 615                 620

Asp Lys Leu Asn Val Lys Ile Ser Asp Leu Gly Leu Phe Arg Glu Val
625                 630                 635                 640

Tyr Ala Ala Asp Tyr Tyr Lys Leu Leu Gly Asn Ser Leu Leu Pro Ile
                645                 650                 655

Arg Trp Met Ala Pro Glu Ala Ile Met Tyr Gly Lys Phe Ser Ile Asp
            660                 665                 670

Ser Asp Ile Trp Ser Tyr Gly Val Val Leu Trp Glu Val Phe Ser Tyr
        675                 680                 685

Gly Leu Gln Pro Tyr Cys Gly Tyr Ser Asn Gln Asp Val Val Glu Met
    690                 695                 700

Ile Arg Asn Arg Gln Val Leu Pro Cys Pro Asp Asp Cys Pro Ala Trp
705                 710                 715                 720

Val Tyr Ala Leu Met Ile Glu Cys Trp Asn Glu Phe Pro Ser Arg Arg
                725                 730                 735

Pro Arg Phe Lys Asp Ile His Ser Arg Leu Arg Ala Trp Gly Asn Leu
            740                 745                 750
```

Ser Asn Tyr Asn Ser Ser Ala Gln Thr Ser Gly Ala Ser Asn Thr Thr
755 760 765

Gln Thr Ser Ser Leu Ser Thr Ser Pro Val Ser Asn Val Ser Asn Ala
770 775 780

Arg Tyr Val Gly Pro Lys Gln Lys Ala Pro Pro Phe Pro Gln Pro Gln
785 790 795 800

Phe Ile Pro Met Lys Gly Gln Ile Arg Pro Met Val Pro Pro Pro Gln
805 810 815

Leu Tyr Val Pro Val Asn Gly Tyr Gln Pro Val Pro Ala Tyr Gly Ala
820 825 830

Tyr Leu Pro Asn Phe Tyr Pro Val Gln Ile Pro Met Gln Met Ala Pro
835 840 845

Gln Gln Val Pro Pro Gln Met Val Pro Lys Pro Ser Ser His His Ser
850 855 860

Gly Ser Gly Ser Thr Ser Thr Gly Tyr Val Thr Thr Ala Pro Ser Asn
865 870 875 880

Thr Ser Met Ala Asp Arg Ala Ala Leu Leu Ser Glu Gly Ala Asp Asp
885 890 895

Thr Gln Asn Ala Pro Glu Asp Gly Ala Gln Ser Thr Val Gln Glu Ala
900 905 910

Glu Glu Glu Glu Glu Gly Ser Val Pro Glu Thr Glu Leu Leu Gly Asp
915 920 925

Cys Asp Thr Leu Gln Val Asp Glu Ala Gln Val Gln Leu Glu Ala
930 935 940

<210> 457
<211> 855
<212> PRT
<213> Homo sapiens

<400> 457

Met Ile Leu Ile Pro Arg Met Leu Leu Val Leu Phe Leu Leu Leu Pro
1 5 10 15

Ile Leu Ser Ser Ala Lys Ala Gln Val Asn Pro Ala Ile Cys Arg Tyr
20 25 30

Pro Leu Gly Met Ser Gly Gly Gln Ile Pro Asp Glu Asp Ile Thr Ala
35 40 45

```
Ser Ser Gln Trp Ser Glu Ser Thr Ala Ala Lys Tyr Gly Arg Leu Asp
    50                  55                  60

Ser Glu Glu Gly Asp Gly Ala Trp Cys Pro Glu Ile Pro Val Glu Pro
65                  70                  75                  80

Asp Asp Leu Lys Glu Phe Leu Gln Ile Asp Leu His Thr Leu His Phe
                85                  90                  95

Ile Thr Leu Val Gly Thr Gln Gly Arg His Ala Gly Gly His Gly Ile
            100                 105                 110

Glu Phe Ala Pro Met Tyr Lys Ile Asn Tyr Ser Arg Asp Gly Thr Arg
        115                 120                 125

Trp Ile Ser Trp Arg Asn Arg His Gly Lys Gln Val Leu Asp Gly Asn
    130                 135                 140

Ser Asn Pro Tyr Asp Ile Phe Leu Lys Asp Leu Glu Pro Pro Ile Val
145                 150                 155                 160

Ala Arg Phe Val Arg Phe Ile Pro Val Thr Asp His Ser Met Asn Val
                165                 170                 175

Cys Met Arg Val Glu Leu Tyr Gly Cys Val Trp Leu Asp Gly Leu Val
            180                 185                 190

Ser Tyr Asn Ala Pro Ala Gly Gln Gln Phe Val Leu Pro Gly Gly Ser
        195                 200                 205

Ile Ile Tyr Leu Asn Asp Ser Val Tyr Asp Gly Ala Val Gly Tyr Ser
    210                 215                 220

Met Thr Glu Gly Leu Gly Gln Leu Thr Asp Gly Val Ser Gly Leu Asp
225                 230                 235                 240

Asp Phe Thr Gln Thr His Glu Tyr His Val Trp Pro Gly Tyr Asp Tyr
                245                 250                 255

Val Gly Trp Arg Asn Glu Ser Ala Thr Asn Gly Tyr Ile Glu Ile Met
            260                 265                 270

Phe Glu Phe Asp Arg Ile Arg Asn Phe Thr Thr Met Lys Val His Cys
        275                 280                 285

Asn Asn Met Phe Ala Lys Gly Val Lys Ile Phe Lys Glu Val Gln Cys
    290                 295                 300

Tyr Phe Arg Ser Glu Ala Ser Glu Trp Glu Pro Asn Ala Ile Ser Phe
305                 310                 315                 320
```

```
Pro Leu Val Leu Asp Asp Val Asn Pro Ser Ala Arg Phe Val Thr Val
                325                 330                 335

Pro Leu His His Arg Met Ala Ser Ala Ile Lys Cys Gln Tyr His Phe
            340                 345                 350

Ala Asp Thr Trp Met Met Phe Ser Glu Ile Thr Phe Gln Ser Asp Ala
        355                 360                 365

Ala Met Tyr Asn Asn Ser Glu Ala Leu Pro Thr Ser Pro Met Ala Pro
    370                 375                 380

Thr Thr Tyr Asp Pro Met Leu Lys Val Asp Asp Ser Asn Thr Arg Ile
385                 390                 395                 400

Leu Ile Gly Cys Leu Val Ala Ile Ile Phe Ile Leu Leu Ala Ile Ile
                405                 410                 415

Val Ile Ile Leu Trp Arg Gln Phe Trp Gln Lys Met Leu Glu Lys Ala
            420                 425                 430

Ser Arg Arg Met Leu Asp Asp Glu Met Thr Val Ser Leu Ser Leu Pro
        435                 440                 445

Ser Asp Ser Ser Met Phe Asn Asn Asn Arg Ser Ser Ser Pro Ser Glu
    450                 455                 460

Gln Gly Ser Asn Ser Thr Tyr Asp Arg Ile Phe Pro Leu Arg Pro Asp
465                 470                 475                 480

Tyr Gln Glu Pro Ser Arg Leu Ile Arg Lys Leu Pro Glu Phe Ala Pro
                485                 490                 495

Gly Glu Glu Glu Ser Gly Cys Ser Gly Val Val Lys Pro Val Gln Pro
            500                 505                 510

Ser Gly Pro Glu Gly Val Pro His Tyr Ala Glu Ala Asp Ile Val Asn
        515                 520                 525

Leu Gln Gly Val Thr Gly Gly Asn Thr Tyr Ser Val Pro Ala Val Thr
    530                 535                 540

Met Asp Leu Leu Ser Gly Lys Asp Val Ala Val Glu Glu Phe Pro Arg
545                 550                 555                 560

Lys Leu Leu Thr Phe Lys Glu Lys Leu Gly Glu Gly Gln Phe Gly Glu
                565                 570                 575

Val His Leu Cys Glu Val Glu Gly Met Glu Lys Phe Lys Asp Lys Asp
            580                 585                 590
```

```
Phe Ala Leu Asp Val Ser Ala Asn Gln Pro Val Leu Val Ala Val Lys
        595                 600                 605

Met Leu Arg Ala Asp Ala Asn Lys Asn Ala Arg Asn Asp Phe Leu Lys
    610                 615                 620

Glu Ile Lys Ile Met Ser Arg Leu Lys Asp Pro Asn Ile Ile His Leu
625                 630                 635                 640

Leu Ala Val Cys Ile Thr Asp Asp Pro Leu Cys Met Ile Thr Glu Tyr
                645                 650                 655

Met Glu Asn Gly Asp Leu Asn Gln Phe Leu Ser Arg His Glu Pro Pro
            660                 665                 670

Asn Ser Ser Ser Ser Asp Val Arg Thr Val Ser Tyr Thr Asn Leu Lys
        675                 680                 685

Phe Met Ala Thr Gln Ile Ala Ser Gly Met Lys Tyr Leu Ser Ser Leu
    690                 695                 700

Asn Phe Val His Arg Asp Leu Ala Thr Arg Asn Cys Leu Val Gly Lys
705                 710                 715                 720

Asn Tyr Thr Ile Lys Ile Ala Asp Phe Gly Met Ser Arg Asn Leu Tyr
                725                 730                 735

Ser Gly Asp Tyr Tyr Arg Ile Gln Gly Arg Ala Val Leu Pro Ile Arg
            740                 745                 750

Trp Met Ser Trp Glu Ser Ile Leu Leu Gly Lys Phe Thr Thr Ala Ser
        755                 760                 765

Asp Val Trp Ala Phe Gly Val Thr Leu Trp Glu Thr Phe Thr Phe Cys
    770                 775                 780

Gln Glu Gln Pro Tyr Ser Gln Leu Ser Asp Glu Gln Val Ile Glu Asn
785                 790                 795                 800

Thr Gly Glu Phe Phe Arg Asp Gln Gly Arg Gln Thr Tyr Leu Pro Gln
                805                 810                 815

Pro Ala Ile Cys Pro Asp Ser Val Tyr Lys Leu Met Leu Ser Cys Trp
            820                 825                 830

Arg Arg Asp Thr Lys Asn Arg Pro Ser Phe Gln Glu Ile His Leu Leu
        835                 840                 845

Leu Leu Gln Gln Gly Asp Glu
    850                 855
```

<210> 458
<211> 1089
<212> PRT
<213> Homo sapiens

<400> 458

```
Met Gly Thr Ser His Pro Ala Phe Leu Val Leu Gly Cys Leu Leu Thr
1               5                  10                  15

Gly Leu Ser Leu Ile Leu Cys Gln Leu Ser Leu Pro Ser Ile Leu Pro
            20                  25                  30

Asn Glu Asn Glu Lys Val Val Gln Leu Asn Ser Ser Phe Ser Leu Arg
        35                  40                  45

Cys Phe Gly Glu Ser Glu Val Ser Trp Gln Tyr Pro Met Ser Glu Glu
    50                  55                  60

Glu Ser Ser Asp Val Glu Ile Arg Asn Glu Glu Asn Asn Ser Gly Leu
65                  70                  75                  80

Phe Val Thr Val Leu Glu Val Ser Ser Ala Ser Ala Ala His Thr Gly
                85                  90                  95

Leu Tyr Thr Cys Tyr Tyr Asn His Thr Gln Thr Glu Glu Asn Glu Leu
            100                 105                 110

Glu Gly Arg His Ile Tyr Ile Tyr Val Pro Asp Pro Asp Val Ala Phe
        115                 120                 125

Val Pro Leu Gly Met Thr Asp Tyr Leu Val Ile Val Glu Asp Asp Asp
    130                 135                 140

Ser Ala Ile Ile Pro Cys Arg Thr Thr Asp Pro Glu Thr Pro Val Thr
145                 150                 155                 160

Leu His Asn Ser Glu Gly Val Val Pro Ala Ser Tyr Asp Ser Arg Gln
                165                 170                 175

Gly Phe Asn Gly Thr Phe Thr Val Gly Pro Tyr Ile Cys Glu Ala Thr
            180                 185                 190

Val Lys Gly Lys Lys Phe Gln Thr Ile Pro Phe Asn Val Tyr Ala Leu
        195                 200                 205

Lys Ala Thr Ser Glu Leu Asp Leu Glu Met Glu Ala Leu Lys Thr Val
    210                 215                 220

Tyr Lys Ser Gly Glu Thr Ile Val Val Thr Cys Ala Val Phe Asn Asn
225                 230                 235                 240
```

```
Glu Val Val Asp Leu Gln Trp Thr Tyr Pro Gly Glu Val Lys Gly Lys
                245                 250                 255

Gly Ile Thr Met Leu Glu Glu Ile Lys Val Pro Ser Ile Lys Leu Val
            260                 265                 270

Tyr Thr Leu Thr Val Pro Glu Ala Thr Val Lys Asp Ser Gly Asp Tyr
        275                 280                 285

Glu Cys Ala Ala Arg Gln Ala Thr Arg Glu Val Lys Glu Met Lys Lys
    290                 295                 300

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

Phe Ser Gln Leu Glu Ala Val Asn Leu His Glu Val Lys His Phe Val
                325                 330                 335

Val Glu Val Arg Ala Tyr Pro Pro Pro Arg Ile Ser Trp Leu Lys Asn
            340                 345                 350

Asn Leu Thr Leu Ile Glu Asn Leu Thr Glu Ile Thr Thr Asp Val Glu
        355                 360                 365

Lys Ile Gln Glu Ile Arg Tyr Arg Ser Lys Leu Lys Leu Ile Arg Ala
    370                 375                 380

Lys Glu Glu Asp Ser Gly His Tyr Thr Ile Val Ala Gln Asn Glu Asp
385                 390                 395                 400

Ala Val Lys Ser Tyr Thr Phe Glu Leu Leu Thr Gln Val Pro Ser Ser
                405                 410                 415

Ile Leu Asp Leu Val Asp Asp His His Gly Ser Thr Gly Gly Gln Thr
            420                 425                 430

Val Arg Cys Thr Ala Glu Gly Thr Pro Leu Pro Asp Ile Glu Trp Met
        435                 440                 445

Ile Cys Lys Asp Ile Lys Lys Cys Asn Asn Glu Thr Ser Trp Thr Ile
    450                 455                 460

Leu Ala Asn Asn Val Ser Asn Ile Ile Thr Glu Ile His Ser Arg Asp
465                 470                 475                 480

Arg Ser Thr Val Glu Gly Arg Val Thr Phe Ala Lys Val Glu Glu Thr
                485                 490                 495

Ile Ala Val Arg Cys Leu Ala Lys Asn Leu Leu Gly Ala Glu Asn Arg
            500                 505                 510
```

```
Glu Leu Lys Leu Val Ala Pro Thr Leu Arg Ser Glu Leu Thr Val Ala
        515                 520                 525

Ala Ala Val Leu Val Leu Leu Val Ile Val Ile Ile Ser Leu Ile Val
    530                 535                 540

Leu Val Val Ile Trp Lys Gln Lys Pro Arg Tyr Glu Ile Arg Trp Arg
545                 550                 555                 560

Val Ile Glu Ser Ile Ser Pro Asp Gly His Glu Tyr Ile Tyr Val Asp
                565                 570                 575

Pro Met Gln Leu Pro Tyr Asp Ser Arg Trp Glu Phe Pro Arg Asp Gly
            580                 585                 590

Leu Val Leu Gly Arg Val Leu Gly Ser Gly Ala Phe Gly Lys Val Val
        595                 600                 605

Glu Gly Thr Ala Tyr Gly Leu Ser Arg Ser Gln Pro Val Met Lys Val
    610                 615                 620

Ala Val Lys Met Leu Lys Pro Thr Ala Arg Ser Ser Glu Lys Gln Ala
625                 630                 635                 640

Leu Met Ser Glu Leu Lys Ile Met Thr His Leu Gly Pro His Leu Asn
                645                 650                 655

Ile Val Asn Leu Leu Gly Ala Cys Thr Lys Ser Gly Pro Ile Tyr Ile
            660                 665                 670

Ile Thr Glu Tyr Cys Phe Tyr Gly Asp Leu Val Asn Tyr Leu His Lys
        675                 680                 685

Asn Arg Asp Ser Phe Leu Ser His His Pro Glu Lys Pro Lys Lys Glu
    690                 695                 700

Leu Asp Ile Phe Gly Leu Asn Pro Ala Asp Glu Ser Thr Arg Ser Tyr
705                 710                 715                 720

Val Ile Leu Ser Phe Glu Asn Asn Gly Asp Tyr Met Asp Met Lys Gln
                725                 730                 735

Ala Asp Thr Thr Gln Tyr Val Pro Met Leu Glu Arg Lys Glu Val Ser
            740                 745                 750

Lys Tyr Ser Asp Ile Gln Arg Ser Leu Tyr Asp Arg Pro Ala Ser Tyr
        755                 760                 765

Lys Lys Lys Ser Met Leu Asp Ser Glu Val Lys Asn Leu Leu Ser Asp
    770                 775                 780
```

```
Asp Asn Ser Glu Gly Leu Thr Leu Leu Asp Leu Leu Ser Phe Thr Tyr
785                 790                 795                 800

Gln Val Ala Arg Gly Met Glu Phe Leu Ala Ser Lys Asn Cys Val His
                805                 810                 815

Arg Asp Leu Ala Ala Arg Asn Val Leu Leu Ala Gln Gly Lys Ile Val
            820                 825                 830

Lys Ile Cys Asp Phe Gly Leu Ala Arg Asp Ile Met His Asp Ser Asn
        835                 840                 845

Tyr Val Ser Lys Gly Ser Thr Phe Leu Pro Val Lys Trp Met Ala Pro
    850                 855                 860

Glu Ser Ile Phe Asp Asn Leu Tyr Thr Thr Leu Ser Asp Val Trp Ser
865                 870                 875                 880

Tyr Gly Ile Leu Leu Trp Glu Ile Phe Ser Leu Gly Gly Thr Pro Tyr
                885                 890                 895

Pro Gly Met Met Val Asp Ser Thr Phe Tyr Asn Lys Ile Lys Ser Gly
            900                 905                 910

Tyr Arg Met Ala Lys Pro Asp His Ala Thr Ser Glu Val Tyr Glu Ile
        915                 920                 925

Met Val Lys Cys Trp Asn Ser Glu Pro Glu Lys Arg Pro Ser Phe Tyr
    930                 935                 940

His Leu Ser Glu Ile Val Glu Asn Leu Leu Pro Gly Gln Tyr Lys Lys
945                 950                 955                 960

Ser Tyr Glu Lys Ile His Leu Asp Phe Leu Lys Ser Asp His Pro Ala
                965                 970                 975

Val Ala Arg Met Arg Val Asp Ser Asp Asn Ala Tyr Ile Gly Val Thr
            980                 985                 990

Tyr Lys Asn Glu Glu Asp Lys Leu  Lys Asp Trp Glu Gly  Gly Leu Asp
        995                 1000                1005

Glu Gln  Arg Leu Ser Ala Asp  Ser Gly Tyr Ile Ile  Pro Leu Pro
    1010                1015                1020

Asp Ile  Asp Pro Val Pro Glu  Glu Glu Asp Leu Gly  Lys Arg Asn
    1025                1030                1035

Arg His  Ser Ser Gln Thr Ser  Glu Glu Ser Ala Ile  Glu Thr Gly
    1040                1045                1050
```

Ser Ser Ser Ser Thr Phe Ile Lys Arg Glu Asp Glu Thr Ile Glu
1055 1060 1065

Asp Ile Asp Met Met Asp Asp Ile Gly Ile Asp Ser Ser Asp Leu
1070 1075 1080

Val Glu Asp Ser Phe Leu
1085

<210> 459
<211> 1106
<212> PRT
<213> Homo sapiens

<400> 459

Met Arg Leu Pro Gly Ala Met Pro Ala Leu Ala Leu Lys Gly Glu Leu
1 5 10 15

Leu Leu Leu Ser Leu Leu Leu Leu Leu Glu Pro Gln Ile Ser Gln Gly
20 25 30

Leu Val Val Thr Pro Pro Gly Pro Glu Leu Val Leu Asn Val Ser Ser
35 40 45

Thr Phe Val Leu Thr Cys Ser Gly Ser Ala Pro Val Val Trp Glu Arg
50 55 60

Met Ser Gln Glu Pro Pro Gln Glu Met Ala Lys Ala Gln Asp Gly Thr
65 70 75 80

Phe Ser Ser Val Leu Thr Leu Thr Asn Leu Thr Gly Leu Asp Thr Gly
85 90 95

Glu Tyr Phe Cys Thr His Asn Asp Ser Arg Gly Leu Glu Thr Asp Glu
100 105 110

Arg Lys Arg Leu Tyr Ile Phe Val Pro Asp Pro Thr Val Gly Phe Leu
115 120 125

Pro Asn Asp Ala Glu Glu Leu Phe Ile Phe Leu Thr Glu Ile Thr Glu
130 135 140

Ile Thr Ile Pro Cys Arg Val Thr Asp Pro Gln Leu Val Val Thr Leu
145 150 155 160

His Glu Lys Lys Gly Asp Val Ala Leu Pro Val Pro Tyr Asp His Gln
165 170 175

Arg Gly Phe Ser Gly Ile Phe Glu Asp Arg Ser Tyr Ile Cys Lys Thr
180 185 190

Thr Ile Gly Asp Arg Glu Val Asp Ser Asp Ala Tyr Tyr Val Tyr Arg

195 200 205

Leu Gln Val Ser Ser Ile Asn Val Ser Val Asn Ala Val Gln Thr Val
210 215 220

Val Arg Gln Gly Glu Asn Ile Thr Leu Met Cys Ile Val Ile Gly Asn
225 230 235 240

Glu Val Val Asn Phe Glu Trp Thr Tyr Pro Arg Lys Glu Ser Gly Arg
245 250 255

Leu Val Glu Pro Val Thr Asp Phe Leu Leu Asp Met Pro Tyr His Ile
260 265 270

Arg Ser Ile Leu His Ile Pro Ser Ala Glu Leu Glu Asp Ser Gly Thr
275 280 285

Tyr Thr Cys Asn Val Thr Glu Ser Val Asn Asp His Gln Asp Glu Lys
290 295 300

Ala Ile Asn Ile Thr Val Val Glu Ser Gly Tyr Val Arg Leu Leu Gly
305 310 315 320

Glu Val Gly Thr Leu Gln Phe Ala Glu Leu His Arg Ser Arg Thr Leu
325 330 335

Gln Val Val Phe Glu Ala Tyr Pro Pro Pro Thr Val Leu Trp Phe Lys
340 345 350

Asp Asn Arg Thr Leu Gly Asp Ser Ser Ala Gly Glu Ile Ala Leu Ser
355 360 365

Thr Arg Asn Val Ser Glu Thr Arg Tyr Val Ser Glu Leu Thr Leu Val
370 375 380

Arg Val Lys Val Ala Glu Ala Gly His Tyr Thr Met Arg Ala Phe His
385 390 395 400

Glu Asp Ala Glu Val Gln Leu Ser Phe Gln Leu Gln Ile Asn Val Pro
405 410 415

Val Arg Val Leu Glu Leu Ser Glu Ser His Pro Asp Ser Gly Glu Gln
420 425 430

Thr Val Arg Cys Arg Gly Arg Gly Met Pro Gln Pro Asn Ile Ile Trp
435 440 445

Ser Ala Cys Arg Asp Leu Lys Arg Cys Pro Arg Glu Leu Pro Pro Thr
450 455 460

Leu Leu Gly Asn Ser Ser Glu Glu Glu Ser Gln Leu Glu Thr Asn Val

465 470 475 480

Thr Tyr Trp Glu Glu Glu Gln Glu Phe Glu Val Val Ser Thr Leu Arg
485 490 495

Leu Gln His Val Asp Arg Pro Leu Ser Val Arg Cys Thr Leu Arg Asn
500 505 510

Ala Val Gly Gln Asp Thr Gln Glu Val Ile Val Val Pro His Ser Leu
515 520 525

Pro Phe Lys Val Val Val Ile Ser Ala Ile Leu Ala Leu Val Val Leu
530 535 540

Thr Ile Ile Ser Leu Ile Ile Leu Ile Met Leu Trp Gln Lys Lys Pro
545 550 555 560

Arg Tyr Glu Ile Arg Trp Lys Val Ile Glu Ser Val Ser Ser Asp Gly
565 570 575

His Glu Tyr Ile Tyr Val Asp Pro Met Gln Leu Pro Tyr Asp Ser Thr
580 585 590

Trp Glu Leu Pro Arg Asp Gln Leu Val Leu Gly Arg Thr Leu Gly Ser
595 600 605

Gly Ala Phe Gly Gln Val Val Glu Ala Thr Ala His Gly Leu Ser His
610 615 620

Ser Gln Ala Thr Met Lys Val Ala Val Lys Met Leu Lys Ser Thr Ala
625 630 635 640

Arg Ser Ser Glu Lys Gln Ala Leu Met Ser Glu Leu Lys Ile Met Ser
645 650 655

His Leu Gly Pro His Leu Asn Val Val Asn Leu Leu Gly Ala Cys Thr
660 665 670

Lys Gly Gly Pro Ile Tyr Ile Ile Thr Glu Tyr Cys Arg Tyr Gly Asp
675 680 685

Leu Val Asp Tyr Leu His Arg Asn Lys His Thr Phe Leu Gln His His
690 695 700

Ser Asp Lys Arg Arg Pro Pro Ser Ala Glu Leu Tyr Ser Asn Ala Leu
705 710 715 720

Pro Val Gly Leu Pro Leu Pro Ser His Val Ser Leu Thr Gly Glu Ser
725 730 735

Asp Gly Gly Tyr Met Asp Met Ser Lys Asp Glu Ser Val Asp Tyr Val

740 745 750

Pro Met Leu Asp Met Lys Gly Asp Val Lys Tyr Ala Asp Ile Glu Ser
755 760 765

Ser Asn Tyr Met Ala Pro Tyr Asp Asn Tyr Val Pro Ser Ala Pro Glu
770 775 780

Arg Thr Cys Arg Ala Thr Leu Ile Asn Glu Ser Pro Val Leu Ser Tyr
785 790 795 800

Met Asp Leu Val Gly Phe Ser Tyr Gln Val Ala Asn Gly Met Glu Phe
805 810 815

Leu Ala Ser Lys Asn Cys Val His Arg Asp Leu Ala Ala Arg Asn Val
820 825 830

Leu Ile Cys Glu Gly Lys Leu Val Lys Ile Cys Asp Phe Gly Leu Ala
835 840 845

Arg Asp Ile Met Arg Asp Ser Asn Tyr Ile Ser Lys Gly Ser Thr Phe
850 855 860

Leu Pro Leu Lys Trp Met Ala Pro Glu Ser Ile Phe Asn Ser Leu Tyr
865 870 875 880

Thr Thr Leu Ser Asp Val Trp Ser Phe Gly Ile Leu Leu Trp Glu Ile
885 890 895

Phe Thr Leu Gly Gly Thr Pro Tyr Pro Glu Leu Pro Met Asn Glu Gln
900 905 910

Phe Tyr Asn Ala Ile Lys Arg Gly Tyr Arg Met Ala Gln Pro Ala His
915 920 925

Ala Ser Asp Glu Ile Tyr Glu Ile Met Gln Lys Cys Trp Glu Glu Lys
930 935 940

Phe Glu Ile Arg Pro Pro Phe Ser Gln Leu Val Leu Leu Leu Glu Arg
945 950 955 960

Leu Leu Gly Glu Gly Tyr Lys Lys Lys Tyr Gln Gln Val Asp Glu Glu
965 970 975

Phe Leu Arg Ser Asp His Pro Ala Ile Leu Arg Ser Gln Ala Arg Leu
980 985 990

Pro Gly Phe His Gly Leu Arg Ser Pro Leu Asp Thr Ser Ser Val Leu
995 1000 1005

Tyr Thr Ala Val Gln Pro Asn Glu Gly Asp Asn Asp Tyr Ile Ile

1010 1015 1020

Pro Leu Pro Asp Pro Lys Pro Glu Val Ala Asp Glu Gly Pro Leu
1025 1030 1035

Glu Gly Ser Pro Ser Leu Ala Ser Ser Thr Leu Asn Glu Val Asn
1040 1045 1050

Thr Ser Ser Thr Ile Ser Cys Asp Ser Pro Leu Glu Pro Gln Asp
1055 1060 1065

Glu Pro Glu Pro Glu Pro Gln Leu Glu Leu Gln Val Glu Pro Glu
1070 1075 1080

Pro Glu Leu Glu Gln Leu Pro Asp Ser Gly Cys Pro Ala Pro Arg
1085 1090 1095

Ala Glu Ala Glu Asp Ser Phe Leu
1100 1105

<210> 460
<211> 894
<212> PRT
<213> Homo sapiens

<400> 460

Met Ala Trp Arg Cys Pro Arg Met Gly Arg Val Pro Leu Ala Trp Cys
1 5 10 15

Leu Ala Leu Cys Gly Trp Ala Cys Met Ala Pro Arg Gly Thr Gln Ala
20 25 30

Glu Glu Ser Pro Phe Val Gly Asn Pro Gly Asn Ile Thr Gly Ala Arg
35 40 45

Gly Leu Thr Gly Thr Leu Arg Cys Gln Leu Gln Val Gln Gly Glu Pro
50 55 60

Pro Glu Val His Trp Leu Arg Asp Gly Gln Ile Leu Glu Leu Ala Asp
65 70 75 80

Ser Thr Gln Thr Gln Val Pro Leu Gly Glu Asp Glu Gln Asp Asp Trp
85 90 95

Ile Val Val Ser Gln Leu Arg Ile Thr Ser Leu Gln Leu Ser Asp Thr
100 105 110

Gly Gln Tyr Gln Cys Leu Val Phe Leu Gly His Gln Thr Phe Val Ser
115 120 125

Gln Pro Gly Tyr Val Gly Leu Glu Gly Leu Pro Tyr Phe Leu Glu Glu
130 135 140

```
Pro Glu Asp Arg Thr Val Ala Ala Asn Thr Pro Phe Asn Leu Ser Cys
145                 150                 155                 160

Gln Ala Gln Gly Pro Pro Glu Pro Val Asp Leu Leu Trp Leu Gln Asp
                165                 170                 175

Ala Val Pro Leu Ala Thr Ala Pro Gly His Gly Pro Gln Arg Ser Leu
            180                 185                 190

His Val Pro Gly Leu Asn Lys Thr Ser Ser Phe Ser Cys Glu Ala His
        195                 200                 205

Asn Ala Lys Gly Val Thr Thr Ser Arg Thr Ala Thr Ile Thr Val Leu
    210                 215                 220

Pro Gln Gln Pro Arg Asn Leu His Leu Val Ser Arg Gln Pro Thr Glu
225                 230                 235                 240

Leu Glu Val Ala Trp Thr Pro Gly Leu Ser Gly Ile Tyr Pro Leu Thr
                245                 250                 255

His Cys Thr Leu Gln Ala Val Leu Ser Asp Asp Gly Met Gly Ile Gln
            260                 265                 270

Ala Gly Glu Pro Asp Pro Pro Glu Glu Pro Leu Thr Ser Gln Ala Ser
        275                 280                 285

Val Pro Pro His Gln Leu Arg Leu Gly Ser Leu His Pro His Thr Pro
    290                 295                 300

Tyr His Ile Arg Val Ala Cys Thr Ser Ser Gln Gly Pro Ser Ser Trp
305                 310                 315                 320

Thr His Trp Leu Pro Val Glu Thr Pro Glu Gly Val Pro Leu Gly Pro
                325                 330                 335

Pro Glu Asn Ile Ser Ala Thr Arg Asn Gly Ser Gln Ala Phe Val His
            340                 345                 350

Trp Gln Glu Pro Arg Ala Pro Leu Gln Gly Thr Leu Leu Gly Tyr Arg
        355                 360                 365

Leu Ala Tyr Gln Gly Gln Asp Thr Pro Glu Val Leu Met Asp Ile Gly
    370                 375                 380

Leu Arg Gln Glu Val Thr Leu Glu Leu Gln Gly Asp Gly Ser Val Ser
385                 390                 395                 400

Asn Leu Thr Val Cys Val Ala Ala Tyr Thr Ala Ala Gly Asp Gly Pro
                405                 410                 415
```

Trp Ser Leu Pro Val Pro Leu Glu Ala Trp Arg Pro Gly Gln Ala Gln
420 425 430

Pro Val His Gln Leu Val Lys Glu Pro Ser Thr Pro Ala Phe Ser Trp
435 440 445

Pro Trp Trp Tyr Val Leu Leu Gly Ala Val Val Ala Ala Ala Cys Val
450 455 460

Leu Ile Leu Ala Leu Phe Leu Val His Arg Arg Lys Lys Glu Thr Arg
465 470 475 480

Tyr Gly Glu Val Phe Glu Pro Thr Val Glu Arg Gly Glu Leu Val Val
485 490 495

Arg Tyr Arg Val Arg Lys Ser Tyr Ser Arg Arg Thr Thr Glu Ala Thr
500 505 510

Leu Asn Ser Leu Gly Ile Ser Glu Glu Leu Lys Glu Lys Leu Arg Asp
515 520 525

Val Met Val Asp Arg His Lys Val Ala Leu Gly Lys Thr Leu Gly Glu
530 535 540

Gly Glu Phe Gly Ala Val Met Glu Gly Gln Leu Asn Gln Asp Asp Ser
545 550 555 560

Ile Leu Lys Val Ala Val Lys Thr Met Lys Ile Ala Ile Cys Thr Arg
565 570 575

Ser Glu Leu Glu Asp Phe Leu Ser Glu Ala Val Cys Met Lys Glu Phe
580 585 590

Asp His Pro Asn Val Met Arg Leu Ile Gly Val Cys Phe Gln Gly Ser
595 600 605

Glu Arg Glu Ser Phe Pro Ala Pro Val Val Ile Leu Pro Phe Met Lys
610 615 620

His Gly Asp Leu His Ser Phe Leu Leu Tyr Ser Arg Leu Gly Asp Gln
625 630 635 640

Pro Val Tyr Leu Pro Thr Gln Met Leu Val Lys Phe Met Ala Asp Ile
645 650 655

Ala Ser Gly Met Glu Tyr Leu Ser Thr Lys Arg Phe Ile His Arg Asp
660 665 670

Leu Ala Ala Arg Asn Cys Met Leu Asn Glu Asn Met Ser Val Cys Val
675 680 685

```
Ala Asp Phe Gly Leu Ser Lys Lys Ile Tyr Asn Gly Asp Tyr Tyr Arg
    690                 695                 700

Gln Gly Arg Ile Ala Lys Met Pro Val Lys Trp Ile Ala Ile Glu Ser
705                 710                 715                 720

Leu Ala Asp Arg Val Tyr Thr Ser Lys Ser Asp Val Trp Ser Phe Gly
                725                 730                 735

Val Thr Met Trp Glu Ile Ala Thr Arg Gly Gln Thr Pro Tyr Pro Gly
            740                 745                 750

Val Glu Asn Ser Glu Ile Tyr Asp Tyr Leu Arg Gln Gly Asn Arg Leu
        755                 760                 765

Lys Gln Pro Ala Asp Cys Leu Asp Gly Leu Tyr Ala Leu Met Ser Arg
    770                 775                 780

Cys Trp Glu Leu Asn Pro Gln Asp Arg Pro Ser Phe Thr Glu Leu Arg
785                 790                 795                 800

Glu Asp Leu Glu Asn Thr Leu Lys Ala Leu Pro Pro Ala Gln Glu Pro
                805                 810                 815

Asp Glu Ile Leu Tyr Val Asn Met Asp Glu Gly Gly Gly Tyr Pro Glu
            820                 825                 830

Pro Pro Gly Ala Ala Gly Gly Ala Asp Pro Pro Thr Gln Pro Asp Pro
        835                 840                 845

Lys Asp Ser Cys Ser Cys Leu Thr Ala Ala Glu Val His Pro Ala Gly
    850                 855                 860

Arg Tyr Val Leu Cys Pro Ser Thr Thr Pro Ser Pro Ala Gln Pro Ala
865                 870                 875                 880

Asp Arg Gly Ser Pro Ala Ala Pro Gly Gln Glu Asp Gly Ala
                885                 890
```

<210> 461
<211> 1070
<212> PRT
<213> Homo sapiens

<400> 461

```
Met Gly Ala Ala Arg Gly Ser Pro Ala Arg Pro Arg Arg Leu Pro Leu
1               5                   10                  15

Leu Ser Val Leu Leu Leu Pro Leu Leu Gly Gly Thr Gln Thr Ala Ile
            20                  25                  30
```

```
Val Phe Ile Lys Gln Pro Ser Ser Gln Asp Ala Leu Gln Gly Arg Arg
        35                  40                  45

Ala Leu Leu Arg Cys Glu Val Glu Ala Pro Gly Pro Val His Val Tyr
    50                  55                  60

Trp Leu Leu Asp Gly Ala Pro Val Gln Asp Thr Glu Arg Arg Phe Ala
65                  70                  75                  80

Gln Gly Ser Ser Leu Ser Phe Ala Ala Val Asp Arg Leu Gln Asp Ser
                85                  90                  95

Gly Thr Phe Gln Cys Val Ala Arg Asp Asp Val Thr Gly Glu Glu Ala
            100                 105                 110

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

Val Val Leu Lys His Pro Ala Ser Glu Ala Glu Ile Gln Pro Gln Thr
    130                 135                 140

Gln Val Thr Leu Arg Cys His Ile Asp Gly His Pro Arg Pro Thr Tyr
145                 150                 155                 160

Gln Trp Phe Arg Asp Gly Thr Pro Leu Ser Asp Gly Gln Ser Asn His
                165                 170                 175

Thr Val Ser Ser Lys Glu Arg Asn Leu Thr Leu Arg Pro Ala Gly Pro
            180                 185                 190

Glu His Ser Gly Leu Tyr Ser Cys Cys Ala His Ser Ala Phe Gly Gln
        195                 200                 205

Ala Cys Ser Ser Gln Asn Phe Thr Leu Ser Ile Ala Asp Glu Ser Phe
    210                 215                 220

Ala Arg Val Val Leu Ala Pro Gln Asp Val Val Val Ala Arg Tyr Glu
225                 230                 235                 240

Glu Ala Met Phe His Cys Gln Phe Ser Ala Gln Pro Pro Pro Ser Leu
                245                 250                 255

Gln Trp Leu Phe Glu Asp Glu Thr Pro Ile Thr Asn Arg Ser Arg Pro
            260                 265                 270

Pro His Leu Arg Arg Ala Thr Val Phe Ala Asn Gly Ser Leu Leu Leu
        275                 280                 285

Thr Gln Val Arg Pro Arg Asn Ala Gly Ile Tyr Arg Cys Ile Gly Gln
    290                 295                 300
```

```
Gly Gln Arg Gly Pro Pro Ile Ile Leu Glu Ala Thr Leu His Leu Ala
305                 310                 315                 320

Glu Ile Glu Asp Met Pro Leu Phe Glu Pro Arg Val Phe Thr Ala Gly
                325                 330                 335

Ser Glu Glu Arg Val Thr Cys Leu Pro Pro Lys Gly Leu Pro Glu Pro
            340                 345                 350

Ser Val Trp Trp Glu His Ala Gly Val Arg Leu Pro Thr His Gly Arg
        355                 360                 365

Val Tyr Gln Lys Gly His Glu Leu Val Leu Ala Asn Ile Ala Glu Ser
    370                 375                 380

Asp Ala Gly Val Tyr Thr Cys His Ala Ala Asn Leu Ala Gly Gln Arg
385                 390                 395                 400

Arg Gln Asp Val Asn Ile Thr Val Ala Thr Val Pro Ser Trp Leu Lys
                405                 410                 415

Lys Pro Gln Asp Ser Gln Leu Glu Glu Gly Lys Pro Gly Tyr Leu Asp
            420                 425                 430

Cys Leu Thr Gln Ala Thr Pro Lys Pro Thr Val Val Trp Tyr Arg Asn
        435                 440                 445

Gln Met Leu Ile Ser Glu Asp Ser Arg Phe Glu Val Phe Lys Asn Gly
    450                 455                 460

Thr Leu Arg Ile Asn Ser Val Glu Val Tyr Asp Gly Thr Trp Tyr Arg
465                 470                 475                 480

Cys Met Ser Ser Thr Pro Ala Gly Ser Ile Glu Ala Gln Ala Arg Val
                485                 490                 495

Gln Val Leu Glu Lys Leu Lys Phe Thr Pro Pro Pro Gln Pro Gln Gln
            500                 505                 510

Cys Met Glu Phe Asp Lys Glu Ala Thr Val Pro Cys Ser Ala Thr Gly
        515                 520                 525

Arg Glu Lys Pro Thr Ile Lys Trp Glu Arg Ala Asp Gly Ser Ser Leu
    530                 535                 540

Pro Glu Trp Val Thr Asp Asn Ala Gly Thr Leu His Phe Ala Arg Val
545                 550                 555                 560

Thr Arg Asp Asp Ala Gly Asn Tyr Thr Cys Ile Ala Ser Asn Gly Pro
                565                 570                 575
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Gln Gly Gln Ile Arg Ala His Val Gln Leu Thr Val Ala Val Phe Ile
            580                 585                 590

Thr Phe Lys Val Glu Pro Glu Arg Thr Thr Val Tyr Gln Gly His Thr
        595                 600                 605

Ala Leu Leu Gln Cys Glu Ala Gln Gly Asp Pro Lys Pro Leu Ile Gln
    610                 615                 620

Trp Lys Gly Lys Asp Arg Ile Leu Asp Pro Thr Lys Leu Gly Pro Arg
625                 630                 635                 640

Met His Ile Phe Gln Asn Gly Ser Leu Val Ile His Asp Val Ala Pro
                645                 650                 655

Glu Asp Ser Gly Arg Tyr Thr Cys Ile Ala Gly Asn Ser Cys Asn Ile
            660                 665                 670

Lys His Thr Glu Ala Pro Leu Tyr Val Val Asp Lys Pro Val Pro Glu
        675                 680                 685

Glu Ser Glu Gly Pro Gly Ser Pro Pro Pro Tyr Lys Met Ile Gln Thr
    690                 695                 700

Ile Gly Leu Ser Val Gly Ala Ala Val Ala Tyr Ile Ile Ala Val Leu
705                 710                 715                 720

Gly Leu Met Phe Tyr Cys Lys Lys Arg Cys Lys Ala Lys Arg Leu Gln
                725                 730                 735

Lys Gln Pro Glu Gly Glu Glu Pro Glu Met Glu Cys Leu Asn Gly Gly
            740                 745                 750

Pro Leu Gln Asn Gly Gln Pro Ser Ala Glu Ile Gln Glu Glu Val Ala
        755                 760                 765

Leu Thr Ser Leu Gly Ser Gly Pro Ala Ala Thr Asn Lys Arg His Ser
    770                 775                 780

Thr Ser Asp Lys Met His Phe Pro Arg Ser Ser Leu Gln Pro Ile Thr
785                 790                 795                 800

Thr Leu Gly Lys Ser Glu Phe Gly Glu Val Phe Leu Ala Lys Ala Gln
                805                 810                 815

Gly Leu Glu Glu Gly Val Ala Glu Thr Leu Val Leu Val Lys Ser Leu
            820                 825                 830

Gln Ser Lys Asp Glu Gln Gln Gln Leu Asp Phe Arg Arg Glu Leu Glu
        835                 840                 845
```

```
Met Phe Gly Lys Leu Asn His Ala Asn Val Val Arg Leu Leu Gly Leu
    850                 855                 860

Cys Arg Glu Ala Glu Pro His Tyr Met Val Leu Glu Tyr Val Asp Leu
865                 870                 875                 880

Gly Asp Leu Lys Gln Phe Leu Arg Ile Ser Lys Ser Lys Asp Glu Lys
                885                 890                 895

Leu Lys Ser Gln Pro Leu Ser Thr Lys Gln Lys Val Ala Leu Cys Thr
            900                 905                 910

Gln Val Ala Leu Gly Met Glu His Leu Ser Asn Asn Arg Phe Val His
        915                 920                 925

Lys Asp Leu Ala Ala Arg Asn Cys Leu Val Ser Ala Gln Arg Gln Val
    930                 935                 940

Lys Val Ser Ala Leu Gly Leu Ser Lys Asp Val Tyr Asn Ser Glu Tyr
945                 950                 955                 960

Tyr His Phe Arg Gln Ala Trp Val Pro Leu Arg Trp Met Ser Pro Glu
                965                 970                 975

Ala Ile Leu Glu Gly Asp Phe Ser Thr Lys Ser Asp Val Trp Ala Phe
            980                 985                 990

Gly Val Leu Met Trp Glu Val Phe  Thr His Gly Glu Met  Pro His Gly
        995                 1000                1005

Gly Gln  Ala Asp Asp Glu Val  Leu Ala Asp Leu Gln  Ala Gly Lys
    1010                1015                1020

Ala Arg  Leu Pro Gln Pro Glu  Gly Cys Pro Ser Lys  Leu Tyr Arg
    1025                1030                1035

Leu Met  Gln Arg Cys Trp Ala  Leu Ser Pro Lys Asp  Arg Pro Ser
    1040                1045                1050

Phe Ser  Glu Ile Ala Ser Ala  Leu Gly Asp Ser Thr  Val Asp Ser
    1055                1060                1065

Lys Pro
    1070
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<210> 462
<211> 1114
<212> PRT
<213> Homo sapiens

<400> 462

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

Leu Leu Leu Pro Leu Leu Gly Lys Val Ala Leu Gly Leu Tyr Phe Ser
            20                  25                  30

Arg Asp Ala Tyr Trp Glu Lys Leu Tyr Val Asp Gln Ala Ala Gly Thr
        35                  40                  45

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

Ser Phe Arg Leu Gly Gln His Leu Tyr Gly Thr Tyr Arg Thr Arg Leu
65                  70                  75                  80

His Glu Asn Asn Trp Ile Cys Ile Gln Glu Asp Thr Gly Leu Leu Tyr
                85                  90                  95

Leu Asn Arg Ser Leu Asp His Ser Ser Trp Glu Lys Leu Ser Val Arg
            100                 105                 110

Asn Arg Gly Phe Pro Leu Leu Thr Val Tyr Leu Lys Val Phe Leu Ser
        115                 120                 125

Pro Thr Ser Leu Arg Glu Gly Glu Cys Gln Trp Pro Gly Cys Ala Arg
    130                 135                 140

Val Tyr Phe Ser Phe Phe Asn Thr Ser Phe Pro Ala Cys Ser Ser Leu
145                 150                 155                 160

Lys Pro Arg Glu Leu Cys Phe Pro Glu Thr Arg Pro Ser Phe Arg Ile
                165                 170                 175

Arg Glu Asn Arg Pro Pro Gly Thr Phe His Gln Phe Arg Leu Leu Pro
            180                 185                 190

Val Gln Phe Leu Cys Pro Asn Ile Ser Val Ala Tyr Arg Leu Leu Glu
        195                 200                 205

Gly Glu Gly Leu Pro Phe Arg Cys Ala Pro Asp Ser Leu Glu Val Ser
    210                 215                 220

Thr Arg Trp Ala Leu Asp Arg Glu Gln Arg Glu Lys Tyr Glu Leu Val
225                 230                 235                 240

Ala Val Cys Thr Val His Ala Gly Ala Arg Glu Glu Val Val Met Val
                245                 250                 255

Pro Phe Pro Val Thr Val Tyr Asp Glu Asp Asp Ser Ala Pro Thr Phe
            260                 265                 270
```

```
Pro Ala Gly Val Asp Thr Ala Ser Ala Val Val Glu Phe Lys Arg Lys
        275                 280                 285

Glu Asp Thr Val Val Ala Thr Leu Arg Val Phe Asp Ala Asp Val Val
    290                 295                 300

Pro Ala Ser Gly Glu Leu Val Arg Arg Tyr Thr Ser Thr Leu Leu Pro
305                 310                 315                 320

Gly Asp Thr Trp Ala Gln Gln Thr Phe Arg Val Glu His Trp Pro Asn
                325                 330                 335

Glu Thr Ser Val Gln Ala Asn Gly Ser Phe Val Arg Ala Thr Val His
            340                 345                 350

Asp Tyr Arg Leu Val Leu Asn Arg Asn Leu Ser Ile Ser Glu Asn Arg
        355                 360                 365

Thr Met Gln Leu Ala Val Leu Val Asn Asp Ser Asp Phe Gln Gly Pro
    370                 375                 380

Gly Ala Gly Val Leu Leu Leu His Phe Asn Val Ser Val Leu Pro Val
385                 390                 395                 400

Ser Leu His Leu Pro Ser Thr Tyr Ser Leu Ser Val Ser Arg Arg Ala
                405                 410                 415

Arg Arg Phe Ala Gln Ile Gly Lys Val Cys Val Glu Asn Cys Gln Ala
            420                 425                 430

Phe Ser Gly Ile Asn Val Gln Tyr Lys Leu His Ser Ser Gly Ala Asn
        435                 440                 445

Cys Ser Thr Leu Gly Val Val Thr Ser Ala Glu Asp Thr Ser Gly Ile
    450                 455                 460

Leu Phe Val Asn Asp Thr Lys Ala Leu Arg Arg Pro Lys Cys Ala Glu
465                 470                 475                 480

Leu His Tyr Met Val Val Ala Thr Asp Gln Gln Thr Ser Arg Gln Ala
                485                 490                 495

Gln Ala Gln Leu Leu Val Thr Val Glu Gly Ser Tyr Val Ala Glu Glu
            500                 505                 510

Ala Gly Cys Pro Leu Ser Cys Ala Val Ser Lys Arg Arg Leu Glu Cys
        515                 520                 525

Glu Glu Cys Gly Gly Leu Gly Ser Pro Thr Gly Arg Cys Glu Trp Arg
    530                 535                 540
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```
Gln Gly Asp Gly Lys Gly Ile Thr Arg Asn Phe Ser Thr Cys Ser Pro
545                 550                 555                 560

Ser Thr Lys Thr Cys Pro Asp Gly His Cys Asp Val Val Glu Thr Gln
                565                 570                 575

Asp Ile Asn Ile Cys Pro Gln Asp Cys Leu Arg Gly Ser Ile Val Gly
            580                 585                 590

Gly His Glu Pro Gly Glu Pro Arg Gly Ile Lys Ala Gly Tyr Gly Thr
        595                 600                 605

Cys Asn Cys Phe Pro Glu Glu Glu Lys Cys Phe Cys Glu Pro Glu Asp
    610                 615                 620

Ile Gln Asp Pro Leu Cys Asp Glu Leu Cys Arg Thr Val Ile Ala Ala
625                 630                 635                 640

Ala Val Leu Phe Ser Phe Ile Val Ser Val Leu Leu Ser Ala Phe Cys
                645                 650                 655

Ile His Cys Tyr His Lys Phe Ala His Lys Pro Pro Ile Ser Ser Ala
            660                 665                 670

Glu Met Thr Phe Arg Arg Pro Ala Gln Ala Phe Pro Val Ser Tyr Ser
        675                 680                 685

Ser Ser Gly Ala Arg Arg Pro Ser Leu Asp Ser Met Glu Asn Gln Val
    690                 695                 700

Ser Val Asp Ala Phe Lys Ile Leu Glu Asp Pro Lys Trp Glu Phe Pro
705                 710                 715                 720

Arg Lys Asn Leu Val Leu Gly Lys Thr Leu Gly Glu Gly Glu Phe Gly
                725                 730                 735

Lys Val Val Lys Ala Thr Ala Phe His Leu Lys Gly Arg Ala Gly Tyr
            740                 745                 750

Thr Thr Val Ala Val Lys Met Leu Lys Glu Asn Ala Ser Pro Ser Glu
        755                 760                 765

Leu Arg Asp Leu Leu Ser Glu Phe Asn Val Leu Lys Gln Val Asn His
    770                 775                 780

Pro His Val Ile Lys Leu Tyr Gly Ala Cys Ser Gln Asp Gly Pro Leu
785                 790                 795                 800

Leu Leu Ile Val Glu Tyr Ala Lys Tyr Gly Ser Leu Arg Gly Phe Leu
                805                 810                 815
```

```
Arg Glu Ser Arg Lys Val Gly Pro Gly Tyr Leu Gly Ser Gly Gly Ser
            820                 825                 830

Arg Asn Ser Ser Ser Leu Asp His Pro Asp Glu Arg Ala Leu Thr Met
        835                 840                 845

Gly Asp Leu Ile Ser Phe Ala Trp Gln Ile Ser Gln Gly Met Gln Tyr
    850                 855                 860

Leu Ala Glu Met Lys Leu Val His Arg Asp Leu Ala Ala Arg Asn Ile
865                 870                 875                 880

Leu Val Ala Glu Gly Arg Lys Met Lys Ile Ser Asp Phe Gly Leu Ser
                885                 890                 895

Arg Asp Val Tyr Glu Glu Asp Ser Tyr Val Lys Arg Ser Gln Gly Arg
            900                 905                 910

Ile Pro Val Lys Trp Met Ala Ile Glu Ser Leu Phe Asp His Ile Tyr
        915                 920                 925

Thr Thr Gln Ser Asp Val Trp Ser Phe Gly Val Leu Leu Trp Glu Ile
    930                 935                 940

Val Thr Leu Gly Gly Asn Pro Tyr Pro Gly Ile Pro Pro Glu Arg Leu
945                 950                 955                 960

Phe Asn Leu Leu Lys Thr Gly His Arg Met Glu Arg Pro Asp Asn Cys
                965                 970                 975

Ser Glu Glu Met Tyr Arg Leu Met Leu Gln Cys Trp Lys Gln Glu Pro
            980                 985                 990

Asp Lys Arg Pro Val Phe Ala Asp  Ile Ser Lys Asp Leu  Glu Lys Met
        995                 1000                1005

Met Val  Lys Arg Arg Asp Tyr  Leu Asp Leu Ala Ala  Ser Thr Pro
    1010                1015                1020

Ser Asp  Ser Leu Ile Tyr Asp  Asp Gly Leu Ser Glu  Glu Glu Thr
    1025                1030                1035

Pro Leu  Val Asp Cys Asn Asn  Ala Pro Leu Pro Arg  Ala Leu Pro
    1040                1045                1050

Ser Thr  Trp Ile Glu Asn Lys  Leu Tyr Gly Met Ser  Asp Pro Asn
    1055                1060                1065

Trp Pro  Gly Glu Ser Pro Val  Pro Leu Thr Arg Ala  Asp Gly Thr
    1070                1075                1080
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Asn Thr Gly Phe Pro Arg Tyr Pro Asn Asp Ser Val Tyr Ala Asn
1085 1090 1095

Trp Met Leu Ser Pro Ser Ala Ala Lys Leu Met Asp Thr Phe Asp
1100 1105 1110

Ser

<210> 463
<211> 2347
<212> PRT
<213> Homo sapiens

<400> 463

Met Lys Asn Ile Tyr Cys Leu Ile Pro Lys Leu Val Asn Phe Ala Thr
1 5 10 15

Leu Gly Cys Leu Trp Ile Ser Val Val Gln Cys Thr Val Leu Asn Ser
20 25 30

Cys Leu Lys Ser Cys Val Thr Asn Leu Gly Gln Gln Leu Asp Leu Gly
35 40 45

Thr Pro His Asn Leu Ser Glu Pro Cys Ile Gln Gly Cys His Phe Trp
50 55 60

Asn Ser Val Asp Gln Lys Asn Cys Ala Leu Lys Cys Arg Glu Ser Cys
65 70 75 80

Glu Val Gly Cys Ser Ser Ala Glu Gly Ala Tyr Glu Glu Glu Val Leu
85 90 95

Glu Asn Ala Asp Leu Pro Thr Ala Pro Phe Ala Ser Ser Ile Gly Ser
100 105 110

His Asn Met Thr Leu Arg Trp Lys Ser Ala Asn Phe Ser Gly Val Lys
115 120 125

Tyr Ile Ile Gln Trp Lys Tyr Ala Gln Leu Leu Gly Ser Trp Thr Tyr
130 135 140

Thr Lys Thr Val Ser Arg Pro Ser Tyr Val Val Lys Pro Leu His Pro
145 150 155 160

Phe Thr Glu Tyr Ile Phe Arg Val Val Trp Ile Phe Thr Ala Gln Leu
165 170 175

Gln Leu Tyr Ser Pro Pro Ser Pro Ser Tyr Arg Thr His Pro His Gly
180 185 190

Val Pro Glu Thr Ala Pro Leu Ile Arg Asn Ile Glu Ser Ser Ser Pro

195 200 205

Asp Thr Val Glu Val Ser Trp Asp Pro Pro Gln Phe Pro Gly Gly Pro
210 215 220

Ile Leu Gly Tyr Asn Leu Arg Leu Ile Ser Lys Asn Gln Lys Leu Asp
225 230 235 240

Ala Gly Thr Gln Arg Thr Ser Phe Gln Phe Tyr Ser Thr Leu Pro Asn
245 250 255

Thr Ile Tyr Arg Phe Ser Ile Ala Ala Val Asn Glu Val Gly Glu Gly
260 265 270

Pro Glu Ala Glu Ser Ser Ile Thr Thr Ser Ser Ser Ala Val Gln Gln
275 280 285

Glu Glu Gln Trp Leu Phe Leu Ser Arg Lys Thr Ser Leu Arg Lys Arg
290 295 300

Ser Leu Lys His Leu Val Asp Glu Ala His Cys Leu Arg Leu Asp Ala
305 310 315 320

Ile Tyr His Asn Ile Thr Gly Ile Ser Val Asp Val His Gln Gln Ile
325 330 335

Val Tyr Phe Ser Glu Gly Thr Leu Ile Trp Ala Lys Lys Ala Ala Asn
340 345 350

Met Ser Asp Val Ser Asp Leu Arg Ile Phe Tyr Arg Gly Ser Gly Leu
355 360 365

Ile Ser Ser Ile Ser Ile Asp Trp Leu Tyr Gln Arg Met Tyr Phe Ile
370 375 380

Met Asp Glu Leu Val Cys Val Cys Asp Leu Glu Asn Cys Ser Asn Ile
385 390 395 400

Glu Glu Ile Thr Pro Pro Ser Ile Ser Ala Pro Gln Lys Ile Val Ala
405 410 415

Asp Ser Tyr Asn Gly Tyr Val Phe Tyr Leu Leu Arg Asp Gly Ile Tyr
420 425 430

Arg Ala Asp Leu Pro Val Pro Ser Gly Arg Cys Ala Glu Ala Val Arg
435 440 445

Ile Val Glu Ser Cys Thr Leu Lys Asp Phe Ala Ile Lys Pro Gln Ala
450 455 460

Lys Arg Ile Ile Tyr Phe Asn Asp Thr Ala Gln Val Phe Met Ser Thr

465 470 475 480

Phe Leu Asp Gly Ser Ala Ser His Leu Ile Leu Pro Arg Ile Pro Phe
485 490 495

Ala Asp Val Lys Ser Phe Ala Cys Glu Asn Asn Asp Phe Leu Val Thr
500 505 510

Asp Gly Lys Val Ile Phe Gln Gln Asp Ala Leu Ser Phe Asn Glu Phe
515 520 525

Ile Val Gly Cys Asp Leu Ser His Ile Glu Glu Phe Gly Phe Gly Asn
530 535 540

Leu Val Ile Phe Gly Ser Ser Ser Gln Leu His Pro Leu Pro Gly Arg
545 550 555 560

Pro Gln Glu Leu Ser Val Leu Phe Gly Ser His Gln Ala Leu Val Gln
565 570 575

Trp Lys Pro Pro Ala Leu Ala Ile Gly Ala Asn Val Ile Leu Ile Ser
580 585 590

Asp Ile Ile Glu Leu Phe Glu Leu Gly Pro Ser Ala Trp Gln Asn Trp
595 600 605

Thr Tyr Glu Val Lys Val Ser Thr Gln Asp Pro Pro Glu Val Thr His
610 615 620

Ile Phe Leu Asn Ile Ser Gly Thr Met Leu Asn Val Pro Glu Leu Gln
625 630 635 640

Ser Ala Met Lys Tyr Lys Val Ser Val Arg Ala Ser Ser Pro Lys Arg
645 650 655

Pro Gly Pro Trp Ser Glu Pro Ser Val Gly Thr Thr Leu Val Pro Ala
660 665 670

Ser Glu Pro Pro Phe Ile Met Ala Val Lys Glu Asp Gly Leu Trp Ser
675 680 685

Lys Pro Leu Asn Ser Phe Gly Pro Gly Glu Phe Leu Ser Ser Asp Ile
690 695 700

Gly Asn Val Ser Asp Met Asp Trp Tyr Asn Asn Ser Leu Tyr Tyr Ser
705 710 715 720

Asp Thr Lys Gly Asp Val Phe Val Trp Leu Leu Asn Gly Thr Asp Ile
725 730 735

Ser Glu Asn Tyr His Leu Pro Ser Ile Ala Gly Ala Gly Ala Leu Ala

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            740                 745                 750

Phe Glu Trp Leu Gly His Phe Leu Tyr Trp Ala Gly Lys Thr Tyr Val
        755                 760                 765

Ile Gln Arg Gln Ser Val Leu Thr Gly His Thr Asp Ile Val Thr His
    770                 775                 780

Val Lys Leu Leu Val Asn Asp Met Val Val Asp Ser Val Gly Gly Tyr
785                 790                 795                 800

Leu Tyr Trp Thr Thr Leu Tyr Ser Val Glu Ser Thr Arg Leu Asn Gly
                805                 810                 815

Glu Ser Ser Leu Val Leu Gln Thr Gln Pro Trp Phe Ser Gly Lys Lys
            820                 825                 830

Val Ile Ala Leu Thr Leu Asp Leu Ser Asp Gly Leu Leu Tyr Trp Leu
        835                 840                 845

Val Gln Asp Ser Gln Cys Ile His Leu Tyr Thr Ala Val Leu Arg Gly
    850                 855                 860

Gln Ser Thr Gly Asp Thr Thr Ile Thr Glu Phe Ala Ala Trp Ser Thr
865                 870                 875                 880

Ser Glu Ile Ser Gln Asn Ala Leu Met Tyr Tyr Ser Gly Arg Leu Phe
                885                 890                 895

Trp Ile Asn Gly Phe Arg Ile Ile Thr Thr Gln Glu Ile Gly Gln Lys
            900                 905                 910

Thr Ser Val Ser Val Leu Glu Pro Ala Arg Phe Asn Gln Phe Thr Ile
        915                 920                 925

Ile Gln Thr Ser Leu Lys Pro Leu Pro Gly Asn Phe Ser Phe Thr Pro
    930                 935                 940

Lys Val Ile Pro Asp Ser Val Gln Glu Ser Ser Phe Arg Ile Glu Gly
945                 950                 955                 960

Asn Ala Ser Ser Phe Gln Ile Leu Trp Asn Gly Pro Pro Ala Val Asp
                965                 970                 975

Trp Gly Val Val Phe Tyr Ser Val Glu Phe Ser Ala His Ser Lys Phe
            980                 985                 990

Leu Ala Ser Glu Gln His Ser Leu  Pro Val Phe Thr Val  Glu Gly Leu
        995                 1000                1005

Glu Pro  Tyr Ala Leu Phe Asn  Leu Ser Val Thr Pro  Tyr Thr Tyr
```

1010 1015 1020

Trp Gly Lys Gly Pro Lys Thr Ser Leu Ser Leu Arg Ala Pro Glu
1025 1030 1035

Thr Val Pro Ser Ala Pro Glu Asn Pro Arg Ile Phe Ile Leu Pro
1040 1045 1050

Ser Gly Lys Cys Cys Asn Lys Asn Glu Val Val Val Glu Phe Arg
1055 1060 1065

Trp Asn Lys Pro Lys His Glu Asn Gly Val Leu Thr Lys Phe Glu
1070 1075 1080

Ile Phe Tyr Asn Ile Ser Asn Gln Ser Ile Thr Asn Lys Thr Cys
1085 1090 1095

Glu Asp Trp Ile Ala Val Asn Val Thr Pro Ser Val Met Ser Phe
1100 1105 1110

Gln Leu Glu Gly Met Ser Pro Arg Cys Phe Ile Ala Phe Gln Val
1115 1120 1125

Arg Ala Phe Thr Ser Lys Gly Pro Gly Pro Tyr Ala Asp Val Val
1130 1135 1140

Lys Ser Thr Thr Ser Glu Ile Asn Pro Phe Pro His Leu Ile Thr
1145 1150 1155

Leu Leu Gly Asn Lys Ile Val Phe Leu Asp Met Asp Gln Asn Gln
1160 1165 1170

Val Val Trp Thr Phe Ser Ala Glu Arg Val Ile Ser Ala Val Cys
1175 1180 1185

Tyr Thr Ala Asp Asn Glu Met Gly Tyr Tyr Ala Glu Gly Asp Ser
1190 1195 1200

Leu Phe Leu Leu His Leu His Asn Arg Ser Ser Ser Glu Leu Phe
1205 1210 1215

Gln Asp Ser Leu Val Phe Asp Ile Thr Val Ile Thr Ile Asp Trp
1220 1225 1230

Ile Ser Arg His Leu Tyr Phe Ala Leu Lys Glu Ser Gln Asn Gly
1235 1240 1245

Met Gln Val Phe Asp Val Asp Leu Glu His Lys Val Lys Tyr Pro
1250 1255 1260

Arg Glu Val Lys Ile His Asn Arg Asn Ser Thr Ile Ile Ser Phe

1265 1270 1275

Ser Val Tyr Pro Leu Leu Ser Arg Leu Tyr Trp Thr Glu Val Ser
1280 1285 1290

Asn Phe Gly Tyr Gln Met Phe Tyr Tyr Ser Ile Ile Ser His Thr
1295 1300 1305

Leu His Arg Ile Leu Gln Pro Thr Ala Thr Asn Gln Gln Asn Lys
1310 1315 1320

Arg Asn Gln Cys Ser Cys Asn Val Thr Glu Phe Glu Leu Ser Gly
1325 1330 1335

Ala Met Ala Ile Asp Thr Ser Asn Leu Glu Lys Pro Leu Ile Tyr
1340 1345 1350

Phe Ala Lys Ala Gln Glu Ile Trp Ala Met Asp Leu Glu Gly Cys
1355 1360 1365

Gln Cys Trp Arg Val Ile Thr Val Pro Ala Met Leu Ala Gly Lys
1370 1375 1380

Thr Leu Val Ser Leu Thr Val Asp Gly Asp Leu Ile Tyr Trp Ile
1385 1390 1395

Ile Thr Ala Lys Asp Ser Thr Gln Ile Tyr Gln Ala Lys Lys Gly
1400 1405 1410

Asn Gly Ala Ile Val Ser Gln Val Lys Ala Leu Arg Ser Arg His
1415 1420 1425

Ile Leu Ala Tyr Ser Ser Val Met Gln Pro Phe Pro Asp Lys Ala
1430 1435 1440

Phe Leu Ser Leu Ala Ser Asp Thr Val Glu Pro Thr Ile Leu Asn
1445 1450 1455

Ala Thr Asn Thr Ser Leu Thr Ile Arg Leu Pro Leu Ala Lys Thr
1460 1465 1470

Asn Leu Thr Trp Tyr Gly Ile Thr Ser Pro Thr Pro Thr Tyr Leu
1475 1480 1485

Val Tyr Tyr Ala Glu Val Asn Asp Arg Lys Asn Ser Ser Asp Leu
1490 1495 1500

Lys Tyr Arg Ile Leu Glu Phe Gln Asp Ser Ile Ala Leu Ile Glu
1505 1510 1515

Asp Leu Gln Pro Phe Ser Thr Tyr Met Ile Gln Ile Ala Val Lys

1520 1525 1530

Asn Tyr Tyr Ser Asp Pro Leu Glu His Leu Pro Pro Gly Lys Glu
1535 1540 1545

Ile Trp Gly Lys Thr Lys Asn Gly Val Pro Glu Ala Val Gln Leu
1550 1555 1560

Ile Asn Thr Thr Val Arg Ser Asp Thr Ser Leu Ile Ile Ser Trp
1565 1570 1575

Arg Glu Ser His Lys Pro Asn Gly Pro Lys Glu Ser Val Arg Tyr
1580 1585 1590

Gln Leu Ala Ile Ser His Leu Ala Leu Ile Pro Glu Thr Pro Leu
1595 1600 1605

Arg Gln Ser Glu Phe Pro Asn Gly Arg Leu Thr Leu Leu Val Thr
1610 1615 1620

Arg Leu Ser Gly Gly Asn Ile Tyr Val Leu Lys Val Leu Ala Cys
1625 1630 1635

His Ser Glu Glu Met Trp Cys Thr Glu Ser His Pro Val Thr Val
1640 1645 1650

Glu Met Phe Asn Thr Pro Glu Lys Pro Tyr Ser Leu Val Pro Glu
1655 1660 1665

Asn Thr Ser Leu Gln Phe Asn Trp Lys Ala Pro Leu Asn Val Asn
1670 1675 1680

Leu Ile Arg Phe Trp Val Glu Leu Gln Lys Trp Lys Tyr Asn Glu
1685 1690 1695

Phe Tyr His Val Lys Thr Ser Cys Ser Gln Gly Pro Ala Tyr Val
1700 1705 1710

Cys Asn Ile Thr Asn Leu Gln Pro Tyr Thr Ser Tyr Asn Val Arg
1715 1720 1725

Val Val Val Val Tyr Lys Thr Gly Glu Asn Ser Thr Ser Leu Pro
1730 1735 1740

Glu Ser Phe Lys Thr Lys Ala Gly Val Pro Asn Lys Pro Gly Ile
1745 1750 1755

Pro Lys Leu Leu Glu Gly Ser Lys Asn Ser Ile Gln Trp Glu Lys
1760 1765 1770

Ala Glu Asp Asn Gly Cys Arg Ile Thr Tyr Tyr Ile Leu Glu Ile

1775 1780 1785

Arg Lys Ser Thr Ser Asn Asn Leu Gln Asn Gln Asn Leu Arg Trp
1790 1795 1800

Lys Met Thr Phe Asn Gly Ser Cys Ser Ser Val Cys Thr Trp Lys
1805 1810 1815

Ser Lys Asn Leu Lys Gly Ile Phe Gln Phe Arg Val Val Ala Ala
1820 1825 1830

Asn Asn Leu Gly Phe Gly Glu Tyr Ser Gly Ile Ser Glu Asn Ile
1835 1840 1845

Ile Leu Val Gly Asp Asp Phe Trp Ile Pro Glu Thr Ser Phe Ile
1850 1855 1860

Leu Thr Ile Ile Val Gly Ile Phe Leu Val Val Thr Ile Pro Leu
1865 1870 1875

Thr Phe Val Trp His Arg Arg Leu Lys Asn Gln Lys Ser Ala Lys
1880 1885 1890

Glu Gly Val Thr Val Leu Ile Asn Glu Asp Lys Glu Leu Ala Glu
1895 1900 1905

Leu Arg Gly Leu Ala Ala Gly Val Gly Leu Ala Asn Ala Cys Tyr
1910 1915 1920

Ala Ile His Thr Leu Pro Thr Gln Glu Glu Ile Glu Asn Leu Pro
1925 1930 1935

Ala Phe Pro Arg Glu Lys Leu Thr Leu Arg Leu Leu Leu Gly Ser
1940 1945 1950

Gly Ala Phe Gly Glu Val Tyr Glu Gly Thr Ala Val Asp Ile Leu
1955 1960 1965

Gly Val Gly Ser Gly Glu Ile Lys Val Ala Val Lys Thr Leu Lys
1970 1975 1980

Lys Gly Ser Thr Asp Gln Glu Lys Ile Glu Phe Leu Lys Glu Ala
1985 1990 1995

His Leu Met Ser Lys Phe Asn His Pro Asn Ile Leu Lys Gln Leu
2000 2005 2010

Gly Val Cys Leu Leu Asn Glu Pro Gln Tyr Ile Ile Leu Glu Leu
2015 2020 2025

Met Glu Gly Gly Asp Leu Leu Thr Tyr Leu Arg Lys Ala Arg Met

2030 2035 2040

Ala Thr Phe Tyr Gly Pro Leu Leu Thr Leu Val Asp Leu Val Asp
2045 2050 2055

Leu Cys Val Asp Ile Ser Lys Gly Cys Val Tyr Leu Glu Arg Met
2060 2065 2070

His Phe Ile His Arg Asp Leu Ala Ala Arg Asn Cys Leu Val Ser
2075 2080 2085

Val Lys Asp Tyr Thr Ser Pro Arg Ile Val Lys Ile Gly Asp Phe
2090 2095 2100

Gly Leu Ala Arg Asp Ile Tyr Lys Asn Asp Tyr Tyr Arg Lys Arg
2105 2110 2115

Gly Glu Gly Leu Leu Pro Val Arg Trp Met Ala Pro Glu Ser Leu
2120 2125 2130

Met Asp Gly Ile Phe Thr Thr Gln Ser Asp Val Trp Ser Phe Gly
2135 2140 2145

Ile Leu Ile Trp Glu Ile Leu Thr Leu Gly His Gln Pro Tyr Pro
2150 2155 2160

Ala His Ser Asn Leu Asp Val Leu Asn Tyr Val Gln Thr Gly Gly
2165 2170 2175

Arg Leu Glu Pro Pro Arg Asn Cys Pro Asp Asp Leu Trp Asn Leu
2180 2185 2190

Met Thr Gln Cys Trp Ala Gln Glu Pro Asp Gln Arg Pro Thr Phe
2195 2200 2205

His Arg Ile Gln Asp Gln Leu Gln Leu Phe Arg Asn Phe Phe Leu
2210 2215 2220

Asn Ser Ile Tyr Lys Ser Arg Asp Glu Ala Asn Asn Ser Gly Val
2225 2230 2235

Ile Asn Glu Ser Phe Glu Gly Glu Asp Gly Asp Val Ile Cys Leu
2240 2245 2250

Asn Ser Asp Asp Ile Met Pro Val Ala Leu Met Glu Thr Lys Asn
2255 2260 2265

Arg Glu Gly Leu Asn Tyr Met Val Leu Ala Thr Glu Cys Gly Gln
2270 2275 2280

Gly Glu Glu Lys Ser Glu Gly Pro Leu Gly Ser Gln Glu Ser Glu

2285 2290 2295

Ser Cys Gly Leu Arg Lys Glu Glu Lys Glu Pro His Ala Asp Lys
2300 2305 2310

Asp Phe Cys Gln Glu Lys Gln Val Ala Tyr Cys Pro Ser Gly Lys
2315 2320 2325

Pro Glu Gly Leu Asn Tyr Ala Cys Leu Thr His Ser Gly Tyr Gly
2330 2335 2340

Asp Gly Ser Asp
2345

<210> 464
<211> 607
<212> PRT
<213> Homo sapiens

<400> 464

Met Arg Gly Ala Ala Arg Leu Gly Arg Pro Gly Arg Ser Cys Leu Pro
1 5 10 15

Gly Ala Arg Gly Leu Arg Ala Pro Pro Pro Pro Pro Leu Leu Leu Leu
20 25 30

Leu Ala Leu Leu Pro Leu Leu Pro Ala Pro Gly Ala Ala Ala Ala Pro
35 40 45

Ala Pro Arg Pro Pro Glu Leu Gln Ser Ala Ser Ala Gly Pro Ser Val
50 55 60

Ser Leu Tyr Leu Ser Glu Asp Glu Val Arg Arg Leu Ile Gly Leu Asp
65 70 75 80

Ala Glu Leu Tyr Tyr Val Arg Asn Asp Leu Ile Ser His Tyr Ala Leu
85 90 95

Ser Phe Ser Leu Leu Val Pro Ser Glu Thr Asn Phe Leu His Phe Thr
100 105 110

Trp His Ala Lys Ser Lys Val Glu Tyr Lys Leu Gly Phe Gln Val Asp
115 120 125

Asn Val Leu Ala Met Asp Met Pro Gln Val Asn Ile Ser Val Gln Gly
130 135 140

Glu Val Pro Arg Thr Leu Ser Val Phe Arg Val Glu Leu Ser Cys Thr
145 150 155 160

Gly Lys Val Asp Ser Glu Val Met Ile Leu Met Gln Leu Asn Leu Thr
165 170 175

```
Val Asn Ser Ser Lys Asn Phe Thr Val Leu Asn Phe Lys Arg Arg Lys
            180                 185                 190

Met Cys Tyr Lys Lys Leu Glu Glu Val Lys Thr Ser Ala Leu Asp Lys
        195                 200                 205

Asn Thr Ser Arg Thr Ile Tyr Asp Pro Val His Ala Ala Pro Thr Thr
    210                 215                 220

Ser Thr Arg Val Phe Tyr Ile Ser Val Gly Val Cys Cys Ala Val Ile
225                 230                 235                 240

Phe Leu Val Ala Ile Ile Leu Ala Val Leu His Leu His Ser Met Lys
                245                 250                 255

Arg Ile Glu Leu Asp Asp Ser Ile Ser Ala Ser Ser Ser Ser Gln Gly
            260                 265                 270

Leu Ser Gln Pro Ser Thr Gln Thr Thr Gln Tyr Leu Arg Ala Asp Thr
        275                 280                 285

Pro Asn Asn Ala Thr Pro Ile Thr Ser Tyr Pro Thr Leu Arg Ile Glu
    290                 295                 300

Lys Asn Asp Leu Arg Ser Val Thr Leu Leu Glu Ala Lys Gly Lys Val
305                 310                 315                 320

Lys Asp Ile Ala Ile Ser Arg Glu Arg Ile Thr Leu Lys Asp Val Leu
                325                 330                 335

Gln Glu Gly Thr Phe Gly Arg Ile Phe His Gly Ile Leu Ile Asp Glu
            340                 345                 350

Lys Asp Pro Asn Lys Glu Lys Gln Ala Phe Val Lys Thr Val Lys Asp
        355                 360                 365

Gln Ala Ser Glu Ile Gln Val Thr Met Met Leu Thr Glu Ser Cys Lys
    370                 375                 380

Leu Arg Gly Leu His His Arg Asn Leu Leu Pro Ile Thr His Val Cys
385                 390                 395                 400

Ile Glu Glu Gly Glu Lys Pro Met Val Ile Leu Pro Tyr Met Asn Trp
                405                 410                 415

Gly Asn Leu Lys Leu Phe Leu Arg Gln Cys Lys Leu Val Glu Ala Asn
            420                 425                 430

Asn Pro Gln Ala Ile Ser Gln Gln Asp Leu Val His Met Ala Ile Gln
        435                 440                 445
```

```
Ile Ala Cys Gly Met Ser Tyr Leu Ala Arg Arg Glu Val Ile His Lys
    450                 455                 460

Asp Leu Ala Ala Arg Asn Cys Val Ile Asp Asp Thr Leu Gln Val Lys
465                 470                 475                 480

Ile Thr Asp Asn Ala Leu Ser Arg Asp Leu Phe Pro Met Asp Tyr His
                485                 490                 495

Cys Leu Gly Asp Asn Glu Asn Arg Pro Val Arg Trp Met Ala Leu Glu
            500                 505                 510

Ser Leu Val Asn Asn Glu Phe Ser Ser Ala Ser Asp Val Trp Ala Phe
        515                 520                 525

Gly Val Thr Leu Trp Glu Leu Met Thr Leu Gly Gln Thr Pro Tyr Val
    530                 535                 540

Asp Ile Asp Pro Phe Glu Met Ala Ala Tyr Leu Lys Asp Gly Tyr Arg
545                 550                 555                 560

Ile Ala Gln Pro Ile Asn Cys Pro Asp Glu Leu Phe Ala Val Met Ala
                565                 570                 575

Cys Cys Trp Ala Leu Asp Pro Glu Glu Arg Pro Lys Phe Gln Gln Leu
            580                 585                 590

Val Gln Cys Leu Thr Glu Phe His Ala Ala Leu Gly Ala Tyr Val
        595                 600                 605


<210>  465
<211>  1124
<212>  PRT
<213>  Homo sapiens

<400>  465

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

Ser Gly Thr Val Glu Gly Ala Met Asp Leu Ile Leu Ile Asn Ser Leu
            20                  25                  30

Pro Leu Val Ser Asp Ala Glu Thr Ser Leu Thr Cys Ile Ala Ser Gly
        35                  40                  45

Trp Arg Pro His Glu Pro Ile Thr Ile Gly Arg Asp Phe Glu Ala Leu
    50                  55                  60

Met Asn Gln His Gln Asp Pro Leu Glu Val Thr Gln Asp Val Thr Arg
65                  70                  75                  80
```

```
Glu Trp Ala Lys Lys Val Val Trp Lys Arg Glu Lys Ala Ser Lys Ile
                85                  90                  95

Asn Gly Ala Tyr Phe Cys Glu Gly Arg Val Arg Gly Glu Ala Ile Arg
            100                 105                 110

Ile Arg Thr Met Lys Met Arg Gln Gln Ala Ser Phe Leu Pro Ala Thr
        115                 120                 125

Leu Thr Met Thr Val Asp Lys Gly Asp Asn Val Asn Ile Ser Phe Lys
    130                 135                 140

Lys Val Leu Ile Lys Glu Glu Asp Ala Val Ile Tyr Lys Asn Gly Ser
145                 150                 155                 160

Phe Ile His Ser Val Pro Arg His Glu Val Pro Asp Ile Leu Glu Val
                165                 170                 175

His Leu Pro His Ala Gln Pro Gln Asp Ala Gly Val Tyr Ser Ala Arg
            180                 185                 190

Tyr Ile Gly Gly Asn Leu Phe Thr Ser Ala Phe Thr Arg Leu Ile Val
        195                 200                 205

Arg Arg Cys Glu Ala Gln Lys Trp Gly Pro Glu Cys Asn His Leu Cys
    210                 215                 220

Thr Ala Cys Met Asn Asn Gly Val Cys His Glu Asp Thr Gly Glu Cys
225                 230                 235                 240

Ile Cys Pro Pro Gly Phe Met Gly Arg Thr Cys Glu Lys Ala Cys Glu
                245                 250                 255

Leu His Thr Phe Gly Arg Thr Cys Lys Glu Arg Cys Ser Gly Gln Glu
            260                 265                 270

Gly Cys Lys Ser Tyr Val Phe Cys Leu Pro Asp Pro Tyr Gly Cys Ser
        275                 280                 285

Cys Ala Thr Gly Trp Lys Gly Leu Gln Cys Asn Glu Ala Cys His Pro
    290                 295                 300

Gly Phe Tyr Gly Pro Asp Cys Lys Leu Arg Cys Ser Cys Asn Asn Gly
305                 310                 315                 320

Glu Met Cys Asp Arg Phe Gln Gly Cys Leu Cys Ser Pro Gly Trp Gln
                325                 330                 335

Gly Leu Gln Cys Glu Arg Glu Gly Ile Pro Arg Met Thr Pro Lys Ile
            340                 345                 350
```

```
Val Asp Leu Pro Asp His Ile Glu Val Asn Ser Gly Lys Phe Asn Pro
        355                 360                 365

Ile Cys Lys Ala Ser Gly Trp Pro Leu Pro Thr Asn Glu Glu Met Thr
    370                 375                 380

Leu Val Lys Pro Asp Gly Thr Val Leu His Pro Lys Asp Phe Asn His
385                 390                 395                 400

Thr Asp His Phe Ser Val Ala Ile Phe Thr Ile His Arg Ile Leu Pro
                405                 410                 415

Pro Asp Ser Gly Val Trp Val Cys Ser Val Asn Thr Val Ala Gly Met
            420                 425                 430

Val Glu Lys Pro Phe Asn Ile Ser Val Lys Val Leu Pro Lys Pro Leu
        435                 440                 445

Asn Ala Pro Asn Val Ile Asp Thr Gly His Asn Phe Ala Val Ile Asn
    450                 455                 460

Ile Ser Ser Glu Pro Tyr Phe Gly Asp Gly Pro Ile Lys Ser Lys Lys
465                 470                 475                 480

Leu Leu Tyr Lys Pro Val Asn His Tyr Glu Ala Trp Gln His Ile Gln
                485                 490                 495

Val Thr Asn Glu Ile Val Thr Leu Asn Tyr Leu Glu Pro Arg Thr Glu
            500                 505                 510

Tyr Glu Leu Cys Val Gln Leu Val Arg Arg Gly Glu Gly Gly Glu Gly
        515                 520                 525

His Pro Gly Pro Val Arg Arg Phe Thr Thr Ala Ser Ile Gly Leu Pro
    530                 535                 540

Pro Pro Arg Gly Leu Asn Leu Leu Pro Lys Ser Gln Thr Thr Leu Asn
545                 550                 555                 560

Leu Thr Trp Gln Pro Ile Phe Pro Ser Ser Glu Asp Asp Phe Tyr Val
                565                 570                 575

Glu Val Glu Arg Arg Ser Val Gln Lys Ser Asp Gln Gln Asn Ile Lys
            580                 585                 590

Val Pro Gly Asn Leu Thr Ser Val Leu Leu Asn Asn Leu His Pro Arg
        595                 600                 605

Glu Gln Tyr Val Val Arg Ala Arg Val Asn Thr Lys Ala Gln Gly Glu
    610                 615                 620
```

```
Trp Ser Glu Asp Leu Thr Ala Trp Thr Leu Ser Asp Ile Leu Pro Pro
625                 630                 635                 640

Gln Pro Glu Asn Ile Lys Ile Ser Asn Ile Thr His Ser Ser Ala Val
                645                 650                 655

Ile Ser Trp Thr Ile Leu Asp Gly Tyr Ser Ile Ser Ser Ile Thr Ile
            660                 665                 670

Arg Tyr Lys Val Gln Gly Lys Asn Glu Asp Gln His Val Asp Val Lys
        675                 680                 685

Ile Lys Asn Ala Thr Ile Thr Gln Tyr Gln Leu Lys Gly Leu Glu Pro
    690                 695                 700

Glu Thr Ala Tyr Gln Val Asp Ile Phe Ala Glu Asn Asn Ile Gly Ser
705                 710                 715                 720

Ser Asn Pro Ala Phe Ser His Glu Leu Val Thr Leu Pro Glu Ser Gln
                725                 730                 735

Ala Pro Ala Asp Leu Gly Gly Gly Lys Met Leu Leu Ile Ala Ile Leu
            740                 745                 750

Gly Ser Ala Gly Met Thr Cys Leu Thr Val Leu Leu Ala Phe Leu Ile
        755                 760                 765

Ile Leu Gln Leu Lys Arg Ala Asn Val Gln Arg Arg Met Ala Gln Ala
    770                 775                 780

Phe Gln Asn Val Arg Glu Glu Pro Ala Val Gln Phe Asn Ser Gly Thr
785                 790                 795                 800

Leu Ala Leu Asn Arg Lys Val Lys Asn Asn Pro Asp Pro Thr Ile Tyr
                805                 810                 815

Pro Val Leu Asp Trp Asn Asp Ile Lys Phe Gln Asp Val Ile Gly Glu
            820                 825                 830

Gly Asn Phe Gly Gln Val Leu Lys Ala Arg Ile Lys Lys Asp Gly Leu
        835                 840                 845

Arg Met Asp Ala Ala Ile Lys Arg Met Lys Glu Tyr Ala Ser Lys Asp
    850                 855                 860

Asp His Arg Asp Phe Ala Gly Glu Leu Glu Val Leu Cys Lys Leu Gly
865                 870                 875                 880

His His Pro Asn Ile Ile Asn Leu Leu Gly Ala Cys Glu His Arg Gly
                885                 890                 895
```

```
Tyr Leu Tyr Leu Ala Ile Glu Tyr Ala Pro His Gly Asn Leu Leu Asp
            900                 905                 910

Phe Leu Arg Lys Ser Arg Val Leu Glu Thr Asp Pro Ala Phe Ala Ile
        915                 920                 925

Ala Asn Ser Thr Ala Ser Thr Leu Ser Ser Gln Gln Leu Leu His Phe
    930                 935                 940

Ala Ala Asp Val Ala Arg Gly Met Asp Tyr Leu Ser Gln Lys Gln Phe
945                 950                 955                 960

Ile His Arg Asp Leu Ala Ala Arg Asn Ile Leu Val Gly Glu Asn Tyr
                965                 970                 975

Val Ala Lys Ile Ala Asp Phe Gly Leu Ser Arg Gly Gln Glu Val Tyr
            980                 985                 990

Val Lys Lys Thr Met Gly Arg Leu  Pro Val Arg Trp Met  Ala Ile Glu
        995                 1000                1005

Ser Leu  Asn Tyr Ser Val Tyr  Thr Thr Asn Ser Asp  Val Trp Ser
    1010                1015                1020

Tyr Gly  Val Leu Leu Trp Glu  Ile Val Ser Leu Gly  Gly Thr Pro
    1025                1030                1035

Tyr Cys  Gly Met Thr Cys Ala  Glu Leu Tyr Glu Lys  Leu Pro Gln
    1040                1045                1050

Gly Tyr  Arg Leu Glu Lys Pro  Leu Asn Cys Asp Asp  Glu Val Tyr
    1055                1060                1065

Asp Leu  Met Arg Gln Cys Trp  Arg Glu Lys Pro Tyr  Glu Arg Pro
    1070                1075                1080

Ser Phe  Ala Gln Ile Leu Val  Ser Leu Asn Arg Met  Leu Glu Glu
    1085                1090                1095

Arg Lys  Thr Tyr Val Asn Thr  Thr Leu Tyr Glu Lys  Phe Thr Tyr
    1100                1105                1110

Ala Gly  Ile Asp Cys Ser Ala  Glu Glu Ala Ala
    1115                1120
```

<210> 466
<211> 1138
<212> PRT
<213> Homo sapiens

<400> 466

```
Met Val Trp Arg Val Pro Pro Phe Leu Leu Pro Ile Leu Phe Leu Ala
1               5                  10                  15

Ser His Val Gly Ala Ala Val Asp Leu Thr Leu Leu Ala Asn Leu Arg
            20                  25                  30

Leu Thr Asp Pro Gln Arg Phe Phe Leu Thr Cys Val Ser Gly Glu Ala
        35                  40                  45

Gly Ala Gly Arg Gly Ser Asp Ala Trp Gly Pro Pro Leu Leu Leu Glu
    50                  55                  60

Lys Asp Asp Arg Ile Val Arg Thr Pro Pro Gly Pro Pro Leu Arg Leu
65                  70                  75                  80

Ala Arg Asn Gly Ser His Gln Val Thr Leu Arg Gly Phe Ser Lys Pro
                85                  90                  95

Ser Asp Leu Val Gly Val Phe Ser Cys Val Gly Gly Ala Gly Ala Arg
            100                 105                 110

Arg Thr Arg Val Ile Tyr Val His Asn Ser Pro Gly Ala His Leu Leu
        115                 120                 125

Pro Asp Lys Val Thr His Thr Val Asn Lys Gly Asp Thr Ala Val Leu
    130                 135                 140

Ser Ala Arg Val His Lys Glu Lys Gln Thr Asp Val Ile Trp Lys Ser
145                 150                 155                 160

Asn Gly Ser Tyr Phe Tyr Thr Leu Asp Trp His Glu Ala Gln Asp Gly
                165                 170                 175

Arg Phe Leu Leu Gln Leu Pro Asn Val Gln Pro Pro Ser Ser Gly Ile
            180                 185                 190

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

Arg Leu Ile Val Arg Gly Cys Gly Ala Gly Arg Trp Gly Pro Gly Cys
    210                 215                 220

Thr Lys Glu Cys Pro Gly Cys Leu His Gly Gly Val Cys His Asp His
225                 230                 235                 240

Asp Gly Glu Cys Val Cys Pro Pro Gly Phe Thr Gly Thr Arg Cys Glu
                245                 250                 255

Gln Ala Cys Arg Glu Gly Arg Phe Gly Gln Ser Cys Gln Glu Gln Cys
            260                 265                 270
```

```
Pro Gly Ile Ser Gly Cys Arg Gly Leu Thr Phe Cys Leu Pro Asp Pro
        275                 280                 285

Tyr Gly Cys Ser Cys Gly Ser Gly Trp Arg Gly Ser Gln Cys Gln Glu
    290                 295                 300

Ala Cys Ala Pro Gly His Phe Gly Ala Asp Cys Arg Leu Gln Cys Gln
305                 310                 315                 320

Cys Gln Asn Gly Gly Thr Cys Asp Arg Phe Ser Gly Cys Val Cys Pro
                325                 330                 335

Ser Gly Trp His Gly Val His Cys Glu Lys Ser Asp Arg Ile Pro Gln
            340                 345                 350

Ile Leu Asn Met Ala Ser Glu Leu Glu Phe Asn Leu Glu Thr Met Pro
        355                 360                 365

Arg Ile Asn Cys Ala Ala Ala Gly Asn Pro Phe Pro Val Arg Gly Ser
    370                 375                 380

Ile Glu Leu Arg Lys Pro Asp Gly Thr Val Leu Leu Ser Thr Lys Ala
385                 390                 395                 400

Ile Val Glu Pro Glu Lys Thr Thr Ala Glu Phe Glu Val Pro Arg Leu
                405                 410                 415

Val Leu Ala Asp Ser Gly Phe Trp Glu Cys Arg Val Ser Thr Ser Gly
            420                 425                 430

Gly Gln Asp Ser Arg Arg Phe Lys Val Asn Val Lys Val Pro Pro Val
        435                 440                 445

Pro Leu Ala Ala Pro Arg Leu Leu Thr Lys Gln Ser Arg Gln Leu Val
    450                 455                 460

Val Ser Pro Leu Val Ser Phe Ser Gly Asp Gly Pro Ile Ser Thr Val
465                 470                 475                 480

Arg Leu His Tyr Arg Pro Gln Asp Ser Thr Met Asp Trp Ser Thr Ile
                485                 490                 495

Val Val Asp Pro Ser Glu Asn Val Thr Leu Met Asn Leu Arg Pro Lys
            500                 505                 510

Thr Gly Tyr Ser Val Arg Val Gln Leu Ser Arg Pro Gly Glu Gly Gly
        515                 520                 525

Glu Gly Ala Trp Gly Pro Pro Thr Leu Met Thr Thr Asp Cys Pro Glu
    530                 535                 540
```

```
Pro Leu Leu Gln Pro Trp Leu Glu Gly Trp His Val Glu Gly Thr Asp
545                 550                 555                 560

Arg Leu Arg Val Ser Trp Ser Leu Pro Leu Val Pro Gly Pro Leu Val
                565                 570                 575

Gly Asp Gly Phe Leu Leu Arg Leu Trp Asp Gly Thr Arg Gly Gln Glu
            580                 585                 590

Arg Arg Glu Asn Val Ser Ser Pro Gln Ala Arg Thr Ala Leu Leu Thr
        595                 600                 605

Gly Leu Thr Pro Gly Thr His Tyr Gln Leu Asp Val Gln Leu Tyr His
    610                 615                 620

Cys Thr Leu Leu Gly Pro Ala Ser Pro Pro Ala His Val Leu Leu Pro
625                 630                 635                 640

Pro Ser Gly Pro Pro Ala Pro Arg His Leu His Ala Gln Ala Leu Ser
                645                 650                 655

Asp Ser Glu Ile Gln Leu Thr Trp Lys His Pro Glu Ala Leu Pro Gly
            660                 665                 670

Pro Ile Ser Lys Tyr Val Val Glu Val Gln Val Ala Gly Gly Ala Gly
        675                 680                 685

Asp Pro Leu Trp Ile Asp Val Asp Arg Pro Glu Glu Thr Ser Thr Ile
    690                 695                 700

Ile Arg Gly Leu Asn Ala Ser Thr Arg Tyr Leu Phe Arg Met Arg Ala
705                 710                 715                 720

Ser Ile Gln Gly Leu Gly Asp Trp Ser Asn Thr Val Glu Glu Ser Thr
                725                 730                 735

Leu Gly Asn Gly Leu Gln Ala Glu Gly Pro Val Gln Glu Ser Arg Ala
            740                 745                 750

Ala Glu Glu Gly Leu Asp Gln Gln Leu Ile Leu Ala Val Val Gly Ser
        755                 760                 765

Val Ser Ala Thr Cys Leu Thr Ile Leu Ala Ala Leu Leu Thr Leu Val
    770                 775                 780

Cys Ile Arg Arg Ser Cys Leu His Arg Arg Arg Thr Phe Thr Tyr Gln
785                 790                 795                 800

Ser Gly Ser Gly Glu Glu Thr Ile Leu Gln Phe Ser Ser Gly Thr Leu
                805                 810                 815
```

```
Thr Leu Thr Arg Arg Pro Lys Leu Gln Pro Glu Pro Leu Ser Tyr Pro
            820                 825                 830

Val Leu Glu Trp Glu Asp Ile Thr Phe Glu Asp Leu Ile Gly Glu Gly
        835                 840                 845

Asn Phe Gly Gln Val Ile Arg Ala Met Ile Lys Lys Asp Gly Leu Lys
    850                 855                 860

Met Asn Ala Ala Ile Lys Met Leu Lys Glu Tyr Ala Ser Glu Asn Asp
865                 870                 875                 880

His Arg Asp Phe Ala Gly Glu Leu Glu Val Leu Cys Lys Leu Gly His
                885                 890                 895

His Pro Asn Ile Ile Asn Leu Leu Gly Ala Cys Lys Asn Arg Gly Tyr
            900                 905                 910

Leu Tyr Ile Ala Ile Glu Tyr Ala Pro Tyr Gly Asn Leu Leu Asp Phe
        915                 920                 925

Leu Arg Lys Ser Arg Val Leu Glu Thr Asp Pro Ala Phe Ala Arg Glu
    930                 935                 940

His Gly Thr Ala Ser Thr Leu Ser Ser Arg Gln Leu Leu Arg Phe Ala
945                 950                 955                 960

Ser Asp Ala Ala Asn Gly Met Gln Tyr Leu Ser Glu Lys Gln Phe Ile
                965                 970                 975

His Arg Asp Leu Ala Ala Arg Asn Val Leu Val Gly Glu Asn Leu Ala
            980                 985                 990

Ser Lys Ile Ala Asp Phe Gly Leu  Ser Arg Gly Glu Glu  Val Tyr Val
        995                 1000                1005

Lys Lys  Thr Met Gly Arg Leu  Pro Val Arg Trp Met  Ala Ile Glu
    1010                1015                1020

Ser Leu  Asn Tyr Ser Val Tyr  Thr Thr Lys Ser Asp  Val Trp Ser
    1025                1030                1035

Phe Gly  Val Leu Leu Trp Glu  Ile Val Ser Leu Gly  Gly Thr Pro
    1040                1045                1050

Tyr Cys  Gly Met Thr Cys Ala  Glu Leu Tyr Glu Lys  Leu Pro Gln
    1055                1060                1065

Gly Tyr  Arg Met Glu Gln Pro  Arg Asn Cys Asp Asp  Glu Val Tyr
    1070                1075                1080
```

Glu Leu Met Arg Gln Cys Trp Arg Asp Arg Pro Tyr Glu Arg Pro
1085 1090 1095

Pro Phe Ala Gln Ile Ala Leu Gln Leu Gly Arg Met Leu Glu Ala
1100 1105 1110

Arg Lys Ala Tyr Val Asn Met Ser Leu Phe Glu Asn Phe Thr Tyr
1115 1120 1125

Ala Gly Ile Asp Ala Thr Ala Glu Glu Ala
1130 1135

<210> 467
<211> 890
<212> PRT
<213> Homo sapiens

<400> 467

Met Ala Leu Arg Arg Ser Met Gly Arg Pro Gly Leu Pro Pro Leu Pro
1 5 10 15

Leu Pro Pro Pro Pro Arg Leu Gly Leu Leu Leu Ala Ala Leu Ala Ser
20 25 30

Leu Leu Leu Pro Glu Ser Ala Ala Ala Gly Leu Lys Leu Met Gly Ala
35 40 45

Pro Val Lys Leu Thr Val Ser Gln Gly Gln Pro Val Lys Leu Asn Cys
50 55 60

Ser Val Glu Gly Met Glu Glu Pro Asp Ile Gln Trp Val Lys Asp Gly
65 70 75 80

Ala Val Val Gln Asn Leu Asp Gln Leu Tyr Ile Pro Val Ser Glu Gln
85 90 95

His Trp Ile Gly Phe Leu Ser Leu Lys Ser Val Glu Arg Ser Asp Ala
100 105 110

Gly Arg Tyr Trp Cys Gln Val Glu Asp Gly Gly Glu Thr Glu Ile Ser
115 120 125

Gln Pro Val Trp Leu Thr Val Glu Gly Val Pro Phe Phe Thr Val Glu
130 135 140

Pro Lys Asp Leu Ala Val Pro Pro Asn Ala Pro Phe Gln Leu Ser Cys
145 150 155 160

Glu Ala Val Gly Pro Pro Glu Pro Val Thr Ile Val Trp Trp Arg Gly
165 170 175

Thr Thr Lys Ile Gly Gly Pro Ala Pro Ser Pro Ser Val Leu Asn Val

180 185 190

Thr Gly Val Thr Gln Ser Thr Met Phe Ser Cys Glu Ala His Asn Leu
195 200 205

Lys Gly Leu Ala Ser Ser Arg Thr Ala Thr Val His Leu Gln Ala Leu
210 215 220

Pro Ala Ala Pro Phe Asn Ile Thr Val Thr Lys Leu Ser Ser Ser Asn
225 230 235 240

Ala Ser Val Ala Trp Met Pro Gly Ala Asp Gly Arg Ala Leu Leu Gln
245 250 255

Ser Cys Thr Val Gln Val Thr Gln Ala Pro Gly Gly Trp Glu Val Leu
260 265 270

Ala Val Val Val Pro Val Pro Pro Phe Thr Cys Leu Leu Arg Asp Leu
275 280 285

Val Pro Ala Thr Asn Tyr Ser Leu Arg Val Arg Cys Ala Asn Ala Leu
290 295 300

Gly Pro Ser Pro Tyr Ala Asp Trp Val Pro Phe Gln Thr Lys Gly Leu
305 310 315 320

Ala Pro Ala Ser Ala Pro Gln Asn Leu His Ala Ile Arg Thr Asp Ser
325 330 335

Gly Leu Ile Leu Glu Trp Glu Glu Val Ile Pro Glu Ala Pro Leu Glu
340 345 350

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

Gln Asp Glu Leu Thr Val Glu Gly Thr Arg Ala Asn Leu Thr Gly Trp
370 375 380

Asp Pro Gln Lys Asp Leu Ile Val Arg Val Cys Val Ser Asn Ala Val
385 390 395 400

Gly Cys Gly Pro Trp Ser Gln Pro Leu Val Val Ser Ser His Asp Arg
405 410 415

Ala Gly Gln Gln Gly Pro Pro His Ser Arg Thr Ser Trp Val Pro Val
420 425 430

Val Leu Gly Val Leu Thr Ala Leu Val Thr Ala Ala Ala Leu Ala Leu
435 440 445

Ile Leu Leu Arg Lys Arg Arg Lys Glu Thr Arg Phe Gly Gln Ala Phe

450 455 460

Asp Ser Val Met Ala Arg Gly Glu Pro Ala Val His Phe Arg Ala Ala
465 470 475 480

Arg Ser Phe Asn Arg Glu Arg Pro Glu Arg Ile Glu Ala Thr Leu Asp
485 490 495

Ser Leu Gly Ile Ser Asp Glu Leu Lys Glu Lys Leu Glu Asp Val Leu
500 505 510

Ile Pro Glu Gln Gln Phe Thr Leu Gly Arg Met Leu Gly Lys Gly Glu
515 520 525

Phe Gly Ser Val Arg Glu Ala Gln Leu Lys Gln Glu Asp Gly Ser Phe
530 535 540

Val Lys Val Ala Val Lys Met Leu Lys Ala Asp Ile Ile Ala Ser Ser
545 550 555 560

Asp Ile Glu Glu Phe Leu Arg Glu Ala Ala Cys Met Lys Glu Phe Asp
565 570 575

His Pro His Val Ala Lys Leu Val Gly Val Ser Leu Arg Ser Arg Ala
580 585 590

Lys Gly Arg Leu Pro Ile Pro Met Val Ile Leu Pro Phe Met Lys His
595 600 605

Gly Asp Leu His Ala Phe Leu Leu Ala Ser Arg Ile Gly Glu Asn Pro
610 615 620

Phe Asn Leu Pro Leu Gln Thr Leu Ile Arg Phe Met Val Asp Ile Ala
625 630 635 640

Cys Gly Met Glu Tyr Leu Ser Ser Arg Asn Phe Ile His Arg Asp Leu
645 650 655

Ala Ala Arg Asn Cys Met Leu Ala Glu Asp Met Thr Val Cys Val Ala
660 665 670

Asp Phe Gly Leu Ser Arg Lys Ile Tyr Ser Gly Asp Tyr Tyr Arg Gln
675 680 685

Gly Cys Ala Ser Lys Leu Pro Val Lys Trp Leu Ala Leu Glu Ser Leu
690 695 700

Ala Asp Asn Leu Tyr Thr Val Gln Ser Asp Val Trp Ala Phe Gly Val
705 710 715 720

Thr Met Trp Glu Ile Met Thr Arg Gly Gln Thr Pro Tyr Ala Gly Ile

725 730 735

Glu Asn Ala Glu Ile Tyr Asn Tyr Leu Ile Gly Gly Asn Arg Leu Lys
740 745 750

Gln Pro Pro Glu Cys Met Glu Asp Val Tyr Asp Leu Met Tyr Gln Cys
755 760 765

Trp Ser Ala Asp Pro Lys Gln Arg Pro Ser Phe Thr Cys Leu Arg Met
770 775 780

Glu Leu Glu Asn Ile Leu Gly Gln Leu Ser Val Leu Ser Ala Ser Gln
785 790 795 800

Asp Pro Leu Tyr Ile Asn Ile Glu Arg Ala Glu Glu Pro Thr Ala Gly
805 810 815

Gly Ser Leu Glu Leu Pro Gly Arg Asp Gln Pro Tyr Ser Gly Ala Gly
820 825 830

Asp Gly Ser Gly Met Gly Ala Val Gly Gly Thr Pro Ser Asp Cys Arg
835 840 845

Tyr Ile Leu Thr Pro Gly Gly Leu Ala Glu Gln Pro Gly Gln Ala Glu
850 855 860

His Gln Pro Glu Ser Pro Leu Asn Glu Thr Gln Arg Leu Leu Leu Leu
865 870 875 880

Gln Gln Gly Leu Leu Pro His Ser Ser Cys
885 890

<210> 468
<211> 913
<212> PRT
<213> Homo sapiens

<400> 468

Met Gly Pro Glu Ala Leu Ser Ser Leu Leu Leu Leu Leu Leu Val Ala
1 5 10 15

Ser Gly Asp Ala Asp Met Lys Gly His Phe Asp Pro Ala Lys Cys Arg
20 25 30

Tyr Ala Leu Gly Met Gln Asp Arg Thr Ile Pro Asp Ser Asp Ile Ser
35 40 45

Ala Ser Ser Ser Trp Ser Asp Ser Thr Ala Ala Arg His Ser Arg Leu
50 55 60

Glu Ser Ser Asp Gly Asp Gly Ala Trp Cys Pro Ala Gly Ser Val Phe
65 70 75 80

```
Pro Lys Glu Glu Glu Tyr Leu Gln Val Asp Leu Gln Arg Leu His Leu
                85                  90                  95

Val Ala Leu Val Gly Thr Gln Gly Arg His Ala Gly Gly Leu Gly Lys
            100                 105                 110

Glu Phe Ser Arg Ser Tyr Arg Leu Arg Tyr Ser Arg Asp Gly Arg Arg
        115                 120                 125

Trp Met Gly Trp Lys Asp Arg Trp Gly Gln Glu Val Ile Ser Gly Asn
    130                 135                 140

Glu Asp Pro Glu Gly Val Val Leu Lys Asp Leu Gly Pro Pro Met Val
145                 150                 155                 160

Ala Arg Leu Val Arg Phe Tyr Pro Arg Ala Asp Arg Val Met Ser Val
                165                 170                 175

Cys Leu Arg Val Glu Leu Tyr Gly Cys Leu Trp Arg Asp Gly Leu Leu
            180                 185                 190

Ser Tyr Thr Ala Pro Val Gly Gln Thr Met Tyr Leu Ser Glu Ala Val
        195                 200                 205

Tyr Leu Asn Asp Ser Thr Tyr Asp Gly His Thr Val Gly Gly Leu Gln
    210                 215                 220

Tyr Gly Gly Leu Gly Gln Leu Ala Asp Gly Val Val Gly Leu Asp Asp
225                 230                 235                 240

Phe Arg Lys Ser Gln Glu Leu Arg Val Trp Pro Gly Tyr Asp Tyr Val
                245                 250                 255

Gly Trp Ser Asn His Ser Phe Ser Ser Gly Tyr Val Glu Met Glu Phe
            260                 265                 270

Glu Phe Asp Arg Leu Arg Ala Phe Gln Ala Met Gln Val His Cys Asn
        275                 280                 285

Asn Met His Thr Leu Gly Ala Arg Leu Pro Gly Gly Val Glu Cys Arg
    290                 295                 300

Phe Arg Arg Gly Pro Ala Met Ala Trp Glu Gly Glu Pro Met Arg His
305                 310                 315                 320

Asn Leu Gly Gly Asn Leu Gly Asp Pro Arg Ala Arg Ala Val Ser Val
                325                 330                 335

Pro Leu Gly Gly Arg Val Ala Arg Phe Leu Gln Cys Arg Phe Leu Phe
            340                 345                 350
```

```
Ala Gly Pro Trp Leu Leu Phe Ser Glu Ile Ser Phe Ile Ser Asp Val
        355                 360                 365

Val Asn Asn Ser Ser Pro Ala Leu Gly Gly Thr Phe Pro Pro Ala Pro
    370                 375                 380

Trp Trp Pro Pro Gly Pro Pro Pro Thr Asn Phe Ser Ser Leu Glu Leu
385                 390                 395                 400

Glu Pro Arg Gly Gln Gln Pro Val Ala Lys Ala Glu Gly Ser Pro Thr
                405                 410                 415

Ala Ile Leu Ile Gly Cys Leu Val Ala Ile Ile Leu Leu Leu Leu Leu
            420                 425                 430

Ile Ile Ala Leu Met Leu Trp Arg Leu His Trp Arg Arg Leu Leu Ser
        435                 440                 445

Lys Ala Glu Arg Arg Val Leu Glu Glu Glu Leu Thr Val His Leu Ser
    450                 455                 460

Val Pro Gly Asp Thr Ile Leu Ile Asn Asn Arg Pro Gly Pro Arg Glu
465                 470                 475                 480

Pro Pro Pro Tyr Gln Glu Pro Arg Pro Arg Gly Asn Pro Pro His Ser
                485                 490                 495

Ala Pro Cys Val Pro Asn Gly Ser Ala Leu Leu Leu Ser Asn Pro Ala
            500                 505                 510

Tyr Arg Leu Leu Leu Ala Thr Tyr Ala Arg Pro Pro Arg Gly Pro Gly
        515                 520                 525

Pro Pro Thr Pro Ala Trp Ala Lys Pro Thr Asn Thr Gln Ala Tyr Ser
    530                 535                 540

Gly Asp Tyr Met Glu Pro Glu Lys Pro Gly Ala Pro Leu Leu Pro Pro
545                 550                 555                 560

Pro Pro Gln Asn Ser Val Pro His Tyr Ala Glu Ala Asp Ile Val Thr
                565                 570                 575

Leu Gln Gly Val Thr Gly Gly Asn Thr Tyr Ala Val Pro Ala Leu Pro
            580                 585                 590

Pro Gly Ala Val Gly Asp Gly Pro Pro Arg Val Asp Phe Pro Arg Ser
        595                 600                 605

Arg Leu Arg Phe Lys Glu Lys Leu Gly Glu Gly Gln Phe Gly Glu Val
    610                 615                 620
```

```
His Leu Cys Glu Val Asp Ser Pro Gln Asp Leu Val Ser Leu Asp Phe
625                 630                 635                 640

Pro Leu Asn Val Arg Lys Gly His Pro Leu Leu Val Ala Val Lys Ile
                645                 650                 655

Leu Arg Pro Asp Ala Thr Lys Asn Ala Arg Asn Asp Phe Leu Lys Glu
            660                 665                 670

Val Lys Ile Met Ser Arg Leu Lys Asp Pro Asn Ile Ile Arg Leu Leu
        675                 680                 685

Gly Val Cys Val Gln Asp Asp Pro Leu Cys Met Ile Thr Asp Tyr Met
    690                 695                 700

Glu Asn Gly Asp Leu Asn Gln Phe Leu Ser Ala His Gln Leu Glu Asp
705                 710                 715                 720

Lys Ala Ala Glu Gly Ala Pro Gly Asp Gly Gln Ala Ala Gln Gly Pro
                725                 730                 735

Thr Ile Ser Tyr Pro Met Leu Leu His Val Ala Ala Gln Ile Ala Ser
            740                 745                 750

Gly Met Arg Tyr Leu Ala Thr Leu Asn Phe Val His Arg Asp Leu Ala
        755                 760                 765

Thr Arg Asn Cys Leu Val Gly Glu Asn Phe Thr Ile Lys Ile Ala Asp
    770                 775                 780

Phe Gly Met Ser Arg Asn Leu Tyr Ala Gly Asp Tyr Tyr Arg Val Gln
785                 790                 795                 800

Gly Arg Ala Val Leu Pro Ile Arg Trp Met Ala Trp Glu Cys Ile Leu
                805                 810                 815

Met Gly Lys Phe Thr Thr Ala Ser Asp Val Trp Ala Phe Gly Val Thr
            820                 825                 830

Leu Trp Glu Val Leu Met Leu Cys Arg Ala Gln Pro Phe Gly Gln Leu
        835                 840                 845

Thr Asp Glu Gln Val Ile Glu Asn Ala Gly Glu Phe Phe Arg Asp Gln
    850                 855                 860

Gly Arg Gln Val Tyr Leu Ser Arg Pro Pro Ala Cys Pro Gln Gly Leu
865                 870                 875                 880

Tyr Glu Leu Met Leu Arg Cys Trp Ser Arg Glu Ser Glu Gln Arg Pro
                885                 890                 895
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Pro Phe Ser Gln Leu His Arg Phe Leu Ala Glu Asp Ala Leu Asn Thr
            900                 905                 910

Val
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<213> Homo sapiens

<400> 469

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Met Ser Ser Ser Phe Phe Asn Pro Ser Phe Ala Phe Ser Ser His Phe
1               5                  10                  15

Asp Pro Asp Gly Ala Pro Leu Ser Glu Leu Ser Trp Pro Ser Ser Leu
            20                  25                  30

Ala Val Val Ala Val Ser Phe Ser Gly Leu Phe Ala Val Ile Val Leu
        35                  40                  45

Met Leu Ala Cys Leu Cys Cys Lys Lys Gly Gly Ile Gly Phe Lys Glu
    50                  55                  60

Phe Glu Asn Ala Glu Gly Asp Glu Tyr Ala Ala Asp Leu Ala Gln Gly
65                  70                  75                  80

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

Leu Thr Glu Val Ser Leu Pro Met Ala Lys Gln Pro Gly Arg Ser Val
            100                 105                 110

Gln Leu Leu Lys Ser Thr Asp Val Gly Arg His Ser Leu Leu Tyr Leu
        115                 120                 125

Lys Glu Ile Gly Arg Gly Trp Phe Gly Lys Val Phe Leu Gly Glu Val
    130                 135                 140

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

Ser Ala Ser Val Gln Glu Gln Met Gln Phe Leu Glu Glu Val Gln Pro
                165                 170                 175

Tyr Arg Ala Leu Lys His Ser Asn Leu Leu Gln Cys Leu Ala Gln Cys
            180                 185                 190

Ala Glu Val Thr Pro Tyr Leu Leu Val Met Glu Phe Cys Pro Leu Gly
        195                 200                 205
```

```
Asp Leu Lys Gly Tyr Leu Arg Ser Cys Arg Val Ala Glu Ser Met Ala
    210                 215                 220

Pro Asp Pro Arg Thr Leu Gln Arg Met Ala Cys Glu Val Ala Cys Gly
225                 230                 235                 240

Val Leu His Leu His Arg Asn Asn Phe Val His Ser Asp Leu Ala Leu
                245                 250                 255

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

Gly Leu Ala His Cys Lys Tyr Arg Glu Asp Tyr Phe Val Thr Ala Asp
        275                 280                 285

Gln Leu Trp Val Pro Leu Arg Trp Ile Ala Pro Glu Leu Val Asp Glu
    290                 295                 300

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

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

Pro Tyr Pro Gln His Ser Asp Gln Gln Val Leu Ala Tyr Thr Val Arg
            340                 345                 350

Glu Gln Gln Leu Lys Leu Pro Lys Pro Gln Leu Gln Leu Thr Leu Ser
        355                 360                 365

Asp Arg Trp Tyr Glu Val Met Gln Phe Cys Trp Leu Gln Pro Glu Gln
    370                 375                 380

Arg Pro Thr Ala Glu Glu Val His Leu Leu Leu Ser Tyr Leu Cys Ala
385                 390                 395                 400

Lys Gly Ala Thr Glu Ala Glu Glu Glu Phe Glu Arg Arg Trp Arg Ser
                405                 410                 415

Leu Arg Pro Gly Gly Gly Gly Val Gly Pro Gly Pro Gly Ala Ala Gly
            420                 425                 430

Pro Met Leu Gly Gly Val Val Glu Leu Ala Ala Ala Ser Ser Phe Pro
        435                 440                 445

Leu Leu Glu Gln Phe Ala Gly Asp Gly Phe His Ala Asp Gly Asp Asp
    450                 455                 460

Val Leu Thr Val Thr Glu Thr Ser Arg Gly Leu Asn Phe Glu Tyr Lys
465                 470                 475                 480
```

```
Trp Glu Ala Gly Arg Gly Ala Glu Ala Phe Pro Ala Thr Leu Ser Pro
                485                 490                 495

Gly Arg Thr Ala Arg Leu Gln Glu Leu Cys Ala Pro Asp Gly Ala Pro
            500                 505                 510

Pro Gly Val Val Pro Val Leu Ser Ala His Ser Pro Ser Leu Gly Ser
        515                 520                 525

Glu Tyr Phe Ile Arg Leu Glu Glu Ala Ala Pro Ala Ala Gly His Asp
    530                 535                 540

Pro Asp Cys Ala Gly Cys Ala Pro Ser Pro Pro Ala Thr Ala Asp Gln
545                 550                 555                 560

Asp Asp Asp Ser Asp Gly Ser Thr Ala Ala Ser Leu Ala Met Glu Pro
                565                 570                 575

Leu Leu Gly His Gly Pro Pro Val Asp Val Pro Trp Gly Arg Gly Asp
            580                 585                 590

His Tyr Pro Arg Arg Ser Leu Ala Arg Asp Pro Leu Cys Pro Ser Arg
        595                 600                 605

Ser Pro Ser Pro Ser Ala Gly Pro Leu Ser Leu Ala Glu Gly Gly Ala
    610                 615                 620

Glu Asp Ala Asp Trp Gly Val Ala Ala Phe Cys Pro Ala Phe Phe Glu
625                 630                 635                 640

Asp Pro Leu Gly Thr Ser Pro Leu Gly Ser Ser Gly Ala Pro Pro Leu
                645                 650                 655

Pro Leu Thr Gly Glu Asp Glu Leu Glu Glu Val Gly Ala Arg Arg Ala
            660                 665                 670

Ala Gln Arg Gly His Trp Arg Ser Asn Val Ser Ala Asn Asn Asn Ser
        675                 680                 685

Gly Ser Arg Cys Pro Glu Ser Trp Asp Pro Val Ser Ala Gly Gly His
    690                 695                 700

Ala Glu Gly Cys Pro Ser Pro Lys Gln Thr Pro Arg Ala Ser Pro Glu
705                 710                 715                 720

Pro Gly Tyr Pro Gly Glu Pro Leu Leu Gly Leu Gln Ala Ala Ser Ala
                725                 730                 735

Gln Glu Pro Gly Cys Cys Pro Gly Leu Pro His Leu Cys Ser Ala Gln
            740                 745                 750
```

```
Gly Leu Ala Pro Ala Pro Cys Leu Val Thr Pro Ser Trp Thr Glu Thr
        755                 760                 765

Ala Ser Ser Gly Gly Asp His Pro Gln Ala Glu Pro Lys Leu Ala Thr
    770                 775                 780

Glu Ala Glu Gly Thr Thr Gly Pro Arg Leu Pro Leu Pro Ser Val Pro
785                 790                 795                 800

Ser Pro Ser Gln Glu Gly Ala Pro Leu Pro Ser Glu Glu Ala Ser Ala
                805                 810                 815

Pro Asp Ala Pro Asp Ala Leu Pro Asp Ser Pro Thr Pro Ala Thr Gly
            820                 825                 830

Gly Glu Val Ser Ala Ile Lys Leu Ala Ser Ala Leu Asn Gly Ser Ser
        835                 840                 845

Ser Ser Pro Glu Val Glu Ala Pro Ser Ser Glu Asp Glu Asp Thr Ala
    850                 855                 860

Glu Ala Thr Ser Gly Ile Phe Thr Asp Thr Ser Ser Asp Gly Leu Gln
865                 870                 875                 880

Ala Arg Arg Pro Asp Val Val Pro Ala Phe Arg Ser Leu Gln Lys Gln
                885                 890                 895

Val Gly Thr Pro Asp Ser Leu Asp Ser Leu Asp Ile Pro Ser Ser Ala
            900                 905                 910

Ser Asp Gly Gly Tyr Glu Val Phe Ser Pro Ser Ala Thr Gly Pro Ser
        915                 920                 925

Gly Gly Gln Pro Arg Ala Leu Asp Ser Gly Tyr Asp Thr Glu Asn Tyr
    930                 935                 940

Glu Ser Pro Glu Phe Val Leu Lys Glu Ala Gln Glu Gly Cys Glu Pro
945                 950                 955                 960

Gln Ala Phe Ala Glu Leu Ala Ser Glu Gly Glu Gly Pro Gly Pro Glu
                965                 970                 975

Thr Arg Leu Ser Thr Ser Leu Ser Gly Leu Asn Glu Lys Asn Pro Tyr
            980                 985                 990

Arg Asp Ser Ala Tyr Phe Ser Asp  Leu Glu Ala Glu Ala  Glu Ala Thr
        995                 1000                1005

Ser Gly  Pro Glu Lys Lys Cys  Gly Gly Asp Arg Ala  Pro Gly Pro
    1010                1015                1020
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```
Glu Leu  Gly Leu Pro Ser Thr  Gly Gln Pro Ser Glu  Gln Val Cys
    1025                1030                1035

Leu Arg  Pro Gly Val Ser Gly  Glu Ala Gln Gly Ser  Gly Pro Gly
    1040                1045                1050

Glu Val  Leu Pro Pro Leu Leu  Gln Leu Glu Gly Ser  Ser Pro Glu
    1055                1060                1065

Pro Ser  Thr Cys Pro Ser Gly  Leu Val Pro Glu Pro  Pro Glu Pro
    1070                1075                1080

Gln Gly  Pro Ala Lys Val Arg  Pro Gly Pro Ser Pro  Ser Cys Ser
    1085                1090                1095

Gln Phe  Phe Leu Leu Thr Pro  Val Pro Leu Arg Ser  Glu Gly Asn
    1100                1105                1110

Ser Ser  Glu Phe Gln Gly Pro  Pro Gly Leu Leu Ser  Gly Pro Ala
    1115                1120                1125

Pro Gln  Lys Arg Met Gly Gly  Pro Gly Thr Pro Arg  Ala Pro Leu
    1130                1135                1140

Arg Leu  Ala Leu Pro Gly Leu  Pro Ala Ala Leu Glu  Gly Arg Pro
    1145                1150                1155

Glu Glu  Glu Glu Glu Asp Ser  Glu Asp Ser Asp Glu  Ser Asp Glu
    1160                1165                1170

Glu Leu  Arg Cys Tyr Ser Val  Gln Glu Pro Ser Glu  Asp Ser Glu
    1175                1180                1185

Glu Glu  Ala Pro Ala Val Pro  Val Val Val Ala Glu  Ser Gln Ser
    1190                1195                1200

Ala Arg  Asn Leu Arg Ser Leu  Leu Lys Met Pro Ser  Leu Leu Ser
    1205                1210                1215

Glu Thr  Phe Cys Glu Asp Leu  Glu Arg Lys Lys Lys  Ala Val Ser
    1220                1225                1230

Phe Phe  Asp Asp Val Thr Val  Tyr Leu Phe Asp Gln  Glu Ser Pro
    1235                1240                1245

Thr Arg  Glu Leu Gly Glu Pro  Phe Pro Gly Ala Lys  Glu Ser Pro
    1250                1255                1260

Pro Thr  Phe Leu Arg Gly Ser  Pro Gly Ser Pro Ser  Ala Pro Asn
    1265                1270                1275
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```
Arg Pro  Gln Gln Ala Asp Gly  Ser Pro Asn Gly Ser  Thr Ala Glu
    1280                 1285                 1290

Glu Gly  Gly Gly Phe Ala Trp  Asp Asp Asp Phe Pro  Leu Met Thr
    1295                 1300                 1305

Ala Lys  Ala Ala Phe Ala Met  Ala Leu Asp Pro Ala  Ala Pro Ala
    1310                 1315                 1320

Pro Ala  Ala Pro Thr Pro Thr  Pro Ala Pro Phe Ser  Arg Phe Thr
    1325                 1330                 1335

Val Ser  Pro Ala Pro Thr Ser  Arg Phe Ser Ile Thr  His Val Ser
    1340                 1345                 1350

Asp Ser  Asp Ala Glu Ser Lys  Arg Gly Pro Glu Ala  Gly Ala Gly
    1355                 1360                 1365

Gly Glu  Ser Lys Glu Ala
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Arg Met Phe Pro Asn Ala Pro Tyr Leu
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<400> 471

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Lys Leu Val Val Val Gly Ala Gly Gly Val
1               5                   10
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<400> 472

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Lys Leu Val Val Val Gly Ala Val Gly Val
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1 5 10

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<400> 473

Lys Leu Val Val Val Gly Ala Cys Gly Val
1 5 10

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<400> 474

Lys Leu Val Val Val Gly Ala Asp Gly Val
1 5 10

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<400> 475

Val Val Gly Ala Val Gly Val Gly Lys
1 5

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<400> 476

Val Val Gly Ala Cys Gly Val Gly Lys
1 5

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<400> 477

Val Val Gly Ala Gly Gly Val Gly Lys
1 5

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<400> 478

Lys Ile Thr Asp Phe Gly Leu Ala Lys
1 5

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<400> 479

Lys Ile Thr Asp Phe Gly Arg Ala Lys
1 5

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Val Leu Gln Glu Leu Asn Val Thr Val
1 5

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Glu Ala Asp Pro Thr Gly His Ser Tyr
1 5

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Leu Leu Gly Arg Asn Ser Phe Glu Val
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Ser Thr Thr Pro Pro Pro Gly Thr Arg Val
1 5 10

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Glu Leu Ala Gly Ile Gly Ile Leu Thr Val
1 5 10

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Ile Met Asp Gln Val Pro Phe Ser Val
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Asn Leu Val Pro Met Val Ala Thr Val
1 5

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Ala Ile Ile Arg Ile Leu Gln Gln Leu
1 5

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Val Leu His Asp Asp Leu Leu Glu Ala
1 5

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Val Leu Arg Asp Asp Leu Leu Glu Ala
1 5

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<400> 490

Ser Leu Leu Met Trp Ile Thr Gln Val
1 5

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<400> 491

Leu Leu Asp Phe Val Arg Phe Met Gly Val
1 5 10

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<400> 492

Phe Met Asn Lys Phe Ile Tyr Glu Ile
1 5

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<400> 493

Lys Ile Phe Gly Ser Leu Ala Phe Leu
1 5

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<400> 494

Gly Val Leu Pro Ala Leu Pro Gln Val
1 5

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Phe Leu Leu Thr Arg Ile Leu Thr Ile
1 5

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His Leu Ser Pro Ile Asp Cys Glu Val
1 5

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Leu Thr Ser Met Trp Ser Pro Ala Val
1 5

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His Leu Asp His Pro His Pro Ala Val
1 5

<210> 499
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Ser Leu Ser Val Met Ser Ser Asn Val
1 5

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<400> 500

Met Met Ala Trp Ser Asp Asn Lys Ile
1 5

<210> 501
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Thr Gln Ile Gly Ile Glu Trp Asn Leu
1 5

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Cys Leu Phe Glu Met Gln Asp Pro Ala
1 5

<210> 503
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<400> 503

Tyr Leu Ser His Pro Ser Cys Asn Val
1 5

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Gly Ile Glu Trp Asn Leu Ser Pro Val
1 5

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<400> 505

Gly Leu Gly Cys Ser Pro Ala Ser Ile
1 5

<210> 506
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<400> 506

Arg Gln Ala Phe Glu Phe Pro Gln Ile

1 5

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<400> 507

Arg Gln Ala Phe Glu Phe Pro Gln Ile
1 5

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Gly Met Trp Thr Asp Thr Phe Glu Phe
1 5

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<400> 509

Tyr Leu Asn Trp Gln Asp Thr Ala Val
1 5

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Val Leu Trp Gly Pro Ile Thr Gln Ile
1 5

<210> 511
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<400> 511

Thr Leu Asp His Thr Gly Val Val Val
1 5

<210> 512
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Thr Met Gly Val Trp Leu His Ile Ala
1 5

<210> 513
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<400> 513

Thr Met Gly Val Trp Leu His Ile Ala
1 5

<210> 514
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Lys Val Trp Val Gln Gly His Tyr Leu
1 5

<210> 515
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Lys Ile Asn Cys Asn Asn Phe Arg Leu
1 5

<210> 516
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Gly Ser Gly Gly Ser
1 5

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Gly Gly Gly Ser
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Gly Gly Ser Gly
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Gly Gly Ser Gly Gly
1 5

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<400> 520

Gly Ser Gly Ser Gly
1 5

<210> 521
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<400> 521

Gly Ser Gly Gly Gly
1 5

<210> 522
<211> 5
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<400> 522

Gly Gly Gly Ser Gly
1 5

<210> 523
<211> 5
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<400> 523

Gly Ser Ser Ser Gly
1 5

<210> 524
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<400> 524

Asp Lys Thr His Thr
1 5

<210> 525
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Cys Pro Pro Cys
1

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Cys Pro Glu Pro Lys Ser Cys Asp Thr Pro Pro Pro Cys Pro Arg
1 5 10 15

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<400> 527

Glu Leu Lys Thr Pro Leu Gly Asp Thr Thr His Thr
1 5 10

<210> 528
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Lys Ser Cys Asp Lys Thr His Thr Cys Pro
1 5 10

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<400> 529

Lys Cys Cys Val Asp Cys Pro
1 5

<210> 530
<211> 7
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<400> 530

Lys Tyr Gly Pro Pro Cys Pro
1 5

<210> 531

<211> 15
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Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro
1 5 10 15

<210> 532
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<400> 532

Glu Arg Lys Cys Cys Val Glu Cys Pro Pro Cys Pro
1 5 10

<210> 533
<211> 17
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<400> 533

Glu Leu Lys Thr Pro Leu Gly Asp Thr Thr His Thr Cys Pro Arg Cys
1 5 10 15

Pro

<210> 534
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Ser Pro Asn Met Val Pro His Ala His His Ala Gln
1 5 10

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<213> Artificial sequence

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<400> 535

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Glu Pro Lys Ser Cys Asp Lys Thr Tyr Thr Cys Pro Pro Cys Pro
1               5                   10                  15


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<220>
<223>  synthetic amino acid sequence

<400>  536

Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala
1               5                   10                  15


Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly
            20                  25                  30


Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp
        35                  40                  45


<210>  537
<211>  24
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic amino acid sequence

<400>  537

Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu
1               5                   10                  15


Ser Leu Val Ile Thr Leu Tyr Cys
            20


<210>  538
<211>  23
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic amino acid sequence

<400>  538

Leu Gly Leu Leu Val Ala Gly Val Leu Val Leu Leu Val Ser Leu Gly
1               5                   10                  15


Val Ala Ile His Leu Cys Cys
            20


<210>  539
<211>  25
<212>  PRT
<213>  Artificial sequence
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<220>
<223> synthetic amino acid sequence

<400> 539

Ala Leu Ile Val Leu Gly Gly Val Ala Gly Leu Leu Leu Phe Ile Gly
1 5 10 15

Leu Gly Ile Phe Phe Cys Val Arg Cys
20 25

<210> 540
<211> 23
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 540

Leu Cys Tyr Leu Leu Asp Gly Ile Leu Phe Ile Tyr Gly Val Ile Leu
1 5 10 15

Thr Ala Leu Phe Leu Arg Val
20

<210> 541
<211> 26
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 541

Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu Leu
1 5 10 15

Val Thr Val Ala Phe Ile Ile Phe Trp Val
20 25

<210> 542
<211> 26
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 542

Val Ala Ala Ile Leu Gly Leu Gly Leu Val Leu Gly Leu Leu Gly Pro
1 5 10 15

Leu Ala Ile Leu Leu Ala Leu Tyr Leu Leu
20 25

<210> 543

<211> 24
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 543

Ala Leu Pro Ala Ala Leu Ala Val Ile Ser Phe Leu Leu Gly Leu Gly
1 5 10 15

Leu Gly Val Ala Cys Val Leu Ala
20

<210> 544
<211> 42
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 544

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
1 5 10 15

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
20 25 30

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu
35 40

<210> 545
<211> 44
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 545

Phe Trp Val Arg Ser Lys Arg Ser Arg Leu Leu His Ser Asp Tyr Met
1 5 10 15

Asn Met Thr Pro Arg Arg Pro Gly Pro Thr Arg Lys His Tyr Gln Pro
20 25 30

Tyr Ala Pro Pro Arg Asp Phe Ala Ala Tyr Arg Ser
35 40

<210> 546
<211> 35
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 546

Thr Lys Lys Lys Tyr Ser Ser Ser Val His Asp Pro Asn Gly Glu Tyr
1 5 10 15

Met Phe Met Arg Ala Val Asn Thr Ala Lys Lys Ser Arg Leu Thr Asp
20 25 30

Val Thr Leu
35

<210> 547
<211> 37
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 547

Arg Arg Asp Gln Arg Leu Pro Pro Asp Ala His Lys Pro Pro Gly Gly
1 5 10 15

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

Thr Leu Ala Lys Ile
35

<210> 548
<211> 114
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 548

Cys Cys Leu Arg Arg His Gln Gly Lys Gln Asn Glu Leu Ser Asp Thr
1 5 10 15

Ala Gly Arg Glu Ile Asn Leu Val Asp Ala His Leu Lys Ser Glu Gln
20 25 30

Thr Glu Ala Ser Thr Arg Gln Asn Ser Gln Val Leu Leu Ser Glu Thr
35 40 45

Gly Ile Tyr Asp Asn Asp Pro Asp Leu Cys Phe Arg Met Gln Glu Gly
50 55 60

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

Val Tyr Ala Ser Leu Asn His Ser Val Ile Gly Pro Asn Ser Arg Leu

85 90 95

Ala Arg Asn Val Lys Glu Ala Pro Thr Glu Tyr Ala Ser Ile Cys Val
100 105 110

Arg Ser

<210> 549
<211> 49
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 549

His Gln Arg Arg Lys Tyr Arg Ser Asn Lys Gly Glu Ser Pro Val Glu
1 5 10 15

Pro Ala Glu Pro Cys Arg Tyr Ser Cys Pro Arg Glu Glu Glu Gly Ser
20 25 30

Thr Ile Pro Ile Gln Glu Asp Tyr Arg Lys Pro Glu Pro Ala Cys Ser
35 40 45

Pro

<210> 550
<211> 187
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 550

Arg Arg Ala Cys Arg Lys Arg Ile Arg Gln Lys Leu His Leu Cys Tyr
1 5 10 15

Pro Val Gln Thr Ser Gln Pro Lys Leu Glu Leu Val Asp Ser Arg Pro
20 25 30

Arg Arg Ser Ser Thr Gln Leu Arg Ser Gly Ala Ser Val Thr Glu Pro
35 40 45

Val Ala Glu Glu Arg Gly Leu Met Ser Gln Pro Leu Met Glu Thr Cys
50 55 60

His Ser Val Gly Ala Ala Tyr Leu Glu Ser Leu Pro Leu Gln Asp Ala
65 70 75 80

Ser Pro Ala Gly Gly Pro Ser Ser Pro Arg Asp Leu Pro Glu Pro Arg

85 90 95

Val Ser Thr Glu His Thr Asn Asn Lys Ile Glu Lys Ile Tyr Ile Met
100 105 110

Lys Ala Asp Thr Val Ile Val Gly Thr Val Lys Ala Glu Leu Pro Glu
115 120 125

Gly Arg Gly Leu Ala Gly Pro Ala Glu Pro Glu Leu Glu Glu Glu Leu
130 135 140

Glu Ala Asp His Thr Pro His Tyr Pro Glu Gln Glu Thr Glu Pro Pro
145 150 155 160

Leu Gly Ser Cys Ser Asp Val Met Leu Ser Val Glu Glu Glu Gly Lys
165 170 175

Glu Asp Pro Leu Pro Thr Ala Ala Ser Gly Lys
180 185

<210> 551
<211> 54
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 551

His Ile Trp Gln Leu Arg Ser Gln Cys Met Trp Pro Arg Glu Thr Gln
1 5 10 15

Leu Leu Leu Glu Val Pro Pro Ser Thr Glu Asp Ala Arg Ser Cys Gln
20 25 30

Phe Pro Glu Glu Glu Arg Gly Glu Arg Ser Ala Glu Glu Lys Gly Arg
35 40 45

Leu Gly Asp Leu Trp Val
50

<210> 552
<211> 60
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 552

Cys Val Lys Arg Arg Lys Pro Arg Gly Asp Val Val Lys Val Ile Val
1 5 10 15

Ser Val Gln Arg Lys Arg Gln Glu Ala Glu Gly Glu Ala Thr Val Ile

20 25 30

Glu Ala Leu Gln Ala Pro Pro Asp Val Thr Thr Val Ala Val Glu Glu
35 40 45

Thr Ile Pro Ser Phe Thr Gly Arg Ser Pro Asn His
50 55 60

<210> 553
<211> 203
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 553

Cys Ser Ser Asp Asp Arg Gly His Ser Ser Leu Thr Asn Ser Pro Leu
1 5 10 15

Asp Ser Ser Cys Lys Glu Ser Ser Val Ser Val Thr Ser Pro Ser Gly
20 25 30

Val Ser Ser Ser Thr Ser Gly Gly Val Ser Ser Thr Ser Asn Met His
35 40 45

Gly Ser Leu Leu Gln Glu Lys His Arg Ile Leu His Lys Leu Leu Gln
50 55 60

Asn Gly Asn Ser Pro Ala Glu Val Ala Lys Ile Thr Ala Glu Ala Thr
65 70 75 80

Gly Lys Asp Thr Ser Ser Ile Thr Ser Cys Gly Asp Gly Asn Val Val
85 90 95

Lys Gln Glu Gln Leu Ser Pro Lys Lys Lys Glu Asn Asn Ala Leu Leu
100 105 110

Arg Tyr Leu Leu Asp Arg Asp Asp Pro Ser Asp Ala Leu Ser Lys Glu
115 120 125

Leu Gln Pro Gln Val Glu Gly Val Asp Asn Lys Met Ser Gln Cys Thr
130 135 140

Ser Ser Thr Ile Pro Ser Ser Ser Gln Glu Lys Asp Pro Lys Ile Lys
145 150 155 160

Thr Glu Thr Ser Glu Glu Gly Ser Gly Asp Leu Asp Asn Leu Asp Ala
165 170 175

Ile Leu Gly Asp Leu Thr Ser Ser Asp Phe Tyr Asn Asn Ser Ile Ser
180 185 190

Ser Asn Gly Ser His Leu Gly Thr Lys Gln Gln
195 200

<210> 554
<211> 78
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 554

Met His Gly Ser Leu Leu Gln Glu Lys His Arg Ile Leu His Lys Leu
1 5 10 15

Leu Gln Asn Gly Asn Ser Pro Ala Glu Val Ala Lys Ile Thr Ala Glu
20 25 30

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

Val Val Lys Gln Glu Gln Leu Ser Pro Lys Lys Lys Glu Asn Asn Ala
50 55 60

Leu Leu Arg Tyr Leu Leu Asp Arg Asp Asp Pro Ser Asp Ala
65 70 75

<210> 555
<211> 301
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 555

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

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

Asp Thr Lys Asp Ile Gly Leu Pro Glu Ile Thr Pro Lys Leu Glu Arg
35 40 45

Leu Asp Ser Lys Thr Asp Pro Ala Ser Asn Thr Lys Leu Ile Ala Met
50 55 60

Lys Thr Glu Lys Glu Glu Met Ser Phe Glu Pro Gly Asp Gln Pro Gly
65 70 75 80

Ser Glu Leu Asp Asn Leu Glu Glu Ile Leu Asp Asp Leu Gln Asn Ser
85 90 95

```
Gln Leu Pro Gln Leu Phe Pro Asp Thr Arg Pro Gly Ala Pro Ala Gly
            100                 105                 110

Ser Val Asp Lys Gln Ala Ile Ile Asn Asp Leu Met Gln Leu Thr Ala
        115                 120                 125

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

Ile Ser Gln Ser Thr Phe Asn Asn Pro Arg Pro Gly Gln Leu Gly Arg
145                 150                 155                 160

Leu Leu Pro Asn Gln Asn Leu Pro Leu Asp Ile Thr Leu Gln Ser Pro
                165                 170                 175

Thr Gly Ala Gly Pro Phe Pro Pro Ile Arg Asn Ser Ser Pro Tyr Ser
            180                 185                 190

Val Ile Pro Gln Pro Gly Met Met Gly Asn Gln Gly Met Ile Gly Asn
        195                 200                 205

Gln Gly Asn Leu Gly Asn Ser Ser Thr Gly Met Ile Gly Asn Ser Ala
    210                 215                 220

Ser Arg Pro Thr Met Pro Ser Gly Glu Trp Ala Pro Gln Ser Ser Ala
225                 230                 235                 240

Val Arg Val Thr Cys Ala Ala Thr Thr Ser Ala Met Asn Arg Pro Val
                245                 250                 255

Gln Gly Gly Met Ile Arg Asn Pro Ala Ala Ser Ile Pro Met Arg Pro
            260                 265                 270

Ser Ser Gln Pro Gly Gln Arg Gln Thr Leu Gln Ser Gln Val Met Asn
        275                 280                 285

Ile Gly Pro Ser Glu Leu Glu Met Asn Met Gly Gly Pro
    290                 295                 300


<210>  556
<211>  270
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic amino acid sequence

<400>  556

Asn Tyr Gly Thr Asn Pro Gly Thr Pro Pro Ala Ser Thr Ser Pro Phe
1               5                   10                  15

Ser Gln Leu Ala Ala Asn Pro Glu Ala Ser Leu Ala Asn Arg Asn Ser
```

20 25 30

Met Val Ser Arg Gly Met Thr Gly Asn Ile Gly Gly Gln Phe Gly Thr
35 40 45

Gly Ile Asn Pro Gln Met Gln Gln Asn Val Phe Gln Tyr Pro Gly Ala
50 55 60

Gly Met Val Pro Gln Gly Glu Ala Asn Phe Ala Pro Ser Leu Ser Pro
65 70 75 80

Gly Ser Ser Met Val Pro Met Pro Ile Pro Pro Pro Gln Ser Ser Leu
85 90 95

Leu Gln Gln Thr Pro Pro Ala Ser Gly Tyr Gln Ser Pro Asp Met Lys
100 105 110

Ala Trp Gln Gln Gly Ala Ile Gly Asn Asn Asn Val Phe Ser Gln Ala
115 120 125

Val Gln Asn Gln Pro Thr Pro Ala Gln Pro Gly Val Tyr Asn Asn Met
130 135 140

Ser Ile Thr Val Ser Met Ala Gly Gly Asn Thr Asn Val Gln Asn Met
145 150 155 160

Asn Pro Met Met Ala Gln Met Gln Met Ser Ser Leu Gln Met Pro Gly
165 170 175

Met Asn Thr Val Cys Pro Glu Gln Ile Asn Asp Pro Ala Leu Arg His
180 185 190

Thr Gly Leu Tyr Cys Asn Gln Leu Ser Ser Thr Asp Leu Leu Lys Thr
195 200 205

Glu Ala Asp Gly Thr Gln Gln Val Gln Gln Val Gln Val Phe Ala Asp
210 215 220

Val Gln Cys Thr Val Asn Leu Val Gly Gly Asp Pro Tyr Leu Asn Gln
225 230 235 240

Pro Gly Pro Leu Gly Thr Gln Lys Pro Thr Ser Gly Pro Gln Thr Pro
245 250 255

Gln Ala Gln Gln Lys Ser Leu Leu Gln Gln Leu Leu Thr Glu
260 265 270

<210> 557
<211> 702
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 557

```
Lys Arg His His His Glu Val Leu Arg Gln Gly Leu Ala Phe Ser Gln
1               5                  10                  15

Ile Tyr Arg Phe Ser Leu Ser Asp Gly Thr Leu Val Ala Ala Gln Thr
            20                  25                  30

Lys Ser Lys Leu Ile Arg Ser Gln Thr Thr Asn Glu Pro Gln Leu Val
        35                  40                  45

Ile Ser Leu His Met Leu His Arg Glu Gln Asn Val Cys Val Met Asn
    50                  55                  60

Pro Asp Leu Thr Gly Gln Thr Met Gly Lys Pro Leu Asn Pro Ile Ser
65                  70                  75                  80

Ser Asn Ser Pro Ala His Gln Ala Leu Cys Ser Gly Asn Pro Gly Gln
                85                  90                  95

Asp Met Thr Leu Ser Ser Asn Ile Asn Phe Pro Ile Asn Gly Pro Lys
            100                 105                 110

Glu Gln Met Gly Met Pro Met Gly Arg Phe Gly Gly Ser Gly Gly Met
        115                 120                 125

Asn His Val Ser Gly Met Gln Ala Thr Thr Pro Gln Gly Ser Asn Tyr
    130                 135                 140

Ala Leu Lys Met Asn Ser Pro Ser Gln Ser Ser Pro Gly Met Asn Pro
145                 150                 155                 160

Gly Gln Pro Thr Ser Met Leu Ser Pro Arg His Arg Met Ser Pro Gly
                165                 170                 175

Val Ala Gly Ser Pro Arg Ile Pro Pro Ser Gln Phe Ser Pro Ala Gly
            180                 185                 190

Ser Leu His Ser Pro Val Gly Val Cys Ser Ser Thr Gly Asn Ser His
        195                 200                 205

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

His Gly Val Ser Leu Gly Ser Ser Leu Ala Ser Pro Asp Leu Lys Met
225                 230                 235                 240

Gly Asn Leu Gln Asn Ser Pro Val Asn Met Asn Pro Pro Pro Leu Ser
                245                 250                 255
```

```
Lys Met Gly Ser Leu Asp Ser Lys Asp Cys Phe Gly Leu Tyr Gly Glu
            260                 265                 270

Pro Ser Glu Gly Thr Thr Gly Gln Ala Glu Ser Ser Cys His Pro Gly
        275                 280                 285

Glu Gln Lys Glu Thr Asn Asp Pro Asn Leu Pro Pro Ala Val Ser Ser
    290                 295                 300

Glu Arg Ala Asp Gly Gln Ser Arg Leu His Asp Ser Lys Gly Gln Thr
305                 310                 315                 320

Lys Leu Leu Gln Leu Leu Thr Thr Lys Ser Asp Gln Met Glu Pro Ser
                325                 330                 335

Pro Leu Ala Ser Ser Leu Ser Asp Thr Asn Lys Asp Ser Thr Gly Ser
            340                 345                 350

Leu Pro Gly Ser Gly Ser Thr His Gly Thr Ser Leu Lys Glu Lys His
        355                 360                 365

Lys Ile Leu His Arg Leu Leu Gln Asp Ser Ser Ser Pro Val Asp Leu
    370                 375                 380

Ala Lys Leu Thr Ala Glu Ala Thr Gly Lys Asp Leu Ser Gln Glu Ser
385                 390                 395                 400

Ser Ser Thr Ala Pro Gly Ser Glu Val Thr Ile Lys Gln Glu Pro Val
                405                 410                 415

Ser Pro Lys Lys Lys Glu Asn Ala Leu Leu Arg Tyr Leu Leu Asp Lys
            420                 425                 430

Asp Asp Thr Lys Asp Ile Gly Leu Pro Glu Ile Thr Pro Lys Leu Glu
        435                 440                 445

Arg Leu Asp Ser Lys Thr Asp Pro Ala Ser Asn Thr Lys Leu Ile Ala
    450                 455                 460

Met Lys Thr Glu Lys Glu Glu Met Ser Phe Glu Pro Gly Asp Gln Pro
465                 470                 475                 480

Gly Ser Glu Leu Asp Asn Leu Glu Glu Ile Leu Asp Asp Leu Gln Asn
                485                 490                 495

Ser Gln Leu Pro Gln Leu Phe Pro Asp Thr Arg Pro Gly Ala Pro Ala
            500                 505                 510

Gly Ser Val Asp Lys Gln Ala Ile Ile Asn Asp Leu Met Gln Leu Thr
        515                 520                 525
```

```
Ala Glu Asn Ser Pro Val Thr Pro Val Gly Ala Gln Lys Thr Ala Leu
    530                 535                 540

Arg Ile Ser Gln Ser Thr Phe Asn Asn Pro Arg Pro Gly Gln Leu Gly
545                 550                 555                 560

Arg Leu Leu Pro Asn Gln Asn Leu Pro Leu Asp Ile Thr Leu Gln Ser
                565                 570                 575

Pro Thr Gly Ala Gly Pro Phe Pro Pro Ile Arg Asn Ser Ser Pro Tyr
            580                 585                 590

Ser Val Ile Pro Gln Pro Gly Met Met Gly Asn Gln Gly Met Ile Gly
        595                 600                 605

Asn Gln Gly Asn Leu Gly Asn Ser Ser Thr Gly Met Ile Gly Asn Ser
    610                 615                 620

Ala Ser Arg Pro Thr Met Pro Ser Gly Glu Trp Ala Pro Gln Ser Ser
625                 630                 635                 640

Ala Val Arg Val Thr Cys Ala Ala Thr Thr Ser Ala Met Asn Arg Pro
                645                 650                 655

Val Gln Gly Gly Met Ile Arg Asn Pro Ala Ala Ser Ile Pro Met Arg
            660                 665                 670

Pro Ser Ser Gln Pro Gly Gln Arg Gln Thr Leu Gln Ser Gln Val Met
        675                 680                 685

Asn Ile Gly Pro Ser Glu Leu Glu Met Asn Met Gly Gly Pro
    690                 695                 700


<210>  558
<211>  270
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic amino acid sequence

<400>  558

Asn Tyr Gly Thr Asn Pro Gly Thr Pro Pro Ala Ser Thr Ser Pro Phe
1               5                   10                  15

Ser Gln Leu Ala Ala Asn Pro Glu Ala Ser Leu Ala Asn Arg Asn Ser
            20                  25                  30

Met Val Ser Arg Gly Met Thr Gly Asn Ile Gly Gly Gln Phe Gly Thr
        35                  40                  45

Gly Ile Asn Pro Gln Met Gln Gln Asn Val Phe Gln Tyr Pro Gly Ala
```

50 55 60

Gly Met Val Pro Gln Gly Glu Ala Asn Phe Ala Pro Ser Leu Ser Pro
65 70 75 80

Gly Ser Ser Met Val Pro Met Pro Ile Pro Pro Pro Gln Ser Ser Leu
85 90 95

Leu Gln Gln Thr Pro Pro Ala Ser Gly Tyr Gln Ser Pro Asp Met Lys
100 105 110

Ala Trp Gln Gln Gly Ala Ile Gly Asn Asn Asn Val Phe Ser Gln Ala
115 120 125

Val Gln Asn Gln Pro Thr Pro Ala Gln Pro Gly Val Tyr Asn Asn Met
130 135 140

Ser Ile Thr Val Ser Met Ala Gly Gly Asn Thr Asn Val Gln Asn Met
145 150 155 160

Asn Pro Met Met Ala Gln Met Gln Met Ser Ser Leu Gln Met Pro Gly
165 170 175

Met Asn Thr Val Cys Pro Glu Gln Ile Asn Asp Pro Ala Leu Arg His
180 185 190

Thr Gly Leu Tyr Cys Asn Gln Leu Ser Ser Thr Asp Leu Leu Lys Thr
195 200 205

Glu Ala Asp Gly Thr Gln Gln Val Gln Gln Val Gln Val Phe Ala Asp
210 215 220

Val Gln Cys Thr Val Asn Leu Val Gly Gly Asp Pro Tyr Leu Asn Gln
225 230 235 240

Pro Gly Pro Leu Gly Thr Gln Lys Pro Thr Ser Gly Pro Gln Thr Pro
245 250 255

Gln Ala Gln Gln Lys Ser Leu Leu Gln Gln Leu Leu Thr Glu
260 265 270

<210> 559
<211> 702
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 559

Lys Arg His His His Glu Val Leu Arg Gln Gly Leu Ala Phe Ser Gln
1 5 10 15

```
Ile Tyr Arg Phe Ser Leu Ser Asp Gly Thr Leu Val Ala Ala Gln Thr
            20                  25                  30

Lys Ser Lys Leu Ile Arg Ser Gln Thr Thr Asn Glu Pro Gln Leu Val
        35                  40                  45

Ile Ser Leu His Met Leu His Arg Glu Gln Asn Val Cys Val Met Asn
    50                  55                  60

Pro Asp Leu Thr Gly Gln Thr Met Gly Lys Pro Leu Asn Pro Ile Ser
65                  70                  75                  80

Ser Asn Ser Pro Ala His Gln Ala Leu Cys Ser Gly Asn Pro Gly Gln
                85                  90                  95

Asp Met Thr Leu Ser Ser Asn Ile Asn Phe Pro Ile Asn Gly Pro Lys
            100                 105                 110

Glu Gln Met Gly Met Pro Met Gly Arg Phe Gly Gly Ser Gly Gly Met
        115                 120                 125

Asn His Val Ser Gly Met Gln Ala Thr Thr Pro Gln Gly Ser Asn Tyr
    130                 135                 140

Ala Leu Lys Met Asn Ser Pro Ser Gln Ser Ser Pro Gly Met Asn Pro
145                 150                 155                 160

Gly Gln Pro Thr Ser Met Leu Ser Pro Arg His Arg Met Ser Pro Gly
                165                 170                 175

Val Ala Gly Ser Pro Arg Ile Pro Pro Ser Gln Phe Ser Pro Ala Gly
            180                 185                 190

Ser Leu His Ser Pro Val Gly Val Cys Ser Ser Thr Gly Asn Ser His
        195                 200                 205

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

His Gly Val Ser Leu Gly Ser Ser Leu Ala Ser Pro Asp Leu Lys Met
225                 230                 235                 240

Gly Asn Leu Gln Asn Ser Pro Val Asn Met Asn Pro Pro Pro Leu Ser
                245                 250                 255

Lys Met Gly Ser Leu Asp Ser Lys Asp Cys Phe Gly Leu Tyr Gly Glu
            260                 265                 270

Pro Ser Glu Gly Thr Thr Gly Gln Ala Glu Ser Ser Cys His Pro Gly
        275                 280                 285
```

```
Glu Gln Lys Glu Thr Asn Asp Pro Asn Leu Pro Pro Ala Val Ser Ser
    290                 295                 300

Glu Arg Ala Asp Gly Gln Ser Arg Leu His Asp Ser Lys Gly Gln Thr
305                 310                 315                 320

Lys Leu Leu Gln Leu Leu Thr Thr Lys Ser Asp Gln Met Glu Pro Ser
                325                 330                 335

Pro Leu Ala Ser Ser Leu Ser Asp Thr Asn Lys Asp Ser Thr Gly Ser
            340                 345                 350

Leu Pro Gly Ser Gly Ser Thr His Gly Thr Ser Leu Lys Glu Lys His
        355                 360                 365

Lys Ile Leu His Arg Leu Leu Gln Asp Ser Ser Ser Pro Val Asp Leu
    370                 375                 380

Ala Lys Leu Thr Ala Glu Ala Thr Gly Lys Asp Leu Ser Gln Glu Ser
385                 390                 395                 400

Ser Ser Thr Ala Pro Gly Ser Glu Val Thr Ile Lys Gln Glu Pro Val
                405                 410                 415

Ser Pro Lys Lys Lys Glu Asn Ala Leu Leu Arg Tyr Leu Leu Asp Lys
            420                 425                 430

Asp Asp Thr Lys Asp Ile Gly Leu Pro Glu Ile Thr Pro Lys Leu Glu
        435                 440                 445

Arg Leu Asp Ser Lys Thr Asp Pro Ala Ser Asn Thr Lys Leu Ile Ala
    450                 455                 460

Met Lys Thr Glu Lys Glu Glu Met Ser Phe Glu Pro Gly Asp Gln Pro
465                 470                 475                 480

Gly Ser Glu Leu Asp Asn Leu Glu Glu Ile Leu Asp Asp Leu Gln Asn
                485                 490                 495

Ser Gln Leu Pro Gln Leu Phe Pro Asp Thr Arg Pro Gly Ala Pro Ala
            500                 505                 510

Gly Ser Val Asp Lys Gln Ala Ile Ile Asn Asp Leu Met Gln Leu Thr
        515                 520                 525

Ala Glu Asn Ser Pro Val Thr Pro Val Gly Ala Gln Lys Thr Ala Leu
    530                 535                 540

Arg Ile Ser Gln Ser Thr Phe Asn Asn Pro Arg Pro Gly Gln Leu Gly
545                 550                 555                 560
```

```
Arg Leu Leu Pro Asn Gln Asn Leu Pro Leu Asp Ile Thr Leu Gln Ser
                565                 570                 575

Pro Thr Gly Ala Gly Pro Phe Pro Pro Ile Arg Asn Ser Ser Pro Tyr
            580                 585                 590

Ser Val Ile Pro Gln Pro Gly Met Met Gly Asn Gln Gly Met Ile Gly
        595                 600                 605

Asn Gln Gly Asn Leu Gly Asn Ser Ser Thr Gly Met Ile Gly Asn Ser
    610                 615                 620

Ala Ser Arg Pro Thr Met Pro Ser Gly Glu Trp Ala Pro Gln Ser Ser
625                 630                 635                 640

Ala Val Arg Val Thr Cys Ala Ala Thr Thr Ser Ala Met Asn Arg Pro
                645                 650                 655

Val Gln Gly Gly Met Ile Arg Asn Pro Ala Ala Ser Ile Pro Met Arg
            660                 665                 670

Pro Ser Ser Gln Pro Gly Gln Arg Gln Thr Leu Gln Ser Gln Val Met
        675                 680                 685

Asn Ile Gly Pro Ser Glu Leu Glu Met Asn Met Gly Gly Pro
    690                 695                 700
```

<210> 560
<211> 8
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 560

```
Leu Leu Arg Tyr Leu Leu Asp Lys
1               5
```

<210> 561
<211> 270
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 561

```
Asn Tyr Gly Thr Asn Pro Gly Thr Pro Pro Ala Ser Thr Ser Pro Phe
1               5                   10                  15

Ser Gln Leu Ala Ala Asn Pro Glu Ala Ser Leu Ala Asn Arg Asn Ser
            20                  25                  30
```

```
Met Val Ser Arg Gly Met Thr Gly Asn Ile Gly Gly Gln Phe Gly Thr
        35                  40                  45

Gly Ile Asn Pro Gln Met Gln Gln Asn Val Phe Gln Tyr Pro Gly Ala
    50                  55                  60

Gly Met Val Pro Gln Gly Glu Ala Asn Phe Ala Pro Ser Leu Ser Pro
65                  70                  75                  80

Gly Ser Ser Met Val Pro Met Pro Ile Pro Pro Pro Gln Ser Ser Leu
                85                  90                  95

Leu Gln Gln Thr Pro Pro Ala Ser Gly Tyr Gln Ser Pro Asp Met Lys
            100                 105                 110

Ala Trp Gln Gln Gly Ala Ile Gly Asn Asn Asn Val Phe Ser Gln Ala
        115                 120                 125

Val Gln Asn Gln Pro Thr Pro Ala Gln Pro Gly Val Tyr Asn Asn Met
    130                 135                 140

Ser Ile Thr Val Ser Met Ala Gly Gly Asn Thr Asn Val Gln Asn Met
145                 150                 155                 160

Asn Pro Met Met Ala Gln Met Gln Met Ser Ser Leu Gln Met Pro Gly
                165                 170                 175

Met Asn Thr Val Cys Pro Glu Gln Ile Asn Asp Pro Ala Leu Arg His
            180                 185                 190

Thr Gly Leu Tyr Cys Asn Gln Leu Ser Ser Thr Asp Leu Leu Lys Thr
        195                 200                 205

Glu Ala Asp Gly Thr Gln Gln Val Gln Gln Val Gln Val Phe Ala Asp
    210                 215                 220

Val Gln Cys Thr Val Asn Leu Val Gly Gly Asp Pro Tyr Leu Asn Gln
225                 230                 235                 240

Pro Gly Pro Leu Gly Thr Gln Lys Pro Thr Ser Gly Pro Gln Thr Pro
                245                 250                 255

Gln Ala Gln Gln Lys Ser Leu Leu Gln Gln Leu Leu Thr Glu
            260                 265                 270
```

<210> 562
<211> 702
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 562

Lys Arg His His His Glu Val Leu Arg Gln Gly Leu Ala Phe Ser Gln
1 5 10 15

Ile Tyr Arg Phe Ser Leu Ser Asp Gly Thr Leu Val Ala Ala Gln Thr
20 25 30

Lys Ser Lys Leu Ile Arg Ser Gln Thr Thr Asn Glu Pro Gln Leu Val
35 40 45

Ile Ser Leu His Met Leu His Arg Glu Gln Asn Val Cys Val Met Asn
50 55 60

Pro Asp Leu Thr Gly Gln Thr Met Gly Lys Pro Leu Asn Pro Ile Ser
65 70 75 80

Ser Asn Ser Pro Ala His Gln Ala Leu Cys Ser Gly Asn Pro Gly Gln
85 90 95

Asp Met Thr Leu Ser Ser Asn Ile Asn Phe Pro Ile Asn Gly Pro Lys
100 105 110

Glu Gln Met Gly Met Pro Met Gly Arg Phe Gly Gly Ser Gly Gly Met
115 120 125

Asn His Val Ser Gly Met Gln Ala Thr Thr Pro Gln Gly Ser Asn Tyr
130 135 140

Ala Leu Lys Met Asn Ser Pro Ser Gln Ser Ser Pro Gly Met Asn Pro
145 150 155 160

Gly Gln Pro Thr Ser Met Leu Ser Pro Arg His Arg Met Ser Pro Gly
165 170 175

Val Ala Gly Ser Pro Arg Ile Pro Pro Ser Gln Phe Ser Pro Ala Gly
180 185 190

Ser Leu His Ser Pro Val Gly Val Cys Ser Ser Thr Gly Asn Ser His
195 200 205

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

His Gly Val Ser Leu Gly Ser Ser Leu Ala Ser Pro Asp Leu Lys Met
225 230 235 240

Gly Asn Leu Gln Asn Ser Pro Val Asn Met Asn Pro Pro Pro Leu Ser
245 250 255

Lys Met Gly Ser Leu Asp Ser Lys Asp Cys Phe Gly Leu Tyr Gly Glu

260 265 270

Pro Ser Glu Gly Thr Thr Gly Gln Ala Glu Ser Ser Cys His Pro Gly
275 280 285

Glu Gln Lys Glu Thr Asn Asp Pro Asn Leu Pro Pro Ala Val Ser Ser
290 295 300

Glu Arg Ala Asp Gly Gln Ser Arg Leu His Asp Ser Lys Gly Gln Thr
305 310 315 320

Lys Leu Leu Gln Leu Leu Thr Thr Lys Ser Asp Gln Met Glu Pro Ser
325 330 335

Pro Leu Ala Ser Ser Leu Ser Asp Thr Asn Lys Asp Ser Thr Gly Ser
340 345 350

Leu Pro Gly Ser Gly Ser Thr His Gly Thr Ser Leu Lys Glu Lys His
355 360 365

Lys Ile Leu His Arg Leu Leu Gln Asp Ser Ser Ser Pro Val Asp Leu
370 375 380

Ala Lys Leu Thr Ala Glu Ala Thr Gly Lys Asp Leu Ser Gln Glu Ser
385 390 395 400

Ser Ser Thr Ala Pro Gly Ser Glu Val Thr Ile Lys Gln Glu Pro Val
405 410 415

Ser Pro Lys Lys Lys Glu Asn Ala Leu Leu Arg Tyr Leu Leu Asp Lys
420 425 430

Asp Asp Thr Lys Asp Ile Gly Leu Pro Glu Ile Thr Pro Lys Leu Glu
435 440 445

Arg Leu Asp Ser Lys Thr Asp Pro Ala Ser Asn Thr Lys Leu Ile Ala
450 455 460

Met Lys Thr Glu Lys Glu Glu Met Ser Phe Glu Pro Gly Asp Gln Pro
465 470 475 480

Gly Ser Glu Leu Asp Asn Leu Glu Glu Ile Leu Asp Asp Leu Gln Asn
485 490 495

Ser Gln Leu Pro Gln Leu Phe Pro Asp Thr Arg Pro Gly Ala Pro Ala
500 505 510

Gly Ser Val Asp Lys Gln Ala Ile Ile Asn Asp Leu Met Gln Leu Thr
515 520 525

Ala Glu Asn Ser Pro Val Thr Pro Val Gly Ala Gln Lys Thr Ala Leu

530 535 540

Arg Ile Ser Gln Ser Thr Phe Asn Asn Pro Arg Pro Gly Gln Leu Gly
545 550 555 560

Arg Leu Leu Pro Asn Gln Asn Leu Pro Leu Asp Ile Thr Leu Gln Ser
565 570 575

Pro Thr Gly Ala Gly Pro Phe Pro Pro Ile Arg Asn Ser Ser Pro Tyr
580 585 590

Ser Val Ile Pro Gln Pro Gly Met Met Gly Asn Gln Gly Met Ile Gly
595 600 605

Asn Gln Gly Asn Leu Gly Asn Ser Ser Thr Gly Met Ile Gly Asn Ser
610 615 620

Ala Ser Arg Pro Thr Met Pro Ser Gly Glu Trp Ala Pro Gln Ser Ser
625 630 635 640

Ala Val Arg Val Thr Cys Ala Ala Thr Thr Ser Ala Met Asn Arg Pro
645 650 655

Val Gln Gly Gly Met Ile Arg Asn Pro Ala Ala Ser Ile Pro Met Arg
660 665 670

Pro Ser Ser Gln Pro Gly Gln Arg Gln Thr Leu Gln Ser Gln Val Met
675 680 685

Asn Ile Gly Pro Ser Glu Leu Glu Met Asn Met Gly Gly Pro
690 695 700

<210> 563
<211> 24
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 563

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

Leu Met Gly Ser Phe Asp Asp Lys
20

<210> 564
<211> 4
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<220>
<221> MISC_FEATURE
<222> (2)..(3)
<223> the amino acid at this position may be any amino acid

<220>
<221> MISC_FEATURE
<222> (4)..(4)
<223> the amino acid at this position may be L or I

<400> 564

Tyr Xaa Xaa Xaa
1

<210> 565
<211> 16
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<220>
<221> MISC_FEATURE
<222> (2)..(3)
<223> the amino acid at this position may be any amino acid

<220>
<221> MISC_FEATURE
<222> (4)..(4)
<223> the amino acid at this position may be a L or I

<220>
<221> MISC_FEATURE
<222> (5)..(12)
<223> 6-8 amino acids may be present at these positions and, when present, the amino acids may be any amino acid

<220>
<221> MISC_FEATURE
<222> (14)..(15)
<223> the amino acid at this position may be any amino acid

<220>
<221> MISC_FEATURE
<222> (16)..(16)
<223> the amino acid at this position may be a L or I

<400> 565

Tyr Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Tyr Xaa Xaa Xaa
1 5 10 15

<210> 566
<211> 113
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 566

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Met Gly Gly Leu Glu Pro Cys Ser Arg Leu Leu Leu Leu Pro Leu Leu
1               5                  10                  15

Leu Ala Val Ser Gly Leu Arg Pro Val Gln Ala Gln Ala Gln Ser Asp
            20                  25                  30

Cys Ser Cys Ser Thr Val Ser Pro Gly Val Leu Ala Gly Ile Val Met
        35                  40                  45

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

Gly Arg Leu Val Pro Arg Gly Arg Gly Ala Ala Glu Ala Ala Thr Arg
65                  70                  75                  80

Lys Gln Arg Ile Thr Glu Thr Glu Ser Pro Tyr Gln Glu Leu Gln Gly
                85                  90                  95

Gln Arg Ser Asp Val Tyr Ser Asp Leu Asn Thr Gln Arg Pro Tyr Tyr
            100                 105                 110

Lys
```

<210> 567
<211> 112
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 567

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Met Gly Gly Leu Glu Pro Cys Ser Arg Leu Leu Leu Leu Pro Leu Leu
1               5                  10                  15

Leu Ala Val Ser Gly Leu Arg Pro Val Gln Ala Gln Ala Gln Ser Asp
            20                  25                  30

Cys Ser Cys Ser Thr Val Ser Pro Gly Val Leu Ala Gly Ile Val Met
        35                  40                  45

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

Gly Arg Leu Val Pro Arg Gly Arg Gly Ala Ala Glu Ala Thr Arg Lys
65                  70                  75                  80

Gln Arg Ile Thr Glu Thr Glu Ser Pro Tyr Gln Glu Leu Gln Gly Gln
                85                  90                  95

Arg Ser Asp Val Tyr Ser Asp Leu Asn Thr Gln Arg Pro Tyr Tyr Lys
```

100 105 110

<210> 568
<211> 102
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 568

Met Gly Gly Leu Glu Pro Cys Ser Arg Leu Leu Leu Leu Pro Leu Leu
1 5 10 15

Leu Ala Val Ser Asp Cys Ser Cys Ser Thr Val Ser Pro Gly Val Leu
20 25 30

Ala Gly Ile Val Met Gly Asp Leu Val Leu Thr Val Leu Ile Ala Leu
35 40 45

Ala Val Tyr Phe Leu Gly Arg Leu Val Pro Arg Gly Arg Gly Ala Ala
50 55 60

Glu Ala Ala Thr Arg Lys Gln Arg Ile Thr Glu Thr Glu Ser Pro Tyr
65 70 75 80

Gln Glu Leu Gln Gly Gln Arg Ser Asp Val Tyr Ser Asp Leu Asn Thr
85 90 95

Gln Arg Pro Tyr Tyr Lys
100

<210> 569
<211> 101
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 569

Met Gly Gly Leu Glu Pro Cys Ser Arg Leu Leu Leu Leu Pro Leu Leu
1 5 10 15

Leu Ala Val Ser Asp Cys Ser Cys Ser Thr Val Ser Pro Gly Val Leu
20 25 30

Ala Gly Ile Val Met Gly Asp Leu Val Leu Thr Val Leu Ile Ala Leu
35 40 45

Ala Val Tyr Phe Leu Gly Arg Leu Val Pro Arg Gly Arg Gly Ala Ala
50 55 60

Glu Ala Thr Arg Lys Gln Arg Ile Thr Glu Thr Glu Ser Pro Tyr Gln

65 70 75 80

Glu Leu Gln Gly Gln Arg Ser Asp Val Tyr Ser Asp Leu Asn Thr Gln
85 90 95

Arg Pro Tyr Tyr Lys
100

<210> 570
<211> 21
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 570

Glu Ser Pro Tyr Gln Glu Leu Gln Gly Gln Arg Ser Asp Val Tyr Ser
1 5 10 15

Asp Leu Asn Thr Gln
20

<210> 571
<211> 86
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 571

Met Ile Pro Ala Val Val Leu Leu Leu Leu Leu Val Glu Gln Ala
1 5 10 15

Ala Ala Leu Gly Glu Pro Gln Leu Cys Tyr Ile Leu Asp Ala Ile Leu
20 25 30

Phe Leu Tyr Gly Ile Val Leu Thr Leu Leu Tyr Cys Arg Leu Lys Ile
35 40 45

Gln Val Arg Lys Ala Ala Ile Thr Ser Tyr Glu Lys Ser Asp Gly Val
50 55 60

Tyr Thr Gly Leu Ser Thr Arg Asn Gln Glu Thr Tyr Glu Thr Leu Lys
65 70 75 80

His Glu Lys Pro Pro Gln
85

<210> 572
<211> 21
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 572

Asp Gly Val Tyr Thr Gly Leu Ser Thr Arg Asn Gln Glu Thr Tyr Glu
1 5 10 15

Thr Leu Lys His Glu
20

<210> 573
<211> 171
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 573

Met Glu His Ser Thr Phe Leu Ser Gly Leu Val Leu Ala Thr Leu Leu
1 5 10 15

Ser Gln Val Ser Pro Phe Lys Ile Pro Ile Glu Glu Leu Glu Asp Arg
20 25 30

Val Phe Val Asn Cys Asn Thr Ser Ile Thr Trp Val Glu Gly Thr Val
35 40 45

Gly Thr Leu Leu Ser Asp Ile Thr Arg Leu Asp Leu Gly Lys Arg Ile
50 55 60

Leu Asp Pro Arg Gly Ile Tyr Arg Cys Asn Gly Thr Asp Ile Tyr Lys
65 70 75 80

Asp Lys Glu Ser Thr Val Gln Val His Tyr Arg Met Cys Gln Ser Cys
85 90 95

Val Glu Leu Asp Pro Ala Thr Val Ala Gly Ile Ile Val Thr Asp Val
100 105 110

Ile Ala Thr Leu Leu Leu Ala Leu Gly Val Phe Cys Phe Ala Gly His
115 120 125

Glu Thr Gly Arg Leu Ser Gly Ala Ala Asp Thr Gln Ala Leu Leu Arg
130 135 140

Asn Asp Gln Val Tyr Gln Pro Leu Arg Asp Arg Asp Asp Ala Gln Tyr
145 150 155 160

Ser His Leu Gly Gly Asn Trp Ala Arg Asn Lys
165 170

<210> 574

<211> 127
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 574

Met Glu His Ser Thr Phe Leu Ser Gly Leu Val Leu Ala Thr Leu Leu
1 5 10 15

Ser Gln Val Ser Pro Phe Lys Ile Pro Ile Glu Glu Leu Glu Asp Arg
20 25 30

Val Phe Val Asn Cys Asn Thr Ser Ile Thr Trp Val Glu Gly Thr Val
35 40 45

Gly Thr Leu Leu Ser Asp Ile Thr Arg Leu Asp Leu Gly Lys Arg Ile
50 55 60

Leu Asp Pro Arg Gly Ile Tyr Arg Cys Asn Gly Thr Asp Ile Tyr Lys
65 70 75 80

Asp Lys Glu Ser Thr Val Gln Val His Tyr Arg Thr Ala Asp Thr Gln
85 90 95

Ala Leu Leu Arg Asn Asp Gln Val Tyr Gln Pro Leu Arg Asp Arg Asp
100 105 110

Asp Ala Gln Tyr Ser His Leu Gly Gly Asn Trp Ala Arg Asn Lys
115 120 125

<210> 575
<211> 21
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 575

Asp Gln Val Tyr Gln Pro Leu Arg Asp Arg Asp Asp Ala Gln Tyr Ser
1 5 10 15

His Leu Gly Gly Asn
20

<210> 576
<211> 207
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 576

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Met Gln Ser Gly Thr His Trp Arg Val Leu Gly Leu Cys Leu Leu Ser
1               5                  10                  15

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

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

Cys Pro Gln Tyr Pro Gly Ser Glu Ile Leu Trp Gln His Asn Asp Lys
    50                  55                  60

Asn Ile Gly Gly Asp Glu Asp Asp Lys Asn Ile Gly Ser Asp Glu Asp
65                  70                  75                  80

His Leu Ser Leu Lys Glu Phe Ser Glu Leu Glu Gln Ser Gly Tyr Tyr
                85                  90                  95

Val Cys Tyr Pro Arg Gly Ser Lys Pro Glu Asp Ala Asn Phe Tyr Leu
            100                 105                 110

Tyr Leu Arg Ala Arg Val Cys Glu Asn Cys Met Glu Met Asp Val Met
        115                 120                 125

Ser Val Ala Thr Ile Val Ile Val Asp Ile Cys Ile Thr Gly Gly Leu
    130                 135                 140

Leu Leu Leu Val Tyr Tyr Trp Ser Lys Asn Arg Lys Ala Lys Ala Lys
145                 150                 155                 160

Pro Val Thr Arg Gly Ala Gly Ala Gly Gly Arg Gln Arg Gly Gln Asn
                165                 170                 175

Lys Glu Arg Pro Pro Pro Val Pro Asn Pro Asp Tyr Glu Pro Ile Arg
            180                 185                 190

Lys Gly Gln Arg Asp Leu Tyr Ser Gly Leu Asn Gln Arg Arg Ile
        195                 200                 205


<210>  577
<211>  21
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic amino acid sequence

<400>  577

Asn Pro Asp Tyr Glu Pro Ile Arg Lys Gly Gln Arg Asp Leu Tyr Ser
1               5                  10                  15

Gly Leu Asn Gln Arg
```

20

<210> 578
<211> 182
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 578

Met Glu Gln Gly Lys Gly Leu Ala Val Leu Ile Leu Ala Ile Ile Leu
1 5 10 15

Leu Gln Gly Thr Leu Ala Gln Ser Ile Lys Gly Asn His Leu Val Lys
20 25 30

Val Tyr Asp Tyr Gln Glu Asp Gly Ser Val Leu Leu Thr Cys Asp Ala
35 40 45

Glu Ala Lys Asn Ile Thr Trp Phe Lys Asp Gly Lys Met Ile Gly Phe
50 55 60

Leu Thr Glu Asp Lys Lys Lys Trp Asn Leu Gly Ser Asn Ala Lys Asp
65 70 75 80

Pro Arg Gly Met Tyr Gln Cys Lys Gly Ser Gln Asn Lys Ser Lys Pro
85 90 95

Leu Gln Val Tyr Tyr Arg Met Cys Gln Asn Cys Ile Glu Leu Asn Ala
100 105 110

Ala Thr Ile Ser Gly Phe Leu Phe Ala Glu Ile Val Ser Ile Phe Val
115 120 125

Leu Ala Val Gly Val Tyr Phe Ile Ala Gly Gln Asp Gly Val Arg Gln
130 135 140

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

Gln Pro Leu Lys Asp Arg Glu Asp Asp Gln Tyr Ser His Leu Gln Gly
165 170 175

Asn Gln Leu Arg Arg Asn
180

<210> 579
<211> 21
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 579

Asp Gln Leu Tyr Gln Pro Leu Lys Asp Arg Glu Asp Asp Gln Tyr Ser
1 5 10 15

His Leu Gln Gly Asn
20

<210> 580
<211> 163
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 580

Met Lys Trp Lys Ala Leu Phe Thr Ala Ala Ile Leu Gln Ala Gln Leu
1 5 10 15

Pro Ile Thr Glu Ala Gln Ser Phe Gly Leu Leu Asp Pro Lys Leu Cys
20 25 30

Tyr Leu Leu Asp Gly Ile Leu Phe Ile Tyr Gly Val Ile Leu Thr Ala
35 40 45

Leu Phe Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr
50 55 60

Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg
65 70 75 80

Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met
85 90 95

Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu
100 105 110

Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys
115 120 125

Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu
130 135 140

Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu
145 150 155 160

Pro Pro Arg

<210> 581
<211> 164
<212> PRT

<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 581

Met Lys Trp Lys Ala Leu Phe Thr Ala Ala Ile Leu Gln Ala Gln Leu
1 5 10 15

Pro Ile Thr Glu Ala Gln Ser Phe Gly Leu Leu Asp Pro Lys Leu Cys
20 25 30

Tyr Leu Leu Asp Gly Ile Leu Phe Ile Tyr Gly Val Ile Leu Thr Ala
35 40 45

Leu Phe Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr
50 55 60

Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg
65 70 75 80

Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met
85 90 95

Gly Gly Lys Pro Gln Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn
100 105 110

Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met
115 120 125

Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly
130 135 140

Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala
145 150 155 160

Leu Pro Pro Arg

<210> 582
<211> 112
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 582

Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly
1 5 10 15

Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr
20 25 30

Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys
35 40 45

Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys
50 55 60

Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg
65 70 75 80

Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala
85 90 95

Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
100 105 110

<210> 583
<211> 21
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 583

Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp
1 5 10 15

Val Leu Asp Lys Arg
20

<210> 584
<211> 22
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 584

Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr
1 5 10 15

Ser Glu Ile Gly Met Lys
20

<210> 585
<211> 21
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 585

Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp

1 5 10 15

Ala Leu His Met Gln
20

<210> 586
<211> 226
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 586

Met Pro Gly Gly Pro Gly Val Leu Gln Ala Leu Pro Ala Thr Ile Phe
1 5 10 15

Leu Leu Phe Leu Leu Ser Ala Val Tyr Leu Gly Pro Gly Cys Gln Ala
20 25 30

Leu Trp Met His Lys Val Pro Ala Ser Leu Met Val Ser Leu Gly Glu
35 40 45

Asp Ala His Phe Gln Cys Pro His Asn Ser Ser Asn Asn Ala Asn Val
50 55 60

Thr Trp Trp Arg Val Leu His Gly Asn Tyr Thr Trp Pro Pro Glu Phe
65 70 75 80

Leu Gly Pro Gly Glu Asp Pro Asn Gly Thr Leu Ile Ile Gln Asn Val
85 90 95

Asn Lys Ser His Gly Gly Ile Tyr Val Cys Arg Val Gln Glu Gly Asn
100 105 110

Glu Ser Tyr Gln Gln Ser Cys Gly Thr Tyr Leu Arg Val Arg Gln Pro
115 120 125

Pro Pro Arg Pro Phe Leu Asp Met Gly Glu Gly Thr Lys Asn Arg Ile
130 135 140

Ile Thr Ala Glu Gly Ile Ile Leu Leu Phe Cys Ala Val Val Pro Gly
145 150 155 160

Thr Leu Leu Leu Phe Arg Lys Arg Trp Gln Asn Glu Lys Leu Gly Leu
165 170 175

Asp Ala Gly Asp Glu Tyr Glu Asp Glu Asn Leu Tyr Glu Gly Leu Asn
180 185 190

Leu Asp Asp Cys Ser Met Tyr Glu Asp Ile Ser Arg Gly Leu Gln Gly
195 200 205

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

Lys Pro
225

<210> 587
<211> 188
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 587

Met Pro Gly Gly Pro Gly Val Leu Gln Ala Leu Pro Ala Thr Ile Phe
1 5 10 15

Leu Leu Phe Leu Leu Ser Ala Val Tyr Leu Gly Pro Gly Cys Gln Ala
20 25 30

Leu Trp Met His Lys Val Pro Ala Ser Leu Met Val Ser Leu Gly Glu
35 40 45

Asp Ala His Phe Gln Cys Pro His Asn Ser Ser Asn Asn Ala Asn Val
50 55 60

Thr Trp Trp Arg Val Leu His Gly Asn Tyr Thr Trp Pro Pro Glu Phe
65 70 75 80

Leu Gly Pro Gly Glu Asp Pro Asn Glu Pro Pro Pro Arg Pro Phe Leu
85 90 95

Asp Met Gly Glu Gly Thr Lys Asn Arg Ile Ile Thr Ala Glu Gly Ile
100 105 110

Ile Leu Leu Phe Cys Ala Val Val Pro Gly Thr Leu Leu Leu Phe Arg
115 120 125

Lys Arg Trp Gln Asn Glu Lys Leu Gly Leu Asp Ala Gly Asp Glu Tyr
130 135 140

Glu Asp Glu Asn Leu Tyr Glu Gly Leu Asn Leu Asp Asp Cys Ser Met
145 150 155 160

Tyr Glu Asp Ile Ser Arg Gly Leu Gln Gly Thr Tyr Gln Asp Val Gly
165 170 175

Ser Leu Asn Ile Gly Asp Val Gln Leu Glu Lys Pro
180 185

<210> 588

<211> 21
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 588

Glu Asn Leu Tyr Glu Gly Leu Asn Leu Asp Asp Cys Ser Met Tyr Glu
1 5 10 15

Asp Ile Ser Arg Gly
20

<210> 589
<211> 20
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 589

Arg Pro Arg Arg Ser Pro Ala Gln Asp Gly Lys Val Tyr Ile Asn Met
1 5 10 15

Pro Gly Arg Gly
20

<210> 590
<211> 20
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 590

Arg Pro Arg Arg Ser Pro Ala Gln Asp Gly Lys Val Tyr Ile Asn Met
1 5 10 15

Pro Gly Arg Gly
20

<210> 591
<211> 68
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 591

Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu
1 5 10 15

Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg Ser

20 25 30

Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro Gly
35 40 45

Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe Ala
50 55 60

Ala Tyr Arg Ser
65

<210> 592
<211> 68
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 592

Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu
1 5 10 15

Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg Ser
20 25 30

Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro Gly
35 40 45

Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe Ala
50 55 60

Ala Tyr Arg Ser
65

<210> 593
<211> 619
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 593

Met Pro Asp Pro Ala Ala His Leu Pro Phe Phe Tyr Gly Ser Ile Ser
1 5 10 15

Arg Ala Glu Ala Glu Glu His Leu Lys Leu Ala Gly Met Ala Asp Gly
20 25 30

Leu Phe Leu Leu Arg Gln Cys Leu Arg Ser Leu Gly Gly Tyr Val Leu
35 40 45

Ser Leu Val His Asp Val Arg Phe His His Phe Pro Ile Glu Arg Gln

50 55 60

Leu Asn Gly Thr Tyr Ala Ile Ala Gly Gly Lys Ala His Cys Gly Pro
65 70 75 80

Ala Glu Leu Cys Glu Phe Tyr Ser Arg Asp Pro Asp Gly Leu Pro Cys
85 90 95

Asn Leu Arg Lys Pro Cys Asn Arg Pro Ser Gly Leu Glu Pro Gln Pro
100 105 110

Gly Val Phe Asp Cys Leu Arg Asp Ala Met Val Arg Asp Tyr Val Arg
115 120 125

Gln Thr Trp Lys Leu Glu Gly Glu Ala Leu Glu Gln Ala Ile Ile Ser
130 135 140

Gln Ala Pro Gln Val Glu Lys Leu Ile Ala Thr Thr Ala His Glu Arg
145 150 155 160

Met Pro Trp Tyr His Ser Ser Leu Thr Arg Glu Glu Ala Glu Arg Lys
165 170 175

Leu Tyr Ser Gly Ala Gln Thr Asp Gly Lys Phe Leu Leu Arg Pro Arg
180 185 190

Lys Glu Gln Gly Thr Tyr Ala Leu Ser Leu Ile Tyr Gly Lys Thr Val
195 200 205

Tyr His Tyr Leu Ile Ser Gln Asp Lys Ala Gly Lys Tyr Cys Ile Pro
210 215 220

Glu Gly Thr Lys Phe Asp Thr Leu Trp Gln Leu Val Glu Tyr Leu Lys
225 230 235 240

Leu Lys Ala Asp Gly Leu Ile Tyr Cys Leu Lys Glu Ala Cys Pro Asn
245 250 255

Ser Ser Ala Ser Asn Ala Ser Gly Ala Ala Ala Pro Thr Leu Pro Ala
260 265 270

His Pro Ser Thr Leu Thr His Pro Gln Arg Arg Ile Asp Thr Leu Asn
275 280 285

Ser Asp Gly Tyr Thr Pro Glu Pro Ala Arg Ile Thr Ser Pro Asp Lys
290 295 300

Pro Arg Pro Met Pro Met Asp Thr Ser Val Tyr Glu Ser Pro Tyr Ser
305 310 315 320

Asp Pro Glu Glu Leu Lys Asp Lys Lys Leu Phe Leu Lys Arg Asp Asn

325 330 335

Leu Leu Ile Ala Asp Ile Glu Leu Gly Cys Gly Asn Phe Gly Ser Val
340 345 350

Arg Gln Gly Val Tyr Arg Met Arg Lys Lys Gln Ile Asp Val Ala Ile
355 360 365

Lys Val Leu Lys Gln Gly Thr Glu Lys Ala Asp Thr Glu Glu Met Met
370 375 380

Arg Glu Ala Gln Ile Met His Gln Leu Asp Asn Pro Tyr Ile Val Arg
385 390 395 400

Leu Ile Gly Val Cys Gln Ala Glu Ala Leu Met Leu Val Met Glu Met
405 410 415

Ala Gly Gly Gly Pro Leu His Lys Phe Leu Val Gly Lys Arg Glu Glu
420 425 430

Ile Pro Val Ser Asn Val Ala Glu Leu Leu His Gln Val Ser Met Gly
435 440 445

Met Lys Tyr Leu Glu Glu Lys Asn Phe Val His Arg Asp Leu Ala Ala
450 455 460

Arg Asn Val Leu Leu Val Asn Arg His Tyr Ala Lys Ile Ser Asp Phe
465 470 475 480

Gly Leu Ser Lys Ala Leu Gly Ala Asp Asp Ser Tyr Tyr Thr Ala Arg
485 490 495

Ser Ala Gly Lys Trp Pro Leu Lys Trp Tyr Ala Pro Glu Cys Ile Asn
500 505 510

Phe Arg Lys Phe Ser Ser Arg Ser Asp Val Trp Ser Tyr Gly Val Thr
515 520 525

Met Trp Glu Ala Leu Ser Tyr Gly Gln Lys Pro Tyr Lys Lys Met Lys
530 535 540

Gly Pro Glu Val Met Ala Phe Ile Glu Gln Gly Lys Arg Met Glu Cys
545 550 555 560

Pro Pro Glu Cys Pro Pro Glu Leu Tyr Ala Leu Met Ser Asp Cys Trp
565 570 575

Ile Tyr Lys Trp Glu Asp Arg Pro Asp Phe Leu Thr Val Glu Gln Arg
580 585 590

Met Arg Ala Cys Tyr Tyr Ser Leu Ala Ser Lys Val Glu Gly Pro Pro

595 600 605

Gly Ser Thr Gln Lys Ala Glu Ala Ala Cys Ala
610 615

<210> 594
<211> 9
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<400> 594

Tyr Pro Tyr Asp Val Pro Asp Tyr Ala
1 5

<210> 595
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<400> 595

Asp Tyr Lys Asp Asp Asp Asp Lys
1 5

<210> 596
<211> 10
<212> PRT
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<220>
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<400> 596

Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu
1 5 10

<210> 597
<211> 5
<212> PRT
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<220>
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<400> 597

His His His His His
1 5

<210> 598
<211> 6
<212> PRT
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<400> 598

His His His His His His
1 5

<210> 599
<211> 10
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 599

Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu
1 5 10

<210> 600
<211> 8
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<400> 600

Asp Tyr Lys Asp Asp Asp Asp Lys
1 5

<210> 601
<211> 8
<212> PRT
<213> Artificial sequence

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<400> 601

Trp Ser His Pro Gln Phe Glu Lys
1 5

<210> 602
<211> 9
<212> PRT
<213> Artificial sequence

<220>
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<400> 602

Tyr Pro Tyr Asp Val Pro Asp Tyr Ala
1 5

<210> 603
<211> 5
<212> PRT

<213> Artificial sequence

<220>
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<400> 603

Arg Tyr Ile Arg Ser
1 5

<210> 604
<211> 4
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<400> 604

Phe His His Thr
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<213> Artificial sequence

<220>
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<400> 605

Trp Glu Ala Ala Ala Arg Glu Ala Cys Cys Arg Glu Cys Cys Ala Arg
1 5 10 15

Ala

<210> 606
<211> 75
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 606

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
1 5 10 15

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
20 25 30

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Ser Arg Gly Ser Gly Ser
35 40 45

Gly Ser Thr Ser Pro Lys Lys Glu Asn Asn Ala Leu Leu Arg Tyr Leu
50 55 60

Leu Asp Arg Asp Asp Pro Ser Asp Ala Gly Ser
65 70 75

<210> 607
<211> 477
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 607

Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu
1 5 10 15

Ser Leu Val Ile Thr Leu Tyr Cys Ser Leu Lys Arg Gly Arg Lys Lys
20 25 30

Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr
35 40 45

Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly
50 55 60

Gly Cys Glu Leu Gly Ser Gly Ser Gly Ser Gly Ser Gly Ser Gly Ser
65 70 75 80

Gly Ser Thr Ser Glu Ser Ala Asp Leu Arg Ala Leu Ala Lys His Leu
85 90 95

Tyr Asp Ser Tyr Ile Lys Ser Phe Pro Leu Thr Lys Ala Lys Ala Arg
100 105 110

Ala Ile Leu Thr Gly Lys Thr Thr Asp Lys Ser Pro Phe Val Ile Tyr
115 120 125

Asp Met Asn Ser Leu Met Met Gly Glu Asp Lys Ile Lys Phe Lys His
130 135 140

Ile Thr Pro Leu Gln Glu Gln Ser Lys Glu Val Ala Ile Arg Ile Phe
145 150 155 160

Gln Gly Cys Gln Phe Arg Ser Val Glu Ala Val Gln Glu Ile Thr Glu
165 170 175

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

Val Thr Leu Leu Lys Tyr Gly Val His Glu Ile Ile Tyr Thr Met Leu
195 200 205

Ala Ser Leu Met Asn Lys Asp Gly Val Leu Ile Ser Glu Gly Gln Gly

210 215 220

Phe Met Thr Arg Glu Phe Leu Lys Ser Leu Arg Lys Pro Phe Gly Asp
225 230 235 240

Phe Met Glu Pro Lys Phe Glu Phe Ala Val Lys Phe Asn Ala Leu Glu
245 250 255

Leu Asp Asp Ser Asp Leu Ala Ile Phe Ile Ala Val Ile Ile Leu Ser
260 265 270

Gly Asp Arg Pro Gly Leu Leu Asn Val Lys Pro Ile Glu Asp Ile Gln
275 280 285

Asp Asn Leu Leu Gln Ala Leu Glu Leu Gln Leu Lys Leu Asn His Pro
290 295 300

Glu Ser Ser Gln Leu Phe Ala Lys Leu Leu Gln Lys Met Thr Asp Leu
305 310 315 320

Arg Gln Ile Val Thr Glu His Val Gln Leu Leu Gln Val Ile Lys Lys
325 330 335

Thr Glu Thr Asp Met Ser Leu His Pro Leu Leu Gln Glu Ile Tyr Lys
340 345 350

Asp Leu Tyr Gly Ser Gly Ser Gly Ser Gly Ser Ser Leu Arg Val Lys
355 360 365

Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln
370 375 380

Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
385 390 395 400

Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
405 410 415

Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
420 425 430

Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
435 440 445

Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
450 455 460

Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
465 470 475

<210> 608

<211> 388
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 608

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Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly
1               5                  10                  15

Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr
            20                  25                  30

Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Ile
        35                  40                  45

Tyr His Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln
65                  70                  75                  80

Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr
                85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Thr Gly Gly Gly Gly Ser
            100                 105                 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Lys Leu Gln Glu
        115                 120                 125

Ser Gly Pro Gly Leu Val Ala Pro Ser Gln Ser Leu Ser Val Thr Cys
    130                 135                 140

Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg
145                 150                 155                 160

Gln Pro Pro Arg Lys Gly Leu Glu Trp Leu Gly Val Ile Trp Gly Ser
                165                 170                 175

Glu Thr Thr Tyr Tyr Asn Ser Ala Leu Lys Ser Arg Leu Thr Ile Ile
            180                 185                 190

Lys Asp Asn Ser Lys Ser Gln Val Phe Leu Lys Met Asn Ser Leu Gln
        195                 200                 205

Thr Asp Asp Thr Ala Ile Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly
    210                 215                 220

Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val
225                 230                 235                 240
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Ser Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr
                245                 250                 255

Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala
            260                 265                 270

Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile
        275                 280                 285

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

Leu Val Ile Thr Leu Tyr Cys Ser Leu Lys Arg Gly Arg Lys Lys Leu
305                 310                 315                 320

Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln
                325                 330                 335

Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly
            340                 345                 350

Cys Glu Leu Ser Arg Gly Ser Gly Ser Gly Ser Thr Ser Pro Lys Lys
        355                 360                 365

Glu Asn Asn Ala Leu Leu Arg Tyr Leu Leu Asp Arg Asp Asp Pro Ser
    370                 375                 380

Asp Ala Gly Ser
385


<210>  609
<211>  477
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic amino acid sequence

<400>  609

Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu
1               5                   10                  15

Ser Leu Val Ile Thr Leu Tyr Cys Ser Leu Lys Arg Gly Arg Lys Lys
            20                  25                  30

Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr
        35                  40                  45

Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly
    50                  55                  60

Gly Cys Glu Leu Gly Ser Gly Ser Gly Ser Gly Ser Gly Ser Gly Ser
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65 70 75 80

Gly Ser Thr Ser Glu Ser Ala Asp Leu Arg Ala Leu Ala Lys His Leu
85 90 95

Tyr Asp Ser Tyr Ile Lys Ser Phe Pro Leu Thr Lys Ala Lys Ala Arg
100 105 110

Ala Ile Leu Thr Gly Lys Thr Thr Asp Lys Ser Pro Phe Val Ile Tyr
115 120 125

Asp Met Asn Ser Leu Met Met Gly Glu Asp Lys Ile Lys Phe Lys His
130 135 140

Ile Thr Pro Leu Gln Glu Gln Ser Lys Glu Val Ala Ile Arg Ile Phe
145 150 155 160

Gln Gly Cys Gln Phe Arg Ser Val Glu Ala Val Gln Glu Ile Thr Glu
165 170 175

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

Val Thr Leu Leu Lys Tyr Gly Val His Glu Ile Ile Tyr Thr Met Leu
195 200 205

Ala Ser Leu Met Asn Lys Asp Gly Val Leu Ile Ser Glu Gly Gln Gly
210 215 220

Phe Met Thr Arg Glu Phe Leu Lys Ser Leu Arg Lys Pro Phe Gly Asp
225 230 235 240

Phe Met Glu Pro Lys Phe Glu Phe Ala Val Lys Phe Asn Ala Leu Glu
245 250 255

Leu Asp Asp Ser Asp Leu Ala Ile Phe Ile Ala Val Ile Ile Leu Ser
260 265 270

Gly Asp Arg Pro Gly Leu Leu Asn Val Lys Pro Ile Glu Asp Ile Gln
275 280 285

Asp Asn Leu Leu Gln Ala Leu Glu Leu Gln Leu Lys Leu Asn His Pro
290 295 300

Glu Ser Ser Gln Leu Phe Ala Lys Leu Leu Gln Lys Met Thr Asp Leu
305 310 315 320

Arg Gln Ile Val Thr Glu His Val Gln Leu Leu Gln Val Ile Lys Lys
325 330 335

Thr Glu Thr Asp Met Ser Leu His Pro Leu Leu Gln Glu Ile Tyr Lys

340 345 350

Asp Leu Tyr Gly Ser Gly Ser Gly Ser Gly Ser Ser Leu Arg Val Lys
355 360 365

Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln
370 375 380

Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
385 390 395 400

Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
405 410 415

Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
420 425 430

Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
435 440 445

Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
450 455 460

Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
465 470 475

<210> 610
<211> 445
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 610

Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly
1 5 10 15

Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Ile
35 40 45

Tyr His Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln
65 70 75 80

Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

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Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Thr Gly Gly Gly Gly Ser
            100                 105                 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Lys Leu Gln Glu
        115                 120                 125

Ser Gly Pro Gly Leu Val Ala Pro Ser Gln Ser Leu Ser Val Thr Cys
    130                 135                 140

Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg
145                 150                 155                 160

Gln Pro Pro Arg Lys Gly Leu Glu Trp Leu Gly Val Ile Trp Gly Ser
                165                 170                 175

Glu Thr Thr Tyr Tyr Asn Ser Ala Leu Lys Ser Arg Leu Thr Ile Ile
            180                 185                 190

Lys Asp Asn Ser Lys Ser Gln Val Phe Leu Lys Met Asn Ser Leu Gln
        195                 200                 205

Thr Asp Asp Thr Ala Ile Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly
    210                 215                 220

Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val
225                 230                 235                 240

Ser Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr
                245                 250                 255

Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala
            260                 265                 270

Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile
        275                 280                 285

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

Leu Val Ile Thr Leu Tyr Cys Ser Leu Lys Arg Gly Arg Lys Lys Leu
305                 310                 315                 320

Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln
                325                 330                 335

Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly
            340                 345                 350

Cys Glu Leu Ser Arg Gly Ser Gly Ser Gly Ser Thr Ser Met His Gly
        355                 360                 365
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Ser Leu Leu Gln Glu Lys His Arg Ile Leu His Lys Leu Leu Gln Asn
370 375 380

Gly Asn Ser Pro Ala Glu Val Ala Lys Ile Thr Ala Glu Ala Thr Gly
385 390 395 400

Lys Asp Thr Ser Ser Ile Thr Ser Cys Gly Asp Gly Asn Val Val Lys
405 410 415

Gln Glu Gln Leu Ser Pro Lys Lys Lys Glu Asn Asn Ala Leu Leu Arg
420 425 430

Tyr Leu Leu Asp Arg Asp Asp Pro Ser Asp Ala Gly Ser
435 440 445

<210> 611
<211> 477
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 611

Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu
1 5 10 15

Ser Leu Val Ile Thr Leu Tyr Cys Ser Leu Lys Arg Gly Arg Lys Lys
20 25 30

Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr
35 40 45

Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly
50 55 60

Gly Cys Glu Leu Gly Ser Gly Ser Gly Ser Gly Ser Gly Ser Gly Ser
65 70 75 80

Gly Ser Thr Ser Glu Ser Ala Asp Leu Arg Ala Leu Ala Lys His Leu
85 90 95

Tyr Asp Ser Tyr Ile Lys Ser Phe Pro Leu Thr Lys Ala Lys Ala Arg
100 105 110

Ala Ile Leu Thr Gly Lys Thr Thr Asp Lys Ser Pro Phe Val Ile Tyr
115 120 125

Asp Met Asn Ser Leu Met Met Gly Glu Asp Lys Ile Lys Phe Lys His
130 135 140

Ile Thr Pro Leu Gln Glu Gln Ser Lys Glu Val Ala Ile Arg Ile Phe

145 150 155 160

Gln Gly Cys Gln Phe Arg Ser Val Glu Ala Val Gln Glu Ile Thr Glu
165 170 175

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

Val Thr Leu Leu Lys Tyr Gly Val His Glu Ile Ile Tyr Thr Met Leu
195 200 205

Ala Ser Leu Met Asn Lys Asp Gly Val Leu Ile Ser Glu Gly Gln Gly
210 215 220

Phe Met Thr Arg Glu Phe Leu Lys Ser Leu Arg Lys Pro Phe Gly Asp
225 230 235 240

Phe Met Glu Pro Lys Phe Glu Phe Ala Val Lys Phe Asn Ala Leu Glu
245 250 255

Leu Asp Asp Ser Asp Leu Ala Ile Phe Ile Ala Val Ile Ile Leu Ser
260 265 270

Gly Asp Arg Pro Gly Leu Leu Asn Val Lys Pro Ile Glu Asp Ile Gln
275 280 285

Asp Asn Leu Leu Gln Ala Leu Glu Leu Gln Leu Lys Leu Asn His Pro
290 295 300

Glu Ser Ser Gln Leu Phe Ala Lys Leu Leu Gln Lys Met Thr Asp Leu
305 310 315 320

Arg Gln Ile Val Thr Glu His Val Gln Leu Leu Gln Val Ile Lys Lys
325 330 335

Thr Glu Thr Asp Met Ser Leu His Pro Leu Leu Gln Glu Ile Tyr Lys
340 345 350

Asp Leu Tyr Gly Ser Gly Ser Gly Ser Gly Ser Ser Leu Arg Val Lys
355 360 365

Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln
370 375 380

Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
385 390 395 400

Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
405 410 415

Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met

420 425 430

Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
435 440 445

Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
450 455 460

Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
465 470 475

<210> 612
<211> 445
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 612

Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly
1 5 10 15

Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Ile
35 40 45

Tyr His Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln
65 70 75 80

Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Thr Gly Gly Gly Gly Ser
100 105 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Lys Leu Gln Glu
115 120 125

Ser Gly Pro Gly Leu Val Ala Pro Ser Gln Ser Leu Ser Val Thr Cys
130 135 140

Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg
145 150 155 160

Gln Pro Pro Arg Lys Gly Leu Glu Trp Leu Gly Val Ile Trp Gly Ser
165 170 175

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Glu Thr Thr Tyr Tyr Asn Ser Ala Leu Lys Ser Arg Leu Thr Ile Ile
            180                 185                 190

Lys Asp Asn Ser Lys Ser Gln Val Phe Leu Lys Met Asn Ser Leu Gln
        195                 200                 205

Thr Asp Asp Thr Ala Ile Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly
    210                 215                 220

Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val
225                 230                 235                 240

Ser Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr
                245                 250                 255

Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala
            260                 265                 270

Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile
        275                 280                 285

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

Leu Val Ile Thr Leu Tyr Cys Ser Leu Lys Arg Gly Arg Lys Lys Leu
305                 310                 315                 320

Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln
                325                 330                 335

Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly
            340                 345                 350

Cys Glu Leu Ser Arg Gly Ser Gly Ser Gly Ser Thr Ser Pro Lys Lys
        355                 360                 365

Glu Asn Asn Ala Leu Leu Arg Tyr Leu Leu Asp Arg Asp Asp Pro Ser
    370                 375                 380

Asp Ala Gly Gly Gly Ser Gly Gly Gly Ser Pro Lys Lys Glu Asn Asn
385                 390                 395                 400

Ala Leu Leu Arg Tyr Leu Leu Asp Arg Asp Asp Pro Ser Asp Ala Gly
                405                 410                 415

Gly Gly Ser Gly Gly Gly Ser Lys Lys Glu Asn Asn Ala Leu Leu Arg
            420                 425                 430

Tyr Leu Leu Asp Arg Asp Asp Pro Ser Asp Ala Gly Ser
        435                 440                 445
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<210> 613
<211> 477
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 613

Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu
1 5 10 15

Ser Leu Val Ile Thr Leu Tyr Cys Ser Leu Lys Arg Gly Arg Lys Lys
20 25 30

Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr
35 40 45

Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly
50 55 60

Gly Cys Glu Leu Gly Ser Gly Ser Gly Ser Gly Ser Gly Ser Gly Ser
65 70 75 80

Gly Ser Thr Ser Glu Ser Ala Asp Leu Arg Ala Leu Ala Lys His Leu
85 90 95

Tyr Asp Ser Tyr Ile Lys Ser Phe Pro Leu Thr Lys Ala Lys Ala Arg
100 105 110

Ala Ile Leu Thr Gly Lys Thr Thr Asp Lys Ser Pro Phe Val Ile Tyr
115 120 125

Asp Met Asn Ser Leu Met Met Gly Glu Asp Lys Ile Lys Phe Lys His
130 135 140

Ile Thr Pro Leu Gln Glu Gln Ser Lys Glu Val Ala Ile Arg Ile Phe
145 150 155 160

Gln Gly Cys Gln Phe Arg Ser Val Glu Ala Val Gln Glu Ile Thr Glu
165 170 175

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

Val Thr Leu Leu Lys Tyr Gly Val His Glu Ile Ile Tyr Thr Met Leu
195 200 205

Ala Ser Leu Met Asn Lys Asp Gly Val Leu Ile Ser Glu Gly Gln Gly
210 215 220

Phe Met Thr Arg Glu Phe Leu Lys Ser Leu Arg Lys Pro Phe Gly Asp

225 230 235 240

Phe Met Glu Pro Lys Phe Glu Phe Ala Val Lys Phe Asn Ala Leu Glu
245 250 255

Leu Asp Asp Ser Asp Leu Ala Ile Phe Ile Ala Val Ile Ile Leu Ser
260 265 270

Gly Asp Arg Pro Gly Leu Leu Asn Val Lys Pro Ile Glu Asp Ile Gln
275 280 285

Asp Asn Leu Leu Gln Ala Leu Glu Leu Gln Leu Lys Leu Asn His Pro
290 295 300

Glu Ser Ser Gln Leu Phe Ala Lys Leu Leu Gln Lys Met Thr Asp Leu
305 310 315 320

Arg Gln Ile Val Thr Glu His Val Gln Leu Leu Gln Val Ile Lys Lys
325 330 335

Thr Glu Thr Asp Met Ser Leu His Pro Leu Leu Gln Glu Ile Tyr Lys
340 345 350

Asp Leu Tyr Gly Ser Gly Ser Gly Ser Gly Ser Ser Leu Arg Val Lys
355 360 365

Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln
370 375 380

Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
385 390 395 400

Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
405 410 415

Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
420 425 430

Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
435 440 445

Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
450 455 460

Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
465 470 475

<210> 614
<211> 117
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 614

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
1 5 10 15

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
20 25 30

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Ser Arg Gly Ser Gly Ser
35 40 45

Gly Ser Thr Ser Asp Ala Phe Gln Leu Arg Gln Leu Ile Leu Arg Gly
50 55 60

Leu Gln Asp Asp Gly Gly Gly Ser Gly Gly Gly Ser Asp Ala Phe Gln
65 70 75 80

Leu Arg Gln Leu Ile Leu Arg Gly Leu Gln Asp Asp Gly Gly Gly Ser
85 90 95

Gly Gly Gly Ser Asp Ala Phe Gln Leu Arg Gln Leu Ile Leu Arg Gly
100 105 110

Leu Gln Asp Asp Gly
115

<210> 615
<211> 381
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 615

Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu
1 5 10 15

Ser Leu Val Ile Thr Leu Tyr Cys Ser Leu Lys Arg Gly Arg Lys Lys
20 25 30

Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr
35 40 45

Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly
50 55 60

Gly Cys Glu Leu Gly Ser Gly Ser Gly Ser Gly Ser Gly Ser Gly Ser
65 70 75 80

Gly Ser Thr Ser Asp Arg Arg Gly Gly Arg Met Leu Lys His Lys Arg

85 90 95

Gln Arg Asp Asp Gly Glu Gly Arg Gly Glu Val Gly Ser Ala Gly Asp
100 105 110

Met Arg Ala Ala Asn Leu Trp Pro Ser Pro Leu Met Ile Lys Arg Ser
115 120 125

Lys Lys Asn Ser Leu Ala Leu Ser Leu Thr Ala Asp Gln Met Val Ser
130 135 140

Ala Leu Leu Asp Ala Glu Pro Pro Ile Leu Tyr Ser Glu Tyr Asp Pro
145 150 155 160

Thr Arg Pro Phe Ser Glu Ala Ser Met Met Gly Leu Leu Thr Asn Leu
165 170 175

Ala Asp Arg Glu Leu Val His Met Ile Asn Trp Ala Lys Arg Val Pro
180 185 190

Gly Phe Val Asp Leu Thr Leu His Asp Gln Val His Leu Leu Glu Cys
195 200 205

Ala Trp Leu Glu Ile Leu Met Ile Gly Leu Val Trp Arg Ser Met Glu
210 215 220

His Pro Gly Lys Leu Leu Phe Ala Pro Asn Leu Leu Leu Asp Arg Asn
225 230 235 240

Gln Gly Lys Cys Val Glu Gly Met Val Glu Ile Phe Asp Met Leu Leu
245 250 255

Ala Thr Ser Ser Arg Phe Arg Met Met Asn Leu Gln Gly Glu Glu Phe
260 265 270

Val Cys Leu Lys Ser Ile Ile Leu Leu Asn Ser Gly Val Tyr Thr Phe
275 280 285

Leu Ser Ser Thr Leu Lys Ser Leu Glu Glu Lys Asp His Ile His Arg
290 295 300

Val Leu Asp Lys Ile Thr Asp Thr Leu Ile His Leu Met Ala Lys Ala
305 310 315 320

Gly Leu Thr Leu Gln Gln Gln His Gln Arg Leu Ala Gln Leu Leu Leu
325 330 335

Ile Leu Ser His Ile Arg His Met Ser Asn Lys Gly Met Glu His Leu
340 345 350

Tyr Ser Met Lys Cys Lys Asn Val Val Pro Leu Tyr Asp Leu Leu Leu

355 360 365

Glu Met Leu Asp Ala His Arg Leu His Ala Pro Thr Ser
370 375 380

<210> 616
<211> 431
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 616

Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly
1 5 10 15

Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Ile
35 40 45

Tyr His Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln
65 70 75 80

Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Thr Gly Gly Gly Gly Ser
100 105 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Lys Leu Gln Glu
115 120 125

Ser Gly Pro Gly Leu Val Ala Pro Ser Gln Ser Leu Ser Val Thr Cys
130 135 140

Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg
145 150 155 160

Gln Pro Pro Arg Lys Gly Leu Glu Trp Leu Gly Val Ile Trp Gly Ser
165 170 175

Glu Thr Thr Tyr Tyr Asn Ser Ala Leu Lys Ser Arg Leu Thr Ile Ile
180 185 190

Lys Asp Asn Ser Lys Ser Gln Val Phe Leu Lys Met Asn Ser Leu Gln
195 200 205

```
Thr Asp Asp Thr Ala Ile Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly
    210                 215                 220

Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val
225                 230                 235                 240

Ser Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr
                245                 250                 255

Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala
            260                 265                 270

Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile
        275                 280                 285

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

Leu Val Ile Thr Leu Tyr Cys Ser Leu Lys Arg Gly Arg Lys Lys Leu
305                 310                 315                 320

Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln
                325                 330                 335

Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly
            340                 345                 350

Cys Glu Leu Ser Arg Gly Ser Gly Ser Gly Ser Thr Ser Asp Ala Phe
        355                 360                 365

Gln Leu Arg Gln Leu Ile Leu Arg Gly Leu Gln Asp Asp Gly Gly Gly
    370                 375                 380

Ser Gly Gly Gly Ser Asp Ala Phe Gln Leu Arg Gln Leu Ile Leu Arg
385                 390                 395                 400

Gly Leu Gln Asp Asp Gly Gly Gly Ser Gly Gly Gly Ser Asp Ala Phe
                405                 410                 415

Gln Leu Arg Gln Leu Ile Leu Arg Gly Leu Gln Asp Asp Gly Ser
            420                 425                 430
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<210> 617
<211> 429
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 617

```
Met Ile His Leu Gly His Ile Leu Phe Leu Leu Leu Leu Pro Val Ala
```

1 5 10 15

Ala Ala Gln Thr Thr Pro Gly Glu Arg Ser Ser Leu Pro Ala Phe Tyr
20 25 30

Pro Gly Thr Ser Gly Ser Cys Ser Gly Cys Gly Ser Leu Ser Leu Pro
35 40 45

Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu
50 55 60

Ser Leu Val Ile Thr Leu Tyr Cys Ser Leu Lys Arg Gly Arg Lys Lys
65 70 75 80

Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr
85 90 95

Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly
100 105 110

Gly Cys Glu Leu Gly Ser Gly Ser Gly Ser Gly Ser Gly Ser Gly Ser
115 120 125

Gly Ser Thr Ser Asp Arg Arg Gly Gly Arg Met Leu Lys His Lys Arg
130 135 140

Gln Arg Asp Asp Gly Glu Gly Arg Gly Glu Val Gly Ser Ala Gly Asp
145 150 155 160

Met Arg Ala Ala Asn Leu Trp Pro Ser Pro Leu Met Ile Lys Arg Ser
165 170 175

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

Ala Leu Leu Asp Ala Glu Pro Pro Ile Leu Tyr Ser Glu Tyr Asp Pro
195 200 205

Thr Arg Pro Phe Ser Glu Ala Ser Met Met Gly Leu Leu Thr Asn Leu
210 215 220

Ala Asp Arg Glu Leu Val His Met Ile Asn Trp Ala Lys Arg Val Pro
225 230 235 240

Gly Phe Val Asp Leu Thr Leu His Asp Gln Val His Leu Leu Glu Cys
245 250 255

Ala Trp Leu Glu Ile Leu Met Ile Gly Leu Val Trp Arg Ser Met Glu
260 265 270

His Pro Gly Lys Leu Leu Phe Ala Pro Asn Leu Leu Leu Asp Arg Asn

275 280 285

Gln Gly Lys Cys Val Glu Gly Met Val Glu Ile Phe Asp Met Leu Leu
290 295 300

Ala Thr Ser Ser Arg Phe Arg Met Met Asn Leu Gln Gly Glu Glu Phe
305 310 315 320

Val Cys Leu Lys Ser Ile Ile Leu Leu Asn Ser Gly Val Tyr Thr Phe
325 330 335

Leu Ser Ser Thr Leu Lys Ser Leu Glu Glu Lys Asp His Ile His Arg
340 345 350

Val Leu Asp Lys Ile Thr Asp Thr Leu Ile His Leu Met Ala Lys Ala
355 360 365

Gly Leu Thr Leu Gln Gln Gln His Gln Arg Leu Ala Gln Leu Leu Leu
370 375 380

Ile Leu Ser His Ile Arg His Met Ser Asn Lys Gly Met Glu His Leu
385 390 395 400

Tyr Ser Met Lys Cys Lys Asn Val Val Pro Leu Tyr Asp Leu Leu Leu
405 410 415

Glu Met Leu Asp Ala His Arg Leu His Ala Pro Thr Ser
420 425

<210> 618
<211> 42
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 618

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
1 5 10 15

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
20 25 30

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu
35 40

<210> 619
<211> 44
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 619

Phe Trp Val Arg Ser Lys Arg Ser Arg Leu Leu His Ser Asp Tyr Met
1 5 10 15

Asn Met Thr Pro Arg Arg Pro Gly Pro Thr Arg Lys His Tyr Gln Pro
20 25 30

Tyr Ala Pro Pro Arg Asp Phe Ala Ala Tyr Arg Ser
35 40

<210> 620
<211> 35
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 620

Thr Lys Lys Lys Tyr Ser Ser Ser Val His Asp Pro Asn Gly Glu Tyr
1 5 10 15

Met Phe Met Arg Ala Val Asn Thr Ala Lys Lys Ser Arg Leu Thr Asp
20 25 30

Val Thr Leu
35

<210> 621
<211> 37
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 621

Arg Arg Asp Gln Arg Leu Pro Pro Asp Ala His Lys Pro Pro Gly Gly
1 5 10 15

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

Thr Leu Ala Lys Ile
35

<210> 622
<211> 114
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 622

```
Cys Cys Leu Arg Arg His Gln Gly Lys Gln Asn Glu Leu Ser Asp Thr
1               5                   10                  15

Ala Gly Arg Glu Ile Asn Leu Val Asp Ala His Leu Lys Ser Glu Gln
            20                  25                  30

Thr Glu Ala Ser Thr Arg Gln Asn Ser Gln Val Leu Leu Ser Glu Thr
        35                  40                  45

Gly Ile Tyr Asp Asn Asp Pro Asp Leu Cys Phe Arg Met Gln Glu Gly
    50                  55                  60

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

Val Tyr Ala Ser Leu Asn His Ser Val Ile Gly Pro Asn Ser Arg Leu
                85                  90                  95

Ala Arg Asn Val Lys Glu Ala Pro Thr Glu Tyr Ala Ser Ile Cys Val
            100                 105                 110

Arg Ser
```

<210> 623
<211> 49
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 623

```
His Gln Arg Arg Lys Tyr Arg Ser Asn Lys Gly Glu Ser Pro Val Glu
1               5                   10                  15

Pro Ala Glu Pro Cys Arg Tyr Ser Cys Pro Arg Glu Glu Glu Gly Ser
            20                  25                  30

Thr Ile Pro Ile Gln Glu Asp Tyr Arg Lys Pro Glu Pro Ala Cys Ser
        35                  40                  45

Pro
```

<210> 624
<211> 187
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 624

```
Arg Arg Ala Cys Arg Lys Arg Ile Arg Gln Lys Leu His Leu Cys Tyr
1               5                   10                  15

Pro Val Gln Thr Ser Gln Pro Lys Leu Glu Leu Val Asp Ser Arg Pro
            20                  25                  30

Arg Arg Ser Ser Thr Gln Leu Arg Ser Gly Ala Ser Val Thr Glu Pro
        35                  40                  45

Val Ala Glu Glu Arg Gly Leu Met Ser Gln Pro Leu Met Glu Thr Cys
    50                  55                  60

His Ser Val Gly Ala Ala Tyr Leu Glu Ser Leu Pro Leu Gln Asp Ala
65                  70                  75                  80

Ser Pro Ala Gly Gly Pro Ser Ser Pro Arg Asp Leu Pro Glu Pro Arg
                85                  90                  95

Val Ser Thr Glu His Thr Asn Asn Lys Ile Glu Lys Ile Tyr Ile Met
            100                 105                 110

Lys Ala Asp Thr Val Ile Val Gly Thr Val Lys Ala Glu Leu Pro Glu
        115                 120                 125

Gly Arg Gly Leu Ala Gly Pro Ala Glu Pro Glu Leu Glu Glu Glu Leu
    130                 135                 140

Glu Ala Asp His Thr Pro His Tyr Pro Glu Gln Glu Thr Glu Pro Pro
145                 150                 155                 160

Leu Gly Ser Cys Ser Asp Val Met Leu Ser Val Glu Glu Glu Gly Lys
                165                 170                 175

Glu Asp Pro Leu Pro Thr Ala Ala Ser Gly Lys
            180                 185


<210>  625
<211>  54
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic amino acid sequence

<400>  625

His Ile Trp Gln Leu Arg Ser Gln Cys Met Trp Pro Arg Glu Thr Gln
1               5                   10                  15

Leu Leu Leu Glu Val Pro Pro Ser Thr Glu Asp Ala Arg Ser Cys Gln
            20                  25                  30

Phe Pro Glu Glu Glu Arg Gly Glu Arg Ser Ala Glu Glu Lys Gly Arg
```

35 40 45

Leu Gly Asp Leu Trp Val
50

<210> 626
<211> 60
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 626

Cys Val Lys Arg Arg Lys Pro Arg Gly Asp Val Val Lys Val Ile Val
1 5 10 15

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

Glu Ala Leu Gln Ala Pro Pro Asp Val Thr Thr Val Ala Val Glu Glu
35 40 45

Thr Ile Pro Ser Phe Thr Gly Arg Ser Pro Asn His
50 55 60

<210> 627
<211> 113
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 627

Met Gly Gly Leu Glu Pro Cys Ser Arg Leu Leu Leu Leu Pro Leu Leu
1 5 10 15

Leu Ala Val Ser Gly Leu Arg Pro Val Gln Ala Gln Ala Gln Ser Asp
20 25 30

Cys Ser Cys Ser Thr Val Ser Pro Gly Val Leu Ala Gly Ile Val Met
35 40 45

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

Gly Arg Leu Val Pro Arg Gly Arg Gly Ala Ala Glu Ala Ala Thr Arg
65 70 75 80

Lys Gln Arg Ile Thr Glu Thr Glu Ser Pro Tyr Gln Glu Leu Gln Gly
85 90 95

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

100 105 110

Lys

<210> 628
<211> 112
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 628

Met Gly Gly Leu Glu Pro Cys Ser Arg Leu Leu Leu Leu Pro Leu Leu
1 5 10 15

Leu Ala Val Ser Gly Leu Arg Pro Val Gln Ala Gln Ala Gln Ser Asp
20 25 30

Cys Ser Cys Ser Thr Val Ser Pro Gly Val Leu Ala Gly Ile Val Met
35 40 45

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

Gly Arg Leu Val Pro Arg Gly Arg Gly Ala Ala Glu Ala Thr Arg Lys
65 70 75 80

Gln Arg Ile Thr Glu Thr Glu Ser Pro Tyr Gln Glu Leu Gln Gly Gln
85 90 95

Arg Ser Asp Val Tyr Ser Asp Leu Asn Thr Gln Arg Pro Tyr Tyr Lys
100 105 110

<210> 629
<211> 102
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 629

Met Gly Gly Leu Glu Pro Cys Ser Arg Leu Leu Leu Leu Pro Leu Leu
1 5 10 15

Leu Ala Val Ser Asp Cys Ser Cys Ser Thr Val Ser Pro Gly Val Leu
20 25 30

Ala Gly Ile Val Met Gly Asp Leu Val Leu Thr Val Leu Ile Ala Leu
35 40 45

Ala Val Tyr Phe Leu Gly Arg Leu Val Pro Arg Gly Arg Gly Ala Ala

50 55 60

Glu Ala Ala Thr Arg Lys Gln Arg Ile Thr Glu Thr Glu Ser Pro Tyr
65 70 75 80

Gln Glu Leu Gln Gly Gln Arg Ser Asp Val Tyr Ser Asp Leu Asn Thr
85 90 95

Gln Arg Pro Tyr Tyr Lys
100

<210> 630
<211> 101
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 630

Met Gly Gly Leu Glu Pro Cys Ser Arg Leu Leu Leu Leu Pro Leu Leu
1 5 10 15

Leu Ala Val Ser Asp Cys Ser Cys Ser Thr Val Ser Pro Gly Val Leu
20 25 30

Ala Gly Ile Val Met Gly Asp Leu Val Leu Thr Val Leu Ile Ala Leu
35 40 45

Ala Val Tyr Phe Leu Gly Arg Leu Val Pro Arg Gly Arg Gly Ala Ala
50 55 60

Glu Ala Thr Arg Lys Gln Arg Ile Thr Glu Thr Glu Ser Pro Tyr Gln
65 70 75 80

Glu Leu Gln Gly Gln Arg Ser Asp Val Tyr Ser Asp Leu Asn Thr Gln
85 90 95

Arg Pro Tyr Tyr Lys
100

<210> 631
<211> 21
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 631

Glu Ser Pro Tyr Gln Glu Leu Gln Gly Gln Arg Ser Asp Val Tyr Ser
1 5 10 15

Asp Leu Asn Thr Gln

20

<210> 632
<211> 86
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 632

Met Ile Pro Ala Val Val Leu Leu Leu Leu Leu Val Glu Gln Ala
1 5 10 15

Ala Ala Leu Gly Glu Pro Gln Leu Cys Tyr Ile Leu Asp Ala Ile Leu
20 25 30

Phe Leu Tyr Gly Ile Val Leu Thr Leu Leu Tyr Cys Arg Leu Lys Ile
35 40 45

Gln Val Arg Lys Ala Ala Ile Thr Ser Tyr Glu Lys Ser Asp Gly Val
50 55 60

Tyr Thr Gly Leu Ser Thr Arg Asn Gln Glu Thr Tyr Glu Thr Leu Lys
65 70 75 80

His Glu Lys Pro Pro Gln
85

<210> 633
<211> 21
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 633

Asp Gly Val Tyr Thr Gly Leu Ser Thr Arg Asn Gln Glu Thr Tyr Glu
1 5 10 15

Thr Leu Lys His Glu
20

<210> 634
<211> 171
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 634

Met Glu His Ser Thr Phe Leu Ser Gly Leu Val Leu Ala Thr Leu Leu
1 5 10 15

Ser Gln Val Ser Pro Phe Lys Ile Pro Ile Glu Glu Leu Glu Asp Arg
            20   25   30

Val Phe Val Asn Cys Asn Thr Ser Ile Thr Trp Val Glu Gly Thr Val
        35   40   45

Gly Thr Leu Leu Ser Asp Ile Thr Arg Leu Asp Leu Gly Lys Arg Ile
    50   55   60

Leu Asp Pro Arg Gly Ile Tyr Arg Cys Asn Gly Thr Asp Ile Tyr Lys
65   70   75   80

Asp Lys Glu Ser Thr Val Gln Val His Tyr Arg Met Cys Gln Ser Cys
                85   90   95

Val Glu Leu Asp Pro Ala Thr Val Ala Gly Ile Ile Val Thr Asp Val
            100   105   110

Ile Ala Thr Leu Leu Leu Ala Leu Gly Val Phe Cys Phe Ala Gly His
        115   120   125

Glu Thr Gly Arg Leu Ser Gly Ala Ala Asp Thr Gln Ala Leu Leu Arg
    130   135   140

Asn Asp Gln Val Tyr Gln Pro Leu Arg Asp Arg Asp Asp Ala Gln Tyr
145   150   155   160

Ser His Leu Gly Gly Asn Trp Ala Arg Asn Lys
                165   170

<210> 635
<211> 127
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 635

Met Glu His Ser Thr Phe Leu Ser Gly Leu Val Leu Ala Thr Leu Leu
1   5   10   15

Ser Gln Val Ser Pro Phe Lys Ile Pro Ile Glu Glu Leu Glu Asp Arg
            20   25   30

Val Phe Val Asn Cys Asn Thr Ser Ile Thr Trp Val Glu Gly Thr Val
        35   40   45

Gly Thr Leu Leu Ser Asp Ile Thr Arg Leu Asp Leu Gly Lys Arg Ile
    50   55   60

Leu Asp Pro Arg Gly Ile Tyr Arg Cys Asn Gly Thr Asp Ile Tyr Lys

65 70 75 80

Asp Lys Glu Ser Thr Val Gln Val His Tyr Arg Thr Ala Asp Thr Gln
85 90 95

Ala Leu Leu Arg Asn Asp Gln Val Tyr Gln Pro Leu Arg Asp Arg Asp
100 105 110

Asp Ala Gln Tyr Ser His Leu Gly Gly Asn Trp Ala Arg Asn Lys
115 120 125

<210> 636
<211> 21
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 636

Asp Gln Val Tyr Gln Pro Leu Arg Asp Arg Asp Asp Ala Gln Tyr Ser
1 5 10 15

His Leu Gly Gly Asn
20

<210> 637
<211> 207
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 637

Met Gln Ser Gly Thr His Trp Arg Val Leu Gly Leu Cys Leu Leu Ser
1 5 10 15

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

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

Cys Pro Gln Tyr Pro Gly Ser Glu Ile Leu Trp Gln His Asn Asp Lys
50 55 60

Asn Ile Gly Gly Asp Glu Asp Asp Lys Asn Ile Gly Ser Asp Glu Asp
65 70 75 80

His Leu Ser Leu Lys Glu Phe Ser Glu Leu Glu Gln Ser Gly Tyr Tyr
85 90 95

Val Cys Tyr Pro Arg Gly Ser Lys Pro Glu Asp Ala Asn Phe Tyr Leu

100 105 110

Tyr Leu Arg Ala Arg Val Cys Glu Asn Cys Met Glu Met Asp Val Met
115 120 125

Ser Val Ala Thr Ile Val Ile Val Asp Ile Cys Ile Thr Gly Gly Leu
130 135 140

Leu Leu Leu Val Tyr Tyr Trp Ser Lys Asn Arg Lys Ala Lys Ala Lys
145 150 155 160

Pro Val Thr Arg Gly Ala Gly Ala Gly Gly Arg Gln Arg Gly Gln Asn
165 170 175

Lys Glu Arg Pro Pro Pro Val Pro Asn Pro Asp Tyr Glu Pro Ile Arg
180 185 190

Lys Gly Gln Arg Asp Leu Tyr Ser Gly Leu Asn Gln Arg Arg Ile
195 200 205

<210> 638
<211> 21
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 638

Asn Pro Asp Tyr Glu Pro Ile Arg Lys Gly Gln Arg Asp Leu Tyr Ser
1 5 10 15

Gly Leu Asn Gln Arg
20

<210> 639
<211> 182
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 639

Met Glu Gln Gly Lys Gly Leu Ala Val Leu Ile Leu Ala Ile Ile Leu
1 5 10 15

Leu Gln Gly Thr Leu Ala Gln Ser Ile Lys Gly Asn His Leu Val Lys
20 25 30

Val Tyr Asp Tyr Gln Glu Asp Gly Ser Val Leu Leu Thr Cys Asp Ala
35 40 45

Glu Ala Lys Asn Ile Thr Trp Phe Lys Asp Gly Lys Met Ile Gly Phe

50 55 60

Leu Thr Glu Asp Lys Lys Lys Trp Asn Leu Gly Ser Asn Ala Lys Asp
65 70 75 80

Pro Arg Gly Met Tyr Gln Cys Lys Gly Ser Gln Asn Lys Ser Lys Pro
85 90 95

Leu Gln Val Tyr Tyr Arg Met Cys Gln Asn Cys Ile Glu Leu Asn Ala
100 105 110

Ala Thr Ile Ser Gly Phe Leu Phe Ala Glu Ile Val Ser Ile Phe Val
115 120 125

Leu Ala Val Gly Val Tyr Phe Ile Ala Gly Gln Asp Gly Val Arg Gln
130 135 140

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

Gln Pro Leu Lys Asp Arg Glu Asp Asp Gln Tyr Ser His Leu Gln Gly
165 170 175

Asn Gln Leu Arg Arg Asn
180

<210> 640
<211> 21
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 640

Asp Gln Leu Tyr Gln Pro Leu Lys Asp Arg Glu Asp Asp Gln Tyr Ser
1 5 10 15

His Leu Gln Gly Asn
20

<210> 641
<211> 163
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 641

Met Lys Trp Lys Ala Leu Phe Thr Ala Ala Ile Leu Gln Ala Gln Leu
1 5 10 15

Pro Ile Thr Glu Ala Gln Ser Phe Gly Leu Leu Asp Pro Lys Leu Cys

20 25 30

Tyr Leu Leu Asp Gly Ile Leu Phe Ile Tyr Gly Val Ile Leu Thr Ala
35 40 45

Leu Phe Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr
50 55 60

Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg
65 70 75 80

Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met
85 90 95

Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu
100 105 110

Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys
115 120 125

Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu
130 135 140

Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu
145 150 155 160

Pro Pro Arg

<210> 642
<211> 164
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 642

Met Lys Trp Lys Ala Leu Phe Thr Ala Ala Ile Leu Gln Ala Gln Leu
1 5 10 15

Pro Ile Thr Glu Ala Gln Ser Phe Gly Leu Leu Asp Pro Lys Leu Cys
20 25 30

Tyr Leu Leu Asp Gly Ile Leu Phe Ile Tyr Gly Val Ile Leu Thr Ala
35 40 45

Leu Phe Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr
50 55 60

Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg
65 70 75 80

Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met
85 90 95

Gly Gly Lys Pro Gln Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn
100 105 110

Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met
115 120 125

Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly
130 135 140

Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala
145 150 155 160

Leu Pro Pro Arg

<210> 643
<211> 112
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 643

Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly
1 5 10 15

Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr
20 25 30

Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys
35 40 45

Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys
50 55 60

Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg
65 70 75 80

Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala
85 90 95

Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
100 105 110

<210> 644
<211> 21
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 644

Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp
1 5 10 15

Val Leu Asp Lys Arg
20

<210> 645
<211> 22
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 645

Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr
1 5 10 15

Ser Glu Ile Gly Met Lys
20

<210> 646
<211> 21
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 646

Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp
1 5 10 15

Ala Leu His Met Gln
20

<210> 647
<211> 226
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 647

Met Pro Gly Gly Pro Gly Val Leu Gln Ala Leu Pro Ala Thr Ile Phe
1 5 10 15

Leu Leu Phe Leu Leu Ser Ala Val Tyr Leu Gly Pro Gly Cys Gln Ala
20 25 30

Leu Trp Met His Lys Val Pro Ala Ser Leu Met Val Ser Leu Gly Glu

35 40 45

Asp Ala His Phe Gln Cys Pro His Asn Ser Ser Asn Asn Ala Asn Val
50 55 60

Thr Trp Trp Arg Val Leu His Gly Asn Tyr Thr Trp Pro Pro Glu Phe
65 70 75 80

Leu Gly Pro Gly Glu Asp Pro Asn Gly Thr Leu Ile Ile Gln Asn Val
85 90 95

Asn Lys Ser His Gly Gly Ile Tyr Val Cys Arg Val Gln Glu Gly Asn
100 105 110

Glu Ser Tyr Gln Gln Ser Cys Gly Thr Tyr Leu Arg Val Arg Gln Pro
115 120 125

Pro Pro Arg Pro Phe Leu Asp Met Gly Glu Gly Thr Lys Asn Arg Ile
130 135 140

Ile Thr Ala Glu Gly Ile Ile Leu Leu Phe Cys Ala Val Val Pro Gly
145 150 155 160

Thr Leu Leu Leu Phe Arg Lys Arg Trp Gln Asn Glu Lys Leu Gly Leu
165 170 175

Asp Ala Gly Asp Glu Tyr Glu Asp Glu Asn Leu Tyr Glu Gly Leu Asn
180 185 190

Leu Asp Asp Cys Ser Met Tyr Glu Asp Ile Ser Arg Gly Leu Gln Gly
195 200 205

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

Lys Pro
225

<210> 648
<211> 188
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 648

Met Pro Gly Gly Pro Gly Val Leu Gln Ala Leu Pro Ala Thr Ile Phe
1 5 10 15

Leu Leu Phe Leu Leu Ser Ala Val Tyr Leu Gly Pro Gly Cys Gln Ala
20 25 30

Leu Trp Met His Lys Val Pro Ala Ser Leu Met Val Ser Leu Gly Glu
35 40 45

Asp Ala His Phe Gln Cys Pro His Asn Ser Ser Asn Asn Ala Asn Val
50 55 60

Thr Trp Trp Arg Val Leu His Gly Asn Tyr Thr Trp Pro Pro Glu Phe
65 70 75 80

Leu Gly Pro Gly Glu Asp Pro Asn Glu Pro Pro Pro Arg Pro Phe Leu
85 90 95

Asp Met Gly Glu Gly Thr Lys Asn Arg Ile Ile Thr Ala Glu Gly Ile
100 105 110

Ile Leu Leu Phe Cys Ala Val Val Pro Gly Thr Leu Leu Leu Phe Arg
115 120 125

Lys Arg Trp Gln Asn Glu Lys Leu Gly Leu Asp Ala Gly Asp Glu Tyr
130 135 140

Glu Asp Glu Asn Leu Tyr Glu Gly Leu Asn Leu Asp Asp Cys Ser Met
145 150 155 160

Tyr Glu Asp Ile Ser Arg Gly Leu Gln Gly Thr Tyr Gln Asp Val Gly
165 170 175

Ser Leu Asn Ile Gly Asp Val Gln Leu Glu Lys Pro
180 185

<210> 649
<211> 21
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 649

Glu Asn Leu Tyr Glu Gly Leu Asn Leu Asp Asp Cys Ser Met Tyr Glu
1 5 10 15

Asp Ile Ser Arg Gly
20

<210> 650
<211> 20
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 650

Arg Pro Arg Arg Ser Pro Ala Gln Asp Gly Lys Val Tyr Ile Asn Met
1 5 10 15

Pro Gly Arg Gly
20

<210> 651
<211> 20
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 651

Arg Pro Arg Arg Ser Pro Ala Gln Asp Gly Lys Val Tyr Ile Asn Met
1 5 10 15

Pro Gly Arg Gly
20

<210> 652
<211> 68
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 652

Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu
1 5 10 15

Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg Ser
20 25 30

Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro Gly
35 40 45

Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe Ala
50 55 60

Ala Tyr Arg Ser
65

<210> 653
<211> 68
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 653

Phe Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu

1 5 10 15

Leu Val Thr Val Ala Phe Ile Ile Phe Trp Val Arg Ser Lys Arg Ser
20 25 30

Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro Arg Arg Pro Gly
35 40 45

Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro Arg Asp Phe Ala
50 55 60

Ala Tyr Arg Ser
65

<210> 654
<211> 619
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 654

Met Pro Asp Pro Ala Ala His Leu Pro Phe Phe Tyr Gly Ser Ile Ser
1 5 10 15

Arg Ala Glu Ala Glu Glu His Leu Lys Leu Ala Gly Met Ala Asp Gly
20 25 30

Leu Phe Leu Leu Arg Gln Cys Leu Arg Ser Leu Gly Gly Tyr Val Leu
35 40 45

Ser Leu Val His Asp Val Arg Phe His His Phe Pro Ile Glu Arg Gln
50 55 60

Leu Asn Gly Thr Tyr Ala Ile Ala Gly Gly Lys Ala His Cys Gly Pro
65 70 75 80

Ala Glu Leu Cys Glu Phe Tyr Ser Arg Asp Pro Asp Gly Leu Pro Cys
85 90 95

Asn Leu Arg Lys Pro Cys Asn Arg Pro Ser Gly Leu Glu Pro Gln Pro
100 105 110

Gly Val Phe Asp Cys Leu Arg Asp Ala Met Val Arg Asp Tyr Val Arg
115 120 125

Gln Thr Trp Lys Leu Glu Gly Glu Ala Leu Glu Gln Ala Ile Ile Ser
130 135 140

Gln Ala Pro Gln Val Glu Lys Leu Ile Ala Thr Thr Ala His Glu Arg
145 150 155 160

```
Met Pro Trp Tyr His Ser Ser Leu Thr Arg Glu Glu Ala Glu Arg Lys
                165                 170                 175

Leu Tyr Ser Gly Ala Gln Thr Asp Gly Lys Phe Leu Leu Arg Pro Arg
            180                 185                 190

Lys Glu Gln Gly Thr Tyr Ala Leu Ser Leu Ile Tyr Gly Lys Thr Val
        195                 200                 205

Tyr His Tyr Leu Ile Ser Gln Asp Lys Ala Gly Lys Tyr Cys Ile Pro
    210                 215                 220

Glu Gly Thr Lys Phe Asp Thr Leu Trp Gln Leu Val Glu Tyr Leu Lys
225                 230                 235                 240

Leu Lys Ala Asp Gly Leu Ile Tyr Cys Leu Lys Glu Ala Cys Pro Asn
                245                 250                 255

Ser Ser Ala Ser Asn Ala Ser Gly Ala Ala Ala Pro Thr Leu Pro Ala
            260                 265                 270

His Pro Ser Thr Leu Thr His Pro Gln Arg Arg Ile Asp Thr Leu Asn
        275                 280                 285

Ser Asp Gly Tyr Thr Pro Glu Pro Ala Arg Ile Thr Ser Pro Asp Lys
    290                 295                 300

Pro Arg Pro Met Pro Met Asp Thr Ser Val Tyr Glu Ser Pro Tyr Ser
305                 310                 315                 320

Asp Pro Glu Glu Leu Lys Asp Lys Lys Leu Phe Leu Lys Arg Asp Asn
                325                 330                 335

Leu Leu Ile Ala Asp Ile Glu Leu Gly Cys Gly Asn Phe Gly Ser Val
            340                 345                 350

Arg Gln Gly Val Tyr Arg Met Arg Lys Lys Gln Ile Asp Val Ala Ile
        355                 360                 365

Lys Val Leu Lys Gln Gly Thr Glu Lys Ala Asp Thr Glu Glu Met Met
    370                 375                 380

Arg Glu Ala Gln Ile Met His Gln Leu Asp Asn Pro Tyr Ile Val Arg
385                 390                 395                 400

Leu Ile Gly Val Cys Gln Ala Glu Ala Leu Met Leu Val Met Glu Met
                405                 410                 415

Ala Gly Gly Gly Pro Leu His Lys Phe Leu Val Gly Lys Arg Glu Glu
            420                 425                 430
```

```
Ile Pro Val Ser Asn Val Ala Glu Leu Leu His Gln Val Ser Met Gly
        435                 440                 445

Met Lys Tyr Leu Glu Glu Lys Asn Phe Val His Arg Asp Leu Ala Ala
    450                 455                 460

Arg Asn Val Leu Leu Val Asn Arg His Tyr Ala Lys Ile Ser Asp Phe
465                 470                 475                 480

Gly Leu Ser Lys Ala Leu Gly Ala Asp Asp Ser Tyr Tyr Thr Ala Arg
                485                 490                 495

Ser Ala Gly Lys Trp Pro Leu Lys Trp Tyr Ala Pro Glu Cys Ile Asn
            500                 505                 510

Phe Arg Lys Phe Ser Ser Arg Ser Asp Val Trp Ser Tyr Gly Val Thr
        515                 520                 525

Met Trp Glu Ala Leu Ser Tyr Gly Gln Lys Pro Tyr Lys Lys Met Lys
    530                 535                 540

Gly Pro Glu Val Met Ala Phe Ile Glu Gln Gly Lys Arg Met Glu Cys
545                 550                 555                 560

Pro Pro Glu Cys Pro Pro Glu Leu Tyr Ala Leu Met Ser Asp Cys Trp
                565                 570                 575

Ile Tyr Lys Trp Glu Asp Arg Pro Asp Phe Leu Thr Val Glu Gln Arg
            580                 585                 590

Met Arg Ala Cys Tyr Tyr Ser Leu Ala Ser Lys Val Glu Gly Pro Pro
        595                 600                 605

Gly Ser Thr Gln Lys Ala Glu Ala Ala Cys Ala
    610                 615


<210>  655
<211>  24
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic amino acid sequence

<400>  655

Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu
1               5                   10                  15

Ser Leu Val Ile Thr Leu Tyr Cys
            20


<210>  656
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<211> 23
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 656

Leu Gly Leu Leu Val Ala Gly Val Leu Val Leu Leu Val Ser Leu Gly
1 5 10 15

Val Ala Ile His Leu Cys Cys
20

<210> 657
<211> 25
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 657

Ala Leu Ile Val Leu Gly Gly Val Ala Gly Leu Leu Leu Phe Ile Gly
1 5 10 15

Leu Gly Ile Phe Phe Cys Val Arg Cys
20 25

<210> 658
<211> 23
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 658

Leu Cys Tyr Leu Leu Asp Gly Ile Leu Phe Ile Tyr Gly Val Ile Leu
1 5 10 15

Thr Ala Leu Phe Leu Arg Val
20

<210> 659
<211> 26
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 659

Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu Leu
1 5 10 15

Val Thr Val Ala Phe Ile Ile Phe Trp Val

20 25

<210> 660
<211> 26
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 660

Val Ala Ala Ile Leu Gly Leu Gly Leu Val Leu Gly Leu Leu Gly Pro
1 5 10 15

Leu Ala Ile Leu Leu Ala Leu Tyr Leu Leu
20 25

<210> 661
<211> 24
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 661

Ala Leu Pro Ala Ala Leu Ala Val Ile Ser Phe Leu Leu Gly Leu Gly
1 5 10 15

Leu Gly Val Ala Cys Val Leu Ala
20

<210> 662
<211> 203
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 662

Cys Ser Ser Asp Asp Arg Gly His Ser Ser Leu Thr Asn Ser Pro Leu
1 5 10 15

Asp Ser Ser Cys Lys Glu Ser Ser Val Ser Val Thr Ser Pro Ser Gly
20 25 30

Val Ser Ser Ser Thr Ser Gly Gly Val Ser Ser Thr Ser Asn Met His
35 40 45

Gly Ser Leu Leu Gln Glu Lys His Arg Ile Leu His Lys Leu Leu Gln
50 55 60

Asn Gly Asn Ser Pro Ala Glu Val Ala Lys Ile Thr Ala Glu Ala Thr
65 70 75 80

```
Gly Lys Asp Thr Ser Ser Ile Thr Ser Cys Gly Asp Gly Asn Val Val
                85                  90                  95

Lys Gln Glu Gln Leu Ser Pro Lys Lys Lys Glu Asn Asn Ala Leu Leu
            100                 105                 110

Arg Tyr Leu Leu Asp Arg Asp Asp Pro Ser Asp Ala Leu Ser Lys Glu
        115                 120                 125

Leu Gln Pro Gln Val Glu Gly Val Asp Asn Lys Met Ser Gln Cys Thr
    130                 135                 140

Ser Ser Thr Ile Pro Ser Ser Ser Gln Glu Lys Asp Pro Lys Ile Lys
145                 150                 155                 160

Thr Glu Thr Ser Glu Glu Gly Ser Gly Asp Leu Asp Asn Leu Asp Ala
                165                 170                 175

Ile Leu Gly Asp Leu Thr Ser Ser Asp Phe Tyr Asn Asn Ser Ile Ser
            180                 185                 190

Ser Asn Gly Ser His Leu Gly Thr Lys Gln Gln
        195                 200


<210>  663
<211>  301
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic amino acid sequence

<400>  663

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

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

Asp Thr Lys Asp Ile Gly Leu Pro Glu Ile Thr Pro Lys Leu Glu Arg
        35                  40                  45

Leu Asp Ser Lys Thr Asp Pro Ala Ser Asn Thr Lys Leu Ile Ala Met
    50                  55                  60

Lys Thr Glu Lys Glu Glu Met Ser Phe Glu Pro Gly Asp Gln Pro Gly
65                  70                  75                  80

Ser Glu Leu Asp Asn Leu Glu Glu Ile Leu Asp Asp Leu Gln Asn Ser
                85                  90                  95

Gln Leu Pro Gln Leu Phe Pro Asp Thr Arg Pro Gly Ala Pro Ala Gly
```

100 105 110

Ser Val Asp Lys Gln Ala Ile Ile Asn Asp Leu Met Gln Leu Thr Ala
115 120 125

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

Ile Ser Gln Ser Thr Phe Asn Asn Pro Arg Pro Gly Gln Leu Gly Arg
145 150 155 160

Leu Leu Pro Asn Gln Asn Leu Pro Leu Asp Ile Thr Leu Gln Ser Pro
165 170 175

Thr Gly Ala Gly Pro Phe Pro Pro Ile Arg Asn Ser Ser Pro Tyr Ser
180 185 190

Val Ile Pro Gln Pro Gly Met Met Gly Asn Gln Gly Met Ile Gly Asn
195 200 205

Gln Gly Asn Leu Gly Asn Ser Ser Thr Gly Met Ile Gly Asn Ser Ala
210 215 220

Ser Arg Pro Thr Met Pro Ser Gly Glu Trp Ala Pro Gln Ser Ser Ala
225 230 235 240

Val Arg Val Thr Cys Ala Ala Thr Thr Ser Ala Met Asn Arg Pro Val
245 250 255

Gln Gly Gly Met Ile Arg Asn Pro Ala Ala Ser Ile Pro Met Arg Pro
260 265 270

Ser Ser Gln Pro Gly Gln Arg Gln Thr Leu Gln Ser Gln Val Met Asn
275 280 285

Ile Gly Pro Ser Glu Leu Glu Met Asn Met Gly Gly Pro
290 295 300

<210> 664
<211> 270
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 664

Asn Tyr Gly Thr Asn Pro Gly Thr Pro Pro Ala Ser Thr Ser Pro Phe
1 5 10 15

Ser Gln Leu Ala Ala Asn Pro Glu Ala Ser Leu Ala Asn Arg Asn Ser
20 25 30

```
Met Val Ser Arg Gly Met Thr Gly Asn Ile Gly Gly Gln Phe Gly Thr
        35                  40                  45

Gly Ile Asn Pro Gln Met Gln Gln Asn Val Phe Gln Tyr Pro Gly Ala
    50                  55                  60

Gly Met Val Pro Gln Gly Glu Ala Asn Phe Ala Pro Ser Leu Ser Pro
65                  70                  75                  80

Gly Ser Ser Met Val Pro Met Pro Ile Pro Pro Pro Gln Ser Ser Leu
                85                  90                  95

Leu Gln Gln Thr Pro Pro Ala Ser Gly Tyr Gln Ser Pro Asp Met Lys
            100                 105                 110

Ala Trp Gln Gln Gly Ala Ile Gly Asn Asn Asn Val Phe Ser Gln Ala
        115                 120                 125

Val Gln Asn Gln Pro Thr Pro Ala Gln Pro Gly Val Tyr Asn Asn Met
    130                 135                 140

Ser Ile Thr Val Ser Met Ala Gly Gly Asn Thr Asn Val Gln Asn Met
145                 150                 155                 160

Asn Pro Met Met Ala Gln Met Gln Met Ser Ser Leu Gln Met Pro Gly
                165                 170                 175

Met Asn Thr Val Cys Pro Glu Gln Ile Asn Asp Pro Ala Leu Arg His
            180                 185                 190

Thr Gly Leu Tyr Cys Asn Gln Leu Ser Ser Thr Asp Leu Leu Lys Thr
        195                 200                 205

Glu Ala Asp Gly Thr Gln Gln Val Gln Gln Val Gln Val Phe Ala Asp
    210                 215                 220

Val Gln Cys Thr Val Asn Leu Val Gly Gly Asp Pro Tyr Leu Asn Gln
225                 230                 235                 240

Pro Gly Pro Leu Gly Thr Gln Lys Pro Thr Ser Gly Pro Gln Thr Pro
                245                 250                 255

Gln Ala Gln Gln Lys Ser Leu Leu Gln Gln Leu Leu Thr Glu
            260                 265                 270
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<210> 665
<211> 702
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 665

Lys Arg His His His Glu Val Leu Arg Gln Gly Leu Ala Phe Ser Gln
1 5 10 15

Ile Tyr Arg Phe Ser Leu Ser Asp Gly Thr Leu Val Ala Ala Gln Thr
20 25 30

Lys Ser Lys Leu Ile Arg Ser Gln Thr Thr Asn Glu Pro Gln Leu Val
35 40 45

Ile Ser Leu His Met Leu His Arg Glu Gln Asn Val Cys Val Met Asn
50 55 60

Pro Asp Leu Thr Gly Gln Thr Met Gly Lys Pro Leu Asn Pro Ile Ser
65 70 75 80

Ser Asn Ser Pro Ala His Gln Ala Leu Cys Ser Gly Asn Pro Gly Gln
85 90 95

Asp Met Thr Leu Ser Ser Asn Ile Asn Phe Pro Ile Asn Gly Pro Lys
100 105 110

Glu Gln Met Gly Met Pro Met Gly Arg Phe Gly Gly Ser Gly Gly Met
115 120 125

Asn His Val Ser Gly Met Gln Ala Thr Thr Pro Gln Gly Ser Asn Tyr
130 135 140

Ala Leu Lys Met Asn Ser Pro Ser Gln Ser Ser Pro Gly Met Asn Pro
145 150 155 160

Gly Gln Pro Thr Ser Met Leu Ser Pro Arg His Arg Met Ser Pro Gly
165 170 175

Val Ala Gly Ser Pro Arg Ile Pro Pro Ser Gln Phe Ser Pro Ala Gly
180 185 190

Ser Leu His Ser Pro Val Gly Val Cys Ser Ser Thr Gly Asn Ser His
195 200 205

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

His Gly Val Ser Leu Gly Ser Ser Leu Ala Ser Pro Asp Leu Lys Met
225 230 235 240

Gly Asn Leu Gln Asn Ser Pro Val Asn Met Asn Pro Pro Pro Leu Ser
245 250 255

Lys Met Gly Ser Leu Asp Ser Lys Asp Cys Phe Gly Leu Tyr Gly Glu

260 265 270

Pro Ser Glu Gly Thr Thr Gly Gln Ala Glu Ser Ser Cys His Pro Gly
275 280 285

Glu Gln Lys Glu Thr Asn Asp Pro Asn Leu Pro Pro Ala Val Ser Ser
290 295 300

Glu Arg Ala Asp Gly Gln Ser Arg Leu His Asp Ser Lys Gly Gln Thr
305 310 315 320

Lys Leu Leu Gln Leu Leu Thr Thr Lys Ser Asp Gln Met Glu Pro Ser
325 330 335

Pro Leu Ala Ser Ser Leu Ser Asp Thr Asn Lys Asp Ser Thr Gly Ser
340 345 350

Leu Pro Gly Ser Gly Ser Thr His Gly Thr Ser Leu Lys Glu Lys His
355 360 365

Lys Ile Leu His Arg Leu Leu Gln Asp Ser Ser Ser Pro Val Asp Leu
370 375 380

Ala Lys Leu Thr Ala Glu Ala Thr Gly Lys Asp Leu Ser Gln Glu Ser
385 390 395 400

Ser Ser Thr Ala Pro Gly Ser Glu Val Thr Ile Lys Gln Glu Pro Val
405 410 415

Ser Pro Lys Lys Lys Glu Asn Ala Leu Leu Arg Tyr Leu Leu Asp Lys
420 425 430

Asp Asp Thr Lys Asp Ile Gly Leu Pro Glu Ile Thr Pro Lys Leu Glu
435 440 445

Arg Leu Asp Ser Lys Thr Asp Pro Ala Ser Asn Thr Lys Leu Ile Ala
450 455 460

Met Lys Thr Glu Lys Glu Glu Met Ser Phe Glu Pro Gly Asp Gln Pro
465 470 475 480

Gly Ser Glu Leu Asp Asn Leu Glu Glu Ile Leu Asp Asp Leu Gln Asn
485 490 495

Ser Gln Leu Pro Gln Leu Phe Pro Asp Thr Arg Pro Gly Ala Pro Ala
500 505 510

Gly Ser Val Asp Lys Gln Ala Ile Ile Asn Asp Leu Met Gln Leu Thr
515 520 525

Ala Glu Asn Ser Pro Val Thr Pro Val Gly Ala Gln Lys Thr Ala Leu

530 535 540

Arg Ile Ser Gln Ser Thr Phe Asn Asn Pro Arg Pro Gly Gln Leu Gly
545 550 555 560

Arg Leu Leu Pro Asn Gln Asn Leu Pro Leu Asp Ile Thr Leu Gln Ser
565 570 575

Pro Thr Gly Ala Gly Pro Phe Pro Pro Ile Arg Asn Ser Ser Pro Tyr
580 585 590

Ser Val Ile Pro Gln Pro Gly Met Met Gly Asn Gln Gly Met Ile Gly
595 600 605

Asn Gln Gly Asn Leu Gly Asn Ser Ser Thr Gly Met Ile Gly Asn Ser
610 615 620

Ala Ser Arg Pro Thr Met Pro Ser Gly Glu Trp Ala Pro Gln Ser Ser
625 630 635 640

Ala Val Arg Val Thr Cys Ala Ala Thr Thr Ser Ala Met Asn Arg Pro
645 650 655

Val Gln Gly Gly Met Ile Arg Asn Pro Ala Ala Ser Ile Pro Met Arg
660 665 670

Pro Ser Ser Gln Pro Gly Gln Arg Gln Thr Leu Gln Ser Gln Val Met
675 680 685

Asn Ile Gly Pro Ser Glu Leu Glu Met Asn Met Gly Gly Pro
690 695 700

<210> 666
<211> 270
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 666

Asn Tyr Gly Thr Asn Pro Gly Thr Pro Pro Ala Ser Thr Ser Pro Phe
1 5 10 15

Ser Gln Leu Ala Ala Asn Pro Glu Ala Ser Leu Ala Asn Arg Asn Ser
20 25 30

Met Val Ser Arg Gly Met Thr Gly Asn Ile Gly Gly Gln Phe Gly Thr
35 40 45

Gly Ile Asn Pro Gln Met Gln Gln Asn Val Phe Gln Tyr Pro Gly Ala
50 55 60

```
Gly Met Val Pro Gln Gly Glu Ala Asn Phe Ala Pro Ser Leu Ser Pro
65                  70                  75                  80

Gly Ser Ser Met Val Pro Met Pro Ile Pro Pro Pro Gln Ser Ser Leu
                85                  90                  95

Leu Gln Gln Thr Pro Pro Ala Ser Gly Tyr Gln Ser Pro Asp Met Lys
            100                 105                 110

Ala Trp Gln Gln Gly Ala Ile Gly Asn Asn Asn Val Phe Ser Gln Ala
        115                 120                 125

Val Gln Asn Gln Pro Thr Pro Ala Gln Pro Gly Val Tyr Asn Asn Met
    130                 135                 140

Ser Ile Thr Val Ser Met Ala Gly Gly Asn Thr Asn Val Gln Asn Met
145                 150                 155                 160

Asn Pro Met Met Ala Gln Met Gln Met Ser Ser Leu Gln Met Pro Gly
                165                 170                 175

Met Asn Thr Val Cys Pro Glu Gln Ile Asn Asp Pro Ala Leu Arg His
            180                 185                 190

Thr Gly Leu Tyr Cys Asn Gln Leu Ser Ser Thr Asp Leu Leu Lys Thr
        195                 200                 205

Glu Ala Asp Gly Thr Gln Gln Val Gln Gln Val Gln Val Phe Ala Asp
    210                 215                 220

Val Gln Cys Thr Val Asn Leu Val Gly Gly Asp Pro Tyr Leu Asn Gln
225                 230                 235                 240

Pro Gly Pro Leu Gly Thr Gln Lys Pro Thr Ser Gly Pro Gln Thr Pro
                245                 250                 255

Gln Ala Gln Gln Lys Ser Leu Leu Gln Gln Leu Leu Thr Glu
            260                 265                 270


<210>  667
<211>  702
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic amino acid sequence

<400>  667

Lys Arg His His His Glu Val Leu Arg Gln Gly Leu Ala Phe Ser Gln
1               5                   10                  15

Ile Tyr Arg Phe Ser Leu Ser Asp Gly Thr Leu Val Ala Ala Gln Thr
```

20 25 30

Lys Ser Lys Leu Ile Arg Ser Gln Thr Thr Asn Glu Pro Gln Leu Val
35 40 45

Ile Ser Leu His Met Leu His Arg Glu Gln Asn Val Cys Val Met Asn
50 55 60

Pro Asp Leu Thr Gly Gln Thr Met Gly Lys Pro Leu Asn Pro Ile Ser
65 70 75 80

Ser Asn Ser Pro Ala His Gln Ala Leu Cys Ser Gly Asn Pro Gly Gln
85 90 95

Asp Met Thr Leu Ser Ser Asn Ile Asn Phe Pro Ile Asn Gly Pro Lys
100 105 110

Glu Gln Met Gly Met Pro Met Gly Arg Phe Gly Gly Ser Gly Gly Met
115 120 125

Asn His Val Ser Gly Met Gln Ala Thr Thr Pro Gln Gly Ser Asn Tyr
130 135 140

Ala Leu Lys Met Asn Ser Pro Ser Gln Ser Ser Pro Gly Met Asn Pro
145 150 155 160

Gly Gln Pro Thr Ser Met Leu Ser Pro Arg His Arg Met Ser Pro Gly
165 170 175

Val Ala Gly Ser Pro Arg Ile Pro Pro Ser Gln Phe Ser Pro Ala Gly
180 185 190

Ser Leu His Ser Pro Val Gly Val Cys Ser Ser Thr Gly Asn Ser His
195 200 205

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

His Gly Val Ser Leu Gly Ser Ser Leu Ala Ser Pro Asp Leu Lys Met
225 230 235 240

Gly Asn Leu Gln Asn Ser Pro Val Asn Met Asn Pro Pro Pro Leu Ser
245 250 255

Lys Met Gly Ser Leu Asp Ser Lys Asp Cys Phe Gly Leu Tyr Gly Glu
260 265 270

Pro Ser Glu Gly Thr Thr Gly Gln Ala Glu Ser Ser Cys His Pro Gly
275 280 285

Glu Gln Lys Glu Thr Asn Asp Pro Asn Leu Pro Pro Ala Val Ser Ser

290 295 300

Glu Arg Ala Asp Gly Gln Ser Arg Leu His Asp Ser Lys Gly Gln Thr
305 310 315 320

Lys Leu Leu Gln Leu Leu Thr Thr Lys Ser Asp Gln Met Glu Pro Ser
325 330 335

Pro Leu Ala Ser Ser Leu Ser Asp Thr Asn Lys Asp Ser Thr Gly Ser
340 345 350

Leu Pro Gly Ser Gly Ser Thr His Gly Thr Ser Leu Lys Glu Lys His
355 360 365

Lys Ile Leu His Arg Leu Leu Gln Asp Ser Ser Ser Pro Val Asp Leu
370 375 380

Ala Lys Leu Thr Ala Glu Ala Thr Gly Lys Asp Leu Ser Gln Glu Ser
385 390 395 400

Ser Ser Thr Ala Pro Gly Ser Glu Val Thr Ile Lys Gln Glu Pro Val
405 410 415

Ser Pro Lys Lys Lys Glu Asn Ala Leu Leu Arg Tyr Leu Leu Asp Lys
420 425 430

Asp Asp Thr Lys Asp Ile Gly Leu Pro Glu Ile Thr Pro Lys Leu Glu
435 440 445

Arg Leu Asp Ser Lys Thr Asp Pro Ala Ser Asn Thr Lys Leu Ile Ala
450 455 460

Met Lys Thr Glu Lys Glu Glu Met Ser Phe Glu Pro Gly Asp Gln Pro
465 470 475 480

Gly Ser Glu Leu Asp Asn Leu Glu Glu Ile Leu Asp Asp Leu Gln Asn
485 490 495

Ser Gln Leu Pro Gln Leu Phe Pro Asp Thr Arg Pro Gly Ala Pro Ala
500 505 510

Gly Ser Val Asp Lys Gln Ala Ile Ile Asn Asp Leu Met Gln Leu Thr
515 520 525

Ala Glu Asn Ser Pro Val Thr Pro Val Gly Ala Gln Lys Thr Ala Leu
530 535 540

Arg Ile Ser Gln Ser Thr Phe Asn Asn Pro Arg Pro Gly Gln Leu Gly
545 550 555 560

Arg Leu Leu Pro Asn Gln Asn Leu Pro Leu Asp Ile Thr Leu Gln Ser

565 570 575

Pro Thr Gly Ala Gly Pro Phe Pro Pro Ile Arg Asn Ser Ser Pro Tyr
580 585 590

Ser Val Ile Pro Gln Pro Gly Met Met Gly Asn Gln Gly Met Ile Gly
595 600 605

Asn Gln Gly Asn Leu Gly Asn Ser Ser Thr Gly Met Ile Gly Asn Ser
610 615 620

Ala Ser Arg Pro Thr Met Pro Ser Gly Glu Trp Ala Pro Gln Ser Ser
625 630 635 640

Ala Val Arg Val Thr Cys Ala Ala Thr Thr Ser Ala Met Asn Arg Pro
645 650 655

Val Gln Gly Gly Met Ile Arg Asn Pro Ala Ala Ser Ile Pro Met Arg
660 665 670

Pro Ser Ser Gln Pro Gly Gln Arg Gln Thr Leu Gln Ser Gln Val Met
675 680 685

Asn Ile Gly Pro Ser Glu Leu Glu Met Asn Met Gly Gly Pro
690 695 700

<210> 668
<211> 8
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 668

Leu Leu Arg Tyr Leu Leu Asp Lys
1 5

<210> 669
<211> 24
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 669

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

Leu Met Gly Ser Phe Asp Asp Lys
20

<210> 670

<211> 9
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 670

Ser Leu Leu Met Trp Ile Thr Gln Cys
1 5

<210> 671
<211> 9
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 671

Ser Leu Leu Met Trp Ile Thr Gln Cys
1 5

<210> 672
<211> 9
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 672

Ser Leu Leu Met Trp Ile Thr Gln Cys
1 5

<210> 673
<211> 9
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 673

Ser Leu Leu Met Trp Ile Thr Gln Cys
1 5

<210> 674
<211> 9
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 674

Ser Leu Leu Met Trp Ile Thr Gln Cys
1 5

<210> 675
<211> 275
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 675

Met Glu Thr Leu Leu Gly Leu Leu Ile Leu Trp Leu Gln Leu Gln Trp
1 5 10 15

Val Ser Ser Lys Gln Glu Val Thr Gln Ile Pro Ala Ala Leu Ser Val
20 25 30

Pro Glu Gly Glu Asn Leu Val Leu Asn Cys Ser Phe Thr Asp Ser Ala
35 40 45

Ile Tyr Asn Leu Gln Trp Phe Arg Gln Asp Pro Gly Lys Gly Leu Thr
50 55 60

Ser Leu Leu Leu Ile Gln Ser Ser Gln Arg Glu Gln Thr Ser Gly Arg
65 70 75 80

Leu Asn Ala Ser Leu Asp Lys Ser Ser Gly Arg Ser Thr Leu Tyr Ile
85 90 95

Ala Ala Ser Gln Pro Gly Asp Ser Ala Thr Tyr Leu Cys Ala Val Arg
100 105 110

Pro Thr Ser Gly Gly Ser Tyr Ile Pro Thr Phe Gly Arg Gly Thr Ser
115 120 125

Leu Ile Val His Pro Pro Asn Ile Gln Asn Pro Asp Pro Ala Val Tyr
130 135 140

Gln Leu Arg Asp Ser Lys Ser Ser Asp Lys Ser Val Cys Leu Phe Thr
145 150 155 160

Asp Phe Asp Ser Gln Thr Asn Val Ser Gln Ser Lys Asp Ser Asp Val
165 170 175

Tyr Ile Thr Asp Lys Thr Val Leu Asp Met Arg Ser Met Asp Phe Lys
180 185 190

Ser Asn Ser Ala Val Ala Trp Ser Asn Lys Ser Asp Phe Ala Cys Ala
195 200 205

Asn Ala Phe Asn Asn Ser Ile Ile Pro Glu Asp Thr Phe Phe Pro Ser
210 215 220

Pro Glu Ser Ser Cys Asp Val Lys Leu Val Glu Lys Ser Phe Glu Thr

225 230 235 240

Asp Thr Asn Leu Asn Phe Gln Asn Leu Ser Val Ile Gly Phe Arg Ile
245 250 255

Leu Leu Leu Lys Val Ala Gly Phe Asn Leu Leu Met Thr Leu Arg Leu
260 265 270

Trp Ser Ser
275

<210> 676
<211> 275
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 676

Met Glu Thr Leu Leu Gly Leu Leu Ile Leu Trp Leu Gln Leu Gln Trp
1 5 10 15

Val Ser Ser Lys Gln Glu Val Thr Gln Ile Pro Ala Ala Leu Ser Val
20 25 30

Pro Glu Gly Glu Asn Leu Val Leu Asn Cys Ser Phe Thr Asp Ser Ala
35 40 45

Ile Tyr Asn Leu Gln Trp Phe Arg Gln Asp Pro Gly Lys Gly Leu Thr
50 55 60

Ser Leu Leu Leu Ile Gln Ser Ser Gln Arg Glu Gln Thr Ser Gly Arg
65 70 75 80

Leu Asn Ala Ser Leu Asp Lys Ser Ser Gly Arg Ser Thr Leu Tyr Ile
85 90 95

Ala Ala Ser Gln Pro Gly Asp Ser Ala Thr Tyr Leu Cys Ala Val Arg
100 105 110

Pro Leu Tyr Gly Gly Ser Tyr Ile Pro Thr Phe Gly Arg Gly Thr Ser
115 120 125

Leu Ile Val His Pro Pro Asn Ile Gln Asn Pro Asp Pro Ala Val Tyr
130 135 140

Gln Leu Arg Asp Ser Lys Ser Ser Asp Lys Ser Val Cys Leu Phe Thr
145 150 155 160

Asp Phe Asp Ser Gln Thr Asn Val Ser Gln Ser Lys Asp Ser Asp Val
165 170 175

Tyr Ile Thr Asp Lys Thr Val Leu Asp Met Arg Ser Met Asp Phe Lys
180 185 190

Ser Asn Ser Ala Val Ala Trp Ser Asn Lys Ser Asp Phe Ala Cys Ala
195 200 205

Asn Ala Phe Asn Asn Ser Ile Ile Pro Glu Asp Thr Phe Phe Pro Ser
210 215 220

Pro Glu Ser Ser Cys Asp Val Lys Leu Val Glu Lys Ser Phe Glu Thr
225 230 235 240

Asp Thr Asn Leu Asn Phe Gln Asn Leu Ser Val Ile Gly Phe Arg Ile
245 250 255

Leu Leu Leu Lys Val Ala Gly Phe Asn Leu Leu Met Thr Leu Arg Leu
260 265 270

Trp Ser Ser
275

<210> 677
<211> 309
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 677

Met Ser Ile Gly Leu Leu Cys Cys Ala Ala Leu Ser Leu Leu Trp Ala
1 5 10 15

Gly Pro Val Asn Ala Gly Val Thr Gln Thr Pro Lys Phe Gln Val Leu
20 25 30

Lys Thr Gly Gln Ser Met Thr Leu Gln Cys Ala Gln Asp Met Asn His
35 40 45

Glu Tyr Met Ser Trp Tyr Arg Gln Asp Pro Gly Met Gly Leu Arg Leu
50 55 60

Ile His Tyr Ser Val Gly Ala Gly Ile Thr Asp Gln Gly Glu Val Pro
65 70 75 80

Asn Gly Tyr Asn Val Ser Arg Ser Thr Thr Glu Asp Phe Pro Leu Arg
85 90 95

Leu Leu Ser Ala Ala Pro Ser Gln Thr Ser Val Tyr Phe Cys Ala Ser
100 105 110

Ser Tyr Val Gly Asn Thr Gly Glu Leu Phe Phe Gly Glu Gly Ser Arg

115 120 125

Leu Thr Val Leu Glu Asp Leu Asn Lys Val Phe Pro Pro Glu Val Ala
130 135 140

Val Phe Glu Pro Ser Glu Ala Glu Ile Ser His Thr Gln Lys Ala Thr
145 150 155 160

Leu Val Cys Leu Ala Thr Gly Phe Phe Pro Asp His Val Glu Leu Ser
165 170 175

Trp Trp Val Asn Gly Lys Glu Val His Ser Gly Val Ser Thr Asp Pro
180 185 190

Gln Pro Leu Lys Glu Gln Pro Ala Leu Asn Asp Ser Arg Tyr Cys Leu
195 200 205

Ser Ser Arg Leu Arg Val Ser Ala Thr Phe Trp Gln Asn Pro Arg Asn
210 215 220

His Phe Arg Cys Gln Val Gln Phe Tyr Gly Leu Ser Glu Asn Asp Glu
225 230 235 240

Trp Thr Gln Asp Arg Ala Lys Pro Val Thr Gln Ile Val Ser Ala Glu
245 250 255

Ala Trp Gly Arg Ala Asp Cys Gly Phe Thr Ser Val Ser Tyr Gln Gln
260 265 270

Gly Val Leu Ser Ala Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala
275 280 285

Thr Leu Tyr Ala Val Leu Val Ser Ala Leu Val Leu Met Ala Met Val
290 295 300

Lys Arg Lys Asp Phe
305

<210> 678
<211> 309
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 678

Met Ser Ile Gly Leu Leu Cys Cys Ala Ala Leu Ser Leu Leu Trp Ala
1 5 10 15

Gly Pro Val Asn Ala Gly Val Thr Gln Thr Pro Lys Phe Gln Val Leu
20 25 30

```
Lys Thr Gly Gln Ser Met Thr Leu Gln Cys Ala Gln Asp Met Asn His
        35                  40                  45

Glu Tyr Met Ser Trp Tyr Arg Gln Asp Pro Gly Met Gly Leu Arg Leu
    50                  55                  60

Ile His Tyr Ser Val Ala Ala Gly Ile Thr Asp Gln Gly Glu Val Pro
65                  70                  75                  80

Asn Gly Tyr Asn Val Ser Arg Ser Thr Thr Glu Asp Phe Pro Leu Arg
                85                  90                  95

Leu Leu Ser Ala Ala Pro Ser Gln Thr Ser Val Tyr Phe Cys Ala Ser
            100                 105                 110

Ser Tyr Val Gly Asn Thr Gly Glu Leu Phe Phe Gly Glu Gly Ser Arg
        115                 120                 125

Leu Thr Val Leu Glu Asp Leu Asn Lys Val Phe Pro Pro Glu Val Ala
    130                 135                 140

Val Phe Glu Pro Ser Glu Ala Glu Ile Ser His Thr Gln Lys Ala Thr
145                 150                 155                 160

Leu Val Cys Leu Ala Thr Gly Phe Phe Pro Asp His Val Glu Leu Ser
                165                 170                 175

Trp Trp Val Asn Gly Lys Glu Val His Ser Gly Val Ser Thr Asp Pro
            180                 185                 190

Gln Pro Leu Lys Glu Gln Pro Ala Leu Asn Asp Ser Arg Tyr Cys Leu
        195                 200                 205

Ser Ser Arg Leu Arg Val Ser Ala Thr Phe Trp Gln Asn Pro Arg Asn
    210                 215                 220

His Phe Arg Cys Gln Val Gln Phe Tyr Gly Leu Ser Glu Asn Asp Glu
225                 230                 235                 240

Trp Thr Gln Asp Arg Ala Lys Pro Val Thr Gln Ile Val Ser Ala Glu
                245                 250                 255

Ala Trp Gly Arg Ala Asp Cys Gly Phe Thr Ser Val Ser Tyr Gln Gln
            260                 265                 270

Gly Val Leu Ser Ala Thr Ile Leu Tyr Glu Ile Leu Leu Gly Lys Ala
        275                 280                 285

Thr Leu Tyr Ala Val Leu Val Ser Ala Leu Val Leu Met Ala Met Val
    290                 295                 300
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Lys Arg Lys Asp Phe
305

<210> 679
<211> 208
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 679

Met Gln Glu Val Thr Gln Ile Pro Ala Ala Leu Ser Val Pro Glu Gly
1 5 10 15

Glu Asn Leu Val Leu Asn Cys Ser Phe Thr Asp Ser Ala Ile Tyr Asn
20 25 30

Leu Gln Trp Phe Arg Gln Asp Pro Gly Lys Gly Leu Thr Ser Leu Leu
35 40 45

Leu Ile Gln Ser Ser Gln Arg Glu Gln Thr Ser Gly Arg Leu Asn Ala
50 55 60

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

Gln Pro Gly Asp Ser Ala Thr Tyr Leu Cys Ala Val Arg Pro Thr Ser
85 90 95

Gly Gly Ser Tyr Ile Pro Thr Phe Gly Arg Gly Thr Ser Leu Ile Val
100 105 110

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

Ser Lys Ser Ser Asp Lys Ser Val Cys Leu Phe Thr Asp Phe Asp Ser
130 135 140

Gln Thr Asn Val Ser Gln Ser Lys Asp Ser Asp Val Tyr Ile Thr Asp
145 150 155 160

Lys Thr Val Leu Asp Met Arg Ser Met Asp Phe Lys Ser Asn Ser Ala
165 170 175

Val Ala Trp Ser Asn Lys Ser Asp Phe Ala Cys Ala Asn Ala Phe Asn
180 185 190

Asn Ser Ile Ile Pro Glu Asp Thr Phe Phe Pro Ser Pro Glu Ser Ser
195 200 205

<210> 680

<211> 242
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 680

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Met Gly Val Thr Gln Thr Pro Lys Phe Gln Val Leu Lys Thr Gly Gln
1               5                  10                  15

Ser Met Thr Leu Gln Cys Ala Gln Asp Met Asn His Glu Tyr Met Ser
            20                  25                  30

Trp Tyr Arg Gln Asp Pro Gly Met Gly Leu Arg Leu Ile His Tyr Ser
        35                  40                  45

Val Gly Ala Gly Ile Thr Asp Gln Gly Glu Val Pro Asn Gly Tyr Asn
    50                  55                  60

Val Ser Arg Ser Thr Thr Glu Asp Phe Pro Leu Arg Leu Leu Ser Ala
65                  70                  75                  80

Ala Pro Ser Gln Thr Ser Val Tyr Phe Cys Ala Ser Ser Tyr Val Gly
                85                  90                  95

Asn Thr Gly Glu Leu Phe Phe Gly Glu Gly Ser Arg Leu Thr Val Leu
            100                 105                 110

Glu Asp Leu Lys Asn Val Phe Pro Pro Glu Val Ala Val Phe Glu Pro
        115                 120                 125

Ser Glu Ala Glu Ile Ser His Thr Gln Lys Ala Thr Leu Val Cys Leu
    130                 135                 140

Ala Thr Gly Phe Tyr Pro Asp His Val Glu Leu Ser Trp Trp Val Asn
145                 150                 155                 160

Gly Lys Glu Val His Ser Gly Val Ser Thr Asp Pro Gln Pro Leu Lys
                165                 170                 175

Glu Gln Pro Ala Leu Asn Asp Ser Arg Tyr Ala Leu Ser Ser Arg Leu
            180                 185                 190

Arg Val Ser Ala Thr Phe Trp Gln Asp Pro Arg Asn His Phe Arg Cys
        195                 200                 205

Gln Val Gln Phe Tyr Gly Leu Ser Glu Asn Asp Glu Trp Thr Gln Asp
    210                 215                 220

Arg Ala Lys Pro Val Thr Gln Ile Val Ser Ala Glu Ala Trp Gly Arg
225                 230                 235                 240
```

Ala Asp

<210> 681
<211> 98
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 681

Ile Cys Ser Arg Ala Ala Arg Gly Thr Ile Gly Ala Arg Arg Thr Gly
1 5 10 15

Gln Pro Leu Lys Glu Asp Pro Ser Ala Val Pro Val Phe Ser Val Asp
20 25 30

Tyr Gly Glu Leu Asp Phe Gln Trp Arg Glu Lys Thr Pro Glu Pro Pro
35 40 45

Val Pro Cys Val Pro Glu Gln Thr Glu Tyr Ala Thr Ile Val Phe Pro
50 55 60

Ser Gly Met Gly Thr Ser Ser Pro Ala Arg Arg Gly Ser Ala Asp Gly
65 70 75 80

Pro Arg Ser Ala Gln Pro Leu Arg Pro Glu Asp Gly His Cys Ser Trp
85 90 95

Pro Leu

<210> 682
<211> 39
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 682

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

Tyr Val Lys Met Pro Pro Thr Glu Pro Glu Cys Glu Lys Gln Phe Gln
20 25 30

Pro Tyr Phe Ile Pro Ile Asn
35

<210> 683
<211> 258
<212> PRT

<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 683

Tyr Asp Leu Leu Gln Arg Leu Gly Gly Gly Thr Tyr Gly Glu Val Phe
1 5 10 15

Lys Ala Arg Asp Lys Val Ser Gly Asp Leu Val Ala Leu Lys Met Val
20 25 30

Lys Met Glu Pro Asp Asp Asp Val Ser Thr Leu Gln Lys Glu Ile Leu
35 40 45

Ile Leu Lys Thr Cys Arg His Ala Asn Ile Val Ala Tyr His Gly Ser
50 55 60

Tyr Leu Trp Leu Gln Lys Leu Trp Ile Cys Met Glu Phe Cys Gly Ala
65 70 75 80

Gly Ser Leu Gln Asp Ile Tyr Gln Val Thr Gly Ser Leu Ser Glu Leu
85 90 95

Gln Ile Ser Tyr Val Cys Arg Glu Val Leu Gln Gly Leu Ala Tyr Leu
100 105 110

His Ser Gln Lys Lys Ile His Arg Asp Ile Lys Gly Ala Asn Ile Leu
115 120 125

Ile Asn Asp Ala Gly Glu Val Arg Leu Ala Asp Phe Gly Ile Ser Ala
130 135 140

Gln Ile Gly Ala Thr Leu Ala Arg Arg Leu Ser Phe Ile Gly Thr Pro
145 150 155 160

Tyr Trp Met Ala Pro Glu Val Ala Ala Val Ala Leu Lys Gly Gly Tyr
165 170 175

Asn Glu Leu Cys Asp Ile Trp Ser Leu Gly Ile Thr Ala Ile Glu Leu
180 185 190

Ala Glu Leu Gln Pro Pro Leu Phe Asp Val His Pro Leu Arg Val Leu
195 200 205

Phe Leu Met Thr Lys Ser Gly Tyr Gln Pro Pro Arg Leu Lys Glu Lys
210 215 220

Gly Lys Trp Ser Ala Ala Phe His Asn Phe Ile Lys Val Thr Leu Thr
225 230 235 240

Lys Ser Pro Lys Lys Arg Pro Ser Ala Thr Lys Met Leu Ser His Gln

245 250 255

Leu Val

<210> 684
<211> 272
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 684

Phe Trp Glu Glu Phe Glu Ser Leu Gln Lys Gln Glu Val Lys Asn Leu
1 5 10 15

His Gln Arg Leu Glu Gly Gln Arg Pro Glu Asn Lys Gly Lys Asn Arg
20 25 30

Tyr Lys Asn Ile Leu Pro Phe Asp His Ser Arg Val Ile Leu Gln Gly
35 40 45

Arg Asp Ser Asn Ile Pro Gly Ser Asp Tyr Ile Asn Ala Asn Tyr Ile
50 55 60

Lys Asn Gln Leu Leu Gly Pro Asp Glu Asn Ala Lys Thr Tyr Ile Ala
65 70 75 80

Ser Gln Gly Cys Leu Glu Ala Thr Val Asn Asp Phe Trp Gln Met Ala
85 90 95

Trp Gln Glu Asn Ser Arg Val Ile Val Met Thr Thr Arg Glu Val Glu
100 105 110

Lys Gly Arg Asn Lys Cys Val Pro Tyr Trp Pro Glu Val Gly Met Gln
115 120 125

Arg Ala Tyr Gly Pro Tyr Ser Val Thr Asn Cys Gly Glu His Asp Thr
130 135 140

Thr Glu Tyr Lys Leu Arg Thr Leu Gln Val Ser Pro Leu Asp Asn Gly
145 150 155 160

Asp Leu Ile Arg Glu Ile Trp His Tyr Gln Tyr Leu Ser Trp Pro Asp
165 170 175

His Gly Val Pro Ser Glu Pro Gly Gly Val Leu Ser Phe Leu Asp Gln
180 185 190

Ile Asn Gln Arg Gln Glu Ser Leu Pro His Ala Gly Pro Ile Ile Val
195 200 205

His Cys Ser Ala Gly Ile Gly Arg Thr Gly Thr Ile Ile Val Ile Asp
210 215 220

Met Leu Met Glu Asn Ile Ser Thr Lys Gly Leu Asp Cys Asp Ile Asp
225 230 235 240

Ile Gln Lys Thr Ile Gln Met Val Arg Ala Gln Arg Ser Gly Met Val
245 250 255

Gln Thr Glu Ala Gln Tyr Lys Phe Ile Tyr Val Ala Ile Ala Gln Phe
260 265 270

<210> 685
<211> 275
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 685

Phe Trp Glu Glu Phe Glu Thr Leu Gln Gln Gln Glu Cys Lys Leu Leu
1 5 10 15

Tyr Ser Arg Lys Glu Gly Gln Arg Gln Glu Asn Lys Asn Lys Asn Arg
20 25 30

Tyr Lys Asn Ile Leu Pro Phe Asp His Thr Arg Val Val Leu His Asp
35 40 45

Gly Asp Pro Asn Glu Pro Val Ser Asp Tyr Ile Asn Ala Asn Ile Ile
50 55 60

Met Pro Glu Phe Glu Thr Lys Cys Asn Asn Ser Lys Pro Lys Lys Ser
65 70 75 80

Tyr Ile Ala Thr Gln Gly Cys Leu Gln Asn Thr Val Asn Asp Phe Trp
85 90 95

Arg Met Val Phe Gln Glu Asn Ser Arg Val Ile Val Met Thr Thr Lys
100 105 110

Glu Val Glu Arg Gly Lys Ser Lys Cys Val Lys Tyr Trp Pro Asp Glu
115 120 125

Tyr Ala Leu Lys Glu Tyr Gly Val Met Arg Val Arg Asn Val Lys Glu
130 135 140

Ser Ala Ala His Asp Tyr Thr Leu Arg Glu Leu Lys Leu Ser Lys Val
145 150 155 160

Gly Gln Ala Leu Leu Gln Gly Asn Thr Glu Arg Thr Val Trp Gln Tyr

165 170 175

His Phe Arg Thr Trp Pro Asp His Gly Val Pro Ser Asp Pro Gly Gly
180 185 190

Val Leu Asp Phe Leu Glu Glu Val His His Lys Gln Glu Ser Ile Met
195 200 205

Asp Ala Gly Pro Val Val Val His Cys Ser Ala Gly Ile Gly Arg Thr
210 215 220

Gly Thr Phe Ile Val Ile Asp Ile Leu Ile Asp Ile Ile Arg Glu Lys
225 230 235 240

Gly Val Asp Cys Asp Ile Asp Val Pro Lys Thr Ile Gln Met Val Arg
245 250 255

Ser Gln Arg Ser Gly Met Val Gln Thr Glu Ala Gln Tyr Arg Phe Ile
260 265 270

Tyr Met Ala
275

<210> 686
<211> 270
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 686

Gly Pro Gln Lys Arg Cys Leu Phe Val Cys Arg His Gly Glu Arg Met
1 5 10 15

Asp Val Val Phe Gly Lys Tyr Trp Leu Ser Gln Cys Phe Asp Ala Lys
20 25 30

Gly Arg Tyr Ile Arg Thr Asn Leu Asn Met Pro His Ser Leu Pro Gln
35 40 45

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

Phe Gly Cys Met Gln Ala Arg Leu Val Gly Glu Ala Leu Leu Glu Ser
65 70 75 80

Asn Thr Ile Ile Asp His Val Tyr Cys Ser Pro Ser Leu Arg Cys Val
85 90 95

Gln Thr Ala His Asn Ile Leu Lys Gly Leu Gln Gln Glu Asn His Leu
100 105 110

```
Lys Ile Arg Val Glu Pro Gly Leu Phe Glu Trp Thr Lys Trp Val Ala
        115                 120                 125

Gly Ser Thr Leu Pro Ala Trp Ile Pro Pro Ser Glu Leu Ala Ala Ala
    130                 135                 140

Asn Leu Ser Val Asp Thr Thr Tyr Arg Pro His Ile Pro Ile Ser Lys
145                 150                 155                 160

Leu Val Val Ser Glu Ser Tyr Asp Thr Tyr Ile Ser Arg Ser Phe Gln
                165                 170                 175

Val Thr Lys Glu Ile Ile Ser Glu Cys Lys Ser Lys Gly Asn Asn Ile
            180                 185                 190

Leu Ile Val Ala His Ala Ser Ser Leu Glu Ala Cys Thr Cys Gln Leu
        195                 200                 205

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

Lys Ile Pro Tyr Leu Gly Phe Cys Ser Cys Glu Glu Leu Gly Glu Thr
225                 230                 235                 240

Gly Ile Trp Gln Leu Thr Asp Pro Pro Ile Leu Pro Leu Thr His Gly
                245                 250                 255

Pro Thr Gly Gly Phe Asn Trp Arg Glu Thr Leu Leu Gln Glu
            260                 265                 270


<210>  687
<211>  255
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic amino acid sequence

<400>  687

Leu Lys Leu Leu Gln Thr Ile Gly Lys Gly Glu Phe Gly Asp Val Met
1               5                   10                  15

Leu Gly Asp Tyr Arg Gly Asn Lys Val Ala Val Lys Cys Ile Lys Asn
            20                  25                  30

Asp Ala Thr Ala Gln Ala Phe Leu Ala Glu Ala Ser Val Met Thr Gln
        35                  40                  45

Leu Arg His Ser Asn Leu Val Gln Leu Leu Gly Val Ile Val Glu Glu
    50                  55                  60

Lys Gly Gly Leu Tyr Ile Val Thr Glu Tyr Met Ala Lys Gly Ser Leu
```

65 70 75 80

Val Asp Tyr Leu Arg Ser Arg Gly Arg Ser Val Leu Gly Gly Asp Cys
85 90 95

Leu Leu Lys Phe Ser Leu Asp Val Cys Glu Ala Met Glu Tyr Leu Glu
100 105 110

Gly Asn Asn Phe Val His Arg Asp Leu Ala Ala Arg Asn Val Leu Val
115 120 125

Ser Glu Asp Asn Val Ala Lys Val Ser Asp Phe Gly Leu Thr Lys Glu
130 135 140

Ala Ser Ser Thr Gln Asp Thr Gly Lys Leu Pro Val Lys Trp Thr Ala
145 150 155 160

Pro Glu Ala Leu Arg Glu Lys Lys Phe Ser Thr Lys Ser Asp Val Trp
165 170 175

Ser Phe Gly Ile Leu Leu Trp Glu Ile Tyr Ser Phe Gly Arg Val Pro
180 185 190

Tyr Pro Arg Ile Pro Leu Lys Asp Val Val Pro Arg Val Glu Lys Gly
195 200 205

Tyr Lys Met Asp Ala Pro Asp Gly Cys Pro Pro Ala Val Tyr Glu Val
210 215 220

Met Lys Asn Cys Trp His Leu Asp Ala Ala Met Arg Pro Ser Phe Leu
225 230 235 240

Gln Leu Arg Glu Gln Leu Glu His Ile Lys Thr His Glu Leu His
245 250 255

<210> 688
<211> 24
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 688

Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu
1 5 10 15

Ser Leu Val Ile Thr Leu Tyr Cys
20

<210> 689
<211> 23
<212> PRT

<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 689

Leu Gly Leu Leu Val Ala Gly Val Leu Val Leu Leu Val Ser Leu Gly
1 5 10 15

Val Ala Ile His Leu Cys Cys
20

<210> 690
<211> 25
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 690

Ala Leu Ile Val Leu Gly Gly Val Ala Gly Leu Leu Leu Phe Ile Gly
1 5 10 15

Leu Gly Ile Phe Phe Cys Val Arg Cys
20 25

<210> 691
<211> 23
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 691

Leu Cys Tyr Leu Leu Asp Gly Ile Leu Phe Ile Tyr Gly Val Ile Leu
1 5 10 15

Thr Ala Leu Phe Leu Arg Val
20

<210> 692
<211> 26
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 692

Trp Val Leu Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu Leu
1 5 10 15

Val Thr Val Ala Phe Ile Ile Phe Trp Val
20 25

<210> 693
<211> 26
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 693

Val Ala Ala Ile Leu Gly Leu Gly Leu Val Leu Gly Leu Leu Gly Pro
1 5 10 15

Leu Ala Ile Leu Leu Ala Leu Tyr Leu Leu
20 25

<210> 694
<211> 24
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 694

Ala Leu Pro Ala Ala Leu Ala Val Ile Ser Phe Leu Leu Gly Leu Gly
1 5 10 15

Leu Gly Val Ala Cys Val Leu Ala
20

<210> 695
<211> 271
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 695

Glu Ser Ala Asp Leu Arg Ala Leu Ala Lys His Leu Tyr Asp Ser Tyr
1 5 10 15

Ile Lys Ser Phe Pro Leu Thr Lys Ala Lys Ala Arg Ala Ile Leu Thr
20 25 30

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

Leu Met Met Gly Glu Asp Lys Ile Lys Phe Lys His Ile Thr Pro Leu
50 55 60

Gln Glu Gln Ser Lys Glu Val Ala Ile Arg Ile Phe Gln Gly Cys Gln
65 70 75 80

Phe Arg Ser Val Glu Ala Val Gln Glu Ile Thr Glu Tyr Ala Lys Ser

85 90 95

Ile Pro Gly Phe Val Asn Leu Asp Leu Asn Asp Gln Val Thr Leu Leu
100 105 110

Lys Tyr Gly Val His Glu Ile Ile Tyr Thr Met Leu Ala Ser Leu Met
115 120 125

Asn Lys Asp Gly Val Leu Ile Ser Glu Gly Gln Gly Phe Met Thr Arg
130 135 140

Glu Phe Leu Lys Ser Leu Arg Lys Pro Phe Gly Asp Phe Met Glu Pro
145 150 155 160

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

Asp Leu Ala Ile Phe Ile Ala Val Ile Ile Leu Ser Gly Asp Arg Pro
180 185 190

Gly Leu Leu Asn Val Lys Pro Ile Glu Asp Ile Gln Asp Asn Leu Leu
195 200 205

Gln Ala Leu Glu Leu Gln Leu Lys Leu Asn His Pro Glu Ser Ser Gln
210 215 220

Leu Phe Ala Lys Leu Leu Gln Lys Met Thr Asp Leu Arg Gln Ile Val
225 230 235 240

Thr Glu His Val Gln Leu Leu Gln Val Ile Lys Lys Thr Glu Thr Asp
245 250 255

Met Ser Leu His Pro Leu Leu Gln Glu Ile Tyr Lys Asp Leu Tyr
260 265 270

<210> 696
<211> 21
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 696

Pro Lys Lys Glu Asn Asn Ala Leu Leu Arg Tyr Leu Leu Asp Arg Asp
1 5 10 15

Asp Pro Ser Asp Ala
20

<210> 697
<211> 79
<212> PRT

<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 697

Pro Lys Lys Glu Asn Asn Ala Leu Leu Arg Tyr Leu Leu Asp Arg Asp
1 5 10 15

Asp Pro Ser Asp Ala Gly Gly Gly Ser Gly Gly Gly Ser Pro Lys Lys
20 25 30

Glu Asn Asn Ala Leu Leu Arg Tyr Leu Leu Asp Arg Asp Asp Pro Ser
35 40 45

Asp Ala Gly Gly Gly Ser Gly Gly Gly Ser Pro Lys Lys Glu Asn Asn
50 55 60

Ala Leu Leu Arg Tyr Leu Leu Asp Arg Asp Asp Pro Ser Asp Ala
65 70 75

<210> 698
<211> 78
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 698

Met His Gly Ser Leu Leu Gln Glu Lys His Arg Ile Leu His Lys Leu
1 5 10 15

Leu Gln Asn Gly Asn Ser Pro Ala Glu Val Ala Lys Ile Thr Ala Glu
20 25 30

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

Val Val Lys Gln Glu Gln Leu Ser Pro Lys Lys Lys Glu Asn Asn Ala
50 55 60

Leu Leu Arg Tyr Leu Leu Asp Arg Asp Asp Pro Ser Asp Ala
65 70 75

<210> 699
<211> 419
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 699

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu

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1               5                  10                  15

His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Asp
            20                  25                  30

Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly Asp
        35                  40                  45

Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr Leu
    50                  55                  60

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

His Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
                85                  90                  95

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

Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr
        115                 120                 125

Phe Gly Gly Gly Thr Lys Leu Glu Ile Thr Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Lys Leu Gln Glu Ser
145                 150                 155                 160

Gly Pro Gly Leu Val Ala Pro Ser Gln Ser Leu Ser Val Thr Cys Thr
                165                 170                 175

Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg Gln
            180                 185                 190

Pro Pro Arg Lys Gly Leu Glu Trp Leu Gly Val Ile Trp Gly Ser Glu
        195                 200                 205

Thr Thr Tyr Tyr Asn Ser Ala Leu Lys Ser Arg Leu Thr Ile Ile Lys
    210                 215                 220

Asp Asn Ser Lys Ser Gln Val Phe Leu Lys Met Asn Ser Leu Gln Thr
225                 230                 235                 240

Asp Asp Thr Ala Ile Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly Gly
                245                 250                 255

Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser
            260                 265                 270

Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile
```

275 280 285

Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala
290 295 300

Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr
305 310 315 320

Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu
325 330 335

Val Ile Thr Leu Tyr Cys Ser Leu Lys Arg Gly Arg Lys Lys Leu Leu
340 345 350

Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu
355 360 365

Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys
370 375 380

Glu Leu Ser Arg Gly Ser Gly Ser Gly Ser Thr Ser Pro Lys Lys Glu
385 390 395 400

Asn Asn Ala Leu Leu Arg Tyr Leu Leu Asp Arg Asp Asp Pro Ser Asp
405 410 415

Ala Gly Ser

<210> 700
<211> 476
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 700

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Asp
20 25 30

Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly Asp
35 40 45

Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr Leu
50 55 60

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

```
His Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
                85                  90                  95

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

Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr
        115                 120                 125

Phe Gly Gly Gly Thr Lys Leu Glu Ile Thr Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Lys Leu Gln Glu Ser
145                 150                 155                 160

Gly Pro Gly Leu Val Ala Pro Ser Gln Ser Leu Ser Val Thr Cys Thr
                165                 170                 175

Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg Gln
            180                 185                 190

Pro Pro Arg Lys Gly Leu Glu Trp Leu Gly Val Ile Trp Gly Ser Glu
        195                 200                 205

Thr Thr Tyr Tyr Asn Ser Ala Leu Lys Ser Arg Leu Thr Ile Ile Lys
    210                 215                 220

Asp Asn Ser Lys Ser Gln Val Phe Leu Lys Met Asn Ser Leu Gln Thr
225                 230                 235                 240

Asp Asp Thr Ala Ile Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly Gly
                245                 250                 255

Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser
            260                 265                 270

Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile
        275                 280                 285

Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala
    290                 295                 300

Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr
305                 310                 315                 320

Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu
                325                 330                 335

Val Ile Thr Leu Tyr Cys Ser Leu Lys Arg Gly Arg Lys Lys Leu Leu
            340                 345                 350
```

```
Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu
        355                 360                 365

Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys
    370                 375                 380

Glu Leu Ser Arg Gly Ser Gly Ser Gly Ser Thr Ser Met His Gly Ser
385                 390                 395                 400

Leu Leu Gln Glu Lys His Arg Ile Leu His Lys Leu Leu Gln Asn Gly
                405                 410                 415

Asn Ser Pro Ala Glu Val Ala Lys Ile Thr Ala Glu Ala Thr Gly Lys
            420                 425                 430

Asp Thr Ser Ser Ile Thr Ser Cys Gly Asp Gly Asn Val Val Lys Gln
        435                 440                 445

Glu Gln Leu Ser Pro Lys Lys Lys Glu Asn Asn Ala Leu Leu Arg Tyr
    450                 455                 460

Leu Leu Asp Arg Asp Asp Pro Ser Asp Ala Gly Ser
465                 470                 475
```

<210> 701
<211> 476
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 701

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15

His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Asp
            20                  25                  30

Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly Asp
        35                  40                  45

Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr Leu
    50                  55                  60

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

His Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
                85                  90                  95

Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln Glu
```

100 105 110

Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr
115 120 125

Phe Gly Gly Gly Thr Lys Leu Glu Ile Thr Gly Gly Gly Gly Ser Gly
130 135 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Lys Leu Gln Glu Ser
145 150 155 160

Gly Pro Gly Leu Val Ala Pro Ser Gln Ser Leu Ser Val Thr Cys Thr
165 170 175

Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg Gln
180 185 190

Pro Pro Arg Lys Gly Leu Glu Trp Leu Gly Val Ile Trp Gly Ser Glu
195 200 205

Thr Thr Tyr Tyr Asn Ser Ala Leu Lys Ser Arg Leu Thr Ile Ile Lys
210 215 220

Asp Asn Ser Lys Ser Gln Val Phe Leu Lys Met Asn Ser Leu Gln Thr
225 230 235 240

Asp Asp Thr Ala Ile Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly Gly
245 250 255

Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser
260 265 270

Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile
275 280 285

Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala
290 295 300

Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr
305 310 315 320

Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu
325 330 335

Val Ile Thr Leu Tyr Cys Ser Leu Lys Arg Gly Arg Lys Lys Leu Leu
340 345 350

Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu
355 360 365

Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys

370 375 380

Glu Leu Ser Arg Gly Ser Gly Ser Gly Ser Thr Ser Pro Lys Lys Glu
385 390 395 400

Asn Asn Ala Leu Leu Arg Tyr Leu Leu Asp Arg Asp Asp Pro Ser Asp
405 410 415

Ala Gly Gly Gly Ser Gly Gly Gly Ser Pro Lys Lys Glu Asn Asn Ala
420 425 430

Leu Leu Arg Tyr Leu Leu Asp Arg Asp Asp Pro Ser Asp Ala Gly Gly
435 440 445

Gly Ser Gly Gly Gly Ser Lys Lys Glu Asn Asn Ala Leu Leu Arg Tyr
450 455 460

Leu Leu Asp Arg Asp Asp Pro Ser Asp Ala Gly Ser
465 470 475

<210> 702
<211> 775
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 702

Met Ile His Leu Gly His Ile Leu Phe Leu Leu Leu Leu Pro Val Ala
1 5 10 15

Ala Ala Gln Thr Thr Pro Gly Glu Arg Ser Ser Leu Pro Ala Phe Tyr
20 25 30

Pro Gly Thr Ser Gly Ser Cys Ser Gly Cys Gly Ser Leu Ser Leu Pro
35 40 45

Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu
50 55 60

Ser Leu Val Ile Thr Leu Tyr Cys Ser Leu Lys Arg Gly Arg Lys Lys
65 70 75 80

Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr
85 90 95

Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly
100 105 110

Gly Cys Glu Leu Gly Ser Gly Ser Gly Ser Gly Ser Gly Ser Gly Ser
115 120 125

```
Gly Ser Thr Ser Glu Ser Ala Asp Leu Arg Ala Leu Ala Lys His Leu
    130                 135                 140

Tyr Asp Ser Tyr Ile Lys Ser Phe Pro Leu Thr Lys Ala Lys Ala Arg
145                 150                 155                 160

Ala Ile Leu Thr Gly Lys Thr Thr Asp Lys Ser Pro Phe Val Ile Tyr
                165                 170                 175

Asp Met Asn Ser Leu Met Met Gly Glu Asp Lys Ile Lys Phe Lys His
            180                 185                 190

Ile Thr Pro Leu Gln Glu Gln Ser Lys Glu Val Ala Ile Arg Ile Phe
        195                 200                 205

Gln Gly Cys Gln Phe Arg Ser Val Glu Ala Val Gln Glu Ile Thr Glu
    210                 215                 220

Tyr Ala Lys Ser Ile Pro Gly Phe Val Asn Leu Asp Leu Asn Asp Gln
225                 230                 235                 240

Val Thr Leu Leu Lys Tyr Gly Val His Glu Ile Ile Tyr Thr Met Leu
                245                 250                 255

Ala Ser Leu Met Asn Lys Asp Gly Val Leu Ile Ser Glu Gly Gln Gly
            260                 265                 270

Phe Met Thr Arg Glu Phe Leu Lys Ser Leu Arg Lys Pro Phe Gly Asp
        275                 280                 285

Phe Met Glu Pro Lys Phe Glu Phe Ala Val Lys Phe Asn Ala Leu Glu
    290                 295                 300

Leu Asp Asp Ser Asp Leu Ala Ile Phe Ile Ala Val Ile Ile Leu Ser
305                 310                 315                 320

Gly Asp Arg Pro Gly Leu Leu Asn Val Lys Pro Ile Glu Asp Ile Gln
                325                 330                 335

Asp Asn Leu Leu Gln Ala Leu Glu Leu Gln Leu Lys Leu Asn His Pro
            340                 345                 350

Glu Ser Ser Gln Leu Phe Ala Lys Leu Leu Gln Lys Met Thr Asp Leu
        355                 360                 365

Arg Gln Ile Val Thr Glu His Val Gln Leu Leu Gln Val Ile Lys Lys
    370                 375                 380

Thr Glu Thr Asp Met Ser Leu His Pro Leu Leu Gln Glu Ile Tyr Lys
385                 390                 395                 400
```

```
Asp Leu Tyr Gly Ser Gly Ser Gly Ser Gly Ser Ser Leu Arg Val Lys
                405                 410                 415

Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln
            420                 425                 430

Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
        435                 440                 445

Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
    450                 455                 460

Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
465                 470                 475                 480

Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
                485                 490                 495

Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
            500                 505                 510

Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg Ser Arg Gly
        515                 520                 525

Ser Gly Ser Gly Ser Gly Ser Met Val Ser Lys Gly Glu Glu Asp Asn
    530                 535                 540

Met Ala Ile Ile Lys Glu Phe Met Arg Phe Lys Val His Met Glu Gly
545                 550                 555                 560

Ser Val Asn Gly His Glu Phe Glu Ile Glu Gly Glu Gly Glu Gly Arg
                565                 570                 575

Pro Tyr Glu Gly Thr Gln Thr Ala Lys Leu Lys Val Thr Lys Gly Gly
            580                 585                 590

Pro Leu Pro Phe Ala Trp Asp Ile Leu Ser Pro Gln Phe Met Tyr Gly
        595                 600                 605

Ser Lys Ala Tyr Val Lys His Pro Ala Asp Ile Pro Asp Tyr Leu Lys
    610                 615                 620

Leu Ser Phe Pro Glu Gly Phe Lys Trp Glu Arg Val Met Asn Phe Glu
625                 630                 635                 640

Asp Gly Gly Val Val Thr Val Thr Gln Asp Ser Ser Leu Gln Asp Gly
                645                 650                 655

Glu Phe Ile Tyr Lys Val Lys Leu Arg Gly Thr Asn Phe Pro Ser Asp
            660                 665                 670
```

Gly Pro Val Met Gln Lys Lys Thr Met Gly Trp Glu Ala Ser Ser Glu
675 680 685

Arg Met Tyr Pro Glu Asp Gly Ala Leu Lys Gly Glu Ile Lys Gln Arg
690 695 700

Leu Lys Leu Lys Asp Gly Gly His Tyr Asp Ala Glu Val Lys Thr Thr
705 710 715 720

Tyr Lys Ala Lys Lys Pro Val Gln Leu Pro Gly Ala Tyr Asn Val Asn
725 730 735

Ile Lys Leu Asp Ile Thr Ser His Asn Glu Asp Tyr Thr Ile Val Glu
740 745 750

Gln Tyr Glu Arg Ala Glu Gly Arg His Ser Thr Gly Gly Met Asp Glu
755 760 765

Leu Tyr Lys Cys Val Thr Asp
770 775

<210> 703
<211> 297
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 703

Asp Arg Arg Gly Gly Arg Met Leu Lys His Lys Arg Gln Arg Asp Asp
1 5 10 15

Gly Glu Gly Arg Gly Glu Val Gly Ser Ala Gly Asp Met Arg Ala Ala
20 25 30

Asn Leu Trp Pro Ser Pro Leu Met Ile Lys Arg Ser Lys Lys Asn Ser
35 40 45

Leu Ala Leu Ser Leu Thr Ala Asp Gln Met Val Ser Ala Leu Leu Asp
50 55 60

Ala Glu Pro Pro Ile Leu Tyr Ser Glu Tyr Asp Pro Thr Arg Pro Phe
65 70 75 80

Ser Glu Ala Ser Met Met Gly Leu Leu Thr Asn Leu Ala Asp Arg Glu
85 90 95

Leu Val His Met Ile Asn Trp Ala Lys Arg Val Pro Gly Phe Val Asp
100 105 110

Leu Thr Leu His Asp Gln Val His Leu Leu Glu Cys Ala Trp Leu Glu

115 120 125

Ile Leu Met Ile Gly Leu Val Trp Arg Ser Met Glu His Pro Gly Lys
130 135 140

Leu Leu Phe Ala Pro Asn Leu Leu Leu Asp Arg Asn Gln Gly Lys Cys
145 150 155 160

Val Glu Gly Met Val Glu Ile Phe Asp Met Leu Leu Ala Thr Ser Ser
165 170 175

Arg Phe Arg Met Met Asn Leu Gln Gly Glu Glu Phe Val Cys Leu Lys
180 185 190

Ser Ile Ile Leu Leu Asn Ser Gly Val Tyr Thr Phe Leu Ser Ser Thr
195 200 205

Leu Lys Ser Leu Glu Glu Lys Asp His Ile His Arg Val Leu Asp Lys
210 215 220

Ile Thr Asp Thr Leu Ile His Leu Met Ala Lys Ala Gly Leu Thr Leu
225 230 235 240

Gln Gln Gln His Gln Arg Leu Ala Gln Leu Leu Leu Ile Leu Ser His
245 250 255

Ile Arg His Met Ser Asn Lys Gly Met Glu His Leu Tyr Ser Met Lys
260 265 270

Cys Lys Asn Val Val Pro Leu Tyr Asp Leu Leu Leu Glu Met Leu Asp
275 280 285

Ala His Arg Leu His Ala Pro Thr Ser
290 295

<210> 704
<211> 297
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 704

Asp Arg Arg Gly Gly Arg Met Leu Lys His Lys Arg Gln Arg Asp Asp
1 5 10 15

Gly Glu Gly Arg Gly Glu Val Gly Ser Ala Gly Asp Met Arg Ala Ala
20 25 30

Asn Leu Trp Pro Ser Pro Leu Met Ile Lys Arg Ser Lys Lys Asn Ser
35 40 45

```
Leu Ala Leu Ser Leu Thr Ala Asp Gln Met Val Ser Ala Leu Leu Asp
    50                  55                  60

Ala Glu Pro Pro Ile Leu Tyr Ser Glu Tyr Asp Pro Thr Arg Pro Phe
65                  70                  75                  80

Ser Glu Ala Ser Met Met Gly Leu Leu Thr Asn Leu Ala Asp Arg Glu
                85                  90                  95

Leu Val His Met Ile Asn Trp Ala Lys Arg Val Pro Gly Phe Val Asp
            100                 105                 110

Leu Thr Leu His Asp Gln Val His Leu Leu Glu Cys Ala Trp Leu Glu
        115                 120                 125

Ile Leu Met Ile Gly Leu Val Trp Arg Ser Met Glu His Pro Gly Lys
    130                 135                 140

Leu Leu Phe Ala Pro Asn Leu Leu Leu Asp Arg Asn Gln Gly Lys Cys
145                 150                 155                 160

Val Glu Gly Met Val Glu Ile Phe Asp Met Leu Leu Ala Thr Ser Ser
                165                 170                 175

Arg Phe Arg Met Met Asn Leu Gln Gly Glu Glu Phe Val Cys Leu Lys
            180                 185                 190

Ser Ile Ile Leu Leu Asn Ser Gly Val Tyr Thr Phe Leu Ser Ser Thr
        195                 200                 205

Leu Lys Ser Leu Glu Glu Lys Asp His Ile His Arg Val Leu Asp Lys
    210                 215                 220

Ile Thr Asp Thr Leu Ile His Leu Met Ala Lys Ala Gly Leu Thr Leu
225                 230                 235                 240

Gln Gln Gln His Gln Arg Leu Ala Gln Leu Leu Leu Ile Leu Ser His
                245                 250                 255

Ile Arg His Met Ser Asn Lys Gly Met Glu His Leu Tyr Ser Met Lys
            260                 265                 270

Cys Lys Asn Val Val Pro Leu Phe Asp Leu Leu Leu Glu Met Leu Asp
        275                 280                 285

Ala His Arg Leu His Ala Pro Thr Ser
    290                 295

<210>  705
<211>  297
<212>  PRT
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<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 705

Asp Arg Arg Gly Gly Arg Met Leu Lys His Lys Arg Gln Arg Asp Asp
1 5 10 15

Gly Glu Gly Arg Gly Glu Val Gly Ser Ala Gly Asp Met Arg Ala Ala
20 25 30

Asn Leu Trp Pro Ser Pro Leu Met Ile Lys Arg Ser Lys Lys Asn Ser
35 40 45

Leu Ala Leu Ser Leu Thr Ala Asp Gln Met Val Ser Ala Leu Leu Asp
50 55 60

Ala Glu Pro Pro Ile Leu Tyr Ser Glu Tyr Asp Pro Thr Arg Pro Phe
65 70 75 80

Ser Glu Ala Ser Met Met Gly Leu Leu Thr Asn Leu Ala Asp Arg Glu
85 90 95

Leu Val His Met Ile Asn Trp Ala Lys Arg Val Pro Gly Phe Val Asp
100 105 110

Leu Thr Leu His Asp Gln Val His Leu Leu Glu Cys Ala Trp Leu Glu
115 120 125

Ile Leu Met Ile Gly Leu Val Trp Arg Ser Met Glu His Pro Gly Lys
130 135 140

Leu Leu Phe Ala Pro Asn Leu Leu Leu Asp Arg Asn Gln Gly Lys Cys
145 150 155 160

Val Glu Gly Met Val Glu Ile Phe Asp Met Leu Leu Ala Thr Ser Ser
165 170 175

Arg Phe Arg Met Met Asn Leu Gln Gly Glu Glu Phe Val Cys Leu Lys
180 185 190

Ser Ile Ile Leu Leu Asn Ser Gly Val Tyr Thr Phe Leu Ser Ser Thr
195 200 205

Leu Lys Ser Leu Glu Glu Lys Asp His Ile His Arg Val Leu Asp Lys
210 215 220

Ile Thr Asp Thr Leu Ile His Leu Met Ala Lys Ala Gly Leu Thr Leu
225 230 235 240

Gln Gln Gln His Gln Arg Leu Ala Gln Leu Leu Leu Ile Leu Ser His

245 250 255

Ile Arg His Met Ser Asn Lys Arg Met Glu His Leu Tyr Ser Met Lys
260 265 270

Cys Lys Asn Val Val Pro Leu Phe Asp Leu Leu Leu Glu Met Leu Asp
275 280 285

Ala His Arg Leu His Ala Pro Thr Ser
290 295

<210> 706
<211> 60
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 706

Ser Gly Ser Gly Pro Gly Ser Arg Glu Trp Phe Lys Asp Met Leu Gly
1 5 10 15

Gly Gly Ser Gly Gly Gly Ser Ser Gly Ser Gly Pro Gly Ser Arg Glu
20 25 30

Trp Phe Lys Asp Met Leu Gly Gly Gly Ser Gly Gly Gly Ser Ser Gly
35 40 45

Ser Gly Pro Gly Ser Arg Glu Trp Phe Lys Asp Met
50 55 60

<210> 707
<211> 64
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 707

Asp Ala Phe Gln Leu Arg Gln Leu Ile Leu Arg Gly Leu Gln Asp Asp
1 5 10 15

Gly Gly Gly Ser Gly Gly Gly Ser Asp Ala Phe Gln Leu Arg Gln Leu
20 25 30

Ile Leu Arg Gly Leu Gln Asp Asp Gly Gly Gly Ser Gly Gly Gly Ser
35 40 45

Asp Ala Phe Gln Leu Arg Gln Leu Ile Leu Arg Gly Leu Gln Asp Asp
50 55 60

<210> 708

<211> 459
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 708

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15

His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Asp
            20                  25                  30

Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly Asp
        35                  40                  45

Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr Leu
    50                  55                  60

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

His Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
                85                  90                  95

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

Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr
        115                 120                 125

Phe Gly Gly Gly Thr Lys Leu Glu Ile Thr Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Lys Leu Gln Glu Ser
145                 150                 155                 160

Gly Pro Gly Leu Val Ala Pro Ser Gln Ser Leu Ser Val Thr Cys Thr
                165                 170                 175

Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg Gln
            180                 185                 190

Pro Pro Arg Lys Gly Leu Glu Trp Leu Gly Val Ile Trp Gly Ser Glu
        195                 200                 205

Thr Thr Tyr Tyr Asn Ser Ala Leu Lys Ser Arg Leu Thr Ile Ile Lys
    210                 215                 220

Asp Asn Ser Lys Ser Gln Val Phe Leu Lys Met Asn Ser Leu Gln Thr
225                 230                 235                 240
```

```
Asp Asp Thr Ala Ile Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly Gly
                245                 250                 255

Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser
            260                 265                 270

Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile
        275                 280                 285

Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala
    290                 295                 300

Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr
305                 310                 315                 320

Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu
                325                 330                 335

Val Ile Thr Leu Tyr Cys Ser Leu Lys Arg Gly Arg Lys Lys Leu Leu
            340                 345                 350

Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu
        355                 360                 365

Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys
    370                 375                 380

Glu Leu Ser Arg Gly Ser Gly Ser Gly Ser Thr Ser Ser Gly Ser Gly
385                 390                 395                 400

Pro Gly Ser Arg Glu Trp Phe Lys Asp Met Leu Gly Gly Gly Ser Gly
                405                 410                 415

Gly Gly Ser Ser Gly Ser Gly Pro Gly Ser Arg Glu Trp Phe Lys Asp
            420                 425                 430

Met Leu Gly Gly Gly Ser Gly Gly Gly Ser Ser Gly Ser Gly Pro Gly
        435                 440                 445

Ser Arg Glu Trp Phe Lys Asp Met Leu Gly Ser
    450                 455


<210>  709
<211>  462
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic amino acid sequence

<400>  709

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
```

1 5 10 15

His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Asp
20 25 30

Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly Asp
35 40 45

Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr Leu
50 55 60

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

His Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
85 90 95

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

Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr
115 120 125

Phe Gly Gly Gly Thr Lys Leu Glu Ile Thr Gly Gly Gly Gly Ser Gly
130 135 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Lys Leu Gln Glu Ser
145 150 155 160

Gly Pro Gly Leu Val Ala Pro Ser Gln Ser Leu Ser Val Thr Cys Thr
165 170 175

Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg Gln
180 185 190

Pro Pro Arg Lys Gly Leu Glu Trp Leu Gly Val Ile Trp Gly Ser Glu
195 200 205

Thr Thr Tyr Tyr Asn Ser Ala Leu Lys Ser Arg Leu Thr Ile Ile Lys
210 215 220

Asp Asn Ser Lys Ser Gln Val Phe Leu Lys Met Asn Ser Leu Gln Thr
225 230 235 240

Asp Asp Thr Ala Ile Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly Gly
245 250 255

Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser
260 265 270

Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile

275 280 285

Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala
290 295 300

Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr
305 310 315 320

Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu
325 330 335

Val Ile Thr Leu Tyr Cys Ser Leu Lys Arg Gly Arg Lys Lys Leu Leu
340 345 350

Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu
355 360 365

Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys
370 375 380

Glu Leu Ser Arg Gly Ser Gly Ser Gly Ser Thr Ser Asp Ala Phe Gln
385 390 395 400

Leu Arg Gln Leu Ile Leu Arg Gly Leu Gln Asp Asp Gly Gly Gly Ser
405 410 415

Gly Gly Gly Ser Asp Ala Phe Gln Leu Arg Gln Leu Ile Leu Arg Gly
420 425 430

Leu Gln Asp Asp Gly Gly Gly Ser Gly Gly Gly Ser Asp Ala Phe Gln
435 440 445

Leu Arg Gln Leu Ile Leu Arg Gly Leu Gln Asp Asp Gly Ser
450 455 460

<210> 710
<211> 801
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 710

Met Ile His Leu Gly His Ile Leu Phe Leu Leu Leu Leu Pro Val Ala
1 5 10 15

Ala Ala Gln Thr Thr Pro Gly Glu Arg Ser Ser Leu Pro Ala Phe Tyr
20 25 30

Pro Gly Thr Ser Gly Ser Cys Ser Gly Cys Gly Ser Leu Ser Leu Pro
35 40 45

```
Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu
    50                  55                  60

Ser Leu Val Ile Thr Leu Tyr Cys Ser Leu Lys Arg Gly Arg Lys Lys
65                  70                  75                  80

Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr
                85                  90                  95

Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly
            100                 105                 110

Gly Cys Glu Leu Gly Ser Gly Ser Gly Ser Gly Ser Gly Ser Gly Ser
        115                 120                 125

Gly Ser Thr Ser Asp Arg Arg Gly Gly Arg Met Leu Lys His Lys Arg
    130                 135                 140

Gln Arg Asp Asp Gly Glu Gly Arg Gly Glu Val Gly Ser Ala Gly Asp
145                 150                 155                 160

Met Arg Ala Ala Asn Leu Trp Pro Ser Pro Leu Met Ile Lys Arg Ser
                165                 170                 175

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

Ala Leu Leu Asp Ala Glu Pro Pro Ile Leu Tyr Ser Glu Tyr Asp Pro
        195                 200                 205

Thr Arg Pro Phe Ser Glu Ala Ser Met Met Gly Leu Leu Thr Asn Leu
    210                 215                 220

Ala Asp Arg Glu Leu Val His Met Ile Asn Trp Ala Lys Arg Val Pro
225                 230                 235                 240

Gly Phe Val Asp Leu Thr Leu His Asp Gln Val His Leu Leu Glu Cys
                245                 250                 255

Ala Trp Leu Glu Ile Leu Met Ile Gly Leu Val Trp Arg Ser Met Glu
            260                 265                 270

His Pro Gly Lys Leu Leu Phe Ala Pro Asn Leu Leu Leu Asp Arg Asn
        275                 280                 285

Gln Gly Lys Cys Val Glu Gly Met Val Glu Ile Phe Asp Met Leu Leu
    290                 295                 300

Ala Thr Ser Ser Arg Phe Arg Met Met Asn Leu Gln Gly Glu Glu Phe
305                 310                 315                 320
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Val Cys Leu Lys Ser Ile Ile Leu Leu Asn Ser Gly Val Tyr Thr Phe
                325                 330                 335

Leu Ser Ser Thr Leu Lys Ser Leu Glu Glu Lys Asp His Ile His Arg
            340                 345                 350

Val Leu Asp Lys Ile Thr Asp Thr Leu Ile His Leu Met Ala Lys Ala
        355                 360                 365

Gly Leu Thr Leu Gln Gln Gln His Gln Arg Leu Ala Gln Leu Leu Leu
    370                 375                 380

Ile Leu Ser His Ile Arg His Met Ser Asn Lys Gly Met Glu His Leu
385                 390                 395                 400

Tyr Ser Met Lys Cys Lys Asn Val Val Pro Leu Tyr Asp Leu Leu Leu
                405                 410                 415

Glu Met Leu Asp Ala His Arg Leu His Ala Pro Thr Ser Gly Ser Gly
            420                 425                 430

Ser Gly Ser Gly Ser Ser Leu Arg Val Lys Phe Ser Arg Ser Ala Asp
        435                 440                 445

Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn
    450                 455                 460

Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg
465                 470                 475                 480

Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly
                485                 490                 495

Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu
            500                 505                 510

Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu
        515                 520                 525

Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His
    530                 535                 540

Met Gln Ala Leu Pro Pro Arg Ser Arg Gly Ser Gly Ser Gly Ser Gly
545                 550                 555                 560

Ser Met Val Ser Lys Gly Glu Glu Asp Asn Met Ala Ile Ile Lys Glu
                565                 570                 575

Phe Met Arg Phe Lys Val His Met Glu Gly Ser Val Asn Gly His Glu
            580                 585                 590
```

Phe Glu Ile Glu Gly Glu Gly Glu Gly Arg Pro Tyr Glu Gly Thr Gln
595 600 605

Thr Ala Lys Leu Lys Val Thr Lys Gly Gly Pro Leu Pro Phe Ala Trp
610 615 620

Asp Ile Leu Ser Pro Gln Phe Met Tyr Gly Ser Lys Ala Tyr Val Lys
625 630 635 640

His Pro Ala Asp Ile Pro Asp Tyr Leu Lys Leu Ser Phe Pro Glu Gly
645 650 655

Phe Lys Trp Glu Arg Val Met Asn Phe Glu Asp Gly Gly Val Val Thr
660 665 670

Val Thr Gln Asp Ser Ser Leu Gln Asp Gly Glu Phe Ile Tyr Lys Val
675 680 685

Lys Leu Arg Gly Thr Asn Phe Pro Ser Asp Gly Pro Val Met Gln Lys
690 695 700

Lys Thr Met Gly Trp Glu Ala Ser Ser Glu Arg Met Tyr Pro Glu Asp
705 710 715 720

Gly Ala Leu Lys Gly Glu Ile Lys Gln Arg Leu Lys Leu Lys Asp Gly
725 730 735

Gly His Tyr Asp Ala Glu Val Lys Thr Thr Tyr Lys Ala Lys Lys Pro
740 745 750

Val Gln Leu Pro Gly Ala Tyr Asn Val Asn Ile Lys Leu Asp Ile Thr
755 760 765

Ser His Asn Glu Asp Tyr Thr Ile Val Glu Gln Tyr Glu Arg Ala Glu
770 775 780

Gly Arg His Ser Thr Gly Gly Met Asp Glu Leu Tyr Lys Cys Val Thr
785 790 795 800

Asp

<210> 711
<211> 801
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 711

Met Ile His Leu Gly His Ile Leu Phe Leu Leu Leu Leu Pro Val Ala

1 5 10 15

Ala Ala Gln Thr Thr Pro Gly Glu Arg Ser Ser Leu Pro Ala Phe Tyr
20 25 30

Pro Gly Thr Ser Gly Ser Cys Ser Gly Cys Gly Ser Leu Ser Leu Pro
35 40 45

Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu
50 55 60

Ser Leu Val Ile Thr Leu Tyr Cys Ser Leu Lys Arg Gly Arg Lys Lys
65 70 75 80

Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr
85 90 95

Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly
100 105 110

Gly Cys Glu Leu Gly Ser Gly Ser Gly Ser Gly Ser Gly Ser Gly Ser
115 120 125

Gly Ser Thr Ser Asp Arg Arg Gly Gly Arg Met Leu Lys His Lys Arg
130 135 140

Gln Arg Asp Asp Gly Glu Gly Arg Gly Glu Val Gly Ser Ala Gly Asp
145 150 155 160

Met Arg Ala Ala Asn Leu Trp Pro Ser Pro Leu Met Ile Lys Arg Ser
165 170 175

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

Ala Leu Leu Asp Ala Glu Pro Pro Ile Leu Tyr Ser Glu Tyr Asp Pro
195 200 205

Thr Arg Pro Phe Ser Glu Ala Ser Met Met Gly Leu Leu Thr Asn Leu
210 215 220

Ala Asp Arg Glu Leu Val His Met Ile Asn Trp Ala Lys Arg Val Pro
225 230 235 240

Gly Phe Val Asp Leu Thr Leu His Asp Gln Val His Leu Leu Glu Cys
245 250 255

Ala Trp Leu Glu Ile Leu Met Ile Gly Leu Val Trp Arg Ser Met Glu
260 265 270

His Pro Gly Lys Leu Leu Phe Ala Pro Asn Leu Leu Leu Asp Arg Asn

275 280 285

Gln Gly Lys Cys Val Glu Gly Met Val Glu Ile Phe Asp Met Leu Leu
290 295 300

Ala Thr Ser Ser Arg Phe Arg Met Met Asn Leu Gln Gly Glu Glu Phe
305 310 315 320

Val Cys Leu Lys Ser Ile Ile Leu Leu Asn Ser Gly Val Tyr Thr Phe
325 330 335

Leu Ser Ser Thr Leu Lys Ser Leu Glu Glu Lys Asp His Ile His Arg
340 345 350

Val Leu Asp Lys Ile Thr Asp Thr Leu Ile His Leu Met Ala Lys Ala
355 360 365

Gly Leu Thr Leu Gln Gln Gln His Gln Arg Leu Ala Gln Leu Leu Leu
370 375 380

Ile Leu Ser His Ile Arg His Met Ser Asn Lys Gly Met Glu His Leu
385 390 395 400

Tyr Ser Met Lys Cys Lys Asn Val Val Pro Leu Phe Asp Leu Leu Leu
405 410 415

Glu Met Leu Asp Ala His Arg Leu His Ala Pro Thr Ser Gly Ser Gly
420 425 430

Ser Gly Ser Gly Ser Ser Leu Arg Val Lys Phe Ser Arg Ser Ala Asp
435 440 445

Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn
450 455 460

Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg
465 470 475 480

Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly
485 490 495

Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu
500 505 510

Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu
515 520 525

Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His
530 535 540

Met Gln Ala Leu Pro Pro Arg Ser Arg Gly Ser Gly Ser Gly Ser Gly

545 550 555 560

Ser Met Val Ser Lys Gly Glu Glu Asp Asn Met Ala Ile Ile Lys Glu
565 570 575

Phe Met Arg Phe Lys Val His Met Glu Gly Ser Val Asn Gly His Glu
580 585 590

Phe Glu Ile Glu Gly Glu Gly Glu Gly Arg Pro Tyr Glu Gly Thr Gln
595 600 605

Thr Ala Lys Leu Lys Val Thr Lys Gly Gly Pro Leu Pro Phe Ala Trp
610 615 620

Asp Ile Leu Ser Pro Gln Phe Met Tyr Gly Ser Lys Ala Tyr Val Lys
625 630 635 640

His Pro Ala Asp Ile Pro Asp Tyr Leu Lys Leu Ser Phe Pro Glu Gly
645 650 655

Phe Lys Trp Glu Arg Val Met Asn Phe Glu Asp Gly Gly Val Val Thr
660 665 670

Val Thr Gln Asp Ser Ser Leu Gln Asp Gly Glu Phe Ile Tyr Lys Val
675 680 685

Lys Leu Arg Gly Thr Asn Phe Pro Ser Asp Gly Pro Val Met Gln Lys
690 695 700

Lys Thr Met Gly Trp Glu Ala Ser Ser Glu Arg Met Tyr Pro Glu Asp
705 710 715 720

Gly Ala Leu Lys Gly Glu Ile Lys Gln Arg Leu Lys Leu Lys Asp Gly
725 730 735

Gly His Tyr Asp Ala Glu Val Lys Thr Thr Tyr Lys Ala Lys Lys Pro
740 745 750

Val Gln Leu Pro Gly Ala Tyr Asn Val Asn Ile Lys Leu Asp Ile Thr
755 760 765

Ser His Asn Glu Asp Tyr Thr Ile Val Glu Gln Tyr Glu Arg Ala Glu
770 775 780

Gly Arg His Ser Thr Gly Gly Met Asp Glu Leu Tyr Lys Cys Val Thr
785 790 795 800

Asp

<210> 712

<211> 801
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 712

```
Met Ile His Leu Gly His Ile Leu Phe Leu Leu Leu Leu Pro Val Ala
1               5                   10                  15


Ala Ala Gln Thr Thr Pro Gly Glu Arg Ser Ser Leu Pro Ala Phe Tyr
            20                  25                  30


Pro Gly Thr Ser Gly Ser Cys Ser Gly Cys Gly Ser Leu Ser Leu Pro
        35                  40                  45


Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu
    50                  55                  60


Ser Leu Val Ile Thr Leu Tyr Cys Ser Leu Lys Arg Gly Arg Lys Lys
65                  70                  75                  80


Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr
                85                  90                  95


Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly
            100                 105                 110


Gly Cys Glu Leu Gly Ser Gly Ser Gly Ser Gly Ser Gly Ser Gly Ser
        115                 120                 125


Gly Ser Thr Ser Asp Arg Arg Gly Gly Arg Met Leu Lys His Lys Arg
    130                 135                 140


Gln Arg Asp Asp Gly Glu Gly Arg Gly Glu Val Gly Ser Ala Gly Asp
145                 150                 155                 160


Met Arg Ala Ala Asn Leu Trp Pro Ser Pro Leu Met Ile Lys Arg Ser
                165                 170                 175


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


Ala Leu Leu Asp Ala Glu Pro Pro Ile Leu Tyr Ser Glu Tyr Asp Pro
        195                 200                 205


Thr Arg Pro Phe Ser Glu Ala Ser Met Met Gly Leu Leu Thr Asn Leu
    210                 215                 220


Ala Asp Arg Glu Leu Val His Met Ile Asn Trp Ala Lys Arg Val Pro
225                 230                 235                 240
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Gly Phe Val Asp Leu Thr Leu His Asp Gln Val His Leu Leu Glu Cys
                245                 250                 255

Ala Trp Leu Glu Ile Leu Met Ile Gly Leu Val Trp Arg Ser Met Glu
            260                 265                 270

His Pro Gly Lys Leu Leu Phe Ala Pro Asn Leu Leu Leu Asp Arg Asn
        275                 280                 285

Gln Gly Lys Cys Val Glu Gly Met Val Glu Ile Phe Asp Met Leu Leu
    290                 295                 300

Ala Thr Ser Ser Arg Phe Arg Met Met Asn Leu Gln Gly Glu Glu Phe
305                 310                 315                 320

Val Cys Leu Lys Ser Ile Ile Leu Leu Asn Ser Gly Val Tyr Thr Phe
                325                 330                 335

Leu Ser Ser Thr Leu Lys Ser Leu Glu Glu Lys Asp His Ile His Arg
            340                 345                 350

Val Leu Asp Lys Ile Thr Asp Thr Leu Ile His Leu Met Ala Lys Ala
        355                 360                 365

Gly Leu Thr Leu Gln Gln Gln His Gln Arg Leu Ala Gln Leu Leu Leu
    370                 375                 380

Ile Leu Ser His Ile Arg His Met Ser Asn Lys Arg Met Glu His Leu
385                 390                 395                 400

Tyr Ser Met Lys Cys Lys Asn Val Val Pro Leu Phe Asp Leu Leu Leu
                405                 410                 415

Glu Met Leu Asp Ala His Arg Leu His Ala Pro Thr Ser Gly Ser Gly
            420                 425                 430

Ser Gly Ser Gly Ser Ser Leu Arg Val Lys Phe Ser Arg Ser Ala Asp
        435                 440                 445

Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn
    450                 455                 460

Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg
465                 470                 475                 480

Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly
                485                 490                 495

Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu
            500                 505                 510
```

```
Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu
        515                 520                 525

Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His
    530                 535                 540

Met Gln Ala Leu Pro Pro Arg Ser Arg Gly Ser Gly Ser Gly Ser Gly
545                 550                 555                 560

Ser Met Val Ser Lys Gly Glu Glu Asp Asn Met Ala Ile Ile Lys Glu
                565                 570                 575

Phe Met Arg Phe Lys Val His Met Glu Gly Ser Val Asn Gly His Glu
            580                 585                 590

Phe Glu Ile Glu Gly Glu Gly Glu Gly Arg Pro Tyr Glu Gly Thr Gln
        595                 600                 605

Thr Ala Lys Leu Lys Val Thr Lys Gly Gly Pro Leu Pro Phe Ala Trp
    610                 615                 620

Asp Ile Leu Ser Pro Gln Phe Met Tyr Gly Ser Lys Ala Tyr Val Lys
625                 630                 635                 640

His Pro Ala Asp Ile Pro Asp Tyr Leu Lys Leu Ser Phe Pro Glu Gly
                645                 650                 655

Phe Lys Trp Glu Arg Val Met Asn Phe Glu Asp Gly Gly Val Val Thr
            660                 665                 670

Val Thr Gln Asp Ser Ser Leu Gln Asp Gly Glu Phe Ile Tyr Lys Val
        675                 680                 685

Lys Leu Arg Gly Thr Asn Phe Pro Ser Asp Gly Pro Val Met Gln Lys
    690                 695                 700

Lys Thr Met Gly Trp Glu Ala Ser Ser Glu Arg Met Tyr Pro Glu Asp
705                 710                 715                 720

Gly Ala Leu Lys Gly Glu Ile Lys Gln Arg Leu Lys Leu Lys Asp Gly
                725                 730                 735

Gly His Tyr Asp Ala Glu Val Lys Thr Thr Tyr Lys Ala Lys Lys Pro
            740                 745                 750

Val Gln Leu Pro Gly Ala Tyr Asn Val Asn Ile Lys Leu Asp Ile Thr
        755                 760                 765

Ser His Asn Glu Asp Tyr Thr Ile Val Glu Gln Tyr Glu Arg Ala Glu
    770                 775                 780
```

Gly Arg His Ser Thr Gly Gly Met Asp Glu Leu Tyr Lys Cys Val Thr
785 790 795 800

Asp

<210> 713
<211> 781
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 713

Met Ile His Leu Gly His Ile Leu Phe Leu Leu Leu Leu Pro Val Ala
1 5 10 15

Ala Ala Gln Thr Thr Pro Gly Glu Arg Ser Ser Leu Pro Ala Phe Tyr
20 25 30

Pro Gly Thr Ser Gly Ser Cys Ser Gly Cys Gly Ser Leu Ser Leu Pro
35 40 45

Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu
50 55 60

Ser Leu Val Ile Thr Leu Tyr Cys Ser Leu Lys Arg Gly Arg Lys Lys
65 70 75 80

Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr
85 90 95

Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly
100 105 110

Gly Cys Glu Leu Gly Ser Gly Ser Gly Ser Gly Ser Gly Ser Gly Ser
115 120 125

Gly Ser Thr Ser Asp Arg Arg Gly Gly Arg Met Leu Lys His Lys Arg
130 135 140

Gln Arg Asp Asp Gly Glu Gly Arg Gly Glu Val Gly Ser Ala Gly Asp
145 150 155 160

Met Arg Ala Ala Asn Leu Trp Pro Ser Pro Leu Met Ile Lys Arg Ser
165 170 175

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

Ala Leu Leu Asp Ala Glu Pro Pro Ile Leu Tyr Ser Glu Tyr Asp Pro

195 200 205

Thr Arg Pro Phe Ser Glu Ala Ser Met Met Gly Leu Leu Thr Asn Leu
210 215 220

Ala Asp Arg Glu Leu Val His Met Ile Asn Trp Ala Lys Arg Val Pro
225 230 235 240

Gly Phe Val Asp Leu Thr Leu His Asp Gln Val His Leu Leu Glu Cys
245 250 255

Ala Trp Leu Glu Ile Leu Met Ile Gly Leu Val Trp Arg Ser Met Glu
260 265 270

His Pro Gly Lys Leu Leu Phe Ala Pro Asn Leu Leu Leu Asp Arg Asn
275 280 285

Gln Gly Lys Cys Val Glu Gly Met Val Glu Ile Phe Asp Met Leu Leu
290 295 300

Ala Thr Ser Ser Arg Phe Arg Met Met Asn Leu Gln Gly Glu Glu Phe
305 310 315 320

Val Cys Leu Lys Ser Ile Ile Leu Leu Asn Ser Gly Val Tyr Thr Phe
325 330 335

Leu Ser Ser Thr Leu Lys Ser Leu Glu Glu Lys Asp His Ile His Arg
340 345 350

Val Leu Asp Lys Ile Thr Asp Thr Leu Ile His Leu Met Ala Lys Ala
355 360 365

Gly Leu Thr Leu Gln Gln Gln His Gln Arg Leu Ala Gln Leu Leu Leu
370 375 380

Ile Leu Ser His Ile Arg His Met Ser Asn Lys Gly Met Glu His Leu
385 390 395 400

Tyr Ser Met Lys Cys Lys Asn Val Ala Gly Ser Gly Ser Gly Ser Gly
405 410 415

Ser Ser Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr
420 425 430

Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg
435 440 445

Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met
450 455 460

Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu

```
465                 470                 475                 480

Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys
                485                 490                 495

Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu
            500                 505                 510

Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu
        515                 520                 525

Pro Pro Arg Ser Arg Gly Ser Gly Ser Gly Ser Gly Ser Met Val Ser
    530                 535                 540

Lys Gly Glu Glu Asp Asn Met Ala Ile Ile Lys Glu Phe Met Arg Phe
545                 550                 555                 560

Lys Val His Met Glu Gly Ser Val Asn Gly His Glu Phe Glu Ile Glu
                565                 570                 575

Gly Glu Gly Glu Gly Arg Pro Tyr Glu Gly Thr Gln Thr Ala Lys Leu
            580                 585                 590

Lys Val Thr Lys Gly Gly Pro Leu Pro Phe Ala Trp Asp Ile Leu Ser
        595                 600                 605

Pro Gln Phe Met Tyr Gly Ser Lys Ala Tyr Val Lys His Pro Ala Asp
    610                 615                 620

Ile Pro Asp Tyr Leu Lys Leu Ser Phe Pro Glu Gly Phe Lys Trp Glu
625                 630                 635                 640

Arg Val Met Asn Phe Glu Asp Gly Gly Val Val Thr Val Thr Gln Asp
                645                 650                 655

Ser Ser Leu Gln Asp Gly Glu Phe Ile Tyr Lys Val Lys Leu Arg Gly
            660                 665                 670

Thr Asn Phe Pro Ser Asp Gly Pro Val Met Gln Lys Lys Thr Met Gly
        675                 680                 685

Trp Glu Ala Ser Ser Glu Arg Met Tyr Pro Glu Asp Gly Ala Leu Lys
    690                 695                 700

Gly Glu Ile Lys Gln Arg Leu Lys Leu Lys Asp Gly Gly His Tyr Asp
705                 710                 715                 720

Ala Glu Val Lys Thr Thr Tyr Lys Ala Lys Lys Pro Val Gln Leu Pro
                725                 730                 735

Gly Ala Tyr Asn Val Asn Ile Lys Leu Asp Ile Thr Ser His Asn Glu
```

740 745 750

Asp Tyr Thr Ile Val Glu Gln Tyr Glu Arg Ala Glu Gly Arg His Ser
755 760 765

Thr Gly Gly Met Asp Glu Leu Tyr Lys Cys Val Thr Asp
770 775 780

<210> 714
<211> 781
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 714

Met Ile His Leu Gly His Ile Leu Phe Leu Leu Leu Leu Pro Val Ala
1 5 10 15

Ala Ala Gln Thr Thr Pro Gly Glu Arg Ser Ser Leu Pro Ala Phe Tyr
20 25 30

Pro Gly Thr Ser Gly Ser Cys Ser Gly Cys Gly Ser Leu Ser Leu Pro
35 40 45

Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu
50 55 60

Ser Leu Val Ile Thr Leu Tyr Cys Ser Leu Lys Arg Gly Arg Lys Lys
65 70 75 80

Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr
85 90 95

Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly
100 105 110

Gly Cys Glu Leu Gly Ser Gly Ser Gly Ser Gly Ser Gly Ser Gly Ser
115 120 125

Gly Ser Thr Ser Asp Arg Arg Gly Gly Arg Met Leu Lys His Lys Arg
130 135 140

Gln Arg Asp Asp Gly Glu Gly Arg Gly Glu Val Gly Ser Ala Gly Asp
145 150 155 160

Met Arg Ala Ala Asn Leu Trp Pro Ser Pro Leu Met Ile Lys Arg Ser
165 170 175

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

```
Ala Leu Leu Asp Ala Glu Pro Pro Ile Leu Tyr Ser Glu Tyr Asp Pro
        195                 200                 205

Thr Arg Pro Phe Ser Glu Ala Ser Met Met Gly Leu Leu Thr Asn Leu
    210                 215                 220

Ala Asp Arg Glu Leu Val His Met Ile Asn Trp Ala Lys Arg Val Pro
225                 230                 235                 240

Gly Phe Val Asp Leu Thr Leu His Asp Gln Val His Leu Leu Glu Cys
                245                 250                 255

Ala Trp Leu Glu Ile Leu Met Ile Gly Leu Val Trp Arg Ser Met Glu
            260                 265                 270

His Pro Gly Lys Leu Leu Phe Ala Pro Asn Leu Leu Leu Asp Arg Asn
        275                 280                 285

Gln Gly Lys Cys Val Glu Gly Met Val Glu Ile Phe Asp Met Leu Leu
    290                 295                 300

Ala Thr Ser Ser Arg Phe Arg Met Met Asn Leu Gln Gly Glu Glu Phe
305                 310                 315                 320

Val Cys Leu Lys Ser Ile Ile Leu Leu Asn Ser Gly Val Tyr Thr Phe
                325                 330                 335

Leu Ser Ser Thr Leu Lys Ser Leu Glu Glu Lys Asp His Ile His Arg
            340                 345                 350

Val Leu Asp Lys Ile Thr Asp Thr Leu Ile His Leu Met Ala Lys Ala
        355                 360                 365

Gly Leu Thr Leu Gln Gln Gln His Gln Arg Leu Ala Gln Leu Leu Leu
    370                 375                 380

Ile Leu Ser His Ile Arg His Met Ser Asn Lys Arg Met Glu His Leu
385                 390                 395                 400

Tyr Ser Met Lys Cys Lys Asn Val Ala Gly Ser Gly Ser Gly Ser Gly
                405                 410                 415

Ser Ser Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr
            420                 425                 430

Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg
        435                 440                 445

Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met
    450                 455                 460
```

```
Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu
465                 470                 475                 480

Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys
                485                 490                 495

Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu
            500                 505                 510

Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu
        515                 520                 525

Pro Pro Arg Ser Arg Gly Ser Gly Ser Gly Ser Gly Ser Met Val Ser
    530                 535                 540

Lys Gly Glu Glu Asp Asn Met Ala Ile Ile Lys Glu Phe Met Arg Phe
545                 550                 555                 560

Lys Val His Met Glu Gly Ser Val Asn Gly His Glu Phe Glu Ile Glu
                565                 570                 575

Gly Glu Gly Glu Gly Arg Pro Tyr Glu Gly Thr Gln Thr Ala Lys Leu
            580                 585                 590

Lys Val Thr Lys Gly Gly Pro Leu Pro Phe Ala Trp Asp Ile Leu Ser
        595                 600                 605

Pro Gln Phe Met Tyr Gly Ser Lys Ala Tyr Val Lys His Pro Ala Asp
    610                 615                 620

Ile Pro Asp Tyr Leu Lys Leu Ser Phe Pro Glu Gly Phe Lys Trp Glu
625                 630                 635                 640

Arg Val Met Asn Phe Glu Asp Gly Gly Val Val Thr Val Thr Gln Asp
                645                 650                 655

Ser Ser Leu Gln Asp Gly Glu Phe Ile Tyr Lys Val Lys Leu Arg Gly
            660                 665                 670

Thr Asn Phe Pro Ser Asp Gly Pro Val Met Gln Lys Lys Thr Met Gly
        675                 680                 685

Trp Glu Ala Ser Ser Glu Arg Met Tyr Pro Glu Asp Gly Ala Leu Lys
    690                 695                 700

Gly Glu Ile Lys Gln Arg Leu Lys Leu Lys Asp Gly Gly His Tyr Asp
705                 710                 715                 720

Ala Glu Val Lys Thr Thr Tyr Lys Ala Lys Lys Pro Val Gln Leu Pro
                725                 730                 735
```

Gly Ala Tyr Asn Val Asn Ile Lys Leu Asp Ile Thr Ser His Asn Glu
740 745 750

Asp Tyr Thr Ile Val Glu Gln Tyr Glu Arg Ala Glu Gly Arg His Ser
755 760 765

Thr Gly Gly Met Asp Glu Leu Tyr Lys Cys Val Thr Asp
770 775 780

<210> 715
<211> 465
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 715

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Asp
20 25 30

Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly Asp
35 40 45

Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr Leu
50 55 60

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

His Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
85 90 95

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

Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr
115 120 125

Phe Gly Gly Gly Thr Lys Leu Glu Ile Thr Gly Gly Gly Gly Ser Gly
130 135 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Lys Leu Gln Glu Ser
145 150 155 160

Gly Pro Gly Leu Val Ala Pro Ser Gln Ser Leu Ser Val Thr Cys Thr
165 170 175

Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg Gln

```
            180                 185                 190

Pro Pro Arg Lys Gly Leu Glu Trp Leu Gly Val Ile Trp Gly Ser Glu
        195                 200                 205

Thr Thr Tyr Tyr Asn Ser Ala Leu Lys Ser Arg Leu Thr Ile Ile Lys
    210                 215                 220

Asp Asn Ser Lys Ser Gln Val Phe Leu Lys Met Asn Ser Leu Gln Thr
225                 230                 235                 240

Asp Asp Thr Ala Ile Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly Gly
                245                 250                 255

Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser
            260                 265                 270

Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile
        275                 280                 285

Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala
    290                 295                 300

Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr
305                 310                 315                 320

Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu
                325                 330                 335

Val Ile Thr Leu Tyr Cys Ser Leu Lys Arg Gly Arg Lys Lys Leu Leu
            340                 345                 350

Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu
        355                 360                 365

Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys
    370                 375                 380

Glu Leu Ser Arg Gly Ser Gly Ser Gly Ser Thr Ser Pro Arg Gln Gly
385                 390                 395                 400

Ser Ile Leu Tyr Ser Met Leu Thr Ser Ala Lys Gln Thr Gly Gly Gly
                405                 410                 415

Ser Gly Gly Gly Ser Pro Arg Gln Gly Ser Ile Leu Tyr Ser Met Leu
            420                 425                 430

Thr Ser Ala Lys Gln Thr Gly Gly Gly Ser Gly Gly Gly Ser Pro Arg
        435                 440                 445

Gln Gly Ser Ile Leu Tyr Ser Met Leu Thr Ser Ala Lys Gln Thr Gly
```

450 455 460

Ser
465

<210> 716
<211> 471
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 716

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Asp
20 25 30

Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly Asp
35 40 45

Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr Leu
50 55 60

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

His Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
85 90 95

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

Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr
115 120 125

Phe Gly Gly Gly Thr Lys Leu Glu Ile Thr Gly Gly Gly Gly Ser Gly
130 135 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Lys Leu Gln Glu Ser
145 150 155 160

Gly Pro Gly Leu Val Ala Pro Ser Gln Ser Leu Ser Val Thr Cys Thr
165 170 175

Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg Gln
180 185 190

Pro Pro Arg Lys Gly Leu Glu Trp Leu Gly Val Ile Trp Gly Ser Glu
195 200 205

```
Thr Thr Tyr Tyr Asn Ser Ala Leu Lys Ser Arg Leu Thr Ile Ile Lys
    210                 215                 220

Asp Asn Ser Lys Ser Gln Val Phe Leu Lys Met Asn Ser Leu Gln Thr
225                 230                 235                 240

Asp Asp Thr Ala Ile Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly Gly
                245                 250                 255

Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser
            260                 265                 270

Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile
        275                 280                 285

Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala
    290                 295                 300

Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr
305                 310                 315                 320

Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu
                325                 330                 335

Val Ile Thr Leu Tyr Cys Ser Leu Lys Arg Gly Arg Lys Lys Leu Leu
            340                 345                 350

Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu
        355                 360                 365

Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys
    370                 375                 380

Glu Leu Ser Arg Gly Ser Gly Ser Gly Ser Thr Ser Leu Thr Glu Arg
385                 390                 395                 400

His Lys Ile Leu His Arg Leu Leu Gln Glu Gly Ser Pro Ser Asp Gly
                405                 410                 415

Gly Gly Ser Gly Gly Gly Ser Leu Thr Glu Arg His Lys Ile Leu His
            420                 425                 430

Arg Leu Leu Gln Glu Gly Ser Pro Ser Asp Gly Gly Gly Ser Gly Gly
        435                 440                 445

Gly Ser Leu Thr Glu Arg His Lys Ile Leu His Arg Leu Leu Gln Glu
    450                 455                 460

Gly Ser Pro Ser Asp Gly Ser
465                 470
```

<210> 717
<211> 465
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 717

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Asp
20 25 30

Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly Asp
35 40 45

Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr Leu
50 55 60

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

His Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
85 90 95

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

Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr
115 120 125

Phe Gly Gly Gly Thr Lys Leu Glu Ile Thr Gly Gly Gly Gly Ser Gly
130 135 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Lys Leu Gln Glu Ser
145 150 155 160

Gly Pro Gly Leu Val Ala Pro Ser Gln Ser Leu Ser Val Thr Cys Thr
165 170 175

Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg Gln
180 185 190

Pro Pro Arg Lys Gly Leu Glu Trp Leu Gly Val Ile Trp Gly Ser Glu
195 200 205

Thr Thr Tyr Tyr Asn Ser Ala Leu Lys Ser Arg Leu Thr Ile Ile Lys
210 215 220

Asp Asn Ser Lys Ser Gln Val Phe Leu Lys Met Asn Ser Leu Gln Thr

225 230 235 240

Asp Asp Thr Ala Ile Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly Gly
245 250 255

Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser
260 265 270

Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile
275 280 285

Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala
290 295 300

Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr
305 310 315 320

Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu
325 330 335

Val Ile Thr Leu Tyr Cys Ser Leu Lys Arg Gly Arg Lys Lys Leu Leu
340 345 350

Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu
355 360 365

Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys
370 375 380

Glu Leu Ser Arg Gly Ser Gly Ser Gly Ser Thr Ser Ser Lys Gly Gln
385 390 395 400

Thr Lys Leu Leu Gln Leu Leu Thr Thr Lys Ser Asp Gln Gly Gly Gly
405 410 415

Ser Gly Gly Gly Ser Ser Lys Gly Gln Thr Lys Leu Leu Gln Leu Leu
420 425 430

Thr Thr Lys Ser Asp Gln Gly Gly Gly Ser Gly Gly Gly Ser Ser Lys
435 440 445

Gly Gln Thr Lys Leu Leu Gln Leu Leu Thr Thr Lys Ser Asp Gln Gly
450 455 460

Ser
465

<210> 718
<211> 465
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 718

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15

His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Asp
            20                  25                  30

Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly Asp
        35                  40                  45

Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr Leu
    50                  55                  60

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

His Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
                85                  90                  95

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

Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr
        115                 120                 125

Phe Gly Gly Gly Thr Lys Leu Glu Ile Thr Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Lys Leu Gln Glu Ser
145                 150                 155                 160

Gly Pro Gly Leu Val Ala Pro Ser Gln Ser Leu Ser Val Thr Cys Thr
                165                 170                 175

Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg Gln
            180                 185                 190

Pro Pro Arg Lys Gly Leu Glu Trp Leu Gly Val Ile Trp Gly Ser Glu
        195                 200                 205

Thr Thr Tyr Tyr Asn Ser Ala Leu Lys Ser Arg Leu Thr Ile Ile Lys
    210                 215                 220

Asp Asn Ser Lys Ser Gln Val Phe Leu Lys Met Asn Ser Leu Gln Thr
225                 230                 235                 240

Asp Asp Thr Ala Ile Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly Gly
                245                 250                 255
```

```
Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser
            260                 265                 270

Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile
        275                 280                 285

Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala
    290                 295                 300

Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr
305                 310                 315                 320

Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu
                325                 330                 335

Val Ile Thr Leu Tyr Cys Ser Leu Lys Arg Gly Arg Lys Lys Leu Leu
            340                 345                 350

Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu
        355                 360                 365

Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys
    370                 375                 380

Glu Leu Ser Arg Gly Ser Gly Ser Gly Ser Thr Ser Ala Glu Glu Pro
385                 390                 395                 400

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

Ser Gly Gly Gly Ser Ala Glu Glu Pro Ser Leu Leu Lys Lys Leu Leu
            420                 425                 430

Leu Ala Pro Ala Asn Thr Gly Gly Gly Ser Gly Gly Gly Ser Ala Glu
        435                 440                 445

Glu Pro Ser Leu Leu Lys Lys Leu Leu Leu Ala Pro Ala Asn Thr Gly
    450                 455                 460

Ser
465
```

<210> 719
<211> 465
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 719

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
```

```
1               5                  10                  15

His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Asp
            20                  25                  30

Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly Asp
        35                  40                  45

Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr Leu
    50                  55                  60

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

His Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
                85                  90                  95

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

Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr
        115                 120                 125

Phe Gly Gly Gly Thr Lys Leu Glu Ile Thr Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Lys Leu Gln Glu Ser
145                 150                 155                 160

Gly Pro Gly Leu Val Ala Pro Ser Gln Ser Leu Ser Val Thr Cys Thr
                165                 170                 175

Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg Gln
            180                 185                 190

Pro Pro Arg Lys Gly Leu Glu Trp Leu Gly Val Ile Trp Gly Ser Glu
        195                 200                 205

Thr Thr Tyr Tyr Asn Ser Ala Leu Lys Ser Arg Leu Thr Ile Ile Lys
    210                 215                 220

Asp Asn Ser Lys Ser Gln Val Phe Leu Lys Met Asn Ser Leu Gln Thr
225                 230                 235                 240

Asp Asp Thr Ala Ile Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly Gly
                245                 250                 255

Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser
            260                 265                 270

Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile
```

275 280 285

Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala
290 295 300

Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr
305 310 315 320

Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu
325 330 335

Val Ile Thr Leu Tyr Cys Ser Leu Lys Arg Gly Arg Lys Lys Leu Leu
340 345 350

Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu
355 360 365

Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys
370 375 380

Glu Leu Ser Arg Gly Ser Gly Ser Gly Ser Thr Ser Ala Ala Asn Asn
385 390 395 400

Ser Leu Leu Leu His Leu Leu Lys Ser Gln Thr Ile Pro Gly Gly Gly
405 410 415

Ser Gly Gly Gly Ser Ala Ala Asn Asn Ser Leu Leu Leu His Leu Leu
420 425 430

Lys Ser Gln Thr Ile Pro Gly Gly Gly Ser Gly Gly Gly Ser Ala Ala
435 440 445

Asn Asn Ser Leu Leu Leu His Leu Leu Lys Ser Gln Thr Ile Pro Gly
450 455 460

Ser
465

<210> 720
<211> 820
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 720

Met Ile His Leu Gly His Ile Leu Phe Leu Leu Leu Leu Pro Val Ala
1 5 10 15

Ala Ala Gln Thr Thr Pro Gly Glu Arg Ser Ser Leu Pro Ala Phe Tyr
20 25 30

```
Pro Gly Thr Ser Gly Ser Cys Ser Gly Cys Gly Ser Leu Ser Leu Pro
        35                  40                  45

Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu
    50                  55                  60

Ser Leu Val Ile Thr Leu Tyr Cys Ser Leu Lys Arg Gly Arg Lys Lys
65                  70                  75                  80

Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr
                85                  90                  95

Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly
            100                 105                 110

Gly Cys Glu Leu Gly Ser Gly Ser Gly Ser Gly Ser Gly Ser Gly Ser
        115                 120                 125

Gly Ser Thr Ser Val Lys Cys Gly Ser Arg Arg Glu Arg Cys Gly Tyr
    130                 135                 140

Arg Leu Val Arg Arg Gln Arg Ser Ala Asp Glu Gln Leu His Cys Ala
145                 150                 155                 160

Gly Lys Ala Lys Arg Ser Gly Gly His Ala Pro Arg Val Arg Glu Leu
                165                 170                 175

Leu Leu Asp Ala Leu Ser Pro Glu Gln Leu Val Leu Thr Leu Leu Glu
            180                 185                 190

Ala Glu Pro Pro His Val Leu Ile Ser Arg Pro Ser Ala Pro Phe Thr
        195                 200                 205

Glu Ala Ser Met Met Met Ser Leu Thr Lys Leu Ala Asp Lys Glu Leu
    210                 215                 220

Val His Met Ile Ser Trp Ala Lys Lys Ile Pro Gly Phe Val Glu Leu
225                 230                 235                 240

Ser Leu Phe Asp Gln Val Arg Leu Leu Glu Ser Cys Trp Met Glu Val
                245                 250                 255

Leu Met Met Gly Leu Met Trp Arg Ser Ile Asp His Pro Gly Lys Leu
            260                 265                 270

Ile Phe Ala Pro Asp Leu Val Leu Asp Arg Asp Glu Gly Lys Cys Val
        275                 280                 285

Glu Gly Ile Leu Glu Ile Phe Asp Met Leu Leu Ala Thr Thr Ser Arg
    290                 295                 300
```

```
Phe Arg Glu Leu Lys Leu Gln His Lys Glu Tyr Leu Cys Val Lys Ala
305                 310                 315                 320

Met Ile Leu Leu Asn Ser Ser Met Tyr Pro Leu Val Thr Ala Thr Gln
                325                 330                 335

Asp Ala Asp Ser Ser Arg Lys Leu Ala His Leu Leu Asn Ala Val Thr
            340                 345                 350

Asp Ala Leu Val Trp Val Ile Ala Lys Ser Gly Ile Ser Ser Gln Gln
        355                 360                 365

Gln Ser Met Arg Leu Ala Asn Leu Leu Met Leu Leu Ser His Val Arg
    370                 375                 380

His Ala Ser Asn Lys Gly Met Glu His Leu Leu Asn Met Lys Cys Lys
385                 390                 395                 400

Asn Val Val Pro Val Tyr Asp Leu Leu Leu Glu Met Leu Asn Ala His
                405                 410                 415

Val Leu Arg Gly Cys Lys Ser Ser Ile Thr Gly Ser Glu Cys Ser Pro
            420                 425                 430

Ala Glu Asp Ser Lys Ser Lys Glu Gly Ser Gln Asn Pro Gln Ser Gln
        435                 440                 445

Gly Ser Gly Ser Gly Ser Gly Ser Ser Leu Arg Val Lys Phe Ser Arg
    450                 455                 460

Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu Tyr Asn
465                 470                 475                 480

Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg
                485                 490                 495

Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro
            500                 505                 510

Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala
        515                 520                 525

Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His
    530                 535                 540

Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp
545                 550                 555                 560

Ala Leu His Met Gln Ala Leu Pro Pro Arg Ser Arg Gly Ser Gly Ser
                565                 570                 575
```

```
Gly Ser Gly Ser Met Val Ser Lys Gly Glu Glu Asp Asn Met Ala Ile
            580                 585                 590

Ile Lys Glu Phe Met Arg Phe Lys Val His Met Glu Gly Ser Val Asn
        595                 600                 605

Gly His Glu Phe Glu Ile Glu Gly Glu Gly Glu Gly Arg Pro Tyr Glu
    610                 615                 620

Gly Thr Gln Thr Ala Lys Leu Lys Val Thr Lys Gly Gly Pro Leu Pro
625                 630                 635                 640

Phe Ala Trp Asp Ile Leu Ser Pro Gln Phe Met Tyr Gly Ser Lys Ala
                645                 650                 655

Tyr Val Lys His Pro Ala Asp Ile Pro Asp Tyr Leu Lys Leu Ser Phe
            660                 665                 670

Pro Glu Gly Phe Lys Trp Glu Arg Val Met Asn Phe Glu Asp Gly Gly
        675                 680                 685

Val Val Thr Val Thr Gln Asp Ser Ser Leu Gln Asp Gly Glu Phe Ile
    690                 695                 700

Tyr Lys Val Lys Leu Arg Gly Thr Asn Phe Pro Ser Asp Gly Pro Val
705                 710                 715                 720

Met Gln Lys Lys Thr Met Gly Trp Glu Ala Ser Ser Glu Arg Met Tyr
                725                 730                 735

Pro Glu Asp Gly Ala Leu Lys Gly Glu Ile Lys Gln Arg Leu Lys Leu
            740                 745                 750

Lys Asp Gly Gly His Tyr Asp Ala Glu Val Lys Thr Thr Tyr Lys Ala
        755                 760                 765

Lys Lys Pro Val Gln Leu Pro Gly Ala Tyr Asn Val Asn Ile Lys Leu
    770                 775                 780

Asp Ile Thr Ser His Asn Glu Asp Tyr Thr Ile Val Glu Gln Tyr Glu
785                 790                 795                 800

Arg Ala Glu Gly Arg His Ser Thr Gly Gly Met Asp Glu Leu Tyr Lys
                805                 810                 815

Cys Val Thr Asp
            820
```

<210> 721
<211> 456
<212> PRT

<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 721

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Asp
20 25 30

Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly Asp
35 40 45

Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr Leu
50 55 60

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

His Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
85 90 95

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

Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr
115 120 125

Phe Gly Gly Gly Thr Lys Leu Glu Ile Thr Gly Gly Gly Gly Ser Gly
130 135 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Lys Leu Gln Glu Ser
145 150 155 160

Gly Pro Gly Leu Val Ala Pro Ser Gln Ser Leu Ser Val Thr Cys Thr
165 170 175

Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg Gln
180 185 190

Pro Pro Arg Lys Gly Leu Glu Trp Leu Gly Val Ile Trp Gly Ser Glu
195 200 205

Thr Thr Tyr Tyr Asn Ser Ala Leu Lys Ser Arg Leu Thr Ile Ile Lys
210 215 220

Asp Asn Ser Lys Ser Gln Val Phe Leu Lys Met Asn Ser Leu Gln Thr
225 230 235 240

Asp Asp Thr Ala Ile Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly Gly

245 250 255

Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser
260 265 270

Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile
275 280 285

Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala
290 295 300

Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr
305 310 315 320

Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu
325 330 335

Val Ile Thr Leu Tyr Cys Ser Leu Lys Arg Gly Arg Lys Lys Leu Leu
340 345 350

Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu
355 360 365

Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys
370 375 380

Glu Leu Ser Arg Gly Ser Gly Ser Gly Ser Thr Ser Gln Ala Gln Gln
385 390 395 400

Lys Ser Leu Leu Gln Gln Leu Leu Thr Glu Gly Gly Gly Ser Gly Gly
405 410 415

Gly Ser Gln Ala Gln Gln Lys Ser Leu Leu Gln Gln Leu Leu Thr Glu
420 425 430

Gly Gly Gly Ser Gly Gly Gly Ser Gln Ala Gln Gln Lys Ser Leu Leu
435 440 445

Gln Gln Leu Leu Thr Glu Gly Ser
450 455

<210> 722
<211> 462
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic amino acid sequence

<400> 722

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

```
His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Asp
            20                  25                  30

Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly Asp
        35                  40                  45

Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr Leu
    50                  55                  60

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

His Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
                85                  90                  95

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

Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr
        115                 120                 125

Phe Gly Gly Gly Thr Lys Leu Glu Ile Thr Gly Gly Gly Gly Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Lys Leu Gln Glu Ser
145                 150                 155                 160

Gly Pro Gly Leu Val Ala Pro Ser Gln Ser Leu Ser Val Thr Cys Thr
                165                 170                 175

Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg Gln
            180                 185                 190

Pro Pro Arg Lys Gly Leu Glu Trp Leu Gly Val Ile Trp Gly Ser Glu
        195                 200                 205

Thr Thr Tyr Tyr Asn Ser Ala Leu Lys Ser Arg Leu Thr Ile Ile Lys
    210                 215                 220

Asp Asn Ser Lys Ser Gln Val Phe Leu Lys Met Asn Ser Leu Gln Thr
225                 230                 235                 240

Asp Asp Thr Ala Ile Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly Gly
                245                 250                 255

Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser
            260                 265                 270

Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile
        275                 280                 285
```

```
Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala
    290                 295                 300

Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr
305                 310                 315                 320

Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu
                325                 330                 335

Val Ile Thr Leu Tyr Cys Ser Leu Lys Arg Gly Arg Lys Lys Leu Leu
            340                 345                 350

Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu
        355                 360                 365

Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys
    370                 375                 380

Glu Leu Ser Arg Gly Ser Gly Ser Gly Ser Thr Ser Asp Ala Phe Gln
385                 390                 395                 400

Leu Arg Gln Leu Ile Leu Arg Gly Leu Gln Asp Asp Gly Gly Gly Ser
                405                 410                 415

Gly Gly Gly Ser Asp Ala Phe Gln Leu Arg Gln Leu Ile Leu Arg Gly
            420                 425                 430

Leu Gln Asp Asp Gly Gly Gly Ser Gly Gly Gly Ser Asp Ala Phe Gln
        435                 440                 445

Leu Arg Gln Leu Ile Leu Arg Gly Leu Gln Asp Asp Gly Ser
    450                 455                 460


<210>  723
<211>  820
<212>  PRT
<213>  Artificial sequence

<220>
<223>  synthetic amino acid sequence

<400>  723

Met Ile His Leu Gly His Ile Leu Phe Leu Leu Leu Leu Pro Val Ala
1               5                   10                  15

Ala Ala Gln Thr Thr Pro Gly Glu Arg Ser Ser Leu Pro Ala Phe Tyr
            20                  25                  30

Pro Gly Thr Ser Gly Ser Cys Ser Gly Cys Gly Ser Leu Ser Leu Pro
        35                  40                  45

Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu
```

50 55 60

Ser Leu Val Ile Thr Leu Tyr Cys Ser Leu Lys Arg Gly Arg Lys Lys
65 70 75 80

Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr
85 90 95

Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly
100 105 110

Gly Cys Glu Leu Gly Ser Gly Ser Gly Ser Gly Ser Gly Ser Gly Ser
115 120 125

Gly Ser Thr Ser Val Lys Cys Gly Ser Arg Arg Glu Arg Cys Gly Tyr
130 135 140

Arg Leu Val Arg Arg Gln Arg Ser Ala Asp Glu Gln Leu His Cys Ala
145 150 155 160

Gly Lys Ala Lys Arg Ser Gly Gly His Ala Pro Arg Val Arg Glu Leu
165 170 175

Leu Leu Asp Ala Leu Ser Pro Glu Gln Leu Val Leu Thr Leu Leu Glu
180 185 190

Ala Glu Pro Pro His Val Leu Ile Ser Arg Pro Ser Ala Pro Phe Thr
195 200 205

Glu Ala Ser Met Met Met Ser Leu Thr Lys Leu Ala Asp Lys Glu Leu
210 215 220

Val His Met Ile Ser Trp Ala Lys Lys Ile Pro Gly Phe Val Glu Leu
225 230 235 240

Ser Leu Phe Asp Gln Val Arg Leu Leu Glu Ser Cys Trp Met Glu Val
245 250 255

Leu Met Met Gly Leu Met Trp Arg Ser Ile Asp His Pro Gly Lys Leu
260 265 270

Ile Phe Ala Pro Asp Leu Val Leu Asp Arg Asp Glu Gly Lys Cys Val
275 280 285

Glu Gly Ile Leu Glu Ile Phe Asp Met Leu Leu Ala Thr Thr Ser Arg
290 295 300

Phe Arg Glu Leu Lys Leu Gln His Lys Glu Tyr Leu Cys Val Lys Ala
305 310 315 320

Met Ile Leu Leu Asn Ser Ser Met Tyr Pro Leu Val Thr Ala Thr Gln

325 330 335

Asp Ala Asp Ser Ser Arg Lys Leu Ala His Leu Leu Asn Ala Val Thr
340 345 350

Asp Ala Leu Val Trp Val Ile Ala Lys Ser Gly Ile Ser Ser Gln Gln
355 360 365

Gln Ser Met Arg Leu Ala Asn Leu Leu Met Leu Leu Ser His Val Arg
370 375 380

His Ala Ser Asn Lys Gly Met Glu His Leu Leu Asn Met Lys Cys Lys
385 390 395 400

Asn Val Val Pro Val Tyr Asp Leu Leu Leu Glu Met Leu Asn Ala His
405 410 415

Val Leu Arg Gly Cys Lys Ser Ser Ile Thr Gly Ser Glu Cys Ser Pro
420 425 430

Ala Glu Asp Ser Lys Ser Lys Glu Gly Ser Gln Asn Pro Gln Ser Gln
435 440 445

Gly Ser Gly Ser Gly Ser Gly Ser Ser Leu Arg Val Lys Phe Ser Arg
450 455 460

Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu Tyr Asn
465 470 475 480

Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg
485 490 495

Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro
500 505 510

Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala
515 520 525

Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His
530 535 540

Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp
545 550 555 560

Ala Leu His Met Gln Ala Leu Pro Pro Arg Ser Arg Gly Ser Gly Ser
565 570 575

Gly Ser Gly Ser Met Val Ser Lys Gly Glu Glu Asp Asn Met Ala Ile
580 585 590

Ile Lys Glu Phe Met Arg Phe Lys Val His Met Glu Gly Ser Val Asn

595 600 605

Gly His Glu Phe Glu Ile Glu Gly Glu Gly Glu Gly Arg Pro Tyr Glu
610 615 620

Gly Thr Gln Thr Ala Lys Leu Lys Val Thr Lys Gly Gly Pro Leu Pro
625 630 635 640

Phe Ala Trp Asp Ile Leu Ser Pro Gln Phe Met Tyr Gly Ser Lys Ala
645 650 655

Tyr Val Lys His Pro Ala Asp Ile Pro Asp Tyr Leu Lys Leu Ser Phe
660 665 670

Pro Glu Gly Phe Lys Trp Glu Arg Val Met Asn Phe Glu Asp Gly Gly
675 680 685

Val Val Thr Val Thr Gln Asp Ser Ser Leu Gln Asp Gly Glu Phe Ile
690 695 700

Tyr Lys Val Lys Leu Arg Gly Thr Asn Phe Pro Ser Asp Gly Pro Val
705 710 715 720

Met Gln Lys Lys Thr Met Gly Trp Glu Ala Ser Ser Glu Arg Met Tyr
725 730 735

Pro Glu Asp Gly Ala Leu Lys Gly Glu Ile Lys Gln Arg Leu Lys Leu
740 745 750

Lys Asp Gly Gly His Tyr Asp Ala Glu Val Lys Thr Thr Tyr Lys Ala
755 760 765

Lys Lys Pro Val Gln Leu Pro Gly Ala Tyr Asn Val Asn Ile Lys Leu
770 775 780

Asp Ile Thr Ser His Asn Glu Asp Tyr Thr Ile Val Glu Gln Tyr Glu
785 790 795 800

Arg Ala Glu Gly Arg His Ser Thr Gly Gly Met Asp Glu Leu Tyr Lys
805 810 815

Cys Val Thr Asp
820