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(54) Title: METHODS AND COMPOSITIONS FOR CANCER TREATMENT RELATING TO BRCA1 BRCT DOMAIN RECOGNITION OF PHOSPHORYLATED BACH1

(57) Abstract: The present invention relates to compounds (e.g., peptidomimetics and non-peptides) that treat, prevent or stabilize cellular proliferative disorders and methods of treating, preventing, or stabilizing such disorders. The invention also provides three-dimensional structures of a BRCT domain-BACH1 phosphopeptide complex.

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METHODS AND COMPOSITIONS FOR CANCER TREATMENT RELATING TO BRCA1 BRCT DOMAIN RECOGNITION OF PHOSPHORYLATED BACH1

Statement as to Federally Sponsored Research

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Background of the Invention

The present invention relates to compounds (e.g. peptidomimetics) that inhibit cellular proliferation involving a protein having tandem BRCT domains and methods of treating proliferative disorders. Methods of designing and discovering such compounds are also provided. Applicants have discovered the three-dimensional structure of a BRCT domain-BACH1 phosphopeptide complex.

The breast-cancer susceptibility protein, BRCA1, plays important roles in cell cycle control, transcriptional regulation, chromatin remodelling, and the response to DNA-damage. BRCA1 is a large, modular protein of 1,863 amino-acid residues containing an N-terminal RING domain, a central region rich in SQ/TQ dipeptide pairs, and tandem BRCT (BRCA1 C-terminal) domains. BRCA1 interacts with a large number of protein partners at different stages of the cell cycle and following genotoxic stress. For example, BRCA1 interacts with the DNA helicase BACH1 during S and G2 in normally cycling cells, whereas BRCA1 interacts with a subset of ATM/ATR substrates in response to DNA damage. In both S-phase and irradiated/mutagen-treated cells, BRCA1 localizes to distinct nuclear foci thought to represent sites of DNA-damage where BRCA1 is thought to function, at least in part, as a scaffold for the assembly of DNA-repair complexes.

Mutations in BRCA1 occur in 50% of women with inherited breast cancer and up to 90% of women with combined breast and ovarian cancer. Most frameshift and deletion mutants truncate all or part of the BRCT repeats, while more than 70 missense mutations lie within the BRCT domains themselves. BRCT domains are α/β structures that occur singly or as multiple repeats in a number of proteins, in addition to BRCA1, that are involved in cell-cycle regulation and DNA-damage responses. Comprised of 80–100 amino acids, BRCT domains are generally thought to function as protein-protein recognition modules.

There exists a need to better understand the mechanism by which defects in the BRCA1 pathway mediate cancer and a need for therapies that may be provided to prevent or treat the resulting cancers. Specifically, there is a need to better understand the function that the BRCT domains of BRCA1 play in this process.

Summary of the Invention

We recently discovered that a subset of tandem BRCT domains, including those of BRCA1, function as phosphoserine/phosphothreonine (pSer/pThr)-binding modules, indicating that some BRCT-mediated interactions with proteins involved in DNA-damage and cell-cycle control are regulated by protein phosphorylation. Oriented peptide library screening of tandem BRCT domains revealed phospho-dependent binding specificity extending from the pSer/pThr+1 to the pSer/pThr+5 position, with particularly strong selection for aromatic or aromatic/aliphatic residues in the pSer/pThr+3 position. High affinity phosphopeptides selected by *in vitro* oriented library screens were able to block the interaction of the tandem BRCT domains of BRCA1 and the transcriptional regulator PTIP with ATM/ATR-phosphorylated substrates. We concluded that the tumor-suppressor function of BRCA1 may directly depend on this interaction

since its disruption is sufficient to abrogate the G2-M checkpoint following DNA damage.

To determine the structural basis for phosphopeptide binding and phosphopeptide-motif selection, and investigate alternative structural mechanisms underlying BRCA1 BRCT mutations and cancer predisposition, we solved the high resolution X-ray crystal structure of the BRCA1 tandem BRCT repeats bound to a BACH1 phosphopeptide. We now provide a molecular rationale for phosphospecific binding, and show that a set of cancer-associated BRCA1 BRCT mutations eliminate phosphopeptide binding *in vitro* and BACH1 phosphoprotein binding *in vivo*, or alter the phosphopeptide recognition motif for the BRCA1 tandem BRCT domains. Our findings reveal a structural basis for mutation-associated loss of BRCA1 function. This discovery has allowed us to design compounds for the treatment of proliferative diseases associated with BRCA1 and further methods for designing and identifying additional compounds.

Accordingly, in a first aspect, the invention features a computer that includes a processor in communication with a memory which has stored therein (a) at least one atomic coordinate, or a surrogate thereof, for all of the non-hydrogen atoms listed in Table 2 from each of a first group of residues that includes Ser1655, Gly1656, and Lys1702 of BRCA1 tandem BRCT domain complexed with a BACH1 phosphopeptide, or at least one atomic coordinate, or a surrogate thereof, for all of the non-hydrogen atoms listed in Table 2 from each of a second group of residues that includes Phe1704, Met1775, and Leu1839 of the tandem BRCT domain, or atomic coordinates that have a root mean square deviation of less than 3Å from the coordinates of either the first or second groups of residues; and (b) a program for generating a three-dimensional model of the coordinates. In an embodiment, the memory has stored therein atomic coordinates for all of the non-hydrogen atoms, or surrogates thereof, of either the first or second group of residues, or atomic coordinates that have a root mean square

deviation of less than 3Å from the coordinates of either the first or second groups of residues.

In another aspect, the invention features a computer that includes a processor in communication with a memory that has stored therein a pharmacophore model of a compound that binds to a tandem BRCT domain and a program for displaying the model, where the model includes at least one of the following: (a) a phosphate group on a phosphorylated residue of the phosphopeptide that participates in at least one hydrogen-bonding interaction; and (b) a phenylalanine or tyrosine residue at the +3 position of the phosphopeptide, where the phenylalanine or tyrosine side chain is directed towards the surface of the tandem BRCT domain. In one embodiment, the tandem BRCT domain is a BRCA1 tandem BRCT domain. In another embodiment, the tandem BRCT domain is a PTIP tandem BRCT domain.

In another aspect, the invention features a computer that includes a processor in electrical communication with a memory that has stored therein a pharmacophore model of BRCA1 tandem BRCT domain ligands and a program for displaying the model which includes at least three of the following parameters:

(a) a hydrogen bond acceptor group that forms a hydrogen bond with the side chain hydroxyl group of Ser1655 of the BRCA1 tandem BRCT domain, where the distance between the hydrogen of the hydroxyl group and the acceptor group is less than 4 Ångstroms;

(b) a hydrogen bond acceptor group that forms a hydrogen bond with the backbone amide group of Gly1656 of the BRCA1 tandem BRCT domain, where the distance between the hydrogen of the amide group and the acceptor group is less than 4 Ångstroms;

(c) a hydrogen bond acceptor group that forms a hydrogen bond with the side chain amine group of Lys1702 of the BRCA1 tandem BRCT domain, where

the distance between a hydrogen of the amine group and the acceptor group is less than 4 Ångstroms;

(d) a hydrogen bond acceptor group that forms a hydrogen bond with a water molecule, where the water molecule in turn forms a hydrogen bond with the backbone amide group of Leu1657 of the BRCA1 tandem BRCT domain, where the distance between the hydrogen of the amide group and the acceptor group is less than 6 Ångstroms;

(e) a hydrogen bond acceptor group that forms a hydrogen bond with a water molecule, where the water molecule in turn forms a hydrogen bond with a second water molecule, where the second water molecule in turn forms a hydrogen bond with the backbone amide group of Leu1701 of the BRCA1 tandem BRCT domain, where the distance between the hydrogen of the amide group and the acceptor group is less than 8 Ångstroms;

(f) a hydrogen bond acceptor group that forms a hydrogen bond with a water molecule, where the water molecule in turn forms a hydrogen bond with a second water molecule, where the second water in turn forms a hydrogen bond with a third water molecule, where the third water molecule in turn forms a hydrogen bond with the backbone carbonyl group of Asn1774, where the distance between the oxygen of the carbonyl group and the acceptor group is less than 11 Ångstroms;

(g) a hydrogen bond acceptor group that forms a hydrogen bond with a water molecule, where the water molecule in turn forms a hydrogen bond with a second water molecule, where the second water molecule in turn forms a hydrogen bond with a third water molecule, where the third water molecule in turn forms a hydrogen bond with a fourth water molecule, where the fourth water molecule in turn forms a hydrogen bond with the backbone amide group of Ile1680 of the BRCA1 tandem BRCT domain, where the distance between the hydrogen of the amide group and the acceptor group is less than 10 Ångstroms;

(h) a hydrogen bond acceptor group that forms a hydrogen bond with a water molecule, where the water molecule in turn forms a hydrogen bond with a second water molecule, where the second water molecule in turn forms a hydrogen bond with a third water molecule, where the third water molecule in turn forms a hydrogen bond with a fourth water molecule, where the fourth water molecule in turn forms a hydrogen bond with the side chain amide group of Gln1779 of the BRCA1 tandem BRCT domain, where the distance between the hydrogen of the amide group and the acceptor group is less than 14 Ångstroms;

(i) a hydrogen bond acceptor group that forms a hydrogen bond with a water molecule, where the water molecule in turn forms a hydrogen bond with the backbone amide group of Arg1699 of the BRCA1 tandem BRCT domain, where the distance between the hydrogen of the amide group and the acceptor group is less than 7 Ångstroms;

(j) a hydrogen bond acceptor group that forms a hydrogen bond with a water molecule, where the water molecule in turn forms a hydrogen bond with the side chain carboxyl group of Glu1698 of the BRCA1 tandem BRCT domain, where the distance between an oxygen of the carboxyl group and the acceptor group is less than 6 Ångstroms;

(k) a hydrogen bond acceptor group that forms a hydrogen bond with the side chain guanidinium group of Arg1699 of the BRCA1 tandem BRCT domain, where the distance between a hydrogen of the side guanidinium group and the acceptor group is less than 4 Ångstroms;

(l) a hydrogen bond donor group that forms a hydrogen bond with the side chain carbonyl group of Arg1699 of the BRCA1 tandem BRCT domain, where the distance between the hydrogen of the donor group and the carbonyl oxygen is less than 4 Ångstroms;

(m) a hydrophobic group that is less than 5 Ångstroms away from an atom of Phe1704, Met1775, or Leu1839 of the BRCA1 tandem BRCT domain.

(n) a hydrogen bond acceptor group that forms a hydrogen bond with a water molecule, where the water molecule in turn forms a hydrogen bond with the side chain carboxyl group of Glu1836 of the BRCA1 tandem BRCT domain, where the distance between an oxygen of the carboxyl group and the acceptor group is less than 6 Ångstroms; or

(o) a hydrogen bond donor group that forms a hydrogen bond with the side chain carboxyl group of Asp1840 of the BRCA1 tandem BRCT domain, where the distance between the hydrogen of the donor group and a carboxyl oxygen is less than 4 Ångstroms.

In another aspect, the invention features a method of producing a structure for a candidate compound for a BRCA1 tandem BRCT domain that includes the steps of:

(a) providing a three-dimensional structure of the tandem BRCT domain having at least one atomic coordinate, or a surrogate thereof, for all of the non-hydrogen atoms listed in Table 2 from each of a first group of residues that includes Ser1655, Gly1656, and Lys1702 of BRCA1 tandem BRCT domain complexed with a BACH1 phosphopeptide, or at least one atomic coordinate, or a surrogate thereof, for all of the non-hydrogen atoms listed in Table 2 from each of a second group of residues that includes Phe1704, Met1775, and Leu1839 of the tandem BRCT domain, or atomic coordinates that have a root mean square deviation of less than 3Å from the coordinates of either the first or second groups of residues; and

(b) producing a structure for a candidate compound where the structure defines a molecule having sufficient surface complementary to the tandem BRCT domain structure to bind the tandem BRCT domain in an aqueous solution.

In one embodiment, the memory has stored therein atomic coordinates for all of the non-hydrogen atoms, or surrogates thereof, of either the first or second group of residues, or atomic coordinates that have a root mean square deviation of

less than 3Å from the coordinates of either the first or second groups of residues.

In another embodiment, the candidate compound is a peptidomimetic compound. Desirable examples of peptidomimetic compounds include those that include a phosphate moiety or a phosphonate moiety. In another embodiment, the compound binds a tandem BRCT domain.

In another aspect, the invention features a compound having a structure produced by a method that includes the steps of:

(a) providing a three-dimensional structure of the tandem BRCT domain having at least one atomic coordinate, or a surrogate thereof, for all of the non-hydrogen atoms listed in Table 2 from each of a first group of residues that includes Ser1655, Gly1656, and Lys1702 of BRCA1 tandem BRCT domain complexed with a BACH1 phosphopeptide, or at least one atomic coordinate, or a surrogate thereof, for all of the non-hydrogen atoms listed in Table 2 from each of a second group of residues that includes Phe1704, Met1775, and Leu1839 of the tandem BRCT domain, or atomic coordinates that have a root mean square deviation of less than 3Å from the coordinates of either the first or second groups of residues; and

(b) producing a structure for a candidate compound where the structure defines a molecule having sufficient surface complementary to the tandem BRCT domain structure to bind the tandem BRCT domain in an aqueous solution.

In an embodiment, the memory has stored therein atomic coordinates for all of the non-hydrogen atoms, or surrogates thereof, of either the first or second group of residues, or atomic coordinates that have a root mean square deviation of less than 3Å from the coordinates of either the first or second groups of residues.

In another aspect, the invention features a crystal of a complex comprising a tandem BRCT domain bound to a phosphopeptide. In one embodiment, the tandem BRCT domain is a PTIP tandem BRCT domain. In another embodiment, the phosphopeptide includes the amino acid sequence [pSer/pThr]-X-X-[Phe/Tyr].

In one example, the +1 position of the phosphopeptide can be proline. In another example the phosphopeptide includes the amino acid sequence Ser-Arg-Ser-Thr-pSer-Pro-Thr-Phe-Asn-Lys. In another embodiment, the tandem BRCT domain is a BRCA1 tandem BRCT domain. In one example, the tandem BRCT domain is $BRCA1_{1646-1859}$. In other examples, the tandem BRCT domain can be $BRCA1_{1646-1863}$ or $BRCA1_{1633-1863}$. In yet another embodiment, the crystal has a space group of $P3_221$ and a unit cell dimension of a = b = 65.8 Å and c = 93.1 Å).

In another aspect, the invention features a method for selecting or identifying a compound that is a modulator of phosphopeptide binding to a BRCA1 tandem BRCT domain that includes the steps of:

a) contacting a BACH1 phosphopeptide and the tandem BRCT domain under conditions that allow for the formation of a complex between the phosphopeptide and the tandem BRCT domain;

b) contacting the complex of step (a) with a candidate compound; and

c) measuring the displacement of the phosphopeptide from the tandem BRCT domain, where the displacement of the phosphopeptide from the tandem BRCT domain indicates that the candidate compound is a peptidomimetic compound that modulates phosphopeptide binding to a tandem BRCT domain.

In one embodiment, the candidate compound is identified using rational drug design. In another embodiment, the compound modulates phosphopeptide binding to a tandem BRCT domain.

In another aspect, the invention features a method for treating or inhibiting cellular proliferation in a subject that includes administering any of the compounds of the invention in an amount sufficient to treat or inhibit the cellular proliferative disorder in the subject. In one embodiment, the method further includes administering a chemotherapeutic agent, where the phosphopeptide and the chemotherapeutic agent are administered in amounts sufficient to inhibit the cellular proliferative disorder in the subject, and where the chemotherapeutic agent

is administered simultaneously or within twenty-eight days of administering the phosphopeptide. Examples of useful chemotherapeutic agent are listed in Table 3.

In another embodiment, the method further includes radiation therapy, where the phosphopeptide and the radiation therapy are administered in amounts sufficient to treat or inhibit the cellular proliferative disorder in the subject, and where the radiation therapy is administered simultaneously or within twenty-eight days of administering the phosphopeptide.

The cellular proliferative disorder can be a neoplasm or cancer, such as, for example, those cancers selected from the group consisting of acoustic neuroma, acute leukemia, acute lymphocytic leukemia, acute monocytic leukemia, acute myeloblastic leukemia, acute myelocytic leukemia, acute myelomonocytic leukemia, acute promyelocytic leukemia, acute erythroleukemia, adenocarcinoma, angiosarcoma, astrocytoma, basal cell carcinoma, bile duct carcinoma, bladder carcinoma, brain cancer, breast cancer, bronchogenic carcinoma, cervical cancer, chondrosarcoma, chordoma, choriocarcinoma, chronic leukemia, chronic lymphocytic leukemia, chronic myelocytic leukemia, colon cancer, colon carcinoma, craniopharyngioma, cystadenocarcinoma, embryonal carcinoma, endotheliosarcoma, ependymoma, epithelial carcinoma, Ewing's tumor, glioma, heavy chain disease, hemangioblastoma, hepatoma, Hodgkin's disease, large cell carcinoma, leiomyosarcoma, liposarcoma, lung cancer, lung carcinoma, lymphangioendotheliosarcoma, lymphangiosarcoma, macroglobulinemia, medullary carcinoma, medulloblastoma, melanoma, meningioma, mesothelioma, myxosarcoma, neuroblastoma, non-Hodgkin's disease, oligodendriglioma, osteogenic sarcoma, ovarian cancer, pancreatic cancer, papillary adenocarcinomas, papillary carcinoma, pinealoma, polycythemia vera, prostate cancer, rhabdomyosarcoma, renal cell carcinoma, retinoblastoma, schwannoma, sebaceous gland carcinoma, seminoma, small cell lung carcinoma, squamous cell carcinoma, sweat gland carcinoma, synovioma, testicular cancer, uterine cancer,

Waldenstrom's fibrosarcoma, and Wilm's tumor.

Any of the compounds of the invention can be in prodrug form, such as, for example, those prodrugs that include hydrolysable esters (e.g., methyl esters) or sulfonate groups. Other useful prodrugs of compounds of the invention are those in which a charged group of the compound is masked or those in which the prodrug includes a caged compound.

The invention also features a pharmaceutical composition that includes any of the compounds of the invention, or prodrugs thereof, and a pharmaceutically acceptable excipient.

Definitions

As used throughout this specification and the appended claims, the following terms have the meanings specified.

As used herein, the terms "alkyl" and the prefix "alk-" are inclusive of both straight chain and branched chain groups and of cyclic groups, i.e., cycloalkyl and cycloalkenyl groups. Cyclic groups can be monocyclic or polycyclic and preferably have from 3 to 8 ring carbon atoms, inclusive. Exemplary cyclic groups include cyclopropyl, cyclopentyl, cyclohexyl, and adamantyl groups.

By an "amino acid fragment" is meant an amino acid residue that has been incorporated into a peptide chain via its alpha carboxyl, its alpha nitrogen, or both. A terminal amino acid is any natural or unnatural amino acid residue at the amino-terminus or the carboxy-terminus. An internal amino acid is any natural or unnatural amino acid residue that is not a terminal amino acid.

By "analog" is meant a molecule that is not identical but has analogous features. For example, a polypeptide analog retains the biological activity of a corresponding naturally-occurring polypeptide, while having certain biochemical modifications that enhance the analog's function relative to a naturally occurring polypeptide. Such biochemical modifications could increase the analog's protease

resistance, membrane permeability, or half-life, without altering, for example, ligand binding. An analog may include an unnatural amino acid.

By "antigenicity" is meant the ability of a substance to elicit an immune response. As one example, a compound may elicit an immune response through interaction with an antibody.

By "apoptosis" is meant the process of cell death where a dying cell displays at least one of a set of well-characterized biological hallmarks, including cell membrane blebbing, cell soma shrinkage, chromatin condensation, or DNA laddering.

By "aromatic residue" is meant an aromatic group having a ring system with conjugated π electrons (e.g., phenyl or imidazole). The ring of the aryl group is preferably 5 to 6 atoms. The aromatic ring may be exclusively composed of carbon atoms or may be composed of a mixture of carbon atoms and heteroatoms. Preferred heteroatoms include nitrogen, oxygen, sulfur, and phosphorous. Aryl groups may optionally include monocyclic, bicyclic, or tricyclic rings, where each ring has preferably five or six members. The aryl group may be substituted or unsubstituted. Exemplary substituents include alkyl, hydroxyl, alkoxy, aryloxy, sulfhydryl, alkylthio, arylthio, halo, fluoroalkyl, carboxyl, carboxyalkyl, amino, aminoalkyl, monosubstituted amino, disubstituted amino, and quaternary amino groups.

By "aryl" is meant a carbocyclic aromatic ring or ring system. Unless otherwise specified, aryl groups are from 6 to 18 carbons. Examples of aryl groups include phenyl, naphthyl, biphenyl, fluorenyl, and indenyl groups.

Aryl, heteroaryl, and heterocyclyl groups may be unsubstituted or substituted by one or more substituents selected from the group consisting of C_{1-5} alkyl, hydroxy, halo, nitro, C_{1-5} alkoxy, C_{1-5} alkylthio, trihalomethyl, C_{1-5} acyl, arylcarbonyl, heteroarylcarbonyl, nitrile, C_{1-5} alkoxycarbonyl, oxo, arylalkyl

(wherein the alkyl group has from 1 to 5 carbon atoms) and heteroarylalkyl (wherein the alkyl group has from 1 to 5 carbon atoms).

By "atomic coordinates" (or "structural coordinates") is meant those mathematical three-dimensional coordinates of the atoms in a crystalline material derived from mathematical equations related to the patterns obtained on diffraction of x-rays by the atoms (x-ray scattering centers) of the crystalline material. The diffraction data are used to calculate an electron density map of the unit cell of the crystal. These electron density maps are used to establish the positions of the individual atoms within the unit cell of the crystal. Atomic coordinates can be transformed, as is known to those skilled in the art, to different coordinate systems (i.e., surrogate systems) without affecting the relative positions of the atoms.

By "BACH1 nucleic acid" is meant a nucleic acid, or analog thereof, that encodes all or a portion of a BACH1 polypeptide or is substantially identical to all or a portion of the nucleic acid sequence of Genbank Accession No. 13661818.

By "BACH1 polypeptide" is meant a polypeptide substantially identical to all or a portion of the polypeptide sequence of Genbank Accession No. 13661819, or analog thereof.

By "BACH1 phosphopeptide" is meant a phosphorylated polypeptide substantially identical to all or a portion of the polypepide sequence of Genbank Accession No. 13661819, or analog thereof, and having binding activity to a BRCA1 tandem BRCT domain.

By "basic pocket" is meant a discrete region of a molecule possessing net positive charge at pH 7.0. Such a region may be able to interact with a second molecule of complementary shape, charge, or other features, for example a therapeutic candidate compound. In one embodiment, such a region may be able to interact with a negatively charged group such as a phosphate moiety of a ligand. The basic pocket of a BRCA1 tandem BRCT domain is minimally defined by the BRCA1 tandem BRCT domain residues Ser1655, Gly1656, and Lys1702.

By "biased phosphopeptide library" is meant a phosphoserine, phosphothreonine, and/or phosphotyrosine degenerate peptide library, wherein specific amino acid residues of the phosphopeptide are fixed so as to be expressed in all phosphopeptides in the specific library. For instance, a biased phosphopeptide library can be synthesized to contain the core sequence Ser-pSer-Pro or Ser-pThr-Pro. In a desirable embodiment, the amino acid residue adjacent to the phosphoserine, phosphothreonine, or phosphotyrosine residue is also fixed.

By "binding to BRCA1" is meant having a physicochemical affinity for BRCA1. Binding may be measured by any of the methods of the invention, for example using an *in vitro* translation binding assay.

By "biological activity" is meant a polypeptide or other compound having structural, regulatory, or biochemical functions of a naturally occurring molecule. For example, one biological activity of a BRCA1 tandem BRCT domain is phosphopeptide binding, which may be measured using *in vivo* or *in vitro* binding assays.

By "BRCA1 biological activity" is meant at least one of the following: function in a DNA damage response pathway, cell cycle control, transcriptional regulation, chromatin remodeling, or phosphopeptide binding. In one assay for BRCA1 biological activity, the ability of BRCA1, or a fragment or mutant thereof comprising a tandem BRCT domain, to bind a BACH1 phosphopeptide is measured.

By "BRCA1 nucleic acid" is meant a nucleic acid that encodes all or a portion of BRCA1 or is substantially identical to all or a portion of the nucleic acid sequence of Genbank Accession No. 30039658, or analog thereof.

By "BRCA1 polypeptide" is meant a polypeptide substantially identical to all or a portion of the polypeptide sequence of Genbank Accession No. 30039659, or analog thereof, and having BRCA1 biological activity.

By "BRCT domain" is meant a polypeptide of at least 80 amino acids that, together with a second BRCT domain, functions to bind phosphoserine- and phosphothreonine-containing polypeptides. In one embodiment, a BRCT domain is a polypeptide sequence that adopts a three-dimensional structure comprising at least three alpha helices and four beta strands.

By "BRCT nucleic acid" is meant a nucleic acid that encodes at least one tandem BRCT domain, or analog thereof. For example, a nucleic acid substantially identical to PTIP BC033781[21707457], or NM_007349 (PAX transcription activation domain interacting protein 1 mRNA) or Gene Bank Accession No: AY273801[30039658], is a BRCT nucleic acid.

By "BRCA1 tandem BRCT domain mutant" is meant a polypeptide encoded by at least one mutation of a BRCA1 nucleic acid.

By "caged compound" is meant a biologically active molecule coupled to a cleavable moiety such that the resulting coupled compound lacks biological activity as long as the moiety remains attached. Such a moiety prevents bioaction by sterically shielding one or more chemical groups of the molecule. The moiety may be removed by any means, including enymatic, chemical, or photolytic; removal of the moiety results in restoration of the molecule's biological activity.

By "candidate compound" is meant any nucleic acid molecule, polypeptide, or other small molecule, that is assayed for its ability to alter gene or protein expression levels, or the biological activity of a gene or protein by employing one of the assay methods described herein. Candidate compounds include, for example, peptides, polypeptides, synthesized organic molecules, naturally occurring organic molecules, nucleic acid molecules, and components thereof.

By "cellular proliferative disorder" or "disease or disorder characterized by inappropriate cell cycle regulation" is meant any pathological condition in which there is an abnormal increase or decrease in cell proliferation. Exemplary cellular

proliferative disorders include cancer or neoplasms, inflammatory diseases, or hyperplasias (e.g. some forms of hypertension, prostatic hyperplasia).

By "chemotherapeutic agent" is meant one or more chemical agents used in the treatment or control of proliferative diseases, including cancer. Chemotherapeutic agents include cytotoxic and cytostatic agents. Examples of chemotherapeutic agents include cytotoxic and cytostatic agents such as alemtuzumab, altretamine, aminoglutethimide, amsacrine, anastrozole, azacitidine, bicalutamide, bleomycin, busulfan, capecitabine, carboplatin, carmustine, celecoxib, chlorambucil, 2-chlorodeoxyadenosine, cisplatin, colchicine, cyclophosphamide, cytarabine, cytoxan, dacarbazine, dactinomycin, daunorubicin, docetaxel, doxorubicin, epirubicin, estramustine phosphate, etodolac, etoposide, exemestane, floxuridine, fludarabine, 5-fluorouracil, flutamide, formestane, gemcitabine, gentuzumab, goserelin, hexamethylmelamine, hydroxyurea, hypericin, ifosfamide, imatinib, interferon, irinotecan, letrozole, leuporelin, lomustine, mechlorethamine, melphalen, mercaptopurine, 6-mercaptopurine, methotrexate, mitomycin, mitotane, mitoxantrone, nilutamide, paclitaxel, pentostatin, procarbazine, raltitrexed, rituximab, rofecoxib, streptozocin, tamoxifen, temozolomide, teniposide, 6-thioguanine, topotecan, toremofine, trastuzumab, vinblastine, vincristine, vindesine, and vinorelbine, or any combination of these. Other chemotherapeutic agents include, but are not limited to, those listed in Table 3.

By "three-dimensional model" is meant a three-dimensional representation of a molecule's structure. Computer modeling may be used to generate such a model in conjunction with structural data. These data could include x-ray crystallographic data, nuclear magnetic resonance data, electron microscopy data, or any other source of experimental or theoretical data useful for generating a model of a molecule or complex of molecules.

By "complex" is meant a chemical association of two or more molecules. Complexes may include a network of weak electrostatic bonds that maintain the association of the molecules. Other types of interactions, such as covalent, ionic, hydrogen bond, hydrophobic, or van der Waals interactions, may be present instead of or in addition to electrostatic bonds between members of a complex.

By "computer modeling" is meant the application of a computational program to determine one or more of the following: the location and binding proximity of a ligand to a binding moiety, the occupied space of a bound ligand, the amount of complementary contact surface between a binding moiety and a ligand, the deformation energy of binding of a given ligand to a binding moiety, and some estimate of hydrogen bonding strength, van der Waals interaction, hydrophobic interaction, and/or electrostatic interaction energies between ligand and binding moiety. Computer modeling can also provide comparisons between the features of a model system and a candidate compound. For example, a computer modeling experiment can compare a pharmacophore model of the invention with a candidate compound to assess the fit of the candidate compound with the model. Examples of techniques useful in the above evaluations include: quantum mechanics, molecular mechanics, molecular dynamics, Monte Carlo sampling, systematic searches and distance geometry methods. Further descriptions of computer modeling programs are provided elsewhere herein.

By "detectably-labeled" is meant any means for marking and identifying the presence of a molecule, e.g. a phosphopeptide or a peptidomimetic small molecule that interacts with a BRCA1 tandem BRCT domain. Methods for detectably-labeling a molecule are well known in the art and include, without limitation, radionuclides (e.g., with an isotope such as ^{32}P, ^{33}P, ^{125}I, or ^{35}S), nonradioactive labeling (e.g., chemiluminescent labeling or fluorescein labeling), and epitope tags.

If required, molecules can be differentially labeled using markers that can distinguish the presence of multiply distinct molecules. For example, a phosphopeptide that interacts with a PBD domain can be labeled with fluorescein and a PBD domain polypeptide can be labeled with Texas Red. The presence of the phosphopeptide can be monitored simultaneously with the presence of the PBD.

By "drug" is meant a compound of the present invention that is, within the scope of sound medical judgment, suitable for use in contact with the tissues of humans and animals without undue toxicity, irritation, allergic response, and the like, commensurate with a reasonable benefit/risk ratio, and effective for their intended use, as well as the zwitterionic forms, where possible, of the compounds of the invention.

By "fragment" is meant a portion of a polypeptide or nucleic acid having a region that is substantially identical to a portion of a reference protein or nucleic acid and retains at least 50% or 75%, more preferably 80%, 90%, or 95%, or even 99% of at least one biological activity of the reference protein or nucleic acid.

By "inhibitory fragment" is meant a portion of a polypeptide or nucleic acid having a region that is substantially identical to a portion of a reference protein or nucleic acid and inhibits biological activity of the reference protein or nucleic acid by at least 5%, more desirably, by at least 10%, even more desirably, by at least 25%, 50%, or 75%, and most desirably, by 90% or more.

By "halide" or "halogen" or "halo" is meant bromine, chlorine, iodine, or fluorine.

By "heteroaryl" is meant an aromatic ring or ring system that contains at least one ring hetero-atom (e.g., O, S, N). Unless otherwise specified, heteroaryl groups are from 1 to 9 carbons.. Heteroaryl groups include furanyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, triazolyl, oxadiazolyl, oxatriazolyl, pyridyl, pyridazyl, pyrimidyl, pyrazyl, triazyl,

benzofuranyl, isobenzofuranyl, benzothienyl, indole, indazolyl, indolizinyl, benzisoxazolyl, quinolinyl, isoquinolinyl, cinnolinyl, quinazolinyl, naphtyridinyl, phthalazinyl, phenanthrolinyl, purinyl, and carbazolyl groups.

By "heterocycle" is meant a non-aromatic ring or ring system that contains at least one ring heteroatom (e.g., O, S, N). Unless otherwise specified, heterocyclic groups are from 1 to 9 carbons. Heterocyclic groups include, for example, dihydropyrrolyl, tetrahydropyrrolyl, piperazinyl, pyranyl, dihydropyranyl, tetrahydropyranyl, tetrahydrofuranyl, dihydrothiophene, tetrahydrothiophene, and morpholinyl groups.

By "hydrophobic pocket" is meant a discrete region of a molecule possessing hydrophobic character. Such a region may be able to interact with a second molecule of complementary shape, charge, or other features, for example a therapeutic candidate compound. In one embodiment, such a region may be able to interact with a hydrophobic group such as an aromatic side chain of a ligand. The hydrophobic pocket of a BRCA1 tandem BRCT domain is minimally defined by the BRCA1 tandem BRCT domain residues Phe1704, Met1775, and Leu1839.

By "hydrogen bond acceptor (HBA)" is meant any atom that has a lone pair of electrons available for interacting with a hydrogen atom. Typical hydrogen bond acceptors include oxygen, sulfur, or nitrogen atoms, including those oxygen or nitrogen atoms that are SP_2-hybridized.

By "hydrogen bond donor (HBD)" is meant a heteroatom, such as, for example, an oxygen, sulfur, or nitrogen, that bears a hydrogen.

By "isolated polynucleotide" is meant a nucleic acid (e.g., a DNA) that is free of the genes which, in the naturally-occurring genome of the organism from which the nucleic acid molecule of the invention is derived, flank the gene. The term therefore includes, for example, a recombinant DNA that is incorporated into a vector; into an autonomously replicating plasmid or virus; or into the genomic DNA of a prokaryote or eukaryote; or that exists as a separate molecule

(for example, a cDNA or a genomic or cDNA fragment produced by PCR or restriction endonuclease digestion) independent of other sequences. In addition, the term includes an RNA molecule which is transcribed from a DNA molecule, as well as a recombinant DNA which is part of a hybrid gene encoding additional polypeptide sequence.

By "main-chain atoms" or "main chain group" are meant those atoms in an amino acid, peptide, or protein that include the carbon and oxygen atom(s) of an amino acid's C1 carboxyl or carbonyl group; an amino acid's C2 carbon, and any hydrogen atom(s) bonded to the C2 carbon; and an amino acid's alpha-amine, and any hydrogen atom(s) bonded to the alpha amine.

By "modulate" is meant a change, such as an decrease or increase. For example, the change could refer to a biological activity. Desirably, the change is either an increase or a decrease of at least 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or 95% in expression or biological activity, relative to a reference or to control expression or activity, for example the expression or biological activity of a naturally occurring BRCA1 polypeptide.

By "mutation" is meant an alteration in a naturally-occurring or reference nucleic acid sequence, such as an insertion, a deletion, a substitution, or a frameshift mutation. Desirably, the nucleic acid sequence has at least one base pair alteration from a naturally-occurring sequence.

By "neoplasia" is meant a disease characterized by the pathological proliferation of a cell or tissue and its subsequent migration to or invasion of other tissues or organs. Neoplasia growth is typically uncontrolled and progressive, and occurs under conditions that would not elicit, or would cause cessation of, multiplication of normal cells. Neoplasias can affect a variety of cell types, tissues, or organs, including but not limited to an organ selected from the group consisting of bladder, bone, brain, breast, cartilage, glia, esophagus, fallopian tube, gallbladder, heart, intestines, kidney, liver, lung, lymph node, nervous tissue,

ovaries, pancreas, prostate, skeletal muscle, skin, spinal cord, spleen, stomach, testes, thymus, thyroid, trachea, urogenital tract, ureter, urethra, uterus, and vagina, or a tissue or cell type thereof. Neoplasias include cancers, such as acoustic neuroma, acute leukemia, acute lymphocytic leukemia, acute monocytic leukemia, acute myeloblastic leukemia, acute myelocytic leukemia, acute myelomonocytic leukemia, acute promyelocytic leukemia, acute erythroleukemia, adenocarcinoma, angiosarcoma, astrocytoma, basal cell carcinoma, bile duct carcinoma, bladder carcinoma, brain cancer, breast cancer, bronchogenic carcinoma, cervical cancer, chondrosarcoma, chordoma, choriocarcinoma, chronic leukemia, chronic lymphocytic leukemia, chronic myelocytic leukemia, colon cancer, colon carcinoma, craniopharyngioma, cystadenocarcinoma, embryonal carcinoma, endotheliosarcoma, ependymoma, epithelial carcinoma, Ewing's tumor, glioma, heavy chain disease, hemangioblastoma, hepatoma, Hodgkin's disease, large cell carcinoma, leiomyosarcoma, liposarcoma, lung cancer, lung carcinoma, lymphangioendotheliosarcoma, lymphangiosarcoma, macroglobulinemia, medullary carcinoma, medulloblastoma, melanoma, meningioma, mesothelioma, myxosarcoma, neuroblastoma, non-Hodgkin's disease, oligodendriglioma, osteogenic sarcoma, ovarian cancer, pancreatic cancer, papillary adenocarcinomas, papillary carcinoma, pinealoma, polycythemia vera, prostate cancer, rhabdomyosarcoma, renal cell carcinoma, retinoblastoma, schwannoma, sebaceous gland carcinoma, seminoma, small cell lung carcinoma, squamous cell carcinoma, sweat gland carcinoma, synovioma, testicular cancer, uterine cancer, Waldenstrom's fibrosarcoma, and Wilm's tumor.

By "nucleic acid" is meant an oligomer or polymer of ribonucleic acid or deoxyribonucleic acid, or analog thereof. This term includes oligomers consisting of naturally occurring bases, sugars, and intersugar (backbone) linkages as well as oligomers having non-naturally occurring portions which function similarly. Such modified or substituted oligonucleotides are often preferred over native forms

because of properties such as, for example, enhanced cellular uptake and increased stability in the presence of nucleases.

Specific examples of some preferred nucleic acids may contain phosphorothioates, phosphotriesters, methyl phosphonates, short chain alkyl or cycloalkyl intersugar linkages or short chain heteroatomic or heterocyclic intersugar linkages. Most preferred are those with CH_2 –NH—O—CH_2, CH_2—$N(CH_3)$—O—CH_2, CH_2—O—$N(CH_3)$—CH_2, CH_2—$N(CH_3)$—$N(CH_3)$—CH_2 and O—$N(CH_3)$—CH_2—CH_2 backbones (where phosphodiester is O—P—O—CH_2). Also preferred are oligonucleotides having morpholino backbone structures (Summerton, J.E. and Weller, D.D., U.S. Pat. No: 5,034,506). In other preferred embodiments, such as the protein-nucleic acid (PNA) backbone, the phosphodiester backbone of the oligonucleotide may be replaced with a polyamide backbone, the bases being bound directly or indirectly to the aza nitrogen atoms of the polyamide backbone (P.E. Nielsen et al. *Science* 199: 254, 1997). Other preferred oligonucleotides may contain alkyl and halogen-substituted sugar moieties comprising one of the following at the 2' position: OH, SH, SCH_3, F, OCN, $O(CH_2)_nNH_2$ or $O(CH_2)_n$ CH_3, where n is from 1 to about 10; C_1 to C_{10} lower alkyl, substituted lower alkyl, alkaryl or aralkyl; Cl; Br; CN; CF_3; OCF_3; O-, S-, or N-alkyl; O-, S-, or N-alkenyl; $SOCH_3$; SO_2CH_3; ONO_2; NO_2; N_3; NH_2; heterocycloalkyl; heterocycloalkaryl; aminoalkylamino; polyalkylamino; substituted silyl; an RNA cleaving group; a conjugate; a reporter group; an intercalator; a group for improving the pharmacokinetic properties of an oligonucleotide; or a group for improving the pharmacodynamic properties of an oligonucleotide and other substituents having similar properties. Oligonucleotides may also have sugar mimetics such as cyclobutyls in place of the pentofuranosyl group.

Other preferred embodiments may include at least one modified base form. Some specific examples of such modified bases include 2-(amino)adenine, 2-

(methylamino)adenine, 2-(imidazolylalkyl)adenine, 2-(aminoalklyamino)adenine, or other heterosubstituted alkyladenines.

By "OE1," "OE2," "OD1," and "OD2," the following is meant. By "OE1" is meant the side chain oxygen of a glutamic acid residue such that the torsion angle formed by the side chain atoms CB (the beta carbon), CD (the delta carbon), CG (the gamma carbon), and OE1 is between –90 and 90 degrees.

By "OE2" is meant the side chain oxygen of a glutamic acid residue such that the torsion angle formed by the side chain atoms CB (the beta carbon), CD (the delta carbon), CG (the gamma carbon), and OE2 is not between –90 and 90 degrees.

By "OD1" is meant the side chain oxygen of an aspartic acid residue such that the torsion angle formed by the side chain atoms CA (the alpha carbon), CB, CG, and OD1 is between –90 and 90 degrees.

By "OD2" is meant the side chain oxygen of an aspartic acid residue such that the torsion angle formed by the side chain atoms CA, CB, CG, and OD2 is not between –90 and 90 degrees.

Other amino acid residue side chain atoms are similarly defined, where torsion angle of the instant atom, combined with the three most adjacent atoms connecting the instant atom to the main chain carboxyl group is measured and the instant atom is assigned a "1" designation if the torsion angle is between –90 and 90 degrees and a "2" designation if the torsion angle is not between –90 and 90 degrees. For symmetrical side chain ring atoms in tyrosine and phenylalanine residues, ring atoms including or most nearly connected to the two instant ring atoms are assigned a "CD1" designation if the torsion angle formed by CA, CB, CG, and CD1 is between –90 and 90 degrees and a "CD2" designation if the torsion angle formed by CA, CB, CG, and CD2 is not between –90 and 90 degrees.

By "peptide" is meant any compound composed of amino acids, amino acid analogs, chemically bound together. In general, the amino acids are chemically bound together via amide linkages (CONH); however, the amino acids may be bound together by other chemical bonds known in the art. For example, the amino acids may be bound by amine linkages. Peptide as used herein includes oligomers of amino acids, amino acid analog, or small and large peptides, including polypeptides.

By a "peptidomimetic" is meant a compound that is capable of mimicking or antagonizing the biological actions of a natural parent peptide. A peptidomimetic may include non-peptidic structural elements, unnatural peptides, synthesized organic molecules, naturally occurring organic molecules, nucleic acid molecules, and components thereof. Identification of a peptidomimetic can be accomplished by screening methods incorporating a binding pair and identifying compounds that displace the binding pair. Alternatively, a peptidomimetic can be designed *in silico*, by molecular modeling of a known protein-protein interaction, for example, the interaction of a phosphopeptide of the invention and a PBD. Desirably, the peptidomimetic will displace one member of a binding pair by occupying the same binding interface. More desirably the peptidomimetic will have a higher binding affinity to the binding interface.

By "pharmaceutically acceptable excipient" is meant a carrier that is physiologically acceptable to the subject to which it is administered and that preserves the therapeutic properties of the compound with which it is administered. One exemplary pharmaceutically acceptable excipient is physiological saline. Other physiologically acceptable excipients and their formulations are known to one skilled in the art and described, for example, in "Remington: The Science and Practice of Pharmacy" (20th ed., ed. A.R. Gennaro AR., 2000, Lippincott Williams & Wilkins).

By "pharmacophore" or "pharmacophore model" is meant the ensemble of steric and electronic features that is used to optimize supramolecular interactions with a specific biological target structure and to trigger (or to block) its biological response. A pharmacophore can be considered as the largest common denominator shared by a set of active molecules. Pharmacophore models are particularly useful in drug design.

In some embodiments, molecules may be derivatized with groups that introduce useful pharmacodynamic properties, such as those that transform an analog into a prodrug. Such groups are known to those skilled in the art, examples of which can be found in Testa and Mayer, Hydrolysis in Drug and Prodrug Metabolism: Chemistry, Biochemistry and Enzymology, published by Vch. Verlagsgesellschaft Mbh. (2003), which is hereby incorporated by reference.

By "phosphopeptide" or "phosphoprotein" means a polypeptide in which one or more phosphate moieties are covalently linked to serine, threonine, tyrosine, aspartic acid, histidine amino acid residues, or amino acid analogs. A peptide can be phosphorylated to the extent of the number of serine, threonine, tyrosine, or histidine amino acid residues that is present. Desirably, a phosphopeptide is phosphorylated at 4 independent Ser/Thr/Tyr residues, at 3 independent Ser/Thr/Tyr residues, or at 2 independent Ser/Thr/Tyr residues. Most desirably, a phosphopeptide is phosphorylated at one Ser/Thr/Tyr residue regardless of the presence of multiple Ser, Thr, or Tyr residues.

Typically, a phosphopeptide is produced by expression in a prokaryotic or eukaryotic cell under appropriate conditions or in translation extracts where the peptide is subsequently isolated, and phosphorylated using an appropriate kinase. Alternatively, a phosphopeptide may be synthesized by standard chemical methods, for example, using N-α-FMOC-protected amino acids (including appropriate phosphoamino acids). In a desired embodiment, the use of non-hydrolysable phosphate analogs can be incorporated to produce non-hydrolysable

phosphopeptides (Jenkins et al., *J. Am. Chem. Soc.*, 124:6584-6593, 2002; herein incorporated by reference). Such methods of protein synthesis are commonly used and practiced by standard methods in molecular biology and protein biochemistry (Ausubel *et al.*, Current Protocols in Molecular Biology, John Wiley & Sons, New York, NY, 1994, J. Sambrook and D. Russel, Molecular Cloning: A Laboratory Manual, 3rd Edition, Cold Spring Harbor Laboratory Press, Woodbury NY, 2000). Desirably, a phosphopeptide employed in the invention is generally not longer than 100 amino acid residues in length, desirably less than 50 residues, more desirably less than 25 residues, 20 residues, 15 residues. Most desirably the phosphopeptide is 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acid residues long.

By a "Polo-like kinase" (Plk) is meant a polypeptide substantially identical to a Polo-like kinase amino acid sequence, having serine/threonine kinase activity, and having at least one Polo-box domain consisting of 2 Polo-boxes. Exemplary Polo-like kinase polypeptides include Plk-1 (GenBank Accession Number NP_005021); Plk-2 (GenBank Accession Number NP_006613); and Plk-3 (GenBank Accession Number NP_004064). Additional Polo-like kinase polypeptides include GenBank Accession Numbers P53350, and Q07832.

Structurally, Polo or Polo-like kinases have a unique amino terminus followed by a serine/threonine kinase domain, a linker region, a Polo-box (PB1), a linker sequence, a second Polo-box (PB 2), and a small stretch of 12-20 amino acids at the carboxy terminus.

In desirable embodiments, Polo-like kinases include *Saccaromyces cereviseae*, Cdc5, *Schizosaccaromyces pombe*, Plo-1, *Drosophila melanogaster*, Polo, *Xenopus laevis*, Plx (Plx-1, -2, -3), and mammalian Plk-1, Prk/Fnk, Snk, and Cnk. The Polo-box is approximately 70 amino acids in length.

By "Polo-like kinase biological activity" is meant any biological activity associated with Polo-like kinases, such as serine/threonine kinase activity.

Other biological activities of Polo-like kinases include the localization of the kinase to the centrosomes, spindle apparatus, and microtubular organizing centers (MOCs).

By "Polo-like kinase (PLK) nucleic acid molecule" is meant a nucleic acid, or nucleic acid analog, that encodes a Polo-like kinase polypeptide. For example, a Plk-1 nucleic acid molecule is substantially identical to the nucleic acid sequence of GenBank Accession Number X73458 or NM_005030; a Plk-2/SNK nucleic acid molecule is substantially identical to NM_006622; a Plk-3 nucleic acid molecule is substantially identical to NM_004073; a Plx-1 nucleotide sequence is substantially identical to the nucleic acid sequence of GenBank Accession Number U58205; and a Polo nucleic acid molecule is substantially identical to the nucleic acid sequence of GenBank Accession Number AY095028 or NM_079455.

By "polypeptide" is meant any chain of at least two naturally-occurring amino acids, or unnatural amino acids (e.g., those amino acids that do not occur in nature) regardless of post-translational modification (e.g., glycosylation or phosphorylation), constituting all or part of a naturally-occurring or unnatural polypeptide or peptide, as is described herein. Naturally occurring amino acids include any one of the following: alanine (A or Ala), cysteine (C or Cys), aspartic acid (D or Asp), glutamic acid (E or Glu), phenylalanine (F or Phe), glycine (G or Gly), histidine (H, or His), isoleucine (I or Ile), lysine (K or Lys), leucine (L or Leu), methionine (M or Met), asparagine (N or Asn), proline (P or Pro), hydroxyproline (Hyp), glutamine (Q or Gln), arginine (R or Arg), serine (S or Ser), threonine (T or Thr), valine (V or Val), tryptophan (W or Trp), and tyrosine (Y or Tyr). Other amino acids that may also be incorporated into a polypeptide include Ornithine (O or Orn) and hydroxyproline (Hyp).

Polypeptides or derivatives thereof may be fused or attached to another protein or peptide, for example, as a Glutathione-S-Transferase (GST) fusion polypeptide. Other commonly employed fusion polypeptides include, but are not

limited to, maltose-binding protein, *Staphylococcus aureus* protein A, Flag-Tag, HA-tag, green fluorescent proteins (e.g., eGFP, eYFP, eCFP, GFP, YFP, CFP), red fluorescent protein, polyhistidine (6xHis), and cellulose-binding protein.

By "prodrug" is meant a compound that is modified *in vivo*, resulting in formation of a biologically active drug compound, for example by hydrolysis in blood. A thorough discussion of prodrug modifications is provided in T. Higuchi and V. Stella, Pro-drugs as Novel Delivery Systems, Vol. 14 of the A.C.S. Symposium Series, Edward B. Roche, ed., Bioreversible Carriers in Drug Design, American Pharmaceutical Association and Pergamon Press, 1987, and Judkins et al., Synthetic Communications 26(23):4351-4367, 1996, each of which is incorporated herein by reference.

By "PTIP" or "Pax2 *trans*-activation domain-interacting protein" is meant a polypeptide, or analog thereof, substantially identical to Genebank Accession No: AAH33781.1or NP_031375, and having PTIP biological activity.

By "PTIP biological activity" is meant function in a DNA damage response pathway or phosphopeptide binding. In one assay for PTIP biological activity, the ability of PTIP, or a fragment or mutant thereof comprising a tandem BRCT domain, to bind a phosphopeptide is measured.

By "PTIP biological activity" is meant function in a DNA damage response pathway or phosphopeptide binding.

By "PTIP nucleic acid" is meant a nucleic acid, or analog thereof, substantially identical to Genebank Accession No:21707457 or NM_007349.

By "purified" is meant separated from other components that naturally accompany it. Typically, a factor is substantially pure when it is at least 50%, by weight, free from proteins, antibodies, and naturally-occurring organic molecules with which it is naturally associated. Desirably, the factor is at least 75%, more desirably, at least 90%, and most desirably, at least 99%, by weight, pure. A substantially pure factor may be obtained by chemical synthesis, separation of the

factor from natural sources, or production of the factor in a recombinant host cell that does not naturally produce the factor. Proteins, vesicles, and organelles may be purified by one skilled in the art using standard techniques such as those described by Coligan *et al.* (*Current Protocols in Protein Science*, John Wiley & Sons, New York, 2000). The factor is desirably at least 2, 5, or 10 times as pure as the starting material, as measured using polyacrylamide gel electrophoresis or column chromatography (including HPLC) analysis (Coligan *et al.*, *supra*). Exemplary methods of purification include (i) salting-out, *i.e.*, $(NH_4)_2SO_4$ precipitation; (ii) conventional chromatography, *e.g.*, ion exchange, size exclusion, hydrophobic interaction, or reverse-phase; (iii) affinity chromatography, *e.g.*, immunoaffinity, active site affinity, dye affinity, or immobilized-metal affinity; and (iv) preparative electrophoresis, *e.g.*, isoelectric focusing or native PAGE.

By "rational drug design" is meant the design or selection of drugs using information about the structure of the drugs' protein target as a basis for the design or selection.

By "salt bridge" is meant an electrostatic interaction between groups in a protein structure that results in the formation of a non-covalent interaction between an ionizable hydrogen of a hydrogen bond donor group and a heteroatom of a hydrogen bond acceptor group. Typically, salt bridges are formed between the hydrogen atom of the side chain carboxyl group of an aspartic acid or a glutamic acid and a side chain nitrogen atom found in lysine, ornithine, arginine, histidine, or tryptophan.

By "side chain atoms" or "side chain group" are meant those atoms in an amino acid, peptide, or protein that do not include the carbon and oxygen atom(s) of an amino acid's C1 carboxyl or carbonyl group; an amino acid's C2 carbon, and any hydrogen atoms bonded to the C2 carbon; and an amino acid's alpha-amine, and any hydrogen atom(s) bonded to the alpha amine.

By "space group" is meant a collection of symmetry elements of the unit cell of a crystal.

By "subject" is meant any animal (e.g., a human). Other animals that can be treated using the methods, compositions, and kits of the invention include horses, dogs, cats, pigs, goats, rabbits, hamsters, monkeys, guinea pigs, rats, mice, lizards, snakes, sheep, cattle, fish, and birds.

By "substantially identical" is meant a polypeptide or nucleic acid exhibiting at least 75%, but preferably 85%, more preferably 90%, most preferably 95%, or even 99% identity to a reference amino acid or nucleic acid sequence. For polypeptides, the length of comparison sequences will generally be at least 35 amino acids, preferably at least 45 amino acids, more preferably at least 55 amino acids, and most preferably 70 amino acids. For nucleic acids, the length of comparison sequences will generally be at least 60 nucleotides, preferably at least 90 nucleotides, and more preferably at least 120 nucleotides.

Sequence identity is typically measured using sequence analysis software with the default parameters specified therein (e.g., Sequence Analysis Software Package of the Genetics Computer Group, University of Wisconsin Biotechnology Center, 1710 University Avenue, Madison, WI 53705). This software program matches similar sequences by assigning degrees of homology to various substitutions, deletions, and other modifications. Conservative substitutions typically include substitutions within the following groups: glycine, alanine, valine, isoleucine, leucine, methionine; aspartic acid, glutamic acid, asparagine, glutamine; serine, threonine; lysine, arginine; and phenylalanine, tyrosine.

By "surrogate," in the context of atomic coordinates, is meant any modification (e.g., mathematical modification or scaling) of the coordinates that preserves the relative relationships among the coordinates.

By "tandem BRCT domain" is meant a protein having at least 2 tandem BRCT domains. For example, a protein substantially identical to the polypeptide sequence of AAH33781, NP_031375, or Genbank Accession NO. 30039659.

By "treating," "stabilizing," or "preventing" a disease, disorder, or condition is meant preventing or delaying an initial or subsequent occurrence of a disease, disorder, or condition; increasing the disease-free survival time between the disappearance of a condition and its reoccurrence; stabilizing or reducing an adverse symptom associated with a condition; or inhibiting, slowing, or stabilizing the progression of a condition. Desirably, at least 20, 40, 60, 80, 90, or 95% of the treated subjects have a complete remission in which all evidence of the disease disappears. In another desirable embodiment, the length of time a patient survives after being diagnosed with a condition and treated with a compound of the invention is at least 20, 40, 60, 80, 100, 200, or even 500% greater than (i) the average amount of time an untreated patient survives or (ii) the average amount of time a patient treated with another therapy survives.

By "unit cell" is meant the fundamental repeating unit of a crystal.

By "unnatural amino acid" is meant an organic compound that has a structure similar to a natural amino acid, where it mimics the structure and reactivity of a natural amino acid. The unnatural amino acid as defined herein generally increases or enhances the properties of a peptide (e.g., selectivity, stability, binding affinity) when the unnatural amino acid is either substituted for a natural amino acid or incorporated into a peptide.

Unnatural amino acids and peptides including such amino acids are described in U.S. Patent No. 6,566,330 and 6,555,522.

Other features and advantages of the invention will be apparent from the following description of the desirable embodiments thereof, and from the claims.

Brief Description of the Drawings

Figure 1A and Figure 1B depict the structure of a BRCA1 tandem BRCT domain complexed with a BACH1 phosphopeptide. Figure 1A is a ribbon representation of a BRCA1 tandem BRCT domain in complex with a pSer-containing BACH1 peptide shown as stick representation. The BACH1 phosphopeptide binds at the interface between the two BRCT repeats. The secondary-structure elements in BRCT2 are labelled 'prime' to differentiate them from the secondary-structure elements in BRCT1. Areas of 3_{10}-helix are not labelled. Figure 1B is an electron density map ($2F_o$-F_c) covering the BACH1 phosphopeptide.

Figure 2A and Figure 2B depict BRCA1 BRCT cancer-linked mutations and sequence conservation in relation to the BACH1 phosphopeptide binding-site. Figure 2A is a molecular surface representation of a BRCA1 tandem BRCT domain showing how the cancer-associated mutations S1655F, D1692Y, C1697R, R1699Q, S1715R, M1775R and Y1853X cluster with respect to the phosphopeptide binding-site. Figure 2B is a comparison of the front and back views of the molecular surface showing the clustering of residues conserved in human, chimp, mouse, rat, chicken and Xenopus BRCA1 tandem BRCT domains. The BACH1 peptide binds in a conserved phosphopeptide binding-groove.

Figure 3A, Figure 3B, and Figure 3C depict the functional effects of tandem BRCT domain mutations. Figure 3A is a schematic representation of protein-peptide contacts between a BRCA1 tandem BRCT domain and the BACH1 phosphopeptide. Hydrogen bonds, Van der Waals interactions and water molecules are denoted by dashed lines, crescents, and circles respectively. In Figure 3B, the wild-type and mutant myc-tagged BRCA1 tandem BRCT domain constructs containing the indicated mutations were analysed for binding to a bead-immobilized optimal tandem BRCT domain-interacting phosphopeptide, YDIpSQVFPF, or its non-phosphorylated counterpart. The weak phospho-

independent binding of the R1699Q mutant was observed using 10-fold more sample input than used in the other lanes. In Figure 3C, U2OS cells transfected with wild-type and mutant myc-tagged BRCA1 tandem BRCT domain constructs were analysed for association with endogenous BACH1.

Figure 4A , Figure 4B, and Figure 4C reveal that the Phe +3 position of the BACH1 phosphopeptide is essential for BRCA1 tandem BRCT domain binding-specificity. Figure 4A shows that residues Phe 1704, Met 1775, and Leu 1704 from a BRCA1 tandem BRCT domain form a hydrophobic pocket to accommodate the Phe +3 position of the BACH1 phosphopeptide. In Figure 4B, superposition of the crystal structure of a BRCA1 M1775R tandem BRCT domain mutant with the wild-type:BACH1 phosphopeptide complex reveals that this mutation occludes the BACH1 Phe +3 position. Figure 4C depicts BRCA1 wild type tandem BRCT domain and the M1775R mutant binding to a BACH1 phosphopeptide spot array. The M1775R mutant spot blot was performed using 10 times the amount of protein and was exposed to film for a significantly longer amount of time than the wild-type protein.

Figure 5A and Figure 5B depict the localization of BRCA1 BRCT domains to nuclear phosphoproteins. Figure 5A depicts the localization of wild-type, M1775R, or K1702M/S1655A versions of myc-tagged BRCA1 tandem BRCT domains in un-irradiated U2OS cells prior to (left panels) or following (right panels) extraction using Triton X-100-containing buffers. Bars indicate 25 μm. Figure 5B depicts localization following Triton X-100 extraction as in Figure 5A two hours following exposure of cells to 10 Gy of γ-radiation. Extracted cells were also stained using an anti-pSer/pThr-Gln epitope antibody that recognizes the phosphorylation motif generated by the DNA damage-response kinases ATM and ATR. Bars indicate 10 μm.

Description of the Invention

Structure of the BRCA1 BRCT:BACH1 Phosphopeptide Complex

The BRCA1 tandem BRCT domains bound to the interacting phosphopeptide from BACH1 (residues 986–995) was crystallized and its structure solved at 1.85Å resolution by X-ray diffraction (Figure 1A and Figure 1B). Phases were determined by molecular replacement using the previously determined structure of the un-liganded BRCA1 tandem BRCT domains (PDB ID 1JNX) as a search model (see Table 1). Difference Fourier maps revealed well-defined electron density for the phosphopeptide allowing modelling of eight residues corresponding to BACH1 Ser988 – Lys995. Each BRCT repeat forms a compact domain (Figure 1A) in which a central, four-stranded beta-sheet is packed against two helices, α1 and α3, on one side and a single helix, α2 on the other. The two domains pack together through interaction between α2 of BRCT1 and the α1'/α3' pair of BRCT2. A linker region connecting the two BRCT domains contains a β-hairpin-like structure βL and a short helical region, αL, that forms part of the interface through interactions with α2 of BRCT1 and the N-terminal end of α3' from BRCT2. Overall, the structure of the tandem BRCT domain:phosphopeptide complex is similar to that of the un-liganded domains (rmsd ~ 0.4Å for all Cα atoms). However, superposition of the individual BRCT repeats reveals that phosphopeptide-binding is associated with a slight relative rotation of each BRCT domain and a translation of BRCT1 helix α1 towards the cleft between the domains.

The BACH1 phosphopeptide binds in an extended conformation to a groove located at the highly conserved interface between the N- and C-terminal BRCT domains (Figure 1A and Figure 2A), consistent with the requirement of both domains for efficient phosphopeptide binding. This mode of binding is distinct from that observed in the phospho-independent interaction between p53 and the

tandem BRCT domains of 53BP-1, which occurs primarily through the linker region. Our structure clearly shows that the phospho-dependent interactions that are necessary and sufficient for formation of the BACH1/BRCA1 complex occur on the opposite side of the BRCT-BRCT interface from those involved in the p53:53BP-1 interaction.

BRCA1 BRCT:Phosphopeptide Specificity

BRCA1 tandem BRCT domain binding to library-selected peptides *in vitro*, and to phosphorylated BACH1 *in vivo* is dominated by the presence of a phosphoserine/threonine and a phenylalanine three residues C-terminal to it (Phe +3). This is now confirmed by our structure which shows that the BACH1 pSer 990 phosphate moiety binds to a basic pocket through three direct hydrogen-bonding interactions involving the side chains of Ser1655 and Lys1702, and the main-chain NH of Gly1656 (Figure 3A). All three of these residues are located in BRCT1 and all are absolutely conserved in BRCA1 homologues. Ser1655 and Gly1656 are situated within the loop preceding α1 and are brought into proximity with the phosphate moiety as a result of the conformational change that occurs upon phosphopeptide binding. Intriguingly, a S1655F mutation has been identified in a single breast cancer patient, although its link to disease has not been confirmed. In addition to these direct interactions, the phosphate, and some peptide main-chain atoms are also tethered through networks of water molecules, many of which are tetrahedrally hydrogen bonded (Figure 3A). Indirect protein-solvent-phosphate contacts are unusual in phospho-dependent protein-protein interactions but have been observed previously in structures of phosphopeptide complexes of the human Plk1 Polo-box domain.

The Phe +3 peptide side-chain fits into a hydrophobic pocket at the BRCT interface consisting of the side chains of Phe1704, Met1775 and Leu1839

contributed from both BRCT domains (Figure 3A and Figure 4A). This finding rationalizes the strong selection for aromatic amino acids in the +3 position of the binding motif seen in peptide library experiments, as well as the observation of Yu et al. that mutation of Phe993 to Ala eliminates BRCA1:BACH1 binding. Additional hydrogen-bonds with the main-chain N and C=O atoms of Phe +3 are supplied by main- and side-chain atoms from Arg1699, a site of mutation also associated with cancer predisposition. The phosphorylated Ser990 of BACH1 is preceded by an Arg residue in the –3 position and followed by a proline residue in the +1 position, suggesting potential Ser990 phosphorylation by either basophilic and/or proline-directed kinases. The BRCA1 tandem BRCT domains are also known to interact with pSQ-containing motifs characteristic of PI 3-kinase-like kinases such as ATM and ATR. In the tandem BRCT:BACH1 phosphopeptide co-crystal structure, there are no direct interactions between the +1 Pro side chain and the BRCT domains. Instead, this residue participates in only a single water-mediated hydrogen bond involving its carbonyl oxygen (Figure 3A), consistent with the idea that various types of protein kinases can generate tandem BRCT phospho-binding motifs. The Lys +5 side chain makes two salt-bridging interactions with residues in BRCT2 (Figure 3A), consistent with the Lys selection observed in this position by spot blot and peptide library experiments.

Cancer-Associated BRCA1 BRCT Mutations

Residues that form or stabilize the phosphopeptide binding surface, and the domain-domain interface, are among the most highly conserved portions of the molecule in BRCA1 orthologues from humans, primates, rats and mice (Figure 2B). Interestingly, these regions correlate strongly with the location of cancer-associated mutations (Figure 2A). Some cancer-associated mutations may disrupt the global BRCT fold while others are more likely to specifically interfere with

ligand binding. Approximately 80 tumor-derived mutations have been identified within the BRCA1 tandem BRCT domains, though only a few of these have been subsequently confirmed to result in cancer predisposition including D1692Y, C1697R, R1699W, A1708E, S1715R, G1738E, P1749R, M1775R, 5382InsC (a frameshift mutation that results in a stop codon at position 1829), and Y1853X (which truncates the last 11 residues). Most of these cluster at or near the phosphopeptide-interacting surface (Figure 2A). Two of these mutated residues, Arg1699 and Met1775, directly interact with residues in the phosphopeptide (Figure 3A). Two others, Pro1749 and Gly1738, are located at the BRCT1/BRCT2 interface beneath the molecular surface and their effects are likely to be mediated through alterations in the relative orientation of the tandem BRCT motifs that our structure suggests is necessary for phospho-dependent interactions with partner proteins.

To verify the phosphoserine phosphate interactions observed in the X-ray structure and to investigate the effects of the most common tumor-derived point mutations, we investigated the binding of a panel of site-directed mutant BRCA1 tandem BRCT domains to the interacting region of BACH1. Binding was determined by measuring the ability of *in vitro* transcribed and translated proteins to bind to either phosphorylated and non-phosphorylated biotinylated peptides (Figure 3B). Wild-type BRCA1 tandem BRCT domains clearly bind to phosphorylated but not non-phosphorylated peptides, while mutation of the conserved Ser1655 and Lys1702, alone or in combination, completely abolished the interaction. Five *bona fide* cancer-linked mutations, P1749R, G1738E, M1775R, Y1853X and 5382InsC, all result in complete loss of phosphopeptide binding. A mutation R1699W is cancer-linked and a second, R1699Q, has been detected in breast cancer patients but has not yet been directly related to disease-predisposition. We surmised that the glutamine side-chain might still participate in main-chain hydrogen bonding to the peptide and this is, indeed, the only BRCA1

tandem BRCT domain mutant that retained a small degree of binding in our assays. Somewhat surprisingly, however, the R1699Q mutant largely loses phospho-specificity, and instead bound to both phosphorylated and non-phosphorylated peptides.

To investigate the *in vivo* binding of cancer-predisposing mutant BRCA1 tandem BRCT domains to endogenous BACH1, we transfected U2OS cells with a vector encoding the C-terminal 550 amino acids of BRCA1 containing a myc tag and an SV40 nuclear localization sequence as described by Chen et al. As shown in Figure 3C, interaction between the wild type BRCA1 tandem BRCT domains with full-length BACH1 was easily detected. In contrast, no *in vivo* interaction was observed between BACH1 and mutant BRCA1 tandem BRCT domains that disrupt phosphate-binding or predispose to breast and ovarian cancer. All of these cancer-associated mutant proteins were expressed at comparable levels when transfected into mammalian cells (Figure 3C), suggesting that gross structural destabilization is unlikely to account for their cancer proclivity.

Interpretation of the structural effects of the M1775R mutation is simplified since the X-ray crystal structure of the M1775R tandem BRCT domain mutant has been determined (PDB ID 1N5O), revealing a nearly identical structure as the wild-type protein with an average rmsd of 0.35 Å for all Cα atoms. Superposition of the mutant structure with that of our BACH1 complex shows that the guanidine portion of the substituent arginine side-chain extrudes into the tandem BRCT cleft, where it occupies the binding site for the essential Phe +3 of the phosphopeptide (Figure 4A and Figure 4B). In this case, loss of phosphopeptide-binding *in vitro* and BACH1 binding *in vivo* appear to be attributable to the severe steric clash of the Arg1775 side-chain with an important determinant of phospholigand specificity and affinity. The M1775R mutant protein does, however, bind weakly to a BACH1 phosphopeptide in which the +3 Phe is mutated to Asp or Glu (Figure 4C). This is consistent with the introduction of a basic residue at the pSer +3

binding site and with the observation that this mutation creates new anion binding sites in the M1775R crystal structure. Thus, in addition to disrupting the native BRCA1:BACH1 interaction, this mutation may also result in the formation of inappropriate BRCA1 BRCT interactions.

Phosphopeptide-Binding and Nuclear Foci Formation

Subcellular localization and nuclear foci formation by the wild type, S1655A/K1702M phosphopeptide-binding mutant and the M1775R cancer-associated mutant BRCA1 BRCT domains were studied before and after DNA damage in unsynchronized U2OS cells (Figure 5A and Figure 5B). To maximize visualization of nuclear foci, the cells were permeabilized with buffers containing 0.5% Triton X-100 prior to fixation and immunostaining. In un-extracted cells the wild-type BRCT domains and both of the mutant BRCT proteins showed equivalent diffuse nuclear localization. Extraction of the un-irradiated cells prior to fixation resulted in near complete loss of BRCT domain staining in all cases (Figure 5A). Under these conditions, less than 5% of the wild-type and M1775R tandem BRCT-containing cells displayed 5 or more nuclear foci, and no foci were observed with the S1655A/K1702M double mutant. When the cells were irradiated with 10 Gy of γ-irradiation, and 2 hrs later permeabilized, fixed, and stained, nearly all of the cells containing the wild-type BRCA1 tandem BRCT domains demonstrated sharp punctate nuclear foci that largely co-localized with the staining pattern of an anti-pSer/pThr-Gln epitope antibody that recognizes ATM- and ATR-phosphorylated substrates (Figure 5B). In contrast, the S1655A/K1702M mutant protein displayed only faint staining with a very fine granular pattern that completely failed to co-localize with pSer/pThr-Gln staining. This failure of foci formation and pSer/pThr-Gln co-localization is strong evidence that the phospho-binding function of the BRCA1 tandem BRCT domains is critical for normal subcellular localization following DNA damage. The M1775R

mutant protein that binds weakly to phosphopeptides with a different specificity than the wild-type BRCA1 BRCT domains also formed punctate nuclear foci, although these were slightly reduced in number and showed less co-localization with pSer/pThr-Gln staining foci than the wild-type protein. This localization might result from synergistic weak binding to alternative non-optimal phosphorylated ligands present in high abundance in nuclear foci following DNA damage, as has been observed for other phosphopeptide-binding domain interactions.

Analysis of BRCA1 tandem BRCT domain-BACH1 phosphopeptide structure

The 1.85Å BRCA1 tandem BRCT domain:phosphopeptide structure described here is the highest resolution X-ray structure of any BRCT domain structure solved to date, and provides an enhanced structural framework within which the molecular basis of breast and ovarian cancer can be further investigated. The structure reveals why tandem BRCT repeats, rather than single BRCT domains, are required for binding to pSer- or pThr-containing phosphopeptides with high affinity and specificity, since motif recognition is mediated by residues contributed from both domains across the domain-domain interface. In addition, the structure rationalizes the observation that the BRCA1 BRCT domains do not bind to pTyr-containing sequences, since the phosphate recognition pocket appears too shallow to accept a bulky phenyl ring. Despite the fact that not all tandem BRCT domains appear to bind phosphopeptides, several residues involved in the binding are relatively conserved. Structures of additional BRCT:phosphopeptide complexes will be necessary to better understand negative determinants of binding.

The BRCA1 tandem BRCT:phosphopeptide structure, in combination with biochemical and cell biological analysis, shows that some pro-oncogenic mutations in the BRCA1 C-terminal domains directly disrupt phosphopeptide

binding or perturb the BRCT interface that forms the phospho-dependent binding surface. Similar conclusions were reached by Williams et al., who reported the structure of the BRCA1 tandem BRCT domains bound to an alternative phosphopeptide determined from oriented peptide library screening, and the un-liganded structures of the M1775R and V1809F mutants.

Like the BRCT domains in PTIP, the BRCT domains in BRCA1 are sufficient for nuclear foci formation in response to DNA damage, and the phospho-binding function appears to be involved in this phenomenon. Four *bona fide* cancer-linked mutations, P1749R, G1738E, 5382InsC, and Y1853X all result in loss of phosphopeptide binding. A fifth mutation, M1775R, binds weakly to phosphopeptides with altered motif specificity, and can still form nuclear foci after DNA damage, however it completely loses the ability to interact with wild-type BACH1. These effects of the Pro1749 and Met1775 lesions confirm the previous observations that these mutations are sufficient to abrogate BRCA1-BACH1 interactions *in vivo*. Since BACH1 mutations have also been shown to be associated with the development of cancer, these findings suggest that the loss of this critical BRCA1 M1775R:BACH1 interaction may be the critical event responsible for cancer predisposition.

Despite the fact that mutations in BRCA1 ultimately predispose women to cancer, wild-type BRCA1 paradoxically constitutes a target for anti-cancer therapy. Given the importance of BRCA1 in homologous recombination and DNA repair, disruption of the pSer-binding function would be expected to result in enhanced sensitivity to chemotherapy and radiation, as has been observed in BRCA1 null murine embryonic stem cells. The structural delineation of the pSer binding surface provides a new target for rational drug design.

Protein Cloning, Expression, and Purification

For crystallization experiments, human BRCA1 BRCTs (residues 1646–1859) were expressed as glutathione *S*-transferase (GST) fusions in pGEX-4T1 (Amersham Pharmacia Biotech) in *Escherichia coli* BL21 at 18°C. The GST was removed by 48-hour treatment with thrombin before gel filtration. A BRCA1 BRCT clone (residues 1313–1863) in pcDNA3 containing a N-terminal Myc-tag and a SV40 nuclear localization sequence was used for the co-immunoprecipitation and immunofluorescence assays. Mutations were generated using the Stratagene Quick Change Mutagenesis Kit, and verified by sequencing. The pGEX-BRCA1 BRCT clone (residues 1633–1863) was described previously and was used for the peptide filter array. Induction of recombinant GST-BRCA1 BRCT domain protein was performed at 37°C for 3 hrs in the presence of 0.4 mM IPTG. The GST-BRCA1 BRCT domains were isolated from bacterial lysates using glutathione agarose, followed by elution with 40mM glutathione, 50mM Tris/HCl (pH 8.1), and dialysis into 50mM Tris/HCl (pH 8.1), 300mM NaCl.

Crystallization and Structure Determination

Crystals were grown at 18°C by microbatch methods. The BACH1 phosphopeptide (SRSTpS^{990}PTFNK) was mixed with the BRCA1 BRCTs in a 1.5:1 stoichiometric excess and concentrated to 0.35mM in a buffer containing 50mM Tris-HCl (pH 7.5), 0.4M NaCl, and 3mM DTT. Crystals grew from 50 mM MES (pH 6.5), 0.1 M $(NH_4)_2SO_4$, and 13% PEG 8K (w/v). Crystals belonged to the trigonal space group $P3_221$ ($a = b = 65.8$ Å, $c = 93.1$ Å, $\alpha = \beta = 90.0°$, $\gamma = 120.0°$) with one complex in the asymmetric unit. Data were collected from flash-cooled crystals at 100K on a Raxis-II detector mounted on a Rigaku RU200 generator. Diffraction data were integrated and scaled using DENZO and SCALEPACK. The structure was solved by molecular replacement using the coordinates 1JNX.brk as a model with AMORE (CCP4 1994). Subsequent

refinement was carried out using REFMAC5 (CCP4 1994) and manual model building in O. Figures were constructed using Pymol.

Peptide Binding

An optimal phosphopeptide for binding the BRCA1 BRCTs was determined by oriented peptide library screening as described previously. This peptide was synthesized in both its phosphorylated and non-phosphorylated form with a biotin group at the N-terminus using N-α-FMOC-protected amino acids and standard BOP/HOBt coupling chemistry. These peptides were conjugated to streptavidin coated beads (Sigma-Aldrich). The wild-type and mutant BRCA1 BRCT domain-containing constructs (residues 1313–1863) were transcribed and translated *in vitro* in the presence of [^{35}S]-methionine using the TNT kit (Promega). The bead-immobilized peptides (10μL of beads) were added to 10 μL of the in vitro translated [^{35}S]-labeled protein pool in 150 μL binding buffer (50 mM Tris-HCl (pH7.6), 150 mM NaCl, 0.5% NP-40, 1 mM EDTA, 2 mM DTT, 8 μg/mL pepstatin, 8 μg mL^{-1} aprotinin, 8 μg mL^{-1} leupeptin, 800 μM Na3VO4, 25 mM NaF). After incubation at 4°C for 3 hours, the beads were washed three times with 200 μL of binding buffer prior to analysis by SDS-PAGE (12.5% (w/v)) and autoradiography.

Peptide Filter Array

An ABIMED peptide arrayer with a computer controlled Gilson diluter and liquid handling robot was used to synthesize peptides onto an amino-PEG cellulose membrane using N-α-FMOC-protected amino acids and DIC/HOBT coupling chemistry. The membranes were blocked in 5% (w/v) milk in Tris-buffered saline containing 0.1% (v/v) Tween-20 (TBS-T) for 1hr at room temperature, incubated with 0.025μM GST-BRCA1 BRCTs or 0.25 μM GST-BRCA1 BRCTs M1775R (residues 1633–1863) in 5% (w/v) milk, 50 mM Tris-

HCl (pH 7.6), 150 mM NaCl, 2 mM EDTA, 2mM DTT for 1 hr at room temperature and washed four times with TBS-T. The membranes were then incubated with anti-GST conjugated HRP (Amersham) in 5% (w/v) milk/TBS-T for 1 hr at room temperature, washed five times with TBS-T, and binding analysed by ECL (Perkin-Elmer).

Co-immunoprecipitation of BRCA1 BRCTs and BACH1

U2OS cells were grown to 50% confluency in 100cm^2 dishes and transfected with the myc-tagged wild-type or mutant BRCA1 BRCT constructs (residues 1313–1863) using FuGene6 transfection reagent (Roche) according to manufacturer's protocol. Cells were collected 30 hrs following transfection, lysed in lysis buffer (50 mM Tris-HCl (pH7.6), 150 mM NaCl, 1.0% NP-40, 5 mM EDTA, 2 mM DTT, 8 μg/mL AEBSF, 8 μg mL^{-1} aprotinin, 8 μg mL^{-1} leupeptin, 2 mM Na_3VO_4, 10 mM NaF and the phosphatase inhibitors microcystin and okadaic acid). Lysates containing equal amounts of protein (3 mg) was incubated with 3 μL of a mouse anti-myc antibody (Cell Signaling) for 2 hr at 4°C and then 10 μL of protein G-sepharose beads (Sigma-Aldrich) were added and samples incubated for an additional 2 hr at 4°C. Beads were washed four times with lysis buffer, bound proteins eluted in SDS-PAGE sample buffer, analysed on 6% polyacrylamide gels, transferred to PVDF membrane, and detected by blotting with rabbit anti-BACH1 antibody. A portion of the lysates were also run and blotted with the anti-BACH1 antibody and the anti-myc antibody to further ensure equal protein loading.

Immunofluorescence and Microscopy

U2OS cells were seeded onto 18mm^2 coverslips and transfected with the BRCA1 BRCT construct (residues 1313–1863) and various mutants using FuGene6 transfection reagent (Roche) according to manufacturer's protocol.

Thirty hours following transfection, the cells were either treated with 10 Gy of ionizing radiation or mock irradiated and allowed to recover for 120 minutes. Cells were fixed in 3% (v/v) paraformaldehyde/2% (w/v) sucrose for 15 min at RT and permeabilized with a 0.5% (v/v) Triton X-100 solution containing 20 mM Tris-HCl (pH 7.8), 75 mM NaCl, 300 mM sucrose, and 3 mM $MgCl_2$ for 15 min at RT. When necessary, proteins were extracted after IR treatment as described previously. In brief, cells were incubated with extraction buffer (10mM PIPES pH6.8, 100mM NaCl, 300mM sucrose, 3mM $MgCl_2$, 1mM EGTA, 0.5% (v/v) Triton X-100) for 5 minutes on ice followed by incubation with extraction stripping buffer (10mM Tris-HCl pH 7.4, 10mM NaCl, 3mM $MgCl_2$, 0.5% (v/v) Triton X-100) for 5 minutes on ice followed by successive washes in ice cold PBS. Slides were fixed as above, stained with primary antibodies at 37°C for 20 min, then stained with a anti-mouse or anti-rabbit secondary antibody for 20 min (Molecular Probes) at 37°C. Primary antibodies used were mouse anti-myc (Cell Signaling) and rabbit anti-(pSer/pThr)Gln (Cell Signaling). Images were collected on a Axioplan2 microscope (Carl Zeiss) and processed using OpenLab software (Improvision).

Coordinates

The atomic coordinates and structure factors have been deposited in the Protein Data Bank (Accession code 1T15). This information is shown in Table 2.

Table 1. Summary of crystallographic analysis. Details of the crystallization and structure determination are provided in the supplementary information. $^{*}R_{sym}$ = $\Sigma_j | \langle I \rangle - I_j | / \Sigma \langle I \rangle$ where I_j is the intensity of the j^{th} reflection and $\langle I \rangle$ is the average intensity. $^{\S}R_{work} = \Sigma_{hkl} | F_{obs} - F_{calc} | / \Sigma_{hkl} F_{obs}$, where R_{free} is equivalent to R_{work} but is calculated for a randomly chosen 5% of reflections omitted from the refinement process.

Data Collection:	
Space group	$P3_221$
Unit cell dimensions	$a = b = 65.8$ Å, $c = 93.1$ Å,
	$\alpha = \beta = 90°$, $\gamma = 120°$
Resolution range (Å)	15.0-1.85
Completeness (%)	93.9
Total observations	165,151
Unique reflections	19,219
Average $I/\sigma(I)$	35.6
R_{sym} * (%)	5.4
Model refinement:	
Resolution (Å)	15.0-1.85
No. of reflections (free)	18,225 (911)
R_{work}/R_{free} § (%)	20.6/22.2
No. of protein atoms	1,750
No. of water atoms	157
rms deviations	
bonds (Å)	0.01
angles (°)	1.35

Table 2

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HEADER    ANTITUMOR PROTEIN                                15-APR-04   1T15
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TITLE    2 THE PHOSPHORYLATED INTERACTING REGION FROM BACH1 HELICASE
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COMPND   2 MOLECULE: BREAST CANCER TYPE 1 SUSCEPTIBILITY PROTEIN;
COMPND   3 CHAIN: A;
COMPND   4 FRAGMENT: BCRT 1, BCRT 2;
COMPND   5 ENGINEERED: YES;
COMPND   6 MOL_ID: 2;
COMPND   7 MOLECULE: BRCA1 INTERACTING PROTEIN C-TERMINAL HELICASE 1;
COMPND   8 CHAIN: B;
COMPND   9 ENGINEERED: YES
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SOURCE   3 ORGANISM_COMMON: HUMAN;
SOURCE   4 GENE: BRCA1;
SOURCE   5 EXPRESSION_SYSTEM: ESCHERICIA COLI;
SOURCE   6 EXPRESSION_SYSTEM_STRAIN: BL21;
SOURCE   7 EXPRESSION_SYSTEM_VECTOR_TYPE: PLASMID;
SOURCE   8 EXPRESSION_SYSTEM_PLASMID: PGEX-4T1;
SOURCE   9 MOL_ID: 2;
SOURCE  10 SYNTHETIC: YES
KEYWDS    PROTEIN-PEPTIDE COMPLEX
EXPDTA    X-RAY DIFFRACTION
AUTHOR    J.A.CLAPPERTON,I.A.MANKE,D.M.LOWERY,T.HO,L.F.HAIRE,
AUTHOR   2 M.B.YAFFE,S.J.SMERDON
JRNL        AUTH   J.A.CLAPPERTON,I.A.MANKE,D.M.LOWERY,T.HO,L.F.HAIRE,
JRNL        AUTH 2 M.B.YAFFE,S.J.SMERDON
JRNL        TITL   STRUCTURE AND MECHANISM OF BRCA1 BRCT DOMAIN
JRNL        TITL 2 RECOGNITION OF PHOSPHORYLATED BACH1 WITH
JRNL        TITL 3 IMPLICATIONS FOR CANCER
JRNL        REF    TO BE PUBLISHED
JRNL        REFN
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REMARK   3   PROGRAM     : REFMAC 5.0
REMARK   3   AUTHORS     : MURSHUDOV,VAGIN,DODSON
REMARK   3
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REMARK   3
REMARK   3  ISOTROPIC THERMAL FACTOR RESTRAINTS.      COUNT   RMS     WEIGHT
REMARK   3   MAIN-CHAIN BOND REFINED ATOMS  (A**2):  NULL ;  NULL ;  NULL
REMARK   3   MAIN-CHAIN BOND OTHER ATOMS    (A**2):  NULL ;  NULL ;  NULL
REMARK   3   MAIN-CHAIN ANGLE REFINED ATOMS (A**2):  NULL ;  NULL ;  NULL
REMARK   3   SIDE-CHAIN BOND REFINED ATOMS  (A**2):  NULL ;  NULL ;  NULL
REMARK   3   SIDE-CHAIN ANGLE REFINED ATOMS (A**2):  NULL ;  NULL ;  NULL
REMARK   3
REMARK   3 ANISOTROPIC THERMAL FACTOR RESTRAINTS.     COUNT   RMS     WEIGHT
REMARK   3   RIGID-BOND RESTRAINTS          (A**2):  NULL ;  NULL ;  NULL
REMARK   3   SPHERICITY; FREE ATOMS         (A**2):  NULL ;  NULL ;  NULL
REMARK   3   SPHERICITY; BONDED ATOMS       (A**2):  NULL ;  NULL ;  NULL
REMARK   3
REMARK   3  NCS RESTRAINTS STATISTICS
REMARK   3   NUMBER OF DIFFERENT NCS GROUPS : 0
REMARK   3
REMARK   3  TLS DETAILS
REMARK   3   NUMBER OF TLS GROUPS  : 0
REMARK   3
REMARK   3  BULK SOLVENT MODELLING.
REMARK   3   METHOD USED : NULL
REMARK   3   PARAMETERS FOR MASK CALCULATION
REMARK   3   VDW PROBE RADIUS    : NULL
REMARK   3   ION PROBE RADIUS    : NULL
REMARK   3   SHRINKAGE RADIUS    : NULL
REMARK   3
REMARK   3  OTHER REFINEMENT REMARKS: NULL
REMARK   4
REMARK   4 1T15 COMPLIES WITH FORMAT V. 2.3, 09-JULY-1998
REMARK 100
REMARK 100 THIS ENTRY HAS BEEN PROCESSED BY RCSB ON 19-APR-2004.
REMARK 100 THE RCSB ID CODE IS RCSB022182.
REMARK 200
REMARK 200 EXPERIMENTAL DETAILS
REMARK 200  EXPERIMENT TYPE                : X-RAY DIFFRACTION
REMARK 200  DATE OF DATA COLLECTION        : 17-JAN-2004
REMARK 200  TEMPERATURE           (KELVIN) : 100.0
REMARK 200  PH                             : 6.50
REMARK 200  NUMBER OF CRYSTALS USED        : 1
REMARK 200
REMARK 200  SYNCHROTRON              (Y/N) : N
REMARK 200  RADIATION SOURCE               : ROTATING ANODE
REMARK 200  BEAMLINE                       : NULL
REMARK 200  X-RAY GENERATOR MODEL          : NULL
REMARK 200  MONOCHROMATIC OR LAUE    (M/L) : M
```

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REMARK 200  WAVELENGTH OR RANGE        (A) : NULL
REMARK 200  MONOCHROMATOR                  : NULL
REMARK 200  OPTICS                         : NULL
REMARK 200
REMARK 200  DETECTOR TYPE                  : IMAGE PLATE
REMARK 200  DETECTOR MANUFACTURER          : RIGAKU RAXIS II
REMARK 200  INTENSITY-INTEGRATION SOFTWARE : DENZO
REMARK 200  DATA SCALING SOFTWARE          : SCALEPACK
REMARK 200
REMARK 200  NUMBER OF UNIQUE REFLECTIONS   : 19219
REMARK 200  RESOLUTION RANGE HIGH      (A) : 1.850
REMARK 200  RESOLUTION RANGE LOW       (A) : 15.000
REMARK 200  REJECTION CRITERIA  (SIGMA(I)) : 2.500
REMARK 200
REMARK 200 OVERALL.
REMARK 200  COMPLETENESS FOR RANGE     (%) : 93.9
REMARK 200  DATA REDUNDANCY                : NULL
REMARK 200  R MERGE                    (I) : NULL
REMARK 200  R SYM                      (I) : NULL
REMARK 200  <I/SIGMA(I)> FOR THE DATA SET  : NULL
REMARK 200
REMARK 200 IN THE HIGHEST RESOLUTION SHELL.
REMARK 200  HIGHEST RESOLUTION SHELL, RANGE HIGH (A) : 1.85
REMARK 200  HIGHEST RESOLUTION SHELL, RANGE LOW  (A) : 1.93
REMARK 200  COMPLETENESS FOR SHELL     (%) : 76.8
REMARK 200  DATA REDUNDANCY IN SHELL       : NULL
REMARK 200  R MERGE FOR SHELL          (I) : NULL
REMARK 200  R SYM FOR SHELL            (I) : NULL
REMARK 200  <I/SIGMA(I)> FOR SHELL         : NULL
REMARK 200
REMARK 200 DIFFRACTION PROTOCOL: SINGLE WAVELENGTH
REMARK 200 METHOD USED TO DETERMINE THE STRUCTURE: MOLECULAR REPLACEMENT
REMARK 200 SOFTWARE USED: AMORE
REMARK 200 STARTING MODEL: NULL
REMARK 200
REMARK 200 REMARK: NULL
REMARK 280
REMARK 280 CRYSTAL
REMARK 280 SOLVENT CONTENT, VS   (%): NULL
REMARK 280 MATTHEWS COEFFICIENT, VM (ANGSTROMS**3/DA): NULL
REMARK 280
REMARK 280 CRYSTALLIZATION CONDITIONS: PEG 8000, AMMONIUM SULPHATE, MES,
REMARK 280  PH 6.5, MICROBATCH, TEMPERATURE 291K
REMARK 290
REMARK 290 CRYSTALLOGRAPHIC SYMMETRY
REMARK 290 SYMMETRY OPERATORS FOR SPACE GROUP: P 32 2 1
REMARK 290
REMARK 290      SYMOP   SYMMETRY
REMARK 290     NNNMMM   OPERATOR
REMARK 290       1555   X,Y,Z
REMARK 290       2555   -Y,X-Y,2/3+Z
REMARK 290       3555   -X+Y,-X,1/3+Z
REMARK 290       4555   Y,X,-Z
REMARK 290       5555   X-Y,-Y,1/3-Z
REMARK 290       6555   -X,-X+Y,2/3-Z
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REMARK 290
REMARK 290      WHERE NNN -> OPERATOR NUMBER
REMARK 290            MMM -> TRANSLATION VECTOR
REMARK 290
REMARK 290 CRYSTALLOGRAPHIC SYMMETRY TRANSFORMATIONS
REMARK 290 THE FOLLOWING TRANSFORMATIONS OPERATE ON THE ATOM/HETATM
REMARK 290 RECORDS IN THIS ENTRY TO PRODUCE CRYSTALLOGRAPHICALLY
REMARK 290 RELATED MOLECULES.
REMARK 290   SMTRY1   1  1.000000  0.000000  0.000000        0.00000
REMARK 290   SMTRY2   1  0.000000  1.000000  0.000000        0.00000
REMARK 290   SMTRY3   1  0.000000  0.000000  1.000000        0.00000
REMARK 290   SMTRY1   2 -0.500000 -0.866025  0.000000        0.00000
REMARK 290   SMTRY2   2  0.866025 -0.500000  0.000000        0.00000
REMARK 290   SMTRY3   2  0.000000  0.000000  1.000000       62.05000
REMARK 290   SMTRY1   3 -0.500000  0.866025  0.000000        0.00000
REMARK 290   SMTRY2   3 -0.866025 -0.500000  0.000000        0.00000
REMARK 290   SMTRY3   3  0.000000  0.000000  1.000000       31.02500
REMARK 290   SMTRY1   4 -0.500000  0.866025  0.000000        0.00000
REMARK 290   SMTRY2   4  0.866025  0.500000  0.000000        0.00000
REMARK 290   SMTRY3   4  0.000000  0.000000 -1.000000        0.00000
REMARK 290   SMTRY1   5  1.000000  0.000000  0.000000        0.00000
REMARK 290   SMTRY2   5  0.000000 -1.000000  0.000000        0.00000
REMARK 290   SMTRY3   5  0.000000  0.000000 -1.000000       31.02500
REMARK 290   SMTRY1   6 -0.500000 -0.866025  0.000000        0.00000
REMARK 290   SMTRY2   6 -0.866025  0.500000  0.000000        0.00000
REMARK 290   SMTRY3   6  0.000000  0.000000 -1.000000       62.05000
REMARK 290
REMARK 290 REMARK: NULL
REMARK 300
REMARK 300 BIOMOLECULE: 1
REMARK 300 THIS ENTRY CONTAINS THE CRYSTALLOGRAPHIC ASYMMETRIC UNIT
REMARK 300 WHICH CONSISTS OF 2 CHAIN(S). SEE REMARK 350 FOR
REMARK 300 INFORMATION ON GENERATING THE BIOLOGICAL MOLECULE(S).
REMARK 350
REMARK 350 GENERATING THE BIOMOLECULE
REMARK 350 COORDINATES FOR A COMPLETE MULTIMER REPRESENTING THE KNOWN
REMARK 350 BIOLOGICALLY SIGNIFICANT OLIGOMERIZATION STATE OF THE
REMARK 350 MOLECULE CAN BE GENERATED BY APPLYING BIOMT TRANSFORMATIONS
REMARK 350 GIVEN BELOW.  BOTH NON-CRYSTALLOGRAPHIC AND
REMARK 350 CRYSTALLOGRAPHIC OPERATIONS ARE GIVEN.
REMARK 350
REMARK 350 BIOMOLECULE: 1
REMARK 350 APPLY THE FOLLOWING TO CHAINS: A, B
REMARK 350   BIOMT1   1  1.000000  0.000000  0.000000        0.00000
REMARK 350   BIOMT2   1  0.000000  1.000000  0.000000        0.00000
REMARK 350   BIOMT3   1  0.000000  0.000000  1.000000        0.00000
REMARK 465
REMARK 465 MISSING RESIDUES
REMARK 465 THE FOLLOWING RESIDUES WERE NOT LOCATED IN THE
REMARK 465 EXPERIMENT. (M=MODEL NUMBER; RES=RESIDUE NAME; C=CHAIN
REMARK 465 IDENTIFIER; SSSEQ=SEQUENCE NUMBER; I=INSERTION CODE.)
REMARK 465
REMARK 465   M RES C SSSEQI
REMARK 465     VAL A  1646
REMARK 465     ASN A  1647
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REMARK 465     LYS A  1648
REMARK 470
REMARK 470 MISSING ATOM
REMARK 470 THE FOLLOWING RESIDUES HAVE MISSING ATOMS(M=MODEL NUMBER;
REMARK 470 RES=RESIDUE NAME; C=CHAIN IDENTIFIER; SSEQ=SEQUENCE NUMBER;
REMARK 470 I=INSERTION CODE):
REMARK 470   M RES CSSEQI  ATOMS
REMARK 470     GLU A1817    CG    CD    OE1   OE2
REMARK 470     ASP A1818    CG    OD1   OD2
REMARK 470     ASN A1819    CG    OD1   ND2
REMARK 500
REMARK 500 GEOMETRY AND STEREOCHEMISTRY
REMARK 500 SUBTOPIC: CLOSE CONTACTS IN SAME ASYMMETRIC UNIT
REMARK 500
REMARK 500 THE FOLLOWING ATOMS ARE IN CLOSE CONTACT.
REMARK 500
REMARK 500  ATM1  RES C  SSEQI   ATM2  RES C  SSEQI
REMARK 500   O    GLU A  1660     O    HOH     154              2.13
DBREF  1T15 A 1649  1859  SWS    P38398   BRC1_HUMAN    1649   1859
DBREF  1T15 B    6    13  GB     14042978 NP_114432      988    995
SEQADV 1T15 SEP B    8  GB   14042978  SER   990 MODIFIED RESIDUE
SEQRES   1 A  214  VAL ASN LYS ARG MET SER MET VAL VAL SER GLY LEU THR
SEQRES   2 A  214  PRO GLU GLU PHE MET LEU VAL TYR LYS PHE ALA ARG LYS
SEQRES   3 A  214  HIS HIS ILE THR LEU THR ASN LEU ILE THR GLU GLU THR
SEQRES   4 A  214  THR HIS VAL VAL MET LYS THR ASP ALA GLU PHE VAL CYS
SEQRES   5 A  214  GLU ARG THR LEU LYS TYR PHE LEU GLY ILE ALA GLY GLY
SEQRES   6 A  214  LYS TRP VAL VAL SER TYR PHE TRP VAL THR GLN SER ILE
SEQRES   7 A  214  LYS GLU ARG LYS MET LEU ASN GLU HIS ASP PHE GLU VAL
SEQRES   8 A  214  ARG GLY ASP VAL VAL ASN GLY ARG ASN HIS GLN GLY PRO
SEQRES   9 A  214  LYS ARG ALA ARG GLU SER GLN ASP ARG LYS ILE PHE ARG
SEQRES  10 A  214  GLY LEU GLU ILE CYS CYS TYR GLY PRO PHE THR ASN MET
SEQRES  11 A  214  PRO THR ASP GLN LEU GLU TRP MET VAL GLN LEU CYS GLY
SEQRES  12 A  214  ALA SER VAL VAL LYS GLU LEU SER SER PHE THR LEU GLY
SEQRES  13 A  214  THR GLY VAL HIS PRO ILE VAL VAL VAL GLN PRO ASP ALA
SEQRES  14 A  214  TRP THR GLU ASP ASN GLY PHE HIS ALA ILE GLY GLN MET
SEQRES  15 A  214  CYS GLU ALA PRO VAL VAL THR ARG GLU TRP VAL LEU ASP
SEQRES  16 A  214  SER VAL ALA LEU TYR GLN CYS GLN GLU LEU ASP THR TYR
SEQRES  17 A  214  LEU ILE PRO GLN ILE PRO
SEQRES   1 B    8  SER THR SEP PRO THR PHE ASN LYS
MODRES 1T15 SEP B    8  SER  PHOSPHOSERINE
HET    SEP  B   8      10
HETNAM     SEP PHOSPHOSERINE
HETSYN     SEP PHOSPHONOSERINE
FORMUL   2  SEP    C3 H8 N1 O6 P1
FORMUL   3  HOH   *156(H2 O1)
HELIX    1   1 THR A 1658  HIS A 1673  1                                16
HELIX    2   2 THR A 1700  GLY A 1709  1                                10
HELIX    3   3 TYR A 1716  GLU A 1725  1                                10
HELIX    4   4 ASN A 1730  GLU A 1735  5                                 6
HELIX    5   5 GLN A 1747  GLU A 1754  1                                 8
HELIX    6   6 PRO A 1776  CYS A 1787  1                                12
HELIX    7   7 GLU A 1794  PHE A 1798  5                                 5
HELIX    8   8 GLN A 1811  TRP A 1815  5                                 5
HELIX    9   9 ASP A 1818  ALA A 1823  5                                 6
HELIX   10  10 ARG A 1835  TYR A 1845  1                                11
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HELIX   11  11 LEU A 1850  LEU A 1854  5                                    5
SHEET    1   A 4 THR A1675  LEU A1676  0
SHEET    2   A 4 SER A1651  SER A1655  1  N  MET A1652   O  THR A1675
SHEET    3   A 4 HIS A1686  MET A1689  1  O  VAL A1688   N  VAL A1653
SHEET    4   A 4 TRP A1712  SER A1715  1  O  TRP A1712   N  VAL A1687
SHEET    1   B 2 VAL A1696  CYS A1697  0
SHEET    2   B 2 GLY A1738  ASP A1739  1  O  GLY A1738   N  CYS A1697
SHEET    1   C 4 SER A1790  VAL A1791  0
SHEET    2   C 4 GLU A1765  CYS A1768  1  N  ILE A1766   O  SER A1790
SHEET    3   C 4 PRO A1806  VAL A1810  1  O  VAL A1809   N  CYS A1767
SHEET    4   C 4 VAL A1832  THR A1834  1  O  VAL A1833   N  VAL A1808
CISPEP   1 GLY A 1770     PRO A 1771          0         6.36
CRYST1   65.837   65.837   93.075  90.00  90.00 120.00 P 32 2 1       6
ORIGX1      1.000000  0.000000  0.000000        0.00000
ORIGX2      0.000000  1.000000  0.000000        0.00000
ORIGX3      0.000000  0.000000  1.000000        0.00000
SCALE1      0.015189  0.008769  0.000000        0.00000
SCALE2      0.000000  0.017539  0.000000        0.00000
SCALE3      0.000000  0.000000  0.010744        0.00000
ATOM      1  N   ARG A1649      21.350  25.980  38.428  1.00 37.86           N
ATOM      2  CA  ARG A1649      21.167  25.508  37.034  1.00 38.58           C
ATOM      3  C   ARG A1649      19.696  25.211  36.751  1.00 37.92           C
ATOM      4  O   ARG A1649      18.984  26.111  36.309  1.00 39.23           O
ATOM      5  CB  ARG A1649      22.041  24.284  36.737  1.00 38.99           C
ATOM      6  CG  ARG A1649      22.206  24.018  35.247  1.00 40.19           C
ATOM      7  CD  ARG A1649      23.156  24.960  34.544  1.00 41.68           C
ATOM      8  NE  ARG A1649      24.532  24.465  34.472  1.00 41.02           N
ATOM      9  CZ  ARG A1649      24.900  23.213  34.666  1.00 42.27           C
ATOM     10  NH1 ARG A1649      24.012  22.284  34.973  1.00 47.29           N
ATOM     11  NH2 ARG A1649      26.165  22.886  34.560  1.00 44.76           N
ATOM     12  N   MET A1650      19.253  23.967  37.004  1.00 36.61           N
ATOM     13  CA  MET A1650      17.864  23.524  36.769  1.00 34.88           C
ATOM     14  C   MET A1650      17.116  23.314  38.097  1.00 32.87           C
ATOM     15  O   MET A1650      17.716  22.872  39.078  1.00 33.22           O
ATOM     16  CB  MET A1650      17.823  22.184  36.015  1.00 35.73           C
ATOM     17  CG  MET A1650      18.760  22.063  34.822  1.00 39.54           C
ATOM     18  SD  MET A1650      18.701  20.447  33.985  1.00 47.40           S
ATOM     19  CE  MET A1650      17.014  19.948  34.263  1.00 43.86           C
ATOM     20  N   SER A1651      15.816  23.610  38.127  1.00 29.05           N
ATOM     21  CA  SER A1651      15.013  23.420  39.339  1.00 25.47           C
ATOM     22  C   SER A1651      13.556  23.243  38.904  1.00 24.50           C
ATOM     23  O   SER A1651      12.987  24.147  38.272  1.00 23.29           O
ATOM     24  CB  SER A1651      15.169  24.634  40.254  1.00 25.05           C
ATOM     25  OG  SER A1651      14.285  24.568  41.357  1.00 23.07           O
ATOM     26  N   MET A1652      12.958  22.099  39.240  1.00 23.28           N
ATOM     27  CA  MET A1652      11.609  21.768  38.746  1.00 22.67           C
ATOM     28  C   MET A1652      10.503  21.815  39.789  1.00 21.96           C
ATOM     29  O   MET A1652      10.752  21.600  40.963  1.00 21.38           O
ATOM     30  CB  MET A1652      11.582  20.346  38.170  1.00 22.94           C
ATOM     31  CG  MET A1652      12.716  19.972  37.236  1.00 26.44           C
ATOM     32  SD  MET A1652      12.543  18.260  36.657  1.00 29.06           S
ATOM     33  CE  MET A1652      12.877  17.308  38.164  1.00 29.60           C
ATOM     34  N   VAL A1653       9.280  22.103  39.333  1.00 21.77           N
ATOM     35  CA  VAL A1653       8.073  21.861  40.127  1.00 21.44           C
ATOM     36  C   VAL A1653       7.194  21.046  39.176  1.00 21.79           C
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ATOM	37	O	VAL	A1653	7.462	21.019	37.972	1.00	21.55	O
ATOM	38	CB	VAL	A1653	7.348	23.124	40.597	1.00	21.82	C
ATOM	39	CG1	VAL	A1653	8.236	23.964	41.512	1.00	21.08	C
ATOM	40	CG2	VAL	A1653	6.869	23.986	39.400	1.00	21.69	C
ATOM	41	N	VAL	A1654	6.174	20.374	39.710	1.00	22.15	N
ATOM	42	CA	VAL	A1654	5.236	19.649	38.874	1.00	21.91	C
ATOM	43	C	VAL	A1654	3.844	20.185	39.150	1.00	21.96	C
ATOM	44	O	VAL	A1654	3.604	20.860	40.170	1.00	22.10	O
ATOM	45	CB	VAL	A1654	5.243	18.129	39.137	1.00	22.11	C
ATOM	46	CG1	VAL	A1654	6.635	17.546	38.954	1.00	21.48	C
ATOM	47	CG2	VAL	A1654	4.613	17.772	40.509	1.00	21.70	C
ATOM	48	N	SER	A1655	2.921	19.914	38.237	1.00	22.52	N
ATOM	49	CA	SER	A1655	1.561	20.390	38.429	1.00	23.73	C
ATOM	50	C	SER	A1655	0.600	19.446	37.735	1.00	24.21	C
ATOM	51	O	SER	A1655	0.874	18.984	36.633	1.00	23.50	O
ATOM	52	CB	SER	A1655	1.418	21.804	37.847	1.00	23.91	C
ATOM	53	OG	SER	A1655	0.090	22.280	37.999	1.00	25.27	O
ATOM	54	N	GLY	A1656	-0.511	19.142	38.390	1.00	25.03	N
ATOM	55	CA	GLY	A1656	-1.515	18.293	37.784	1.00	26.90	C
ATOM	56	C	GLY	A1656	-1.231	16.813	37.896	1.00	28.26	C
ATOM	57	O	GLY	A1656	-1.951	16.007	37.322	1.00	28.33	O
ATOM	58	N	LEU	A1657	-0.180	16.441	38.624	1.00	29.57	N
ATOM	59	CA	LEU	A1657	0.151	15.039	38.777	1.00	31.48	C
ATOM	60	C	LEU	A1657	-0.445	14.481	40.049	1.00	33.40	C
ATOM	61	O	LEU	A1657	-0.551	15.187	41.046	1.00	33.77	O
ATOM	62	CB	LEU	A1657	1.669	14.835	38.880	1.00	31.30	C
ATOM	63	CG	LEU	A1657	2.557	15.339	37.751	1.00	29.72	C
ATOM	64	CD1	LEU	A1657	3.959	14.805	37.938	1.00	27.61	C
ATOM	65	CD2	LEU	A1657	1.962	14.855	36.430	1.00	31.43	C
ATOM	66	N	THR	A1658	-0.788	13.205	40.012	1.00	35.92	N
ATOM	67	CA	THR	A1658	-1.191	12.497	41.217	1.00	38.84	C
ATOM	68	C	THR	A1658	0.057	12.373	42.092	1.00	40.25	C
ATOM	69	O	THR	A1658	1.182	12.411	41.579	1.00	40.34	O
ATOM	70	CB	THR	A1658	-1.622	11.102	40.860	1.00	38.58	C
ATOM	71	OG1	THR	A1658	-0.515	10.438	40.250	1.00	41.39	O
ATOM	72	CG2	THR	A1658	-2.657	11.119	39.761	1.00	38.93	C
ATOM	73	N	PRO	A1659	-0.140	12.210	43.400	1.00	41.63	N
ATOM	74	CA	PRO	A1659	0.957	12.021	44.353	1.00	42.36	C
ATOM	75	C	PRO	A1659	1.924	10.967	43.837	1.00	43.26	C
ATOM	76	O	PRO	A1659	3.126	11.067	44.074	1.00	43.63	O
ATOM	77	CB	PRO	A1659	0.231	11.484	45.590	1.00	42.81	C
ATOM	78	CG	PRO	A1659	-1.089	12.163	45.531	1.00	41.97	C
ATOM	79	CD	PRO	A1659	-1.456	12.197	44.067	1.00	41.96	C
ATOM	80	N	GLU	A1660	1.389	9.970	43.137	1.00	43.67	N
ATOM	81	CA	GLU	A1660	2.188	8.905	42.561	1.00	44.09	C
ATOM	82	C	GLU	A1660	3.084	9.406	41.447	1.00	44.00	C
ATOM	83	O	GLU	A1660	4.296	9.177	41.457	1.00	44.31	O
ATOM	84	CB	GLU	A1660	1.269	7.843	41.965	1.00	44.71	C
ATOM	85	CG	GLU	A1660	1.888	7.156	40.761	1.00	47.07	C
ATOM	86	CD	GLU	A1660	1.029	6.047	40.195	1.00	52.07	C
ATOM	87	OE1	GLU	A1660	0.453	5.268	40.994	1.00	53.23	O
ATOM	88	OE2	GLU	A1660	0.944	5.952	38.946	1.00	54.35	O
ATOM	89	N	GLU	A1661	2.471	10.056	40.458	1.00	43.83	N
ATOM	90	CA	GLU	A1661	3.201	10.544	39.293	1.00	43.45	C
ATOM	91	C	GLU	A1661	4.341	11.405	39.783	1.00	42.90	C

ATOM	92	O	GLU	A1661	5.428	11.398	39.210	1.00	43.62	O
ATOM	93	CB	GLU	A1661	2.274	11.303	38.321	1.00	43.46	C
ATOM	94	CG	GLU	A1661	1.496	10.413	37.354	1.00	44.55	C
ATOM	95	CD	GLU	A1661	0.316	11.125	36.703	1.00	45.20	C
ATOM	96	OE1	GLU	A1661	-0.205	12.081	37.309	1.00	45.12	O
ATOM	97	OE2	GLU	A1661	-0.092	10.731	35.586	1.00	46.89	O
ATOM	98	N	PHE	A1662	4.094	12.136	40.861	1.00	41.91	N
ATOM	99	CA	PHE	A1662	5.119	12.949	41.478	1.00	42.12	C
ATOM	100	C	PHE	A1662	6.268	12.034	41.906	1.00	41.38	C
ATOM	101	O	PHE	A1662	7.423	12.448	41.923	1.00	40.80	O
ATOM	102	CB	PHE	A1662	4.549	13.703	42.691	1.00	41.81	C
ATOM	103	CG	PHE	A1662	5.567	14.513	43.442	1.00	44.40	C
ATOM	104	CD1	PHE	A1662	6.062	15.689	42.920	1.00	44.89	C
ATOM	105	CD2	PHE	A1662	6.034	14.093	44.671	1.00	45.16	C
ATOM	106	CE1	PHE	A1662	6.994	16.427	43.606	1.00	46.33	C
ATOM	107	CE2	PHE	A1662	6.966	14.816	45.361	1.00	45.74	C
ATOM	108	CZ	PHE	A1662	7.452	15.993	44.830	1.00	46.57	C
ATOM	109	N	MET	A1663	5.941	10.789	42.236	1.00	40.93	N
ATOM	110	CA	MET	A1663	6.961	9.863	42.724	1.00	40.79	C
ATOM	111	C	MET	A1663	7.881	9.337	41.619	1.00	39.37	C
ATOM	112	O	MET	A1663	9.041	9.047	41.875	1.00	39.10	O
ATOM	113	CB	MET	A1663	6.328	8.764	43.579	1.00	41.63	C
ATOM	114	CG	MET	A1663	5.566	9.346	44.780	1.00	44.48	C
ATOM	115	SD	MET	A1663	6.021	11.127	45.033	1.00	54.98	S
ATOM	116	CE	MET	A1663	5.163	11.565	46.534	1.00	49.27	C
ATOM	117	N	LEU	A1664	7.383	9.257	40.386	1.00	38.10	N
ATOM	118	CA	LEU	A1664	8.242	8.893	39.269	1.00	36.62	C
ATOM	119	C	LEU	A1664	9.166	10.076	38.963	1.00	35.32	C
ATOM	120	O	LEU	A1664	10.353	9.882	38.687	1.00	35.19	O
ATOM	121	CB	LEU	A1664	7.444	8.510	38.023	1.00	36.87	C
ATOM	122	CG	LEU	A1664	6.989	7.054	37.865	1.00	38.76	C
ATOM	123	CD1	LEU	A1664	5.785	6.970	36.936	1.00	39.32	C
ATOM	124	CD2	LEU	A1664	8.138	6.155	37.371	1.00	40.42	C
ATOM	125	N	VAL	A1665	8.623	11.294	39.025	1.00	33.46	N
ATOM	126	CA	VAL	A1665	9.435	12.498	38.823	1.00	31.56	C
ATOM	127	C	VAL	A1665	10.462	12.593	39.931	1.00	31.17	C
ATOM	128	O	VAL	A1665	11.626	12.971	39.716	1.00	29.16	O
ATOM	129	CB	VAL	A1665	8.601	13.787	38.830	1.00	32.18	C
ATOM	130	CG1	VAL	A1665	9.514	15.015	38.599	1.00	29.50	C
ATOM	131	CG2	VAL	A1665	7.528	13.727	37.769	1.00	31.04	C
ATOM	132	N	TYR	A1666	10.035	12.225	41.128	1.00	30.24	N
ATOM	133	CA	TYR	A1666	10.951	12.266	42.253	1.00	30.74	C
ATOM	134	C	TYR	A1666	12.106	11.278	42.039	1.00	29.52	C
ATOM	135	O	TYR	A1666	13.252	11.604	42.324	1.00	28.12	O
ATOM	136	CB	TYR	A1666	10.237	11.948	43.558	1.00	32.14	C
ATOM	137	CG	TYR	A1666	11.208	11.829	44.710	1.00	36.82	C
ATOM	138	CD1	TYR	A1666	11.495	12.920	45.512	1.00	41.37	C
ATOM	139	CD2	TYR	A1666	11.851	10.624	44.981	1.00	42.59	C
ATOM	140	CE1	TYR	A1666	12.380	12.816	46.558	1.00	45.38	C
ATOM	141	CE2	TYR	A1666	12.741	10.513	46.026	1.00	45.18	C
ATOM	142	CZ	TYR	A1666	12.999	11.617	46.809	1.00	46.15	C
ATOM	143	OH	TYR	A1666	13.882	11.544	47.858	1.00	49.62	O
ATOM	144	N	LYS	A1667	11.792	10.085	41.541	1.00	29.17	N
ATOM	145	CA	LYS	A1667	12.823	9.070	41.263	1.00	29.54	C
ATOM	146	C	LYS	A1667	13.807	9.593	40.217	1.00	28.96	C

ATOM	147	O	LYS	A1667	15.026	9.510	40.394	1.00	28.65	O
ATOM	148	CB	LYS	A1667	12.174	7.756	40.819	1.00	30.32	C
ATOM	149	CG	LYS	A1667	13.145	6.604	40.600	1.00	33.53	C
ATOM	150	CD	LYS	A1667	12.516	5.477	39.763	1.00	37.99	C
ATOM	151	CE	LYS	A1667	13.599	4.737	38.953	1.00	40.33	C
ATOM	152	NZ	LYS	A1667	13.069	3.904	37.815	1.00	43.44	N
ATOM	153	N	PHE	A1668	13.249	10.137	39.137	1.00	28.47	N
ATOM	154	CA	PHE	A1668	13.986	10.780	38.054	1.00	27.75	C
ATOM	155	C	PHE	A1668	14.944	11.880	38.550	1.00	27.27	C
ATOM	156	O	PHE	A1668	16.136	11.869	38.220	1.00	25.79	O
ATOM	157	CB	PHE	A1668	12.979	11.364	37.057	1.00	28.54	C
ATOM	158	CG	PHE	A1668	13.594	12.000	35.836	1.00	28.84	C
ATOM	159	CD1	PHE	A1668	14.241	11.237	34.875	1.00	32.22	C
ATOM	160	CD2	PHE	A1668	13.470	13.352	35.630	1.00	31.36	C
ATOM	161	CE1	PHE	A1668	14.777	11.837	33.750	1.00	32.35	C
ATOM	162	CE2	PHE	A1668	14.000	13.943	34.508	1.00	32.38	C
ATOM	163	CZ	PHE	A1668	14.662	13.178	33.578	1.00	31.43	C
ATOM	164	N	ALA	A1669	14.424	12.810	39.349	1.00	25.62	N
ATOM	165	CA	ALA	A1669	15.227	13.909	39.883	1.00	26.14	C
ATOM	166	C	ALA	A1669	16.342	13.397	40.770	1.00	26.42	C
ATOM	167	O	ALA	A1669	17.444	13.917	40.744	1.00	27.04	O
ATOM	168	CB	ALA	A1669	14.358	14.888	40.681	1.00	25.21	C
ATOM	169	N	ARG	A1670	16.027	12.413	41.595	1.00	26.98	N
ATOM	170	CA	ARG	A1670	17.024	11.836	42.493	1.00	27.64	C
ATOM	171	C	ARG	A1670	18.174	11.241	41.674	1.00	27.68	C
ATOM	172	O	ARG	A1670	19.340	11.460	41.976	1.00	27.31	O
ATOM	173	CB	ARG	A1670	16.346	10.771	43.343	1.00	28.45	C
ATOM	174	CG	ARG	A1670	17.214	10.070	44.348	1.00	30.59	C
ATOM	175	CD	ARG	A1670	16.421	9.137	45.243	1.00	35.94	C
ATOM	176	NE	ARG	A1670	17.245	8.595	46.310	1.00	37.87	N
ATOM	177	CZ	ARG	A1670	17.559	9.244	47.424	1.00	38.30	C
ATOM	178	NH1	ARG	A1670	17.115	10.473	47.641	1.00	37.07	N
ATOM	179	NH2	ARG	A1670	18.314	8.644	48.333	1.00	38.27	N
ATOM	180	N	LYS	A1671	17.831	10.488	40.634	1.00	27.51	N
ATOM	181	CA	LYS	A1671	18.830	9.814	39.823	1.00	28.46	C
ATOM	182	C	LYS	A1671	19.742	10.798	39.104	1.00	27.96	C
ATOM	183	O	LYS	A1671	20.948	10.602	39.043	1.00	27.41	O
ATOM	184	CB	LYS	A1671	18.150	8.903	38.799	1.00	28.67	C
ATOM	185	CG	LYS	A1671	19.057	8.452	37.645	1.00	30.60	C
ATOM	186	CD	LYS	A1671	18.286	7.499	36.740	1.00	33.67	C
ATOM	187	CE	LYS	A1671	19.181	6.743	35.765	1.00	37.14	C
ATOM	188	NZ	LYS	A1671	18.327	5.889	34.877	1.00	40.72	N
ATOM	189	N	HIS	A1672	19.156	11.871	38.579	1.00	27.95	N
ATOM	190	CA	HIS	A1672	19.902	12.817	37.776	1.00	27.74	C
ATOM	191	C	HIS	A1672	20.394	14.032	38.551	1.00	27.28	C
ATOM	192	O	HIS	A1672	20.975	14.940	37.971	1.00	27.32	O
ATOM	193	CB	HIS	A1672	19.064	13.248	36.571	1.00	28.24	C
ATOM	194	CG	HIS	A1672	18.831	12.144	35.585	1.00	30.19	C
ATOM	195	ND1	HIS	A1672	19.854	11.575	34.856	1.00	30.35	N
ATOM	196	CD2	HIS	A1672	17.699	11.496	35.218	1.00	30.89	C
ATOM	197	CE1	HIS	A1672	19.359	10.631	34.072	1.00	32.84	C
ATOM	198	NE2	HIS	A1672	18.055	10.558	34.278	1.00	29.45	N
ATOM	199	N	HIS	A1673	20.139	14.040	39.854	1.00	27.33	N
ATOM	200	CA	HIS	A1673	20.579	15.125	40.716	1.00	27.56	C
ATOM	201	C	HIS	A1673	20.016	16.447	40.211	1.00	26.59	C

ATOM	202	O	HIS	A1673	20.742	17.422	40.081	1.00	26.83	O
ATOM	203	CB	HIS	A1673	22.105	15.190	40.784	1.00	27.91	C
ATOM	204	CG	HIS	A1673	22.627	15.924	41.984	1.00	29.65	C
ATOM	205	ND1	HIS	A1673	22.540	15.415	43.261	1.00	31.89	N
ATOM	206	CD2	HIS	A1673	23.235	17.127	42.101	1.00	31.98	C
ATOM	207	CE1	HIS	A1673	23.076	16.270	44.116	1.00	29.99	C
ATOM	208	NE2	HIS	A1673	23.506	17.316	43.438	1.00	32.36	N
ATOM	209	N	ILE	A1674	18.723	16.431	39.893	1.00	26.22	N
ATOM	210	CA	ILE	A1674	17.985	17.620	39.472	1.00	25.06	C
ATOM	211	C	ILE	A1674	17.207	18.150	40.668	1.00	23.96	C
ATOM	212	O	ILE	A1674	16.556	17.391	41.375	1.00	24.12	O
ATOM	213	CB	ILE	A1674	16.976	17.245	38.356	1.00	25.75	C
ATOM	214	CG1	ILE	A1674	17.681	16.534	37.193	1.00	26.59	C
ATOM	215	CG2	ILE	A1674	16.239	18.495	37.847	1.00	26.27	C
ATOM	216	CD1	ILE	A1674	16.718	16.040	36.103	1.00	28.27	C
ATOM	217	N	THR	A1675	17.253	19.450	40.882	1.00	22.45	N
ATOM	218	CA	THR	A1675	16.485	20.059	41.959	1.00	22.35	C
ATOM	219	C	THR	A1675	14.987	19.928	41.677	1.00	22.01	C
ATOM	220	O	THR	A1675	14.535	20.297	40.604	1.00	21.54	O
ATOM	221	CB	THR	A1675	16.885	21.538	42.079	1.00	22.30	C
ATOM	222	OG1	THR	A1675	18.262	21.649	42.480	1.00	23.67	O
ATOM	223	CG2	THR	A1675	16.135	22.216	43.198	1.00	21.79	C
ATOM	224	N	LEU	A1676	14.241	19.390	42.636	1.00	21.51	N
ATOM	225	CA	LEU	A1676	12.798	19.250	42.545	1.00	21.73	C
ATOM	226	C	LEU	A1676	12.184	19.848	43.821	1.00	21.93	C
ATOM	227	O	LEU	A1676	12.568	19.463	44.928	1.00	21.14	O
ATOM	228	CB	LEU	A1676	12.409	17.770	42.430	1.00	22.01	C
ATOM	229	CG	LEU	A1676	10.926	17.437	42.592	1.00	22.31	C
ATOM	230	CD1	LEU	A1676	10.079	18.140	41.503	1.00	24.34	C
ATOM	231	CD2	LEU	A1676	10.676	15.920	42.607	1.00	22.73	C
ATOM	232	N	THR	A1677	11.238	20.768	43.675	1.00	21.24	N
ATOM	233	CA	THR	A1677	10.585	21.362	44.839	1.00	21.58	C
ATOM	234	C	THR	A1677	9.065	21.271	44.704	1.00	21.67	C
ATOM	235	O	THR	A1677	8.558	20.984	43.628	1.00	20.01	O
ATOM	236	CB	THR	A1677	10.988	22.842	45.014	1.00	22.16	C
ATOM	237	OG1	THR	A1677	10.362	23.634	43.998	1.00	25.10	O
ATOM	238	CG2	THR	A1677	12.504	23.081	44.774	1.00	21.94	C
ATOM	239	N	ASN	A1678	8.343	21.536	45.790	1.00	21.90	N
ATOM	240	CA	ASN	A1678	6.887	21.534	45.746	1.00	23.71	C
ATOM	241	C	ASN	A1678	6.299	22.921	45.458	1.00	24.19	C
ATOM	242	O	ASN	A1678	5.175	23.041	44.968	1.00	25.65	O
ATOM	243	CB	ASN	A1678	6.313	20.974	47.063	1.00	24.23	C
ATOM	244	CG	ASN	A1678	6.673	21.839	48.285	1.00	24.68	C
ATOM	245	OD1	ASN	A1678	7.688	22.559	48.296	1.00	22.56	O
ATOM	246	ND2	ASN	A1678	5.842	21.767	49.321	1.00	25.85	N
ATOM	247	N	LEU	A1679	7.063	23.958	45.767	1.00	24.17	N
ATOM	248	CA	LEU	A1679	6.622	25.332	45.559	1.00	24.50	C
ATOM	249	C	LEU	A1679	7.396	26.005	44.427	1.00	24.20	C
ATOM	250	O	LEU	A1679	8.614	25.849	44.324	1.00	23.42	O
ATOM	251	CB	LEU	A1679	6.803	26.146	46.850	1.00	25.12	C
ATOM	252	CG	LEU	A1679	6.031	25.602	48.074	1.00	26.29	C
ATOM	253	CD1	LEU	A1679	6.105	26.558	49.255	1.00	25.56	C
ATOM	254	CD2	LEU	A1679	4.580	25.315	47.706	1.00	25.75	C
ATOM	255	N	ILE	A1680	6.691	26.753	43.581	1.00	23.41	N
ATOM	256	CA	ILE	A1680	7.349	27.455	42.495	1.00	23.78	C

ATOM	257	C	ILE	A1680	7.921	28.780	43.027	1.00	24.30	C
ATOM	258	O	ILE	A1680	7.326	29.418	43.904	1.00	23.93	O
ATOM	259	CB	ILE	A1680	6.342	27.681	41.338	1.00	23.69	C
ATOM	260	CG1	ILE	A1680	7.072	28.148	40.073	1.00	24.57	C
ATOM	261	CG2	ILE	A1680	5.259	28.658	41.755	1.00	24.87	C
ATOM	262	CD1	ILE	A1680	6.156	28.205	38.857	1.00	25.47	C
ATOM	263	N	THR	A1681	9.097	29.157	42.541	1.00	24.43	N
ATOM	264	CA	THR	A1681	9.762	30.395	42.951	1.00	25.11	C
ATOM	265	C	THR	A1681	10.402	31.007	41.741	1.00	26.01	C
ATOM	266	O	THR	A1681	10.366	30.429	40.676	1.00	25.92	O
ATOM	267	CB	THR	A1681	10.917	30.103	43.930	1.00	24.96	C
ATOM	268	OG1	THR	A1681	11.958	29.408	43.239	1.00	24.12	O
ATOM	269	CG2	THR	A1681	10.490	29.130	45.002	1.00	24.40	C
ATOM	270	N	GLU	A1682	11.071	32.142	41.921	1.00	27.46	N
ATOM	271	CA	GLU	A1682	11.794	32.757	40.814	1.00	28.87	C
ATOM	272	C	GLU	A1682	12.905	31.869	40.291	1.00	28.73	C
ATOM	273	O	GLU	A1682	13.289	31.986	39.130	1.00	29.06	O
ATOM	274	CB	GLU	A1682	12.405	34.085	41.248	1.00	29.96	C
ATOM	275	CG	GLU	A1682	11.575	34.801	42.284	1.00	34.86	C
ATOM	276	CD	GLU	A1682	11.797	34.244	43.680	1.00	39.53	C
ATOM	277	OE1	GLU	A1682	12.877	34.510	44.255	1.00	45.24	O
ATOM	278	OE2	GLU	A1682	10.906	33.551	44.201	1.00	39.80	O
ATOM	279	N	GLU	A1683	13.447	31.002	41.143	1.00	27.80	N
ATOM	280	CA	GLU	A1683	14.544	30.121	40.732	1.00	27.27	C
ATOM	281	C	GLU	A1683	14.105	28.885	39.941	1.00	25.48	C
ATOM	282	O	GLU	A1683	14.913	28.218	39.297	1.00	24.53	O
ATOM	283	CB	GLU	A1683	15.384	29.710	41.944	1.00	28.00	C
ATOM	284	CG	GLU	A1683	16.135	30.882	42.565	1.00	32.38	C
ATOM	285	CD	GLU	A1683	15.242	31.826	43.357	1.00	38.54	C
ATOM	286	OE1	GLU	A1683	14.320	31.343	44.041	1.00	40.84	O
ATOM	287	OE2	GLU	A1683	15.469	33.061	43.313	1.00	41.64	O
ATOM	288	N	THR	A1684	12.828	28.571	39.988	1.00	23.79	N
ATOM	289	CA	THR	A1684	12.323	27.450	39.200	1.00	22.59	C
ATOM	290	C	THR	A1684	12.605	27.689	37.725	1.00	22.04	C
ATOM	291	O	THR	A1684	12.392	28.788	37.230	1.00	21.76	O
ATOM	292	CB	THR	A1684	10.828	27.366	39.394	1.00	22.67	C
ATOM	293	OG1	THR	A1684	10.549	27.162	40.788	1.00	22.03	O
ATOM	294	CG2	THR	A1684	10.243	26.126	38.640	1.00	21.28	C
ATOM	295	N	THR	A1685	13.111	26.671	37.037	1.00	22.20	N
ATOM	296	CA	THR	A1685	13.356	26.759	35.619	1.00	22.50	C
ATOM	297	C	THR	A1685	12.339	25.966	34.804	1.00	22.65	C
ATOM	298	O	THR	A1685	12.127	26.270	33.629	1.00	22.47	O
ATOM	299	CB	THR	A1685	14.743	26.231	35.282	1.00	22.28	C
ATOM	300	OG1	THR	A1685	14.893	24.913	35.814	1.00	24.12	O
ATOM	301	CG2	THR	A1685	15.841	27.089	35.989	1.00	22.27	C
ATOM	302	N	HIS	A1686	11.735	24.949	35.425	1.00	22.23	N
ATOM	303	CA	HIS	A1686	10.856	24.014	34.729	1.00	22.29	C
ATOM	304	C	HIS	A1686	9.590	23.729	35.498	1.00	22.24	C
ATOM	305	O	HIS	A1686	9.631	23.463	36.700	1.00	22.44	O
ATOM	306	CB	HIS	A1686	11.529	22.643	34.547	1.00	21.81	C
ATOM	307	CG	HIS	A1686	12.730	22.639	33.659	1.00	23.25	C
ATOM	308	ND1	HIS	A1686	13.907	23.282	33.983	1.00	24.02	N
ATOM	309	CD2	HIS	A1686	12.960	22.008	32.484	1.00	23.85	C
ATOM	310	CE1	HIS	A1686	14.794	23.083	33.026	1.00	24.09	C
ATOM	311	NE2	HIS	A1686	14.249	22.303	32.110	1.00	24.68	N

ATOM	312	N	VAL	A1687	8.455	23.760	34.800	1.00	21.33	N
ATOM	313	CA	VAL	A1687	7.193	23.413	35.404	1.00	20.85	C
ATOM	314	C	VAL	A1687	6.746	22.190	34.611	1.00	21.60	C
ATOM	315	O	VAL	A1687	6.501	22.287	33.410	1.00	21.78	O
ATOM	316	CB	VAL	A1687	6.140	24.545	35.251	1.00	21.45	C
ATOM	317	CG1	VAL	A1687	4.751	24.080	35.775	1.00	19.85	C
ATOM	318	CG2	VAL	A1687	6.570	25.788	35.992	1.00	20.28	C
ATOM	319	N	VAL	A1688	6.675	21.036	35.256	1.00	21.42	N
ATOM	320	CA	VAL	A1688	6.325	19.806	34.553	1.00	22.22	C
ATOM	321	C	VAL	A1688	4.828	19.561	34.714	1.00	22.17	C
ATOM	322	O	VAL	A1688	4.344	19.213	35.795	1.00	22.13	O
ATOM	323	CB	VAL	A1688	7.102	18.605	35.107	1.00	22.04	C
ATOM	324	CG1	VAL	A1688	6.714	17.329	34.363	1.00	23.45	C
ATOM	325	CG2	VAL	A1688	8.631	18.867	34.994	1.00	22.73	C
ATOM	326	N	MET	A1689	4.097	19.763	33.630	1.00	22.26	N
ATOM	327	CA	MET	A1689	2.641	19.634	33.672	1.00	22.34	C
ATOM	328	C	MET	A1689	2.161	18.295	33.147	1.00	22.82	C
ATOM	329	O	MET	A1689	2.653	17.812	32.137	1.00	22.06	O
ATOM	330	CB	MET	A1689	1.995	20.655	32.733	1.00	22.42	C
ATOM	331	CG	MET	A1689	2.339	22.103	32.947	1.00	21.00	C
ATOM	332	SD	MET	A1689	1.570	22.779	34.399	1.00	21.36	S
ATOM	333	CE	MET	A1689	-0.176	22.202	34.322	1.00	23.99	C
ATOM	334	N	LYS	A1690	1.140	17.748	33.792	1.00	23.62	N
ATOM	335	CA	LYS	A1690	0.445	16.596	33.234	1.00	25.55	C
ATOM	336	C	LYS	A1690	-0.268	17.100	31.963	1.00	25.64	C
ATOM	337	O	LYS	A1690	-0.953	18.119	31.994	1.00	25.20	O
ATOM	338	CB	LYS	A1690	-0.605	16.107	34.223	1.00	26.03	C
ATOM	339	CG	LYS	A1690	-1.477	14.981	33.698	1.00	29.48	C
ATOM	340	CD	LYS	A1690	-0.635	13.779	33.360	1.00	33.58	C
ATOM	341	CE	LYS	A1690	-1.483	12.536	33.133	1.00	37.81	C
ATOM	342	NZ	LYS	A1690	-0.647	11.273	33.107	1.00	40.65	N
ATOM	343	N	THR	A1691	-0.081	16.395	30.850	1.00	26.37	N
ATOM	344	CA	THR	A1691	-0.747	16.736	29.598	1.00	27.47	C
ATOM	345	C	THR	A1691	-1.366	15.488	28.971	1.00	28.22	C
ATOM	346	O	THR	A1691	-1.142	14.352	29.421	1.00	28.13	O
ATOM	347	CB	THR	A1691	0.224	17.340	28.545	1.00	26.46	C
ATOM	348	OG1	THR	A1691	1.117	16.330	28.052	1.00	27.31	O
ATOM	349	CG2	THR	A1691	1.153	18.411	29.136	1.00	26.70	C
ATOM	350	N	ASP	A1692	-2.126	15.722	27.912	1.00	29.46	N
ATOM	351	CA	ASP	A1692	-2.626	14.643	27.086	1.00	30.31	C
ATOM	352	C	ASP	A1692	-1.538	14.384	26.030	1.00	31.07	C
ATOM	353	O	ASP	A1692	-0.463	15.018	26.058	1.00	30.12	O
ATOM	354	CB	ASP	A1692	-4.006	14.997	26.492	1.00	30.67	C
ATOM	355	CG	ASP	A1692	-3.938	16.065	25.425	1.00	31.94	C
ATOM	356	OD1	ASP	A1692	-2.836	16.523	25.075	1.00	30.65	O
ATOM	357	OD2	ASP	A1692	-4.958	16.496	24.851	1.00	33.80	O
ATOM	358	N	ALA	A1693	-1.770	13.447	25.113	1.00	31.57	N
ATOM	359	CA	ALA	A1693	-0.712	13.074	24.165	1.00	31.83	C
ATOM	360	C	ALA	A1693	-0.273	14.167	23.203	1.00	31.90	C
ATOM	361	O	ALA	A1693	0.763	14.047	22.559	1.00	33.24	O
ATOM	362	CB	ALA	A1693	-1.086	11.776	23.387	1.00	32.02	C
ATOM	363	N	GLU	A1694	-1.056	15.229	23.098	1.00	32.07	N
ATOM	364	CA	GLU	A1694	-0.715	16.332	22.200	1.00	32.13	C
ATOM	365	C	GLU	A1694	-0.143	17.522	22.973	1.00	31.43	C
ATOM	366	O	GLU	A1694	-0.069	18.648	22.455	1.00	31.29	O

ATOM	367	CB	GLU	A1694	-1.938	16.761	21.394	1.00	32.51	C
ATOM	368	CG	GLU	A1694	-2.199	15.883	20.177	1.00	36.64	C
ATOM	369	CD	GLU	A1694	-3.629	15.983	19.665	1.00	40.87	C
ATOM	370	OE1	GLU	A1694	-4.448	16.711	20.268	1.00	43.24	O
ATOM	371	OE2	GLU	A1694	-3.948	15.301	18.659	1.00	45.34	O
ATOM	372	N	PHE	A1695	0.262	17.258	24.209	1.00	30.33	N
ATOM	373	CA	PHE	A1695	0.907	18.267	25.044	1.00	29.76	C
ATOM	374	C	PHE	A1695	-0.009	19.435	25.420	1.00	28.82	C
ATOM	375	O	PHE	A1695	0.433	20.586	25.460	1.00	28.63	O
ATOM	376	CB	PHE	A1695	2.191	18.765	24.380	1.00	30.46	C
ATOM	377	CG	PHE	A1695	3.214	17.676	24.152	1.00	32.35	C
ATOM	378	CD1	PHE	A1695	4.097	17.744	23.096	1.00	34.87	C
ATOM	379	CD2	PHE	A1695	3.276	16.584	25.002	1.00	33.51	C
ATOM	380	CE1	PHE	A1695	5.041	16.741	22.886	1.00	37.03	C
ATOM	381	CE2	PHE	A1695	4.209	15.575	24.800	1.00	35.91	C
ATOM	382	CZ	PHE	A1695	5.091	15.656	23.742	1.00	36.18	C
ATOM	383	N	VAL	A1696	-1.269	19.115	25.714	1.00	27.46	N
ATOM	384	CA	VAL	A1696	-2.256	20.088	26.177	1.00	26.34	C
ATOM	385	C	VAL	A1696	-2.547	19.834	27.643	1.00	26.15	C
ATOM	386	O	VAL	A1696	-2.847	18.695	28.031	1.00	25.67	O
ATOM	387	CB	VAL	A1696	-3.575	19.919	25.419	1.00	26.30	C
ATOM	388	CG1	VAL	A1696	-4.613	20.873	25.965	1.00	27.23	C
ATOM	389	CG2	VAL	A1696	-3.347	20.146	23.922	1.00	26.66	C
ATOM	390	N	CYS	A1697	-2.478	20.884	28.461	1.00	25.76	N
ATOM	391	CA	CYS	A1697	-2.659	20.727	29.907	1.00	25.77	C
ATOM	392	C	CYS	A1697	-3.849	21.495	30.461	1.00	25.66	C
ATOM	393	O	CYS	A1697	-4.570	22.195	29.739	1.00	26.07	O
ATOM	394	CB	CYS	A1697	-1.401	21.198	30.648	1.00	25.57	C
ATOM	395	SG	CYS	A1697	-1.058	22.988	30.437	1.00	25.15	S
ATOM	396	N	GLU	A1698	-4.035	21.361	31.764	1.00	25.40	N
ATOM	397	CA	GLU	A1698	-5.052	22.080	32.494	1.00	25.79	C
ATOM	398	C	GLU	A1698	-4.429	23.376	32.999	1.00	25.04	C
ATOM	399	O	GLU	A1698	-3.221	23.403	33.272	1.00	25.41	O
ATOM	400	CB	GLU	A1698	-5.511	21.288	33.709	1.00	26.56	C
ATOM	401	CG	GLU	A1698	-6.027	19.885	33.408	1.00	29.71	C
ATOM	402	CD	GLU	A1698	-7.536	19.854	33.227	1.00	35.07	C
ATOM	403	OE1	GLU	A1698	-8.084	18.747	33.042	1.00	38.52	O
ATOM	404	OE2	GLU	A1698	-8.172	20.925	33.276	1.00	35.88	O
ATOM	405	N	ARG	A1699	-5.240	24.415	33.147	1.00	23.34	N
ATOM	406	CA	ARG	A1699	-4.765	25.689	33.671	1.00	23.38	C
ATOM	407	C	ARG	A1699	-4.728	25.643	35.186	1.00	23.32	C
ATOM	408	O	ARG	A1699	-5.783	25.723	35.848	1.00	23.77	O
ATOM	409	CB	ARG	A1699	-5.672	26.845	33.226	1.00	23.24	C
ATOM	410	CG	ARG	A1699	-5.728	27.087	31.724	1.00	23.08	C
ATOM	411	CD	ARG	A1699	-6.177	28.513	31.333	1.00	21.06	C
ATOM	412	NE	ARG	A1699	-7.466	28.900	31.915	1.00	24.04	N
ATOM	413	CZ	ARG	A1699	-8.030	30.100	31.750	1.00	23.60	C
ATOM	414	NH1	ARG	A1699	-7.412	31.027	31.038	1.00	22.34	N
ATOM	415	NH2	ARG	A1699	-9.202	30.379	32.306	1.00	26.85	N
ATOM	416	N	THR	A1700	-3.525	25.484	35.733	1.00	23.00	N
ATOM	417	CA	THR	A1700	-3.304	25.581	37.162	1.00	22.49	C
ATOM	418	C	THR	A1700	-2.518	26.849	37.474	1.00	22.18	C
ATOM	419	O	THR	A1700	-1.971	27.496	36.570	1.00	22.02	O
ATOM	420	CB	THR	A1700	-2.488	24.387	37.687	1.00	22.62	C
ATOM	421	OG1	THR	A1700	-1.195	24.364	37.062	1.00	21.16	O

ATOM	422	CG2	THR	A1700	-3.153	23.041	37.288	1.00	22.97	C
ATOM	423	N	LEU	A1701	-2.464	27.209	38.756	1.00	21.41	N
ATOM	424	CA	LEU	A1701	-1.682	28.380	39.170	1.00	21.28	C
ATOM	425	C	LEU	A1701	-0.215	28.229	38.742	1.00	21.03	C
ATOM	426	O	LEU	A1701	0.411	29.185	38.266	1.00	19.46	O
ATOM	427	CB	LEU	A1701	-1.771	28.584	40.679	1.00	21.44	C
ATOM	428	CG	LEU	A1701	-0.943	29.739	41.248	1.00	22.41	C
ATOM	429	CD1	LEU	A1701	-1.233	31.072	40.481	1.00	24.93	C
ATOM	430	CD2	LEU	A1701	-1.225	29.923	42.738	1.00	24.85	C
ATOM	431	N	LYS	A1702	0.335	27.036	38.910	1.00	21.07	N
ATOM	432	CA	LYS	A1702	1.730	26.789	38.500	1.00	21.06	C
ATOM	433	C	LYS	A1702	1.941	26.935	36.992	1.00	21.34	C
ATOM	434	O	LYS	A1702	3.007	27.388	36.548	1.00	21.87	O
ATOM	435	CB	LYS	A1702	2.202	25.406	38.957	1.00	20.84	C
ATOM	436	CG	LYS	A1702	2.683	25.335	40.409	1.00	22.93	C
ATOM	437	CD	LYS	A1702	2.856	23.856	40.785	1.00	26.66	C
ATOM	438	CE	LYS	A1702	3.409	23.668	42.189	1.00	29.07	C
ATOM	439	NZ	LYS	A1702	3.288	22.244	42.623	1.00	28.40	N
ATOM	440	N	TYR	A1703	0.948	26.515	36.207	1.00	20.21	N
ATOM	441	CA	TYR	A1703	0.986	26.735	34.762	1.00	20.07	C
ATOM	442	C	TYR	A1703	1.091	28.240	34.474	1.00	19.96	C
ATOM	443	O	TYR	A1703	1.946	28.676	33.709	1.00	19.76	O
ATOM	444	CB	TYR	A1703	-0.284	26.150	34.120	1.00	19.81	C
ATOM	445	CG	TYR	A1703	-0.563	26.468	32.646	1.00	20.24	C
ATOM	446	CD1	TYR	A1703	0.217	25.914	31.647	1.00	21.50	C
ATOM	447	CD2	TYR	A1703	-1.640	27.283	32.257	1.00	23.08	C
ATOM	448	CE1	TYR	A1703	-0.027	26.145	30.308	1.00	23.12	C
ATOM	449	CE2	TYR	A1703	-1.902	27.531	30.902	1.00	22.29	C
ATOM	450	CZ	TYR	A1703	-1.093	26.956	29.939	1.00	24.64	C
ATOM	451	OH	TYR	A1703	-1.288	27.195	28.596	1.00	24.68	O
ATOM	452	N	PHE	A1704	0.216	29.039	35.089	1.00	20.41	N
ATOM	453	CA	PHE	A1704	0.206	30.483	34.824	1.00	20.31	C
ATOM	454	C	PHE	A1704	1.526	31.143	35.237	1.00	20.81	C
ATOM	455	O	PHE	A1704	2.066	32.006	34.534	1.00	20.33	O
ATOM	456	CB	PHE	A1704	-0.901	31.171	35.624	1.00	19.51	C
ATOM	457	CG	PHE	A1704	-2.280	30.893	35.124	1.00	21.69	C
ATOM	458	CD1	PHE	A1704	-3.223	30.318	35.959	1.00	20.66	C
ATOM	459	CD2	PHE	A1704	-2.651	31.222	33.819	1.00	20.16	C
ATOM	460	CE1	PHE	A1704	-4.510	30.070	35.503	1.00	20.61	C
ATOM	461	CE2	PHE	A1704	-3.933	30.978	33.363	1.00	20.80	C
ATOM	462	CZ	PHE	A1704	-4.862	30.403	34.201	1.00	19.93	C
ATOM	463	N	LEU	A1705	1.997	30.787	36.422	1.00	20.01	N
ATOM	464	CA	LEU	A1705	3.213	31.397	36.934	1.00	20.31	C
ATOM	465	C	LEU	A1705	4.428	30.950	36.125	1.00	20.24	C
ATOM	466	O	LEU	A1705	5.375	31.714	35.969	1.00	20.22	O
ATOM	467	CB	LEU	A1705	3.402	31.071	38.427	1.00	20.87	C
ATOM	468	CG	LEU	A1705	2.374	31.696	39.380	1.00	20.79	C
ATOM	469	CD1	LEU	A1705	2.540	31.143	40.792	1.00	20.90	C
ATOM	470	CD2	LEU	A1705	2.464	33.246	39.405	1.00	21.34	C
ATOM	471	N	GLY	A1706	4.413	29.708	35.647	1.00	19.39	N
ATOM	472	CA	GLY	A1706	5.485	29.208	34.805	1.00	20.05	C
ATOM	473	C	GLY	A1706	5.607	30.040	33.546	1.00	20.85	C
ATOM	474	O	GLY	A1706	6.693	30.522	33.217	1.00	20.83	O
ATOM	475	N	ILE	A1707	4.490	30.229	32.852	1.00	20.24	N
ATOM	476	CA	ILE	A1707	4.482	31.055	31.654	1.00	20.50	C

ATOM	477	C	ILE	A1707	4.835	32.496	32.017	1.00	20.72	C
ATOM	478	O	ILE	A1707	5.659	33.113	31.355	1.00	21.45	O
ATOM	479	CB	ILE	A1707	3.109	31.024	30.963	1.00	20.35	C
ATOM	480	CG1	ILE	A1707	2.826	29.628	30.430	1.00	20.76	C
ATOM	481	CG2	ILE	A1707	3.028	32.074	29.821	1.00	20.87	C
ATOM	482	CD1	ILE	A1707	1.355	29.426	29.970	1.00	20.85	C
ATOM	483	N	ALA	A1708	4.215	33.037	33.065	1.00	21.43	N
ATOM	484	CA	ALA	A1708	4.499	34.419	33.462	1.00	21.67	C
ATOM	485	C	ALA	A1708	5.982	34.623	33.729	1.00	22.15	C
ATOM	486	O	ALA	A1708	6.518	35.700	33.464	1.00	22.03	O
ATOM	487	CB	ALA	A1708	3.680	34.842	34.682	1.00	22.63	C
ATOM	488	N	GLY	A1709	6.655	33.598	34.240	1.00	21.49	N
ATOM	489	CA	GLY	A1709	8.072	33.707	34.538	1.00	21.26	C
ATOM	490	C	GLY	A1709	9.010	33.337	33.400	1.00	21.16	C
ATOM	491	O	GLY	A1709	10.241	33.296	33.572	1.00	20.59	O
ATOM	492	N	GLY	A1710	8.432	33.051	32.237	1.00	20.37	N
ATOM	493	CA	GLY	A1710	9.202	32.698	31.058	1.00	20.60	C
ATOM	494	C	GLY	A1710	9.948	31.380	31.205	1.00	20.86	C
ATOM	495	O	GLY	A1710	10.968	31.165	30.553	1.00	20.62	O
ATOM	496	N	LYS	A1711	9.435	30.493	32.060	1.00	20.95	N
ATOM	497	CA	LYS	A1711	10.079	29.197	32.366	1.00	21.11	C
ATOM	498	C	LYS	A1711	9.794	28.147	31.300	1.00	22.21	C
ATOM	499	O	LYS	A1711	8.994	28.387	30.394	1.00	21.97	O
ATOM	500	CB	LYS	A1711	9.580	28.674	33.729	1.00	20.90	C
ATOM	501	CG	LYS	A1711	9.688	29.696	34.875	1.00	20.67	C
ATOM	502	CD	LYS	A1711	9.203	29.085	36.205	1.00	20.89	C
ATOM	503	CE	LYS	A1711	9.101	30.141	37.337	1.00	21.43	C
ATOM	504	NZ	LYS	A1711	10.410	30.822	37.623	1.00	21.62	N
ATOM	505	N	TRP	A1712	10.476	27.008	31.390	1.00	22.17	N
ATOM	506	CA	TRP	A1712	10.157	25.876	30.542	1.00	23.46	C
ATOM	507	C	TRP	A1712	8.896	25.245	31.085	1.00	23.84	C
ATOM	508	O	TRP	A1712	8.871	24.771	32.223	1.00	24.14	O
ATOM	509	CB	TRP	A1712	11.251	24.820	30.590	1.00	23.18	C
ATOM	510	CG	TRP	A1712	12.374	25.069	29.677	1.00	25.43	C
ATOM	511	CD1	TRP	A1712	13.678	25.337	30.019	1.00	26.48	C
ATOM	512	CD2	TRP	A1712	12.327	25.068	28.250	1.00	25.38	C
ATOM	513	NE1	TRP	A1712	14.433	25.511	28.883	1.00	25.81	N
ATOM	514	CE2	TRP	A1712	13.627	25.344	27.785	1.00	28.43	C
ATOM	515	CE3	TRP	A1712	11.312	24.854	27.309	1.00	25.07	C
ATOM	516	CZ2	TRP	A1712	13.935	25.408	26.426	1.00	27.08	C
ATOM	517	CZ3	TRP	A1712	11.620	24.946	25.960	1.00	24.41	C
ATOM	518	CH2	TRP	A1712	12.914	25.207	25.537	1.00	27.04	C
ATOM	519	N	VAL	A1713	7.851	25.227	30.278	1.00	23.20	N
ATOM	520	CA	VAL	A1713	6.612	24.590	30.687	1.00	23.43	C
ATOM	521	C	VAL	A1713	6.478	23.366	29.784	1.00	23.67	C
ATOM	522	O	VAL	A1713	6.119	23.477	28.620	1.00	23.51	O
ATOM	523	CB	VAL	A1713	5.416	25.546	30.566	1.00	23.85	C
ATOM	524	CG1	VAL	A1713	4.116	24.891	31.096	1.00	22.67	C
ATOM	525	CG2	VAL	A1713	5.695	26.859	31.310	1.00	22.94	C
ATOM	526	N	VAL	A1714	6.778	22.199	30.349	1.00	23.35	N
ATOM	527	CA	VAL	A1714	6.914	20.969	29.586	1.00	23.64	C
ATOM	528	C	VAL	A1714	6.024	19.865	30.092	1.00	23.92	C
ATOM	529	O	VAL	A1714	5.615	19.859	31.260	1.00	24.03	O
ATOM	530	CB	VAL	A1714	8.372	20.455	29.653	1.00	24.06	C
ATOM	531	CG1	VAL	A1714	9.341	21.534	29.107	1.00	23.74	C

ATOM	532	CG2	VAL	A1714	8.732	20.071	31.075	1.00	25.07	C
ATOM	533	N	SER	A1715	5.734	18.916	29.213	1.00	24.41	N
ATOM	534	CA	SER	A1715	4.889	17.780	29.570	1.00	24.54	C
ATOM	535	C	SER	A1715	5.593	16.773	30.451	1.00	24.94	C
ATOM	536	O	SER	A1715	6.801	16.577	30.362	1.00	24.11	O
ATOM	537	CB	SER	A1715	4.466	17.038	28.299	1.00	25.03	C
ATOM	538	OG	SER	A1715	3.778	15.852	28.639	1.00	23.98	O
ATOM	539	N	TYR	A1716	4.797	16.126	31.288	1.00	25.42	N
ATOM	540	CA	TYR	A1716	5.231	15.017	32.125	1.00	26.37	C
ATOM	541	C	TYR	A1716	5.869	13.931	31.247	1.00	27.10	C
ATOM	542	O	TYR	A1716	6.785	13.212	31.683	1.00	26.35	O
ATOM	543	CB	TYR	A1716	4.010	14.514	32.907	1.00	26.21	C
ATOM	544	CG	TYR	A1716	4.195	13.230	33.680	1.00	29.12	C
ATOM	545	CD1	TYR	A1716	3.331	12.154	33.481	1.00	32.06	C
ATOM	546	CD2	TYR	A1716	5.231	13.074	34.608	1.00	28.52	C
ATOM	547	CE1	TYR	A1716	3.486	10.956	34.178	1.00	34.47	C
ATOM	548	CE2	TYR	A1716	5.389	11.881	35.311	1.00	31.81	C
ATOM	549	CZ	TYR	A1716	4.514	10.828	35.094	1.00	34.25	C
ATOM	550	OH	TYR	A1716	4.649	9.641	35.787	1.00	37.87	O
ATOM	551	N	PHE	A1717	5.424	13.826	29.995	1.00	27.52	N
ATOM	552	CA	PHE	A1717	6.034	12.870	29.075	1.00	28.82	C
ATOM	553	C	PHE	A1717	7.538	13.059	28.921	1.00	28.84	C
ATOM	554	O	PHE	A1717	8.240	12.126	28.548	1.00	29.28	O
ATOM	555	CB	PHE	A1717	5.386	12.923	27.680	1.00	29.41	C
ATOM	556	CG	PHE	A1717	4.021	12.301	27.626	1.00	30.82	C
ATOM	557	CD1	PHE	A1717	2.906	13.073	27.348	1.00	32.52	C
ATOM	558	CD2	PHE	A1717	3.857	10.941	27.856	1.00	33.31	C
ATOM	559	CE1	PHE	A1717	1.641	12.504	27.304	1.00	34.86	C
ATOM	560	CE2	PHE	A1717	2.597	10.365	27.815	1.00	34.29	C
ATOM	561	CZ	PHE	A1717	1.489	11.147	27.532	1.00	35.25	C
ATOM	562	N	TRP	A1718	8.042	14.255	29.197	1.00	28.34	N
ATOM	563	CA	TRP	A1718	9.479	14.474	29.109	1.00	28.68	C
ATOM	564	C	TRP	A1718	10.155	13.533	30.080	1.00	29.50	C
ATOM	565	O	TRP	A1718	11.155	12.875	29.758	1.00	29.11	O
ATOM	566	CB	TRP	A1718	9.822	15.914	29.482	1.00	28.52	C
ATOM	567	CG	TRP	A1718	11.271	16.215	29.683	1.00	27.62	C
ATOM	568	CD1	TRP	A1718	12.290	16.042	28.785	1.00	30.51	C
ATOM	569	CD2	TRP	A1718	11.861	16.838	30.832	1.00	27.46	C
ATOM	570	NE1	TRP	A1718	13.476	16.480	29.326	1.00	30.53	N
ATOM	571	CE2	TRP	A1718	13.235	16.979	30.580	1.00	29.14	C
ATOM	572	CE3	TRP	A1718	11.364	17.277	32.064	1.00	28.24	C
ATOM	573	CZ2	TRP	A1718	14.113	17.539	31.509	1.00	29.76	C
ATOM	574	CZ3	TRP	A1718	12.240	17.826	32.984	1.00	30.82	C
ATOM	575	CH2	TRP	A1718	13.598	17.948	32.702	1.00	29.58	C
ATOM	576	N	VAL	A1719	9.606	13.483	31.282	1.00	30.02	N
ATOM	577	CA	VAL	A1719	10.142	12.624	32.316	1.00	31.76	C
ATOM	578	C	VAL	A1719	9.977	11.161	31.922	1.00	33.27	C
ATOM	579	O	VAL	A1719	10.969	10.427	31.827	1.00	33.42	O
ATOM	580	CB	VAL	A1719	9.475	12.912	33.671	1.00	31.63	C
ATOM	581	CG1	VAL	A1719	9.819	11.838	34.710	1.00	31.96	C
ATOM	582	CG2	VAL	A1719	9.889	14.294	34.167	1.00	31.20	C
ATOM	583	N	THR	A1720	8.740	10.743	31.651	1.00	34.96	N
ATOM	584	CA	THR	A1720	8.554	9.313	31.340	1.00	36.85	C
ATOM	585	C	THR	A1720	9.339	8.816	30.131	1.00	38.01	C
ATOM	586	O	THR	A1720	9.913	7.730	30.159	1.00	38.60	O

ATOM	587	CB	THR	A1720	7.081	8.877	31.234	1.00	36.66	C
ATOM	588	OG1	THR	A1720	6.390	9.689	30.279	1.00	36.44	O
ATOM	589	CG2	THR	A1720	6.357	9.118	32.547	1.00	36.41	C
ATOM	590	N	GLN	A1721	9.365	9.602	29.070	1.00	39.54	N
ATOM	591	CA	GLN	A1721	10.134	9.225	27.900	1.00	41.24	C
ATOM	592	C	GLN	A1721	11.631	9.197	28.194	1.00	42.30	C
ATOM	593	O	GLN	A1721	12.342	8.332	27.682	1.00	42.28	O
ATOM	594	CB	GLN	A1721	9.833	10.158	26.732	1.00	41.41	C
ATOM	595	CG	GLN	A1721	10.241	9.612	25.375	1.00	43.88	C
ATOM	596	CD	GLN	A1721	9.451	8.376	24.973	1.00	46.02	C
ATOM	597	OE1	GLN	A1721	9.825	7.679	24.029	1.00	48.31	O
ATOM	598	NE2	GLN	A1721	8.357	8.107	25.678	1.00	47.45	N
ATOM	599	N	SER	A1722	12.114	10.130	29.014	1.00	43.35	N
ATOM	600	CA	SER	A1722	13.541	10.171	29.361	1.00	44.70	C
ATOM	601	C	SER	A1722	13.932	8.901	30.108	1.00	46.65	C
ATOM	602	O	SER	A1722	14.954	8.276	29.812	1.00	46.89	O
ATOM	603	CB	SER	A1722	13.884	11.395	30.219	1.00	44.38	C
ATOM	604	OG	SER	A1722	13.805	12.597	29.478	1.00	42.77	O
ATOM	605	N	ILE	A1723	13.121	8.535	31.092	1.00	48.82	N
ATOM	606	CA	ILE	A1723	13.350	7.313	31.838	1.00	50.90	C
ATOM	607	C	ILE	A1723	13.396	6.162	30.852	1.00	52.25	C
ATOM	608	O	ILE	A1723	14.337	5.363	30.844	1.00	52.74	O
ATOM	609	CB	ILE	A1723	12.201	7.068	32.830	1.00	50.77	C
ATOM	610	CG1	ILE	A1723	12.174	8.140	33.915	1.00	50.32	C
ATOM	611	CG2	ILE	A1723	12.337	5.687	33.463	1.00	51.86	C
ATOM	612	CD1	ILE	A1723	10.961	8.062	34.792	1.00	50.04	C
ATOM	613	N	LYS	A1724	12.374	6.086	30.007	1.00	53.69	N
ATOM	614	CA	LYS	A1724	12.253	4.996	29.045	1.00	54.98	C
ATOM	615	C	LYS	A1724	13.473	4.834	28.133	1.00	55.52	C
ATOM	616	O	LYS	A1724	13.712	3.750	27.595	1.00	55.87	O
ATOM	617	CB	LYS	A1724	10.976	5.163	28.215	1.00	55.06	C
ATOM	618	CG	LYS	A1724	10.795	4.128	27.117	1.00	56.82	C
ATOM	619	CD	LYS	A1724	9.456	4.307	26.404	1.00	59.11	C
ATOM	620	CE	LYS	A1724	9.501	3.770	24.978	1.00	61.01	C
ATOM	621	NZ	LYS	A1724	10.015	2.372	24.900	1.00	62.45	N
ATOM	622	N	GLU	A1725	14.244	5.904	27.967	1.00	55.67	N
ATOM	623	CA	GLU	A1725	15.422	5.862	27.114	1.00	55.94	C
ATOM	624	C	GLU	A1725	16.690	6.032	27.942	1.00	56.09	C
ATOM	625	O	GLU	A1725	17.792	6.166	27.403	1.00	56.28	O
ATOM	626	CB	GLU	A1725	15.335	6.944	26.039	1.00	56.03	C
ATOM	627	CG	GLU	A1725	14.001	6.970	25.312	1.00	56.26	C
ATOM	628	CD	GLU	A1725	14.052	7.765	24.023	1.00	56.75	C
ATOM	629	OE1	GLU	A1725	15.170	8.047	23.543	1.00	57.44	O
ATOM	630	OE2	GLU	A1725	12.975	8.104	23.481	1.00	57.51	O
ATOM	631	N	ARG	A1726	16.517	6.036	29.260	1.00	56.32	N
ATOM	632	CA	ARG	A1726	17.627	6.170	30.200	1.00	56.34	C
ATOM	633	C	ARG	A1726	18.580	7.296	29.833	1.00	56.66	C
ATOM	634	O	ARG	A1726	19.701	7.366	30.341	1.00	56.80	O
ATOM	635	CB	ARG	A1726	18.398	4.856	30.303	1.00	56.21	C
ATOM	636	CG	ARG	A1726	17.587	3.692	30.854	1.00	54.58	C
ATOM	637	CD	ARG	A1726	18.448	2.440	31.127	1.00	52.29	C
ATOM	638	NE	ARG	A1726	17.674	1.297	31.602	1.00	50.00	N
ATOM	639	CZ	ARG	A1726	18.204	0.119	31.936	1.00	49.40	C
ATOM	640	NH1	ARG	A1726	19.518	-0.091	31.853	1.00	49.31	N
ATOM	641	NH2	ARG	A1726	17.418	-0.863	32.356	1.00	48.60	N

ATOM	642	N	LYS	A1727	18.126	8.160	28.931	1.00	56.83	N
ATOM	643	CA	LYS	A1727	18.871	9.338	28.523	1.00	56.73	C
ATOM	644	C	LYS	A1727	18.240	10.517	29.239	1.00	56.20	C
ATOM	645	O	LYS	A1727	17.349	10.347	30.065	1.00	56.46	O
ATOM	646	CB	LYS	A1727	18.713	9.573	27.019	1.00	56.89	C
ATOM	647	CG	LYS	A1727	19.526	8.674	26.096	1.00	58.87	C
ATOM	648	CD	LYS	A1727	19.027	8.815	24.652	1.00	60.89	C
ATOM	649	CE	LYS	A1727	20.012	8.266	23.630	1.00	62.65	C
ATOM	650	NZ	LYS	A1727	19.537	8.509	22.231	1.00	63.70	N
ATOM	651	N	MET	A1728	18.699	11.714	28.903	1.00	55.31	N
ATOM	652	CA	MET	A1728	18.110	12.945	29.403	1.00	54.28	C
ATOM	653	C	MET	A1728	17.630	13.702	28.185	1.00	52.90	C
ATOM	654	O	MET	A1728	18.396	14.434	27.558	1.00	52.58	O
ATOM	655	CB	MET	A1728	19.134	13.791	30.157	1.00	55.12	C
ATOM	656	CG	MET	A1728	19.061	13.657	31.668	1.00	57.13	C
ATOM	657	SD	MET	A1728	17.969	14.835	32.428	1.00	62.34	S
ATOM	658	CE	MET	A1728	18.990	16.316	32.456	1.00	61.18	C
ATOM	659	N	LEU	A1729	16.359	13.526	27.845	1.00	51.17	N
ATOM	660	CA	LEU	A1729	15.822	14.156	26.651	1.00	49.34	C
ATOM	661	C	LEU	A1729	15.739	15.670	26.766	1.00	48.47	C
ATOM	662	O	LEU	A1729	15.840	16.236	27.860	1.00	47.88	O
ATOM	663	CB	LEU	A1729	14.470	13.549	26.287	1.00	49.47	C
ATOM	664	CG	LEU	A1729	14.538	12.037	26.083	1.00	49.29	C
ATOM	665	CD1	LEU	A1729	13.160	11.493	25.790	1.00	49.48	C
ATOM	666	CD2	LEU	A1729	15.506	11.682	24.956	1.00	49.60	C
ATOM	667	N	ASN	A1730	15.564	16.317	25.622	1.00	47.11	N
ATOM	668	CA	ASN	A1730	15.512	17.767	25.549	1.00	46.60	C
ATOM	669	C	ASN	A1730	14.112	18.362	25.753	1.00	45.55	C
ATOM	670	O	ASN	A1730	13.161	17.971	25.080	1.00	44.35	O
ATOM	671	CB	ASN	A1730	16.090	18.222	24.213	1.00	46.97	C
ATOM	672	CG	ASN	A1730	15.670	19.618	23.848	1.00	48.88	C
ATOM	673	OD1	ASN	A1730	15.273	19.882	22.714	1.00	52.48	O
ATOM	674	ND2	ASN	A1730	15.754	20.528	24.805	1.00	50.39	N
ATOM	675	N	GLU	A1731	14.013	19.328	26.670	1.00	44.51	N
ATOM	676	CA	GLU	A1731	12.757	20.025	26.965	1.00	43.45	C
ATOM	677	C	GLU	A1731	11.958	20.402	25.744	1.00	43.01	C
ATOM	678	O	GLU	A1731	10.771	20.100	25.660	1.00	43.43	O
ATOM	679	CB	GLU	A1731	13.020	21.326	27.740	1.00	43.41	C
ATOM	680	CG	GLU	A1731	13.592	21.127	29.119	1.00	41.76	C
ATOM	681	CD	GLU	A1731	15.106	21.125	29.126	1.00	40.50	C
ATOM	682	OE1	GLU	A1731	15.705	21.028	28.039	1.00	41.97	O
ATOM	683	OE2	GLU	A1731	15.689	21.213	30.216	1.00	37.52	O
ATOM	684	N	HIS	A1732	12.606	21.128	24.838	1.00	42.34	N
ATOM	685	CA	HIS	A1732	12.002	21.610	23.605	1.00	41.79	C
ATOM	686	C	HIS	A1732	11.046	20.608	23.027	1.00	40.24	C
ATOM	687	O	HIS	A1732	9.946	20.944	22.603	1.00	40.42	O
ATOM	688	CB	HIS	A1732	13.087	21.831	22.548	1.00	42.72	C
ATOM	689	CG	HIS	A1732	13.424	23.268	22.296	1.00	44.10	C
ATOM	690	ND1	HIS	A1732	14.661	23.800	22.590	1.00	45.91	N
ATOM	691	CD2	HIS	A1732	12.706	24.269	21.731	1.00	45.21	C
ATOM	692	CE1	HIS	A1732	14.685	25.073	22.241	1.00	46.35	C
ATOM	693	NE2	HIS	A1732	13.508	25.385	21.723	1.00	46.39	N
ATOM	694	N	ASP	A1733	11.492	19.362	22.999	1.00	38.11	N
ATOM	695	CA	ASP	A1733	10.734	18.305	22.372	1.00	36.40	C
ATOM	696	C	ASP	A1733	9.461	17.952	23.116	1.00	34.24	C

ATOM	697	O	ASP	A1733	8.641	17.184	22.612	1.00	34.21	O
ATOM	698	CB	ASP	A1733	11.636	17.089	22.171	1.00	37.03	C
ATOM	699	CG	ASP	A1733	12.855	17.424	21.327	1.00	40.13	C
ATOM	700	OD1	ASP	A1733	12.708	18.222	20.371	1.00	42.92	O
ATOM	701	OD2	ASP	A1733	13.991	16.965	21.541	1.00	42.00	O
ATOM	702	N	PHE	A1734	9.274	18.544	24.294	1.00	31.43	N
ATOM	703	CA	PHE	A1734	8.103	18.239	25.088	1.00	29.37	C
ATOM	704	C	PHE	A1734	7.389	19.471	25.613	1.00	27.75	C
ATOM	705	O	PHE	A1734	6.595	19.357	26.524	1.00	27.33	O
ATOM	706	CB	PHE	A1734	8.490	17.353	26.276	1.00	28.85	C
ATOM	707	CG	PHE	A1734	9.074	16.045	25.875	1.00	29.54	C
ATOM	708	CD1	PHE	A1734	10.430	15.924	25.619	1.00	28.38	C
ATOM	709	CD2	PHE	A1734	8.258	14.921	25.748	1.00	29.90	C
ATOM	710	CE1	PHE	A1734	10.971	14.697	25.245	1.00	32.16	C
ATOM	711	CE2	PHE	A1734	8.784	13.709	25.387	1.00	28.92	C
ATOM	712	CZ	PHE	A1734	10.135	13.584	25.137	1.00	29.87	C
ATOM	713	N	GLU	A1735	7.679	20.638	25.049	1.00	26.09	N
ATOM	714	CA	GLU	A1735	7.053	21.874	25.523	1.00	25.44	C
ATOM	715	C	GLU	A1735	5.543	21.806	25.439	1.00	25.07	C
ATOM	716	O	GLU	A1735	4.985	21.250	24.464	1.00	24.68	O
ATOM	717	CB	GLU	A1735	7.563	23.075	24.717	1.00	25.36	C
ATOM	718	CG	GLU	A1735	7.210	24.412	25.355	1.00	25.42	C
ATOM	719	CD	GLU	A1735	7.957	25.570	24.722	1.00	23.84	C
ATOM	720	OE1	GLU	A1735	8.502	25.402	23.597	1.00	23.61	O
ATOM	721	OE2	GLU	A1735	8.007	26.647	25.349	1.00	23.68	O
ATOM	722	N	VAL	A1736	4.845	22.329	26.444	1.00	25.06	N
ATOM	723	CA	VAL	A1736	3.399	22.309	26.312	1.00	24.90	C
ATOM	724	C	VAL	A1736	2.978	23.295	25.233	1.00	24.36	C
ATOM	725	O	VAL	A1736	3.554	24.371	25.120	1.00	23.06	O
ATOM	726	CB	VAL	A1736	2.554	22.340	27.627	1.00	26.50	C
ATOM	727	CG1	VAL	A1736	3.344	22.090	28.906	1.00	25.92	C
ATOM	728	CG2	VAL	A1736	1.468	23.443	27.666	1.00	25.83	C
ATOM	729	N	ARG	A1737	2.039	22.850	24.398	1.00	24.08	N
ATOM	730	CA	ARG	A1737	1.570	23.598	23.229	1.00	24.71	C
ATOM	731	C	ARG	A1737	0.314	24.437	23.486	1.00	24.77	C
ATOM	732	O	ARG	A1737	0.066	25.445	22.801	1.00	24.60	O
ATOM	733	CB	ARG	A1737	1.289	22.617	22.072	1.00	24.14	C
ATOM	734	CG	ARG	A1737	2.478	21.779	21.678	1.00	28.10	C
ATOM	735	CD	ARG	A1737	2.253	20.906	20.461	1.00	33.08	C
ATOM	736	NE	ARG	A1737	3.461	20.144	20.184	1.00	39.98	N
ATOM	737	CZ	ARG	A1737	3.484	18.959	19.584	1.00	42.06	C
ATOM	738	NH1	ARG	A1737	2.359	18.386	19.189	1.00	43.10	N
ATOM	739	NH2	ARG	A1737	4.641	18.348	19.380	1.00	43.46	N
ATOM	740	N	GLY	A1738	-0.483	24.021	24.461	1.00	24.52	N
ATOM	741	CA	GLY	A1738	-1.685	24.761	24.799	1.00	24.68	C
ATOM	742	C	GLY	A1738	-2.378	24.200	26.025	1.00	25.06	C
ATOM	743	O	GLY	A1738	-1.812	23.382	26.766	1.00	25.42	O
ATOM	744	N	ASP	A1739	-3.609	24.638	26.249	1.00	24.43	N
ATOM	745	CA	ASP	A1739	-4.358	24.174	27.400	1.00	24.93	C
ATOM	746	C	ASP	A1739	-5.838	23.971	27.056	1.00	25.86	C
ATOM	747	O	ASP	A1739	-6.301	24.425	26.009	1.00	26.53	O
ATOM	748	CB	ASP	A1739	-4.171	25.134	28.583	1.00	24.27	C
ATOM	749	CG	ASP	A1739	-4.726	26.514	28.323	1.00	25.30	C
ATOM	750	OD1	ASP	A1739	-5.988	26.673	28.306	1.00	22.40	O
ATOM	751	OD2	ASP	A1739	-3.977	27.530	28.174	1.00	25.25	O

ATOM	752	N	VAL	A1740	-6.585	23.334	27.954	1.00	25.85	N
ATOM	753	CA	VAL	A1740	-7.982	22.984	27.668	1.00	27.39	C
ATOM	754	C	VAL	A1740	-8.930	24.169	27.607	1.00	27.48	C
ATOM	755	O	VAL	A1740	-10.110	24.011	27.300	1.00	27.81	O
ATOM	756	CB	VAL	A1740	-8.518	22.016	28.720	1.00	27.51	C
ATOM	757	CG1	VAL	A1740	-7.650	20.753	28.761	1.00	27.72	C
ATOM	758	CG2	VAL	A1740	-8.572	22.721	30.100	1.00	28.36	C
ATOM	759	N	VAL	A1741	-8.422	25.364	27.884	1.00	26.99	N
ATOM	760	CA	VAL	A1741	-9.275	26.541	27.887	1.00	27.27	C
ATOM	761	C	VAL	A1741	-8.992	27.473	26.722	1.00	27.50	C
ATOM	762	O	VAL	A1741	-9.903	27.842	25.956	1.00	27.96	O
ATOM	763	CB	VAL	A1741	-9.165	27.337	29.226	1.00	27.17	C
ATOM	764	CG1	VAL	A1741	-9.882	28.675	29.123	1.00	27.78	C
ATOM	765	CG2	VAL	A1741	-9.723	26.518	30.366	1.00	28.30	C
ATOM	766	N	ASN	A1742	-7.731	27.820	26.535	1.00	26.85	N
ATOM	767	CA	ASN	A1742	-7.425	28.860	25.560	1.00	27.45	C
ATOM	768	C	ASN	A1742	-6.986	28.417	24.171	1.00	27.14	C
ATOM	769	O	ASN	A1742	-6.782	29.261	23.293	1.00	28.01	O
ATOM	770	CB	ASN	A1742	-6.407	29.829	26.163	1.00	26.91	C
ATOM	771	CG	ASN	A1742	-6.965	30.573	27.367	1.00	27.80	C
ATOM	772	OD1	ASN	A1742	-7.852	31.422	27.230	1.00	28.46	O
ATOM	773	ND2	ASN	A1742	-6.462	30.253	28.549	1.00	24.00	N
ATOM	774	N	GLY	A1743	-6.835	27.115	23.961	1.00	26.56	N
ATOM	775	CA	GLY	A1743	-6.395	26.628	22.657	1.00	26.50	C
ATOM	776	C	GLY	A1743	-5.375	25.510	22.722	1.00	26.14	C
ATOM	777	O	GLY	A1743	-4.445	25.548	23.535	1.00	25.14	O
ATOM	778	N	ARG	A1744	-5.507	24.538	21.823	1.00	25.51	N
ATOM	779	CA	ARG	A1744	-4.651	23.369	21.853	1.00	26.02	C
ATOM	780	C	ARG	A1744	-3.241	23.611	21.354	1.00	25.19	C
ATOM	781	O	ARG	A1744	-2.360	22.805	21.626	1.00	25.63	O
ATOM	782	CB	ARG	A1744	-5.281	22.215	21.048	1.00	25.81	C
ATOM	783	CG	ARG	A1744	-6.598	21.754	21.636	1.00	28.55	C
ATOM	784	CD	ARG	A1744	-7.147	20.493	21.013	1.00	30.52	C
ATOM	785	NE	ARG	A1744	-6.331	19.330	21.342	1.00	33.35	N
ATOM	786	CZ	ARG	A1744	-6.394	18.648	22.485	1.00	33.54	C
ATOM	787	NH1	ARG	A1744	-7.241	19.002	23.452	1.00	34.73	N
ATOM	788	NH2	ARG	A1744	-5.606	17.601	22.656	1.00	33.12	N
ATOM	789	N	ASN	A1745	-3.030	24.683	20.591	1.00	24.58	N
ATOM	790	CA	ASN	A1745	-1.707	24.941	20.031	1.00	24.66	C
ATOM	791	C	ASN	A1745	-1.405	26.432	20.007	1.00	24.45	C
ATOM	792	O	ASN	A1745	-0.840	26.930	19.052	1.00	25.27	O
ATOM	793	CB	ASN	A1745	-1.587	24.343	18.613	1.00	25.58	C
ATOM	794	CG	ASN	A1745	-0.138	24.299	18.099	1.00	26.95	C
ATOM	795	OD1	ASN	A1745	0.793	24.017	18.841	1.00	27.90	O
ATOM	796	ND2	ASN	A1745	0.044	24.617	16.831	1.00	31.89	N
ATOM	797	N	HIS	A1746	-1.790	27.145	21.056	1.00	23.66	N
ATOM	798	CA	HIS	A1746	-1.559	28.583	21.102	1.00	23.14	C
ATOM	799	C	HIS	A1746	-0.078	28.956	21.278	1.00	23.27	C
ATOM	800	O	HIS	A1746	0.321	30.099	21.010	1.00	23.59	O
ATOM	801	CB	HIS	A1746	-2.449	29.255	22.157	1.00	23.84	C
ATOM	802	CG	HIS	A1746	-2.192	28.797	23.560	1.00	24.37	C
ATOM	803	ND1	HIS	A1746	-3.190	28.304	24.380	1.00	26.89	N
ATOM	804	CD2	HIS	A1746	-1.057	28.779	24.296	1.00	21.40	C
ATOM	805	CE1	HIS	A1746	-2.681	28.024	25.568	1.00	23.91	C
ATOM	806	NE2	HIS	A1746	-1.383	28.275	25.532	1.00	27.21	N

ATOM	807	N	GLN	A1747	0.726	27.994	21.724	1.00	21.90	N
ATOM	808	CA	GLN	A1747	2.163	28.190	21.903	1.00	22.69	C
ATOM	809	C	GLN	A1747	2.467	29.324	22.880	1.00	22.28	C
ATOM	810	O	GLN	A1747	3.456	30.056	22.737	1.00	21.86	O
ATOM	811	CB	GLN	A1747	2.876	28.416	20.549	1.00	22.24	C
ATOM	812	CG	GLN	A1747	2.880	27.174	19.644	1.00	24.75	C
ATOM	813	CD	GLN	A1747	3.813	26.050	20.128	1.00	28.16	C
ATOM	814	OE1	GLN	A1747	4.806	26.306	20.844	1.00	29.19	O
ATOM	815	NE2	GLN	A1747	3.509	24.808	19.727	1.00	28.13	N
ATOM	816	N	GLY	A1748	1.606	29.463	23.877	1.00	21.59	N
ATOM	817	CA	GLY	A1748	1.817	30.468	24.909	1.00	22.10	C
ATOM	818	C	GLY	A1748	3.136	30.308	25.647	1.00	22.26	C
ATOM	819	O	GLY	A1748	3.865	31.274	25.841	1.00	22.31	O
ATOM	820	N	PRO	A1749	3.453	29.109	26.116	1.00	22.38	N
ATOM	821	CA	PRO	A1749	4.722	28.941	26.832	1.00	22.37	C
ATOM	822	C	PRO	A1749	5.935	29.398	26.013	1.00	21.94	C
ATOM	823	O	PRO	A1749	6.760	30.146	26.542	1.00	22.26	O
ATOM	824	CB	PRO	A1749	4.754	27.450	27.138	1.00	21.64	C
ATOM	825	CG	PRO	A1749	3.282	27.108	27.273	1.00	22.05	C
ATOM	826	CD	PRO	A1749	2.656	27.871	26.103	1.00	23.00	C
ATOM	827	N	LYS	A1750	6.027	28.989	24.755	1.00	21.32	N
ATOM	828	CA	LYS	A1750	7.130	29.403	23.893	1.00	21.74	C
ATOM	829	C	LYS	A1750	7.147	30.925	23.711	1.00	21.91	C
ATOM	830	O	LYS	A1750	8.204	31.531	23.745	1.00	21.20	O
ATOM	831	CB	LYS	A1750	7.006	28.720	22.524	1.00	22.15	C
ATOM	832	CG	LYS	A1750	7.929	29.271	21.427	1.00	22.74	C
ATOM	833	CD	LYS	A1750	7.805	28.392	20.167	1.00	25.81	C
ATOM	834	CE	LYS	A1750	8.765	28.810	19.020	1.00	26.22	C
ATOM	835	NZ	LYS	A1750	8.569	30.219	18.581	1.00	27.71	N
ATOM	836	N	ARG	A1751	5.976	31.536	23.539	1.00	21.71	N
ATOM	837	CA	ARG	A1751	5.911	32.988	23.360	1.00	22.35	C
ATOM	838	C	ARG	A1751	6.449	33.754	24.576	1.00	21.85	C
ATOM	839	O	ARG	A1751	7.170	34.761	24.439	1.00	21.10	O
ATOM	840	CB	ARG	A1751	4.481	33.438	23.026	1.00	23.43	C
ATOM	841	CG	ARG	A1751	4.409	34.828	22.403	1.00	25.25	C
ATOM	842	CD	ARG	A1751	3.261	34.995	21.382	1.00	29.76	C
ATOM	843	NE	ARG	A1751	2.138	34.235	21.862	1.00	31.17	N
ATOM	844	CZ	ARG	A1751	1.632	33.156	21.288	1.00	28.31	C
ATOM	845	NH1	ARG	A1751	2.074	32.710	20.118	1.00	30.77	N
ATOM	846	NH2	ARG	A1751	0.646	32.535	21.897	1.00	27.26	N
ATOM	847	N	ALA	A1752	6.104	33.269	25.766	1.00	21.70	N
ATOM	848	CA	ALA	A1752	6.598	33.888	26.989	1.00	22.04	C
ATOM	849	C	ALA	A1752	8.111	33.729	27.096	1.00	20.96	C
ATOM	850	O	ALA	A1752	8.821	34.668	27.457	1.00	21.13	O
ATOM	851	CB	ALA	A1752	5.911	33.302	28.230	1.00	21.17	C
ATOM	852	N	ARG	A1753	8.609	32.546	26.787	1.00	21.66	N
ATOM	853	CA	ARG	A1753	10.058	32.339	26.834	1.00	22.12	C
ATOM	854	C	ARG	A1753	10.731	33.325	25.907	1.00	22.24	C
ATOM	855	O	ARG	A1753	11.835	33.791	26.166	1.00	23.14	O
ATOM	856	CB	ARG	A1753	10.420	30.971	26.295	1.00	22.42	C
ATOM	857	CG	ARG	A1753	10.230	29.803	27.216	1.00	22.67	C
ATOM	858	CD	ARG	A1753	10.982	28.597	26.699	1.00	23.97	C
ATOM	859	NE	ARG	A1753	10.466	28.027	25.449	1.00	23.88	N
ATOM	860	CZ	ARG	A1753	11.042	28.143	24.244	1.00	24.85	C
ATOM	861	NH1	ARG	A1753	12.135	28.884	24.059	1.00	24.13	N

ATOM	862	NH2	ARG	A1753	10.510	27.520	23.202	1.00	24.17	N
ATOM	863	N	GLU	A1754	10.055	33.627	24.807	1.00	22.93	N
ATOM	864	CA	GLU	A1754	10.653	34.434	23.741	1.00	23.72	C
ATOM	865	C	GLU	A1754	10.301	35.911	23.794	1.00	23.81	C
ATOM	866	O	GLU	A1754	10.743	36.692	22.935	1.00	25.22	O
ATOM	867	CB	GLU	A1754	10.285	33.828	22.368	1.00	23.29	C
ATOM	868	CG	GLU	A1754	10.942	32.469	22.133	1.00	23.30	C
ATOM	869	CD	GLU	A1754	10.563	31.775	20.826	1.00	27.24	C
ATOM	870	OE1	GLU	A1754	9.548	32.149	20.191	1.00	26.54	O
ATOM	871	OE2	GLU	A1754	11.294	30.824	20.437	1.00	25.87	O
ATOM	872	N	SER	A1755	9.561	36.320	24.818	1.00	23.62	N
ATOM	873	CA	SER	A1755	9.093	37.702	24.895	1.00	22.68	C
ATOM	874	C	SER	A1755	9.408	38.385	26.203	1.00	22.66	C
ATOM	875	O	SER	A1755	8.718	39.329	26.600	1.00	22.72	O
ATOM	876	CB	SER	A1755	7.578	37.776	24.658	1.00	22.98	C
ATOM	877	OG	SER	A1755	7.231	37.148	23.453	1.00	23.71	O
ATOM	878	N	GLN	A1756	10.459	37.933	26.872	1.00	22.77	N
ATOM	879	CA	GLN	A1756	10.830	38.532	28.139	1.00	23.68	C
ATOM	880	C	GLN	A1756	11.280	39.990	28.046	1.00	24.52	C
ATOM	881	O	GLN	A1756	11.255	40.693	29.046	1.00	23.97	O
ATOM	882	CB	GLN	A1756	11.873	37.664	28.843	1.00	23.55	C
ATOM	883	CG	GLN	A1756	11.269	36.348	29.285	1.00	23.77	C
ATOM	884	CD	GLN	A1756	10.141	36.562	30.268	1.00	22.15	C
ATOM	885	OE1	GLN	A1756	10.368	37.019	31.393	1.00	25.95	O
ATOM	886	NE2	GLN	A1756	8.917	36.280	29.837	1.00	20.48	N
ATOM	887	N	ASP	A1757	11.673	40.448	26.856	1.00	24.99	N
ATOM	888	CA	ASP	A1757	12.064	41.844	26.689	1.00	25.99	C
ATOM	889	C	ASP	A1757	10.852	42.710	26.355	1.00	25.49	C
ATOM	890	O	ASP	A1757	10.955	43.929	26.283	1.00	25.57	O
ATOM	891	CB	ASP	A1757	13.100	41.996	25.573	1.00	25.79	C
ATOM	892	CG	ASP	A1757	14.477	41.547	25.992	1.00	29.24	C
ATOM	893	OD1	ASP	A1757	14.805	41.582	27.206	1.00	29.38	O
ATOM	894	OD2	ASP	A1757	15.300	41.150	25.151	1.00	30.88	O
ATOM	895	N	ARG	A1758	9.712	42.072	26.132	1.00	25.82	N
ATOM	896	CA	ARG	A1758	8.489	42.796	25.795	1.00	26.34	C
ATOM	897	C	ARG	A1758	7.299	42.146	26.476	1.00	25.48	C
ATOM	898	O	ARG	A1758	6.424	41.527	25.835	1.00	24.95	O
ATOM	899	CB	ARG	A1758	8.279	42.827	24.290	1.00	26.91	C
ATOM	900	CG	ARG	A1758	8.480	41.502	23.592	1.00	30.41	C
ATOM	901	CD	ARG	A1758	7.575	41.327	22.384	1.00	36.98	C
ATOM	902	NE	ARG	A1758	8.224	41.525	21.087	1.00	40.46	N
ATOM	903	CZ	ARG	A1758	7.552	41.854	19.983	1.00	42.63	C
ATOM	904	NH1	ARG	A1758	6.237	42.042	20.049	1.00	42.21	N
ATOM	905	NH2	ARG	A1758	8.183	42.003	18.823	1.00	43.37	N
ATOM	906	N	LYS	A1759	7.271	42.299	27.789	1.00	24.39	N
ATOM	907	CA	LYS	A1759	6.260	41.648	28.600	1.00	24.35	C
ATOM	908	C	LYS	A1759	4.855	42.177	28.314	1.00	24.82	C
ATOM	909	O	LYS	A1759	4.672	43.362	27.997	1.00	24.88	O
ATOM	910	CB	LYS	A1759	6.651	41.729	30.082	1.00	24.38	C
ATOM	911	CG	LYS	A1759	8.007	41.043	30.344	1.00	25.02	C
ATOM	912	CD	LYS	A1759	8.378	41.153	31.823	1.00	24.95	C
ATOM	913	CE	LYS	A1759	9.664	40.425	32.149	1.00	28.10	C
ATOM	914	NZ	LYS	A1759	9.863	40.333	33.620	1.00	31.56	N
ATOM	915	N	ILE	A1760	3.875	41.283	28.408	1.00	24.02	N
ATOM	916	CA	ILE	A1760	2.517	41.583	27.969	1.00	24.54	C

ATOM	917	C	ILE	A1760	1.841	42.700	28.732	1.00	24.57	C
ATOM	918	O	ILE	A1760	1.016	43.414	28.153	1.00	24.53	O
ATOM	919	CB	ILE	A1760	1.636	40.319	27.961	1.00	24.05	C
ATOM	920	CG1	ILE	A1760	1.639	39.637	29.326	1.00	24.38	C
ATOM	921	CG2	ILE	A1760	2.073	39.349	26.852	1.00	23.90	C
ATOM	922	CD1	ILE	A1760	0.599	38.501	29.393	1.00	23.37	C
ATOM	923	N	PHE	A1761	2.215	42.891	30.000	1.00	23.67	N
ATOM	924	CA	PHE	A1761	1.594	43.945	30.784	1.00	24.50	C
ATOM	925	C	PHE	A1761	2.531	45.116	31.029	1.00	25.59	C
ATOM	926	O	PHE	A1761	2.255	45.948	31.885	1.00	25.50	O
ATOM	927	CB	PHE	A1761	1.051	43.428	32.122	1.00	24.34	C
ATOM	928	CG	PHE	A1761	0.008	42.359	31.988	1.00	23.75	C
ATOM	929	CD1	PHE	A1761	-0.098	41.368	32.954	1.00	23.52	C
ATOM	930	CD2	PHE	A1761	-0.836	42.313	30.895	1.00	23.84	C
ATOM	931	CE1	PHE	A1761	-1.025	40.341	32.840	1.00	25.32	C
ATOM	932	CE2	PHE	A1761	-1.788	41.311	30.780	1.00	24.19	C
ATOM	933	CZ	PHE	A1761	-1.883	40.325	31.758	1.00	24.88	C
ATOM	934	N	ARG	A1762	3.618	45.210	30.268	1.00	26.42	N
ATOM	935	CA	ARG	A1762	4.516	46.339	30.439	1.00	27.60	C
ATOM	936	C	ARG	A1762	3.727	47.634	30.257	1.00	27.17	C
ATOM	937	O	ARG	A1762	2.945	47.780	29.327	1.00	26.26	O
ATOM	938	CB	ARG	A1762	5.689	46.269	29.449	1.00	28.28	C
ATOM	939	CG	ARG	A1762	6.633	47.437	29.521	1.00	33.00	C
ATOM	940	CD	ARG	A1762	7.099	47.919	28.120	1.00	42.26	C
ATOM	941	NE	ARG	A1762	5.989	47.979	27.161	1.00	47.60	N
ATOM	942	CZ	ARG	A1762	6.062	48.543	25.953	1.00	51.36	C
ATOM	943	NH1	ARG	A1762	7.192	49.113	25.554	1.00	53.29	N
ATOM	944	NH2	ARG	A1762	5.002	48.553	25.144	1.00	52.45	N
ATOM	945	N	GLY	A1763	3.913	48.562	31.182	1.00	26.92	N
ATOM	946	CA	GLY	A1763	3.252	49.860	31.081	1.00	26.68	C
ATOM	947	C	GLY	A1763	1.835	49.890	31.617	1.00	26.75	C
ATOM	948	O	GLY	A1763	1.106	50.864	31.416	1.00	27.22	O
ATOM	949	N	LEU	A1764	1.428	48.824	32.298	1.00	26.19	N
ATOM	950	CA	LEU	A1764	0.093	48.808	32.886	1.00	25.41	C
ATOM	951	C	LEU	A1764	0.205	48.890	34.403	1.00	25.68	C
ATOM	952	O	LEU	A1764	1.191	48.418	34.975	1.00	25.78	O
ATOM	953	CB	LEU	A1764	-0.637	47.518	32.502	1.00	25.52	C
ATOM	954	CG	LEU	A1764	-0.955	47.286	31.024	1.00	25.66	C
ATOM	955	CD1	LEU	A1764	-1.713	45.958	30.840	1.00	22.88	C
ATOM	956	CD2	LEU	A1764	-1.771	48.432	30.451	1.00	26.36	C
ATOM	957	N	GLU	A1765	-0.782	49.503	35.051	1.00	25.40	N
ATOM	958	CA	GLU	A1765	-0.849	49.516	36.509	1.00	25.54	C
ATOM	959	C	GLU	A1765	-2.077	48.690	36.866	1.00	25.27	C
ATOM	960	O	GLU	A1765	-3.167	49.022	36.444	1.00	24.89	O
ATOM	961	CB	GLU	A1765	-1.046	50.932	37.059	1.00	26.09	C
ATOM	962	CG	GLU	A1765	0.228	51.725	37.201	1.00	28.37	C
ATOM	963	CD	GLU	A1765	0.103	52.849	38.220	1.00	29.58	C
ATOM	964	OE1	GLU	A1765	-1.031	53.182	38.649	1.00	24.60	O
ATOM	965	OE2	GLU	A1765	1.158	53.392	38.585	1.00	31.79	O
ATOM	966	N	ILE	A1766	-1.915	47.640	37.661	1.00	25.07	N
ATOM	967	CA	ILE	A1766	-3.047	46.767	37.965	1.00	25.10	C
ATOM	968	C	ILE	A1766	-3.355	46.639	39.461	1.00	25.75	C
ATOM	969	O	ILE	A1766	-2.452	46.414	40.289	1.00	25.20	O
ATOM	970	CB	ILE	A1766	-2.785	45.356	37.384	1.00	25.40	C
ATOM	971	CG1	ILE	A1766	-2.559	45.413	35.870	1.00	24.46	C

ATOM	972	CG2	ILE	A1766	-3.904	44.395	37.767	1.00	25.24	C
ATOM	973	CD1	ILE	A1766	-2.278	44.030	35.244	1.00	24.35	C
ATOM	974	N	CYS	A1767	-4.628	46.794	39.808	1.00	25.42	N
ATOM	975	CA	CYS	A1767	-5.047	46.584	41.183	1.00	26.50	C
ATOM	976	C	CYS	A1767	-5.880	45.314	41.180	1.00	26.43	C
ATOM	977	O	CYS	A1767	-6.894	45.247	40.485	1.00	26.80	O
ATOM	978	CB	CYS	A1767	-5.873	47.753	41.703	1.00	26.42	C
ATOM	979	SG	CYS	A1767	-6.536	47.543	43.396	1.00	27.72	S
ATOM	980	N	CYS	A1768	-5.419	44.301	41.912	1.00	26.05	N
ATOM	981	CA	CYS	A1768	-6.172	43.066	42.073	1.00	26.62	C
ATOM	982	C	CYS	A1768	-7.088	43.276	43.286	1.00	26.73	C
ATOM	983	O	CYS	A1768	-6.659	43.185	44.438	1.00	26.77	O
ATOM	984	CB	CYS	A1768	-5.220	41.894	42.289	1.00	26.35	C
ATOM	985	SG	CYS	A1768	-4.129	41.599	40.873	1.00	26.54	S
ATOM	986	N	TYR	A1769	-8.345	43.564	42.996	1.00	26.38	N
ATOM	987	CA	TYR	A1769	-9.317	44.004	43.985	1.00	27.38	C
ATOM	988	C	TYR	A1769	-10.229	42.835	44.378	1.00	27.66	C
ATOM	989	O	TYR	A1769	-11.058	42.389	43.593	1.00	26.66	O
ATOM	990	CB	TYR	A1769	-10.100	45.181	43.378	1.00	27.50	C
ATOM	991	CG	TYR	A1769	-10.926	45.996	44.355	1.00	29.17	C
ATOM	992	CD1	TYR	A1769	-10.330	46.866	45.288	1.00	29.79	C
ATOM	993	CD2	TYR	A1769	-12.300	45.931	44.316	1.00	30.16	C
ATOM	994	CE1	TYR	A1769	-11.118	47.608	46.178	1.00	30.57	C
ATOM	995	CE2	TYR	A1769	-13.080	46.678	45.185	1.00	32.31	C
ATOM	996	CZ	TYR	A1769	-12.499	47.486	46.121	1.00	31.34	C
ATOM	997	OH	TYR	A1769	-13.308	48.202	46.974	1.00	30.45	O
ATOM	998	N	GLY	A1770	-10.019	42.327	45.595	1.00	28.90	N
ATOM	999	CA	GLY	A1770	-10.709	41.134	46.094	1.00	29.31	C
ATOM	1000	C	GLY	A1770	-12.176	41.304	46.425	1.00	30.06	C
ATOM	1001	O	GLY	A1770	-12.705	42.422	46.404	1.00	31.36	O
ATOM	1002	N	PRO	A1771	-12.818	40.204	46.807	1.00	30.31	N
ATOM	1003	CA	PRO	A1771	-12.145	38.915	47.043	1.00	29.88	C
ATOM	1004	C	PRO	A1771	-11.942	37.998	45.828	1.00	29.33	C
ATOM	1005	O	PRO	A1771	-12.560	38.177	44.779	1.00	28.62	O
ATOM	1006	CB	PRO	A1771	-13.121	38.183	47.983	1.00	29.86	C
ATOM	1007	CG	PRO	A1771	-14.454	38.880	47.821	1.00	30.66	C
ATOM	1008	CD	PRO	A1771	-14.278	40.096	46.972	1.00	30.69	C
ATOM	1009	N	PHE	A1772	-11.102	36.982	46.013	1.00	28.54	N
ATOM	1010	CA	PHE	A1772	-10.860	35.957	44.996	1.00	27.89	C
ATOM	1011	C	PHE	A1772	-10.924	34.559	45.622	1.00	28.22	C
ATOM	1012	O	PHE	A1772	-10.799	34.406	46.850	1.00	27.52	O
ATOM	1013	CB	PHE	A1772	-9.489	36.138	44.324	1.00	27.92	C
ATOM	1014	CG	PHE	A1772	-9.315	37.458	43.628	1.00	26.98	C
ATOM	1015	CD1	PHE	A1772	-8.686	38.509	44.271	1.00	26.56	C
ATOM	1016	CD2	PHE	A1772	-9.792	37.651	42.345	1.00	27.57	C
ATOM	1017	CE1	PHE	A1772	-8.518	39.744	43.646	1.00	26.59	C
ATOM	1018	CE2	PHE	A1772	-9.633	38.895	41.706	1.00	28.29	C
ATOM	1019	CZ	PHE	A1772	-9.007	39.941	42.370	1.00	24.25	C
ATOM	1020	N	THR	A1773	-11.130	33.547	44.778	1.00	28.39	N
ATOM	1021	CA	THR	A1773	-11.074	32.177	45.232	1.00	29.16	C
ATOM	1022	C	THR	A1773	-10.002	31.383	44.492	1.00	29.03	C
ATOM	1023	O	THR	A1773	-9.651	31.684	43.343	1.00	28.55	O
ATOM	1024	CB	THR	A1773	-12.443	31.458	45.060	1.00	29.72	C
ATOM	1025	OG1	THR	A1773	-12.671	31.172	43.671	1.00	29.53	O
ATOM	1026	CG2	THR	A1773	-13.582	32.392	45.445	1.00	30.21	C

ATOM	1027	N	ASN	A1774	-9.492	30.368	45.186	1.00 29.25	N
ATOM	1028	CA	ASN	A1774	-8.536	29.404	44.644	1.00 30.24	C
ATOM	1029	C	ASN	A1774	-7.206	29.965	44.193	1.00 29.98	C
ATOM	1030	O	ASN	A1774	-6.348	29.239	43.720	1.00 30.34	O
ATOM	1031	CB	ASN	A1774	-9.188	28.599	43.520	1.00 30.62	C
ATOM	1032	CG	ASN	A1774	-10.395	27.829	44.007	1.00 33.86	C
ATOM	1033	OD1	ASN	A1774	-11.327	27.536	43.256	1.00 38.78	O
ATOM	1034	ND2	ASN	A1774	-10.395	27.533	45.297	1.00 34.54	N
ATOM	1035	N	MET	A1775	-7.040	31.253	44.341	1.00 30.26	N
ATOM	1036	CA	MET	A1775	-5.780	31.854	43.959	1.00 30.54	C
ATOM	1037	C	MET	A1775	-5.523	33.037	44.869	1.00 30.62	C
ATOM	1038	O	MET	A1775	-6.146	34.085	44.717	1.00 31.41	O
ATOM	1039	CB	MET	A1775	-5.810	32.262	42.483	1.00 30.05	C
ATOM	1040	CG	MET	A1775	-4.477	32.792	41.944	1.00 30.94	C
ATOM	1041	SD	MET	A1775	-4.637	33.327	40.209	1.00 30.61	S
ATOM	1042	CE	MET	A1775	-4.763	31.773	39.369	1.00 28.57	C
ATOM	1043	N	PRO	A1776	-4.618	32.862	45.829	1.00 30.40	N
ATOM	1044	CA	PRO	A1776	-4.292	33.922	46.781	1.00 29.77	C
ATOM	1045	C	PRO	A1776	-3.943	35.191	46.037	1.00 29.25	C
ATOM	1046	O	PRO	A1776	-3.230	35.183	45.026	1.00 28.93	O
ATOM	1047	CB	PRO	A1776	-3.069	33.387	47.530	1.00 29.89	C
ATOM	1048	CG	PRO	A1776	-3.098	31.908	47.334	1.00 30.76	C
ATOM	1049	CD	PRO	A1776	-3.842	31.634	46.061	1.00 30.92	C
ATOM	1050	N	THR	A1777	-4.458	36.294	46.562	1.00 28.71	N
ATOM	1051	CA	THR	A1777	-4.290	37.596	45.961	1.00 27.45	C
ATOM	1052	C	THR	A1777	-2.855	37.948	45.632	1.00 27.45	C
ATOM	1053	O	THR	A1777	-2.586	38.522	44.577	1.00 25.81	O
ATOM	1054	CB	THR	A1777	-4.870	38.661	46.894	1.00 28.01	C
ATOM	1055	OG1	THR	A1777	-6.289	38.477	46.953	1.00 27.40	O
ATOM	1056	CG2	THR	A1777	-4.683	40.049	46.291	1.00 27.84	C
ATOM	1057	N	ASP	A1778	-1.925	37.632	46.523	1.00 26.91	N
ATOM	1058	CA	ASP	A1778	-0.547	38.018	46.248	1.00 27.03	C
ATOM	1059	C	ASP	A1778	0.121	37.162	45.168	1.00 26.11	C
ATOM	1060	O	ASP	A1778	1.205	37.492	44.695	1.00 26.57	O
ATOM	1061	CB	ASP	A1778	0.313	38.160	47.515	1.00 27.89	C
ATOM	1062	CG	ASP	A1778	0.442	36.877	48.309	1.00 30.00	C
ATOM	1063	OD1	ASP	A1778	0.036	35.787	47.833	1.00 29.81	O
ATOM	1064	OD2	ASP	A1778	0.948	36.893	49.465	1.00 33.69	O
ATOM	1065	N	GLN	A1779	-0.540	36.098	44.751	1.00 25.07	N
ATOM	1066	CA	GLN	A1779	-0.015	35.251	43.684	1.00 24.31	C
ATOM	1067	C	GLN	A1779	-0.510	35.789	42.362	1.00 23.67	C
ATOM	1068	O	GLN	A1779	0.208	35.740	41.357	1.00 22.63	O
ATOM	1069	CB	GLN	A1779	-0.423	33.791	43.873	1.00 24.21	C
ATOM	1070	CG	GLN	A1779	0.120	33.177	45.163	1.00 26.13	C
ATOM	1071	CD	GLN	A1779	1.609	33.436	45.346	1.00 27.16	C
ATOM	1072	OE1	GLN	A1779	2.014	34.357	46.083	1.00 30.91	O
ATOM	1073	NE2	GLN	A1779	2.432	32.653	44.659	1.00 26.73	N
ATOM	1074	N	LEU	A1780	-1.745	36.292	42.357	1.00 23.18	N
ATOM	1075	CA	LEU	A1780	-2.262	36.977	41.179	1.00 23.21	C
ATOM	1076	C	LEU	A1780	-1.404	38.228	40.982	1.00 22.75	C
ATOM	1077	O	LEU	A1780	-1.034	38.558	39.857	1.00 21.45	O
ATOM	1078	CB	LEU	A1780	-3.757	37.347	41.336	1.00 23.73	C
ATOM	1079	CG	LEU	A1780	-4.484	37.965	40.122	1.00 24.76	C
ATOM	1080	CD1	LEU	A1780	-4.382	37.080	38.872	1.00 23.61	C
ATOM	1081	CD2	LEU	A1780	-5.961	38.264	40.472	1.00 23.90	C

ATOM	1082	N	GLU	A1781	-1.053	38.908	42.077	1.00	22.70	N
ATOM	1083	CA	GLU	A1781	-0.215	40.099	41.964	1.00	22.82	C
ATOM	1084	C	GLU	A1781	1.166	39.727	41.433	1.00	22.65	C
ATOM	1085	O	GLU	A1781	1.712	40.398	40.566	1.00	22.98	O
ATOM	1086	CB	GLU	A1781	-0.110	40.829	43.302	1.00	23.74	C
ATOM	1087	CG	GLU	A1781	-1.450	41.413	43.720	1.00	25.21	C
ATOM	1088	CD	GLU	A1781	-1.422	41.983	45.119	1.00	31.15	C
ATOM	1089	OE1	GLU	A1781	-0.600	41.510	45.928	1.00	32.47	O
ATOM	1090	OE2	GLU	A1781	-2.210	42.908	45.403	1.00	31.02	O
ATOM	1091	N	TRP	A1782	1.732	38.643	41.944	1.00	21.92	N
ATOM	1092	CA	TRP	A1782	3.039	38.200	41.452	1.00	21.24	C
ATOM	1093	C	TRP	A1782	2.961	37.904	39.945	1.00	20.76	C
ATOM	1094	O	TRP	A1782	3.822	38.327	39.143	1.00	18.96	O
ATOM	1095	CB	TRP	A1782	3.515	36.973	42.243	1.00	21.65	C
ATOM	1096	CG	TRP	A1782	4.941	36.541	41.916	1.00	23.52	C
ATOM	1097	CD1	TRP	A1782	5.987	37.344	41.526	1.00	25.08	C
ATOM	1098	CD2	TRP	A1782	5.460	35.208	41.972	1.00	23.57	C
ATOM	1099	NE1	TRP	A1782	7.118	36.580	41.329	1.00	25.54	N
ATOM	1100	CE2	TRP	A1782	6.820	35.266	41.599	1.00	23.80	C
ATOM	1101	CE3	TRP	A1782	4.907	33.962	42.302	1.00	24.18	C
ATOM	1102	CZ2	TRP	A1782	7.638	34.122	41.535	1.00	24.52	C
ATOM	1103	CZ3	TRP	A1782	5.723	32.826	42.247	1.00	24.47	C
ATOM	1104	CH2	TRP	A1782	7.067	32.918	41.858	1.00	24.87	C
ATOM	1105	N	MET	A1783	1.910	37.189	39.557	1.00	20.12	N
ATOM	1106	CA	MET	A1783	1.719	36.856	38.156	1.00	21.28	C
ATOM	1107	C	MET	A1783	1.753	38.103	37.272	1.00	21.46	C
ATOM	1108	O	MET	A1783	2.467	38.156	36.259	1.00	22.05	O
ATOM	1109	CB	MET	A1783	0.373	36.142	37.970	1.00	21.69	C
ATOM	1110	CG	MET	A1783	0.220	35.408	36.647	1.00	21.85	C
ATOM	1111	SD	MET	A1783	-1.512	34.881	36.351	1.00	22.73	S
ATOM	1112	CE	MET	A1783	-1.745	33.707	37.731	1.00	22.61	C
ATOM	1113	N	VAL	A1784	0.958	39.103	37.611	1.00	21.18	N
ATOM	1114	CA	VAL	A1784	0.947	40.285	36.755	1.00	21.52	C
ATOM	1115	C	VAL	A1784	2.284	41.013	36.807	1.00	22.09	C
ATOM	1116	O	VAL	A1784	2.729	41.537	35.799	1.00	21.53	O
ATOM	1117	CB	VAL	A1784	-0.276	41.192	37.004	1.00	21.45	C
ATOM	1118	CG1	VAL	A1784	-1.568	40.359	36.842	1.00	21.13	C
ATOM	1119	CG2	VAL	A1784	-0.220	41.862	38.379	1.00	22.13	C
ATOM	1120	N	GLN	A1785	2.948	41.003	37.963	1.00	23.00	N
ATOM	1121	CA	GLN	A1785	4.251	41.649	38.077	1.00	24.82	C
ATOM	1122	C	GLN	A1785	5.294	40.979	37.196	1.00	24.78	C
ATOM	1123	O	GLN	A1785	6.104	41.643	36.540	1.00	24.69	O
ATOM	1124	CB	GLN	A1785	4.741	41.635	39.517	1.00	26.16	C
ATOM	1125	CG	GLN	A1785	4.171	42.738	40.352	1.00	32.52	C
ATOM	1126	CD	GLN	A1785	4.792	42.783	41.733	1.00	37.16	C
ATOM	1127	OE1	GLN	A1785	5.533	43.712	42.055	1.00	41.54	O
ATOM	1128	NE2	GLN	A1785	4.508	41.767	42.546	1.00	41.37	N
ATOM	1129	N	LEU	A1786	5.286	39.658	37.216	1.00	23.87	N
ATOM	1130	CA	LEU	A1786	6.176	38.868	36.384	1.00	23.75	C
ATOM	1131	C	LEU	A1786	5.915	39.218	34.927	1.00	23.54	C
ATOM	1132	O	LEU	A1786	6.806	39.125	34.070	1.00	22.97	O
ATOM	1133	CB	LEU	A1786	5.874	37.391	36.585	1.00	23.20	C
ATOM	1134	CG	LEU	A1786	6.414	36.754	37.873	1.00	23.54	C
ATOM	1135	CD1	LEU	A1786	5.777	35.425	38.059	1.00	24.11	C
ATOM	1136	CD2	LEU	A1786	7.938	36.632	37.805	1.00	24.52	C

ATOM	1137	N	CYS	A1787	4.674	39.602	34.663	1.00	23.42	N
ATOM	1138	CA	CYS	A1787	4.244	39.955	33.309	1.00	23.93	C
ATOM	1139	C	CYS	A1787	4.455	41.436	32.969	1.00	24.40	C
ATOM	1140	O	CYS	A1787	3.934	41.940	31.961	1.00	23.74	O
ATOM	1141	CB	CYS	A1787	2.784	39.549	33.077	1.00	24.32	C
ATOM	1142	SG	CYS	A1787	2.557	37.759	32.865	1.00	24.92	S
ATOM	1143	N	GLY	A1788	5.202	42.136	33.819	1.00	24.77	N
ATOM	1144	CA	GLY	A1788	5.551	43.517	33.535	1.00	24.95	C
ATOM	1145	C	GLY	A1788	4.697	44.588	34.170	1.00	25.18	C
ATOM	1146	O	GLY	A1788	5.039	45.780	34.101	1.00	25.67	O
ATOM	1147	N	ALA	A1789	3.590	44.208	34.805	1.00	25.56	N
ATOM	1148	CA	ALA	A1789	2.741	45.242	35.394	1.00	26.40	C
ATOM	1149	C	ALA	A1789	3.277	45.784	36.709	1.00	27.37	C
ATOM	1150	O	ALA	A1789	4.032	45.112	37.422	1.00	27.03	O
ATOM	1151	CB	ALA	A1789	1.326	44.724	35.606	1.00	26.61	C
ATOM	1152	N	SER	A1790	2.827	46.991	37.034	1.00	27.98	N
ATOM	1153	CA	SER	A1790	3.066	47.591	38.328	1.00	29.61	C
ATOM	1154	C	SER	A1790	1.843	47.255	39.194	1.00	29.23	C
ATOM	1155	O	SER	A1790	0.697	47.460	38.787	1.00	29.69	O
ATOM	1156	CB	SER	A1790	3.250	49.107	38.185	1.00	29.58	C
ATOM	1157	OG	SER	A1790	3.437	49.677	39.464	1.00	35.28	O
ATOM	1158	N	VAL	A1791	2.086	46.689	40.368	1.00	28.99	N
ATOM	1159	CA	VAL	A1791	1.019	46.317	41.279	1.00	29.25	C
ATOM	1160	C	VAL	A1791	0.618	47.514	42.137	1.00	29.63	C
ATOM	1161	O	VAL	A1791	1.466	48.204	42.720	1.00	29.53	O
ATOM	1162	CB	VAL	A1791	1.441	45.133	42.201	1.00	28.68	C
ATOM	1163	CG1	VAL	A1791	0.403	44.903	43.313	1.00	28.69	C
ATOM	1164	CG2	VAL	A1791	1.621	43.862	41.380	1.00	30.13	C
ATOM	1165	N	VAL	A1792	-0.683	47.751	42.202	1.00	29.72	N
ATOM	1166	CA	VAL	A1792	-1.234	48.835	42.994	1.00	30.74	C
ATOM	1167	C	VAL	A1792	-2.142	48.188	44.036	1.00	30.89	C
ATOM	1168	O	VAL	A1792	-2.986	47.378	43.686	1.00	29.79	O
ATOM	1169	CB	VAL	A1792	-2.033	49.793	42.080	1.00	30.90	C
ATOM	1170	CG1	VAL	A1792	-2.978	50.638	42.884	1.00	30.73	C
ATOM	1171	CG2	VAL	A1792	-1.071	50.651	41.236	1.00	31.57	C
ATOM	1172	N	LYS	A1793	-1.970	48.540	45.310	1.00	32.08	N
ATOM	1173	CA	LYS	A1793	-2.735	47.881	46.379	1.00	33.72	C
ATOM	1174	C	LYS	A1793	-4.101	48.496	46.676	1.00	34.33	C
ATOM	1175	O	LYS	A1793	-5.025	47.763	47.014	1.00	35.08	O
ATOM	1176	CB	LYS	A1793	-1.907	47.782	47.669	1.00	34.32	C
ATOM	1177	CG	LYS	A1793	-0.664	46.915	47.555	1.00	36.55	C
ATOM	1178	CD	LYS	A1793	-1.003	45.423	47.603	1.00	40.35	C
ATOM	1179	CE	LYS	A1793	0.256	44.557	47.500	1.00	42.72	C
ATOM	1180	NZ	LYS	A1793	1.199	44.732	48.633	1.00	44.75	N
ATOM	1181	N	GLU	A1794	-4.241	49.819	46.575	1.00	34.78	N
ATOM	1182	CA	GLU	A1794	-5.551	50.454	46.822	1.00	35.65	C
ATOM	1183	C	GLU	A1794	-6.058	51.230	45.606	1.00	34.89	C
ATOM	1184	O	GLU	A1794	-5.267	51.766	44.832	1.00	34.81	O
ATOM	1185	CB	GLU	A1794	-5.500	51.404	48.031	1.00	36.31	C
ATOM	1186	CG	GLU	A1794	-4.507	51.007	49.112	1.00	40.43	C
ATOM	1187	CD	GLU	A1794	-4.908	51.476	50.498	1.00	46.67	C
ATOM	1188	OE1	GLU	A1794	-6.117	51.717	50.739	1.00	49.99	O
ATOM	1189	OE2	GLU	A1794	-4.009	51.585	51.363	1.00	50.69	O
ATOM	1190	N	LEU	A1795	-7.379	51.282	45.436	1.00	34.55	N
ATOM	1191	CA	LEU	A1795	-7.967	52.058	44.341	1.00	34.48	C

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ATOM   1192  C   LEU A1795     -7.456  53.514  44.319  1.00 34.20           C
ATOM   1193  O   LEU A1795     -7.067  54.025  43.275  1.00 34.82           O
ATOM   1194  CB  LEU A1795     -9.496  52.035  44.407  1.00 34.12           C
ATOM   1195  CG  LEU A1795    -10.092  50.631  44.290  1.00 34.35           C
ATOM   1196  CD1 LEU A1795    -11.634  50.609  44.319  1.00 34.41           C
ATOM   1197  CD2 LEU A1795     -9.568  49.911  43.045  1.00 33.04           C
ATOM   1198  N   SER A1796     -7.451  54.170  45.473  1.00 33.85           N
ATOM   1199  CA  SER A1796     -7.001  55.556  45.569  1.00 33.64           C
ATOM   1200  C   SER A1796     -5.520  55.749  45.220  1.00 33.01           C
ATOM   1201  O   SER A1796     -5.047  56.882  45.132  1.00 33.00           O
ATOM   1202  CB  SER A1796     -7.258  56.091  46.982  1.00 33.48           C
ATOM   1203  OG  SER A1796     -6.701  55.215  47.955  1.00 34.78           O
ATOM   1204  N   SER A1797     -4.797  54.651  45.007  1.00 32.29           N
ATOM   1205  CA  SER A1797     -3.349  54.710  44.783  1.00 31.84           C
ATOM   1206  C   SER A1797     -2.869  54.603  43.337  1.00 30.36           C
ATOM   1207  O   SER A1797     -1.666  54.496  43.095  1.00 30.34           O
ATOM   1208  CB  SER A1797     -2.643  53.634  45.610  1.00 32.61           C
ATOM   1209  OG  SER A1797     -2.594  53.987  46.976  1.00 35.22           O
ATOM   1210  N   PHE A1798     -3.787  54.584  42.382  1.00 29.13           N
ATOM   1211  CA  PHE A1798     -3.377  54.544  40.981  1.00 28.27           C
ATOM   1212  C   PHE A1798     -2.633  55.840  40.680  1.00 27.54           C
ATOM   1213  O   PHE A1798     -3.023  56.917  41.142  1.00 26.96           O
ATOM   1214  CB  PHE A1798     -4.591  54.468  40.047  1.00 27.93           C
ATOM   1215  CG  PHE A1798     -5.142  53.089  39.864  1.00 28.24           C
ATOM   1216  CD1 PHE A1798     -6.488  52.829  40.113  1.00 28.79           C
ATOM   1217  CD2 PHE A1798     -4.327  52.048  39.430  1.00 28.00           C
ATOM   1218  CE1 PHE A1798     -7.017  51.554  39.924  1.00 28.17           C
ATOM   1219  CE2 PHE A1798     -4.850  50.775  39.238  1.00 28.78           C
ATOM   1220  CZ  PHE A1798     -6.194  50.525  39.494  1.00 28.31           C
ATOM   1221  N   THR A1799     -1.560  55.726  39.909  1.00 26.11           N
ATOM   1222  CA  THR A1799     -0.850  56.889  39.435  1.00 25.21           C
ATOM   1223  C   THR A1799     -1.724  57.611  38.436  1.00 24.62           C
ATOM   1224  O   THR A1799     -2.408  56.974  37.639  1.00 24.51           O
ATOM   1225  CB  THR A1799      0.388  56.432  38.701  1.00 25.30           C
ATOM   1226  OG1 THR A1799      1.172  55.607  39.573  1.00 24.19           O
ATOM   1227  CG2 THR A1799      1.275  57.623  38.340  1.00 26.71           C
ATOM   1228  N   LEU A1800     -1.683  58.935  38.438  1.00 23.91           N
ATOM   1229  CA  LEU A1800     -2.497  59.685  37.475  1.00 24.00           C
ATOM   1230  C   LEU A1800     -1.670  60.194  36.303  1.00 23.62           C
ATOM   1231  O   LEU A1800     -0.476  60.390  36.425  1.00 23.32           O
ATOM   1232  CB  LEU A1800     -3.176  60.875  38.168  1.00 23.94           C
ATOM   1233  CG  LEU A1800     -4.104  60.525  39.327  1.00 25.45           C
ATOM   1234  CD1 LEU A1800     -4.663  61.829  39.955  1.00 28.64           C
ATOM   1235  CD2 LEU A1800     -5.234  59.638  38.820  1.00 26.80           C
ATOM   1236  N   GLY A1801     -2.314  60.437  35.168  1.00 23.19           N
ATOM   1237  CA  GLY A1801     -1.583  60.954  34.032  1.00 25.22           C
ATOM   1238  C   GLY A1801     -2.114  60.320  32.769  1.00 25.49           C
ATOM   1239  O   GLY A1801     -2.629  59.212  32.788  1.00 26.11           O
ATOM   1240  N   THR A1802     -2.058  61.079  31.681  1.00 26.23           N
ATOM   1241  CA  THR A1802     -2.548  60.612  30.398  1.00 26.84           C
ATOM   1242  C   THR A1802     -1.744  59.425  29.910  1.00 27.25           C
ATOM   1243  O   THR A1802     -2.208  58.689  29.055  1.00 28.30           O
ATOM   1244  CB  THR A1802     -2.467  61.743  29.352  1.00 27.62           C
ATOM   1245  OG1 THR A1802     -1.089  61.967  28.999  1.00 28.27           O
ATOM   1246  CG2 THR A1802     -2.883  63.061  29.977  1.00 25.34           C
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ATOM	1247	N	GLY	A1803	-0.545	59.229	30.446	1.00	27.35	N
ATOM	1248	CA	GLY	A1803	0.317	58.148	30.007	1.00	28.09	C
ATOM	1249	C	GLY	A1803	0.191	56.888	30.834	1.00	27.92	C
ATOM	1250	O	GLY	A1803	0.850	55.874	30.567	1.00	28.48	O
ATOM	1251	N	VAL	A1804	-0.658	56.955	31.852	1.00	27.70	N
ATOM	1252	CA	VAL	A1804	-0.867	55.827	32.741	1.00	27.47	C
ATOM	1253	C	VAL	A1804	-2.065	55.016	32.288	1.00	27.67	C
ATOM	1254	O	VAL	A1804	-3.061	55.587	31.808	1.00	27.02	O
ATOM	1255	CB	VAL	A1804	-1.120	56.308	34.169	1.00	27.03	C
ATOM	1256	CG1	VAL	A1804	-1.325	55.108	35.098	1.00	28.08	C
ATOM	1257	CG2	VAL	A1804	0.052	57.178	34.650	1.00	27.40	C
ATOM	1258	N	HIS	A1805	-1.960	53.690	32.434	1.00	26.47	N
ATOM	1259	CA	HIS	A1805	-3.069	52.823	32.090	1.00	27.22	C
ATOM	1260	C	HIS	A1805	-3.413	51.972	33.303	1.00	26.98	C
ATOM	1261	O	HIS	A1805	-2.804	50.919	33.522	1.00	27.22	O
ATOM	1262	CB	HIS	A1805	-2.675	51.931	30.906	1.00	27.66	C
ATOM	1263	CG	HIS	A1805	-2.300	52.702	29.677	1.00	30.66	C
ATOM	1264	ND1	HIS	A1805	-1.015	53.135	29.433	1.00	33.02	N
ATOM	1265	CD2	HIS	A1805	-3.052	53.155	28.647	1.00	32.98	C
ATOM	1266	CE1	HIS	A1805	-0.990	53.808	28.295	1.00	34.99	C
ATOM	1267	NE2	HIS	A1805	-2.213	53.839	27.801	1.00	33.22	N
ATOM	1268	N	PRO	A1806	-4.364	52.431	34.106	1.00	27.41	N
ATOM	1269	CA	PRO	A1806	-4.797	51.696	35.297	1.00	27.21	C
ATOM	1270	C	PRO	A1806	-5.858	50.685	34.919	1.00	26.94	C
ATOM	1271	O	PRO	A1806	-6.607	50.909	33.976	1.00	26.42	O
ATOM	1272	CB	PRO	A1806	-5.410	52.787	36.169	1.00	27.64	C
ATOM	1273	CG	PRO	A1806	-5.967	53.792	35.167	1.00	27.46	C
ATOM	1274	CD	PRO	A1806	-5.092	53.711	33.947	1.00	28.06	C
ATOM	1275	N	ILE	A1807	-5.886	49.559	35.617	1.00	26.23	N
ATOM	1276	CA	ILE	A1807	-6.886	48.527	35.358	1.00	26.34	C
ATOM	1277	C	ILE	A1807	-7.214	47.876	36.675	1.00	25.82	C
ATOM	1278	O	ILE	A1807	-6.318	47.535	37.437	1.00	26.03	O
ATOM	1279	CB	ILE	A1807	-6.350	47.434	34.411	1.00	26.45	C
ATOM	1280	CG1	ILE	A1807	-5.870	48.039	33.090	1.00	27.84	C
ATOM	1281	CG2	ILE	A1807	-7.435	46.373	34.164	1.00	26.41	C
ATOM	1282	CD1	ILE	A1807	-5.146	47.047	32.202	1.00	30.14	C
ATOM	1283	N	VAL	A1808	-8.494	47.710	36.949	1.00	25.46	N
ATOM	1284	CA	VAL	A1808	-8.921	47.035	38.156	1.00	25.00	C
ATOM	1285	C	VAL	A1808	-9.364	45.636	37.775	1.00	24.67	C
ATOM	1286	O	VAL	A1808	-10.184	45.449	36.864	1.00	24.19	O
ATOM	1287	CB	VAL	A1808	-10.085	47.765	38.830	1.00	25.12	C
ATOM	1288	CG1	VAL	A1808	-10.517	47.022	40.109	1.00	24.18	C
ATOM	1289	CG2	VAL	A1808	-9.692	49.214	39.121	1.00	25.14	C
ATOM	1290	N	VAL	A1809	-8.785	44.647	38.440	1.00	24.13	N
ATOM	1291	CA	VAL	A1809	-9.157	43.267	38.201	1.00	24.25	C
ATOM	1292	C	VAL	A1809	-9.965	42.697	39.381	1.00	24.70	C
ATOM	1293	O	VAL	A1809	-9.548	42.788	40.544	1.00	25.01	O
ATOM	1294	CB	VAL	A1809	-7.905	42.393	37.933	1.00	24.82	C
ATOM	1295	CG1	VAL	A1809	-8.283	40.922	37.783	1.00	23.99	C
ATOM	1296	CG2	VAL	A1809	-7.173	42.872	36.670	1.00	22.98	C
ATOM	1297	N	VAL	A1810	-11.108	42.091	39.068	1.00	25.04	N
ATOM	1298	CA	VAL	A1810	-11.971	41.467	40.068	1.00	25.87	C
ATOM	1299	C	VAL	A1810	-12.497	40.127	39.563	1.00	26.59	C
ATOM	1300	O	VAL	A1810	-12.390	39.811	38.366	1.00	26.21	O
ATOM	1301	CB	VAL	A1810	-13.208	42.337	40.406	1.00	25.71	C

ATOM	1302	CG1	VAL	A1810	-12.789	43.700	40.838	1.00	25.83	C
ATOM	1303	CG2	VAL	A1810	-14.110	42.434	39.204	1.00	27.95	C
ATOM	1304	N	GLN	A1811	-13.042	39.337	40.488	1.00	26.75	N
ATOM	1305	CA	GLN	A1811	-13.658	38.056	40.160	1.00	28.19	C
ATOM	1306	C	GLN	A1811	-15.092	38.105	40.680	1.00	29.04	C
ATOM	1307	O	GLN	A1811	-15.350	37.813	41.849	1.00	28.88	O
ATOM	1308	CB	GLN	A1811	-12.896	36.913	40.834	1.00	27.91	C
ATOM	1309	CG	GLN	A1811	-13.440	35.522	40.535	1.00	26.85	C
ATOM	1310	CD	GLN	A1811	-12.854	34.485	41.485	1.00	27.47	C
ATOM	1311	OE1	GLN	A1811	-11.860	34.757	42.156	1.00	25.51	O
ATOM	1312	NE2	GLN	A1811	-13.458	33.312	41.539	1.00	25.63	N
ATOM	1313	N	PRO	A1812	-16.022	38.501	39.818	1.00	30.07	N
ATOM	1314	CA	PRO	A1812	-17.416	38.692	40.224	1.00	31.43	C
ATOM	1315	C	PRO	A1812	-17.999	37.514	40.991	1.00	32.81	C
ATOM	1316	O	PRO	A1812	-18.689	37.768	41.967	1.00	33.02	O
ATOM	1317	CB	PRO	A1812	-18.153	38.900	38.885	1.00	31.51	C
ATOM	1318	CG	PRO	A1812	-17.111	39.486	37.985	1.00	30.64	C
ATOM	1319	CD	PRO	A1812	-15.808	38.797	38.395	1.00	30.23	C
ATOM	1320	N	ASP	A1813	-17.732	36.275	40.587	1.00	34.65	N
ATOM	1321	CA	ASP	A1813	-18.266	35.115	41.314	1.00	37.52	C
ATOM	1322	C	ASP	A1813	-17.906	35.103	42.795	1.00	38.34	C
ATOM	1323	O	ASP	A1813	-18.681	34.615	43.621	1.00	38.74	O
ATOM	1324	CB	ASP	A1813	-17.768	33.795	40.711	1.00	38.37	C
ATOM	1325	CG	ASP	A1813	-18.495	33.417	39.460	1.00	41.51	C
ATOM	1326	OD1	ASP	A1813	-19.430	34.150	39.052	1.00	46.44	O
ATOM	1327	OD2	ASP	A1813	-18.197	32.396	38.809	1.00	46.11	O
ATOM	1328	N	ALA	A1814	-16.727	35.633	43.120	1.00	39.38	N
ATOM	1329	CA	ALA	A1814	-16.216	35.648	44.485	1.00	40.56	C
ATOM	1330	C	ALA	A1814	-17.056	36.514	45.413	1.00	41.84	C
ATOM	1331	O	ALA	A1814	-17.077	36.292	46.620	1.00	41.65	O
ATOM	1332	CB	ALA	A1814	-14.767	36.106	44.499	1.00	40.28	C
ATOM	1333	N	TRP	A1815	-17.734	37.509	44.849	1.00	43.50	N
ATOM	1334	CA	TRP	A1815	-18.610	38.368	45.632	1.00	45.71	C
ATOM	1335	C	TRP	A1815	-20.000	37.745	45.670	1.00	47.78	C
ATOM	1336	O	TRP	A1815	-20.353	36.930	44.810	1.00	48.50	O
ATOM	1337	CB	TRP	A1815	-18.749	39.754	44.988	1.00	44.99	C
ATOM	1338	CG	TRP	A1815	-17.475	40.465	44.624	1.00	43.59	C
ATOM	1339	CD1	TRP	A1815	-16.396	39.948	43.967	1.00	41.97	C
ATOM	1340	CD2	TRP	A1815	-17.168	41.847	44.864	1.00	43.30	C
ATOM	1341	NE1	TRP	A1815	-15.432	40.915	43.805	1.00	41.30	N
ATOM	1342	CE2	TRP	A1815	-15.881	42.090	44.344	1.00	41.67	C
ATOM	1343	CE3	TRP	A1815	-17.850	42.903	45.477	1.00	43.55	C
ATOM	1344	CZ2	TRP	A1815	-15.263	43.335	44.415	1.00	43.03	C
ATOM	1345	CZ3	TRP	A1815	-17.224	44.158	45.547	1.00	44.60	C
ATOM	1346	CH2	TRP	A1815	-15.946	44.356	45.017	1.00	43.32	C
ATOM	1347	N	THR	A1816	-20.796	38.132	46.659	1.00	50.54	N
ATOM	1348	CA	THR	A1816	-22.199	37.721	46.655	1.00	53.50	C
ATOM	1349	C	THR	A1816	-23.074	38.657	47.466	1.00	54.65	C
ATOM	1350	O	THR	A1816	-22.762	38.981	48.617	1.00	55.39	O
ATOM	1351	CB	THR	A1816	-22.398	36.255	47.066	1.00	53.69	C
ATOM	1352	OG1	THR	A1816	-21.946	35.405	46.004	1.00	55.36	O
ATOM	1353	CG2	THR	A1816	-23.899	35.927	47.141	1.00	54.88	C
ATOM	1354	N	GLU	A1817	-24.170	39.085	46.840	1.00	56.17	N
ATOM	1355	CA	GLU	A1817	-25.099	40.042	47.432	1.00	57.11	C
ATOM	1356	C	GLU	A1817	-24.331	41.344	47.508	1.00	57.59	C

ATOM	1357	O	GLU	A1817	-24.725	42.301	48.181	1.00	58.16	O
ATOM	1358	CB	GLU	A1817	-25.547	39.586	48.817	1.00	57.35	C
ATOM	1359	N	ASP	A1818	-23.211	41.351	46.796	1.00	57.81	N
ATOM	1360	CA	ASP	A1818	-22.324	42.498	46.744	1.00	57.64	C
ATOM	1361	C	ASP	A1818	-22.179	42.973	45.306	1.00	57.34	C
ATOM	1362	O	ASP	A1818	-21.088	42.909	44.731	1.00	57.73	O
ATOM	1363	CB	ASP	A1818	-20.965	42.131	47.324	1.00	58.02	C
ATOM	1364	N	ASN	A1819	-23.281	43.441	44.723	1.00	56.41	N
ATOM	1365	CA	ASN	A1819	-23.259	43.998	43.372	1.00	55.19	C
ATOM	1366	C	ASN	A1819	-22.342	45.215	43.412	1.00	54.27	C
ATOM	1367	O	ASN	A1819	-22.476	46.161	42.629	1.00	54.46	O
ATOM	1368	CB	ASN	A1819	-24.650	44.397	42.941	1.00	55.53	C
ATOM	1369	N	GLY	A1820	-21.402	45.158	44.349	1.00	52.76	N
ATOM	1370	CA	GLY	A1820	-20.465	46.230	44.593	1.00	50.77	C
ATOM	1371	C	GLY	A1820	-19.363	46.312	43.570	1.00	49.40	C
ATOM	1372	O	GLY	A1820	-18.653	47.306	43.551	1.00	49.11	O
ATOM	1373	N	PHE	A1821	-19.208	45.288	42.730	1.00	48.28	N
ATOM	1374	CA	PHE	A1821	-18.168	45.353	41.699	1.00	47.40	C
ATOM	1375	C	PHE	A1821	-18.549	46.301	40.563	1.00	46.77	C
ATOM	1376	O	PHE	A1821	-17.719	46.637	39.721	1.00	46.49	O
ATOM	1377	CB	PHE	A1821	-17.703	43.975	41.190	1.00	47.19	C
ATOM	1378	CG	PHE	A1821	-18.806	43.063	40.718	1.00	46.88	C
ATOM	1379	CD1	PHE	A1821	-19.226	43.075	39.398	1.00	46.67	C
ATOM	1380	CD2	PHE	A1821	-19.378	42.150	41.581	1.00	46.60	C
ATOM	1381	CE1	PHE	A1821	-20.223	42.217	38.957	1.00	46.24	C
ATOM	1382	CE2	PHE	A1821	-20.377	41.286	41.144	1.00	47.04	C
ATOM	1383	CZ	PHE	A1821	-20.798	41.322	39.830	1.00	46.52	C
ATOM	1384	N	HIS	A1822	-19.806	46.737	40.564	1.00	46.27	N
ATOM	1385	CA	HIS	A1822	-20.294	47.691	39.573	1.00	45.79	C
ATOM	1386	C	HIS	A1822	-20.103	49.119	40.075	1.00	45.74	C
ATOM	1387	O	HIS	A1822	-20.285	50.078	39.326	1.00	45.39	O
ATOM	1388	CB	HIS	A1822	-21.783	47.463	39.284	1.00	45.65	C
ATOM	1389	CG	HIS	A1822	-22.080	46.180	38.575	1.00	45.31	C
ATOM	1390	ND1	HIS	A1822	-21.830	45.996	37.233	1.00	45.05	N
ATOM	1391	CD2	HIS	A1822	-22.609	45.016	39.021	1.00	44.73	C
ATOM	1392	CE1	HIS	A1822	-22.191	44.775	36.883	1.00	43.91	C
ATOM	1393	NE2	HIS	A1822	-22.667	44.160	37.949	1.00	44.25	N
ATOM	1394	N	ALA	A1823	-19.730	49.254	41.343	1.00	45.52	N
ATOM	1395	CA	ALA	A1823	-19.566	50.564	41.965	1.00	45.73	C
ATOM	1396	C	ALA	A1823	-18.110	50.992	42.155	1.00	45.82	C
ATOM	1397	O	ALA	A1823	-17.825	51.958	42.868	1.00	45.86	O
ATOM	1398	CB	ALA	A1823	-20.287	50.592	43.296	1.00	45.70	C
ATOM	1399	N	ILE	A1824	-17.188	50.276	41.523	1.00	45.79	N
ATOM	1400	CA	ILE	A1824	-15.773	50.582	41.662	1.00	45.67	C
ATOM	1401	C	ILE	A1824	-15.384	51.862	40.934	1.00	46.07	C
ATOM	1402	O	ILE	A1824	-14.558	52.634	41.418	1.00	45.72	O
ATOM	1403	CB	ILE	A1824	-14.929	49.395	41.174	1.00	45.63	C
ATOM	1404	CG1	ILE	A1824	-15.073	48.222	42.146	1.00	44.55	C
ATOM	1405	CG2	ILE	A1824	-13.470	49.799	41.043	1.00	45.22	C
ATOM	1406	CD1	ILE	A1824	-14.753	46.890	41.537	1.00	44.07	C
ATOM	1407	N	GLY	A1825	-15.992	52.089	39.774	1.00	46.76	N
ATOM	1408	CA	GLY	A1825	-15.716	53.285	38.995	1.00	47.76	C
ATOM	1409	C	GLY	A1825	-16.014	54.561	39.762	1.00	48.36	C
ATOM	1410	O	GLY	A1825	-15.454	55.619	39.475	1.00	48.85	O
ATOM	1411	N	GLN	A1826	-16.895	54.466	40.749	1.00	48.91	N

ATOM	1412	CA	GLN	A1826	-17.243	55.624	41.566	1.00	49.49	C
ATOM	1413	C	GLN	A1826	-16.095	55.971	42.498	1.00	49.02	C
ATOM	1414	O	GLN	A1826	-16.036	57.074	43.029	1.00	49.38	O
ATOM	1415	CB	GLN	A1826	-18.514	55.357	42.382	1.00	49.97	C
ATOM	1416	CG	GLN	A1826	-19.808	55.529	41.598	1.00	51.43	C
ATOM	1417	CD	GLN	A1826	-21.046	55.153	42.403	1.00	54.36	C
ATOM	1418	OE1	GLN	A1826	-20.961	54.399	43.375	1.00	54.97	O
ATOM	1419	NE2	GLN	A1826	-22.198	55.679	41.999	1.00	55.74	N
ATOM	1420	N	MET	A1827	-15.181	55.027	42.695	1.00	48.40	N
ATOM	1421	CA	MET	A1827	-14.037	55.266	43.562	1.00	47.67	C
ATOM	1422	C	MET	A1827	-12.786	55.602	42.761	1.00	46.70	C
ATOM	1423	O	MET	A1827	-11.827	56.145	43.306	1.00	47.08	O
ATOM	1424	CB	MET	A1827	-13.779	54.061	44.476	1.00	48.21	C
ATOM	1425	CG	MET	A1827	-14.996	53.626	45.308	1.00	49.52	C
ATOM	1426	SD	MET	A1827	-14.722	52.190	46.386	1.00	53.09	S
ATOM	1427	CE	MET	A1827	-13.316	52.736	47.333	1.00	51.51	C
ATOM	1428	N	CYS	A1828	-12.784	55.283	41.472	1.00	44.88	N
ATOM	1429	CA	CYS	A1828	-11.607	55.549	40.654	1.00	43.41	C
ATOM	1430	C	CYS	A1828	-11.936	55.581	39.173	1.00	42.27	C
ATOM	1431	O	CYS	A1828	-12.995	55.135	38.760	1.00	42.44	O
ATOM	1432	CB	CYS	A1828	-10.526	54.494	40.913	1.00	43.25	C
ATOM	1433	SG	CYS	A1828	-10.936	52.881	40.228	1.00	41.86	S
ATOM	1434	N	GLU	A1829	-11.012	56.099	38.375	1.00	41.35	N
ATOM	1435	CA	GLU	A1829	-11.222	56.159	36.937	1.00	40.53	C
ATOM	1436	C	GLU	A1829	-10.322	55.150	36.238	1.00	38.88	C
ATOM	1437	O	GLU	A1829	-9.191	55.463	35.880	1.00	38.27	O
ATOM	1438	CB	GLU	A1829	-10.960	57.575	36.409	1.00	41.17	C
ATOM	1439	CG	GLU	A1829	-12.014	58.066	35.424	1.00	44.69	C
ATOM	1440	CD	GLU	A1829	-13.408	58.125	36.030	1.00	48.74	C
ATOM	1441	OE1	GLU	A1829	-13.788	59.192	36.582	1.00	50.05	O
ATOM	1442	OE2	GLU	A1829	-14.139	57.107	35.949	1.00	52.23	O
ATOM	1443	N	ALA	A1830	-10.832	53.935	36.057	1.00	36.81	N
ATOM	1444	CA	ALA	A1830	-10.075	52.873	35.405	1.00	35.20	C
ATOM	1445	C	ALA	A1830	-11.043	51.817	34.936	1.00	33.76	C
ATOM	1446	O	ALA	A1830	-12.043	51.585	35.593	1.00	33.71	O
ATOM	1447	CB	ALA	A1830	-9.087	52.253	36.383	1.00	34.53	C
ATOM	1448	N	PRO	A1831	-10.739	51.139	33.837	1.00	32.71	N
ATOM	1449	CA	PRO	A1831	-11.636	50.086	33.365	1.00	31.65	C
ATOM	1450	C	PRO	A1831	-11.636	48.991	34.425	1.00	30.62	C
ATOM	1451	O	PRO	A1831	-10.646	48.837	35.143	1.00	30.23	O
ATOM	1452	CB	PRO	A1831	-10.972	49.572	32.083	1.00	31.65	C
ATOM	1453	CG	PRO	A1831	-9.751	50.394	31.844	1.00	33.18	C
ATOM	1454	CD	PRO	A1831	-9.529	51.288	33.013	1.00	32.76	C
ATOM	1455	N	VAL	A1832	-12.739	48.267	34.551	1.00	29.96	N
ATOM	1456	CA	VAL	A1832	-12.818	47.182	35.512	1.00	28.63	C
ATOM	1457	C	VAL	A1832	-13.037	45.900	34.724	1.00	28.14	C
ATOM	1458	O	VAL	A1832	-13.941	45.812	33.901	1.00	27.69	O
ATOM	1459	CB	VAL	A1832	-13.948	47.404	36.528	1.00	28.72	C
ATOM	1460	CG1	VAL	A1832	-14.007	46.244	37.501	1.00	28.25	C
ATOM	1461	CG2	VAL	A1832	-13.729	48.702	37.291	1.00	28.99	C
ATOM	1462	N	VAL	A1833	-12.189	44.910	34.960	1.00	26.86	N
ATOM	1463	CA	VAL	A1833	-12.252	43.685	34.192	1.00	26.03	C
ATOM	1464	C	VAL	A1833	-12.229	42.492	35.112	1.00	26.16	C
ATOM	1465	O	VAL	A1833	-11.826	42.601	36.285	1.00	25.71	O
ATOM	1466	CB	VAL	A1833	-11.054	43.581	33.208	1.00	26.25	C

ATOM	1467	CG1	VAL	A1833	-10.997	44.824	32.319	1.00	26.83	C
ATOM	1468	CG2	VAL	A1833	-9.746	43.421	33.962	1.00	25.18	C
ATOM	1469	N	THR	A1834	-12.648	41.352	34.571	1.00	25.65	N
ATOM	1470	CA	THR	A1834	-12.643	40.118	35.330	1.00	25.41	C
ATOM	1471	C	THR	A1834	-11.238	39.535	35.366	1.00	24.80	C
ATOM	1472	O	THR	A1834	-10.394	39.834	34.528	1.00	23.67	O
ATOM	1473	CB	THR	A1834	-13.584	39.050	34.724	1.00	25.08	C
ATOM	1474	OG1	THR	A1834	-13.091	38.637	33.441	1.00	25.48	O
ATOM	1475	CG2	THR	A1834	-14.990	39.602	34.441	1.00	28.02	C
ATOM	1476	N	ARG	A1835	-11.032	38.628	36.307	1.00	24.05	N
ATOM	1477	CA	ARG	A1835	-9.751	37.969	36.450	1.00	23.05	C
ATOM	1478	C	ARG	A1835	-9.403	37.147	35.202	1.00	22.67	C
ATOM	1479	O	ARG	A1835	-8.228	36.913	34.910	1.00	21.59	O
ATOM	1480	CB	ARG	A1835	-9.756	37.116	37.726	1.00	22.89	C
ATOM	1481	CG	ARG	A1835	-8.406	36.494	38.042	1.00	22.82	C
ATOM	1482	CD	ARG	A1835	-8.424	35.599	39.261	1.00	22.87	C
ATOM	1483	NE	ARG	A1835	-9.321	34.457	39.089	1.00	25.40	N
ATOM	1484	CZ	ARG	A1835	-9.597	33.592	40.052	1.00	26.53	C
ATOM	1485	NH1	ARG	A1835	-9.058	33.744	41.259	1.00	27.23	N
ATOM	1486	NH2	ARG	A1835	-10.417	32.580	39.815	1.00	26.16	N
ATOM	1487	N	GLU	A1836	-10.423	36.756	34.441	1.00	22.79	N
ATOM	1488	CA	GLU	A1836	-10.205	36.019	33.195	1.00	23.13	C
ATOM	1489	C	GLU	A1836	-9.402	36.833	32.171	1.00	22.88	C
ATOM	1490	O	GLU	A1836	-8.769	36.256	31.288	1.00	21.70	O
ATOM	1491	CB	GLU	A1836	-11.532	35.565	32.576	1.00	24.07	C
ATOM	1492	CG	GLU	A1836	-12.172	34.356	33.248	1.00	24.34	C
ATOM	1493	CD	GLU	A1836	-11.223	33.154	33.404	1.00	24.86	C
ATOM	1494	OE1	GLU	A1836	-10.656	32.651	32.404	1.00	24.86	O
ATOM	1495	OE2	GLU	A1836	-11.052	32.696	34.549	1.00	24.82	O
ATOM	1496	N	TRP	A1837	-9.454	38.166	32.266	1.00	23.05	N
ATOM	1497	CA	TRP	A1837	-8.649	39.011	31.379	1.00	22.56	C
ATOM	1498	C	TRP	A1837	-7.191	38.684	31.664	1.00	22.15	C
ATOM	1499	O	TRP	A1837	-6.398	38.493	30.756	1.00	21.97	O
ATOM	1500	CB	TRP	A1837	-8.866	40.520	31.577	1.00	22.90	C
ATOM	1501	CG	TRP	A1837	-7.804	41.318	30.821	1.00	23.50	C
ATOM	1502	CD1	TRP	A1837	-7.695	41.457	29.471	1.00	24.18	C
ATOM	1503	CD2	TRP	A1837	-6.681	42.014	31.380	1.00	23.99	C
ATOM	1504	NE1	TRP	A1837	-6.581	42.202	29.155	1.00	24.02	N
ATOM	1505	CE2	TRP	A1837	-5.948	42.565	30.310	1.00	25.57	C
ATOM	1506	CE3	TRP	A1837	-6.234	42.253	32.683	1.00	24.91	C
ATOM	1507	CZ2	TRP	A1837	-4.796	43.333	30.500	1.00	24.16	C
ATOM	1508	CZ3	TRP	A1837	-5.088	43.009	32.869	1.00	23.43	C
ATOM	1509	CH2	TRP	A1837	-4.387	43.544	31.783	1.00	25.83	C
ATOM	1510	N	VAL	A1838	-6.837	38.678	32.940	1.00	22.17	N
ATOM	1511	CA	VAL	A1838	-5.480	38.277	33.300	1.00	21.29	C
ATOM	1512	C	VAL	A1838	-5.183	36.839	32.894	1.00	21.91	C
ATOM	1513	O	VAL	A1838	-4.190	36.571	32.202	1.00	21.90	O
ATOM	1514	CB	VAL	A1838	-5.204	38.421	34.802	1.00	21.57	C
ATOM	1515	CG1	VAL	A1838	-3.828	37.911	35.117	1.00	19.05	C
ATOM	1516	CG2	VAL	A1838	-5.381	39.879	35.267	1.00	21.21	C
ATOM	1517	N	LEU	A1839	-6.009	35.886	33.329	1.00	21.21	N
ATOM	1518	CA	LEU	A1839	-5.729	34.473	33.037	1.00	21.35	C
ATOM	1519	C	LEU	A1839	-5.598	34.144	31.540	1.00	21.35	C
ATOM	1520	O	LEU	A1839	-4.640	33.487	31.136	1.00	20.77	O
ATOM	1521	CB	LEU	A1839	-6.679	33.510	33.778	1.00	21.33	C

ATOM	1522	CG	LEU	A1839	-6.766	33.796	35.290	1.00	21.58	C
ATOM	1523	CD1	LEU	A1839	-7.698	32.787	35.975	1.00	21.78	C
ATOM	1524	CD2	LEU	A1839	-5.377	33.770	35.933	1.00	22.19	C
ATOM	1525	N	ASP	A1840	-6.524	34.620	30.709	1.00	21.59	N
ATOM	1526	CA	ASP	A1840	-6.397	34.364	29.280	1.00	21.84	C
ATOM	1527	C	ASP	A1840	-5.147	35.017	28.690	1.00	22.13	C
ATOM	1528	O	ASP	A1840	-4.446	34.414	27.876	1.00	22.50	O
ATOM	1529	CB	ASP	A1840	-7.605	34.907	28.528	1.00	23.14	C
ATOM	1530	CG	ASP	A1840	-8.875	34.143	28.824	1.00	22.65	C
ATOM	1531	OD1	ASP	A1840	-8.815	33.085	29.483	1.00	22.05	O
ATOM	1532	OD2	ASP	A1840	-9.997	34.564	28.444	1.00	24.79	O
ATOM	1533	N	SER	A1841	-4.878	36.254	29.082	1.00	21.76	N
ATOM	1534	CA	SER	A1841	-3.714	36.959	28.554	1.00	21.52	C
ATOM	1535	C	SER	A1841	-2.415	36.230	28.858	1.00	21.64	C
ATOM	1536	O	SER	A1841	-1.554	36.088	28.008	1.00	21.52	O
ATOM	1537	CB	SER	A1841	-3.650	38.381	29.105	1.00	22.07	C
ATOM	1538	OG	SER	A1841	-4.682	39.186	28.552	1.00	23.47	O
ATOM	1539	N	VAL	A1842	-2.288	35.756	30.084	1.00	20.65	N
ATOM	1540	CA	VAL	A1842	-1.084	35.041	30.486	1.00	20.95	C
ATOM	1541	C	VAL	A1842	-0.908	33.697	29.736	1.00	21.41	C
ATOM	1542	O	VAL	A1842	0.141	33.433	29.151	1.00	22.02	O
ATOM	1543	CB	VAL	A1842	-1.080	34.861	32.003	1.00	20.46	C
ATOM	1544	CG1	VAL	A1842	-0.040	33.761	32.413	1.00	20.51	C
ATOM	1545	CG2	VAL	A1842	-0.827	36.196	32.703	1.00	20.42	C
ATOM	1546	N	ALA	A1843	-1.938	32.859	29.725	1.00	21.20	N
ATOM	1547	CA	ALA	A1843	-1.867	31.560	29.054	1.00	21.99	C
ATOM	1548	C	ALA	A1843	-1.459	31.705	27.595	1.00	22.35	C
ATOM	1549	O	ALA	A1843	-0.686	30.909	27.074	1.00	22.74	O
ATOM	1550	CB	ALA	A1843	-3.227	30.822	29.140	1.00	20.95	C
ATOM	1551	N	LEU	A1844	-2.018	32.702	26.922	1.00	23.32	N
ATOM	1552	CA	LEU	A1844	-1.696	32.943	25.510	1.00	23.68	C
ATOM	1553	C	LEU	A1844	-0.421	33.759	25.346	1.00	24.51	C
ATOM	1554	O	LEU	A1844	0.091	33.894	24.231	1.00	24.87	O
ATOM	1555	CB	LEU	A1844	-2.830	33.742	24.871	1.00	23.66	C
ATOM	1556	CG	LEU	A1844	-4.200	33.049	24.826	1.00	22.84	C
ATOM	1557	CD1	LEU	A1844	-5.296	34.093	24.558	1.00	24.05	C
ATOM	1558	CD2	LEU	A1844	-4.178	31.993	23.742	1.00	23.11	C
ATOM	1559	N	TYR	A1845	0.068	34.296	26.462	1.00	23.99	N
ATOM	1560	CA	TYR	A1845	1.155	35.282	26.493	1.00	24.59	C
ATOM	1561	C	TYR	A1845	0.911	36.357	25.427	1.00	25.26	C
ATOM	1562	O	TYR	A1845	1.784	36.665	24.610	1.00	25.20	O
ATOM	1563	CB	TYR	A1845	2.627	34.733	26.469	1.00	23.49	C
ATOM	1564	CG	TYR	A1845	3.497	35.718	27.236	1.00	23.87	C
ATOM	1565	CD1	TYR	A1845	3.364	35.843	28.618	1.00	21.67	C
ATOM	1566	CD2	TYR	A1845	4.343	36.615	26.575	1.00	22.80	C
ATOM	1567	CE1	TYR	A1845	4.080	36.777	29.334	1.00	22.40	C
ATOM	1568	CE2	TYR	A1845	5.076	37.555	27.288	1.00	23.19	C
ATOM	1569	CZ	TYR	A1845	4.920	37.640	28.664	1.00	22.98	C
ATOM	1570	OH	TYR	A1845	5.604	38.573	29.393	1.00	21.63	O
ATOM	1571	N	GLN	A1846	-0.280	36.928	25.472	1.00	25.19	N
ATOM	1572	CA	GLN	A1846	-0.631	38.011	24.570	1.00	26.63	C
ATOM	1573	C	GLN	A1846	-1.686	38.831	25.279	1.00	26.16	C
ATOM	1574	O	GLN	A1846	-2.706	38.309	25.725	1.00	25.68	O
ATOM	1575	CB	GLN	A1846	-1.120	37.457	23.220	1.00	27.43	C
ATOM	1576	CG	GLN	A1846	-2.621	37.358	23.067	1.00	33.52	C

ATOM	1577	CD	GLN	A1846	-3.019	36.946	21.646	1.00	37.64	C
ATOM	1578	OE1	GLN	A1846	-2.157	36.526	20.863	1.00	41.72	O
ATOM	1579	NE2	GLN	A1846	-4.308	37.049	21.324	1.00	36.71	N
ATOM	1580	N	CYS	A1847	-1.414	40.113	25.449	1.00	26.49	N
ATOM	1581	CA	CYS	A1847	-2.331	40.955	26.185	1.00	27.23	C
ATOM	1582	C	CYS	A1847	-3.663	41.085	25.462	1.00	27.54	C
ATOM	1583	O	CYS	A1847	-3.702	41.666	24.398	1.00	28.42	O
ATOM	1584	CB	CYS	A1847	-1.718	42.334	26.347	1.00	27.25	C
ATOM	1585	SG	CYS	A1847	-2.629	43.347	27.508	1.00	29.32	S
ATOM	1586	N	GLN	A1848	-4.751	40.580	26.043	1.00	28.34	N
ATOM	1587	CA	GLN	A1848	-6.052	40.636	25.370	1.00	28.42	C
ATOM	1588	C	GLN	A1848	-6.686	42.019	25.431	1.00	28.76	C
ATOM	1589	O	GLN	A1848	-6.449	42.788	26.368	1.00	28.33	O
ATOM	1590	CB	GLN	A1848	-7.045	39.637	25.981	1.00	28.38	C
ATOM	1591	CG	GLN	A1848	-6.620	38.171	25.955	1.00	29.42	C
ATOM	1592	CD	GLN	A1848	-6.360	37.694	24.548	1.00	30.00	C
ATOM	1593	OE1	GLN	A1848	-7.299	37.437	23.795	1.00	32.22	O
ATOM	1594	NE2	GLN	A1848	-5.099	37.601	24.179	1.00	28.64	N
ATOM	1595	N	GLU	A1849	-7.512	42.338	24.435	1.00	29.64	N
ATOM	1596	CA	GLU	A1849	-8.286	43.574	24.502	1.00	30.42	C
ATOM	1597	C	GLU	A1849	-9.195	43.461	25.716	1.00	30.05	C
ATOM	1598	O	GLU	A1849	-9.608	42.355	26.082	1.00	30.02	O
ATOM	1599	CB	GLU	A1849	-9.098	43.779	23.217	1.00	30.93	C
ATOM	1600	CG	GLU	A1849	-8.217	43.963	21.988	1.00	32.10	C
ATOM	1601	CD	GLU	A1849	-7.398	45.244	22.035	1.00	34.27	C
ATOM	1602	OE1	GLU	A1849	-7.781	46.199	22.751	1.00	36.49	O
ATOM	1603	OE2	GLU	A1849	-6.353	45.300	21.360	1.00	37.55	O
ATOM	1604	N	LEU	A1850	-9.500	44.582	26.364	1.00	30.45	N
ATOM	1605	CA	LEU	A1850	-10.329	44.543	27.570	1.00	30.93	C
ATOM	1606	C	LEU	A1850	-11.805	44.264	27.326	1.00	31.98	C
ATOM	1607	O	LEU	A1850	-12.518	43.795	28.215	1.00	30.45	O
ATOM	1608	CB	LEU	A1850	-10.236	45.869	28.317	1.00	31.44	C
ATOM	1609	CG	LEU	A1850	-8.838	46.340	28.673	1.00	31.79	C
ATOM	1610	CD1	LEU	A1850	-8.946	47.646	29.435	1.00	33.57	C
ATOM	1611	CD2	LEU	A1850	-8.151	45.270	29.510	1.00	31.94	C
ATOM	1612	N	ASP	A1851	-12.241	44.544	26.104	1.00	33.13	N
ATOM	1613	CA	ASP	A1851	-13.661	44.543	25.747	1.00	34.63	C
ATOM	1614	C	ASP	A1851	-14.556	43.446	26.324	1.00	34.22	C
ATOM	1615	O	ASP	A1851	-15.501	43.744	27.049	1.00	34.06	O
ATOM	1616	CB	ASP	A1851	-13.814	44.586	24.225	1.00	35.68	C
ATOM	1617	CG	ASP	A1851	-12.956	45.662	23.586	1.00	39.32	C
ATOM	1618	OD1	ASP	A1851	-12.616	46.653	24.268	1.00	43.83	O
ATOM	1619	OD2	ASP	A1851	-12.563	45.593	22.404	1.00	44.60	O
ATOM	1620	N	THR	A1852	-14.269	42.189	26.000	1.00	34.07	N
ATOM	1621	CA	THR	A1852	-15.130	41.091	26.421	1.00	33.71	C
ATOM	1622	C	THR	A1852	-15.063	40.806	27.916	1.00	33.36	C
ATOM	1623	O	THR	A1852	-15.854	40.022	28.427	1.00	32.23	O
ATOM	1624	CB	THR	A1852	-14.855	39.781	25.617	1.00	34.36	C
ATOM	1625	OG1	THR	A1852	-13.557	39.261	25.933	1.00	34.49	O
ATOM	1626	CG2	THR	A1852	-14.770	40.057	24.115	1.00	35.54	C
ATOM	1627	N	TYR	A1853	-14.128	41.454	28.615	1.00	32.06	N
ATOM	1628	CA	TYR	A1853	-13.960	41.216	30.037	1.00	31.98	C
ATOM	1629	C	TYR	A1853	-14.523	42.346	30.882	1.00	32.79	C
ATOM	1630	O	TYR	A1853	-14.733	42.181	32.087	1.00	31.91	O
ATOM	1631	CB	TYR	A1853	-12.473	41.022	30.374	1.00	31.05	C

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ATOM   1632  CG  TYR A1853     -11.801  39.933  29.560  1.00 28.55           C
ATOM   1633  CD1 TYR A1853     -11.015  40.249  28.467  1.00 26.82           C
ATOM   1634  CD2 TYR A1853     -11.970  38.591  29.880  1.00 26.26           C
ATOM   1635  CE1 TYR A1853     -10.392  39.262  27.706  1.00 25.64           C
ATOM   1636  CE2 TYR A1853     -11.355  37.595  29.119  1.00 26.13           C
ATOM   1637  CZ  TYR A1853     -10.557  37.943  28.047  1.00 25.03           C
ATOM   1638  OH  TYR A1853      -9.931  36.983  27.280  1.00 24.41           O
ATOM   1639  N   LEU A1854     -14.766  43.492  30.249  1.00 33.66           N
ATOM   1640  CA  LEU A1854     -15.232  44.683  30.965  1.00 34.46           C
ATOM   1641  C   LEU A1854     -16.504  44.494  31.764  1.00 35.09           C
ATOM   1642  O   LEU A1854     -17.434  43.842  31.317  1.00 35.00           O
ATOM   1643  CB  LEU A1854     -15.445  45.852  30.009  1.00 34.47           C
ATOM   1644  CG  LEU A1854     -14.215  46.608  29.509  1.00 35.64           C
ATOM   1645  CD1 LEU A1854     -14.625  47.533  28.359  1.00 36.58           C
ATOM   1646  CD2 LEU A1854     -13.553  47.400  30.639  1.00 34.53           C
ATOM   1647  N   ILE A1855     -16.525  45.077  32.955  1.00 35.82           N
ATOM   1648  CA  ILE A1855     -17.679  45.017  33.834  1.00 37.37           C
ATOM   1649  C   ILE A1855     -18.335  46.389  33.844  1.00 38.72           C
ATOM   1650  O   ILE A1855     -17.672  47.384  34.115  1.00 38.69           O
ATOM   1651  CB  ILE A1855     -17.225  44.649  35.250  1.00 37.41           C
ATOM   1652  CG1 ILE A1855     -16.713  43.208  35.275  1.00 37.27           C
ATOM   1653  CG2 ILE A1855     -18.355  44.861  36.256  1.00 38.04           C
ATOM   1654  CD1 ILE A1855     -15.959  42.856  36.526  1.00 36.90           C
ATOM   1655  N   PRO A1856     -19.636  46.449  33.565  1.00 40.18           N
ATOM   1656  CA  PRO A1856     -20.346  47.738  33.538  1.00 41.38           C
ATOM   1657  C   PRO A1856     -20.243  48.462  34.875  1.00 42.08           C
ATOM   1658  O   PRO A1856     -20.470  47.844  35.908  1.00 42.24           O
ATOM   1659  CB  PRO A1856     -21.806  47.349  33.279  1.00 41.39           C
ATOM   1660  CG  PRO A1856     -21.735  45.980  32.678  1.00 41.56           C
ATOM   1661  CD  PRO A1856     -20.515  45.302  33.267  1.00 40.34           C
ATOM   1662  N   GLN A1857     -19.897  49.744  34.856  1.00 43.27           N
ATOM   1663  CA  GLN A1857     -19.830  50.512  36.094  1.00 44.87           C
ATOM   1664  C   GLN A1857     -20.950  51.546  36.196  1.00 46.28           C
ATOM   1665  O   GLN A1857     -21.118  52.384  35.310  1.00 46.50           O
ATOM   1666  CB  GLN A1857     -18.469  51.196  36.255  1.00 44.60           C
ATOM   1667  CG  GLN A1857     -17.303  50.227  36.463  1.00 43.44           C
ATOM   1668  CD  GLN A1857     -17.454  49.382  37.710  1.00 42.10           C
ATOM   1669  OE1 GLN A1857     -17.500  49.911  38.828  1.00 41.92           O
ATOM   1670  NE2 GLN A1857     -17.525  48.065  37.529  1.00 40.14           N
ATOM   1671  N   ILE A1858     -21.702  51.478  37.291  1.00 47.79           N
ATOM   1672  CA  ILE A1858     -22.771  52.431  37.573  1.00 49.45           C
ATOM   1673  C   ILE A1858     -22.206  53.841  37.743  1.00 50.11           C
ATOM   1674  O   ILE A1858     -21.270  54.048  38.517  1.00 50.29           O
ATOM   1675  CB  ILE A1858     -23.525  51.989  38.838  1.00 49.49           C
ATOM   1676  CG1 ILE A1858     -24.407  50.779  38.511  1.00 50.34           C
ATOM   1677  CG2 ILE A1858     -24.339  53.138  39.414  1.00 50.30           C
ATOM   1678  CD1 ILE A1858     -25.163  50.212  39.698  1.00 51.57           C
ATOM   1679  N   PRO A1859     -22.787  54.808  37.033  1.00 50.83           N
ATOM   1680  CA  PRO A1859     -22.304  56.194  37.052  1.00 51.24           C
ATOM   1681  C   PRO A1859     -22.064  56.721  38.463  1.00 51.47           C
ATOM   1682  O   PRO A1859     -22.991  56.675  39.275  1.00 52.19           O
ATOM   1683  CB  PRO A1859     -23.449  56.967  36.394  1.00 51.29           C
ATOM   1684  CG  PRO A1859     -24.085  55.974  35.484  1.00 51.64           C
ATOM   1685  CD  PRO A1859     -23.980  54.646  36.183  1.00 50.96           C
TER    1686      PRO A1859
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ATOM	1687	N	SER	B	6	-4.459	15.911	41.006	1.00 39.58	N
ATOM	1688	CA	SER	B	6	-3.840	16.534	42.215	1.00 38.75	C
ATOM	1689	C	SER	B	6	-4.833	17.415	42.958	1.00 38.34	C
ATOM	1690	O	SER	B	6	-5.948	17.650	42.500	1.00 39.29	O
ATOM	1691	CB	SER	B	6	-2.601	17.360	41.836	1.00 39.15	C
ATOM	1692	OG	SER	B	6	-2.941	18.694	41.537	1.00 37.83	O
ATOM	1693	N	THR	B	7	-4.414	17.889	44.119	1.00 37.73	N
ATOM	1694	CA	THR	B	7	-5.228	18.771	44.926	1.00 37.38	C
ATOM	1695	C	THR	B	7	-5.255	20.180	44.301	1.00 35.24	C
ATOM	1696	O	THR	B	7	-6.021	21.044	44.739	1.00 35.41	O
ATOM	1697	CB	THR	B	7	-4.596	18.879	46.332	1.00 37.44	C
ATOM	1698	OG1	THR	B	7	-5.022	17.778	47.152	1.00 42.36	O
ATOM	1699	CG2	THR	B	7	-5.131	20.089	47.068	1.00 39.08	C
HETATM	1700	N	SEP	B	8	-4.430	20.416	43.278	1.00 32.99	N
HETATM	1701	CA	SEP	B	8	-4.302	21.772	42.722	1.00 30.87	C
HETATM	1702	CB	SEP	B	8	-3.049	21.883	41.828	1.00 30.51	C
HETATM	1703	OG	SEP	B	8	-1.880	21.560	42.566	1.00 27.95	O
HETATM	1704	C	SEP	B	8	-5.540	22.248	41.957	1.00 29.89	C
HETATM	1705	O	SEP	B	8	-5.979	21.597	41.022	1.00 29.41	O
HETATM	1706	P	SEP	B	8	-0.542	21.347	41.689	1.00 25.10	P
HETATM	1707	O1P	SEP	B	8	-0.407	22.545	40.622	1.00 28.57	O
HETATM	1708	O2P	SEP	B	8	-0.648	19.952	40.948	1.00 26.27	O
HETATM	1709	O3P	SEP	B	8	0.647	21.417	42.775	1.00 27.15	O
ATOM	1710	N	PRO	B	9	-6.089	23.397	42.334	1.00 29.40	N
ATOM	1711	CA	PRO	B	9	-7.257	23.935	41.625	1.00 28.97	C
ATOM	1712	C	PRO	B	9	-6.958	24.139	40.149	1.00 28.38	C
ATOM	1713	O	PRO	B	9	-5.800	24.405	39.790	1.00 27.24	O
ATOM	1714	CB	PRO	B	9	-7.477	25.299	42.281	1.00 29.34	C
ATOM	1715	CG	PRO	B	9	-6.830	25.197	43.625	1.00 29.99	C
ATOM	1716	CD	PRO	B	9	-5.658	24.262	43.446	1.00 29.53	C
ATOM	1717	N	THR	B	10	-7.976	23.976	39.307	1.00 27.13	N
ATOM	1718	CA	THR	B	10	-7.842	24.301	37.891	1.00 27.79	C
ATOM	1719	C	THR	B	10	-8.730	25.495	37.620	1.00 26.89	C
ATOM	1720	O	THR	B	10	-9.653	25.784	38.383	1.00 27.00	O
ATOM	1721	CB	THR	B	10	-8.241	23.136	36.992	1.00 27.55	C
ATOM	1722	OG1	THR	B	10	-9.538	22.661	37.388	1.00 28.31	O
ATOM	1723	CG2	THR	B	10	-7.288	21.952	37.221	1.00 28.82	C
ATOM	1724	N	PHE	B	11	-8.439	26.202	36.542	1.00 26.51	N
ATOM	1725	CA	PHE	B	11	-9.164	27.413	36.253	1.00 27.05	C
ATOM	1726	C	PHE	B	11	-9.842	27.345	34.915	1.00 27.64	C
ATOM	1727	O	PHE	B	11	-9.238	27.618	33.893	1.00 26.95	O
ATOM	1728	CB	PHE	B	11	-8.219	28.598	36.346	1.00 27.22	C
ATOM	1729	CG	PHE	B	11	-7.701	28.786	37.726	1.00 25.62	C
ATOM	1730	CD1	PHE	B	11	-6.608	28.058	38.179	1.00 26.44	C
ATOM	1731	CD2	PHE	B	11	-8.370	29.607	38.603	1.00 25.53	C
ATOM	1732	CE1	PHE	B	11	-6.156	28.188	39.487	1.00 26.35	C
ATOM	1733	CE2	PHE	B	11	-7.925	29.754	39.906	1.00 25.43	C
ATOM	1734	CZ	PHE	B	11	-6.827	29.039	40.350	1.00 26.32	C
ATOM	1735	N	ASN	B	12	-11.116	26.983	34.948	1.00 28.81	N
ATOM	1736	CA	ASN	B	12	-11.895	26.875	33.728	1.00 30.08	C
ATOM	1737	C	ASN	B	12	-12.912	27.998	33.637	1.00 30.52	C
ATOM	1738	O	ASN	B	12	-13.030	28.836	34.548	1.00 31.49	O
ATOM	1739	CB	ASN	B	12	-12.562	25.499	33.633	1.00 30.75	C
ATOM	1740	CG	ASN	B	12	-11.573	24.372	33.782	1.00 32.28	C
ATOM	1741	OD1	ASN	B	12	-10.696	24.185	32.941	1.00 33.02	O

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ATOM   1742  ND2 ASN B  12     -11.699  23.616  34.862  1.00 35.51           N
ATOM   1743  N   LYS B  13     -13.636  28.051  32.526  1.00 30.56           N
ATOM   1744  CA  LYS B  13     -14.613  29.123  32.347  1.00 31.23           C
ATOM   1745  C   LYS B  13     -15.905  28.783  33.072  1.00 32.26           C
ATOM   1746  O   LYS B  13     -16.744  29.665  33.296  1.00 32.52           O
ATOM   1747  CB  LYS B  13     -14.877  29.405  30.862  1.00 31.58           C
ATOM   1748  CG  LYS B  13     -13.653  29.896  30.071  1.00 30.38           C
ATOM   1749  CD  LYS B  13     -13.412  31.388  30.258  1.00 30.46           C
ATOM   1750  CE  LYS B  13     -12.203  31.900  29.451  1.00 28.05           C
ATOM   1751  NZ  LYS B  13     -11.788  33.220  30.019  1.00 26.69           N
TER    1752      LYS B  13
HETATM 1753  O   HOH     2     -13.452  35.972  36.780  1.00 13.79           O
HETATM 1754  O   HOH     3       5.465  30.066  17.850  1.00 21.35           O
HETATM 1755  O   HOH     4      12.653  36.338  25.818  1.00 23.18           O
HETATM 1756  O   HOH     6       3.759  26.707  44.073  1.00 24.12           O
HETATM 1757  O   HOH     7       7.923  26.759  28.024  1.00 24.16           O
HETATM 1758  O   HOH     8       4.534  26.718  23.569  1.00 21.61           O
HETATM 1759  O   HOH     9      21.408  15.707  35.455  1.00 37.40           O
HETATM 1760  O   HOH    10       6.703  37.676  31.585  1.00 21.82           O
HETATM 1761  O   HOH    12     -12.761  40.418  43.310  1.00 26.49           O
HETATM 1762  O   HOH    13       0.402  52.504  33.466  1.00 30.11           O
HETATM 1763  O   HOH    14     -16.205  35.546  38.233  1.00 26.90           O
HETATM 1764  O   HOH    15     -12.691  27.037  37.482  1.00 32.90           O
HETATM 1765  O   HOH    16       1.263  60.489  32.218  1.00 25.18           O
HETATM 1766  O   HOH    17       9.234  36.965  33.821  1.00 26.85           O
HETATM 1767  O   HOH    18      11.279  32.720  35.936  1.00 32.65           O
HETATM 1768  O   HOH    19     -14.783  37.111  32.130  1.00 31.36           O
HETATM 1769  O   HOH    20      15.346  25.795  43.568  1.00 32.73           O
HETATM 1770  O   HOH    21      -5.266  36.132  49.503  1.00 42.15           O
HETATM 1771  O   HOH    22     -11.235  33.894  37.065  1.00 26.80           O
HETATM 1772  O   HOH    23      -0.948  25.060  40.939  1.00 24.62           O
HETATM 1773  O   HOH    25       6.144  20.311  42.468  1.00 25.20           O
HETATM 1774  O   HOH    26      -5.044  60.327  34.893  1.00 32.08           O
HETATM 1775  O   HOH    27      -8.866  49.985  48.098  1.00 32.25           O
HETATM 1776  O   HOH    28      -4.677  57.401  33.408  1.00 31.32           O
HETATM 1777  O   HOH    29      -9.766  37.283  24.696  1.00 33.03           O
HETATM 1778  O   HOH    30     -15.283  49.012  33.433  1.00 29.57           O
HETATM 1779  O   HOH    31       9.082  44.380  28.816  1.00 27.14           O
HETATM 1780  O   HOH    33     -10.873  30.195  35.523  1.00 29.80           O
HETATM 1781  O   HOH    34      -3.525  25.672  41.049  1.00 24.58           O
HETATM 1782  O   HOH    35       2.599  38.538  22.916  1.00 33.63           O
HETATM 1783  O   HOH    36      -7.194  35.792  47.834  1.00 34.60           O
HETATM 1784  O   HOH    37       6.924  24.791  21.372  1.00 28.18           O
HETATM 1785  O   HOH    38       7.239  30.104  29.291  1.00 23.23           O
HETATM 1786  O   HOH    39       7.146  33.205  20.041  1.00 31.82           O
HETATM 1787  O   HOH    40     -12.072  50.005  48.450  1.00 43.04           O
HETATM 1788  O   HOH    41       1.667  13.837  30.563  1.00 28.78           O
HETATM 1789  O   HOH    42      -6.233  51.842  31.514  1.00 32.16           O
HETATM 1790  O   HOH    43      -3.255  44.471  43.526  1.00 34.15           O
HETATM 1791  O   HOH    44      14.799  13.474  48.663  1.00 29.54           O
HETATM 1792  O   HOH    45      -8.201  23.973  33.336  1.00 29.42           O
HETATM 1793  O   HOH    46      -2.591  19.321  33.390  1.00 30.65           O
HETATM 1794  O   HOH    47     -10.285  29.829  47.903  1.00 36.69           O
HETATM 1795  O   HOH    48     -11.849  41.285  24.888  1.00 35.55           O
HETATM 1796  O   HOH    49       2.758  22.327  17.454  1.00 36.72           O
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HETATM 1797  O   HOH    50       4.780  32.302  45.937  1.00 34.60           O
HETATM 1798  O   HOH    51      -0.253  26.099  43.327  1.00 29.48           O
HETATM 1799  O   HOH    52      -6.915  35.455  42.376  1.00 30.40           O
HETATM 1800  O   HOH    53      11.656  24.759  41.744  1.00 27.69           O
HETATM 1801  O   HOH    54      14.117  13.588  43.980  1.00 35.88           O
HETATM 1802  O   HOH    55     -14.123  35.014  30.225  1.00 30.18           O
HETATM 1803  O   HOH    56       1.792  27.942  42.621  1.00 29.19           O
HETATM 1804  O   HOH    57      17.437  25.002  28.429  1.00 31.49           O
HETATM 1805  O   HOH    58      -8.572  47.068  25.046  1.00 37.03           O
HETATM 1806  O   HOH    59      12.243  38.944  24.353  1.00 34.72           O
HETATM 1807  O   HOH    60       1.020  17.759  41.133  1.00 29.32           O
HETATM 1808  O   HOH    61      20.420  13.169  43.660  1.00 38.76           O
HETATM 1809  O   HOH    62      -4.332  27.518  42.865  1.00 30.84           O
HETATM 1810  O   HOH    63     -10.394  23.183  40.730  1.00 39.20           O
HETATM 1811  O   HOH    64       8.578  42.225  35.381  1.00 35.02           O
HETATM 1812  O   HOH    65     -19.050  52.750  39.473  1.00 46.86           O
HETATM 1813  O   HOH    67      19.116  22.461  44.869  1.00 29.06           O
HETATM 1814  O   HOH    69       4.932  48.579  34.082  1.00 41.55           O
HETATM 1815  O   HOH    70       0.674  41.247  23.802  1.00 32.46           O
HETATM 1816  O   HOH    71      -4.735  26.612  19.260  1.00 32.06           O
HETATM 1817  O   HOH    72     -16.624  38.354  30.446  1.00 41.17           O
HETATM 1818  O   HOH    73      -9.563  31.888  24.802  1.00 47.45           O
HETATM 1819  O   HOH    74      -8.024  40.395  22.455  1.00 37.25           O
HETATM 1820  O   HOH    75      22.334  15.119  30.416  1.00 38.23           O
HETATM 1821  O   HOH    76      10.412  36.360  44.040  1.00 53.49           O
HETATM 1822  O   HOH    77       0.194  50.468  45.917  1.00 36.75           O
HETATM 1823  O   HOH    78      11.735  30.457  17.770  1.00 31.20           O
HETATM 1824  O   HOH    79      13.615  30.264  21.492  1.00 31.47           O
HETATM 1825  O   HOH    80       1.981  29.997  44.422  1.00 35.31           O
HETATM 1826  O   HOH    81      -1.459  20.290  20.816  1.00 30.21           O
HETATM 1827  O   HOH    82     -13.609  26.086  30.220  1.00 27.77           O
HETATM 1828  O   HOH    83      -3.780  17.446  35.325  1.00 34.26           O
HETATM 1829  O   HOH    84      -8.279  32.849  46.738  1.00 40.78           O
HETATM 1830  O   HOH    85      -5.186  58.013  42.604  1.00 39.40           O
HETATM 1831  O   HOH    86      -3.704  44.611  23.069  1.00 41.93           O
HETATM 1832  O   HOH    87      -2.399  13.221  36.493  1.00 35.84           O
HETATM 1833  O   HOH    88      10.819  26.096  46.328  1.00 28.53           O
HETATM 1834  O   HOH    89     -15.466  31.518  36.743  1.00 65.91           O
HETATM 1835  O   HOH    90      25.544  18.911  44.692  1.00 44.66           O
HETATM 1836  O   HOH    91     -15.403  35.810  34.537  1.00 31.61           O
HETATM 1837  O   HOH    92      12.209  37.191  20.365  1.00 43.77           O
HETATM 1838  O   HOH    93      -3.822  19.157  19.331  1.00 40.98           O
HETATM 1839  O   HOH    94      -8.775  20.995  23.829  1.00 43.80           O
HETATM 1840  O   HOH    95       5.036  46.212  41.225  1.00 38.26           O
HETATM 1841  O   HOH    96      10.876  37.114  35.849  1.00 37.29           O
HETATM 1842  O   HOH    97      -2.877  37.361  49.248  1.00 43.97           O
HETATM 1843  O   HOH    98       1.058  55.760  42.110  1.00 46.37           O
HETATM 1844  O   HOH    99      -4.680  56.635  36.039  1.00 40.94           O
HETATM 1845  O   HOH   100       8.956  38.521  20.300  1.00 52.56           O
HETATM 1846  O   HOH   101      22.213  12.620  29.359  1.00 39.12           O
HETATM 1847  O   HOH   102       5.384  45.205  25.481  1.00 44.15           O
HETATM 1848  O   HOH   103      12.540  26.873  43.950  1.00 37.63           O
HETATM 1849  O   HOH   104      -7.868  51.651  24.151  1.00 52.45           O
HETATM 1850  O   HOH   106       9.349  33.376  38.461  1.00 31.86           O
HETATM 1851  O   HOH   107      -7.249  56.630  41.970  1.00 40.55           O
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HETATM 1852  O   HOH   108      -5.184  47.738  27.394  1.00 59.47           O
HETATM 1853  O   HOH   109      13.089  34.408  37.600  1.00 44.84           O
HETATM 1854  O   HOH   110       0.705  11.419  30.955  1.00 36.41           O
HETATM 1855  O   HOH   111      -4.798  14.017  42.480  1.00 53.45           O
HETATM 1856  O   HOH   112      -4.843  19.488  39.633  1.00 40.43           O
HETATM 1857  O   HOH   113     -18.670  51.048  32.220  1.00 41.38           O
HETATM 1858  O   HOH   114     -12.102  30.530  38.025  1.00 47.93           O
HETATM 1859  O   HOH   115     -13.776  27.216  27.707  1.00 35.44           O
HETATM 1860  O   HOH   116      -2.334  27.065  44.853  1.00 44.72           O
HETATM 1861  O   HOH   117       2.870  52.316  40.206  1.00 46.36           O
HETATM 1862  O   HOH   118     -18.440  40.445  31.729  1.00 56.81           O
HETATM 1863  O   HOH   119      -6.962  31.452  48.249  1.00 54.20           O
HETATM 1864  O   HOH   120     -10.628  27.328  40.404  1.00 45.21           O
HETATM 1865  O   HOH   122      16.096  24.639  45.922  1.00 37.79           O
HETATM 1866  O   HOH   123      -0.872   8.832  43.975  1.00 49.75           O
HETATM 1867  O   HOH   124     -16.751  49.961  31.151  1.00 39.48           O
HETATM 1868  O   HOH   126      21.867  21.890  45.103  1.00 32.28           O
HETATM 1869  O   HOH   127       0.221  23.594  44.786  1.00 42.23           O
HETATM 1870  O   HOH   129       5.798  20.569  21.887  1.00 38.97           O
HETATM 1871  O   HOH   130       0.027  33.658  49.447  1.00 33.97           O
HETATM 1872  O   HOH   131      17.726  22.984  30.315  1.00 51.39           O
HETATM 1873  O   HOH   133      -7.039  56.697  37.326  1.00 46.16           O
HETATM 1874  O   HOH   134     -18.445  35.870  30.843  1.00 53.20           O
HETATM 1875  O   HOH   135      -1.408  11.649  29.254  1.00 40.99           O
HETATM 1876  O   HOH   136       4.882  31.262  20.482  1.00 36.08           O
HETATM 1877  O   HOH   137     -15.536  34.962  48.398  1.00 38.30           O
HETATM 1878  O   HOH   138       5.748  22.881  20.087  1.00 40.17           O
HETATM 1879  O   HOH   139      -8.361  23.876  24.021  1.00 38.36           O
HETATM 1880  O   HOH   140     -14.676  29.695  41.150  1.00 50.58           O
HETATM 1881  O   HOH   141       9.061  41.220  16.046  1.00 57.28           O
HETATM 1882  O   HOH   142      -1.839  32.308  19.350  1.00 52.87           O
HETATM 1883  O   HOH   143      -5.811  50.543  29.103  1.00 37.21           O
HETATM 1884  O   HOH   144     -12.815  25.160  26.023  1.00 46.91           O
HETATM 1885  O   HOH   145       8.064   6.927  44.309  1.00 47.85           O
HETATM 1886  O   HOH   146      -6.794  49.781  22.800  1.00 51.07           O
HETATM 1887  O   HOH   147     -10.949  48.372  24.823  1.00 52.18           O
HETATM 1888  O   HOH   148     -11.633  30.356  41.316  1.00 35.73           O
HETATM 1889  O   HOH   150      19.648  17.166  27.875  1.00 49.78           O
HETATM 1890  O   HOH   152       1.645   8.928  31.444  1.00 51.22           O
HETATM 1891  O   HOH   153      -2.974  16.595  45.799  1.00 47.36           O
HETATM 1892  O   HOH   154       4.114   7.772  39.862  1.00 44.72           O
HETATM 1893  O   HOH   156      11.495  43.419  29.767  1.00 39.89           O
HETATM 1894  O   HOH   157      14.755  27.975  19.472  1.00 47.52           O
HETATM 1895  O   HOH   159      20.000  25.195  44.085  1.00 56.30           O
HETATM 1896  O   HOH   160      -2.672  23.925  45.847  1.00 50.24           O
HETATM 1897  O   HOH   161       3.604  50.595  35.259  1.00 51.76           O
HETATM 1898  O   HOH   162      19.673  24.416  41.389  1.00 61.54           O
HETATM 1899  O   HOH   163      -6.458  30.497  20.646  1.00 45.53           O
HETATM 1900  O   HOH   164      -6.717  60.196  42.547  1.00 44.71           O
HETATM 1901  O   HOH   166       3.377  39.489  45.416  1.00 51.19           O
HETATM 1902  O   HOH   168      15.857   6.255  34.567  1.00 60.54           O
HETATM 1903  O   HOH   169      -4.347  11.625  25.428  1.00 48.48           O
HETATM 1904  O   HOH   170      -4.966  56.028  29.753  1.00 59.27           O
HETATM 1905  O   HOH   172      -3.276  23.889  48.407  1.00 63.97           O
HETATM 1906  O   HOH   173      16.051   7.381  41.619  1.00 46.25           O
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HETATM 1907  O   HOH   176      10.033  37.532  40.812  1.00 47.17           O
HETATM 1908  O   HOH   179      -7.499  54.256  31.031  1.00 49.63           O
CONECT 1700 1701
CONECT 1701 1700 1702 1704
CONECT 1702 1701 1703
CONECT 1703 1702 1706
CONECT 1704 1701 1705
CONECT 1705 1704
CONECT 1706 1703 1707 1708 1709
CONECT 1707 1706
CONECT 1708 1706
CONECT 1709 1706
MASTER      256    0    1   11   10    0    0    6 1906    2   10   18
END
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Peptide library screening

One skilled in the art would be able to utilize a peptide library screen to identify peptides that bind to a BRCA1 tandem BRCT domain or other biologically relevant binding target. Peptides identified in such a screen, or related compounds, would have potential therapeutic benefit due to their ability to modulate the biological activity of BRCA1.

Phosphoserine and phosphothreonine oriented degenerate peptide libraries consisting of the sequences
Gly-Ala-X-X-X-B-(pSer/pThr)-Gln-J-X-X-X-Ala-Lys-Lys-Lys,
Met-Ala-X-X-X-X-pThr-X-X-X-X-Ala-Lys-Lys-Lys,
and Met-Ala-X-X-X-XpSer-X-X-X-X-X-Ala-Lys-Lys-Lys; where pS is phosphoserine, pT is phosphothreonine; and X denotes all amino acids except Cys. In the (pSer/pThr)-Gln library, B is a biased mixture of the amino acids A, I, L, M, N, P, S, T, V, and J represents a biased mixture of 25% E, 75% X, where X denotes all amino acids except Arg, Cys, His, Lys. Peptides were synthesized using N-α-FMOC-protected amino acids and standard BOP/HOBt coupling chemistry. Peptide library screening was performed using 125 µl of glutathione beads containing saturating amounts of GST-PTIP BRCT or GST-BRCA1 BRCT domains (1-1.5 mg) as described by Yaffe and Cantley (*Methods Enzymol* 328:157-70, 2000). Beads were packed in a 1mL column and incubated with 0.45 mg of the peptide library mixture for 10 minutes at room temperature in PBS (150 mM NaCl, 3 mM KCl, 10 mM Na2HPO4, 2 mm KH2PO4, pH 7.6). Unbound peptides were removed from the column by two washes with PBS containing 1.0% NP-40 followed by two washes with PBS. Bound peptides were eluted with 30% acetic acid for 10 minutes at room temperature, lyophilized, resuspended in H2O, and sequenced by automated Edman degradation on a PROCISE protein microsequencer (Perkin-Elmer Corporation, Norwalk CT). Selectivity values for each amino acid were determined by comparing the relative abundance (mole

percentage) of each amino acid at a particular sequencing cycle in the recovered peptides to that of each amino acid in the original peptide library mixture at the same position.

Prodrugs

Disruption of the BRCA1-BACH1 interaction can be used to promote enhanced sensitivity of cells to chemotherapy and radiation treatment. The treatment, stabilization, or prevention of a disease or disorder associated with BRCA1 can be mediated by administering a compound, peptide, or nucleic acid molecule. In some cases, however, a compound that is effective in disrupting the BRCA1-BACH1 interaction *in vitro* is not an effective therapeutic agent *in vivo*. For example, this could be due to low bioavailability of the compound. One way to circumvent this difficulty is to administer a modified drug, or prodrug, with improved bioavailability that converts naturally to the original compound following administration. Such prodrugs must undergo transformation before exhibiting their full pharmacological effects. Prodrugs contain one or more specialized protective groups that are specifically designed to alter or to eliminate undesirable properties in the parent molecule. Once administered, a prodrug is metabolised in vivo into an active compound.

Prodrugs may be useful for improving one or more of the following characteristics of a drug: solubility, absorption, distribution, metabolization, excretion, site specificity, stability, patient accepability, reduced toxicity, or problems of formulation. For example, an active compound may have poor oral bioavailability, but by attaching an appropriately-chosen covalent linkage that is metabolized in the body, oral bioavailability may improve sufficiently to enable the prodrug to be administered orally without adversely affecting the parent compound's activity within the body.

A prodrug may be carrier-linked, meaning that it contains a group such as an ester that can be removed enzymatically. Optimally, the additional chemical group has little or no pharmacologic activity, and the bond connecting this group to the parent compound is labile to allow for efficient in vivo activation. Such a carrier group may be linked directly to the parent compound (bipartate), or it may be bonded via a linker region (tripartate). Common examples of chemical groups attached to parent compounds to form prodrugs include esters, sulfates, phosphates, alcohols, amides, imines, phenyl carbamates, and carbonyls.

As one example, methylprednisolone is a poorly water-soluble corticosteroid drug. In order to be useful for aqueous injection or ophthalmic administration, this drug must be converted into a prodrug of enhanced solubility. Methylprednisolone sodium succinate ester is much more soluble than the parent compound, and it is rapidly and extensively hydrolysed in vivo by cholinesterases to free methylprednisolone.

Caged compounds may also be used as prodrugs. A caged compound has a photolyzable chemical groups attached that renders the compound biologically inactive. Flash photolysis releases the caging group (and activates the compound) in a spatially or temporally controlled manner.

For further description of the design and use of prodrugs, see Testa and Mayer, Hydrolysis in Drug and Prodrug Metabolism: Chemistry, Biochemistry and Enzymology, published by Vch. Verlagsgesellschaft Mbh. (2003)

Peptidomimetics

Peptide derivatives (e.g. peptidomimetics) include cyclic peptides, peptides obtained by substitution of a natural amino acid residue by the corresponding D-stereoisomer, or by a unnatural amino acid residue, chemical derivatives of the peptides, dual peptides, multimers of the peptides, and peptides fused to other proteins or carriers. A cyclic derivative of a peptide of the invention is one having

two or more additional amino acid residues suitable for cyclization. These residues are often added at the carboxyl terminus and at the amino terminus. A peptide derivative may have one or more amino acid residues replaced by the corresponding D-amino acid residue. In one example, a peptide or peptide derivative of the invention is all-L, all-D, or a mixed D,L-peptide. In another example, an amino acid residue is replaced by a unnatural amino acid residue. Examples of unnatural or derivatized unnatural amino acids include Nα-methyl amino acids, Cα -methyl amino acids, and β-methyl amino acids.

A chemical derivative of a peptide of the invention includes, but is not limited to, a derivative containing additional chemical moieties not normally a part of the peptide. Examples of such derivatives include: (a) N-acyl derivatives of the amino terminal or of another free amino group, where the acyl group may be either an alkanoyl group, e.g., acetyl, hexanoyl, octanoyl, an aroyl group, e.g., benzoyl, or a blocking group such as Fmoc (fluorenylmethyl-O--CO--), carbobenzoxy (benzyl-O--CO--), monomethoxysuccinyl, naphthyl-NH--CO--, acetylamino-caproyl, adamantyl-NH--CO--; (b) esters of the carboxyl terminal or of another free carboxyl or hydroxy groups; (c) amides of the carboxyl terminal or of another free carboxyl groups produced by reaction with ammonia or with a suitable amine; (d) glycosylated derivatives; (e) phosphorylated derivatives; (f) derivatives conjugated to lipophilic moieties, e.g., caproyl, lauryl, stearoyl; and (g) derivatives conjugated to an antibody or other biological ligand. Also included among the chemical derivatives are those derivatives obtained by modification of the peptide bond --CO--NH--, for example, by: (a) reduction to --CH_2 --NH--; (b) alkylation to --CO--N(alkyl)--; and (c) inversion to --NH--CO--. Peptidomimetics may also comprise phosphonate or sulfonate moieties.

A dual peptide of the invention consists of two of the same, or two different, peptides of the invention covalently linked to one another, either directly or through a spacer.

Multimers of the invention consist of polymer molecules formed from a number of the same or different peptides or derivatives thereof.

In one example, a peptide derivative is more resistant to proteolytic degradation than the corresponding non-derivatized peptide. For example, a peptide derivative having D-amino acid substitution(s) in place of one or more L-amino acid residue(s) resists proteolytic cleavage.

In another example, the peptide derivative has increased permeability across a cell membrane as compared to the corresponding non-derivatized peptide. For example, a peptide derivative may have a lipophilic moiety coupled at the amino terminus and/or carboxyl terminus and/or an internal site. Such derivatives are highly preferred when targeting intracellular protein-protein interactions, provided they retain the desired functional activity.

In another example, a peptide derivative binds with increased affinity to a ligand (e.g., a tandem BRCT domain).

The peptides or peptide derivatives of the invention are obtained by any method of peptide synthesis known to those skilled in the art, including synthetic and recombinant techniques. For example, the peptides or peptide derivatives can be obtained by solid phase peptide synthesis which, in brief, consists of coupling the carboxyl group of the C-terminal amino acid to a resin and successively adding N-alpha protected amino acids. The protecting groups may be any such groups known in the art. Before each new amino acid is added to the growing chain, the protecting group of the previous amino acid added to the chain is removed. The coupling of amino acids to appropriate resins has been described by Rivier et al. (U.S. Patent No. 4,244,946). Such solid phase syntheses have been described, for example, by Merrifield, *J. Am. Chem. Soc.* 85:2149, 1964; Vale et al., *Science* 213:1394-1397, 1984; Marki et al., *J. Am. Chem. Soc.* 10:3178, 1981, and in *U. S. Pat. Nos.* 4,305,872 and 4,316,891. In a preferred aspect, an automated peptide synthesizer is employed.

Purification of the synthesized peptides or peptide derivatives is carried out by standard methods, including chromatography (e.g., ion exchange, affinity, and sizing column chromatography), centrifugation, differential solubility, hydrophobicity, or by any other standard technique for the purification of proteins. In one embodiment, thin layer chromatography is employed. In another embodiment, reverse phase HPLC (high performance liquid chromatography) is employed.

Finally, structure-function relationships determined from the peptides, peptide derivatives, and other small molecules of the invention may also be used to prepare analogous molecular structures having similar properties. Thus, the invention is contemplated to include molecules in addition to those expressly disclosed that share the structure, hydrophobicity, charge characteristics and side chain properties of the specific embodiments exemplified herein.

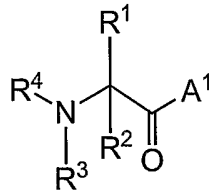
In one example, such derivatives or analogs that have the desired binding activity can be used for binding to a molecule or other target of interest, such as any tandem BRCT domain. Derivatives or analogs that retain, or alternatively lack or inhibit, a desired property-of-interest (e.g., inhibit tandem BRCT binding to a natural ligand), can be used to inhibit the biological activity of a tandem BRCT domain (e.g. from BRCA1 or PTIP).

In particular, peptide derivatives are made by altering amino acid sequences by substitutions, additions, or deletions that provide for functionally equivalent molecules, or for functionally enhanced or diminished molecules, as desired. Due to the degeneracy of the genetic code, other nucleic acid sequences that encode substantially the same amino acid sequence may be used for the production of recombinant peptides. These include, but are not limited to, nucleotide sequences comprising all or portions of a peptide of the invention that is altered by the substitution of different codons that encode a functionally equivalent amino acid residue within the sequence, thus producing a silent change.

The derivatives and analogs of the invention can be produced by various methods known in the art. The manipulations that result in their production can occur at the gene or protein level. For example, a cloned nucleic acid sequence can be modified by any of numerous strategies known in the art (Sambrook et al., 1989, Molecular Cloning, *A Laboratory Manual*, 2d ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y.). The sequence can be cleaved at appropriate sites with restriction endonuclease(s), followed by further enzymatic modification if desired, isolated, and ligated *in vitro*.

Modified Phosphopeptides

A phosphopeptide of the invention may include, but it is not limited to, an unnatural N-terminal amino acid of the formula (III):

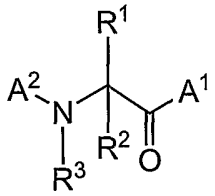


(III)

where A^1 is an amino acid or peptide chain linked via an α-amino group; R^1 and R^3 are independently hydrogen, C_{1-5} branched or linear C_{1-5} alkyl, C_{1-5} alkaryl, heteroaryl, and aryl, each of which are unsubstituted or substituted with a substitutent selected from: 1 to 3 of C_{1-5} alkyl, 1 to 3 of halogen, 1 to 2 of $-OR^5$, $N(R^5)(R^6)$, SR^5, $N\text{-}C(NR^5)NR^6R^7$, methylenedioxy, $-S(O)_mR^5$, 1 to 2 of $-CF_3$, $-OCF_3$, nitro, $-N(R^5)C(O)(R^6)$, $-C(O)OR^5$, $-C(O)N(R^5)(R^6)$, -1H-tetrazol-5-yl, $-SO_2N(R^5)(R^6)$, $-N(R^5)SO_2$ aryl, or $-N(R^5)SO_2R^6$; R^5, R^6 and R^7 are independently selected from hydrogen, C_{1-5} linear or branched alkyl, C_{1-5} alkaryl, aryl, heteroaryl, and C_{3-7} cycloalkyl, and where two C_{1-5} alkyl groups are present on one atom, they optionally are joined to form a C_{3-8} cyclic ring, optionally including oxygen, sulfur or NR^7, where R^7 is hydrogen, or C_{1-5} alkyl, optionally substituted by hydroxyl; R^2

is hydrogen, F, C_{1-5} linear or branched alkyl, C_{1-5} alkaryl; or R^2 and R^1 are joined to form a C_{3-8} cyclic ring, optionally including oxygen, sulfur, or NR^7, where R^7 is hydrogen, or C_{1-5} alkyl, optionally substituted by hydroxyl, or R^2 and R^3 are joined to form a C_{3-8} cyclic ring, optionally substituted by hydroxyl and optionally including oxygen, sulfur or NR^7, where R^7 is hydrogen, or C_{1-5} alkyl; R^2 is hydrogen, F, C_{1-5} linear or branched alkyl, C_{1-5} alkaryl; and R^4 is hydrogen, C_{1-5} branched or linear C_{1-5} alkyl, C_{1-5} alkaryl, heteroaryl, and aryl, each of which are unsubstituted or substituted with a substitutent selected from: 1 to 3 of C_{1-5} alkyl, 1 to 3 of halogen, 1 to 2 of $-OR^5$, $N(R^5)(R^6)$, $N\text{-}C(NR^5)NR^6R^7$, methylenedioxy, $-S(O)_mR^5$ (where m is 0-2), 1 to 2 of $-CF_3$, $-OCF_3$, nitro, $-N(R^5)C(O)(R^6)$, $-N(R^5)C(O)(OR^6)$, $-C(O)OR^5$, $-C(O)N(R^5)(R^6)$, -1H-tetrazol-5-yl, $-SO_2N(R^5)(R^6)$, $-N(R^5)SO_2$ aryl, or $-N(R^5)SO_2R^6$, R^5, R^6 and R^7 are independently selected from hydrogen, C_{1-5} linear or branched alkyl, C_{1-5} alkaryl, aryl, heteroaryl, and C_{3-7} cycloalkyl, and where two C_{1-5} alkyl groups are present on one atom, they optionally are joined to form a C_{3-8} cyclic ring, optionally including oxygen, sulfur or NR^7, where R^7 is hydrogen, or C_{1-5} alkyl, optionally substituted by hydroxyl.

The phosphopeptides of the invention may also include an unnatural internal amino acid of the formula:

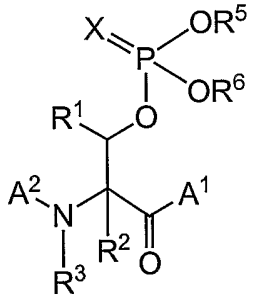


(IV) ,

where A^2 is an amino acid or peptide chain linked via an α-carboxy group; A^1 is an amino acid or peptide chain linked via an α-amino group; R^1 and R^3 are independently hydrogen, C_{1-5} branched or linear C_{1-5} alkyl, C_{1-5} alkaryl, heteroaryl, and aryl, each of which are unsubstituted or substituted with a substitutent selected from: 1 to 3 of C_{1-5} alkyl, 1 to 3 of halogen, 1 to 2 of $-OR^5$, $N(R^5)(R^6)$, SR^5, N-

$C(NR^5)NR^6R^7$, methylenedioxy, $-S(O)_mR^5$ (m is 1-2), 1 to 2 of $-CF_3$, $-OCF_3$, nitro, $-N(R^5)C(O)(R^6)$, $-C(O)OR^5$, $-C(O)N(R^5)(R^6)$, -1H-tetrazol-5-yl, $-SO_2N(R^5)(R^6)$, $-N(R^5)SO_2$ aryl, or $-N(R^5)SO_2R^6$; R^5, R^6 and R^7 are independently selected from hydrogen, C_{1-5} linear or branched alkyl, C_{1-5} alkaryl, aryl, heteroaryl, and C_{3-7} cycloalkyl, and where two C_{1-5} alkyl groups are present on one atom, they optionally are joined to form a C_{3-8} cyclic ring, optionally including oxygen, sulfur or NR^7, where R^7 is hydrogen, or C_{1-5} alkyl, optionally substituted by hydroxyl; and R^2 is hydrogen, F, C_{1-5} linear or branched alkyl, C_{1-5} alkaryl; or R^2 and R^1 are joined to form a C_{3-8} cyclic ring, optionally including oxygen, sulfur or NR^7, where R^7 is hydrogen, or C_{1-5} alkyl, optionally substituted by hydroxyl, or R^2 and R^3 are joined to form a C_{3-8} cyclic ring, optionally substituted by hydroxyl and optionally including oxygen, sulfur or NR^7, where R^7 is hydrogen, or C_{1-5} alkyl.

The invention also includes modifications of the phosphopeptides of the invention, wherein an unnatural internal amino acid of the formula:

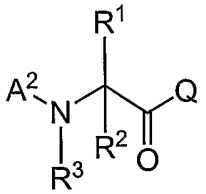


(V)

is present, where A^2 is an amino acid or peptide chain linked via an α-carboxy group; A^1 is an amino acid or peptide chain linked via an α-amino group; R^1 and R^3 are independently hydrogen, C_{1-5} branched or linear C_{1-5} alkyl, and C_{1-5} alkaryl; R^2 is hydrogen, F, C_{1-5} linear or branched alkyl, C_{1-5} alkaryl; or R^2 and R^1 are joined to form a C_{3-8} cyclic ring, optionally including oxygen, sulfur or NR^7, where R^7 is hydrogen, or C_{1-5} alkyl, optionally substituted by hydroxyl; X is O or S; and R^5 and R^6 are independently selected from hydrogen, C_{1-5} linear or

branched alkyl, C_{1-5} alkaryl, aryl, heteroaryl, and C_{3-7} cycloalkyl, and where two C_{1-5} alkyl groups are present on one atom, they optionally are joined to form a C_{3-8} cyclic ring, optionally including oxygen, sulfur or NR^7, where R^7 is hydrogen, or C_{1-5} alkyl, optionally substituted by hydroxyl; or R^5 and R^6 are joined to form a C_{3-8} cyclic ring, optionally including oxygen, sulfur or NR^7, where R^7 is hydrogen, or C_{1-5} alkyl, optionally substituted by hydroxyl.

The phosphopeptides of the invention may also include a C-terminal unnatural internal amino acid of the formula:



(VI) ,

where A^2 is an amino acid or peptide chain linked via an α-carboxy group; R^1 and R^3 are independently hydrogen, C_{1-5} branched or linear C_{1-5} alkyl, C_{1-5} alkaryl, heteroaryl, and aryl, each of which are unsubstituted or substituted with a substitutent selected from: 1 to 3 of C_{1-5} alkyl, 1 to 3 of halogen, 1 to 2 of $-OR^5$, $N(R^5)(R^6)$, SR^5, $N\text{-}C(NR^5)NR^6R^7$, methylenedioxy, $-S(O)_mR^5$, 1 to 2 of $-CF_3$, $-OCF_3$, nitro, $-N(R^5)C(O)(R^6)$, $-C(O)OR^5$, $-C(O)N(R^5)(R^6)$, -1H-tetrazol-5-yl, $-SO_2N(R^5)(R^6)$, $-N(R^5)SO_2$ aryl, or $-N(R^5)SO_2R^6$; R^5, R^6 and R^7 are independently selected from hydrogen, C_{1-5} linear or branched alkyl, C_{1-5} alkaryl, aryl, heteroaryl, and C_{3-7} cycloalkyl, and where two C_{1-5} alkyl groups are present on one atom, they optionally are joined to form a C_{3-8} cyclic ring, optionally including oxygen, sulfur or NR^7, where R^7 is hydrogen, or C_{1-5} alkyl, optionally substituted by hydroxyl; R^2 is hydrogen, F, C_{1-5} linear or branched alkyl, C_{1-5} alkaryl; or R^2 and R^1 are joined to form a C_{3-8} cyclic ring, optionally including oxygen, sulfur or NR^7, where R^7 is hydrogen, or C_{1-5} alkyl, optionally substituted by hydroxyl; or R^2 and R^3 are joined

to form a C_{3-8} cyclic ring, optionally substituted by hydroxyl and optionally including oxygen, sulfur or NR^7, where R^7 is hydrogen, or C_{1-5} alkyl; R^2 is hydrogen, F, C_{1-5} linear or branched alkyl, C_{1-5} alkaryl; and Q is OH , OR^5, or NR^5R^6, where R^5, R^6 are independently selected from hydrogen, C_{1-5} linear or branched alkyl, C_{1-5} alkaryl, aryl, heteroaryl, and C_{3-7} cycloalkyl, and where two C_{1-5} alkyl groups are present on one atom, they optionally are joined to form a C_{3-8} cyclic ring, optionally including oxygen, sulfur or NR^7, where R^7 is hydrogen, or C_{1-5} alkyl, optionally substituted by hydroxyl. Methods well known in the art for modifying peptides are found, for example, in "Remington: The Science and Practice of Pharmacy" (20th ed., ed. A.R. Gennaro, 2000, Lippincott Williams & Wilkins, Philadelphia).

Therapeutic Uses

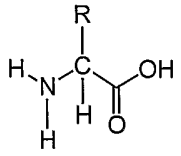
Peptide synthesis and conjugation

Phosphopeptides of the invention are prepared as detailed above. Alternatively, phosphopeptides can be prepared using standard FMOC chemistry on 2-chlorotrityl chloride resin (Int. J. Pept. Prot. Res. 38, 1991, 555-61). Cleavage from the resin is performed using 20% acetic acid in dichloromehane (DCM), which leaves the side chain still blocked. Free terminal carboxylate peptide is then coupled to 4'(aminomethy)-fluorescein (Molecular Probes, A-1351; Eugene, OR) using excess diisopropylcarbodiimide (DIC) in dimethylformamide (DMF) at room temperature. The fluorescent N-C blocked peptide is purified by silica gel chromatography (10% methanol in DCM). The N terminal FMOC group is then removed using piperidine (20%) in DMF, and the N-free peptide, purified by silica gel chromatography (20% methanol in DCM, 0.5% HOAc). Finally, any t-butyl side chain protective groups are removed using 95% trifluoroacetic acid containing 2.5 % water and 2.5 % triisopropyl silane.

The peptide obtained in such a manner should give a single peak by HPLC and is sufficiently pure for carrying on with the assay described below.

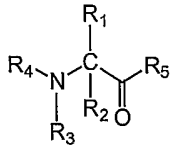
Phosphopeptide Modifications

It is understood that modifications can be made to the amino acid residues of the phosphopeptides of the invention, to enhance or prolong the therapeutic efficacy and/or bioavailability of the phosphopeptide. Accordingly, α-amino acids having the following general formula (I):



(I)

where R defines the specific amino acid residue, may undergo various modifications. Exemplary modifications of α-amino acids, include, but are not limited to, the following formula (II):



(II)

R_1, R_2, R_3, R_4, and R_5, are independently hydrogen, hydroxy, nitro, halo, C_{1-5} branched or linear alkyl, C_{1-5} alkaryl, heteroaryl, and aryl; wherein the alkyl, alkaryl, heteroaryl, and aryl may be unsubstituted or substituted by one or more substituents selected from the group consisting of C_{1-5} alkyl, hydroxy, halo, nitro, C_{1-5} alkoxy, C_{1-5} alkylthio, trihalomethyl, C_{1-5} acyl, arylcarbonyl, heteroarylcarbonyl, nitrile, C_{1-5} alkoxycarbonyl, oxo, arylalkyl (wherein the alkyl group has from 1 to 5 carbon atoms) and heteroarylalkyl (wherein the alkyl group has from 1 to 5carbon atoms); alternatively, R_1 and R_2 are joined to form a C_{3-8} cyclic ring, optionally including oxygen, sulfur or hydrogen, or C_{1-5} alkyl,

optionally substituted by hydroxyl; or R_2 and R_3 are joined to form a C_{3-8} cyclic ring, optionally substituted by hydroxyl and optionally including oxygen, sulfur, C_{1-5} aminoalkyl, or C_{1-5} alkyl. Methods well known in the art for making modifications are found, for example, in "Remington: The Science and Practice of Pharmacy" (20th ed., ed. A.R. Gennaro, 2000, Lippincott Williams & Wilkins), hereby incorporated by reference.

Assays and high throughput assays

Fluorescence polarization assays can be used in displacement assays to identify small molecule peptidomimetics. The following is an exemplary method for use of fluorescence polarization, and should not be viewed as limiting in any way. For screening, all reagents are diluted at the appropriate concentration and the working solution, kept on ice. The working stock concentration for GST and GST fusion proteins are ~4 ng/μL, Fluorescein-labeled phosphopeptides can be used at a concentration of 1.56 fmol/μL, while cold phosphopeptides and peptides at 25 pmol/μL. Samples are incubated at a total volume of 200 μL per well in black flat bottom plates, Biocoat, #359135 low binding (BD BioSciences; Bedford, MA). Assays are started with the successive addition using a Labsystem Multi-Drop 96/384 device (Labsystem; Franklin, MA) of 50μL test compounds, diluted in 10% DMSO (average concentration of 28 μM), 50μL of 50 mM MES-pH 6.5, 50μL of Fluorescein-phosphopeptide, 50μL of GST-BRCA1 tandem BRCT domain fusion, 50μL of unlabeled phosphopeptide, or unphosphorylated peptide can be used as a negative control. Once added, all the plates are placed at 4°C. Following overnight incubation at 4°C, the fluorescence polarization is measured using a Polarion plate reader (Tecan, Research Triangle Park, NC). A xenon flash lamp equipped with an excitation filter of 485 nm and an emission filter of 535 nm. The number of flashes is set at 30. Raw data can then be

converted into a percentage of total interaction(s). All further analysis can be performed using SPOTFIRE data analysis software (SPOTFIRE, Somerville, MA)

Upon selection of active compounds, auto-fluorescence of the hits is measured as well as the fluorescein quenching effect, where a measurement of 2000 or more units indicates auto-fluorescence, while a measurement of 50 units indicates a quenching effect. Confirmed hits can then be analyzed in dose-response curves (IC_{50}) for reconfirmation. Best hits in dose–response curves can then be assessed by isothermal titration calorimetry using a GST-BRCA1 tandem BRCT domain fusion.

Alternate binding and displacement assays

Fluorescence polarization assays are but one means to measure phosphopeptide-protein interactions in a screening strategy. Alternate methods for measuring phosphopeptide-protein interactions are known to the skilled artisan. Such methods include, but are not limited to mass spectrometry (Nelson and Krone, J. Mol. Recognit., 12:77-93, 1999), surface plasmon resonance (Spiga *et al.*, FEBS Lett., 511:33-35, 2002; Rich and Mizka, J. Mol. Recognit., 14:223-8, 2001; Abrantes *et al.*, Anal. Chem., 73:2828-35, 2001), fluorescence resonance energy transfer (FRET) (Bader *et al.*, J. Biomol. Screen, 6:255-64, 2001; Song *et al.*, Anal. Biochem. 291:133-41, 2001; Brockhoff et al., Cytometry, 44:338-48, 2001), bioluminescence resonance energy transfer (BRET) (Angers *et al.*, *Proc. Natl. Acad. Sci. USA*, 97:3684-9, 2000; Xu *et al.*, *Proc. Natl. Acad. Sci. USA*, 96:151-6, 1999), fluorescence quenching (Engelborghs, *Spectrochim. Acta A. Mol. Biomol. Spectros*c., 57:2255-70, 70; Geoghegan *et al.*, *Bioconjug. Chem.* 11:71-7, 2000), fluorescence activated cell scanning/sorting (Barth *et al., J. Mol. Biol.*, 301:751-7, 2000), ELISA, and radioimmunoassay (RIA).

Test extracts and compounds

In general, peptidomimetic compounds that affect phosphopeptide-protein interactions are identified from large libraries of both natural products, synthetic (or semi-synthetic) extracts or chemical libraries, according to methods known in the art.

Those skilled in the art will understand that the precise source of test extracts or compounds is not critical to the screening procedure(s) of the invention. Accordingly, virtually any number of chemical extracts or compounds can be screened using the exemplary methods described herein. Examples of such extracts or compounds include, but are not limited to, plant-, fungal-, prokaryotic- or animal-based extracts, fermentation broths, and synthetic compounds, as well as modifications of existing compounds. Numerous methods are also available for generating random or directed synthesis (e.g., semi-synthesis or total synthesis) of any number of chemical compounds, including, but not limited to, saccharide-, lipid-, peptide-, and nucleic acid-based compounds. Synthetic compound libraries are commercially available from, for example, Brandon Associates (Merrimack, NH) and Aldrich Chemical (Milwaukee, WI)

Alternatively, libraries of natural compounds in the form of bacterial, fungal, plant, and animal extracts are commercially available from a number of sources, including, but not limited to, Biotics (Sussex, UK), Xenova (Slough, UK), Harbor Branch Oceangraphics Institute (Ft. Pierce, FL), and PharmaMar, U.S.A. (Cambridge, MA). In addition, natural and synthetically produced libraries are produced, if desired, according to methods known in the art (e.g., by combinatorial chemistry methods or standard extraction and fractionation methods). Furthermore, if desired, any library or compound may be readily modified using standard chemical, physical, or biochemical methods.

Administration of therapeutic compounds

By selectively disrupting or preventing a phosphoprotein from binding to its natural partner(s) through its binding site, the phosphopeptides of the invention, or derivatives, or peptidomimetics thereof, can significantly alter the biological activity or the biological function of a tandem BRCT domain. Therefore, the phosphopeptides, or derivatives thereof, of the invention can be used for the treatment of a disease or disorder characterized by inappropriate cell cycle regulation or apoptosis.

Diseases or disorders characterized by inappropriate cell cycle regulation, include hyperproliferative disorders, such as neoplasias. Examples of neoplasms include, without limitation, acoustic neuroma, acute leukemia, acute lymphocytic leukemia, acute monocytic leukemia, acute myeloblastic leukemia, acute myelocytic leukemia, acute myelomonocytic leukemia, acute promyelocytic leukemia, acute erythroleukemia, adenocarcinoma, angiosarcoma, astrocytoma, basal cell carcinoma, bile duct carcinoma, bladder carcinoma, brain cancer, breast cancer, bronchogenic carcinoma, cervical cancer, chondrosarcoma, chordoma, choriocarcinoma, chronic leukemia, chronic lymphocytic leukemia, chronic myelocytic leukemia, colon cancer, colon carcinoma, craniopharyngioma, cystadenocarcinoma, embryonal carcinoma, endotheliosarcoma, ependymoma, epithelial carcinoma, Ewing's tumor, glioma, heavy chain disease, hemangioblastoma, hepatoma, Hodgkin's disease, large cell carcinoma, leiomyosarcoma, liposarcoma, lung cancer, lung carcinoma, lymphangioendotheliosarcoma, lymphangiosarcoma, macroglobulinemia, medullary carcinoma, medulloblastoma, melanoma, meningioma, mesothelioma, myxosarcoma, neuroblastoma, non-Hodgkin's disease, oligodendriglioma, osteogenic sarcoma, ovarian cancer, pancreatic cancer, papillary adenocarcinomas, papillary carcinoma, pinealoma, polycythemia vera, prostate cancer, rhabdomyosarcoma, renal cell carcinoma, retinoblastoma, schwannoma, sebaceous

gland carcinoma, seminoma, small cell lung carcinoma, squamous cell carcinoma, sweat gland carcinoma, synovioma, testicular cancer, uterine cancer, Waldenstrom's fibrosarcoma, and Wilm's tumor.

A tandem BRCT domain-binding phosphopeptide or peptidomimetic small molecule may be administered within a pharmaceutically-acceptable diluent, carrier, or excipient, in unit dosage form. Conventional pharmaceutical practice may be employed to provide suitable formulations or compositions to administer the compounds to patients suffering from a disease that is caused by excessive cell proliferation. Administration may begin before the patient is symptomatic. Any appropriate route of administration may be employed, for example, administration may be parenteral, intravenous, intra-arterial, subcutaneous, intramuscular, intracranial, intraorbital, ophthalmic, intraventricular, intracapsular, intraspinal, intracisternal, intraperitoneal, intranasal, aerosol, suppository, or oral administration. For example, therapeutic formulations may be in the form of liquid solutions or suspensions; for oral administration, formulations may be in the form of tablets or capsules; and for intranasal formulations, in the form of powders, nasal drops, or aerosols.

Pharmaceutical formulations

The pharmaceutical compositions of the present invention are prepared in a manner known per se, for example by means of conventional dissolving, lyophilising, mixing, granulating or confectioning processes. Methods well known in the art for making formulations are found, for example, in "Remington: The Science and Practice of Pharmacy" (20th ed., ed. A.R. Gennaro, 2000, Lippincott Williams & Wilkins, Philadelphia).

Solutions of the active ingredient, and also suspensions, and especially isotonic aqueous solutions or suspensions, are preferably used, it being possible, for example in the case of lyophilized compositions that comprise the active

ingredient alone or together with a carrier, for example mannitol, for such solutions or suspensions to be produced prior to use. The pharmaceutical compositions may be sterilized and/or may comprise excipients, for example preservatives, stabilisers, wetting and/or emulsifying agents, solubilisers, salts for regulating the osmotic pressure and/or buffers, and are prepared in a manner known per se, for example by means of conventional dissolving or lyophilising processes. The said solutions or suspensions may comprise viscosity-increasing substances, such as sodium carboxymethylcellulose, carboxymethylcellulose, dextran, poly vinylpyrrolidone or gelatin.

Suspensions in oil comprise as the oil component the vegetable, synthetic or semi-synthetic oils customary for injection purposes. There may be mentioned as such especially liquid fatty acid esters that contain as the acid component a long-chained fatty acid having from 8 to 22, especially from 12 to 22, carbon atoms, for example lauric acid, tridecylic acid, myristic acid, pentadecylic acid, palmitic acid, margaric acid, stearic acid, arachidic acid, behenic acid or corresponding unsaturated acids, for example oleic acid, elaidic acid, erucic acid, brasidic acid or linoleic acid, if desired with the addition of anti oxidants, for example, vitamins E, β-carotene, or 3,5-di-tert-butyl-4-hydroxytoluene. The alcohol component of those fatty acid esters has a maximum of 6 carbon atoms and is a mono- or poly-hydroxy, for example a mono-, di- or tri-hydroxy, alcohol, for example methanol, ethanol, propanol, butanol or pentanol or the isomers thereof, but especially glycol and glycerol. The following examples of fatty acid esters are therefore to be mentioned: ethyl oleate, isopropyl myristate, isopropyl palmitate, "Labrafil M 2375" (poly oxyethylene glycerol trioleate, Gattefoss, Paris), "Miglyol 812" (triglyceride of saturated fatty acids with a chain length of C_8 to C_{12}, Huls AG, Germany), but especially vegetable oils, such as cottonseed oil, almond oil, olive oil, castor oil, sesame oil, soybean oil and more especially groundnut oil.

The injection compositions are prepared in customary manner under sterile conditions; the same applies also to introducing the compositions into ampoules or vials and sealing the containers.

Pharmaceutical compositions for oral administration can be obtained by combining the active ingredient with solid carriers, if desired granulating a resulting mixture, and processing the mixture, if desired or necessary, after the addition of appropriate excipients, into tablets, drage cores or capsules. It is also possible for them to be incorporated into plastics carriers that allow the active ingredients to diffuse or be released in measured amounts.

Suitable carriers are especially fillers, such as sugars, for example lactose, saccharose, mannitol or sorbitol, cellulose preparations and/or calcium phosphates, for example tricalcium phosphate or calcium hydrogen phosphate, and binders, such as starch pastes using for example corn, wheat, rice or potato starch, gelatin, tragacanth, methylcellulose, hydroxypropylmethylcellulose, sodium carboxymethylcellulose and/or polyvinyl-pyrrolidone, and/or, if desired, disintegrates, such as the above-mentioned starches, also carboxymethyl starch, crosslinked polyvinylpyrrolidone, agar, alginic acid or a salt thereof, such as sodium alginate. Excipients are especially flow conditioners and lubricants, for example silicic acid, talc, stearic acid or salts thereof, such as magnesium or calcium stearate, and/or polyethylene glycol. Drage cores are provided with suitable, optionally enteric, coatings, there being used, *inter alia*, concentrated sugar solutions which may comprise gum arabic, talc, polyvinylpyrrolidone, polyethylene glycol and/or titanium dioxide, or coating solutions in suitable organic solvents, or, for the preparation of enteric coatings, solutions of suitable cellulose preparations, such as ethylcellulose phthalate or hydroxypropylmethylcellulose phthalate. Capsules are dry-filled capsules made of gelatin and soft sealed capsules made of gelatin and a plasticiser, such as glycerol or sorbitol. The dry-filled capsules may comprise the active ingredient in the form

of granules, for example with fillers, such as lactose, binders, such as starches, and/or glidants, such as talc or magnesium stearate, and if desired with stabilisers. In soft capsules the active ingredient is preferably dissolved or suspended in suitable oily excipients, such as fatty oils, paraffin oil or liquid polyethylene glycols, it being possible also for stabilisers and/or antibacterial agents to be added. Dyes or pigments may be added to the tablets or drage coatings or the capsule casings, for example for identification purposes or to indicate different doses of active ingredient.

The pharmaceutical compositions comprise from approximately 1% to approximately 95%, preferably from approximately 20% to approximately 90%, active ingredient. Pharmaceutical compositions according to the invention may be, for example, in unit dose form, such as in the form of ampoules, vials, suppositories, drages, tablets or capsules.

The formulations can be administered to human patients in a therapeutically effective amount (e.g., an amount that decreases, suppresses, attenuates, diminishes, arrests, or stabilizes the development or progression of a disease, disorder, or infection in a eukaryotic host organism). The preferred dosage of therapeutic agent to be administered is likely to depend on such variables as the type and extent of the disorder, the overall health status of the particular patient, the formulation of the compound excipients, and its route of administration.

For any of the methods of application described above, a compound that interacts with a tandem BRCT domain may be applied to the site of the needed therapeutic event (for example, by injection), or to tissue in the vicinity of the predicted therapeutic event or to a blood vessel supplying the cells predicted to require enhanced therapy.

The dosages of compounds that interact with a tandem BRCT domain depend on a number of factors, including the size and health of the individual patient, but, generally, between 0.1 mg and 1000 mg inclusive are administered per

day to an adult in any pharmaceutically acceptable formulation. In addition, treatment by any of the approaches described herein may be combined with more traditional therapies.

Combination Therapy

As described above, if desired, treatment with compounds that interact with a tandem BRCT domain may be combined with therapies for the treatment of proliferative disease, such as radiotherapy, surgery, or chemotherapy. Chemotherapeutic agents that may be administered with compounds that interact with a tandem BRCT domain are listed in Table 3.

Table 3

Alkylating agents	cyclophosphamide busulfan ifosfamide melphalan hexamethylmelamine thiotepa chlorambucil dacarbazine carmustine	lomustine procarbazine altretamine estramustine phosphate mechlorethamine streptozocin temozolomide semustine.
Platinum agents	cisplatin oxaliplatin spiroplatinum, carboxyphthalatoplatinum, tetraplatin ormiplatin iproplatin	carboplatinum ZD-0473 (AnorMED) lobaplatin (Aeterna) satraplatin (Johnson Matthey) BBR-3464 (Hoffmann-La Roche) SM-11355 (Sumitomo) AP-5280 (Access)
Antimetabolites	azacytidine gemcitabine capecitabine 5-fluorouracil floxuridine 2-chlorodeoxyadenosine 6-mercaptopurine 6-thioguanine cytarabin 2-fluorodeoxy cytidine methotrexate idatrexate	tomudex trimetrexate deoxycoformycin fludarabine pentostatin raltitrexed hydroxyurea decitabine (SuperGen) clofarabine (Bioenvision) irofulven (MGI Pharma) DMDC (Hoffmann-La Roche) ethynylcytidine (Taiho)

Topoisomerase inhibitors	amsacrine epirubicin etoposide teniposide or mitoxantrone irinotecan (CPT-11) 7-ethyl-10-hydroxy-camptothecin topotecan dexrazoxanet (TopoTarget) pixantrone (Novuspharma) rebeccamycin analogue (Exelixis) BBR-3576 (Novuspharma)	rubitecan (SuperGen) exatecan mesylate (Daiichi) quinamed (ChemGenex) gimatecan (Sigma-Tau) diflomotecan (Beaufour-Ipsen) TAS-103 (Taiho) elsamitrucin (Spectrum) J-107088 (Merck & Co) BNP-1350 (BioNumerik) CKD-602 (Chong Kun Dang) KW-2170 (Kyowa Hakko)

Table 3 (cont.)

Antitumor antibiotics	dactinomycin (actinomycin D) doxorubicin (adriamycin) deoxyrubicin valrubicin daunorubicin (daunomycin) epirubicin therarubicin idarubicin rubidazone plicamycinp porfiromycin cyanomorpholinodoxorubicin mitoxantrone (novantrone)	amonafide azonafide anthrapyrazole oxantrazole losoxantrone bleomycin sulfate (blenoxane) bleomycinic acid bleomycin A bleomycin B mitomycin C MEN-10755 (Menarini) GPX-100 (Gem Pharmaceuticals)
Antimitotic agents	paclitaxel docetaxel colchicine vinblastine vincristine vinorelbine vindesine dolastatin 10 (NCI) rhizoxin (Fujisawa) mivobulin (Warner-Lambert) cemadotin (BASF) RPR 109881A (Aventis) TXD 258 (Aventis) epothilone B (Novartis) T 900607 (Tularik) T 138067 (Tularik) cryptophycin 52 (Eli Lilly) vinflunine (Fabre) auristatin PE (Teikoku Hormone) BMS 247550 (BMS) BMS 184476 (BMS) BMS 188797 (BMS) taxoprexin (Protarga)	SB 408075 (GlaxoSmithKline) E7010 (Abbott) PG-TXL (Cell Therapeutics) IDN 5109 (Bayer) A 105972 (Abbott) A 204197 (Abbott) LU 223651 (BASF) D 24851 (ASTAMedica) ER-86526 (Eisai) combretastatin A4 (BMS) isohomohalichondrin-B (PharmaMar) ZD 6126 (AstraZeneca) PEG-paclitaxel (Enzon) AZ10992 (Asahi) IDN-5109 (Indena) AVLB (Prescient NeuroPharma) azaepothilone B (BMS) BNP-7787 (BioNumerik) CA-4 prodrug (OXiGENE) dolastatin-10 (NIH) CA-4 (OXiGENE)

Table 3 (cont.)

Aromatase inhibitors	aminoglutethimide letrozole anastrazole formestane	exemestane atamestane (BioMedicines) YM-511 (Yamanouchi)
Thymidylate synthase inhibitors	pemetrexed (Eli Lilly) ZD-9331 (BTG)	nolatrexed (Eximias) CoFactor™ (BioKeys)
DNA antagonists	trabectedin (PharmaMar) glufosfamide (Baxter International) albumin + 32P (Isotope Solutions) thymectacin (NewBiotics) edotreotide (Novartis)	mafosfamide (Baxter International) apaziquone (Spectrum Pharmaceuticals) O6 benzyl guanine (Paligent)
Farnesyltransferase inhibitors	arglabin (NuOncology Labs) lonafarnib (Schering-Plough) BAY-43-9006 (Bayer)	tipifarnib (Johnson & Johnson) perillyl alcohol (DOR BioPharma)
Pump inhibitors	CBT-1 (CBA Pharma) tariquidar (Xenova) MS-209 (Schering AG)	zosuquidar trihydrochloride (Eli Lilly) biricodar dicitrate (Vertex)
Histone acetyltransferase inhibitors	tacedinaline (Pfizer) SAHA (Aton Pharma) MS-275 (Schering AG)	pivaloyloxymethyl butyrate (Titan) depsipeptide (Fujisawa)
Metalloproteinase inhibitors	Neovastat (Aeterna Laboratories) marimastat (British Biotech)	CMT-3 (CollaGenex) BMS-275291 (Celltech)
Ribonucleoside reductase inhibitors	gallium maltolate (Titan) triapine (Vion)	tezacitabine (Aventis) didox (Molecules for Health)
TNF alpha agonists/antagonists	virulizin (Lorus Therapeutics) CDC-394 (Celgene)	revimid (Celgene)
Endothelin A receptor antagonist	atrasentan (Abbott) ZD-4054 (AstraZeneca)	YM-598 (Yamanouchi)
Retinoic acid receptor agonists	fenretinide (Johnson & Johnson) LGD-1550 (Ligand)	alitretinoin (Ligand)

Table 3 (cont.)

Immuno-modulators	interferon oncophage (Antigenics) GMK (Progenics) adenocarcinoma vaccine (Biomira) CTP-37 (AVI BioPharma) IRX-2 (Immuno-Rx) PEP-005 (Peplin Biotech) synchrovax vaccines (CTL Immuno) melanoma vaccine (CTL Immuno) p21 RAS vaccine (GemVax)	dexosome therapy (Anosys) pentrix (Australian Cancer Technology) ISF-154 (Tragen) cancer vaccine (Intercell) norelin (Biostar) BLP-25 (Biomira) MGV (Progenics) ß-alethine (Dovetail) CLL therapy (Vasogen)
Hormonal and antihormonal agents	estrogens conjugated estrogens ethinyl estradiol chlortrianisen idenestrol hydroxyprogesterone caproate medroxyprogesterone testosterone testosterone propionate; fluoxymesterone methyltestosterone diethylstilbestrol megestrol tamoxifen toremofine dexamethasone	prednisone methylprednisolone prednisolone aminoglutethimide leuprolide goserelin leuporelin bicalutamide flutamide octreotide nilutamide mitotane P-04 (Novogen) 2-methoxyestradiol (EntreMed) arzoxifene (Eli Lilly)
Photodynamic agents	talaporfin (Light Sciences) Theralux (Theratechnologies) motexafin gadolinium (Pharmacyclics)	Pd-bacteriopheophorbide (Yeda) lutetium texaphyrin (Pharmacyclics) hypericin
Tyrosine Kinase Inhibitors	imatinib (Novartis) leflunomide (Sugen/Pharmacia) ZD1839 (AstraZeneca) erlotinib (Oncogene Science) canertinib (Pfizer) squalamine (Genaera) SU5416 (Pharmacia) SU6668 (Pharmacia) ZD4190 (AstraZeneca) ZD6474 (AstraZeneca) vatalanib (Novartis) PKI166 (Novartis) GW2016 (GlaxoSmithKline) EKB-509 (Wyeth) EKB-569 (Wyeth)	kahalide F (PharmaMar) CEP-701 (Cephalon) CEP-751 (Cephalon) MLN518 (Millenium) PKC412 (Novartis) phenoxodiol () trastuzumab (Genentech) C225 (ImClone) rhu-Mab (Genentech) MDX-H210 (Medarex) 2C4 (Genentech) MDX-447 (Medarex) ABX-EGF (Abgenix) IMC-1C11 (ImClone)

Table 3 (cont.)

Miscellaneous agents	
SR-27897 (CCK A inhibitor, Sanofi-Synthelabo)	BCX-1777 (PNP inhibitor, BioCryst)
tocladesine (cyclic AMP agonist, Ribapharm)	ranpirnase (ribonuclease stimulant, Alfacell)
alvocidib (CDK inhibitor, Aventis)	galarubicin (RNA synthesis inhibitor, Dong-A)
CV-247 (COX-2 inhibitor, Ivy Medical)	tirapazamine (reducing agent, SRI International)
P54 (COX-2 inhibitor, Phytopharm)	N-acetylcysteine (reducing agent, Zambon)
CapCell™ (CYP450 stimulant, Bavarian Nordic)	R-flurbiprofen (NF-kappaB inhibitor, Encore)
GCS-100 (gal3 antagonist, GlycoGenesys)	3CPA (NF-kappaB inhibitor, Active Biotech)
G17DT immunogen (gastrin inhibitor, Aphton)	seocalcitol (vitamin D receptor agonist, Leo)
efaproxiral (oxygenator, Allos Therapeutics)	131-I-TM-601 (DNA antagonist, TransMolecular)
PI-88 (heparanase inhibitor, Progen)	eflornithine (ODC inhibitor , ILEX Oncology)
tesmilifene (histamine antagonist, YM BioSciences)	minodronic acid (osteoclast inhibitor, Yamanouchi)
histamine (histamine H2 receptor agonist, Maxim)	indisulam (p53 stimulant, Eisai)
tiazofurin (IMPDH inhibitor, Ribapharm)	aplidine (PPT inhibitor, PharmaMar)
cilengitide (integrin antagonist, Merck KGaA)	rituximab (CD20 antibody, Genentech)
SR-31747 (IL-1 antagonist, Sanofi-Synthelabo)	gemtuzumab (CD33 antibody, Wyeth Ayerst)
CCI-779 (mTOR kinase inhibitor, Wyeth)	PG2 (hematopoiesis enhancer, Pharmagenesis)
exisulind (PDE V inhibitor, Cell Pathways)	Immunol™ (triclosan oral rinse, Endo)
CP-461 (PDE V inhibitor, Cell Pathways)	triacetyluridine (uridine prodrug , Wellstat)
AG-2037 (GART inhibitor, Pfizer)	SN-4071 (sarcoma agent, Signature BioScience)
WX-UK1 (plasminogen activator inhibitor, Wilex)	TransMID-107™ (immunotoxin, KS Biomedix)
PBI-1402 (PMN stimulant, ProMetic LifeSciences)	PCK-3145 (apoptosis promotor, Procyon)
bortezomib (proteasome inhibitor, Millennium)	doranidazole (apoptosis promotor, Pola)
SRL-172 (T cell stimulant, SR Pharma)	CHS-828 (cytotoxic agent, Leo)
TLK-286 (glutathione S transferase inhibitor, Telik)	trans-retinoic acid (differentiator, NIH)
PT-100 (growth factor agonist, Point Therapeutics)	MX6 (apoptosis promotor, MAXIA)
midostaurin (PKC inhibitor, Novartis)	apomine (apoptosis promotor, ILEX Oncology)
bryostatin-1 (PKC stimulant, GPC Biotech)	urocidin (apoptosis promotor, Bioniche)
CDA-II (apoptosis promotor, Everlife)	Ro-31-7453 (apoptosis promotor, La Roche)
SDX-101 (apoptosis promotor, Salmedix)	brostallicin (apoptosis promotor, Pharmacia)
ceflatonin (apoptosis promotor, ChemGenex)	

Gene Therapy

In another embodiment of the invention, the BRCA1 gene, or another gene encoding for a peptide of the invention, may be administered to a subject using gene therapy techniques. See, generally, Morgan et al., Ann. Rev. Biochem. 62:191-217, 1993; Culver et al., Trends Genet. 10:174-178, 1994; and U.S. Pat. No. 5,399,346 (French et al.). The general principle is to introduce the BRCA1 gene, for example, into a cancer cell in a patient, such that the BRCA1 gene is expressed and produces a BRCA1 polypeptide, or a biologically-active fragment thereof, that can supplement the activity of the endogenous, defective, or absent BRCA1 polypeptide.

A desired mode of gene therapy is to provide the BRCA1 polynucleotide in such a way that it will replicate inside the cell, thereby enhancing and prolonging the interference effect. Thus, the BRCA1 polynucleotide can be operably linked to a suitable promoter, such as the natural promoter of the corresponding gene, a heterologous promoter that is intrinsically active in cancer cells, or a heterologous promoter that can be induced by a suitable agent.

In another aspect of gene therapy according to the invention, a polynucleotide is introduced into a cancer cell such that the polynucleotide interferes with the expression of a BRCA1-related gene, for example, a gene involved in cell cycle regulation (e.g., cdk2). The administered polynucleotide blocks expression of the BRCA1-related gene by forming a complex with the BRCA1-related gene directly, or by complexing with the RNA transcribed from the BRCA1-related gene. Desirably, the construct is designed so that the polynucleotide sequence is complementary to the sequence of the BRCA1-related gene. Thus, once integrated into the cellular genome, the transcript of the administered polynucleotide will be complementary to the transcript of the BRCA1-related gene, and therefore, the polynucleotide will be capable of hybridizing with the BRCA1-related gene transcript. This approach is known as anti-sense therapy or RNAi. See, for example, Culver et al., supra; and Roth, Ann. Surg. Oncol.1:79-86, 1994.

Exemplary disease targets include, but are not limited to, prostate cancer, ovarian cancer, colorectal cancer, stomach cancer, lung cancer, esophageal cancer, head cancer, neck cancer, bladder cancer, squamous cell cancer, breast cancer, cervical cancer, and endometrial cancer.

For general reviews of the methods of gene therapy, see Goldspiel et al., Clinical Pharmacy 12:488-505, 1993; Wu and Wu, Biotherapy 3:87-95, 1991; Tolstoshev, Ann. Rev. Pharmacol. Toxicol. 32:573-596, 1993; Mulligan, Science 260:926-932, 1993; and Morgan and Anderson, supra.

Methods commonly known in the art of recombinant DNA technology that can be used are described in Ausubel et al. supra; and Kriegler, 1990, Gene Transfer and Expression, A Laboratory Manual, Stockton Press, NY.

It is envisioned that a patient that has been diagnosed with, or that has a propensity for developing, a cancer-related condition can be administered a BRCA1 gene, using a suitable method known in the art and as described herein, such that the BRCA1 gene is incorporated into one or more cells of the patient and is expressible by the cell(s) and/or progeny of the cell(s). The method can encompass *in vivo* administration of the BRCA1 gene in a suitable composition, or the method can involve *ex vivo* therapy in which one or more cells of the patient are removed, transformed with the BRCA1 gene, optionally expanded, and readministered to the patient. Expression of the BRCA1 gene in the transformed cells will reactivate BRCA1 activity in the patient, thereby promoting regulation of the cell cycle, as is discussed above, and therefore, inhibition of the cancer-related condition, thus leading to improvement of the diseased condition afflicting the patient.

Transformation of a target cell with a BRCA1 nucleic acid molecule is facilitated by suitable techniques known in the art, such as providing the BRCA1 nucleic acid molecule in the form of a suitable vector, or encapsulation of the BRCA1 nucleic acid molecule in a liposome. The nucleic acid molecule may be provided to the cancer site by an antigen-specific homing mechanism, or by direct injection. In one approach, the nucleic acid molecule is operably linked to a promoter and is contained in an expression vector. In another approach, the nucleic acid molecule is contained in a recombinant viral vector, for example an adenoviral vector (see e.g., Kozarsky and Wilson, Current Opinion in Genetics and Development 3:499-503, 1993; Rosenfeld et al., Science 252:431-434, 1991; Rosenfeld et al., Cell 68:143-155, 1992; and Mastrangeli et al., J. Clin. Invest. 91:225-234, 1993), an adeno-associated viral vector (AAV; see, for example,

Walsh et al., Proc. Soc. Exp. Biol. Med. 204:289-300, 1993), a lentiviral vector, a herpes viral vector, a retroviral vector (see, e.g., Miller et al., 1993, Meth. Enzymol. 217:581-599; Boesen et al., Biotherapy 6:291-302, 1994; Clowes et al., J. Clin. Invest. 93:644-651, 1994; Kiem et al., Blood 83:1467-1473, 1994; Salmons and Gunzberg, Human Gene Therapy 4:129-141, 1993; and Grossman and Wilson, Curr. Opin. in Genetics and Devel. 3:110-114, 1993), a pox virus vector, or a baculoviral vector.

Non-viral vectors can also be used for gene therapy. For example, naked DNA can be delivered via liposomes, receptor-mediated delivery, calcium phosphate transfection, lipofection, electroporation, particle bombardment (gene gun), microinjection, cell fusion, chromosome-mediated gene transfer, microcell-mediated gene transfer, spheroplast fusion, or pressure-mediated gene delivery. Numerous techniques are known in the art for the introduction of foreign genes into cells (see, e.g., Loeffler and Behr, Meth. Enzymol. 217:599-618, 1993; Cohen et al., Meth. Enzymol. 217:618-644, 1993; Cline, Pharmac. Ther. 29:69-92, 1985), and may be used in accordance with the present invention, provided that the necessary developmental and physiological functions of the recipient cells are not disrupted. Usually, the method of transfer includes the transfer of a selectable marker to the cells. The cells are then placed under selection to isolate those cells that have taken up and are expressing the transferred gene. Those transformed cells are then delivered to a patient. The technique should provide for the stable transfer of the gene to the cell, so that the gene is expressible by the cell and preferably heritable and expressible by progeny of the cell.

Preferably, a desired gene is introduced intracellularly and incorporated within the host precursor cell DNA for expression, by homologous recombination (see, e.g., Koller and Smithies, Proc. Natl. Acad. Sci. USA 86:8932-8935, 1989; Zijlstra et al., Nature 342:435-438, 1989).

The vector containing the BRCA1 gene, or a fragment thereof, can be administered as is described above for the administration of a peptide agent or candidate compound of the invention, for example, to an artery at the site of a tumor or other cancerous cell.

Various reports have been presented regarding the efficacy of gene therapy for the treatment of monogeneic diseases, early stage tumors, and cardiovascular disease. (See, e.g., Blaese et al., Science 270:475-480, 1995; Wingo et al., Cancer 82:1197-1207, 1998; Dzao, Keystone Symposium Molecular and Cellular Biology of Gene Therapy, Keystone, Co. January 19-25, 1998; and Isner, Keystone Symposium Molecular and Cellular Biology of Gene Therapy, Keystone, Co. January 19-25, 1998.)

In a preferred embodiment, patients diagnosed with prostate cancer, ovarian cancer, colorectal cancer (e.g., colorectal adenocarcinoma), stomach cancer, lung cancer, esophageal cancer, head cancer, neck cancer, bladder cancer (e.g., bladder transitional cell carcinoma), squamous cell cancer, breast cancer, cervical cancer, or endometrial cancer can be treated using *in vivo* methods consisting of the administration of a recombinant retrovirus containing a BRCA1 cDNA under the control of a promoter (e.g., a prostate-, ovary-, colon-, stomach-, lung-, esophageal-, head-, neck-, bladder-, squamous cell-, breast-, cervical-, or endometrial-specific promoter) for expression in tumor cells. *In vivo* therapy involves transfection of a BRCA1 nucleic acid molecule directly into the cells of a patient without the need for prior removal of those cells from the patient.

In vivo delivery is desirably accomplished by (1) infusing a recombinant retrovirus vector construct into a blood vessel that perfuses the tumor or (2) injecting a recombinant retrovirus vector construct directly into the tumor. In an especially desired *in vivo* embodiment, a catheter is inserted into a blood vessel in the neck of an organism and the tip of the indwelling catheter is advanced with fluoroscopic guidance to a position in an artery that perfuses a portion of the

tumor. It is desired that the tip of an indwelling catheter be placed in proximity to an area of the tumor so that the cells can be directly targeted and transfected. The retroviral construct can also be directly targeted to cancer cells using cancer cell-specific surface antigens, although this is not required. The recombinant retrovirus is administered to patients desirably by means of intravenous administration in any suitable pharmacological composition, either as a bolus or as an infusion over a period of time. Injection of the recombinant retrovirus directly into the tumor, or into a blood vessel that perfuses the tumor will promote incorporation of the BRCA1 cDNA into tumor cells, thereby inhibiting cell growth of the tumor and preventing further tumor formation.

After delivery of a recombinant retrovirus vector construct to the cells of the tumor, the cells are maintained under physiological conditions to allow sufficient time for the retrovirus vector construct to infect the cancer cells and for cellular expression of the BRCA1 polypeptide contained in that construct. A time period sufficient for expression of a BRCA1 polypeptide in a cancer cell varies as is well known in the art depending on the type of retrovirus vector used and the method of delivery. It should also be pointed out that because that the retrovirus vector employed may be replication defective, it may not be capable of replicating in the cells that are ultimately infected.

A retrovirus vector construct is typically delivered in the form of a pharmacological composition that comprises a physiologically acceptable carrier and the retrovirus vector construct. An effective amount of a retrovirus vector construct is delivered, and consists of 1 pfu/cell, 5 pfu/cell, 10 pfu/cell, or 20 pfu/cell, or any other amount that is effective for promoting expression of a BRCA1 polypeptide in the target cancer cells. Means for determining an effective amount of a retrovirus vector construct are well known in the art.

As is also well known in the art, a specific dose level for any particular subject depends upon a variety of factors including the infectivity of the retrovirus

vector, the age, body weight, general health, sex, diet, time of administration, route of administration, rate of excretion, and the severity of the condition of the patient.

Genes other than those encoding BRCA1, such as those encoding BRCA1-binding peptides of the invention (e.g. a gene encoding a BACH1 polypeptide), may alternatively be used in the foregoing methods of gene therapy.

Incorporation by Reference

The following documents are incorporated by reference: 60/426,132, filed November 14, 2002; 60/485,641, filed July 8, 2003; 60/487,899, filed July 17, 2003; and 10/713,978, filed November 14, 2003.

All patents and publications mentioned in this specification are hereby incorporated by reference to the same extent as if each independent publication or patent application was specifically and individually indicated to be incorporated by reference.

Other Embodiments

From the foregoing description, it is apparent that variations and modifications may be made to the invention described herein to adopt it to various usages and conditions. Such embodiments are also within the scope of the following claims.

What is claimed is:

Claims

1. A computer comprising a processor in communication with a memory; said memory having stored therein

(a) at least one atomic coordinate, or surrogates thereof, from Table 2 for each of the following residues: Ser1655, Gly1656, and Lys1702 of a basic pocket of a BRCA1 tandem BRCT domain complexed with a BACH1 phosphopeptide, or residues Phe1704, Met1775, and Leu1839 of a hydrophobic pocket of said tandem BRCT domain, or atomic coordinates that have a root mean square deviation of the coordinates of less than 3Å; and

(b) a program for generating a three-dimensional model of the coordinates.

2. A complex comprising a BRCA1 tandem BRCT domain, or fragment or analog of a BRCA1 tandem BRCT domain, and a BACH1 phosphopeptide.

3. A method for identifying a peptidomimetic compound that may be a modulator of phosphopeptide binding to a BRCA1 tandem BRCT domain, said method comprising the steps of:

a) contacting a BACH1 phosphopeptide and said tandem BRCT domain under conditions allowing the formation of a complex between said phosphopeptide and said tandem BRCT domain;

b) contacting the combination of a), above, with a candidate compound; and

c) measuring the displacement of said phosphopeptide from said tandem BRCT domain, wherein the displacement of said phosphopeptide from said tandem BRCT domain indicates that said candidate compound is a peptidomimetic compound that modulates phosphopeptide binding to a tandem BRCT domain.

4. The method of claim 3, wherein said candidate compound is identified using rational drug design.

5. A computer comprising a processor in communication with a memory; said memory having stored therein a pharmacophore model of a phosphopeptide that binds to a tandem BRCT domain and a program for displaying said model, said model comprising at least one of the following:

(a) a phosphate group on a phosphorylated residue of said phosphopeptide that participates in at least one hydrogen-bonding interaction; and

(b) a phenylalanine or tyrosine residue at the +3 position of said phosphopeptide, wherein said phenylalanine or tyrosine side chain is directed towards the surface of said tandem BRCT domain.

6. The computer of claim 5, wherein said tandem BRCT domain is a BRCA1 tandem BRCT domain.

7. The computer of claim 5, wherein said tandem BRCT domain is a PTIP tandem BRCT domain.

8. A computer comprising a processor in electrical communication with a memory having stored therein a pharmacophore model of BRCA1 tandem BRCT domain ligands and a program for displaying said model which comprises at least three of the following parameters:

(a) a hydrogen bond acceptor group that forms a hydrogen bond with the side chain hydroxyl group of Ser1655 of said BRCA1 tandem BRCT domain, wherein the distance between the hydrogen of said hydroxyl group and said acceptor group is less than 4 Ångstroms;

(b) a hydrogen bond acceptor group that forms a hydrogen bond with the backbone amide group of Gly1656 of said BRCA1 tandem BRCT domain, wherein the distance between the hydrogen of said amide group and said acceptor group is less than 4 Ångstroms;

(c) a hydrogen bond acceptor group that forms a hydrogen bond with the side chain amine group of Lys1702 of said BRCA1 tandem BRCT domain, wherein the distance between a hydrogen of said amine group and said acceptor group is less than 4 Ångstroms;

(d) a hydrogen bond acceptor group that forms a hydrogen bond with a water molecule, wherein said water molecule in turn forms a hydrogen bond with the backbone amide group of Leu1657 of said BRCA1 tandem BRCT domain, wherein the distance between the hydrogen of said amide group and said acceptor group is less than 6 Ångstroms;

(e) a hydrogen bond acceptor group that forms a hydrogen bond with a water molecule, wherein said water molecule in turn forms a hydrogen bond with a second water molecule, wherein said second water molecule in turn forms a hydrogen bond with the backbone amide group of Leu1701 of said BRCA1 tandem BRCT domain, wherein the distance between the hydrogen of said amide group and said acceptor group is less than 8 Ångstroms;

(f) a hydrogen bond acceptor group that forms a hydrogen bond with a water molecule, wherein said water molecule in turn forms a hydrogen bond with a second water molecule, wherein said second water in turn forms a hydrogen bond with a third water molecule, wherein said third water molecule in turn forms a hydrogen bond with the backbone carbonyl group of Asn1774, wherein the distance between the oxygen of said carbonyl group and said acceptor group is less than 11 Ångstroms;

(g) a hydrogen bond acceptor group that forms a hydrogen bond with a water molecule, wherein said water molecule in turn forms a hydrogen bond with a second water molecule, wherein said second water molecule in turn forms a hydrogen bond with a third water molecule, wherein said third water molecule in turn forms a hydrogen bond with a fourth water molecule, wherein said fourth water molecule in turn forms a hydrogen bond with the backbone amide group of Ile1680 of said BRCA1 tandem BRCT domain, wherein the distance between the hydrogen of said amide group and said acceptor group is less than 10 Ångstroms;

(h) a hydrogen bond acceptor group that forms a hydrogen bond with a water molecule, wherein said water molecule in turn forms a hydrogen bond with a second water molecule, wherein said second water molecule in turn forms a hydrogen bond with a third water molecule, wherein said third water molecule in turn forms a hydrogen bond with a fourth water molecule, wherein said fourth water molecule in turn forms a hydrogen bond with the side chain amide group of Gln1779 of said BRCA1 tandem BRCT domain, wherein the distance between the hydrogen of said amide group and said acceptor group is less than 14 Ångstroms;

(i) a hydrogen bond acceptor group that forms a hydrogen bond with a water molecule, wherein said water molecule in turn forms a hydrogen bond with the backbone amide group of Arg1699 of said BRCA1 tandem BRCT domain, wherein the distance between the hydrogen of said amide group and said acceptor group is less than 7 Ångstroms;

(j) a hydrogen bond acceptor group that forms a hydrogen bond with a water molecule, wherein said water molecule in turn forms a hydrogen bond with the side chain carboxyl group of Glu1698 of said BRCA1 tandem BRCT domain, wherein the distance between an oxygen of said carboxyl group and said acceptor group is less than 6 Ångstroms;

(k) a hydrogen bond acceptor group that forms a hydrogen bond with the side chain guanidinium group of Arg1699 of said BRCA1 tandem BRCT domain, wherein the distance between a hydrogen of said side guanidinium group and said acceptor group is less than 4 Ångstroms;

(l) a hydrogen bond donor group that forms a hydrogen bond with the side chain carbonyl group of Arg1699 of said BRCA1 tandem BRCT domain, wherein the distance between the hydrogen of said donor group and the carbonyl oxygen is less than 4 Ångstroms;

(m) a hydrophobic group that is less than 5 Ångstroms away from an atom of Phe1704, Met1775, or Leu1839 of said BRCA1 tandem BRCT domain.

(n) a hydrogen bond acceptor group that forms a hydrogen bond with a water molecule, wherein said water molecule in turn forms a hydrogen bond with the side chain carboxyl group of Glu1836 of said BRCA1 tandem BRCT domain, wherein the distance between an oxygen of said carboxyl group and said acceptor group is less than 6 Ångstroms; or

(o) a hydrogen bond donor group that forms a hydrogen bond with the side chain carboxyl group of Asp1840 of said BRCA1 tandem BRCT domain, wherein the distance between the hydrogen of said donor group and a carboxyl oxygen is less than 4 Ångstroms.

9. A method of producing a structure for a candidate compound for a BRCA1 tandem BRCT domain, said method comprising the steps of:

(a) providing a three-dimensional structure of said tandem BRCT domain having at least one atomic coordinate, or surrogate thereof, from Table 2 for each of the following residues: Ser1655, Gly1656, and Lys1702 of a basic pocket of a BRCA1 tandem BRCT domain, or residues Phe1704, Met1775, and Leu1839 of a hydrophobic pocket of said tandem BRCT domain, or atomic coordinates that have a root mean square deviation of the coordinates of less than 3 Å; and

(b) producing a structure for a candidate compound wherein said structure defines a molecule having sufficient surface complementary to said tandem BRCT domain structure to bind said tandem BRCT domain in an aqueous solution.

10. The method of claim 9, wherein said candidate compound is a peptidomimetic.

11. The method of claim 10, wherein said peptidomimetic comprises a phosphate moiety.

12. The method of claim 10, wherein said peptidomimetic comprises a phosphonate moiety.

13. A compound made by the method of claim 9.

14. A compound having a structure produced by a method comprising the steps of:

(a) providing a three-dimensional structure of a tandem BRCT domain having at least one atomic coordinate, or surrogate thereof, from Table 2 for each of the following residues: Ser1655, Gly1656, and Lys1702 of a basic pocket of a BRCA1 tandem BRCT domain, or residues Phe1704, Met1775, and Leu1839 of a hydrophobic pocket of said tandem BRCT domain, or atomic coordinates that have a root mean square deviation of the coordinates of less than 3 Å; and

(b) producing a structure for a candidate compound wherein said structure defines a molecule having sufficient surface complementary to said tandem BRCT domain structure to bind said tandem BRCT domain in an aqueous solution.

15. A crystal of a complex comprising a tandem BRCT domain bound to a phosphopeptide.

16. The crystal of claim 15, wherein said tandem BRCT domain is a BRCA1 tandem BRCT domain.

17. The crystal of claim 16, wherein said tandem BRCT domain is $BRCA1_{1646-1859}$.

18. The crystal of claim 16, wherein said tandem BRCT domain is $BRCA1_{1646-1863}$ or $BRCA1_{1633-1863}$.

19. The crystal of claim 16, wherein said crystal has a space group of $P3_221$ and a unit cell dimension of a = b = 65.8 Å and c = 93.1 Å).

20. The crystal of claim 15, wherein said tandem BRCT domain is a PTIP tandem BRCT domain.

21. The crystal of claim 15, wherein said phosphopeptide comprises the amino acid sequence [pSer/pThr]-X-X-[Phe/Tyr].

22. The crystal of claim 21, wherein the +1 position of said phosphopeptide is proline.

23. The crystal of claim 21, wherein said phosphopeptide comprises the amino acid sequence Ser-Arg-Ser-Thr-pSer-Pro-Thr-Phe-Asn-Lys.

24. A phosphopeptide comprising the amino acid sequence [pSer/pThr]-X-X-[Phe/Tyr].

25. The phosphopeptide of claim 24, wherein the +1 position of said phosphopeptide is proline.

26. The phosphopeptide of claim 24, wherein said phosphopeptide comprises the amino acid sequence Ser-Arg-Ser-Thr-pSer-Pro-Thr-Phe-Asn-Lys.

27. The compound of claim 14 or the phosphopeptide of claim 24, wherein said compound or said phosphopeptide binds a tandem BRCT domain.

28. The compound of claim 24, wherein said compound modulates phosphopeptide binding to a tandem BRCT domain according to the method of claim 3.

29. A method for treating or inhibiting cellular proliferation in a subject, said method comprising administering the compound of claim 14 or the phosphopeptide of claim 24, wherein said compound or said phosphopeptide is in an amount sufficient to treat or inhibit the cellular proliferative disorder in said subject.

30. The method of claim 29, wherein said method is for the treatment of a subject with a cellular proliferative disorder.

31. The method of claim 29, wherein said method further comprises administering a chemotherapeutic agent, wherein said phosphopeptide and said chemotherapeutic agent are administered in amounts sufficient to inhibit said cellular proliferative disorder in said subject, and wherein said chemotherapeutic agent is administered simultaneously or within twenty-eight days of administering said phosphopeptide.

32. The method of claim 31, wherein said chemotherapeutic agent is selected from one or more of the agents listed in Table 3.

33. The method of claim 30, wherein said method further comprises radiation therapy, wherein said phosphopeptide and said radiation therapy are administered in amounts sufficient to treat or inhibit said cellular proliferative disorder in said subject, and wherein said radiation therapy is administered simultaneously or within twenty-eight days of administering said phosphopeptide.

34. The method of claim 30, wherein said cellular proliferative disorder is a neoplasm.

35. The method of claim 34, wherein said neoplasm is cancer.

36. The method of claim 35, wherein said cancer is selected from the group consisting of acoustic neuroma, acute leukemia, acute lymphocytic leukemia, acute monocytic leukemia, acute myeloblastic leukemia, acute myelocytic leukemia, acute myelomonocytic leukemia, acute promyelocytic leukemia, acute erythroleukemia, adenocarcinoma, angiosarcoma, astrocytoma, basal cell carcinoma, bile duct carcinoma, bladder carcinoma, brain cancer, breast cancer, bronchogenic carcinoma, cervical cancer, chondrosarcoma, chordoma,

choriocarcinoma, chronic leukemia, chronic lymphocytic leukemia, chronic myelocytic leukemia, colon cancer, colon carcinoma, craniopharyngioma, cystadenocarcinoma, embryonal carcinoma, endotheliosarcoma, ependymoma, epithelial carcinoma, Ewing's tumor, glioma, heavy chain disease, hemangioblastoma, hepatoma, Hodgkin's disease, large cell carcinoma, leiomyosarcoma, liposarcoma, lung cancer, lung carcinoma, lymphangioendotheliosarcoma, lymphangiosarcoma, macroglobulinemia, medullary carcinoma, medulloblastoma, melanoma, meningioma, mesothelioma, myxosarcoma, neuroblastoma, non-Hodgkin's disease, oligodendriglioma, osteogenic sarcoma, ovarian cancer, pancreatic cancer, papillary adenocarcinomas, papillary carcinoma, pinealoma, polycythemia vera, prostate cancer, rhabdomyosarcoma, renal cell carcinoma, retinoblastoma, schwannoma, sebaceous gland carcinoma, seminoma, small cell lung carcinoma, squamous cell carcinoma, sweat gland carcinoma, synovioma, testicular cancer, uterine cancer, Waldenstrom's fibrosarcoma, and Wilm's tumor.

37. A prodrug of the compound of claim 14 or the phosphopeptide of claim 24, wherein said prodrug is converted *in vivo* to said compound or said phosphopeptide.

38. The prodrug of claim 37, wherein said prodrug comprises an ester group.

39. The prodrug of claim 38, wherein said ester is a methyl ester.

40. The prodrug of claim 37, wherein said prodrug comprises a sulfonate group.

41. The prodrug of claim 37, wherein said prodrug masks a charged group of said compound or said phosphopeptide.

42. The prodrug of claim 37, wherein said prodrug comprises a caged compound.

43. A pharmaceutical formulation comprising the compound of claim 14 or the phosphopeptide of claim 24.

44. A pharmaceutical formulation comprising the prodrug of claim 38.

Figure 1A

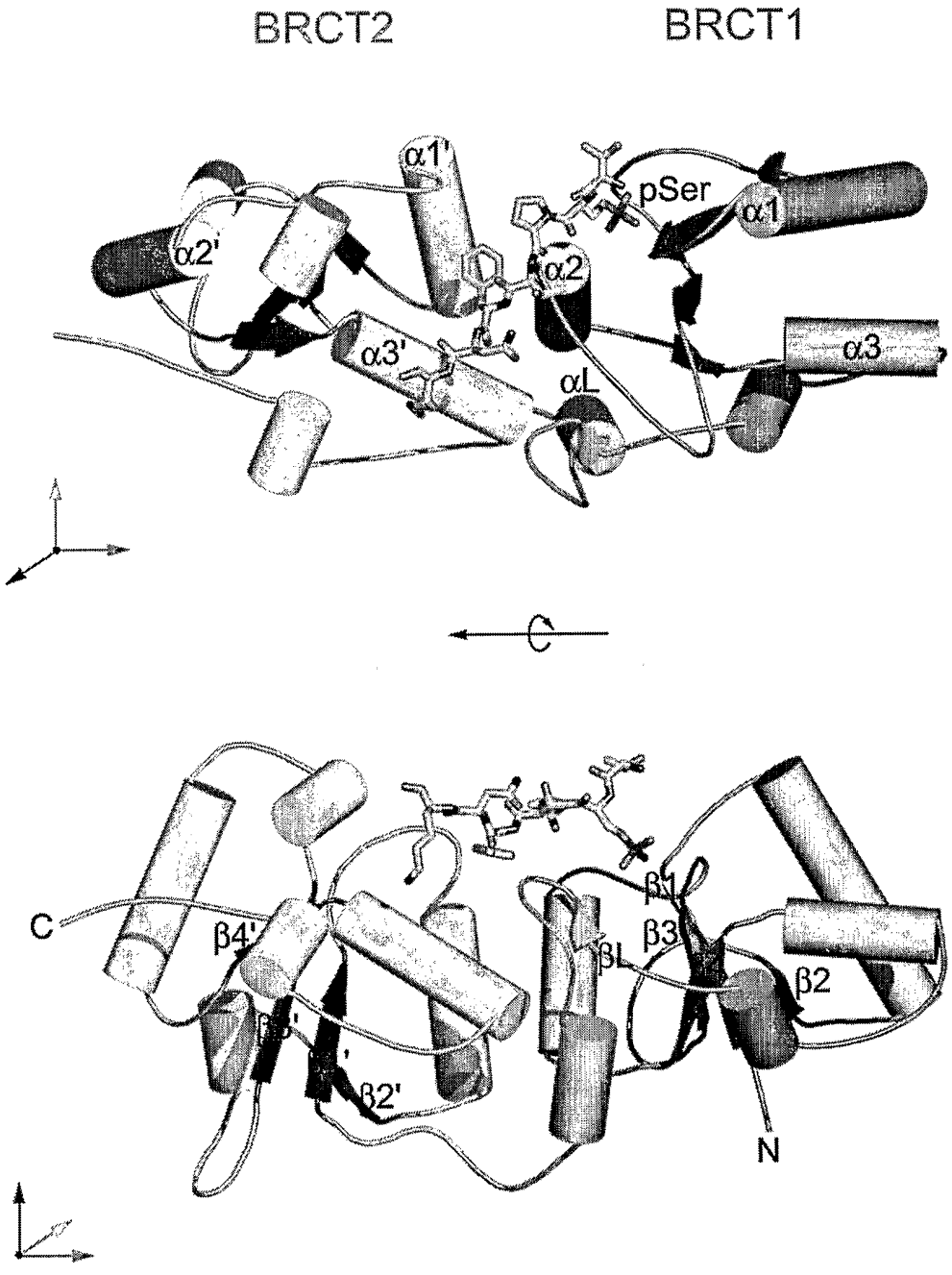


Figure 1B

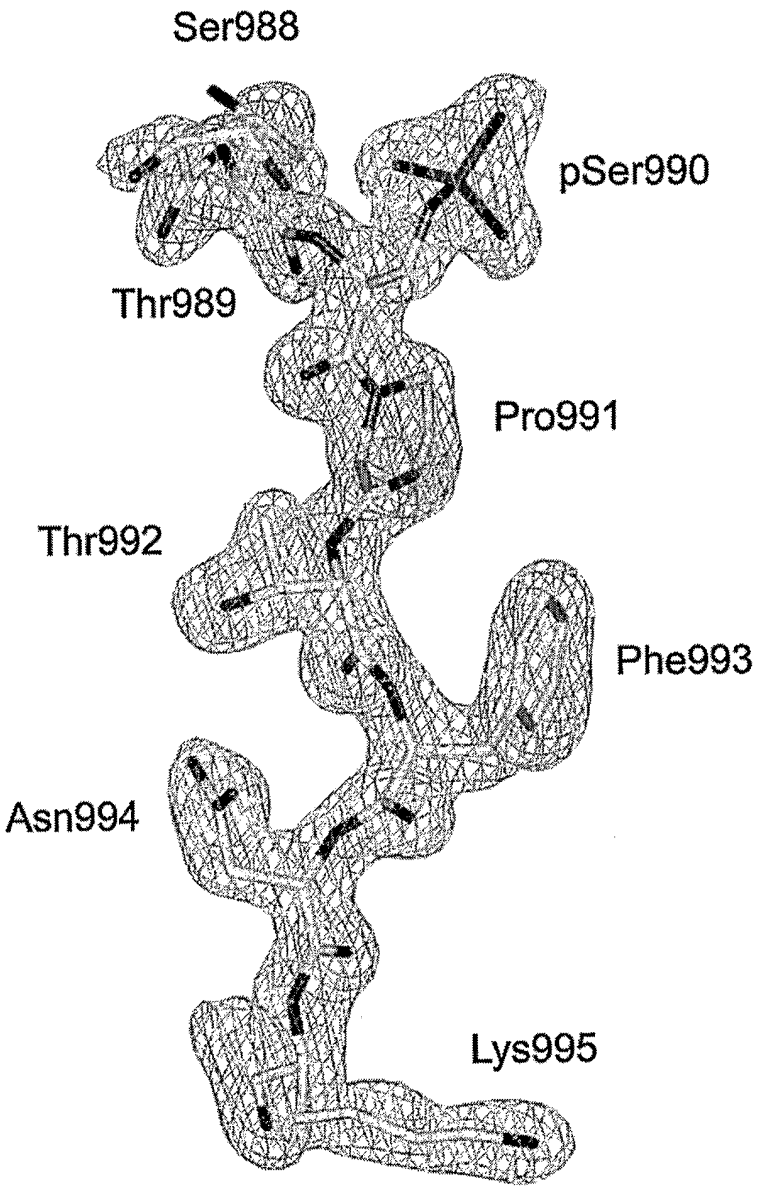


Figure 2A

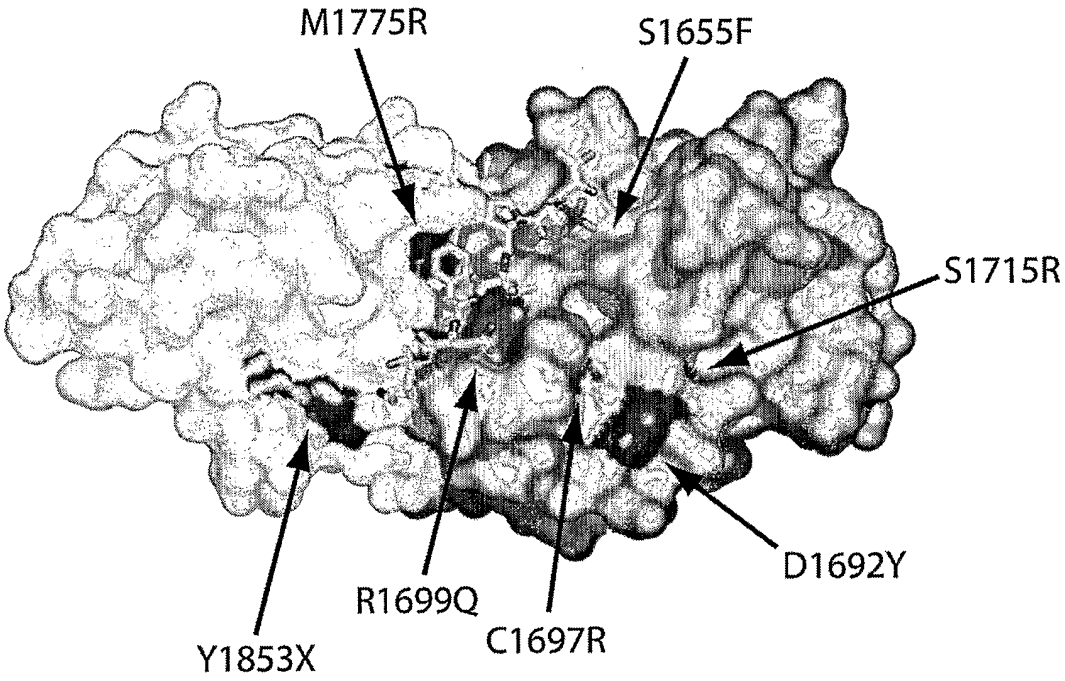


Figure 2B

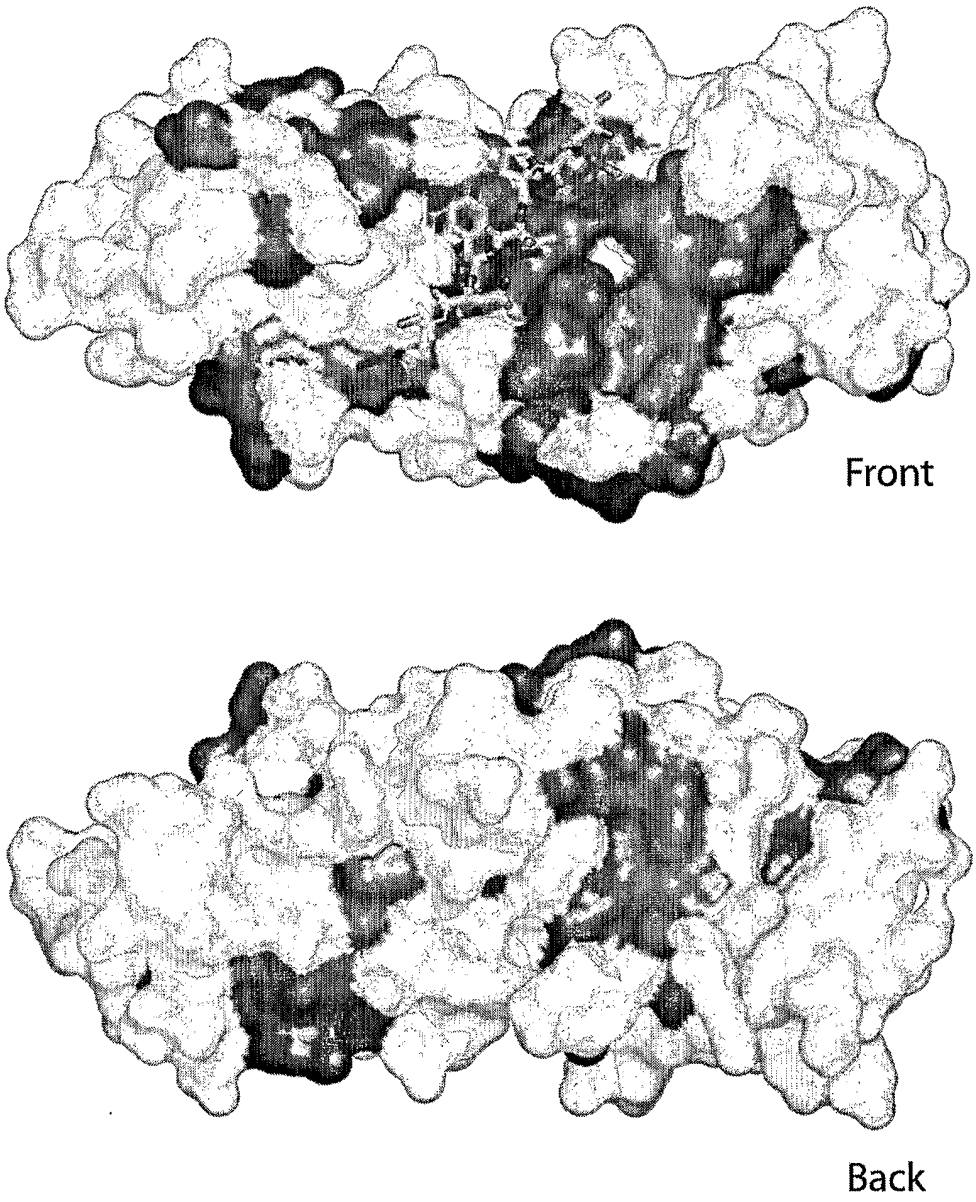


Figure 3A

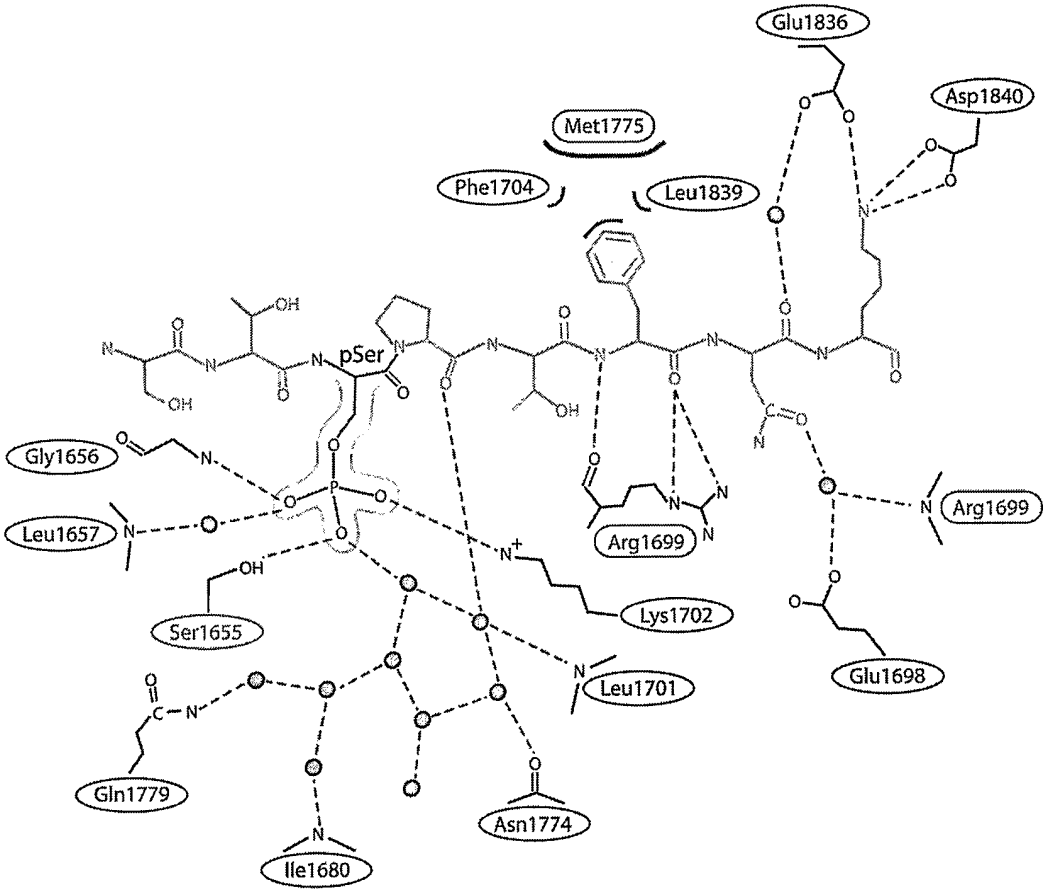

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Figure 3B

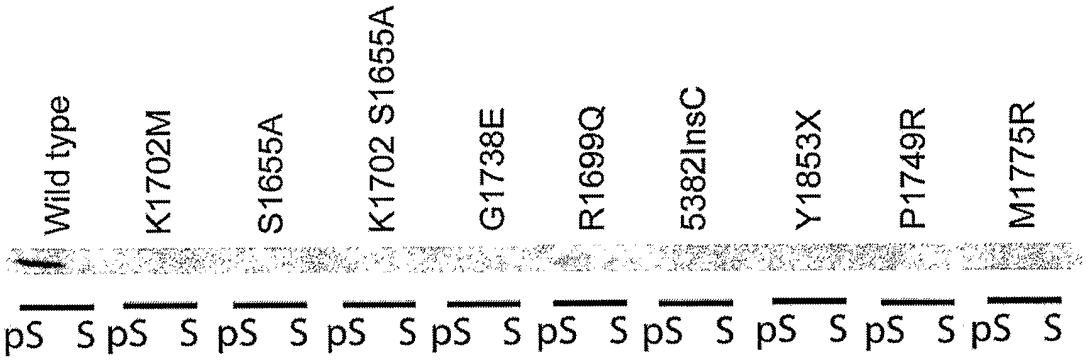

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Figure 3C

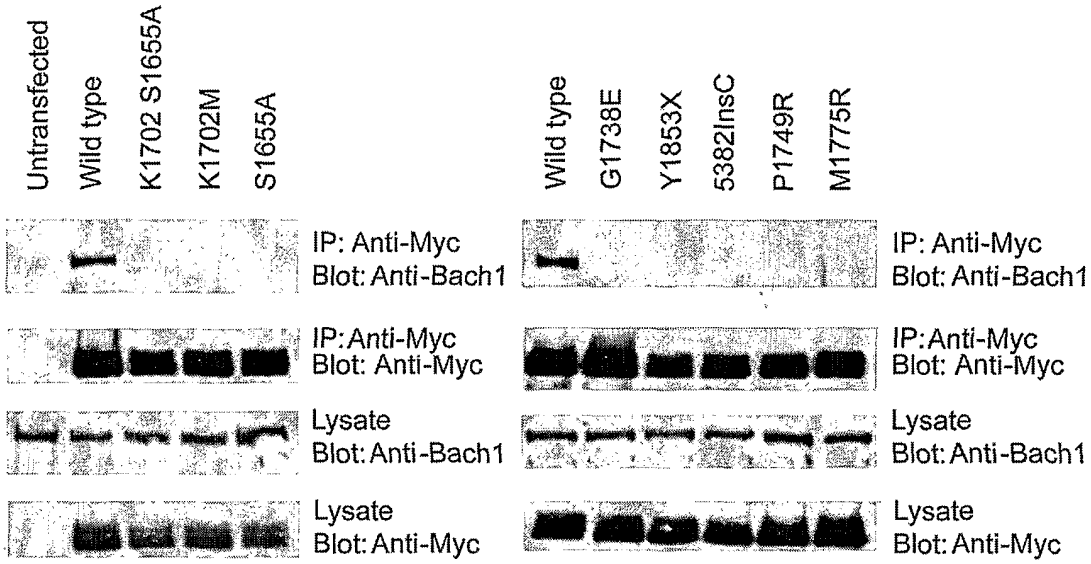

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Figure 4A

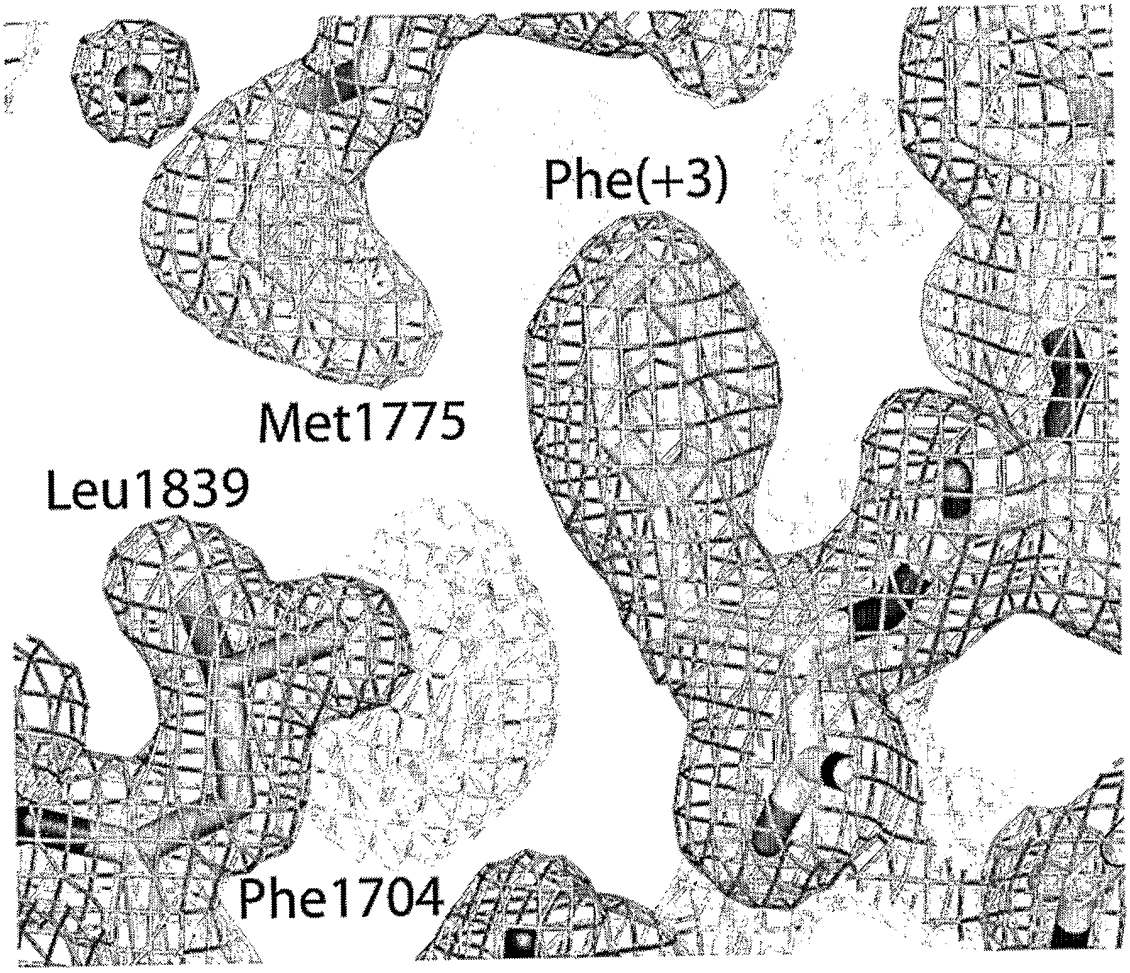


Figure 4B

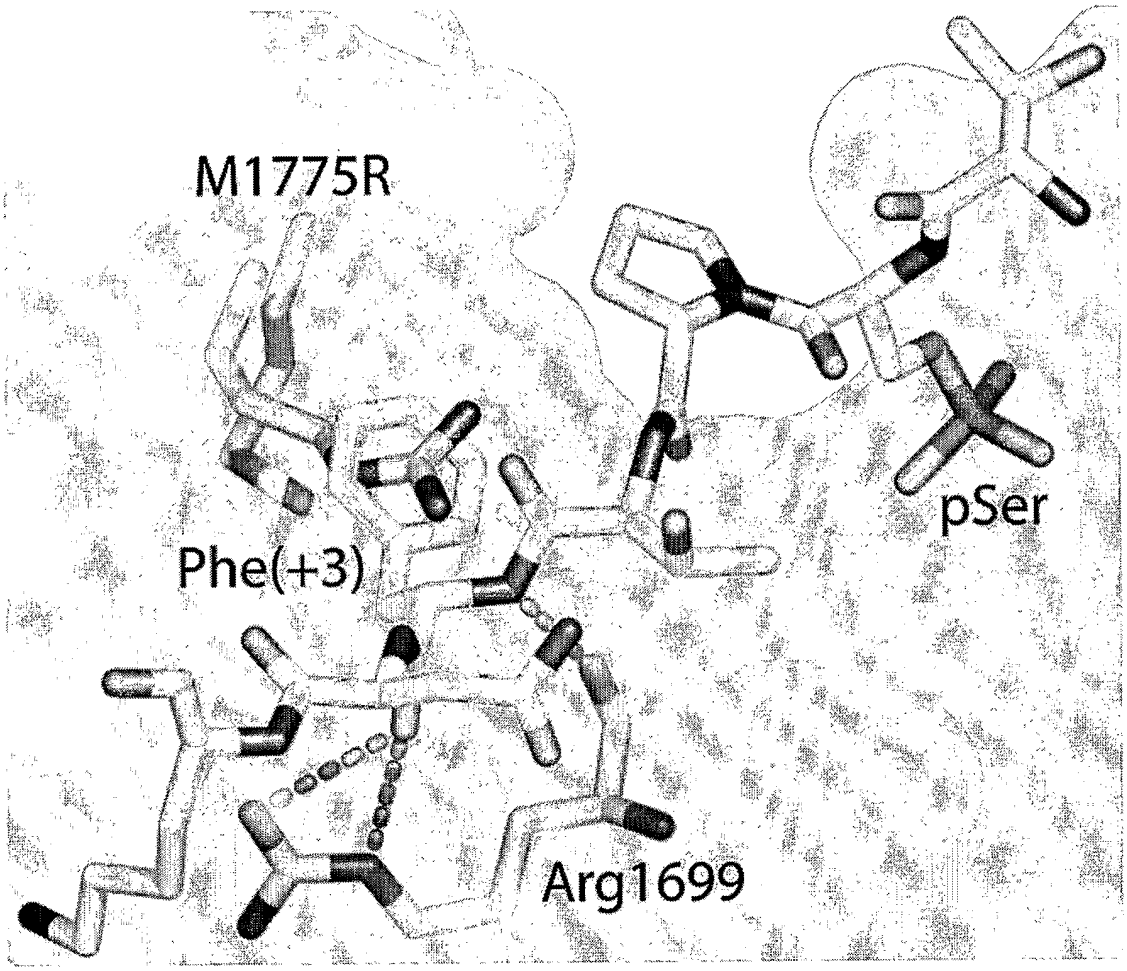


Figure 4C



Figure 5A

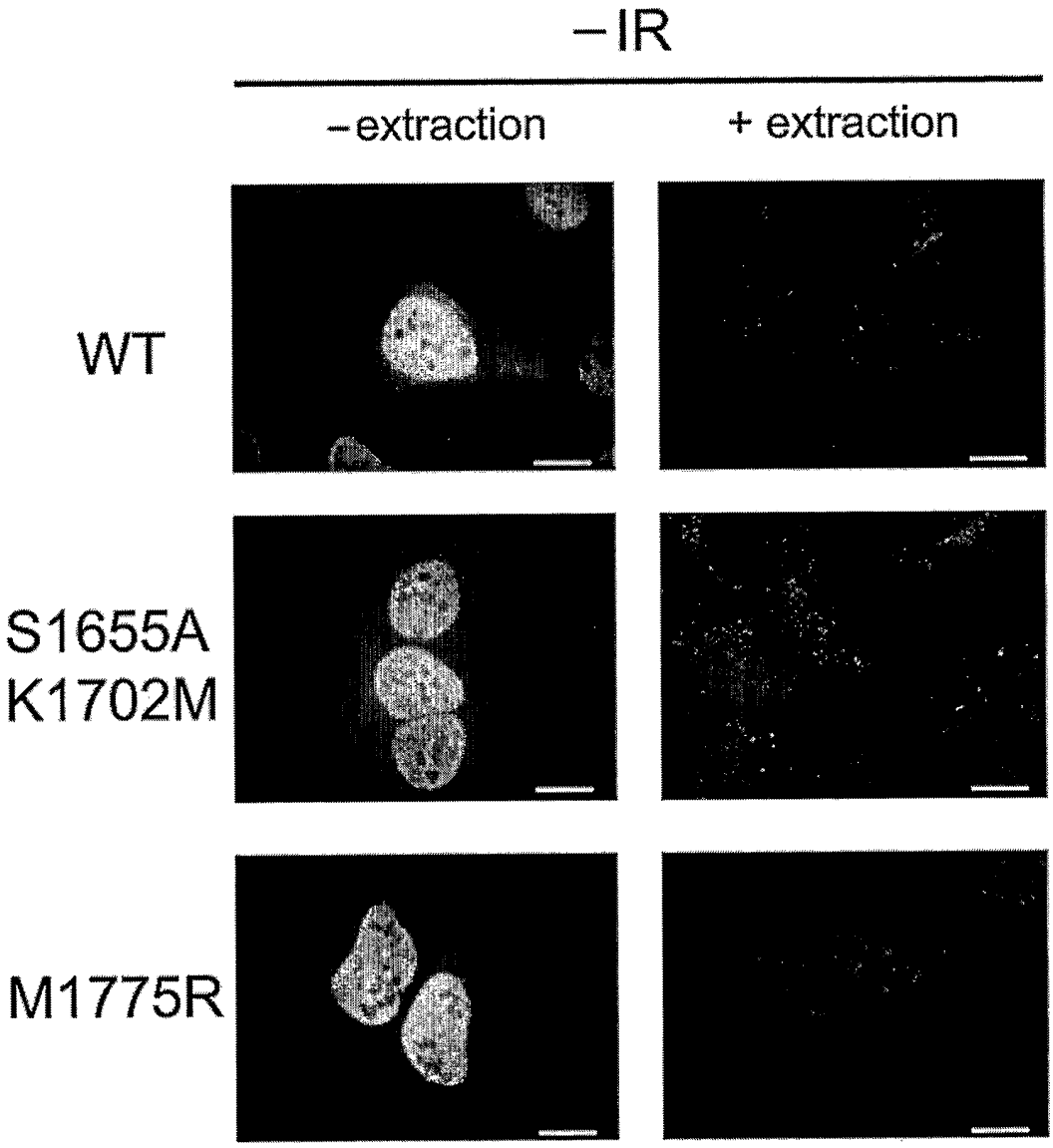
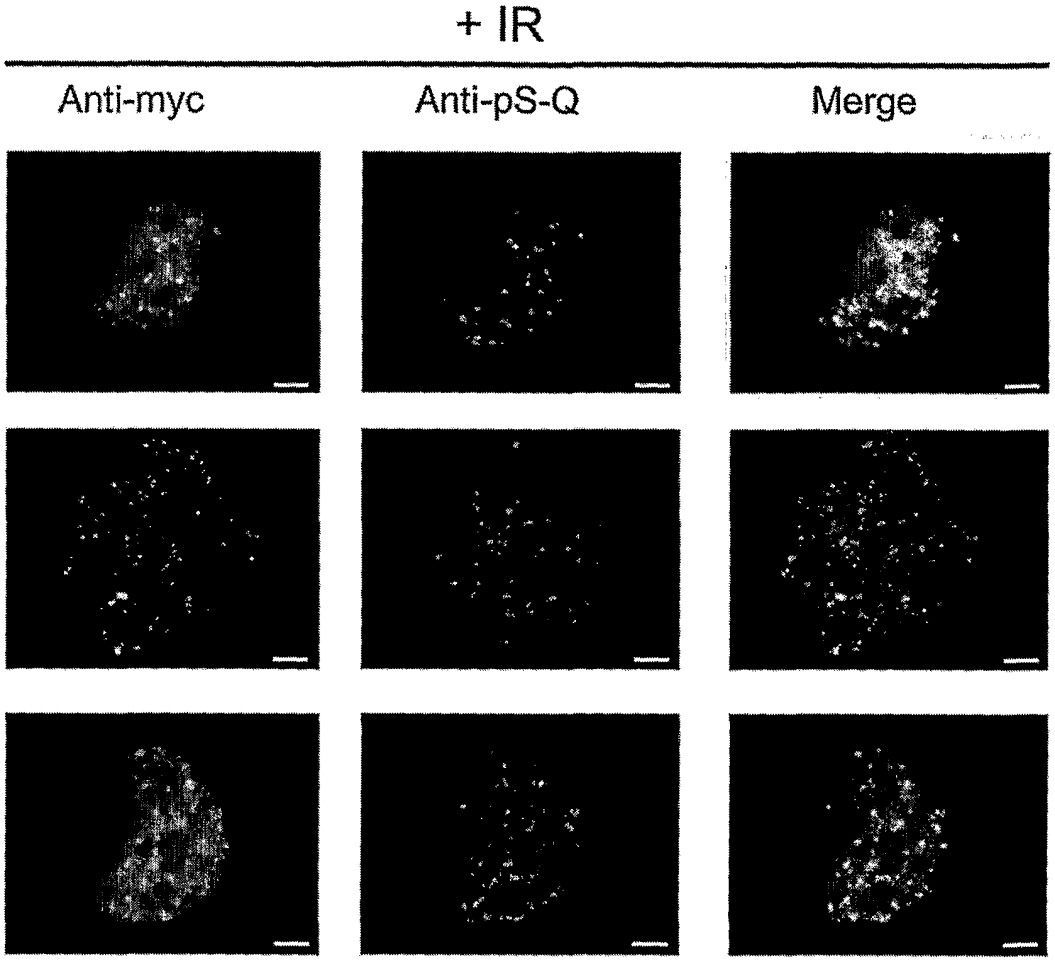


Figure 5B



SEQUENCE LISTING

<110> MASSACHUSETTS INSTITUTE OF TECHNOLOGY et al
Yaffe, Michael B
Clapperton, Julie A
Manke, Isaac A
Lowery, Drew M
Ho, Timmy
Haire, Lesley F
Smerdon, Stephen J

<120> Methods and Compositions For Cancer Treatment Relating to BRCA1 BRCT Domain Recognition of Phosphorylated BACH1

<130> 01997/560WO2

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<151> 2004-05-07

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Ala Met Gln Lys Ile Leu Glu Cys Pro Ile Cys Leu Glu Leu Ile Lys
            20                  25                  30

gaa cct gtc tcc aca aag tgt gac cac ata ttt tgc aaa ttt tgc atg      144
Glu Pro Val Ser Thr Lys Cys Asp His Ile Phe Cys Lys Phe Cys Met
        35                  40                  45

ctg aaa ctt ctc aac cag aag aaa ggg cct tca cag tgt cct tta tgt      192
Leu Lys Leu Leu Asn Gln Lys Lys Gly Pro Ser Gln Cys Pro Leu Cys
    50                  55                  60

aag aat gat ata acc aaa agg agc cta caa gaa agt acg aga ttt agt      240
Lys Asn Asp Ile Thr Lys Arg Ser Leu Gln Glu Ser Thr Arg Phe Ser
65                  70                  75                  80

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Gln Leu Val Glu Glu Leu Leu Lys Ile Ile Cys Ala Phe Gln Leu Asp
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            100                 105                 110

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Asn Ser Pro Glu His Leu Lys Asp Glu Val Ser Ile Ile Gln Ser Met
        115                 120                 125

ggc tac aga aac cgt gcc aaa aga ctt cta cag agt gaa ccc gaa aat      432
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Pro Ser Leu Gln Glu Thr Ser Leu Ser Val Gln Leu Ser Asn Leu Gly
145                 150                 155                 160

act gtg aga act ctg agg aca aag cag cgg ata caa cct caa aag acg      528
Thr Val Arg Thr Leu Arg Thr Lys Gln Arg Ile Gln Pro Gln Lys Thr
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tct gtc tac att gaa ttg gga tct gat tct tct gaa gat acc gtt aat      576
Ser Val Tyr Ile Glu Leu Gly Ser Asp Ser Ser Glu Asp Thr Val Asn
            180                 185                 190

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Lys Ala Thr Tyr Cys Ser Val Gly Asp Gln Glu Leu Leu Gln Ile Thr
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cct caa gga acc agg gat gaa atc agt ttg gat tct gca aaa aag gct      672
Pro Gln Gly Thr Arg Asp Glu Ile Ser Leu Asp Ser Ala Lys Lys Ala
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Pro Cys Gly Thr Asn Thr His Ala Ser Ser Leu Gln His Glu Asn Ser
        275                 280                 285

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Ser Leu Leu Leu Thr Lys Asp Arg Met Asn Val Glu Lys Ala Glu Phe
    290                 295                 300

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Cys Asn Lys Ser Lys Gln Pro Gly Leu Ala Arg Ser Gln His Asn Arg
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                325                 330                 335

gaa aaa aag gta gat ctg aat gct gat ccc ctg tgt gag aga aaa gaa     1056
Glu Lys Lys Val Asp Leu Asn Ala Asp Pro Leu Cys Glu Arg Lys Glu
            340                 345                 350

tgg aat aag cag aaa ctg cca tgc tca gag aat cct aga gat act gaa     1104
Trp Asn Lys Gln Lys Leu Pro Cys Ser Glu Asn Pro Arg Asp Thr Glu
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Trp Phe Ser Arg Ser Asp Glu Leu Leu Gly Ser Asp Asp Ser His Asp
385                 390                 395                 400

ggg gag tct gaa tca aat gcc aaa gta gct gat gta ttg gac gtt cta     1248
Gly Glu Ser Glu Ser Asn Ala Lys Val Ala Asp Val Leu Asp Val Leu
                405                 410                 415

aat gag gta gat gaa tat tct ggt tct tca gag aaa ata gac tta ctg     1296
Asn Glu Val Asp Glu Tyr Ser Gly Ser Ser Glu Lys Ile Asp Leu Leu
            420                 425                 430

gcc agt gat cct cat gag gct tta ata tgt aaa agt gaa aga gtt cac     1344
Ala Ser Asp Pro His Glu Ala Leu Ile Cys Lys Ser Glu Arg Val His
        435                 440                 445

tcc aaa tca gta gag agt aat att gaa gac aaa ata ttt ggg aaa acc     1392
Ser Lys Ser Val Glu Ser Asn Ile Glu Asp Lys Ile Phe Gly Lys Thr
    450                 455                 460

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Leu Ile Ile Gly Ala Phe Val Thr Glu Pro Gln Ile Ile Gln Glu Arg
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Pro Leu Thr Asn Lys Leu Lys Arg Lys Arg Arg Pro Thr Ser Gly Leu
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cat cct gag gat ttt atc aag aaa gca gat ttg gca gtt caa aag act     1584
His Pro Glu Asp Phe Ile Lys Lys Ala Asp Leu Ala Val Gln Lys Thr
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545                 550                 555                 560

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gaa tct gct ttc aaa acg aaa gct gaa cct ata agc agc agt ata agc     1776
Glu Ser Ala Phe Lys Thr Lys Ala Glu Pro Ile Ser Ser Ser Ile Ser
            580                 585                 590

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Asn Arg Leu Arg Arg Lys Ser Ser Thr Arg His Ile His Ala Leu Glu
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625                 630                 635                 640

att gat agt tgt tct agc agt gaa gag ata aag aaa aaa aag tac aac     1968
Ile Asp Ser Cys Ser Ser Ser Glu Glu Ile Lys Lys Lys Lys Tyr Asn
                645                 650                 655

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Gln Met Pro Val Arg His Ser Arg Asn Leu Gln Leu Met Glu Gly Lys
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Glu Pro Ala Thr Gly Ala Lys Lys Ser Asn Lys Pro Asn Glu Gln Thr
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Ser Lys Arg His Asp Ser Asp Thr Phe Pro Glu Leu Lys Leu Thr Asn
    690                 695                 700

gca cct ggt tct ttt act aag tgt tca aat acc agt gaa ctt aaa gaa     2160
Ala Pro Gly Ser Phe Thr Lys Cys Ser Asn Thr Ser Glu Leu Lys Glu
705                 710                 715                 720

ttt gtc aat cct agc ctt cca aga gaa gaa aaa gaa gag aaa cta gaa     2208
Phe Val Asn Pro Ser Leu Pro Arg Glu Glu Lys Glu Glu Lys Leu Glu
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785                 790                 795                 800

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ggt tgt tcc aaa gat aat aga aat gac aca gaa ggc ttt aag tat cca     2496
Gly Cys Ser Lys Asp Asn Arg Asn Asp Thr Glu Gly Phe Lys Tyr Pro
            820                 825                 830

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        835                 840                 845

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865                 870                 875                 880

gaa tgt gca aca ttc tct gcc cac tct ggg tcc tta aag aaa caa agt     2688
Glu Cys Ala Thr Phe Ser Ala His Ser Gly Ser Leu Lys Lys Gln Ser
                885                 890                 895

cca aaa gtc act ttt gaa tgt gaa caa aag gaa gaa aat caa gga aag     2736
Pro Lys Val Thr Phe Glu Cys Glu Gln Lys Glu Glu Asn Gln Gly Lys
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ttt cct gtg gtt ggt cag aaa gat aag cca gtt gat aat gcc aaa tgt     2832
Phe Pro Val Val Gly Gln Lys Asp Lys Pro Val Asp Asn Ala Lys Cys
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Ser Ile Lys Gly Gly Ser Arg Phe Cys Leu Ser Ser Gln Phe Arg Gly
945                 950                 955                 960

aac gaa act gga ctc att act cca aat aaa cat gga ctt tta caa aac     2928
Asn Glu Thr Gly Leu Ile Thr Pro Asn Lys His Gly Leu Leu Gln Asn
                965                 970                 975

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Ser Pro  Glu Arg Glu Met Gly  Asn Glu Asn Ile Pro  Ser Thr Val
    1010                1015                1020

agc aca  att agc cgt aat aac  att aga gaa aat gtt  ttt aaa gaa      3114
Ser Thr  Ile Ser Arg Asn Asn  Ile Arg Glu Asn Val  Phe Lys Glu
    1025                1030                1035

gcc agc  tca agc aat att aat  gaa gta ggt tcc agt  act aat gaa      3159
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gaa gaa  gta gtt cag act gtt  aat aca gat ttc tct  cca tat ctg      3384
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att tca  gat aac tta gaa cag  cct atg gga agt agt  cat gca tct      3429
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    1130                1135                1140

cag gtt  tgt tct gag aca cct  gat gac ctg tta gat  gat ggt gaa      3474
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    1160                1165                1170

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    1205                1210                1215

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    1220                1225                1230

gta aac  aat ata cct tct cag  tct act agg cat agc  acc gtt gct      3744
Val Asn  Asn Ile Pro Ser Gln  Ser Thr Arg His Ser  Thr Val Ala
    1235                1240                1245

acc gag  tgt ctg tct aag aac  aca gag gag aat tta  tta tca ttg      3789
Thr Glu  Cys Leu Ser Lys Asn  Thr Glu Glu Asn Leu  Leu Ser Leu
    1250                1255                1260

aag aat  agc tta aat gac tgc  agt aac cag gta ata  ttg gca aag      3834
Lys Asn  Ser Leu Asn Asp Cys  Ser Asn Gln Val Ile  Leu Ala Lys
    1265                1270                1275

gca tct  cag gaa cat cac ctt  agt gag gaa aca aaa  tgt tct gct      3879
Ala Ser  Gln Glu His His Leu  Ser Glu Glu Thr Lys  Cys Ser Ala
    1280                1285                1290

agc ttg  ttt tct tca cag tgc  agt gaa ttg gaa gac  ttg act gca      3924
Ser Leu  Phe Ser Ser Gln Cys  Ser Glu Leu Glu Asp  Leu Thr Ala
    1295                1300                1305

aat aca  aac acc cag gat cct  ttc ttg att ggt tct  tcc aaa caa      3969
Asn Thr  Asn Thr Gln Asp Pro  Phe Leu Ile Gly Ser  Ser Lys Gln
    1310                1315                1320

atg agg  cat cag tct gaa agc  cag gga gtt ggt ctg  agt gac aag      4014
Met Arg  His Gln Ser Glu Ser  Gln Gly Val Gly Leu  Ser Asp Lys
    1325                1330                1335

gaa ttg  gtt tca gat gat gaa  gaa aga gga acg ggc  ttg gaa gaa      4059
Glu Leu  Val Ser Asp Asp Glu  Glu Arg Gly Thr Gly  Leu Glu Glu
    1340                1345                1350

aat aat  caa gaa gag caa agc  atg gat tca aac tta  ggt gaa gca      4104
Asn Asn  Gln Glu Glu Gln Ser  Met Asp Ser Asn Leu  Gly Glu Ala
    1355                1360                1365

gca tct  ggg tgt gag agt gaa  aca agc gtc tct gaa  gac tgc tca      4149
Ala Ser  Gly Cys Glu Ser Glu  Thr Ser Val Ser Glu  Asp Cys Ser
    1370                1375                1380

ggg cta  tcc tct cag agt gac  att tta acc act cag  cag agg gat      4194
Gly Leu  Ser Ser Gln Ser Asp  Ile Leu Thr Thr Gln  Gln Arg Asp
    1385                1390                1395

acc atg  caa cat aac ctg ata  aag ctc cag cag gaa  atg gct gaa      4239
Thr Met  Gln His Asn Leu Ile  Lys Leu Gln Gln Glu  Met Ala Glu
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    1400                1405                1410

cta gaa  gct gtg tta gaa cag  cat ggg agc cag cct  tct aac agc      4284
Leu Glu  Ala Val Leu Glu Gln  His Gly Ser Gln Pro  Ser Asn Ser
    1415                1420                1425

tac cct  tcc atc ata agt gac  tct tct gcc ctt gag  gac ctg cga      4329
Tyr Pro  Ser Ile Ile Ser Asp  Ser Ser Ala Leu Glu  Asp Leu Arg
    1430                1435                1440

aat cca  gaa caa agc aca tca  gaa aaa gca gta tta  act tca cag      4374
Asn Pro  Glu Gln Ser Thr Ser  Glu Lys Ala Val Leu  Thr Ser Gln
    1445                1450                1455

aaa agt  agt gaa tac cct ata  agc cag aat cca gaa  ggc ctt tct      4419
Lys Ser  Ser Glu Tyr Pro Ile  Ser Gln Asn Pro Glu  Gly Leu Ser
    1460                1465                1470

gct gac  aag ttt gag gtg tct  gca gat agt tct acc  agt aaa aat      4464
Ala Asp  Lys Phe Glu Val Ser  Ala Asp Ser Ser Thr  Ser Lys Asn
    1475                1480                1485

aaa gaa  cca gga gtg gaa agg  tca tcc cct tct aaa  tgc cca tca      4509
Lys Glu  Pro Gly Val Glu Arg  Ser Ser Pro Ser Lys  Cys Pro Ser
    1490                1495                1500

tta gat  gat agg tgg tac atg  cac agt tgc tct ggg  agt ctt cag      4554
Leu Asp  Asp Arg Trp Tyr Met  His Ser Cys Ser Gly  Ser Leu Gln
    1505                1510                1515

aat aga  aac tac cca tct caa  gag gag ctc att aag  gtt gtt gat      4599
Asn Arg  Asn Tyr Pro Ser Gln  Glu Glu Leu Ile Lys  Val Val Asp
    1520                1525                1530

gtg gag  gag caa cag ctg gaa  gag tct ggg cca cac  gat ttg acg      4644
Val Glu  Glu Gln Gln Leu Glu  Glu Ser Gly Pro His  Asp Leu Thr
    1535                1540                1545

gaa aca  tct tac ttg cca agg  caa gat cta gag gga  acc cct tac      4689
Glu Thr  Ser Tyr Leu Pro Arg  Gln Asp Leu Glu Gly  Thr Pro Tyr
    1550                1555                1560

ctg gaa  tct gga atc agc ctc  ttc tct gat gac cct  gaa tct gat      4734
Leu Glu  Ser Gly Ile Ser Leu  Phe Ser Asp Asp Pro  Glu Ser Asp
    1565                1570                1575

cct tct  gaa gac aga gcc cca  gag tca gct cgt gtt  ggc aac ata      4779
Pro Ser  Glu Asp Arg Ala Pro  Glu Ser Ala Arg Val  Gly Asn Ile
    1580                1585                1590

cca tct  tca acc tct gca ttg  aaa gtt ccc caa ttg  aaa gtt gca      4824
Pro Ser  Ser Thr Ser Ala Leu  Lys Val Pro Gln Leu  Lys Val Ala
    1595                1600                1605

gaa tct  gcc cag agt cca gct  gct gct cat act act  gat act gct      4869
Glu Ser  Ala Gln Ser Pro Ala  Ala Ala His Thr Thr  Asp Thr Ala
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    1610                1615                1620

ggg tat  aat gca atg gaa gaa  agt gtg agc agg gag  aag cca gaa      4914
Gly Tyr  Asn Ala Met Glu Glu  Ser Val Ser Arg Glu  Lys Pro Glu
    1625                1630                1635

ttg aca  gct tca aca gaa agg  gtc aac aaa aga atg  tcc atg gtg      4959
Leu Thr  Ala Ser Thr Glu Arg  Val Asn Lys Arg Met  Ser Met Val
    1640                1645                1650

gtg tct  ggc ctg acc cca gaa  gaa ttt atg ctc gtg  tac aag ttt      5004
Val Ser  Gly Leu Thr Pro Glu  Glu Phe Met Leu Val  Tyr Lys Phe
    1655                1660                1665

gcc aga  aaa cac cac atc act  tta act aat cta att  act gaa gag      5049
Ala Arg  Lys His His Ile Thr  Leu Thr Asn Leu Ile  Thr Glu Glu
    1670                1675                1680

act act  cat gtt gtt atg aaa  aca gat gct gag ttt  gtg tgt gaa      5094
Thr Thr  His Val Val Met Lys  Thr Asp Ala Glu Phe  Val Cys Glu
    1685                1690                1695

cgg aca  ctg aaa tat ttt cta  gga att gcg gga gga  aaa tgg gta      5139
Arg Thr  Leu Lys Tyr Phe Leu  Gly Ile Ala Gly Gly  Lys Trp Val
    1700                1705                1710

gtt agc  tat ttc tgg gtg acc  cag tct att aaa gaa  aga aaa atg      5184
Val Ser  Tyr Phe Trp Val Thr  Gln Ser Ile Lys Glu  Arg Lys Met
    1715                1720                1725

ctg aat  gag cat gat ttt gaa  gtc aga gga gat gtg  gtc aat gga      5229
Leu Asn  Glu His Asp Phe Glu  Val Arg Gly Asp Val  Val Asn Gly
    1730                1735                1740

aga aac  cac caa ggt cca aag  cga gca aga gaa tcc  cag gac aga      5274
Arg Asn  His Gln Gly Pro Lys  Arg Ala Arg Glu Ser  Gln Asp Arg
    1745                1750                1755

aag atc  ttc agg ggg cta gaa  atc tgt tgc tat ggg  ccc ttc acc      5319
Lys Ile  Phe Arg Gly Leu Glu  Ile Cys Cys Tyr Gly  Pro Phe Thr
    1760                1765                1770

aac atg  ccc aca gat caa ctg  gaa tgg atg gta cag  ctg tgt ggt      5364
Asn Met  Pro Thr Asp Gln Leu  Glu Trp Met Val Gln  Leu Cys Gly
    1775                1780                1785

gct tct  gtg gtg aag gag ctt  tca tca ttc acc ctt  ggc aca ggt      5409
Ala Ser  Val Val Lys Glu Leu  Ser Ser Phe Thr Leu  Gly Thr Gly
    1790                1795                1800

gtc cac  cca att gtg gtt gtg  cag cca gat gcc tgg  aca gag gac      5454
Val His  Pro Ile Val Val Val  Gln Pro Asp Ala Trp  Thr Glu Asp
    1805                1810                1815

aat ggc  ttc cat gca att ggg  cag atg tgt gag gca  cct gtg gtg      5499
Asn Gly  Phe His Ala Ile Gly  Gln Met Cys Glu Ala  Pro Val Val
```

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    1820                1825                1830

acc cga  gag tgg gtg ttg gac  agt gta gca ctc tac  cag tgc cag      5544
Thr Arg  Glu Trp Val Leu Asp  Ser Val Ala Leu Tyr  Gln Cys Gln
    1835                1840                1845

gag ctg  gac acc tac ctg ata  ccc cag atc ccc cac  agc cac tac      5589
Glu Leu  Asp Thr Tyr Leu Ile  Pro Gln Ile Pro His  Ser His Tyr
    1850                1855                1860

tga                                                               5592
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Ala Met Gln Lys Ile Leu Glu Cys Pro Ile Cys Leu Glu Leu Ile Lys
            20                  25                  30

Glu Pro Val Ser Thr Lys Cys Asp His Ile Phe Cys Lys Phe Cys Met
        35                  40                  45

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

Lys Asn Asp Ile Thr Lys Arg Ser Leu Gln Glu Ser Thr Arg Phe Ser
65                  70                  75                  80

Gln Leu Val Glu Glu Leu Leu Lys Ile Ile Cys Ala Phe Gln Leu Asp
                85                  90                  95

Thr Gly Leu Glu Tyr Ala Asn Ser Tyr Asn Phe Ala Lys Lys Glu Asn
            100                 105                 110

Asn Ser Pro Glu His Leu Lys Asp Glu Val Ser Ile Ile Gln Ser Met
        115                 120                 125

Gly Tyr Arg Asn Arg Ala Lys Arg Leu Leu Gln Ser Glu Pro Glu Asn
    130                 135                 140
```

```
Pro Ser Leu Gln Glu Thr Ser Leu Ser Val Gln Leu Ser Asn Leu Gly
145                 150                 155                 160

Thr Val Arg Thr Leu Arg Thr Lys Gln Arg Ile Gln Pro Gln Lys Thr
                165                 170                 175

Ser Val Tyr Ile Glu Leu Gly Ser Asp Ser Ser Glu Asp Thr Val Asn
            180                 185                 190

Lys Ala Thr Tyr Cys Ser Val Gly Asp Gln Glu Leu Leu Gln Ile Thr
        195                 200                 205

Pro Gln Gly Thr Arg Asp Glu Ile Ser Leu Asp Ser Ala Lys Lys Ala
    210                 215                 220

Ala Cys Glu Phe Ser Glu Thr Asp Val Thr Asn Thr Glu His His Gln
225                 230                 235                 240

Pro Ser Asn Asn Asp Leu Asn Thr Thr Glu Lys Arg Ala Ala Glu Arg
                245                 250                 255

His Pro Glu Lys Tyr Gln Gly Ser Ser Val Ser Asn Leu His Val Glu
            260                 265                 270

Pro Cys Gly Thr Asn Thr His Ala Ser Ser Leu Gln His Glu Asn Ser
        275                 280                 285

Ser Leu Leu Leu Thr Lys Asp Arg Met Asn Val Glu Lys Ala Glu Phe
    290                 295                 300

Cys Asn Lys Ser Lys Gln Pro Gly Leu Ala Arg Ser Gln His Asn Arg
305                 310                 315                 320

Trp Ala Gly Ser Lys Glu Thr Cys Asn Asp Arg Arg Thr Pro Ser Thr
                325                 330                 335

Glu Lys Lys Val Asp Leu Asn Ala Asp Pro Leu Cys Glu Arg Lys Glu
            340                 345                 350

Trp Asn Lys Gln Lys Leu Pro Cys Ser Glu Asn Pro Arg Asp Thr Glu
        355                 360                 365
```

```
Asp Val Pro Trp Ile Thr Leu Asn Ser Ser Ile Gln Lys Val Asn Glu
    370                 375                 380

Trp Phe Ser Arg Ser Asp Glu Leu Leu Gly Ser Asp Asp Ser His Asp
385                 390                 395                 400

Gly Glu Ser Glu Ser Asn Ala Lys Val Ala Asp Val Leu Asp Val Leu
                405                 410                 415

Asn Glu Val Asp Glu Tyr Ser Gly Ser Ser Glu Lys Ile Asp Leu Leu
            420                 425                 430

Ala Ser Asp Pro His Glu Ala Leu Ile Cys Lys Ser Glu Arg Val His
        435                 440                 445

Ser Lys Ser Val Glu Ser Asn Ile Glu Asp Lys Ile Phe Gly Lys Thr
    450                 455                 460

Tyr Arg Lys Lys Ala Ser Leu Pro Asn Leu Ser His Val Thr Glu Asn
465                 470                 475                 480

Leu Ile Ile Gly Ala Phe Val Thr Glu Pro Gln Ile Ile Gln Glu Arg
                485                 490                 495

Pro Leu Thr Asn Lys Leu Lys Arg Lys Arg Arg Pro Thr Ser Gly Leu
            500                 505                 510

His Pro Glu Asp Phe Ile Lys Lys Ala Asp Leu Ala Val Gln Lys Thr
        515                 520                 525

Pro Glu Met Ile Asn Gln Gly Thr Asn Gln Thr Glu Gln Asn Gly Gln
    530                 535                 540

Val Met Asn Ile Thr Asn Ser Gly His Glu Asn Lys Thr Lys Gly Asp
545                 550                 555                 560

Ser Ile Gln Asn Glu Lys Asn Pro Asn Pro Ile Glu Ser Leu Glu Lys
                565                 570                 575

Glu Ser Ala Phe Lys Thr Lys Ala Glu Pro Ile Ser Ser Ser Ile Ser
            580                 585                 590
```

```
Asn Met Glu Leu Glu Leu Asn Ile His Asn Ser Lys Ala Pro Lys Lys
        595                 600                 605

Asn Arg Leu Arg Arg Lys Ser Ser Thr Arg His Ile His Ala Leu Glu
    610                 615                 620

Leu Val Val Ser Arg Asn Leu Ser Pro Pro Asn Cys Thr Glu Leu Gln
625                 630                 635                 640

Ile Asp Ser Cys Ser Ser Ser Glu Glu Ile Lys Lys Lys Lys Tyr Asn
                645                 650                 655

Gln Met Pro Val Arg His Ser Arg Asn Leu Gln Leu Met Glu Gly Lys
            660                 665                 670

Glu Pro Ala Thr Gly Ala Lys Lys Ser Asn Lys Pro Asn Glu Gln Thr
        675                 680                 685

Ser Lys Arg His Asp Ser Asp Thr Phe Pro Glu Leu Lys Leu Thr Asn
    690                 695                 700

Ala Pro Gly Ser Phe Thr Lys Cys Ser Asn Thr Ser Glu Leu Lys Glu
705                 710                 715                 720

Phe Val Asn Pro Ser Leu Pro Arg Glu Glu Lys Glu Glu Lys Leu Glu
                725                 730                 735

Thr Val Lys Val Ser Asn Asn Ala Glu Asp Pro Lys Asp Leu Met Leu
            740                 745                 750

Ser Gly Glu Arg Val Leu Gln Thr Glu Arg Ser Val Glu Ser Ser Ser
        755                 760                 765

Ile Ser Leu Val Pro Gly Thr Asp Tyr Gly Thr Gln Glu Ser Ile Ser
    770                 775                 780

Leu Leu Glu Val Ser Thr Leu Gly Lys Ala Lys Thr Glu Pro Asn Lys
785                 790                 795                 800

Cys Val Ser Gln Cys Ala Ala Phe Glu Asn Pro Lys Gly Leu Ile His
                805                 810                 815
```

```
Gly Cys Ser Lys Asp Asn Arg Asn Asp Thr Glu Gly Phe Lys Tyr Pro
            820                 825                 830

Leu Gly His Glu Val Asn His Ser Arg Glu Thr Ser Ile Glu Met Glu
        835                 840                 845

Glu Ser Glu Leu Asp Ala Gln Tyr Leu Gln Asn Thr Phe Lys Val Ser
    850                 855                 860

Lys Arg Gln Ser Phe Ala Pro Phe Ser Asn Pro Gly Asn Ala Glu Glu
865                 870                 875                 880

Glu Cys Ala Thr Phe Ser Ala His Ser Gly Ser Leu Lys Lys Gln Ser
                885                 890                 895

Pro Lys Val Thr Phe Glu Cys Glu Gln Lys Glu Glu Asn Gln Gly Lys
            900                 905                 910

Asn Glu Ser Asn Ile Lys Pro Val Gln Thr Val Asn Ile Thr Ala Gly
        915                 920                 925

Phe Pro Val Val Gly Gln Lys Asp Lys Pro Val Asp Asn Ala Lys Cys
    930                 935                 940

Ser Ile Lys Gly Gly Ser Arg Phe Cys Leu Ser Ser Gln Phe Arg Gly
945                 950                 955                 960

Asn Glu Thr Gly Leu Ile Thr Pro Asn Lys His Gly Leu Leu Gln Asn
                965                 970                 975

Pro Tyr Arg Ile Pro Pro Leu Phe Pro Ile Lys Ser Phe Val Lys Thr
            980                 985                 990

Lys Cys Lys Lys Asn Leu Leu Glu Glu Asn Phe Glu Glu His Ser Met
        995                 1000                1005

Ser Pro Glu Arg Glu Met Gly Asn Glu Asn Ile Pro Ser Thr Val
    1010                1015                1020

Ser Thr Ile Ser Arg Asn Asn Ile Arg Glu Asn Val Phe Lys Glu
    1025                1030                1035
```

```
Ala Ser  Ser Ser Asn Ile Asn  Glu Val Gly Ser Ser  Thr Asn Glu
    1040                 1045                 1050

Val Gly  Ser Ser Ile Asn Glu  Ile Gly Ser Ser Asp  Glu Asn Ile
    1055                 1060                 1065

Gln Ala  Glu Leu Gly Arg Asn  Arg Gly Pro Lys Leu  Asn Ala Met
    1070                 1075                 1080

Leu Arg  Leu Gly Val Leu Gln  Pro Glu Val Tyr Lys  Gln Ser Leu
    1085                 1090                 1095

Pro Gly  Ser Asn Cys Lys His  Pro Glu Ile Lys Lys  Gln Glu Tyr
    1100                 1105                 1110

Glu Glu  Val Val Gln Thr Val  Asn Thr Asp Phe Ser  Pro Tyr Leu
    1115                 1120                 1125

Ile Ser  Asp Asn Leu Glu Gln  Pro Met Gly Ser Ser  His Ala Ser
    1130                 1135                 1140

Gln Val  Cys Ser Glu Thr Pro  Asp Asp Leu Leu Asp  Asp Gly Glu
    1145                 1150                 1155

Ile Lys  Glu Asp Thr Ser Phe  Ala Glu Asn Asp Ile  Lys Glu Ser
    1160                 1165                 1170

Ser Ala  Val Phe Ser Lys Ser  Val Gln Lys Gly Glu  Leu Ser Arg
    1175                 1180                 1185

Ser Pro  Ser Pro Phe Thr His  Thr His Leu Ala Gln  Gly Tyr Arg
    1190                 1195                 1200

Arg Gly  Ala Lys Lys Leu Glu  Ser Ser Glu Glu Asn  Leu Ser Ser
    1205                 1210                 1215

Glu Asp  Glu Glu Leu Pro Cys  Phe Gln His Leu Leu  Phe Gly Lys
    1220                 1225                 1230

Val Asn  Asn Ile Pro Ser Gln  Ser Thr Arg His Ser  Thr Val Ala
    1235                 1240                 1245
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Thr Glu  Cys Leu Ser Lys Asn  Thr Glu Glu Asn Leu  Leu Ser Leu
    1250                 1255                 1260

Lys Asn  Ser Leu Asn Asp Cys  Ser Asn Gln Val Ile  Leu Ala Lys
    1265                 1270                 1275

Ala Ser  Gln Glu His His Leu  Ser Glu Glu Thr Lys  Cys Ser Ala
    1280                 1285                 1290

Ser Leu  Phe Ser Ser Gln Cys  Ser Glu Leu Glu Asp  Leu Thr Ala
    1295                 1300                 1305

Asn Thr  Asn Thr Gln Asp Pro  Phe Leu Ile Gly Ser  Ser Lys Gln
    1310                 1315                 1320

Met Arg  His Gln Ser Glu Ser  Gln Gly Val Gly Leu  Ser Asp Lys
    1325                 1330                 1335

Glu Leu  Val Ser Asp Asp Glu  Glu Arg Gly Thr Gly  Leu Glu Glu
    1340                 1345                 1350

Asn Asn  Gln Glu Glu Gln Ser  Met Asp Ser Asn Leu  Gly Glu Ala
    1355                 1360                 1365

Ala Ser  Gly Cys Glu Ser Glu  Thr Ser Val Ser Glu  Asp Cys Ser
    1370                 1375                 1380

Gly Leu  Ser Ser Gln Ser Asp  Ile Leu Thr Thr Gln  Gln Arg Asp
    1385                 1390                 1395

Thr Met  Gln His Asn Leu Ile  Lys Leu Gln Gln Glu  Met Ala Glu
    1400                 1405                 1410

Leu Glu  Ala Val Leu Glu Gln  His Gly Ser Gln Pro  Ser Asn Ser
    1415                 1420                 1425

Tyr Pro  Ser Ile Ile Ser Asp  Ser Ser Ala Leu Glu  Asp Leu Arg
    1430                 1435                 1440

Asn Pro  Glu Gln Ser Thr Ser  Glu Lys Ala Val Leu  Thr Ser Gln
    1445                 1450                 1455
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```
Lys Ser  Ser Glu Tyr Pro Ile  Ser Gln Asn Pro Glu  Gly Leu Ser
    1460                 1465                 1470

Ala Asp  Lys Phe Glu Val Ser  Ala Asp Ser Ser Thr  Ser Lys Asn
    1475                 1480                 1485

Lys Glu  Pro Gly Val Glu Arg  Ser Ser Pro Ser Lys  Cys Pro Ser
    1490                 1495                 1500

Leu Asp  Asp Arg Trp Tyr Met  His Ser Cys Ser Gly  Ser Leu Gln
    1505                 1510                 1515

Asn Arg  Asn Tyr Pro Ser Gln  Glu Glu Leu Ile Lys  Val Val Asp
    1520                 1525                 1530

Val Glu  Glu Gln Gln Leu Glu  Glu Ser Gly Pro His  Asp Leu Thr
    1535                 1540                 1545

Glu Thr  Ser Tyr Leu Pro Arg  Gln Asp Leu Glu Gly  Thr Pro Tyr
    1550                 1555                 1560

Leu Glu  Ser Gly Ile Ser Leu  Phe Ser Asp Asp Pro  Glu Ser Asp
    1565                 1570                 1575

Pro Ser  Glu Asp Arg Ala Pro  Glu Ser Ala Arg Val  Gly Asn Ile
    1580                 1585                 1590

Pro Ser  Ser Thr Ser Ala Leu  Lys Val Pro Gln Leu  Lys Val Ala
    1595                 1600                 1605

Glu Ser  Ala Gln Ser Pro Ala  Ala Ala His Thr Thr  Asp Thr Ala
    1610                 1615                 1620

Gly Tyr  Asn Ala Met Glu Glu  Ser Val Ser Arg Glu  Lys Pro Glu
    1625                 1630                 1635

Leu Thr  Ala Ser Thr Glu Arg  Val Asn Lys Arg Met  Ser Met Val
    1640                 1645                 1650

Val Ser  Gly Leu Thr Pro Glu  Glu Phe Met Leu Val  Tyr Lys Phe
    1655                 1660                 1665
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Ala Arg Lys His His Ile Thr Leu Thr Asn Leu Ile Thr Glu Glu
1670 1675 1680

Thr Thr His Val Val Met Lys Thr Asp Ala Glu Phe Val Cys Glu
1685 1690 1695

Arg Thr Leu Lys Tyr Phe Leu Gly Ile Ala Gly Gly Lys Trp Val
1700 1705 1710

Val Ser Tyr Phe Trp Val Thr Gln Ser Ile Lys Glu Arg Lys Met
1715 1720 1725

Leu Asn Glu His Asp Phe Glu Val Arg Gly Asp Val Val Asn Gly
1730 1735 1740

Arg Asn His Gln Gly Pro Lys Arg Ala Arg Glu Ser Gln Asp Arg
1745 1750 1755

Lys Ile Phe Arg Gly Leu Glu Ile Cys Cys Tyr Gly Pro Phe Thr
1760 1765 1770

Asn Met Pro Thr Asp Gln Leu Glu Trp Met Val Gln Leu Cys Gly
1775 1780 1785

Ala Ser Val Val Lys Glu Leu Ser Ser Phe Thr Leu Gly Thr Gly
1790 1795 1800

Val His Pro Ile Val Val Val Gln Pro Asp Ala Trp Thr Glu Asp
1805 1810 1815

Asn Gly Phe His Ala Ile Gly Gln Met Cys Glu Ala Pro Val Val
1820 1825 1830

Thr Arg Glu Trp Val Leu Asp Ser Val Ala Leu Tyr Gln Cys Gln
1835 1840 1845

Glu Leu Asp Thr Tyr Leu Ile Pro Gln Ile Pro His Ser His Tyr
1850 1855 1860

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ttt atg ctc gtg tac aag ttt gcc aga aaa cac cac atc act tta act       96
Phe Met Leu Val Tyr Lys Phe Ala Arg Lys His His Ile Thr Leu Thr
            20                  25                  30

aat cta att act gaa gag act act cat gtt gtt atg aaa aca gat gct      144
Asn Leu Ile Thr Glu Glu Thr Thr His Val Val Met Lys Thr Asp Ala
        35                  40                  45

gag ttt gtg tgt gaa cgg aca ctg aaa tat ttt cta gga att gcg gga      192
Glu Phe Val Cys Glu Arg Thr Leu Lys Tyr Phe Leu Gly Ile Ala Gly
    50                  55                  60

gga aaa tgg gta gtt agc tat ttc tgg gtg acc cag tct att aaa gaa      240
Gly Lys Trp Val Val Ser Tyr Phe Trp Val Thr Gln Ser Ile Lys Glu
65                  70                  75                  80

aga aaa atg ctg aat gag cat gat ttt gaa gtc aga gga gat gtg gtc      288
Arg Lys Met Leu Asn Glu His Asp Phe Glu Val Arg Gly Asp Val Val
                85                  90                  95

aat gga aga aac cac caa ggt cca aag cga gca aga gaa tcc cag gac      336
Asn Gly Arg Asn His Gln Gly Pro Lys Arg Ala Arg Glu Ser Gln Asp
            100                 105                 110

aga aag atc ttc agg ggg cta gaa atc tgt tgc tat ggg ccc ttc acc      384
Arg Lys Ile Phe Arg Gly Leu Glu Ile Cys Cys Tyr Gly Pro Phe Thr
        115                 120                 125

aac atg ccc aca gat caa ctg gaa tgg atg gta cag ctg tgt ggt gct      432
Asn Met Pro Thr Asp Gln Leu Glu Trp Met Val Gln Leu Cys Gly Ala
    130                 135                 140

tct gtg gtg aag gag ctt tca tca ttc acc ctt ggc aca ggt gtc cac      480
Ser Val Val Lys Glu Leu Ser Ser Phe Thr Leu Gly Thr Gly Val His
145                 150                 155                 160

cca att gtg gtt gtg cag cca gat gcc tgg aca gag gac aat ggc ttc      528
Pro Ile Val Val Val Gln Pro Asp Ala Trp Thr Glu Asp Asn Gly Phe
                165                 170                 175

cat gca att ggg cag atg tgt gag gca cct gtg gtg acc cga gag tgg      576
His Ala Ile Gly Gln Met Cys Glu Ala Pro Val Val Thr Arg Glu Trp
            180                 185                 190

gtg ttg gac agt gta gca ctc tac cag tgc cag gag ctg gac acc tac      624
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Val Leu Asp Ser Val Ala Leu Tyr Gln Cys Gln Glu Leu Asp Thr Tyr
195 200 205

ctg ata ccc cag atc ccc 642
Leu Ile Pro Gln Ile Pro
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20 25 30

Asn Leu Ile Thr Glu Glu Thr Thr His Val Val Met Lys Thr Asp Ala
35 40 45

Glu Phe Val Cys Glu Arg Thr Leu Lys Tyr Phe Leu Gly Ile Ala Gly
50 55 60

Gly Lys Trp Val Val Ser Tyr Phe Trp Val Thr Gln Ser Ile Lys Glu
65 70 75 80

Arg Lys Met Leu Asn Glu His Asp Phe Glu Val Arg Gly Asp Val Val
85 90 95

Asn Gly Arg Asn His Gln Gly Pro Lys Arg Ala Arg Glu Ser Gln Asp
100 105 110

Arg Lys Ile Phe Arg Gly Leu Glu Ile Cys Cys Tyr Gly Pro Phe Thr
115 120 125

Asn Met Pro Thr Asp Gln Leu Glu Trp Met Val Gln Leu Cys Gly Ala
130 135 140

Ser Val Val Lys Glu Leu Ser Ser Phe Thr Leu Gly Thr Gly Val His
145 150 155 160

Pro Ile Val Val Val Gln Pro Asp Ala Trp Thr Glu Asp Asn Gly Phe

```
                165                 170                 175

His Ala Ile Gly Gln Met Cys Glu Ala Pro Val Val Thr Arg Glu Trp
            180                 185                 190

Val Leu Asp Ser Val Ala Leu Tyr Gln Cys Gln Glu Leu Asp Thr Tyr
        195                 200                 205

Leu Ile Pro Gln Ile Pro
    210
```

<210> 5
<211> 1653
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (1)..(1653)

<400> 5

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cag gat cct ttc ttg att ggt tct tcc aaa caa atg agg cat cag tct       48
Gln Asp Pro Phe Leu Ile Gly Ser Ser Lys Gln Met Arg His Gln Ser
1               5                   10                  15

gaa agc cag gga gtt ggt ctg agt gac aag gaa ttg gtt tca gat gat       96
Glu Ser Gln Gly Val Gly Leu Ser Asp Lys Glu Leu Val Ser Asp Asp
            20                  25                  30

gaa gaa aga gga acg ggc ttg gaa gaa aat aat caa gaa gag caa agc      144
Glu Glu Arg Gly Thr Gly Leu Glu Glu Asn Asn Gln Glu Glu Gln Ser
        35                  40                  45

atg gat tca aac tta ggt gaa gca gca tct ggg tgt gag agt gaa aca      192
Met Asp Ser Asn Leu Gly Glu Ala Ala Ser Gly Cys Glu Ser Glu Thr
    50                  55                  60

agc gtc tct gaa gac tgc tca ggg cta tcc tct cag agt gac att tta      240
Ser Val Ser Glu Asp Cys Ser Gly Leu Ser Ser Gln Ser Asp Ile Leu
65                  70                  75                  80

acc act cag cag agg gat acc atg caa cat aac ctg ata aag ctc cag      288
Thr Thr Gln Gln Arg Asp Thr Met Gln His Asn Leu Ile Lys Leu Gln
                85                  90                  95

cag gaa atg gct gaa cta gaa gct gtg tta gaa cag cat ggg agc cag      336
Gln Glu Met Ala Glu Leu Glu Ala Val Leu Glu Gln His Gly Ser Gln
            100                 105                 110

cct tct aac agc tac cct tcc atc ata agt gac tct tct gcc ctt gag      384
Pro Ser Asn Ser Tyr Pro Ser Ile Ile Ser Asp Ser Ser Ala Leu Glu
```

```
        115                 120                 125

gac ctg cga aat cca gaa caa agc aca tca gaa aaa gca gta tta act      432
Asp Leu Arg Asn Pro Glu Gln Ser Thr Ser Glu Lys Ala Val Leu Thr
    130                 135                 140

tca cag aaa agt agt gaa tac cct ata agc cag aat cca gaa ggc ctt      480
Ser Gln Lys Ser Ser Glu Tyr Pro Ile Ser Gln Asn Pro Glu Gly Leu
145                 150                 155                 160

tct gct gac aag ttt gag gtg tct gca gat agt tct acc agt aaa aat      528
Ser Ala Asp Lys Phe Glu Val Ser Ala Asp Ser Ser Thr Ser Lys Asn
                165                 170                 175

aaa gaa cca gga gtg gaa agg tca tcc cct tct aaa tgc cca tca tta      576
Lys Glu Pro Gly Val Glu Arg Ser Ser Pro Ser Lys Cys Pro Ser Leu
            180                 185                 190

gat gat agg tgg tac atg cac agt tgc tct ggg agt ctt cag aat aga      624
Asp Asp Arg Trp Tyr Met His Ser Cys Ser Gly Ser Leu Gln Asn Arg
        195                 200                 205

aac tac cca tct caa gag gag ctc att aag gtt gtt gat gtg gag gag      672
Asn Tyr Pro Ser Gln Glu Glu Leu Ile Lys Val Val Asp Val Glu Glu
    210                 215                 220

caa cag ctg gaa gag tct ggg cca cac gat ttg acg gaa aca tct tac      720
Gln Gln Leu Glu Glu Ser Gly Pro His Asp Leu Thr Glu Thr Ser Tyr
225                 230                 235                 240

ttg cca agg caa gat cta gag gga acc cct tac ctg gaa tct gga atc      768
Leu Pro Arg Gln Asp Leu Glu Gly Thr Pro Tyr Leu Glu Ser Gly Ile
                245                 250                 255

agc ctc ttc tct gat gac cct gaa tct gat cct tct gaa gac aga gcc      816
Ser Leu Phe Ser Asp Asp Pro Glu Ser Asp Pro Ser Glu Asp Arg Ala
            260                 265                 270

cca gag tca gct cgt gtt ggc aac ata cca tct tca acc tct gca ttg      864
Pro Glu Ser Ala Arg Val Gly Asn Ile Pro Ser Ser Thr Ser Ala Leu
        275                 280                 285

aaa gtt ccc caa ttg aaa gtt gca gaa tct gcc cag agt cca gct gct      912
Lys Val Pro Gln Leu Lys Val Ala Glu Ser Ala Gln Ser Pro Ala Ala
    290                 295                 300

gct cat act act gat act gct ggg tat aat gca atg gaa gaa agt gtg      960
Ala His Thr Thr Asp Thr Ala Gly Tyr Asn Ala Met Glu Glu Ser Val
305                 310                 315                 320

agc agg gag aag cca gaa ttg aca gct tca aca gaa agg gtc aac aaa     1008
Ser Arg Glu Lys Pro Glu Leu Thr Ala Ser Thr Glu Arg Val Asn Lys
                325                 330                 335

aga atg tcc atg gtg gtg tct ggc ctg acc cca gaa gaa ttt atg ctc     1056
Arg Met Ser Met Val Val Ser Gly Leu Thr Pro Glu Glu Phe Met Leu
```

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                340                 345                 350

gtg tac aag ttt gcc aga aaa cac cac atc act tta act aat cta att     1104
Val Tyr Lys Phe Ala Arg Lys His His Ile Thr Leu Thr Asn Leu Ile
        355                 360                 365

act gaa gag act act cat gtt gtt atg aaa aca gat gct gag ttt gtg     1152
Thr Glu Glu Thr Thr His Val Val Met Lys Thr Asp Ala Glu Phe Val
    370                 375                 380

tgt gaa cgg aca ctg aaa tat ttt cta gga att gcg gga gga aaa tgg     1200
Cys Glu Arg Thr Leu Lys Tyr Phe Leu Gly Ile Ala Gly Gly Lys Trp
385                 390                 395                 400

gta gtt agc tat ttc tgg gtg acc cag tct att aaa gaa aga aaa atg     1248
Val Val Ser Tyr Phe Trp Val Thr Gln Ser Ile Lys Glu Arg Lys Met
                405                 410                 415

ctg aat gag cat gat ttt gaa gtc aga gga gat gtg gtc aat gga aga     1296
Leu Asn Glu His Asp Phe Glu Val Arg Gly Asp Val Val Asn Gly Arg
            420                 425                 430

aac cac caa ggt cca aag cga gca aga gaa tcc cag gac aga aag atc     1344
Asn His Gln Gly Pro Lys Arg Ala Arg Glu Ser Gln Asp Arg Lys Ile
        435                 440                 445

ttc agg ggg cta gaa atc tgt tgc tat ggg ccc ttc acc aac atg ccc     1392
Phe Arg Gly Leu Glu Ile Cys Cys Tyr Gly Pro Phe Thr Asn Met Pro
    450                 455                 460

aca gat caa ctg gaa tgg atg gta cag ctg tgt ggt gct tct gtg gtg     1440
Thr Asp Gln Leu Glu Trp Met Val Gln Leu Cys Gly Ala Ser Val Val
465                 470                 475                 480

aag gag ctt tca tca ttc acc ctt ggc aca ggt gtc cac cca att gtg     1488
Lys Glu Leu Ser Ser Phe Thr Leu Gly Thr Gly Val His Pro Ile Val
                485                 490                 495

gtt gtg cag cca gat gcc tgg aca gag gac aat ggc ttc cat gca att     1536
Val Val Gln Pro Asp Ala Trp Thr Glu Asp Asn Gly Phe His Ala Ile
            500                 505                 510

ggg cag atg tgt gag gca cct gtg gtg acc cga gag tgg gtg ttg gac     1584
Gly Gln Met Cys Glu Ala Pro Val Val Thr Arg Glu Trp Val Leu Asp
        515                 520                 525

agt gta gca ctc tac cag tgc cag gag ctg gac acc tac ctg ata ccc     1632
Ser Val Ala Leu Tyr Gln Cys Gln Glu Leu Asp Thr Tyr Leu Ile Pro
    530                 535                 540

cag atc ccc cac agc cac tac                                        1653
Gln Ile Pro His Ser His Tyr
545                 550
```

<210> 6

<211> 551
<212> PRT
<213> Homo sapiens

<400> 6

Gln Asp Pro Phe Leu Ile Gly Ser Ser Lys Gln Met Arg His Gln Ser
1 5 10 15

Glu Ser Gln Gly Val Gly Leu Ser Asp Lys Glu Leu Val Ser Asp Asp
20 25 30

Glu Glu Arg Gly Thr Gly Leu Glu Glu Asn Asn Gln Glu Glu Gln Ser
35 40 45

Met Asp Ser Asn Leu Gly Glu Ala Ala Ser Gly Cys Glu Ser Glu Thr
50 55 60

Ser Val Ser Glu Asp Cys Ser Gly Leu Ser Ser Gln Ser Asp Ile Leu
65 70 75 80

Thr Thr Gln Gln Arg Asp Thr Met Gln His Asn Leu Ile Lys Leu Gln
85 90 95

Gln Glu Met Ala Glu Leu Glu Ala Val Leu Glu Gln His Gly Ser Gln
100 105 110

Pro Ser Asn Ser Tyr Pro Ser Ile Ile Ser Asp Ser Ser Ala Leu Glu
115 120 125

Asp Leu Arg Asn Pro Glu Gln Ser Thr Ser Glu Lys Ala Val Leu Thr
130 135 140

Ser Gln Lys Ser Ser Glu Tyr Pro Ile Ser Gln Asn Pro Glu Gly Leu
145 150 155 160

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

Lys Glu Pro Gly Val Glu Arg Ser Ser Pro Ser Lys Cys Pro Ser Leu
180 185 190

Asp Asp Arg Trp Tyr Met His Ser Cys Ser Gly Ser Leu Gln Asn Arg
195 200 205

```
Asn Tyr Pro Ser Gln Glu Glu Leu Ile Lys Val Val Asp Val Glu Glu
    210                 215                 220

Gln Gln Leu Glu Glu Ser Gly Pro His Asp Leu Thr Glu Thr Ser Tyr
225                 230                 235                 240

Leu Pro Arg Gln Asp Leu Glu Gly Thr Pro Tyr Leu Glu Ser Gly Ile
                245                 250                 255

Ser Leu Phe Ser Asp Asp Pro Glu Ser Asp Pro Ser Glu Asp Arg Ala
            260                 265                 270

Pro Glu Ser Ala Arg Val Gly Asn Ile Pro Ser Ser Thr Ser Ala Leu
        275                 280                 285

Lys Val Pro Gln Leu Lys Val Ala Glu Ser Ala Gln Ser Pro Ala Ala
    290                 295                 300

Ala His Thr Thr Asp Thr Ala Gly Tyr Asn Ala Met Glu Glu Ser Val
305                 310                 315                 320

Ser Arg Glu Lys Pro Glu Leu Thr Ala Ser Thr Glu Arg Val Asn Lys
                325                 330                 335

Arg Met Ser Met Val Val Ser Gly Leu Thr Pro Glu Glu Phe Met Leu
            340                 345                 350

Val Tyr Lys Phe Ala Arg Lys His His Ile Thr Leu Thr Asn Leu Ile
        355                 360                 365

Thr Glu Glu Thr Thr His Val Val Met Lys Thr Asp Ala Glu Phe Val
    370                 375                 380

Cys Glu Arg Thr Leu Lys Tyr Phe Leu Gly Ile Ala Gly Gly Lys Trp
385                 390                 395                 400

Val Val Ser Tyr Phe Trp Val Thr Gln Ser Ile Lys Glu Arg Lys Met
                405                 410                 415

Leu Asn Glu His Asp Phe Glu Val Arg Gly Asp Val Val Asn Gly Arg
            420                 425                 430
```

```
Asn His Gln Gly Pro Lys Arg Ala Arg Glu Ser Gln Asp Arg Lys Ile
        435                 440                 445

Phe Arg Gly Leu Glu Ile Cys Cys Tyr Gly Pro Phe Thr Asn Met Pro
    450                 455                 460

Thr Asp Gln Leu Glu Trp Met Val Gln Leu Cys Gly Ala Ser Val Val
465                 470                 475                 480

Lys Glu Leu Ser Ser Phe Thr Leu Gly Thr Gly Val His Pro Ile Val
                485                 490                 495

Val Val Gln Pro Asp Ala Trp Thr Glu Asp Asn Gly Phe His Ala Ile
            500                 505                 510

Gly Gln Met Cys Glu Ala Pro Val Val Thr Arg Glu Trp Val Leu Asp
        515                 520                 525

Ser Val Ala Leu Tyr Gln Cys Gln Glu Leu Asp Thr Tyr Leu Ile Pro
    530                 535                 540

Gln Ile Pro His Ser His Tyr
545                 550
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<210> 7
<211> 693
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (1)..(693)

<400> 7

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agc agg gag aag cca gaa ttg aca gct tca aca gaa agg gtc aac aaa        48
Ser Arg Glu Lys Pro Glu Leu Thr Ala Ser Thr Glu Arg Val Asn Lys
1               5                   10                  15

aga atg tcc atg gtg gtg tct ggc ctg acc cca gaa gaa ttt atg ctc        96
Arg Met Ser Met Val Val Ser Gly Leu Thr Pro Glu Glu Phe Met Leu
            20                  25                  30

gtg tac aag ttt gcc aga aaa cac cac atc act tta act aat cta att       144
Val Tyr Lys Phe Ala Arg Lys His His Ile Thr Leu Thr Asn Leu Ile
        35                  40                  45
```

```
act gaa gag act act cat gtt gtt atg aaa aca gat gct gag ttt gtg      192
Thr Glu Glu Thr Thr His Val Val Met Lys Thr Asp Ala Glu Phe Val
    50                  55                  60

tgt gaa cgg aca ctg aaa tat ttt cta gga att gcg gga gga aaa tgg      240
Cys Glu Arg Thr Leu Lys Tyr Phe Leu Gly Ile Ala Gly Gly Lys Trp
65                  70                  75                  80

gta gtt agc tat ttc tgg gtg acc cag tct att aaa gaa aga aaa atg      288
Val Val Ser Tyr Phe Trp Val Thr Gln Ser Ile Lys Glu Arg Lys Met
                85                  90                  95

ctg aat gag cat gat ttt gaa gtc aga gga gat gtg gtc aat gga aga      336
Leu Asn Glu His Asp Phe Glu Val Arg Gly Asp Val Val Asn Gly Arg
            100                 105                 110

aac cac caa ggt cca aag cga gca aga gaa tcc cag gac aga aag atc      384
Asn His Gln Gly Pro Lys Arg Ala Arg Glu Ser Gln Asp Arg Lys Ile
        115                 120                 125

ttc agg ggg cta gaa atc tgt tgc tat ggg ccc ttc acc aac atg ccc      432
Phe Arg Gly Leu Glu Ile Cys Cys Tyr Gly Pro Phe Thr Asn Met Pro
    130                 135                 140

aca gat caa ctg gaa tgg atg gta cag ctg tgt ggt gct tct gtg gtg      480
Thr Asp Gln Leu Glu Trp Met Val Gln Leu Cys Gly Ala Ser Val Val
145                 150                 155                 160

aag gag ctt tca tca ttc acc ctt ggc aca ggt gtc cac cca att gtg      528
Lys Glu Leu Ser Ser Phe Thr Leu Gly Thr Gly Val His Pro Ile Val
                165                 170                 175

gtt gtg cag cca gat gcc tgg aca gag gac aat ggc ttc cat gca att      576
Val Val Gln Pro Asp Ala Trp Thr Glu Asp Asn Gly Phe His Ala Ile
            180                 185                 190

ggg cag atg tgt gag gca cct gtg gtg acc cga gag tgg gtg ttg gac      624
Gly Gln Met Cys Glu Ala Pro Val Val Thr Arg Glu Trp Val Leu Asp
        195                 200                 205

agt gta gca ctc tac cag tgc cag gag ctg gac acc tac ctg ata ccc      672
Ser Val Ala Leu Tyr Gln Cys Gln Glu Leu Asp Thr Tyr Leu Ile Pro
    210                 215                 220

cag atc ccc cac agc cac tac                                         693
Gln Ile Pro His Ser His Tyr
225                 230
```

<210> 8
<211> 231
<212> PRT
<213> Homo sapiens

<400> 8

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Ser Arg Glu Lys Pro Glu Leu Thr Ala Ser Thr Glu Arg Val Asn Lys
1               5                  10                  15

Arg Met Ser Met Val Val Ser Gly Leu Thr Pro Glu Glu Phe Met Leu
            20                  25                  30

Val Tyr Lys Phe Ala Arg Lys His His Ile Thr Leu Thr Asn Leu Ile
        35                  40                  45

Thr Glu Glu Thr Thr His Val Val Met Lys Thr Asp Ala Glu Phe Val
    50                  55                  60

Cys Glu Arg Thr Leu Lys Tyr Phe Leu Gly Ile Ala Gly Gly Lys Trp
65                  70                  75                  80

Val Val Ser Tyr Phe Trp Val Thr Gln Ser Ile Lys Glu Arg Lys Met
                85                  90                  95

Leu Asn Glu His Asp Phe Glu Val Arg Gly Asp Val Val Asn Gly Arg
            100                 105                 110

Asn His Gln Gly Pro Lys Arg Ala Arg Glu Ser Gln Asp Arg Lys Ile
        115                 120                 125

Phe Arg Gly Leu Glu Ile Cys Cys Tyr Gly Pro Phe Thr Asn Met Pro
    130                 135                 140

Thr Asp Gln Leu Glu Trp Met Val Gln Leu Cys Gly Ala Ser Val Val
145                 150                 155                 160

Lys Glu Leu Ser Ser Phe Thr Leu Gly Thr Gly Val His Pro Ile Val
                165                 170                 175

Val Val Gln Pro Asp Ala Trp Thr Glu Asp Asn Gly Phe His Ala Ile
            180                 185                 190

Gly Gln Met Cys Glu Ala Pro Val Val Thr Arg Glu Trp Val Leu Asp
        195                 200                 205

Ser Val Ala Leu Tyr Gln Cys Gln Glu Leu Asp Thr Tyr Leu Ile Pro
    210                 215                 220
```

```
Gln Ile Pro His Ser His Tyr
225                 230


<210>  9
<211>  1863
<212>  PRT
<213>  Homo sapiens

<400>  9

Met Asp Leu Ser Ala Leu Arg Val Glu Glu Val Gln Asn Val Ile Asn
1               5                   10                  15


Ala Met Gln Lys Ile Leu Glu Cys Pro Ile Cys Leu Glu Leu Ile Lys
            20                  25                  30


Glu Pro Val Ser Thr Lys Cys Asp His Ile Phe Cys Lys Phe Cys Met
        35                  40                  45


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


Lys Asn Asp Ile Thr Lys Arg Ser Leu Gln Glu Ser Thr Arg Phe Ser
65                  70                  75                  80


Gln Leu Val Glu Glu Leu Leu Lys Ile Ile Cys Ala Phe Gln Leu Asp
                85                  90                  95


Thr Gly Leu Glu Tyr Ala Asn Ser Tyr Asn Phe Ala Lys Lys Glu Asn
            100                 105                 110


Asn Ser Pro Glu His Leu Lys Asp Glu Val Ser Ile Ile Gln Ser Met
        115                 120                 125


Gly Tyr Arg Asn Arg Ala Lys Arg Leu Leu Gln Ser Glu Pro Glu Asn
    130                 135                 140


Pro Ser Leu Gln Glu Thr Ser Leu Ser Val Gln Leu Ser Asn Leu Gly
145                 150                 155                 160


Thr Val Arg Thr Leu Arg Thr Lys Gln Arg Ile Gln Pro Gln Lys Thr
                165                 170                 175
```

```
Ser Val Tyr Ile Glu Leu Gly Ser Asp Ser Ser Glu Asp Thr Val Asn
            180                 185                 190

Lys Ala Thr Tyr Cys Ser Val Gly Asp Gln Glu Leu Leu Gln Ile Thr
        195                 200                 205

Pro Gln Gly Thr Arg Asp Glu Ile Ser Leu Asp Ser Ala Lys Lys Ala
    210                 215                 220

Ala Cys Glu Phe Ser Glu Thr Asp Val Thr Asn Thr Glu His His Gln
225                 230                 235                 240

Pro Ser Asn Asn Asp Leu Asn Thr Thr Glu Lys Arg Ala Ala Glu Arg
                245                 250                 255

His Pro Glu Lys Tyr Gln Gly Ser Ser Val Ser Asn Leu His Val Glu
            260                 265                 270

Pro Cys Gly Thr Asn Thr His Ala Ser Ser Leu Gln His Glu Asn Ser
        275                 280                 285

Ser Leu Leu Leu Thr Lys Asp Arg Met Asn Val Glu Lys Ala Glu Phe
    290                 295                 300

Cys Asn Lys Ser Lys Gln Pro Gly Leu Ala Arg Ser Gln His Asn Arg
305                 310                 315                 320

Trp Ala Gly Ser Lys Glu Thr Cys Asn Asp Arg Arg Thr Pro Ser Thr
                325                 330                 335

Glu Lys Lys Val Asp Leu Asn Ala Asp Pro Leu Cys Glu Arg Lys Glu
            340                 345                 350

Trp Asn Lys Gln Lys Leu Pro Cys Ser Glu Asn Pro Arg Asp Thr Glu
        355                 360                 365

Asp Val Pro Trp Ile Thr Leu Asn Ser Ser Ile Gln Lys Val Asn Glu
    370                 375                 380

Trp Phe Ser Arg Ser Asp Glu Leu Leu Gly Ser Asp Asp Ser His Asp
385                 390                 395                 400
```

```
Gly Glu Ser Glu Ser Asn Ala Lys Val Ala Asp Val Leu Asp Val Leu
                405                 410                 415

Asn Glu Val Asp Glu Tyr Ser Gly Ser Ser Glu Lys Ile Asp Leu Leu
            420                 425                 430

Ala Ser Asp Pro His Glu Ala Leu Ile Cys Lys Ser Glu Arg Val His
        435                 440                 445

Ser Lys Ser Val Glu Ser Asn Ile Glu Asp Lys Ile Phe Gly Lys Thr
    450                 455                 460

Tyr Arg Lys Lys Ala Ser Leu Pro Asn Leu Ser His Val Thr Glu Asn
465                 470                 475                 480

Leu Ile Ile Gly Ala Phe Val Thr Glu Pro Gln Ile Ile Gln Glu Arg
                485                 490                 495

Pro Leu Thr Asn Lys Leu Lys Arg Lys Arg Arg Pro Thr Ser Gly Leu
            500                 505                 510

His Pro Glu Asp Phe Ile Lys Lys Ala Asp Leu Ala Val Gln Lys Thr
        515                 520                 525

Pro Glu Met Ile Asn Gln Gly Thr Asn Gln Thr Glu Gln Asn Gly Gln
    530                 535                 540

Val Met Asn Ile Thr Asn Ser Gly His Glu Asn Lys Thr Lys Gly Asp
545                 550                 555                 560

Ser Ile Gln Asn Glu Lys Asn Pro Asn Pro Ile Glu Ser Leu Glu Lys
                565                 570                 575

Glu Ser Ala Phe Lys Thr Lys Ala Glu Pro Ile Ser Ser Ser Ile Ser
            580                 585                 590

Asn Met Glu Leu Glu Leu Asn Ile His Asn Ser Lys Ala Pro Lys Lys
        595                 600                 605

Asn Arg Leu Arg Arg Lys Ser Ser Thr Arg His Ile His Ala Leu Glu
    610                 615                 620
```

```
Leu Val Val Ser Arg Asn Leu Ser Pro Pro Asn Cys Thr Glu Leu Gln
625                 630                 635                 640

Ile Asp Ser Cys Ser Ser Ser Glu Glu Ile Lys Lys Lys Lys Tyr Asn
                645                 650                 655

Gln Met Pro Val Arg His Ser Arg Asn Leu Gln Leu Met Glu Gly Lys
            660                 665                 670

Glu Pro Ala Thr Gly Ala Lys Lys Ser Asn Lys Pro Asn Glu Gln Thr
        675                 680                 685

Ser Lys Arg His Asp Ser Asp Thr Phe Pro Glu Leu Lys Leu Thr Asn
    690                 695                 700

Ala Pro Gly Ser Phe Thr Lys Cys Ser Asn Thr Ser Glu Leu Lys Glu
705                 710                 715                 720

Phe Val Asn Pro Ser Leu Pro Arg Glu Glu Lys Glu Glu Lys Leu Glu
                725                 730                 735

Thr Val Lys Val Ser Asn Asn Ala Glu Asp Pro Lys Asp Leu Met Leu
            740                 745                 750

Ser Gly Glu Arg Val Leu Gln Thr Glu Arg Ser Val Glu Ser Ser Ser
        755                 760                 765

Ile Ser Leu Val Pro Gly Thr Asp Tyr Gly Thr Gln Glu Ser Ile Ser
    770                 775                 780

Leu Leu Glu Val Ser Thr Leu Gly Lys Ala Lys Thr Glu Pro Asn Lys
785                 790                 795                 800

Cys Val Ser Gln Cys Ala Ala Phe Glu Asn Pro Lys Gly Leu Ile His
                805                 810                 815

Gly Cys Ser Lys Asp Asn Arg Asn Asp Thr Glu Gly Phe Lys Tyr Pro
            820                 825                 830

Leu Gly His Glu Val Asn His Ser Arg Glu Thr Ser Ile Glu Met Glu
        835                 840                 845
```

```
Glu Ser Glu Leu Asp Ala Gln Tyr Leu Gln Asn Thr Phe Lys Val Ser
    850                 855                 860

Lys Arg Gln Ser Phe Ala Pro Phe Ser Asn Pro Gly Asn Ala Glu Glu
865                 870                 875                 880

Glu Cys Ala Thr Phe Ser Ala His Ser Gly Ser Leu Lys Lys Gln Ser
                885                 890                 895

Pro Lys Val Thr Phe Glu Cys Glu Gln Lys Glu Glu Asn Gln Gly Lys
            900                 905                 910

Asn Glu Ser Asn Ile Lys Pro Val Gln Thr Val Asn Ile Thr Ala Gly
        915                 920                 925

Phe Pro Val Val Gly Gln Lys Asp Lys Pro Val Asp Asn Ala Lys Cys
    930                 935                 940

Ser Ile Lys Gly Gly Ser Arg Phe Cys Leu Ser Ser Gln Phe Arg Gly
945                 950                 955                 960

Asn Glu Thr Gly Leu Ile Thr Pro Asn Lys His Gly Leu Leu Gln Asn
                965                 970                 975

Pro Tyr Arg Ile Pro Pro Leu Phe Pro Ile Lys Ser Phe Val Lys Thr
            980                 985                 990

Lys Cys Lys Lys Asn Leu Leu Glu  Glu Asn Phe Glu Glu  His Ser Met
        995                 1000                1005

Ser Pro  Glu Arg Glu Met Gly  Asn Glu Asn Ile Pro  Ser Thr Val
    1010                1015                1020

Ser Thr  Ile Ser Arg Asn Asn  Ile Arg Glu Asn Val  Phe Lys Glu
    1025                1030                1035

Ala Ser  Ser Ser Asn Ile Asn  Glu Val Gly Ser Ser  Thr Asn Glu
    1040                1045                1050

Val Gly  Ser Ser Ile Asn Glu  Ile Gly Ser Ser Asp  Glu Asn Ile
    1055                1060                1065
```

```
Gln Ala  Glu Leu Gly Arg Asn  Arg Gly Pro Lys Leu  Asn Ala Met
    1070                 1075                 1080

Leu Arg  Leu Gly Val Leu Gln  Pro Glu Val Tyr Lys  Gln Ser Leu
    1085                 1090                 1095

Pro Gly  Ser Asn Cys Lys His  Pro Glu Ile Lys Lys  Gln Glu Tyr
    1100                 1105                 1110

Glu Glu  Val Val Gln Thr Val  Asn Thr Asp Phe Ser  Pro Tyr Leu
    1115                 1120                 1125

Ile Ser  Asp Asn Leu Glu Gln  Pro Met Gly Ser Ser  His Ala Ser
    1130                 1135                 1140

Gln Val  Cys Ser Glu Thr Pro  Asp Asp Leu Leu Asp  Asp Gly Glu
    1145                 1150                 1155

Ile Lys  Glu Asp Thr Ser Phe  Ala Glu Asn Asp Ile  Lys Glu Ser
    1160                 1165                 1170

Ser Ala  Val Phe Ser Lys Ser  Val Gln Lys Gly Glu  Leu Ser Arg
    1175                 1180                 1185

Ser Pro  Ser Pro Phe Thr His  Thr His Leu Ala Gln  Gly Tyr Arg
    1190                 1195                 1200

Arg Gly  Ala Lys Lys Leu Glu  Ser Ser Glu Glu Asn  Leu Ser Ser
    1205                 1210                 1215

Glu Asp  Glu Glu Leu Pro Cys  Phe Gln His Leu Leu  Phe Gly Lys
    1220                 1225                 1230

Val Asn  Asn Ile Pro Ser Gln  Ser Thr Arg His Ser  Thr Val Ala
    1235                 1240                 1245

Thr Glu  Cys Leu Ser Lys Asn  Thr Glu Glu Asn Leu  Leu Ser Leu
    1250                 1255                 1260

Lys Asn  Ser Leu Asn Asp Cys  Ser Asn Gln Val Ile  Leu Ala Lys
    1265                 1270                 1275
```

```
Ala Ser  Gln Glu His His Leu  Ser Glu Glu Thr Lys  Cys Ser Ala
    1280                 1285                 1290

Ser Leu  Phe Ser Ser Gln Cys  Ser Glu Leu Glu Asp  Leu Thr Ala
    1295                 1300                 1305

Asn Thr  Asn Thr Gln Asp Pro  Phe Leu Ile Gly Ser  Ser Lys Gln
    1310                 1315                 1320

Met Arg  His Gln Ser Glu Ser  Gln Gly Val Gly Leu  Ser Asp Lys
    1325                 1330                 1335

Glu Leu  Val Ser Asp Asp Glu  Glu Arg Gly Thr Gly  Leu Glu Glu
    1340                 1345                 1350

Asn Asn  Gln Glu Glu Gln Ser  Met Asp Ser Asn Leu  Gly Glu Ala
    1355                 1360                 1365

Ala Ser  Gly Cys Glu Ser Glu  Thr Ser Val Ser Glu  Asp Cys Ser
    1370                 1375                 1380

Gly Leu  Ser Ser Gln Ser Asp  Ile Leu Thr Thr Gln  Gln Arg Asp
    1385                 1390                 1395

Thr Met  Gln His Asn Leu Ile  Lys Leu Gln Gln Glu  Met Ala Glu
    1400                 1405                 1410

Leu Glu  Ala Val Leu Glu Gln  His Gly Ser Gln Pro  Ser Asn Ser
    1415                 1420                 1425

Tyr Pro  Ser Ile Ile Ser Asp  Ser Ser Ala Leu Glu  Asp Leu Arg
    1430                 1435                 1440

Asn Pro  Glu Gln Ser Thr Ser  Glu Lys Ala Val Leu  Thr Ser Gln
    1445                 1450                 1455

Lys Ser  Ser Glu Tyr Pro Ile  Ser Gln Asn Pro Glu  Gly Leu Ser
    1460                 1465                 1470

Ala Asp  Lys Phe Glu Val Ser  Ala Asp Ser Ser Thr  Ser Lys Asn
    1475                 1480                 1485
```

Lys Glu Pro Gly Val Glu Arg Ser Ser Pro Ser Lys Cys Pro Ser
1490 1495 1500

Leu Asp Asp Arg Trp Tyr Met His Ser Cys Ser Gly Ser Leu Gln
1505 1510 1515

Asn Arg Asn Tyr Pro Ser Gln Glu Glu Leu Ile Lys Val Val Asp
1520 1525 1530

Val Glu Glu Gln Gln Leu Glu Glu Ser Gly Pro His Asp Leu Thr
1535 1540 1545

Glu Thr Ser Tyr Leu Pro Arg Gln Asp Leu Glu Gly Thr Pro Tyr
1550 1555 1560

Leu Glu Ser Gly Ile Ser Leu Phe Ser Asp Asp Pro Glu Ser Asp
1565 1570 1575

Pro Ser Glu Asp Arg Ala Pro Glu Ser Ala Arg Val Gly Asn Ile
1580 1585 1590

Pro Ser Ser Thr Ser Ala Leu Lys Val Pro Gln Leu Lys Val Ala
1595 1600 1605

Glu Ser Ala Gln Ser Pro Ala Ala Ala His Thr Thr Asp Thr Ala
1610 1615 1620

Gly Tyr Asn Ala Met Glu Glu Ser Val Ser Arg Glu Lys Pro Glu
1625 1630 1635

Leu Thr Ala Ser Thr Glu Arg Val Asn Lys Arg Met Ser Met Val
1640 1645 1650

Val Phe Gly Leu Thr Pro Glu Glu Phe Met Leu Val Tyr Lys Phe
1655 1660 1665

Ala Arg Lys His His Ile Thr Leu Thr Asn Leu Ile Thr Glu Glu
1670 1675 1680

Thr Thr His Val Val Met Lys Thr Asp Ala Glu Phe Val Cys Glu
1685 1690 1695

Arg Thr Leu Lys Tyr Phe Leu Gly Ile Ala Gly Gly Lys Trp Val
1700 1705 1710

Val Ser Tyr Phe Trp Val Thr Gln Ser Ile Lys Glu Arg Lys Met
1715 1720 1725

Leu Asn Glu His Asp Phe Glu Val Arg Gly Asp Val Val Asn Gly
1730 1735 1740

Arg Asn His Gln Gly Pro Lys Arg Ala Arg Glu Ser Gln Asp Arg
1745 1750 1755

Lys Ile Phe Arg Gly Leu Glu Ile Cys Cys Tyr Gly Pro Phe Thr
1760 1765 1770

Asn Met Pro Thr Asp Gln Leu Glu Trp Met Val Gln Leu Cys Gly
1775 1780 1785

Ala Ser Val Val Lys Glu Leu Ser Ser Phe Thr Leu Gly Thr Gly
1790 1795 1800

Val His Pro Ile Val Val Val Gln Pro Asp Ala Trp Thr Glu Asp
1805 1810 1815

Asn Gly Phe His Ala Ile Gly Gln Met Cys Glu Ala Pro Val Val
1820 1825 1830

Thr Arg Glu Trp Val Leu Asp Ser Val Ala Leu Tyr Gln Cys Gln
1835 1840 1845

Glu Leu Asp Thr Tyr Leu Ile Pro Gln Ile Pro His Ser His Tyr
1850 1855 1860

<210> 10
<211> 1863
<212> PRT
<213> Homo sapiens

<400> 10

Met Asp Leu Ser Ala Leu Arg Val Glu Glu Val Gln Asn Val Ile Asn
1 5 10 15

Ala Met Gln Lys Ile Leu Glu Cys Pro Ile Cys Leu Glu Leu Ile Lys

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            20                  25                  30

Glu Pro Val Ser Thr Lys Cys Asp His Ile Phe Cys Lys Phe Cys Met
        35                  40                  45

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

Lys Asn Asp Ile Thr Lys Arg Ser Leu Gln Glu Ser Thr Arg Phe Ser
65                  70                  75                  80

Gln Leu Val Glu Glu Leu Leu Lys Ile Ile Cys Ala Phe Gln Leu Asp
                85                  90                  95

Thr Gly Leu Glu Tyr Ala Asn Ser Tyr Asn Phe Ala Lys Lys Glu Asn
            100                 105                 110

Asn Ser Pro Glu His Leu Lys Asp Glu Val Ser Ile Ile Gln Ser Met
        115                 120                 125

Gly Tyr Arg Asn Arg Ala Lys Arg Leu Leu Gln Ser Glu Pro Glu Asn
    130                 135                 140

Pro Ser Leu Gln Glu Thr Ser Leu Ser Val Gln Leu Ser Asn Leu Gly
145                 150                 155                 160

Thr Val Arg Thr Leu Arg Thr Lys Gln Arg Ile Gln Pro Gln Lys Thr
                165                 170                 175

Ser Val Tyr Ile Glu Leu Gly Ser Asp Ser Ser Glu Asp Thr Val Asn
            180                 185                 190

Lys Ala Thr Tyr Cys Ser Val Gly Asp Gln Glu Leu Leu Gln Ile Thr
        195                 200                 205

Pro Gln Gly Thr Arg Asp Glu Ile Ser Leu Asp Ser Ala Lys Lys Ala
    210                 215                 220

Ala Cys Glu Phe Ser Glu Thr Asp Val Thr Asn Thr Glu His His Gln
225                 230                 235                 240

Pro Ser Asn Asn Asp Leu Asn Thr Thr Glu Lys Arg Ala Ala Glu Arg
```

245 250 255

His Pro Glu Lys Tyr Gln Gly Ser Ser Val Ser Asn Leu His Val Glu
260 265 270

Pro Cys Gly Thr Asn Thr His Ala Ser Ser Leu Gln His Glu Asn Ser
275 280 285

Ser Leu Leu Leu Thr Lys Asp Arg Met Asn Val Glu Lys Ala Glu Phe
290 295 300

Cys Asn Lys Ser Lys Gln Pro Gly Leu Ala Arg Ser Gln His Asn Arg
305 310 315 320

Trp Ala Gly Ser Lys Glu Thr Cys Asn Asp Arg Arg Thr Pro Ser Thr
325 330 335

Glu Lys Lys Val Asp Leu Asn Ala Asp Pro Leu Cys Glu Arg Lys Glu
340 345 350

Trp Asn Lys Gln Lys Leu Pro Cys Ser Glu Asn Pro Arg Asp Thr Glu
355 360 365

Asp Val Pro Trp Ile Thr Leu Asn Ser Ser Ile Gln Lys Val Asn Glu
370 375 380

Trp Phe Ser Arg Ser Asp Glu Leu Leu Gly Ser Asp Asp Ser His Asp
385 390 395 400

Gly Glu Ser Glu Ser Asn Ala Lys Val Ala Asp Val Leu Asp Val Leu
405 410 415

Asn Glu Val Asp Glu Tyr Ser Gly Ser Ser Glu Lys Ile Asp Leu Leu
420 425 430

Ala Ser Asp Pro His Glu Ala Leu Ile Cys Lys Ser Glu Arg Val His
435 440 445

Ser Lys Ser Val Glu Ser Asn Ile Glu Asp Lys Ile Phe Gly Lys Thr
450 455 460

Tyr Arg Lys Lys Ala Ser Leu Pro Asn Leu Ser His Val Thr Glu Asn

465 470 475 480

Leu Ile Ile Gly Ala Phe Val Thr Glu Pro Gln Ile Ile Gln Glu Arg
485 490 495

Pro Leu Thr Asn Lys Leu Lys Arg Lys Arg Arg Pro Thr Ser Gly Leu
500 505 510

His Pro Glu Asp Phe Ile Lys Lys Ala Asp Leu Ala Val Gln Lys Thr
515 520 525

Pro Glu Met Ile Asn Gln Gly Thr Asn Gln Thr Glu Gln Asn Gly Gln
530 535 540

Val Met Asn Ile Thr Asn Ser Gly His Glu Asn Lys Thr Lys Gly Asp
545 550 555 560

Ser Ile Gln Asn Glu Lys Asn Pro Asn Pro Ile Glu Ser Leu Glu Lys
565 570 575

Glu Ser Ala Phe Lys Thr Lys Ala Glu Pro Ile Ser Ser Ser Ile Ser
580 585 590

Asn Met Glu Leu Glu Leu Asn Ile His Asn Ser Lys Ala Pro Lys Lys
595 600 605

Asn Arg Leu Arg Arg Lys Ser Ser Thr Arg His Ile His Ala Leu Glu
610 615 620

Leu Val Val Ser Arg Asn Leu Ser Pro Pro Asn Cys Thr Glu Leu Gln
625 630 635 640

Ile Asp Ser Cys Ser Ser Ser Glu Glu Ile Lys Lys Lys Lys Tyr Asn
645 650 655

Gln Met Pro Val Arg His Ser Arg Asn Leu Gln Leu Met Glu Gly Lys
660 665 670

Glu Pro Ala Thr Gly Ala Lys Lys Ser Asn Lys Pro Asn Glu Gln Thr
675 680 685

Ser Lys Arg His Asp Ser Asp Thr Phe Pro Glu Leu Lys Leu Thr Asn

690 695 700

Ala Pro Gly Ser Phe Thr Lys Cys Ser Asn Thr Ser Glu Leu Lys Glu
705 710 715 720

Phe Val Asn Pro Ser Leu Pro Arg Glu Glu Lys Glu Glu Lys Leu Glu
725 730 735

Thr Val Lys Val Ser Asn Asn Ala Glu Asp Pro Lys Asp Leu Met Leu
740 745 750

Ser Gly Glu Arg Val Leu Gln Thr Glu Arg Ser Val Glu Ser Ser Ser
755 760 765

Ile Ser Leu Val Pro Gly Thr Asp Tyr Gly Thr Gln Glu Ser Ile Ser
770 775 780

Leu Leu Glu Val Ser Thr Leu Gly Lys Ala Lys Thr Glu Pro Asn Lys
785 790 795 800

Cys Val Ser Gln Cys Ala Ala Phe Glu Asn Pro Lys Gly Leu Ile His
805 810 815

Gly Cys Ser Lys Asp Asn Arg Asn Asp Thr Glu Gly Phe Lys Tyr Pro
820 825 830

Leu Gly His Glu Val Asn His Ser Arg Glu Thr Ser Ile Glu Met Glu
835 840 845

Glu Ser Glu Leu Asp Ala Gln Tyr Leu Gln Asn Thr Phe Lys Val Ser
850 855 860

Lys Arg Gln Ser Phe Ala Pro Phe Ser Asn Pro Gly Asn Ala Glu Glu
865 870 875 880

Glu Cys Ala Thr Phe Ser Ala His Ser Gly Ser Leu Lys Lys Gln Ser
885 890 895

Pro Lys Val Thr Phe Glu Cys Glu Gln Lys Glu Glu Asn Gln Gly Lys
900 905 910

Asn Glu Ser Asn Ile Lys Pro Val Gln Thr Val Asn Ile Thr Ala Gly

915 920 925

Phe Pro Val Val Gly Gln Lys Asp Lys Pro Val Asp Asn Ala Lys Cys
930 935 940

Ser Ile Lys Gly Gly Ser Arg Phe Cys Leu Ser Ser Gln Phe Arg Gly
945 950 955 960

Asn Glu Thr Gly Leu Ile Thr Pro Asn Lys His Gly Leu Leu Gln Asn
965 970 975

Pro Tyr Arg Ile Pro Pro Leu Phe Pro Ile Lys Ser Phe Val Lys Thr
980 985 990

Lys Cys Lys Lys Asn Leu Leu Glu Glu Asn Phe Glu Glu His Ser Met
995 1000 1005

Ser Pro Glu Arg Glu Met Gly Asn Glu Asn Ile Pro Ser Thr Val
1010 1015 1020

Ser Thr Ile Ser Arg Asn Asn Ile Arg Glu Asn Val Phe Lys Glu
1025 1030 1035

Ala Ser Ser Ser Asn Ile Asn Glu Val Gly Ser Ser Thr Asn Glu
1040 1045 1050

Val Gly Ser Ser Ile Asn Glu Ile Gly Ser Ser Asp Glu Asn Ile
1055 1060 1065

Gln Ala Glu Leu Gly Arg Asn Arg Gly Pro Lys Leu Asn Ala Met
1070 1075 1080

Leu Arg Leu Gly Val Leu Gln Pro Glu Val Tyr Lys Gln Ser Leu
1085 1090 1095

Pro Gly Ser Asn Cys Lys His Pro Glu Ile Lys Lys Gln Glu Tyr
1100 1105 1110

Glu Glu Val Val Gln Thr Val Asn Thr Asp Phe Ser Pro Tyr Leu
1115 1120 1125

Ile Ser Asp Asn Leu Glu Gln Pro Met Gly Ser Ser His Ala Ser

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    1130                1135                1140

Gln Val  Cys Ser Glu Thr Pro  Asp Asp Leu Leu Asp  Asp Gly Glu
    1145                1150                1155

Ile Lys  Glu Asp Thr Ser Phe  Ala Glu Asn Asp Ile  Lys Glu Ser
    1160                1165                1170

Ser Ala  Val Phe Ser Lys Ser  Val Gln Lys Gly Glu  Leu Ser Arg
    1175                1180                1185

Ser Pro  Ser Pro Phe Thr His  Thr His Leu Ala Gln  Gly Tyr Arg
    1190                1195                1200

Arg Gly  Ala Lys Lys Leu Glu  Ser Ser Glu Glu Asn  Leu Ser Ser
    1205                1210                1215

Glu Asp  Glu Glu Leu Pro Cys  Phe Gln His Leu Leu  Phe Gly Lys
    1220                1225                1230

Val Asn  Asn Ile Pro Ser Gln  Ser Thr Arg His Ser  Thr Val Ala
    1235                1240                1245

Thr Glu  Cys Leu Ser Lys Asn  Thr Glu Glu Asn Leu  Leu Ser Leu
    1250                1255                1260

Lys Asn  Ser Leu Asn Asp Cys  Ser Asn Gln Val Ile  Leu Ala Lys
    1265                1270                1275

Ala Ser  Gln Glu His His Leu  Ser Glu Glu Thr Lys  Cys Ser Ala
    1280                1285                1290

Ser Leu  Phe Ser Ser Gln Cys  Ser Glu Leu Glu Asp  Leu Thr Ala
    1295                1300                1305

Asn Thr  Asn Thr Gln Asp Pro  Phe Leu Ile Gly Ser  Ser Lys Gln
    1310                1315                1320

Met Arg  His Gln Ser Glu Ser  Gln Gly Val Gly Leu  Ser Asp Lys
    1325                1330                1335

Glu Leu  Val Ser Asp Asp Glu  Glu Arg Gly Thr Gly  Leu Glu Glu
```

1340 1345 1350

Asn Asn Gln Glu Glu Gln Ser Met Asp Ser Asn Leu Gly Glu Ala
1355 1360 1365

Ala Ser Gly Cys Glu Ser Glu Thr Ser Val Ser Glu Asp Cys Ser
1370 1375 1380

Gly Leu Ser Ser Gln Ser Asp Ile Leu Thr Thr Gln Gln Arg Asp
1385 1390 1395

Thr Met Gln His Asn Leu Ile Lys Leu Gln Gln Glu Met Ala Glu
1400 1405 1410

Leu Glu Ala Val Leu Glu Gln His Gly Ser Gln Pro Ser Asn Ser
1415 1420 1425

Tyr Pro Ser Ile Ile Ser Asp Ser Ser Ala Leu Glu Asp Leu Arg
1430 1435 1440

Asn Pro Glu Gln Ser Thr Ser Glu Lys Ala Val Leu Thr Ser Gln
1445 1450 1455

Lys Ser Ser Glu Tyr Pro Ile Ser Gln Asn Pro Glu Gly Leu Ser
1460 1465 1470

Ala Asp Lys Phe Glu Val Ser Ala Asp Ser Ser Thr Ser Lys Asn
1475 1480 1485

Lys Glu Pro Gly Val Glu Arg Ser Ser Pro Ser Lys Cys Pro Ser
1490 1495 1500

Leu Asp Asp Arg Trp Tyr Met His Ser Cys Ser Gly Ser Leu Gln
1505 1510 1515

Asn Arg Asn Tyr Pro Ser Gln Glu Glu Leu Ile Lys Val Val Asp
1520 1525 1530

Val Glu Glu Gln Gln Leu Glu Glu Ser Gly Pro His Asp Leu Thr
1535 1540 1545

Glu Thr Ser Tyr Leu Pro Arg Gln Asp Leu Glu Gly Thr Pro Tyr

1550 1555 1560

Leu Glu Ser Gly Ile Ser Leu Phe Ser Asp Asp Pro Glu Ser Asp
1565 1570 1575

Pro Ser Glu Asp Arg Ala Pro Glu Ser Ala Arg Val Gly Asn Ile
1580 1585 1590

Pro Ser Ser Thr Ser Ala Leu Lys Val Pro Gln Leu Lys Val Ala
1595 1600 1605

Glu Ser Ala Gln Ser Pro Ala Ala Ala His Thr Thr Asp Thr Ala
1610 1615 1620

Gly Tyr Asn Ala Met Glu Glu Ser Val Ser Arg Glu Lys Pro Glu
1625 1630 1635

Leu Thr Ala Ser Thr Glu Arg Val Asn Lys Arg Met Ser Met Val
1640 1645 1650

Val Ser Gly Leu Thr Pro Glu Glu Phe Met Leu Val Tyr Lys Phe
1655 1660 1665

Ala Arg Lys His His Ile Thr Leu Thr Asn Leu Ile Thr Glu Glu
1670 1675 1680

Thr Thr His Val Val Met Lys Thr Asp Ala Glu Phe Val Cys Glu
1685 1690 1695

Arg Thr Leu Lys Tyr Phe Leu Gly Ile Ala Gly Gly Lys Trp Val
1700 1705 1710

Val Ser Tyr Phe Trp Val Thr Gln Ser Ile Lys Glu Arg Lys Met
1715 1720 1725

Leu Asn Glu His Asp Phe Glu Val Arg Gly Asp Val Val Asn Gly
1730 1735 1740

Arg Asn His Gln Gly Pro Lys Arg Ala Arg Glu Ser Gln Asp Arg
1745 1750 1755

Lys Ile Phe Arg Gly Leu Glu Ile Cys Cys Tyr Gly Pro Phe Thr

1760 1765 1770

Asn Arg Pro Thr Asp Gln Leu Glu Trp Met Val Gln Leu Cys Gly
1775 1780 1785

Ala Ser Val Val Lys Glu Leu Ser Ser Phe Thr Leu Gly Thr Gly
1790 1795 1800

Val His Pro Ile Val Val Val Gln Pro Asp Ala Trp Thr Glu Asp
1805 1810 1815

Asn Gly Phe His Ala Ile Gly Gln Met Cys Glu Ala Pro Val Val
1820 1825 1830

Thr Arg Glu Trp Val Leu Asp Ser Val Ala Leu Tyr Gln Cys Gln
1835 1840 1845

Glu Leu Asp Thr Tyr Leu Ile Pro Gln Ile Pro His Ser His Tyr
1850 1855 1860

<210> 11
<211> 1863
<212> PRT
<213> *Homo sapiens*

<400> 11

Met Asp Leu Ser Ala Leu Arg Val Glu Glu Val Gln Asn Val Ile Asn
1 5 10 15

Ala Met Gln Lys Ile Leu Glu Cys Pro Ile Cys Leu Glu Leu Ile Lys
20 25 30

Glu Pro Val Ser Thr Lys Cys Asp His Ile Phe Cys Lys Phe Cys Met
35 40 45

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

Lys Asn Asp Ile Thr Lys Arg Ser Leu Gln Glu Ser Thr Arg Phe Ser
65 70 75 80

Gln Leu Val Glu Glu Leu Leu Lys Ile Ile Cys Ala Phe Gln Leu Asp
85 90 95

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Thr Gly Leu Glu Tyr Ala Asn Ser Tyr Asn Phe Ala Lys Lys Glu Asn
            100                 105                 110

Asn Ser Pro Glu His Leu Lys Asp Glu Val Ser Ile Ile Gln Ser Met
        115                 120                 125

Gly Tyr Arg Asn Arg Ala Lys Arg Leu Leu Gln Ser Glu Pro Glu Asn
    130                 135                 140

Pro Ser Leu Gln Glu Thr Ser Leu Ser Val Gln Leu Ser Asn Leu Gly
145                 150                 155                 160

Thr Val Arg Thr Leu Arg Thr Lys Gln Arg Ile Gln Pro Gln Lys Thr
                165                 170                 175

Ser Val Tyr Ile Glu Leu Gly Ser Asp Ser Ser Glu Asp Thr Val Asn
            180                 185                 190

Lys Ala Thr Tyr Cys Ser Val Gly Asp Gln Glu Leu Leu Gln Ile Thr
        195                 200                 205

Pro Gln Gly Thr Arg Asp Glu Ile Ser Leu Asp Ser Ala Lys Lys Ala
    210                 215                 220

Ala Cys Glu Phe Ser Glu Thr Asp Val Thr Asn Thr Glu His His Gln
225                 230                 235                 240

Pro Ser Asn Asn Asp Leu Asn Thr Thr Glu Lys Arg Ala Ala Glu Arg
                245                 250                 255

His Pro Glu Lys Tyr Gln Gly Ser Ser Val Ser Asn Leu His Val Glu
            260                 265                 270

Pro Cys Gly Thr Asn Thr His Ala Ser Ser Leu Gln His Glu Asn Ser
        275                 280                 285

Ser Leu Leu Leu Thr Lys Asp Arg Met Asn Val Glu Lys Ala Glu Phe
    290                 295                 300

Cys Asn Lys Ser Lys Gln Pro Gly Leu Ala Arg Ser Gln His Asn Arg
305                 310                 315                 320
```

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Trp Ala Gly Ser Lys Glu Thr Cys Asn Asp Arg Arg Thr Pro Ser Thr
                325                 330                 335

Glu Lys Lys Val Asp Leu Asn Ala Asp Pro Leu Cys Glu Arg Lys Glu
            340                 345                 350

Trp Asn Lys Gln Lys Leu Pro Cys Ser Glu Asn Pro Arg Asp Thr Glu
        355                 360                 365

Asp Val Pro Trp Ile Thr Leu Asn Ser Ser Ile Gln Lys Val Asn Glu
    370                 375                 380

Trp Phe Ser Arg Ser Asp Glu Leu Leu Gly Ser Asp Asp Ser His Asp
385                 390                 395                 400

Gly Glu Ser Glu Ser Asn Ala Lys Val Ala Asp Val Leu Asp Val Leu
                405                 410                 415

Asn Glu Val Asp Glu Tyr Ser Gly Ser Ser Glu Lys Ile Asp Leu Leu
            420                 425                 430

Ala Ser Asp Pro His Glu Ala Leu Ile Cys Lys Ser Glu Arg Val His
        435                 440                 445

Ser Lys Ser Val Glu Ser Asn Ile Glu Asp Lys Ile Phe Gly Lys Thr
    450                 455                 460

Tyr Arg Lys Lys Ala Ser Leu Pro Asn Leu Ser His Val Thr Glu Asn
465                 470                 475                 480

Leu Ile Ile Gly Ala Phe Val Thr Glu Pro Gln Ile Ile Gln Glu Arg
                485                 490                 495

Pro Leu Thr Asn Lys Leu Lys Arg Lys Arg Arg Pro Thr Ser Gly Leu
            500                 505                 510

His Pro Glu Asp Phe Ile Lys Lys Ala Asp Leu Ala Val Gln Lys Thr
        515                 520                 525

Pro Glu Met Ile Asn Gln Gly Thr Asn Gln Thr Glu Gln Asn Gly Gln
    530                 535                 540
```

```
Val Met Asn Ile Thr Asn Ser Gly His Glu Asn Lys Thr Lys Gly Asp
545                 550                 555                 560

Ser Ile Gln Asn Glu Lys Asn Pro Asn Pro Ile Glu Ser Leu Glu Lys
                565                 570                 575

Glu Ser Ala Phe Lys Thr Lys Ala Glu Pro Ile Ser Ser Ser Ile Ser
            580                 585                 590

Asn Met Glu Leu Glu Leu Asn Ile His Asn Ser Lys Ala Pro Lys Lys
        595                 600                 605

Asn Arg Leu Arg Arg Lys Ser Ser Thr Arg His Ile His Ala Leu Glu
    610                 615                 620

Leu Val Val Ser Arg Asn Leu Ser Pro Pro Asn Cys Thr Glu Leu Gln
625                 630                 635                 640

Ile Asp Ser Cys Ser Ser Ser Glu Glu Ile Lys Lys Lys Lys Tyr Asn
                645                 650                 655

Gln Met Pro Val Arg His Ser Arg Asn Leu Gln Leu Met Glu Gly Lys
            660                 665                 670

Glu Pro Ala Thr Gly Ala Lys Lys Ser Asn Lys Pro Asn Glu Gln Thr
        675                 680                 685

Ser Lys Arg His Asp Ser Asp Thr Phe Pro Glu Leu Lys Leu Thr Asn
    690                 695                 700

Ala Pro Gly Ser Phe Thr Lys Cys Ser Asn Thr Ser Glu Leu Lys Glu
705                 710                 715                 720

Phe Val Asn Pro Ser Leu Pro Arg Glu Glu Lys Glu Glu Lys Leu Glu
                725                 730                 735

Thr Val Lys Val Ser Asn Asn Ala Glu Asp Pro Lys Asp Leu Met Leu
            740                 745                 750

Ser Gly Glu Arg Val Leu Gln Thr Glu Arg Ser Val Glu Ser Ser Ser
        755                 760                 765
```

Ile Ser Leu Val Pro Gly Thr Asp Tyr Gly Thr Gln Glu Ser Ile Ser
770 775 780

Leu Leu Glu Val Ser Thr Leu Gly Lys Ala Lys Thr Glu Pro Asn Lys
785 790 795 800

Cys Val Ser Gln Cys Ala Ala Phe Glu Asn Pro Lys Gly Leu Ile His
805 810 815

Gly Cys Ser Lys Asp Asn Arg Asn Asp Thr Glu Gly Phe Lys Tyr Pro
820 825 830

Leu Gly His Glu Val Asn His Ser Arg Glu Thr Ser Ile Glu Met Glu
835 840 845

Glu Ser Glu Leu Asp Ala Gln Tyr Leu Gln Asn Thr Phe Lys Val Ser
850 855 860

Lys Arg Gln Ser Phe Ala Pro Phe Ser Asn Pro Gly Asn Ala Glu Glu
865 870 875 880

Glu Cys Ala Thr Phe Ser Ala His Ser Gly Ser Leu Lys Lys Gln Ser
885 890 895

Pro Lys Val Thr Phe Glu Cys Glu Gln Lys Glu Glu Asn Gln Gly Lys
900 905 910

Asn Glu Ser Asn Ile Lys Pro Val Gln Thr Val Asn Ile Thr Ala Gly
915 920 925

Phe Pro Val Val Gly Gln Lys Asp Lys Pro Val Asp Asn Ala Lys Cys
930 935 940

Ser Ile Lys Gly Gly Ser Arg Phe Cys Leu Ser Ser Gln Phe Arg Gly
945 950 955 960

Asn Glu Thr Gly Leu Ile Thr Pro Asn Lys His Gly Leu Leu Gln Asn
965 970 975

Pro Tyr Arg Ile Pro Pro Leu Phe Pro Ile Lys Ser Phe Val Lys Thr
980 985 990

```
Lys Cys Lys Lys Asn Leu Leu Glu  Glu Asn Phe Glu Glu  His Ser Met
        995                 1000                1005

Ser Pro  Glu Arg Glu Met Gly  Asn Glu Asn Ile Pro  Ser Thr Val
    1010                1015                1020

Ser Thr  Ile Ser Arg Asn Asn  Ile Arg Glu Asn Val  Phe Lys Glu
    1025                1030                1035

Ala Ser  Ser Ser Asn Ile Asn  Glu Val Gly Ser Ser  Thr Asn Glu
    1040                1045                1050

Val Gly  Ser Ser Ile Asn Glu  Ile Gly Ser Ser Asp  Glu Asn Ile
    1055                1060                1065

Gln Ala  Glu Leu Gly Arg Asn  Arg Gly Pro Lys Leu  Asn Ala Met
    1070                1075                1080

Leu Arg  Leu Gly Val Leu Gln  Pro Glu Val Tyr Lys  Gln Ser Leu
    1085                1090                1095

Pro Gly  Ser Asn Cys Lys His  Pro Glu Ile Lys Lys  Gln Glu Tyr
    1100                1105                1110

Glu Glu  Val Val Gln Thr Val  Asn Thr Asp Phe Ser  Pro Tyr Leu
    1115                1120                1125

Ile Ser  Asp Asn Leu Glu Gln  Pro Met Gly Ser Ser  His Ala Ser
    1130                1135                1140

Gln Val  Cys Ser Glu Thr Pro  Asp Asp Leu Leu Asp  Asp Gly Glu
    1145                1150                1155

Ile Lys  Glu Asp Thr Ser Phe  Ala Glu Asn Asp Ile  Lys Glu Ser
    1160                1165                1170

Ser Ala  Val Phe Ser Lys Ser  Val Gln Lys Gly Glu  Leu Ser Arg
    1175                1180                1185

Ser Pro  Ser Pro Phe Thr His  Thr His Leu Ala Gln  Gly Tyr Arg
    1190                1195                1200
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Arg Gly  Ala Lys Lys Leu Glu  Ser Ser Glu Glu Asn  Leu Ser Ser
    1205                 1210                 1215

Glu Asp  Glu Glu Leu Pro Cys  Phe Gln His Leu Leu  Phe Gly Lys
    1220                 1225                 1230

Val Asn  Asn Ile Pro Ser Gln  Ser Thr Arg His Ser  Thr Val Ala
    1235                 1240                 1245

Thr Glu  Cys Leu Ser Lys Asn  Thr Glu Glu Asn Leu  Leu Ser Leu
    1250                 1255                 1260

Lys Asn  Ser Leu Asn Asp Cys  Ser Asn Gln Val Ile  Leu Ala Lys
    1265                 1270                 1275

Ala Ser  Gln Glu His His Leu  Ser Glu Glu Thr Lys  Cys Ser Ala
    1280                 1285                 1290

Ser Leu  Phe Ser Ser Gln Cys  Ser Glu Leu Glu Asp  Leu Thr Ala
    1295                 1300                 1305

Asn Thr  Asn Thr Gln Asp Pro  Phe Leu Ile Gly Ser  Ser Lys Gln
    1310                 1315                 1320

Met Arg  His Gln Ser Glu Ser  Gln Gly Val Gly Leu  Ser Asp Lys
    1325                 1330                 1335

Glu Leu  Val Ser Asp Asp Glu  Glu Arg Gly Thr Gly  Leu Glu Glu
    1340                 1345                 1350

Asn Asn  Gln Glu Glu Gln Ser  Met Asp Ser Asn Leu  Gly Glu Ala
    1355                 1360                 1365

Ala Ser  Gly Cys Glu Ser Glu  Thr Ser Val Ser Glu  Asp Cys Ser
    1370                 1375                 1380

Gly Leu  Ser Ser Gln Ser Asp  Ile Leu Thr Thr Gln  Gln Arg Asp
    1385                 1390                 1395

Thr Met  Gln His Asn Leu Ile  Lys Leu Gln Gln Glu  Met Ala Glu
    1400                 1405                 1410
```

Leu Glu Ala Val Leu Glu Gln His Gly Ser Gln Pro Ser Asn Ser
1415 1420 1425

Tyr Pro Ser Ile Ile Ser Asp Ser Ser Ala Leu Glu Asp Leu Arg
1430 1435 1440

Asn Pro Glu Gln Ser Thr Ser Glu Lys Ala Val Leu Thr Ser Gln
1445 1450 1455

Lys Ser Ser Glu Tyr Pro Ile Ser Gln Asn Pro Glu Gly Leu Ser
1460 1465 1470

Ala Asp Lys Phe Glu Val Ser Ala Asp Ser Ser Thr Ser Lys Asn
1475 1480 1485

Lys Glu Pro Gly Val Glu Arg Ser Ser Pro Ser Lys Cys Pro Ser
1490 1495 1500

Leu Asp Asp Arg Trp Tyr Met His Ser Cys Ser Gly Ser Leu Gln
1505 1510 1515

Asn Arg Asn Tyr Pro Ser Gln Glu Glu Leu Ile Lys Val Val Asp
1520 1525 1530

Val Glu Glu Gln Gln Leu Glu Glu Ser Gly Pro His Asp Leu Thr
1535 1540 1545

Glu Thr Ser Tyr Leu Pro Arg Gln Asp Leu Glu Gly Thr Pro Tyr
1550 1555 1560

Leu Glu Ser Gly Ile Ser Leu Phe Ser Asp Asp Pro Glu Ser Asp
1565 1570 1575

Pro Ser Glu Asp Arg Ala Pro Glu Ser Ala Arg Val Gly Asn Ile
1580 1585 1590

Pro Ser Ser Thr Ser Ala Leu Lys Val Pro Gln Leu Lys Val Ala
1595 1600 1605

Glu Ser Ala Gln Ser Pro Ala Ala Ala His Thr Thr Asp Thr Ala
1610 1615 1620

```
Gly Tyr  Asn Ala Met Glu Glu  Ser Val Ser Arg Glu  Lys Pro Glu
    1625                 1630                 1635

Leu Thr  Ala Ser Thr Glu Arg  Val Asn Lys Arg Met  Ser Met Val
    1640                 1645                 1650

Val Ser  Gly Leu Thr Pro Glu  Glu Phe Met Leu Val  Tyr Lys Phe
    1655                 1660                 1665

Ala Arg  Lys His His Ile Thr  Leu Thr Asn Leu Ile  Thr Glu Glu
    1670                 1675                 1680

Thr Thr  His Val Val Met Lys  Thr Tyr Ala Glu Phe  Val Cys Glu
    1685                 1690                 1695

Arg Thr  Leu Lys Tyr Phe Leu  Gly Ile Ala Gly Gly  Lys Trp Val
    1700                 1705                 1710

Val Ser  Tyr Phe Trp Val Thr  Gln Ser Ile Lys Glu  Arg Lys Met
    1715                 1720                 1725

Leu Asn  Glu His Asp Phe Glu  Val Arg Gly Asp Val  Val Asn Gly
    1730                 1735                 1740

Arg Asn  His Gln Gly Pro Lys  Arg Ala Arg Glu Ser  Gln Asp Arg
    1745                 1750                 1755

Lys Ile  Phe Arg Gly Leu Glu  Ile Cys Cys Tyr Gly  Pro Phe Thr
    1760                 1765                 1770

Asn Met  Pro Thr Asp Gln Leu  Glu Trp Met Val Gln  Leu Cys Gly
    1775                 1780                 1785

Ala Ser  Val Val Lys Glu Leu  Ser Ser Phe Thr Leu  Gly Thr Gly
    1790                 1795                 1800

Val His  Pro Ile Val Val Val  Gln Pro Asp Ala Trp  Thr Glu Asp
    1805                 1810                 1815

Asn Gly  Phe His Ala Ile Gly  Gln Met Cys Glu Ala  Pro Val Val
    1820                 1825                 1830
```

```
Thr Arg  Glu Trp Val Leu Asp  Ser Val Ala Leu Tyr  Gln Cys Gln
    1835                 1840                 1845

Glu Leu  Asp Thr Tyr Leu Ile  Pro Gln Ile Pro His  Ser His Tyr
    1850                 1855                 1860
```

<210> 12
<211> 1863
<212> PRT
<213> Homo sapiens

<400> 12

```
Met Asp Leu Ser Ala Leu Arg Val Glu Glu Val Gln Asn Val Ile Asn
1               5                  10                  15

Ala Met Gln Lys Ile Leu Glu Cys Pro Ile Cys Leu Glu Leu Ile Lys
            20                  25                  30

Glu Pro Val Ser Thr Lys Cys Asp His Ile Phe Cys Lys Phe Cys Met
        35                  40                  45

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

Lys Asn Asp Ile Thr Lys Arg Ser Leu Gln Glu Ser Thr Arg Phe Ser
65                  70                  75                  80

Gln Leu Val Glu Glu Leu Leu Lys Ile Ile Cys Ala Phe Gln Leu Asp
                85                  90                  95

Thr Gly Leu Glu Tyr Ala Asn Ser Tyr Asn Phe Ala Lys Lys Glu Asn
            100                 105                 110

Asn Ser Pro Glu His Leu Lys Asp Glu Val Ser Ile Ile Gln Ser Met
        115                 120                 125

Gly Tyr Arg Asn Arg Ala Lys Arg Leu Leu Gln Ser Glu Pro Glu Asn
    130                 135                 140

Pro Ser Leu Gln Glu Thr Ser Leu Ser Val Gln Leu Ser Asn Leu Gly
145                 150                 155                 160
```

```
Thr Val Arg Thr Leu Arg Thr Lys Gln Arg Ile Gln Pro Gln Lys Thr
                165                 170                 175

Ser Val Tyr Ile Glu Leu Gly Ser Asp Ser Ser Glu Asp Thr Val Asn
            180                 185                 190

Lys Ala Thr Tyr Cys Ser Val Gly Asp Gln Glu Leu Leu Gln Ile Thr
        195                 200                 205

Pro Gln Gly Thr Arg Asp Glu Ile Ser Leu Asp Ser Ala Lys Lys Ala
    210                 215                 220

Ala Cys Glu Phe Ser Glu Thr Asp Val Thr Asn Thr Glu His His Gln
225                 230                 235                 240

Pro Ser Asn Asn Asp Leu Asn Thr Thr Glu Lys Arg Ala Ala Glu Arg
                245                 250                 255

His Pro Glu Lys Tyr Gln Gly Ser Ser Val Ser Asn Leu His Val Glu
            260                 265                 270

Pro Cys Gly Thr Asn Thr His Ala Ser Ser Leu Gln His Glu Asn Ser
        275                 280                 285

Ser Leu Leu Leu Thr Lys Asp Arg Met Asn Val Glu Lys Ala Glu Phe
    290                 295                 300

Cys Asn Lys Ser Lys Gln Pro Gly Leu Ala Arg Ser Gln His Asn Arg
305                 310                 315                 320

Trp Ala Gly Ser Lys Glu Thr Cys Asn Asp Arg Arg Thr Pro Ser Thr
                325                 330                 335

Glu Lys Lys Val Asp Leu Asn Ala Asp Pro Leu Cys Glu Arg Lys Glu
            340                 345                 350

Trp Asn Lys Gln Lys Leu Pro Cys Ser Glu Asn Pro Arg Asp Thr Glu
        355                 360                 365

Asp Val Pro Trp Ile Thr Leu Asn Ser Ser Ile Gln Lys Val Asn Glu
    370                 375                 380
```

```
Trp Phe Ser Arg Ser Asp Glu Leu Leu Gly Ser Asp Asp Ser His Asp
385                 390                 395                 400

Gly Glu Ser Glu Ser Asn Ala Lys Val Ala Asp Val Leu Asp Val Leu
                405                 410                 415

Asn Glu Val Asp Glu Tyr Ser Gly Ser Ser Glu Lys Ile Asp Leu Leu
            420                 425                 430

Ala Ser Asp Pro His Glu Ala Leu Ile Cys Lys Ser Glu Arg Val His
        435                 440                 445

Ser Lys Ser Val Glu Ser Asn Ile Glu Asp Lys Ile Phe Gly Lys Thr
    450                 455                 460

Tyr Arg Lys Lys Ala Ser Leu Pro Asn Leu Ser His Val Thr Glu Asn
465                 470                 475                 480

Leu Ile Ile Gly Ala Phe Val Thr Glu Pro Gln Ile Ile Gln Glu Arg
                485                 490                 495

Pro Leu Thr Asn Lys Leu Lys Arg Lys Arg Arg Pro Thr Ser Gly Leu
            500                 505                 510

His Pro Glu Asp Phe Ile Lys Lys Ala Asp Leu Ala Val Gln Lys Thr
        515                 520                 525

Pro Glu Met Ile Asn Gln Gly Thr Asn Gln Thr Glu Gln Asn Gly Gln
    530                 535                 540

Val Met Asn Ile Thr Asn Ser Gly His Glu Asn Lys Thr Lys Gly Asp
545                 550                 555                 560

Ser Ile Gln Asn Glu Lys Asn Pro Asn Pro Ile Glu Ser Leu Glu Lys
                565                 570                 575

Glu Ser Ala Phe Lys Thr Lys Ala Glu Pro Ile Ser Ser Ser Ile Ser
            580                 585                 590

Asn Met Glu Leu Glu Leu Asn Ile His Asn Ser Lys Ala Pro Lys Lys
        595                 600                 605
```

```
Asn Arg Leu Arg Arg Lys Ser Ser Thr Arg His Ile His Ala Leu Glu
    610                 615                 620

Leu Val Val Ser Arg Asn Leu Ser Pro Pro Asn Cys Thr Glu Leu Gln
625                 630                 635                 640

Ile Asp Ser Cys Ser Ser Ser Glu Glu Ile Lys Lys Lys Lys Tyr Asn
                645                 650                 655

Gln Met Pro Val Arg His Ser Arg Asn Leu Gln Leu Met Glu Gly Lys
            660                 665                 670

Glu Pro Ala Thr Gly Ala Lys Lys Ser Asn Lys Pro Asn Glu Gln Thr
        675                 680                 685

Ser Lys Arg His Asp Ser Asp Thr Phe Pro Glu Leu Lys Leu Thr Asn
    690                 695                 700

Ala Pro Gly Ser Phe Thr Lys Cys Ser Asn Thr Ser Glu Leu Lys Glu
705                 710                 715                 720

Phe Val Asn Pro Ser Leu Pro Arg Glu Glu Lys Glu Glu Lys Leu Glu
                725                 730                 735

Thr Val Lys Val Ser Asn Asn Ala Glu Asp Pro Lys Asp Leu Met Leu
            740                 745                 750

Ser Gly Glu Arg Val Leu Gln Thr Glu Arg Ser Val Glu Ser Ser Ser
        755                 760                 765

Ile Ser Leu Val Pro Gly Thr Asp Tyr Gly Thr Gln Glu Ser Ile Ser
    770                 775                 780

Leu Leu Glu Val Ser Thr Leu Gly Lys Ala Lys Thr Glu Pro Asn Lys
785                 790                 795                 800

Cys Val Ser Gln Cys Ala Ala Phe Glu Asn Pro Lys Gly Leu Ile His
                805                 810                 815

Gly Cys Ser Lys Asp Asn Arg Asn Asp Thr Glu Gly Phe Lys Tyr Pro
            820                 825                 830
```

```
Leu Gly His Glu Val Asn His Ser Arg Glu Thr Ser Ile Glu Met Glu
        835                 840                 845

Glu Ser Glu Leu Asp Ala Gln Tyr Leu Gln Asn Thr Phe Lys Val Ser
    850                 855                 860

Lys Arg Gln Ser Phe Ala Pro Phe Ser Asn Pro Gly Asn Ala Glu Glu
865                 870                 875                 880

Glu Cys Ala Thr Phe Ser Ala His Ser Gly Ser Leu Lys Lys Gln Ser
                885                 890                 895

Pro Lys Val Thr Phe Glu Cys Glu Gln Lys Glu Glu Asn Gln Gly Lys
            900                 905                 910

Asn Glu Ser Asn Ile Lys Pro Val Gln Thr Val Asn Ile Thr Ala Gly
        915                 920                 925

Phe Pro Val Val Gly Gln Lys Asp Lys Pro Val Asp Asn Ala Lys Cys
    930                 935                 940

Ser Ile Lys Gly Gly Ser Arg Phe Cys Leu Ser Ser Gln Phe Arg Gly
945                 950                 955                 960

Asn Glu Thr Gly Leu Ile Thr Pro Asn Lys His Gly Leu Leu Gln Asn
                965                 970                 975

Pro Tyr Arg Ile Pro Pro Leu Phe Pro Ile Lys Ser Phe Val Lys Thr
            980                 985                 990

Lys Cys Lys Lys Asn Leu Leu Glu  Glu Asn Phe Glu Glu  His Ser Met
        995                 1000                1005

Ser Pro  Glu Arg Glu Met Gly  Asn Glu Asn Ile Pro  Ser Thr Val
    1010                1015                1020

Ser Thr  Ile Ser Arg Asn Asn  Ile Arg Glu Asn Val  Phe Lys Glu
    1025                1030                1035

Ala Ser  Ser Ser Asn Ile Asn  Glu Val Gly Ser Ser  Thr Asn Glu
    1040                1045                1050
```

Val Gly Ser Ser Ile Asn Glu Ile Gly Ser Ser Asp Glu Asn Ile
1055 1060 1065

Gln Ala Glu Leu Gly Arg Asn Arg Gly Pro Lys Leu Asn Ala Met
1070 1075 1080

Leu Arg Leu Gly Val Leu Gln Pro Glu Val Tyr Lys Gln Ser Leu
1085 1090 1095

Pro Gly Ser Asn Cys Lys His Pro Glu Ile Lys Lys Gln Glu Tyr
1100 1105 1110

Glu Glu Val Val Gln Thr Val Asn Thr Asp Phe Ser Pro Tyr Leu
1115 1120 1125

Ile Ser Asp Asn Leu Glu Gln Pro Met Gly Ser Ser His Ala Ser
1130 1135 1140

Gln Val Cys Ser Glu Thr Pro Asp Asp Leu Leu Asp Asp Gly Glu
1145 1150 1155

Ile Lys Glu Asp Thr Ser Phe Ala Glu Asn Asp Ile Lys Glu Ser
1160 1165 1170

Ser Ala Val Phe Ser Lys Ser Val Gln Lys Gly Glu Leu Ser Arg
1175 1180 1185

Ser Pro Ser Pro Phe Thr His Thr His Leu Ala Gln Gly Tyr Arg
1190 1195 1200

Arg Gly Ala Lys Lys Leu Glu Ser Ser Glu Glu Asn Leu Ser Ser
1205 1210 1215

Glu Asp Glu Glu Leu Pro Cys Phe Gln His Leu Leu Phe Gly Lys
1220 1225 1230

Val Asn Asn Ile Pro Ser Gln Ser Thr Arg His Ser Thr Val Ala
1235 1240 1245

Thr Glu Cys Leu Ser Lys Asn Thr Glu Glu Asn Leu Leu Ser Leu
1250 1255 1260

Lys Asn Ser Leu Asn Asp Cys Ser Asn Gln Val Ile Leu Ala Lys
1265 1270 1275

Ala Ser Gln Glu His His Leu Ser Glu Glu Thr Lys Cys Ser Ala
1280 1285 1290

Ser Leu Phe Ser Ser Gln Cys Ser Glu Leu Glu Asp Leu Thr Ala
1295 1300 1305

Asn Thr Asn Thr Gln Asp Pro Phe Leu Ile Gly Ser Ser Lys Gln
1310 1315 1320

Met Arg His Gln Ser Glu Ser Gln Gly Val Gly Leu Ser Asp Lys
1325 1330 1335

Glu Leu Val Ser Asp Asp Glu Glu Arg Gly Thr Gly Leu Glu Glu
1340 1345 1350

Asn Asn Gln Glu Glu Gln Ser Met Asp Ser Asn Leu Gly Glu Ala
1355 1360 1365

Ala Ser Gly Cys Glu Ser Glu Thr Ser Val Ser Glu Asp Cys Ser
1370 1375 1380

Gly Leu Ser Ser Gln Ser Asp Ile Leu Thr Thr Gln Gln Arg Asp
1385 1390 1395

Thr Met Gln His Asn Leu Ile Lys Leu Gln Gln Glu Met Ala Glu
1400 1405 1410

Leu Glu Ala Val Leu Glu Gln His Gly Ser Gln Pro Ser Asn Ser
1415 1420 1425

Tyr Pro Ser Ile Ile Ser Asp Ser Ser Ala Leu Glu Asp Leu Arg
1430 1435 1440

Asn Pro Glu Gln Ser Thr Ser Glu Lys Ala Val Leu Thr Ser Gln
1445 1450 1455

Lys Ser Ser Glu Tyr Pro Ile Ser Gln Asn Pro Glu Gly Leu Ser
1460 1465 1470

```
Ala Asp  Lys Phe Glu Val Ser  Ala Asp Ser Ser Thr  Ser Lys Asn
    1475                 1480                 1485

Lys Glu  Pro Gly Val Glu Arg  Ser Ser Pro Ser Lys  Cys Pro Ser
    1490                 1495                 1500

Leu Asp  Asp Arg Trp Tyr Met  His Ser Cys Ser Gly  Ser Leu Gln
    1505                 1510                 1515

Asn Arg  Asn Tyr Pro Ser Gln  Glu Glu Leu Ile Lys  Val Val Asp
    1520                 1525                 1530

Val Glu  Glu Gln Gln Leu Glu  Glu Ser Gly Pro His  Asp Leu Thr
    1535                 1540                 1545

Glu Thr  Ser Tyr Leu Pro Arg  Gln Asp Leu Glu Gly  Thr Pro Tyr
    1550                 1555                 1560

Leu Glu  Ser Gly Ile Ser Leu  Phe Ser Asp Asp Pro  Glu Ser Asp
    1565                 1570                 1575

Pro Ser  Glu Asp Arg Ala Pro  Glu Ser Ala Arg Val  Gly Asn Ile
    1580                 1585                 1590

Pro Ser  Ser Thr Ser Ala Leu  Lys Val Pro Gln Leu  Lys Val Ala
    1595                 1600                 1605

Glu Ser  Ala Gln Ser Pro Ala  Ala Ala His Thr Thr  Asp Thr Ala
    1610                 1615                 1620

Gly Tyr  Asn Ala Met Glu Glu  Ser Val Ser Arg Glu  Lys Pro Glu
    1625                 1630                 1635

Leu Thr  Ala Ser Thr Glu Arg  Val Asn Lys Arg Met  Ser Met Val
    1640                 1645                 1650

Val Ser  Gly Leu Thr Pro Glu  Glu Phe Met Leu Val  Tyr Lys Phe
    1655                 1660                 1665

Ala Arg  Lys His His Ile Thr  Leu Thr Asn Leu Ile  Thr Glu Glu
    1670                 1675                 1680
```

```
Thr Thr  His Val Val Met Lys  Thr Asp Ala Glu Phe  Val Arg Glu
    1685                 1690                 1695

Arg Thr  Leu Lys Tyr Phe Leu  Gly Ile Ala Gly Gly  Lys Trp Val
    1700                 1705                 1710

Val Ser  Tyr Phe Trp Val Thr  Gln Ser Ile Lys Glu  Arg Lys Met
    1715                 1720                 1725

Leu Asn  Glu His Asp Phe Glu  Val Arg Gly Asp Val  Val Asn Gly
    1730                 1735                 1740

Arg Asn  His Gln Gly Pro Lys  Arg Ala Arg Glu Ser  Gln Asp Arg
    1745                 1750                 1755

Lys Ile  Phe Arg Gly Leu Glu  Ile Cys Cys Tyr Gly  Pro Phe Thr
    1760                 1765                 1770

Asn Met  Pro Thr Asp Gln Leu  Glu Trp Met Val Gln  Leu Cys Gly
    1775                 1780                 1785

Ala Ser  Val Val Lys Glu Leu  Ser Ser Phe Thr Leu  Gly Thr Gly
    1790                 1795                 1800

Val His  Pro Ile Val Val Val  Gln Pro Asp Ala Trp  Thr Glu Asp
    1805                 1810                 1815

Asn Gly  Phe His Ala Ile Gly  Gln Met Cys Glu Ala  Pro Val Val
    1820                 1825                 1830

Thr Arg  Glu Trp Val Leu Asp  Ser Val Ala Leu Tyr  Gln Cys Gln
    1835                 1840                 1845

Glu Leu  Asp Thr Tyr Leu Ile  Pro Gln Ile Pro His  Ser His Tyr
    1850                 1855                 1860
```

<210> 13
<211> 1863
<212> PRT
<213> Homo sapiens

<400> 13

```
Met Asp Leu Ser Ala Leu Arg Val Glu Glu Val Gln Asn Val Ile Asn
1               5                  10                  15

Ala Met Gln Lys Ile Leu Glu Cys Pro Ile Cys Leu Glu Leu Ile Lys
            20                  25                  30

Glu Pro Val Ser Thr Lys Cys Asp His Ile Phe Cys Lys Phe Cys Met
        35                  40                  45

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

Lys Asn Asp Ile Thr Lys Arg Ser Leu Gln Glu Ser Thr Arg Phe Ser
65                  70                  75                  80

Gln Leu Val Glu Glu Leu Leu Lys Ile Ile Cys Ala Phe Gln Leu Asp
                85                  90                  95

Thr Gly Leu Glu Tyr Ala Asn Ser Tyr Asn Phe Ala Lys Lys Glu Asn
            100                 105                 110

Asn Ser Pro Glu His Leu Lys Asp Glu Val Ser Ile Ile Gln Ser Met
        115                 120                 125

Gly Tyr Arg Asn Arg Ala Lys Arg Leu Leu Gln Ser Glu Pro Glu Asn
    130                 135                 140

Pro Ser Leu Gln Glu Thr Ser Leu Ser Val Gln Leu Ser Asn Leu Gly
145                 150                 155                 160

Thr Val Arg Thr Leu Arg Thr Lys Gln Arg Ile Gln Pro Gln Lys Thr
                165                 170                 175

Ser Val Tyr Ile Glu Leu Gly Ser Asp Ser Ser Glu Asp Thr Val Asn
            180                 185                 190

Lys Ala Thr Tyr Cys Ser Val Gly Asp Gln Glu Leu Leu Gln Ile Thr
        195                 200                 205

Pro Gln Gly Thr Arg Asp Glu Ile Ser Leu Asp Ser Ala Lys Lys Ala
    210                 215                 220
```

```
Ala Cys Glu Phe Ser Glu Thr Asp Val Thr Asn Thr Glu His His Gln
225                 230                 235                 240

Pro Ser Asn Asn Asp Leu Asn Thr Thr Glu Lys Arg Ala Ala Glu Arg
                245                 250                 255

His Pro Glu Lys Tyr Gln Gly Ser Ser Val Ser Asn Leu His Val Glu
            260                 265                 270

Pro Cys Gly Thr Asn Thr His Ala Ser Ser Leu Gln His Glu Asn Ser
        275                 280                 285

Ser Leu Leu Leu Thr Lys Asp Arg Met Asn Val Glu Lys Ala Glu Phe
    290                 295                 300

Cys Asn Lys Ser Lys Gln Pro Gly Leu Ala Arg Ser Gln His Asn Arg
305                 310                 315                 320

Trp Ala Gly Ser Lys Glu Thr Cys Asn Asp Arg Arg Thr Pro Ser Thr
                325                 330                 335

Glu Lys Lys Val Asp Leu Asn Ala Asp Pro Leu Cys Glu Arg Lys Glu
            340                 345                 350

Trp Asn Lys Gln Lys Leu Pro Cys Ser Glu Asn Pro Arg Asp Thr Glu
        355                 360                 365

Asp Val Pro Trp Ile Thr Leu Asn Ser Ser Ile Gln Lys Val Asn Glu
    370                 375                 380

Trp Phe Ser Arg Ser Asp Glu Leu Leu Gly Ser Asp Asp Ser His Asp
385                 390                 395                 400

Gly Glu Ser Glu Ser Asn Ala Lys Val Ala Asp Val Leu Asp Val Leu
                405                 410                 415

Asn Glu Val Asp Glu Tyr Ser Gly Ser Ser Glu Lys Ile Asp Leu Leu
            420                 425                 430

Ala Ser Asp Pro His Glu Ala Leu Ile Cys Lys Ser Glu Arg Val His
        435                 440                 445
```

Ser Lys Ser Val Glu Ser Asn Ile Glu Asp Lys Ile Phe Gly Lys Thr
450 455 460

Tyr Arg Lys Lys Ala Ser Leu Pro Asn Leu Ser His Val Thr Glu Asn
465 470 475 480

Leu Ile Ile Gly Ala Phe Val Thr Glu Pro Gln Ile Ile Gln Glu Arg
485 490 495

Pro Leu Thr Asn Lys Leu Lys Arg Lys Arg Arg Pro Thr Ser Gly Leu
500 505 510

His Pro Glu Asp Phe Ile Lys Lys Ala Asp Leu Ala Val Gln Lys Thr
515 520 525

Pro Glu Met Ile Asn Gln Gly Thr Asn Gln Thr Glu Gln Asn Gly Gln
530 535 540

Val Met Asn Ile Thr Asn Ser Gly His Glu Asn Lys Thr Lys Gly Asp
545 550 555 560

Ser Ile Gln Asn Glu Lys Asn Pro Asn Pro Ile Glu Ser Leu Glu Lys
565 570 575

Glu Ser Ala Phe Lys Thr Lys Ala Glu Pro Ile Ser Ser Ser Ile Ser
580 585 590

Asn Met Glu Leu Glu Leu Asn Ile His Asn Ser Lys Ala Pro Lys Lys
595 600 605

Asn Arg Leu Arg Arg Lys Ser Ser Thr Arg His Ile His Ala Leu Glu
610 615 620

Leu Val Val Ser Arg Asn Leu Ser Pro Pro Asn Cys Thr Glu Leu Gln
625 630 635 640

Ile Asp Ser Cys Ser Ser Ser Glu Glu Ile Lys Lys Lys Lys Tyr Asn
645 650 655

Gln Met Pro Val Arg His Ser Arg Asn Leu Gln Leu Met Glu Gly Lys
660 665 670

```
Glu Pro Ala Thr Gly Ala Lys Lys Ser Asn Lys Pro Asn Glu Gln Thr
        675                 680                 685

Ser Lys Arg His Asp Ser Asp Thr Phe Pro Glu Leu Lys Leu Thr Asn
    690                 695                 700

Ala Pro Gly Ser Phe Thr Lys Cys Ser Asn Thr Ser Glu Leu Lys Glu
705                 710                 715                 720

Phe Val Asn Pro Ser Leu Pro Arg Glu Glu Lys Glu Glu Lys Leu Glu
                725                 730                 735

Thr Val Lys Val Ser Asn Asn Ala Glu Asp Pro Lys Asp Leu Met Leu
            740                 745                 750

Ser Gly Glu Arg Val Leu Gln Thr Glu Arg Ser Val Glu Ser Ser Ser
        755                 760                 765

Ile Ser Leu Val Pro Gly Thr Asp Tyr Gly Thr Gln Glu Ser Ile Ser
    770                 775                 780

Leu Leu Glu Val Ser Thr Leu Gly Lys Ala Lys Thr Glu Pro Asn Lys
785                 790                 795                 800

Cys Val Ser Gln Cys Ala Ala Phe Glu Asn Pro Lys Gly Leu Ile His
                805                 810                 815

Gly Cys Ser Lys Asp Asn Arg Asn Asp Thr Glu Gly Phe Lys Tyr Pro
            820                 825                 830

Leu Gly His Glu Val Asn His Ser Arg Glu Thr Ser Ile Glu Met Glu
        835                 840                 845

Glu Ser Glu Leu Asp Ala Gln Tyr Leu Gln Asn Thr Phe Lys Val Ser
    850                 855                 860

Lys Arg Gln Ser Phe Ala Pro Phe Ser Asn Pro Gly Asn Ala Glu Glu
865                 870                 875                 880

Glu Cys Ala Thr Phe Ser Ala His Ser Gly Ser Leu Lys Lys Gln Ser
                885                 890                 895
```

```
Pro Lys Val Thr Phe Glu Cys Glu Gln Lys Glu Glu Asn Gln Gly Lys
            900                 905                 910

Asn Glu Ser Asn Ile Lys Pro Val Gln Thr Val Asn Ile Thr Ala Gly
        915                 920                 925

Phe Pro Val Val Gly Gln Lys Asp Lys Pro Val Asp Asn Ala Lys Cys
    930                 935                 940

Ser Ile Lys Gly Gly Ser Arg Phe Cys Leu Ser Ser Gln Phe Arg Gly
945                 950                 955                 960

Asn Glu Thr Gly Leu Ile Thr Pro Asn Lys His Gly Leu Leu Gln Asn
                965                 970                 975

Pro Tyr Arg Ile Pro Pro Leu Phe Pro Ile Lys Ser Phe Val Lys Thr
            980                 985                 990

Lys Cys Lys Lys Asn Leu Leu Glu  Glu Asn Phe Glu Glu  His Ser Met
        995                 1000                1005

Ser Pro  Glu Arg Glu Met Gly  Asn Glu Asn Ile Pro  Ser Thr Val
    1010                1015                1020

Ser Thr  Ile Ser Arg Asn Asn  Ile Arg Glu Asn Val  Phe Lys Glu
    1025                1030                1035

Ala Ser  Ser Ser Asn Ile Asn  Glu Val Gly Ser Ser  Thr Asn Glu
    1040                1045                1050

Val Gly  Ser Ser Ile Asn Glu  Ile Gly Ser Ser Asp  Glu Asn Ile
    1055                1060                1065

Gln Ala  Glu Leu Gly Arg Asn  Arg Gly Pro Lys Leu  Asn Ala Met
    1070                1075                1080

Leu Arg  Leu Gly Val Leu Gln  Pro Glu Val Tyr Lys  Gln Ser Leu
    1085                1090                1095

Pro Gly  Ser Asn Cys Lys His  Pro Glu Ile Lys Lys  Gln Glu Tyr
    1100                1105                1110
```

```
Glu Glu  Val Val Gln Thr Val  Asn Thr Asp Phe Ser  Pro Tyr Leu
    1115                 1120                 1125

Ile Ser  Asp Asn Leu Glu Gln  Pro Met Gly Ser Ser  His Ala Ser
    1130                 1135                 1140

Gln Val  Cys Ser Glu Thr Pro  Asp Asp Leu Leu Asp  Asp Gly Glu
    1145                 1150                 1155

Ile Lys  Glu Asp Thr Ser Phe  Ala Glu Asn Asp Ile  Lys Glu Ser
    1160                 1165                 1170

Ser Ala  Val Phe Ser Lys Ser  Val Gln Lys Gly Glu  Leu Ser Arg
    1175                 1180                 1185

Ser Pro  Ser Pro Phe Thr His  Thr His Leu Ala Gln  Gly Tyr Arg
    1190                 1195                 1200

Arg Gly  Ala Lys Lys Leu Glu  Ser Ser Glu Glu Asn  Leu Ser Ser
    1205                 1210                 1215

Glu Asp  Glu Glu Leu Pro Cys  Phe Gln His Leu Leu  Phe Gly Lys
    1220                 1225                 1230

Val Asn  Asn Ile Pro Ser Gln  Ser Thr Arg His Ser  Thr Val Ala
    1235                 1240                 1245

Thr Glu  Cys Leu Ser Lys Asn  Thr Glu Glu Asn Leu  Leu Ser Leu
    1250                 1255                 1260

Lys Asn  Ser Leu Asn Asp Cys  Ser Asn Gln Val Ile  Leu Ala Lys
    1265                 1270                 1275

Ala Ser  Gln Glu His His Leu  Ser Glu Glu Thr Lys  Cys Ser Ala
    1280                 1285                 1290

Ser Leu  Phe Ser Ser Gln Cys  Ser Glu Leu Glu Asp  Leu Thr Ala
    1295                 1300                 1305

Asn Thr  Asn Thr Gln Asp Pro  Phe Leu Ile Gly Ser  Ser Lys Gln
    1310                 1315                 1320
```

```
Met Arg  His Gln Ser Glu Ser  Gln Gly Val Gly Leu  Ser Asp Lys
    1325                 1330                 1335

Glu Leu  Val Ser Asp Asp Glu  Glu Arg Gly Thr Gly  Leu Glu Glu
    1340                 1345                 1350

Asn Asn  Gln Glu Glu Gln Ser  Met Asp Ser Asn Leu  Gly Glu Ala
    1355                 1360                 1365

Ala Ser  Gly Cys Glu Ser Glu  Thr Ser Val Ser Glu  Asp Cys Ser
    1370                 1375                 1380

Gly Leu  Ser Ser Gln Ser Asp  Ile Leu Thr Thr Gln  Gln Arg Asp
    1385                 1390                 1395

Thr Met  Gln His Asn Leu Ile  Lys Leu Gln Gln Glu  Met Ala Glu
    1400                 1405                 1410

Leu Glu  Ala Val Leu Glu Gln  His Gly Ser Gln Pro  Ser Asn Ser
    1415                 1420                 1425

Tyr Pro  Ser Ile Ile Ser Asp  Ser Ser Ala Leu Glu  Asp Leu Arg
    1430                 1435                 1440

Asn Pro  Glu Gln Ser Thr Ser  Glu Lys Ala Val Leu  Thr Ser Gln
    1445                 1450                 1455

Lys Ser  Ser Glu Tyr Pro Ile  Ser Gln Asn Pro Glu  Gly Leu Ser
    1460                 1465                 1470

Ala Asp  Lys Phe Glu Val Ser  Ala Asp Ser Ser Thr  Ser Lys Asn
    1475                 1480                 1485

Lys Glu  Pro Gly Val Glu Arg  Ser Ser Pro Ser Lys  Cys Pro Ser
    1490                 1495                 1500

Leu Asp  Asp Arg Trp Tyr Met  His Ser Cys Ser Gly  Ser Leu Gln
    1505                 1510                 1515

Asn Arg  Asn Tyr Pro Ser Gln  Glu Glu Leu Ile Lys  Val Val Asp
    1520                 1525                 1530
```

Val Glu Glu Gln Gln Leu Glu Glu Ser Gly Pro His Asp Leu Thr
1535 1540 1545

Glu Thr Ser Tyr Leu Pro Arg Gln Asp Leu Glu Gly Thr Pro Tyr
1550 1555 1560

Leu Glu Ser Gly Ile Ser Leu Phe Ser Asp Asp Pro Glu Ser Asp
1565 1570 1575

Pro Ser Glu Asp Arg Ala Pro Glu Ser Ala Arg Val Gly Asn Ile
1580 1585 1590

Pro Ser Ser Thr Ser Ala Leu Lys Val Pro Gln Leu Lys Val Ala
1595 1600 1605

Glu Ser Ala Gln Ser Pro Ala Ala Ala His Thr Thr Asp Thr Ala
1610 1615 1620

Gly Tyr Asn Ala Met Glu Glu Ser Val Ser Arg Glu Lys Pro Glu
1625 1630 1635

Leu Thr Ala Ser Thr Glu Arg Val Asn Lys Arg Met Ser Met Val
1640 1645 1650

Val Ser Gly Leu Thr Pro Glu Glu Phe Met Leu Val Tyr Lys Phe
1655 1660 1665

Ala Arg Lys His His Ile Thr Leu Thr Asn Leu Ile Thr Glu Glu
1670 1675 1680

Thr Thr His Val Val Met Lys Thr Asp Ala Glu Phe Val Cys Glu
1685 1690 1695

Trp Thr Leu Lys Tyr Phe Leu Gly Ile Ala Gly Gly Lys Trp Val
1700 1705 1710

Val Ser Tyr Phe Trp Val Thr Gln Ser Ile Lys Glu Arg Lys Met
1715 1720 1725

Leu Asn Glu His Asp Phe Glu Val Arg Gly Asp Val Val Asn Gly
1730 1735 1740

Arg Asn His Gln Gly Pro Lys Arg Ala Arg Glu Ser Gln Asp Arg
1745 1750 1755

Lys Ile Phe Arg Gly Leu Glu Ile Cys Cys Tyr Gly Pro Phe Thr
1760 1765 1770

Asn Met Pro Thr Asp Gln Leu Glu Trp Met Val Gln Leu Cys Gly
1775 1780 1785

Ala Ser Val Val Lys Glu Leu Ser Ser Phe Thr Leu Gly Thr Gly
1790 1795 1800

Val His Pro Ile Val Val Val Gln Pro Asp Ala Trp Thr Glu Asp
1805 1810 1815

Asn Gly Phe His Ala Ile Gly Gln Met Cys Glu Ala Pro Val Val
1820 1825 1830

Thr Arg Glu Trp Val Leu Asp Ser Val Ala Leu Tyr Gln Cys Gln
1835 1840 1845

Glu Leu Asp Thr Tyr Leu Ile Pro Gln Ile Pro His Ser His Tyr
1850 1855 1860

<210> 14
<211> 1863
<212> PRT
<213> Homo sapiens

<400> 14

Met Asp Leu Ser Ala Leu Arg Val Glu Glu Val Gln Asn Val Ile Asn
1 5 10 15

Ala Met Gln Lys Ile Leu Glu Cys Pro Ile Cys Leu Glu Leu Ile Lys
20 25 30

Glu Pro Val Ser Thr Lys Cys Asp His Ile Phe Cys Lys Phe Cys Met
35 40 45

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

Lys Asn Asp Ile Thr Lys Arg Ser Leu Gln Glu Ser Thr Arg Phe Ser

65 70 75 80

Gln Leu Val Glu Glu Leu Leu Lys Ile Ile Cys Ala Phe Gln Leu Asp
85 90 95

Thr Gly Leu Glu Tyr Ala Asn Ser Tyr Asn Phe Ala Lys Lys Glu Asn
100 105 110

Asn Ser Pro Glu His Leu Lys Asp Glu Val Ser Ile Ile Gln Ser Met
115 120 125

Gly Tyr Arg Asn Arg Ala Lys Arg Leu Leu Gln Ser Glu Pro Glu Asn
130 135 140

Pro Ser Leu Gln Glu Thr Ser Leu Ser Val Gln Leu Ser Asn Leu Gly
145 150 155 160

Thr Val Arg Thr Leu Arg Thr Lys Gln Arg Ile Gln Pro Gln Lys Thr
165 170 175

Ser Val Tyr Ile Glu Leu Gly Ser Asp Ser Ser Glu Asp Thr Val Asn
180 185 190

Lys Ala Thr Tyr Cys Ser Val Gly Asp Gln Glu Leu Leu Gln Ile Thr
195 200 205

Pro Gln Gly Thr Arg Asp Glu Ile Ser Leu Asp Ser Ala Lys Lys Ala
210 215 220

Ala Cys Glu Phe Ser Glu Thr Asp Val Thr Asn Thr Glu His His Gln
225 230 235 240

Pro Ser Asn Asn Asp Leu Asn Thr Thr Glu Lys Arg Ala Ala Glu Arg
245 250 255

His Pro Glu Lys Tyr Gln Gly Ser Ser Val Ser Asn Leu His Val Glu
260 265 270

Pro Cys Gly Thr Asn Thr His Ala Ser Ser Leu Gln His Glu Asn Ser
275 280 285

Ser Leu Leu Leu Thr Lys Asp Arg Met Asn Val Glu Lys Ala Glu Phe

290 295 300

Cys Asn Lys Ser Lys Gln Pro Gly Leu Ala Arg Ser Gln His Asn Arg
305 310 315 320

Trp Ala Gly Ser Lys Glu Thr Cys Asn Asp Arg Arg Thr Pro Ser Thr
325 330 335

Glu Lys Lys Val Asp Leu Asn Ala Asp Pro Leu Cys Glu Arg Lys Glu
340 345 350

Trp Asn Lys Gln Lys Leu Pro Cys Ser Glu Asn Pro Arg Asp Thr Glu
355 360 365

Asp Val Pro Trp Ile Thr Leu Asn Ser Ser Ile Gln Lys Val Asn Glu
370 375 380

Trp Phe Ser Arg Ser Asp Glu Leu Leu Gly Ser Asp Asp Ser His Asp
385 390 395 400

Gly Glu Ser Glu Ser Asn Ala Lys Val Ala Asp Val Leu Asp Val Leu
405 410 415

Asn Glu Val Asp Glu Tyr Ser Gly Ser Ser Glu Lys Ile Asp Leu Leu
420 425 430

Ala Ser Asp Pro His Glu Ala Leu Ile Cys Lys Ser Glu Arg Val His
435 440 445

Ser Lys Ser Val Glu Ser Asn Ile Glu Asp Lys Ile Phe Gly Lys Thr
450 455 460

Tyr Arg Lys Lys Ala Ser Leu Pro Asn Leu Ser His Val Thr Glu Asn
465 470 475 480

Leu Ile Ile Gly Ala Phe Val Thr Glu Pro Gln Ile Ile Gln Glu Arg
485 490 495

Pro Leu Thr Asn Lys Leu Lys Arg Lys Arg Arg Pro Thr Ser Gly Leu
500 505 510

His Pro Glu Asp Phe Ile Lys Lys Ala Asp Leu Ala Val Gln Lys Thr

```
        515                 520                 525

Pro Glu Met Ile Asn Gln Gly Thr Asn Gln Thr Glu Gln Asn Gly Gln
    530                 535                 540

Val Met Asn Ile Thr Asn Ser Gly His Glu Asn Lys Thr Lys Gly Asp
545                 550                 555                 560

Ser Ile Gln Asn Glu Lys Asn Pro Asn Pro Ile Glu Ser Leu Glu Lys
                565                 570                 575

Glu Ser Ala Phe Lys Thr Lys Ala Glu Pro Ile Ser Ser Ser Ile Ser
            580                 585                 590

Asn Met Glu Leu Glu Leu Asn Ile His Asn Ser Lys Ala Pro Lys Lys
        595                 600                 605

Asn Arg Leu Arg Arg Lys Ser Ser Thr Arg His Ile His Ala Leu Glu
    610                 615                 620

Leu Val Val Ser Arg Asn Leu Ser Pro Pro Asn Cys Thr Glu Leu Gln
625                 630                 635                 640

Ile Asp Ser Cys Ser Ser Ser Glu Glu Ile Lys Lys Lys Lys Tyr Asn
                645                 650                 655

Gln Met Pro Val Arg His Ser Arg Asn Leu Gln Leu Met Glu Gly Lys
            660                 665                 670

Glu Pro Ala Thr Gly Ala Lys Lys Ser Asn Lys Pro Asn Glu Gln Thr
        675                 680                 685

Ser Lys Arg His Asp Ser Asp Thr Phe Pro Glu Leu Lys Leu Thr Asn
    690                 695                 700

Ala Pro Gly Ser Phe Thr Lys Cys Ser Asn Thr Ser Glu Leu Lys Glu
705                 710                 715                 720

Phe Val Asn Pro Ser Leu Pro Arg Glu Glu Lys Glu Glu Lys Leu Glu
                725                 730                 735

Thr Val Lys Val Ser Asn Asn Ala Glu Asp Pro Lys Asp Leu Met Leu
```

740 745 750

Ser Gly Glu Arg Val Leu Gln Thr Glu Arg Ser Val Glu Ser Ser Ser
755 760 765

Ile Ser Leu Val Pro Gly Thr Asp Tyr Gly Thr Gln Glu Ser Ile Ser
770 775 780

Leu Leu Glu Val Ser Thr Leu Gly Lys Ala Lys Thr Glu Pro Asn Lys
785 790 795 800

Cys Val Ser Gln Cys Ala Ala Phe Glu Asn Pro Lys Gly Leu Ile His
805 810 815

Gly Cys Ser Lys Asp Asn Arg Asn Asp Thr Glu Gly Phe Lys Tyr Pro
820 825 830

Leu Gly His Glu Val Asn His Ser Arg Glu Thr Ser Ile Glu Met Glu
835 840 845

Glu Ser Glu Leu Asp Ala Gln Tyr Leu Gln Asn Thr Phe Lys Val Ser
850 855 860

Lys Arg Gln Ser Phe Ala Pro Phe Ser Asn Pro Gly Asn Ala Glu Glu
865 870 875 880

Glu Cys Ala Thr Phe Ser Ala His Ser Gly Ser Leu Lys Lys Gln Ser
885 890 895

Pro Lys Val Thr Phe Glu Cys Glu Gln Lys Glu Glu Asn Gln Gly Lys
900 905 910

Asn Glu Ser Asn Ile Lys Pro Val Gln Thr Val Asn Ile Thr Ala Gly
915 920 925

Phe Pro Val Val Gly Gln Lys Asp Lys Pro Val Asp Asn Ala Lys Cys
930 935 940

Ser Ile Lys Gly Gly Ser Arg Phe Cys Leu Ser Ser Gln Phe Arg Gly
945 950 955 960

Asn Glu Thr Gly Leu Ile Thr Pro Asn Lys His Gly Leu Leu Gln Asn

965 970 975

Pro Tyr Arg Ile Pro Pro Leu Phe Pro Ile Lys Ser Phe Val Lys Thr
980 985 990

Lys Cys Lys Lys Asn Leu Leu Glu Glu Asn Phe Glu Glu His Ser Met
995 1000 1005

Ser Pro Glu Arg Glu Met Gly Asn Glu Asn Ile Pro Ser Thr Val
1010 1015 1020

Ser Thr Ile Ser Arg Asn Asn Ile Arg Glu Asn Val Phe Lys Glu
1025 1030 1035

Ala Ser Ser Ser Asn Ile Asn Glu Val Gly Ser Ser Thr Asn Glu
1040 1045 1050

Val Gly Ser Ser Ile Asn Glu Ile Gly Ser Ser Asp Glu Asn Ile
1055 1060 1065

Gln Ala Glu Leu Gly Arg Asn Arg Gly Pro Lys Leu Asn Ala Met
1070 1075 1080

Leu Arg Leu Gly Val Leu Gln Pro Glu Val Tyr Lys Gln Ser Leu
1085 1090 1095

Pro Gly Ser Asn Cys Lys His Pro Glu Ile Lys Lys Gln Glu Tyr
1100 1105 1110

Glu Glu Val Val Gln Thr Val Asn Thr Asp Phe Ser Pro Tyr Leu
1115 1120 1125

Ile Ser Asp Asn Leu Glu Gln Pro Met Gly Ser Ser His Ala Ser
1130 1135 1140

Gln Val Cys Ser Glu Thr Pro Asp Asp Leu Leu Asp Asp Gly Glu
1145 1150 1155

Ile Lys Glu Asp Thr Ser Phe Ala Glu Asn Asp Ile Lys Glu Ser
1160 1165 1170

Ser Ala Val Phe Ser Lys Ser Val Gln Lys Gly Glu Leu Ser Arg

```
    1175                1180                1185

Ser Pro  Ser Pro Phe Thr His  Thr His Leu Ala Gln  Gly Tyr Arg
    1190                1195                1200

Arg Gly  Ala Lys Lys Leu Glu  Ser Ser Glu Glu Asn  Leu Ser Ser
    1205                1210                1215

Glu Asp  Glu Glu Leu Pro Cys  Phe Gln His Leu Leu  Phe Gly Lys
    1220                1225                1230

Val Asn  Asn Ile Pro Ser Gln  Ser Thr Arg His Ser  Thr Val Ala
    1235                1240                1245

Thr Glu  Cys Leu Ser Lys Asn  Thr Glu Glu Asn Leu  Leu Ser Leu
    1250                1255                1260

Lys Asn  Ser Leu Asn Asp Cys  Ser Asn Gln Val Ile  Leu Ala Lys
    1265                1270                1275

Ala Ser  Gln Glu His His Leu  Ser Glu Glu Thr Lys  Cys Ser Ala
    1280                1285                1290

Ser Leu  Phe Ser Ser Gln Cys  Ser Glu Leu Glu Asp  Leu Thr Ala
    1295                1300                1305

Asn Thr  Asn Thr Gln Asp Pro  Phe Leu Ile Gly Ser  Ser Lys Gln
    1310                1315                1320

Met Arg  His Gln Ser Glu Ser  Gln Gly Val Gly Leu  Ser Asp Lys
    1325                1330                1335

Glu Leu  Val Ser Asp Asp Glu  Glu Arg Gly Thr Gly  Leu Glu Glu
    1340                1345                1350

Asn Asn  Gln Glu Glu Gln Ser  Met Asp Ser Asn Leu  Gly Glu Ala
    1355                1360                1365

Ala Ser  Gly Cys Glu Ser Glu  Thr Ser Val Ser Glu  Asp Cys Ser
    1370                1375                1380

Gly Leu  Ser Ser Gln Ser Asp  Ile Leu Thr Thr Gln  Gln Arg Asp
```

```
    1385                1390                1395

Thr Met  Gln His Asn Leu Ile  Lys Leu Gln Gln Glu  Met Ala Glu
    1400                1405                1410

Leu Glu  Ala Val Leu Glu Gln  His Gly Ser Gln Pro  Ser Asn Ser
    1415                1420                1425

Tyr Pro  Ser Ile Ile Ser Asp  Ser Ser Ala Leu Glu  Asp Leu Arg
    1430                1435                1440

Asn Pro  Glu Gln Ser Thr Ser  Glu Lys Ala Val Leu  Thr Ser Gln
    1445                1450                1455

Lys Ser  Ser Glu Tyr Pro Ile  Ser Gln Asn Pro Glu  Gly Leu Ser
    1460                1465                1470

Ala Asp  Lys Phe Glu Val Ser  Ala Asp Ser Ser Thr  Ser Lys Asn
    1475                1480                1485

Lys Glu  Pro Gly Val Glu Arg  Ser Ser Pro Ser Lys  Cys Pro Ser
    1490                1495                1500

Leu Asp  Asp Arg Trp Tyr Met  His Ser Cys Ser Gly  Ser Leu Gln
    1505                1510                1515

Asn Arg  Asn Tyr Pro Ser Gln  Glu Glu Leu Ile Lys  Val Val Asp
    1520                1525                1530

Val Glu  Glu Gln Gln Leu Glu  Glu Ser Gly Pro His  Asp Leu Thr
    1535                1540                1545

Glu Thr  Ser Tyr Leu Pro Arg  Gln Asp Leu Glu Gly  Thr Pro Tyr
    1550                1555                1560

Leu Glu  Ser Gly Ile Ser Leu  Phe Ser Asp Asp Pro  Glu Ser Asp
    1565                1570                1575

Pro Ser  Glu Asp Arg Ala Pro  Glu Ser Ala Arg Val  Gly Asn Ile
    1580                1585                1590

Pro Ser  Ser Thr Ser Ala Leu  Lys Val Pro Gln Leu  Lys Val Ala
```

1595 1600 1605

Glu Ser Ala Gln Ser Pro Ala Ala Ala His Thr Thr Asp Thr Ala
1610 1615 1620

Gly Tyr Asn Ala Met Glu Glu Ser Val Ser Arg Glu Lys Pro Glu
1625 1630 1635

Leu Thr Ala Ser Thr Glu Arg Val Asn Lys Arg Met Ser Met Val
1640 1645 1650

Val Ser Gly Leu Thr Pro Glu Glu Phe Met Leu Val Tyr Lys Phe
1655 1660 1665

Ala Arg Lys His His Ile Thr Leu Thr Asn Leu Ile Thr Glu Glu
1670 1675 1680

Thr Thr His Val Val Met Lys Thr Asp Ala Glu Phe Val Cys Glu
1685 1690 1695

Gln Thr Leu Lys Tyr Phe Leu Gly Ile Ala Gly Gly Lys Trp Val
1700 1705 1710

Val Ser Tyr Phe Trp Val Thr Gln Ser Ile Lys Glu Arg Lys Met
1715 1720 1725

Leu Asn Glu His Asp Phe Glu Val Arg Gly Asp Val Val Asn Gly
1730 1735 1740

Arg Asn His Gln Gly Pro Lys Arg Ala Arg Glu Ser Gln Asp Arg
1745 1750 1755

Lys Ile Phe Arg Gly Leu Glu Ile Cys Cys Tyr Gly Pro Phe Thr
1760 1765 1770

Asn Met Pro Thr Asp Gln Leu Glu Trp Met Val Gln Leu Cys Gly
1775 1780 1785

Ala Ser Val Val Lys Glu Leu Ser Ser Phe Thr Leu Gly Thr Gly
1790 1795 1800

Val His Pro Ile Val Val Val Gln Pro Asp Ala Trp Thr Glu Asp

1805 1810 1815

Asn Gly Phe His Ala Ile Gly Gln Met Cys Glu Ala Pro Val Val
1820 1825 1830

Thr Arg Glu Trp Val Leu Asp Ser Val Ala Leu Tyr Gln Cys Gln
1835 1840 1845

Glu Leu Asp Thr Tyr Leu Ile Pro Gln Ile Pro His Ser His Tyr
1850 1855 1860

<210> 15
<211> 1863
<212> PRT
<213> Homo sapiens

<400> 15

Met Asp Leu Ser Ala Leu Arg Val Glu Glu Val Gln Asn Val Ile Asn
1 5 10 15

Ala Met Gln Lys Ile Leu Glu Cys Pro Ile Cys Leu Glu Leu Ile Lys
20 25 30

Glu Pro Val Ser Thr Lys Cys Asp His Ile Phe Cys Lys Phe Cys Met
35 40 45

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

Lys Asn Asp Ile Thr Lys Arg Ser Leu Gln Glu Ser Thr Arg Phe Ser
65 70 75 80

Gln Leu Val Glu Glu Leu Leu Lys Ile Ile Cys Ala Phe Gln Leu Asp
85 90 95

Thr Gly Leu Glu Tyr Ala Asn Ser Tyr Asn Phe Ala Lys Lys Glu Asn
100 105 110

Asn Ser Pro Glu His Leu Lys Asp Glu Val Ser Ile Ile Gln Ser Met
115 120 125

Gly Tyr Arg Asn Arg Ala Lys Arg Leu Leu Gln Ser Glu Pro Glu Asn
130 135 140

```
Pro Ser Leu Gln Glu Thr Ser Leu Ser Val Gln Leu Ser Asn Leu Gly
145                 150                 155                 160

Thr Val Arg Thr Leu Arg Thr Lys Gln Arg Ile Gln Pro Gln Lys Thr
                165                 170                 175

Ser Val Tyr Ile Glu Leu Gly Ser Asp Ser Ser Glu Asp Thr Val Asn
            180                 185                 190

Lys Ala Thr Tyr Cys Ser Val Gly Asp Gln Glu Leu Leu Gln Ile Thr
        195                 200                 205

Pro Gln Gly Thr Arg Asp Glu Ile Ser Leu Asp Ser Ala Lys Lys Ala
    210                 215                 220

Ala Cys Glu Phe Ser Glu Thr Asp Val Thr Asn Thr Glu His His Gln
225                 230                 235                 240

Pro Ser Asn Asn Asp Leu Asn Thr Thr Glu Lys Arg Ala Ala Glu Arg
                245                 250                 255

His Pro Glu Lys Tyr Gln Gly Ser Ser Val Ser Asn Leu His Val Glu
            260                 265                 270

Pro Cys Gly Thr Asn Thr His Ala Ser Ser Leu Gln His Glu Asn Ser
        275                 280                 285

Ser Leu Leu Leu Thr Lys Asp Arg Met Asn Val Glu Lys Ala Glu Phe
    290                 295                 300

Cys Asn Lys Ser Lys Gln Pro Gly Leu Ala Arg Ser Gln His Asn Arg
305                 310                 315                 320

Trp Ala Gly Ser Lys Glu Thr Cys Asn Asp Arg Arg Thr Pro Ser Thr
                325                 330                 335

Glu Lys Lys Val Asp Leu Asn Ala Asp Pro Leu Cys Glu Arg Lys Glu
            340                 345                 350

Trp Asn Lys Gln Lys Leu Pro Cys Ser Glu Asn Pro Arg Asp Thr Glu
        355                 360                 365
```

```
Asp Val Pro Trp Ile Thr Leu Asn Ser Ser Ile Gln Lys Val Asn Glu
    370                 375                 380

Trp Phe Ser Arg Ser Asp Glu Leu Leu Gly Ser Asp Asp Ser His Asp
385                 390                 395                 400

Gly Glu Ser Glu Ser Asn Ala Lys Val Ala Asp Val Leu Asp Val Leu
                405                 410                 415

Asn Glu Val Asp Glu Tyr Ser Gly Ser Ser Glu Lys Ile Asp Leu Leu
            420                 425                 430

Ala Ser Asp Pro His Glu Ala Leu Ile Cys Lys Ser Glu Arg Val His
        435                 440                 445

Ser Lys Ser Val Glu Ser Asn Ile Glu Asp Lys Ile Phe Gly Lys Thr
    450                 455                 460

Tyr Arg Lys Lys Ala Ser Leu Pro Asn Leu Ser His Val Thr Glu Asn
465                 470                 475                 480

Leu Ile Ile Gly Ala Phe Val Thr Glu Pro Gln Ile Ile Gln Glu Arg
                485                 490                 495

Pro Leu Thr Asn Lys Leu Lys Arg Lys Arg Arg Pro Thr Ser Gly Leu
            500                 505                 510

His Pro Glu Asp Phe Ile Lys Lys Ala Asp Leu Ala Val Gln Lys Thr
        515                 520                 525

Pro Glu Met Ile Asn Gln Gly Thr Asn Gln Thr Glu Gln Asn Gly Gln
    530                 535                 540

Val Met Asn Ile Thr Asn Ser Gly His Glu Asn Lys Thr Lys Gly Asp
545                 550                 555                 560

Ser Ile Gln Asn Glu Lys Asn Pro Asn Pro Ile Glu Ser Leu Glu Lys
                565                 570                 575

Glu Ser Ala Phe Lys Thr Lys Ala Glu Pro Ile Ser Ser Ser Ile Ser
            580                 585                 590
```

```
Asn Met Glu Leu Glu Leu Asn Ile His Asn Ser Lys Ala Pro Lys Lys
        595                 600                 605

Asn Arg Leu Arg Arg Lys Ser Ser Thr Arg His Ile His Ala Leu Glu
    610                 615                 620

Leu Val Val Ser Arg Asn Leu Ser Pro Pro Asn Cys Thr Glu Leu Gln
625                 630                 635                 640

Ile Asp Ser Cys Ser Ser Ser Glu Glu Ile Lys Lys Lys Lys Tyr Asn
                645                 650                 655

Gln Met Pro Val Arg His Ser Arg Asn Leu Gln Leu Met Glu Gly Lys
            660                 665                 670

Glu Pro Ala Thr Gly Ala Lys Lys Ser Asn Lys Pro Asn Glu Gln Thr
        675                 680                 685

Ser Lys Arg His Asp Ser Asp Thr Phe Pro Glu Leu Lys Leu Thr Asn
    690                 695                 700

Ala Pro Gly Ser Phe Thr Lys Cys Ser Asn Thr Ser Glu Leu Lys Glu
705                 710                 715                 720

Phe Val Asn Pro Ser Leu Pro Arg Glu Glu Lys Glu Glu Lys Leu Glu
                725                 730                 735

Thr Val Lys Val Ser Asn Asn Ala Glu Asp Pro Lys Asp Leu Met Leu
            740                 745                 750

Ser Gly Glu Arg Val Leu Gln Thr Glu Arg Ser Val Glu Ser Ser Ser
        755                 760                 765

Ile Ser Leu Val Pro Gly Thr Asp Tyr Gly Thr Gln Glu Ser Ile Ser
    770                 775                 780

Leu Leu Glu Val Ser Thr Leu Gly Lys Ala Lys Thr Glu Pro Asn Lys
785                 790                 795                 800

Cys Val Ser Gln Cys Ala Ala Phe Glu Asn Pro Lys Gly Leu Ile His
                805                 810                 815
```

```
Gly Cys Ser Lys Asp Asn Arg Asn Asp Thr Glu Gly Phe Lys Tyr Pro
            820                 825                 830

Leu Gly His Glu Val Asn His Ser Arg Glu Thr Ser Ile Glu Met Glu
        835                 840                 845

Glu Ser Glu Leu Asp Ala Gln Tyr Leu Gln Asn Thr Phe Lys Val Ser
    850                 855                 860

Lys Arg Gln Ser Phe Ala Pro Phe Ser Asn Pro Gly Asn Ala Glu Glu
865                 870                 875                 880

Glu Cys Ala Thr Phe Ser Ala His Ser Gly Ser Leu Lys Lys Gln Ser
                885                 890                 895

Pro Lys Val Thr Phe Glu Cys Glu Gln Lys Glu Glu Asn Gln Gly Lys
            900                 905                 910

Asn Glu Ser Asn Ile Lys Pro Val Gln Thr Val Asn Ile Thr Ala Gly
        915                 920                 925

Phe Pro Val Val Gly Gln Lys Asp Lys Pro Val Asp Asn Ala Lys Cys
    930                 935                 940

Ser Ile Lys Gly Gly Ser Arg Phe Cys Leu Ser Ser Gln Phe Arg Gly
945                 950                 955                 960

Asn Glu Thr Gly Leu Ile Thr Pro Asn Lys His Gly Leu Leu Gln Asn
                965                 970                 975

Pro Tyr Arg Ile Pro Pro Leu Phe Pro Ile Lys Ser Phe Val Lys Thr
            980                 985                 990

Lys Cys Lys Lys Asn Leu Leu Glu  Glu Asn Phe Glu Glu  His Ser Met
        995                 1000                1005

Ser Pro  Glu Arg Glu Met Gly  Asn Glu Asn Ile Pro  Ser Thr Val
    1010                1015                1020

Ser Thr  Ile Ser Arg Asn Asn  Ile Arg Glu Asn Val  Phe Lys Glu
    1025                1030                1035
```

Ala Ser Ser Ser Asn Ile Asn Glu Val Gly Ser Ser Thr Asn Glu
1040 1045 1050

Val Gly Ser Ser Ile Asn Glu Ile Gly Ser Ser Asp Glu Asn Ile
1055 1060 1065

Gln Ala Glu Leu Gly Arg Asn Arg Gly Pro Lys Leu Asn Ala Met
1070 1075 1080

Leu Arg Leu Gly Val Leu Gln Pro Glu Val Tyr Lys Gln Ser Leu
1085 1090 1095

Pro Gly Ser Asn Cys Lys His Pro Glu Ile Lys Lys Gln Glu Tyr
1100 1105 1110

Glu Glu Val Val Gln Thr Val Asn Thr Asp Phe Ser Pro Tyr Leu
1115 1120 1125

Ile Ser Asp Asn Leu Glu Gln Pro Met Gly Ser Ser His Ala Ser
1130 1135 1140

Gln Val Cys Ser Glu Thr Pro Asp Asp Leu Leu Asp Asp Gly Glu
1145 1150 1155

Ile Lys Glu Asp Thr Ser Phe Ala Glu Asn Asp Ile Lys Glu Ser
1160 1165 1170

Ser Ala Val Phe Ser Lys Ser Val Gln Lys Gly Glu Leu Ser Arg
1175 1180 1185

Ser Pro Ser Pro Phe Thr His Thr His Leu Ala Gln Gly Tyr Arg
1190 1195 1200

Arg Gly Ala Lys Lys Leu Glu Ser Ser Glu Glu Asn Leu Ser Ser
1205 1210 1215

Glu Asp Glu Glu Leu Pro Cys Phe Gln His Leu Leu Phe Gly Lys
1220 1225 1230

Val Asn Asn Ile Pro Ser Gln Ser Thr Arg His Ser Thr Val Ala
1235 1240 1245

```
Thr Glu  Cys Leu Ser Lys Asn  Thr Glu Glu Asn Leu  Leu Ser Leu
    1250                 1255                 1260

Lys Asn  Ser Leu Asn Asp Cys  Ser Asn Gln Val Ile  Leu Ala Lys
    1265                 1270                 1275

Ala Ser  Gln Glu His His Leu  Ser Glu Glu Thr Lys  Cys Ser Ala
    1280                 1285                 1290

Ser Leu  Phe Ser Ser Gln Cys  Ser Glu Leu Glu Asp  Leu Thr Ala
    1295                 1300                 1305

Asn Thr  Asn Thr Gln Asp Pro  Phe Leu Ile Gly Ser  Ser Lys Gln
    1310                 1315                 1320

Met Arg  His Gln Ser Glu Ser  Gln Gly Val Gly Leu  Ser Asp Lys
    1325                 1330                 1335

Glu Leu  Val Ser Asp Asp Glu  Glu Arg Gly Thr Gly  Leu Glu Glu
    1340                 1345                 1350

Asn Asn  Gln Glu Glu Gln Ser  Met Asp Ser Asn Leu  Gly Glu Ala
    1355                 1360                 1365

Ala Ser  Gly Cys Glu Ser Glu  Thr Ser Val Ser Glu  Asp Cys Ser
    1370                 1375                 1380

Gly Leu  Ser Ser Gln Ser Asp  Ile Leu Thr Thr Gln  Gln Arg Asp
    1385                 1390                 1395

Thr Met  Gln His Asn Leu Ile  Lys Leu Gln Gln Glu  Met Ala Glu
    1400                 1405                 1410

Leu Glu  Ala Val Leu Glu Gln  His Gly Ser Gln Pro  Ser Asn Ser
    1415                 1420                 1425

Tyr Pro  Ser Ile Ile Ser Asp  Ser Ser Ala Leu Glu  Asp Leu Arg
    1430                 1435                 1440

Asn Pro  Glu Gln Ser Thr Ser  Glu Lys Ala Val Leu  Thr Ser Gln
    1445                 1450                 1455
```

```
Lys Ser  Ser Glu Tyr Pro Ile  Ser Gln Asn Pro Glu  Gly Leu Ser
    1460                 1465                 1470

Ala Asp  Lys Phe Glu Val Ser  Ala Asp Ser Ser Thr  Ser Lys Asn
    1475                 1480                 1485

Lys Glu  Pro Gly Val Glu Arg  Ser Ser Pro Ser Lys  Cys Pro Ser
    1490                 1495                 1500

Leu Asp  Asp Arg Trp Tyr Met  His Ser Cys Ser Gly  Ser Leu Gln
    1505                 1510                 1515

Asn Arg  Asn Tyr Pro Ser Gln  Glu Glu Leu Ile Lys  Val Val Asp
    1520                 1525                 1530

Val Glu  Glu Gln Gln Leu Glu  Glu Ser Gly Pro His  Asp Leu Thr
    1535                 1540                 1545

Glu Thr  Ser Tyr Leu Pro Arg  Gln Asp Leu Glu Gly  Thr Pro Tyr
    1550                 1555                 1560

Leu Glu  Ser Gly Ile Ser Leu  Phe Ser Asp Asp Pro  Glu Ser Asp
    1565                 1570                 1575

Pro Ser  Glu Asp Arg Ala Pro  Glu Ser Ala Arg Val  Gly Asn Ile
    1580                 1585                 1590

Pro Ser  Ser Thr Ser Ala Leu  Lys Val Pro Gln Leu  Lys Val Ala
    1595                 1600                 1605

Glu Ser  Ala Gln Ser Pro Ala  Ala Ala His Thr Thr  Asp Thr Ala
    1610                 1615                 1620

Gly Tyr  Asn Ala Met Glu Glu  Ser Val Ser Arg Glu  Lys Pro Glu
    1625                 1630                 1635

Leu Thr  Ala Ser Thr Glu Arg  Val Asn Lys Arg Met  Ser Met Val
    1640                 1645                 1650

Val Ser  Gly Leu Thr Pro Glu  Glu Phe Met Leu Val  Tyr Lys Phe
    1655                 1660                 1665
```

```
Ala Arg  Lys His His Ile Thr  Leu Thr Asn Leu Ile  Thr Glu Glu
    1670                 1675                 1680

Thr Thr  His Val Val Met Lys  Thr Asp Ala Glu Phe  Val Cys Glu
    1685                 1690                 1695

Arg Thr  Leu Lys Tyr Phe Leu  Gly Ile Glu Gly Gly  Lys Trp Val
    1700                 1705                 1710

Val Ser  Tyr Phe Trp Val Thr  Gln Ser Ile Lys Glu  Arg Lys Met
    1715                 1720                 1725

Leu Asn  Glu His Asp Phe Glu  Val Arg Gly Asp Val  Val Asn Gly
    1730                 1735                 1740

Arg Asn  His Gln Gly Pro Lys  Arg Ala Arg Glu Ser  Gln Asp Arg
    1745                 1750                 1755

Lys Ile  Phe Arg Gly Leu Glu  Ile Cys Cys Tyr Gly  Pro Phe Thr
    1760                 1765                 1770

Asn Met  Pro Thr Asp Gln Leu  Glu Trp Met Val Gln  Leu Cys Gly
    1775                 1780                 1785

Ala Ser  Val Val Lys Glu Leu  Ser Ser Phe Thr Leu  Gly Thr Gly
    1790                 1795                 1800

Val His  Pro Ile Val Val Val  Gln Pro Asp Ala Trp  Thr Glu Asp
    1805                 1810                 1815

Asn Gly  Phe His Ala Ile Gly  Gln Met Cys Glu Ala  Pro Val Val
    1820                 1825                 1830

Thr Arg  Glu Trp Val Leu Asp  Ser Val Ala Leu Tyr  Gln Cys Gln
    1835                 1840                 1845

Glu Leu  Asp Thr Tyr Leu Ile  Pro Gln Ile Pro His  Ser His Tyr
    1850                 1855                 1860
```

<210> 16
<211> 1863

<212> PRT
<213> Homo sapiens

<400> 16

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Met Asp Leu Ser Ala Leu Arg Val Glu Glu Val Gln Asn Val Ile Asn
1               5                  10                  15

Ala Met Gln Lys Ile Leu Glu Cys Pro Ile Cys Leu Glu Leu Ile Lys
            20                  25                  30

Glu Pro Val Ser Thr Lys Cys Asp His Ile Phe Cys Lys Phe Cys Met
        35                  40                  45

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

Lys Asn Asp Ile Thr Lys Arg Ser Leu Gln Glu Ser Thr Arg Phe Ser
65                  70                  75                  80

Gln Leu Val Glu Glu Leu Leu Lys Ile Ile Cys Ala Phe Gln Leu Asp
                85                  90                  95

Thr Gly Leu Glu Tyr Ala Asn Ser Tyr Asn Phe Ala Lys Lys Glu Asn
            100                 105                 110

Asn Ser Pro Glu His Leu Lys Asp Glu Val Ser Ile Ile Gln Ser Met
        115                 120                 125

Gly Tyr Arg Asn Arg Ala Lys Arg Leu Leu Gln Ser Glu Pro Glu Asn
    130                 135                 140

Pro Ser Leu Gln Glu Thr Ser Leu Ser Val Gln Leu Ser Asn Leu Gly
145                 150                 155                 160

Thr Val Arg Thr Leu Arg Thr Lys Gln Arg Ile Gln Pro Gln Lys Thr
                165                 170                 175

Ser Val Tyr Ile Glu Leu Gly Ser Asp Ser Ser Glu Asp Thr Val Asn
            180                 185                 190

Lys Ala Thr Tyr Cys Ser Val Gly Asp Gln Glu Leu Leu Gln Ile Thr
        195                 200                 205
```

```
Pro Gln Gly Thr Arg Asp Glu Ile Ser Leu Asp Ser Ala Lys Lys Ala
    210                 215                 220

Ala Cys Glu Phe Ser Glu Thr Asp Val Thr Asn Thr Glu His His Gln
225                 230                 235                 240

Pro Ser Asn Asn Asp Leu Asn Thr Thr Glu Lys Arg Ala Ala Glu Arg
                245                 250                 255

His Pro Glu Lys Tyr Gln Gly Ser Ser Val Ser Asn Leu His Val Glu
            260                 265                 270

Pro Cys Gly Thr Asn Thr His Ala Ser Ser Leu Gln His Glu Asn Ser
        275                 280                 285

Ser Leu Leu Leu Thr Lys Asp Arg Met Asn Val Glu Lys Ala Glu Phe
    290                 295                 300

Cys Asn Lys Ser Lys Gln Pro Gly Leu Ala Arg Ser Gln His Asn Arg
305                 310                 315                 320

Trp Ala Gly Ser Lys Glu Thr Cys Asn Asp Arg Arg Thr Pro Ser Thr
                325                 330                 335

Glu Lys Lys Val Asp Leu Asn Ala Asp Pro Leu Cys Glu Arg Lys Glu
            340                 345                 350

Trp Asn Lys Gln Lys Leu Pro Cys Ser Glu Asn Pro Arg Asp Thr Glu
        355                 360                 365

Asp Val Pro Trp Ile Thr Leu Asn Ser Ser Ile Gln Lys Val Asn Glu
    370                 375                 380

Trp Phe Ser Arg Ser Asp Glu Leu Leu Gly Ser Asp Asp Ser His Asp
385                 390                 395                 400

Gly Glu Ser Glu Ser Asn Ala Lys Val Ala Asp Val Leu Asp Val Leu
                405                 410                 415

Asn Glu Val Asp Glu Tyr Ser Gly Ser Ser Glu Lys Ile Asp Leu Leu
            420                 425                 430
```

```
Ala Ser Asp Pro His Glu Ala Leu Ile Cys Lys Ser Glu Arg Val His
       435                 440                 445

Ser Lys Ser Val Glu Ser Asn Ile Glu Asp Lys Ile Phe Gly Lys Thr
    450                 455                 460

Tyr Arg Lys Lys Ala Ser Leu Pro Asn Leu Ser His Val Thr Glu Asn
465                 470                 475                 480

Leu Ile Ile Gly Ala Phe Val Thr Glu Pro Gln Ile Ile Gln Glu Arg
                485                 490                 495

Pro Leu Thr Asn Lys Leu Lys Arg Lys Arg Arg Pro Thr Ser Gly Leu
            500                 505                 510

His Pro Glu Asp Phe Ile Lys Lys Ala Asp Leu Ala Val Gln Lys Thr
        515                 520                 525

Pro Glu Met Ile Asn Gln Gly Thr Asn Gln Thr Glu Gln Asn Gly Gln
    530                 535                 540

Val Met Asn Ile Thr Asn Ser Gly His Glu Asn Lys Thr Lys Gly Asp
545                 550                 555                 560

Ser Ile Gln Asn Glu Lys Asn Pro Asn Pro Ile Glu Ser Leu Glu Lys
                565                 570                 575

Glu Ser Ala Phe Lys Thr Lys Ala Glu Pro Ile Ser Ser Ser Ile Ser
            580                 585                 590

Asn Met Glu Leu Glu Leu Asn Ile His Asn Ser Lys Ala Pro Lys Lys
        595                 600                 605

Asn Arg Leu Arg Arg Lys Ser Ser Thr Arg His Ile His Ala Leu Glu
    610                 615                 620

Leu Val Val Ser Arg Asn Leu Ser Pro Pro Asn Cys Thr Glu Leu Gln
625                 630                 635                 640

Ile Asp Ser Cys Ser Ser Ser Glu Glu Ile Lys Lys Lys Lys Tyr Asn
                645                 650                 655
```

```
Gln Met Pro Val Arg His Ser Arg Asn Leu Gln Leu Met Glu Gly Lys
            660                 665                 670

Glu Pro Ala Thr Gly Ala Lys Lys Ser Asn Lys Pro Asn Glu Gln Thr
        675                 680                 685

Ser Lys Arg His Asp Ser Asp Thr Phe Pro Glu Leu Lys Leu Thr Asn
    690                 695                 700

Ala Pro Gly Ser Phe Thr Lys Cys Ser Asn Thr Ser Glu Leu Lys Glu
705                 710                 715                 720

Phe Val Asn Pro Ser Leu Pro Arg Glu Glu Lys Glu Glu Lys Leu Glu
                725                 730                 735

Thr Val Lys Val Ser Asn Asn Ala Glu Asp Pro Lys Asp Leu Met Leu
            740                 745                 750

Ser Gly Glu Arg Val Leu Gln Thr Glu Arg Ser Val Glu Ser Ser Ser
        755                 760                 765

Ile Ser Leu Val Pro Gly Thr Asp Tyr Gly Thr Gln Glu Ser Ile Ser
    770                 775                 780

Leu Leu Glu Val Ser Thr Leu Gly Lys Ala Lys Thr Glu Pro Asn Lys
785                 790                 795                 800

Cys Val Ser Gln Cys Ala Ala Phe Glu Asn Pro Lys Gly Leu Ile His
                805                 810                 815

Gly Cys Ser Lys Asp Asn Arg Asn Asp Thr Glu Gly Phe Lys Tyr Pro
            820                 825                 830

Leu Gly His Glu Val Asn His Ser Arg Glu Thr Ser Ile Glu Met Glu
        835                 840                 845

Glu Ser Glu Leu Asp Ala Gln Tyr Leu Gln Asn Thr Phe Lys Val Ser
    850                 855                 860

Lys Arg Gln Ser Phe Ala Pro Phe Ser Asn Pro Gly Asn Ala Glu Glu
865                 870                 875                 880
```

```
Glu Cys Ala Thr Phe Ser Ala His Ser Gly Ser Leu Lys Lys Gln Ser
                885                 890                 895

Pro Lys Val Thr Phe Glu Cys Glu Gln Lys Glu Glu Asn Gln Gly Lys
            900                 905                 910

Asn Glu Ser Asn Ile Lys Pro Val Gln Thr Val Asn Ile Thr Ala Gly
        915                 920                 925

Phe Pro Val Val Gly Gln Lys Asp Lys Pro Val Asp Asn Ala Lys Cys
    930                 935                 940

Ser Ile Lys Gly Gly Ser Arg Phe Cys Leu Ser Ser Gln Phe Arg Gly
945                 950                 955                 960

Asn Glu Thr Gly Leu Ile Thr Pro Asn Lys His Gly Leu Leu Gln Asn
                965                 970                 975

Pro Tyr Arg Ile Pro Pro Leu Phe Pro Ile Lys Ser Phe Val Lys Thr
            980                 985                 990

Lys Cys Lys Lys Asn Leu Leu Glu  Glu Asn Phe Glu Glu  His Ser Met
        995                 1000                1005

Ser Pro  Glu Arg Glu Met Gly  Asn Glu Asn Ile Pro  Ser Thr Val
    1010                1015                1020

Ser Thr  Ile Ser Arg Asn Asn  Ile Arg Glu Asn Val  Phe Lys Glu
    1025                1030                1035

Ala Ser  Ser Ser Asn Ile Asn  Glu Val Gly Ser Ser  Thr Asn Glu
    1040                1045                1050

Val Gly  Ser Ser Ile Asn Glu  Ile Gly Ser Ser Asp  Glu Asn Ile
    1055                1060                1065

Gln Ala  Glu Leu Gly Arg Asn  Arg Gly Pro Lys Leu  Asn Ala Met
    1070                1075                1080

Leu Arg  Leu Gly Val Leu Gln  Pro Glu Val Tyr Lys  Gln Ser Leu
    1085                1090                1095
```

Pro Gly Ser Asn Cys Lys His Pro Glu Ile Lys Lys Gln Glu Tyr
1100 1105 1110

Glu Glu Val Val Gln Thr Val Asn Thr Asp Phe Ser Pro Tyr Leu
1115 1120 1125

Ile Ser Asp Asn Leu Glu Gln Pro Met Gly Ser Ser His Ala Ser
1130 1135 1140

Gln Val Cys Ser Glu Thr Pro Asp Asp Leu Leu Asp Asp Gly Glu
1145 1150 1155

Ile Lys Glu Asp Thr Ser Phe Ala Glu Asn Asp Ile Lys Glu Ser
1160 1165 1170

Ser Ala Val Phe Ser Lys Ser Val Gln Lys Gly Glu Leu Ser Arg
1175 1180 1185

Ser Pro Ser Pro Phe Thr His Thr His Leu Ala Gln Gly Tyr Arg
1190 1195 1200

Arg Gly Ala Lys Lys Leu Glu Ser Ser Glu Glu Asn Leu Ser Ser
1205 1210 1215

Glu Asp Glu Glu Leu Pro Cys Phe Gln His Leu Leu Phe Gly Lys
1220 1225 1230

Val Asn Asn Ile Pro Ser Gln Ser Thr Arg His Ser Thr Val Ala
1235 1240 1245

Thr Glu Cys Leu Ser Lys Asn Thr Glu Glu Asn Leu Leu Ser Leu
1250 1255 1260

Lys Asn Ser Leu Asn Asp Cys Ser Asn Gln Val Ile Leu Ala Lys
1265 1270 1275

Ala Ser Gln Glu His His Leu Ser Glu Glu Thr Lys Cys Ser Ala
1280 1285 1290

Ser Leu Phe Ser Ser Gln Cys Ser Glu Leu Glu Asp Leu Thr Ala
1295 1300 1305

```
Asn Thr  Asn Thr Gln Asp Pro  Phe Leu Ile Gly Ser  Ser Lys Gln
    1310                 1315                 1320

Met Arg  His Gln Ser Glu Ser  Gln Gly Val Gly Leu  Ser Asp Lys
    1325                 1330                 1335

Glu Leu  Val Ser Asp Asp Glu  Glu Arg Gly Thr Gly  Leu Glu Glu
    1340                 1345                 1350

Asn Asn  Gln Glu Glu Gln Ser  Met Asp Ser Asn Leu  Gly Glu Ala
    1355                 1360                 1365

Ala Ser  Gly Cys Glu Ser Glu  Thr Ser Val Ser Glu  Asp Cys Ser
    1370                 1375                 1380

Gly Leu  Ser Ser Gln Ser Asp  Ile Leu Thr Thr Gln  Gln Arg Asp
    1385                 1390                 1395

Thr Met  Gln His Asn Leu Ile  Lys Leu Gln Gln Glu  Met Ala Glu
    1400                 1405                 1410

Leu Glu  Ala Val Leu Glu Gln  His Gly Ser Gln Pro  Ser Asn Ser
    1415                 1420                 1425

Tyr Pro  Ser Ile Ile Ser Asp  Ser Ser Ala Leu Glu  Asp Leu Arg
    1430                 1435                 1440

Asn Pro  Glu Gln Ser Thr Ser  Glu Lys Ala Val Leu  Thr Ser Gln
    1445                 1450                 1455

Lys Ser  Ser Glu Tyr Pro Ile  Ser Gln Asn Pro Glu  Gly Leu Ser
    1460                 1465                 1470

Ala Asp  Lys Phe Glu Val Ser  Ala Asp Ser Ser Thr  Ser Lys Asn
    1475                 1480                 1485

Lys Glu  Pro Gly Val Glu Arg  Ser Ser Pro Ser Lys  Cys Pro Ser
    1490                 1495                 1500

Leu Asp  Asp Arg Trp Tyr Met  His Ser Cys Ser Gly  Ser Leu Gln
    1505                 1510                 1515
```

```
Asn Arg  Asn Tyr Pro Ser Gln  Glu Glu Leu Ile Lys  Val Val Asp
    1520                 1525                 1530

Val Glu  Glu Gln Gln Leu Glu  Glu Ser Gly Pro His  Asp Leu Thr
    1535                 1540                 1545

Glu Thr  Ser Tyr Leu Pro Arg  Gln Asp Leu Glu Gly  Thr Pro Tyr
    1550                 1555                 1560

Leu Glu  Ser Gly Ile Ser Leu  Phe Ser Asp Asp Pro  Glu Ser Asp
    1565                 1570                 1575

Pro Ser  Glu Asp Arg Ala Pro  Glu Ser Ala Arg Val  Gly Asn Ile
    1580                 1585                 1590

Pro Ser  Ser Thr Ser Ala Leu  Lys Val Pro Gln Leu  Lys Val Ala
    1595                 1600                 1605

Glu Ser  Ala Gln Ser Pro Ala  Ala Ala His Thr Thr  Asp Thr Ala
    1610                 1615                 1620

Gly Tyr  Asn Ala Met Glu Glu  Ser Val Ser Arg Glu  Lys Pro Glu
    1625                 1630                 1635

Leu Thr  Ala Ser Thr Glu Arg  Val Asn Lys Arg Met  Ser Met Val
    1640                 1645                 1650

Val Ser  Gly Leu Thr Pro Glu  Glu Phe Met Leu Val  Tyr Lys Phe
    1655                 1660                 1665

Ala Arg  Lys His His Ile Thr  Leu Thr Asn Leu Ile  Thr Glu Glu
    1670                 1675                 1680

Thr Thr  His Val Val Met Lys  Thr Asp Ala Glu Phe  Val Cys Glu
    1685                 1690                 1695

Arg Thr  Leu Lys Tyr Phe Leu  Gly Ile Ala Gly Gly  Lys Trp Val
    1700                 1705                 1710

Val Arg  Tyr Phe Trp Val Thr  Gln Ser Ile Lys Glu  Arg Lys Met
    1715                 1720                 1725
```

```
Leu Asn  Glu His Asp Phe Glu  Val Arg Gly Asp Val  Val Asn Gly
    1730                 1735                 1740

Arg Asn  His Gln Gly Pro Lys  Arg Ala Arg Glu Ser  Gln Asp Arg
    1745                 1750                 1755

Lys Ile  Phe Arg Gly Leu Glu  Ile Cys Cys Tyr Gly  Pro Phe Thr
    1760                 1765                 1770

Asn Met  Pro Thr Asp Gln Leu  Glu Trp Met Val Gln  Leu Cys Gly
    1775                 1780                 1785

Ala Ser  Val Val Lys Glu Leu  Ser Ser Phe Thr Leu  Gly Thr Gly
    1790                 1795                 1800

Val His  Pro Ile Val Val Val  Gln Pro Asp Ala Trp  Thr Glu Asp
    1805                 1810                 1815

Asn Gly  Phe His Ala Ile Gly  Gln Met Cys Glu Ala  Pro Val Val
    1820                 1825                 1830

Thr Arg  Glu Trp Val Leu Asp  Ser Val Ala Leu Tyr  Gln Cys Gln
    1835                 1840                 1845

Glu Leu  Asp Thr Tyr Leu Ile  Pro Gln Ile Pro His  Ser His Tyr
    1850                 1855                 1860
```

<210> 17
<211> 1863
<212> PRT
<213> Homo sapiens

<400> 17

```
Met Asp Leu Ser Ala Leu Arg Val Glu Glu Val Gln Asn Val Ile Asn
1               5                  10                  15

Ala Met Gln Lys Ile Leu Glu Cys Pro Ile Cys Leu Glu Leu Ile Lys
            20                  25                  30

Glu Pro Val Ser Thr Lys Cys Asp His Ile Phe Cys Lys Phe Cys Met
        35                  40                  45
```

```
Leu Lys Leu Leu Asn Gln Lys Lys Gly Pro Ser Gln Cys Pro Leu Cys
    50                  55                  60

Lys Asn Asp Ile Thr Lys Arg Ser Leu Gln Glu Ser Thr Arg Phe Ser
65                  70                  75                  80

Gln Leu Val Glu Glu Leu Leu Lys Ile Ile Cys Ala Phe Gln Leu Asp
                85                  90                  95

Thr Gly Leu Glu Tyr Ala Asn Ser Tyr Asn Phe Ala Lys Lys Glu Asn
            100                 105                 110

Asn Ser Pro Glu His Leu Lys Asp Glu Val Ser Ile Ile Gln Ser Met
        115                 120                 125

Gly Tyr Arg Asn Arg Ala Lys Arg Leu Leu Gln Ser Glu Pro Glu Asn
    130                 135                 140

Pro Ser Leu Gln Glu Thr Ser Leu Ser Val Gln Leu Ser Asn Leu Gly
145                 150                 155                 160

Thr Val Arg Thr Leu Arg Thr Lys Gln Arg Ile Gln Pro Gln Lys Thr
                165                 170                 175

Ser Val Tyr Ile Glu Leu Gly Ser Asp Ser Ser Glu Asp Thr Val Asn
            180                 185                 190

Lys Ala Thr Tyr Cys Ser Val Gly Asp Gln Glu Leu Leu Gln Ile Thr
        195                 200                 205

Pro Gln Gly Thr Arg Asp Glu Ile Ser Leu Asp Ser Ala Lys Lys Ala
    210                 215                 220

Ala Cys Glu Phe Ser Glu Thr Asp Val Thr Asn Thr Glu His His Gln
225                 230                 235                 240

Pro Ser Asn Asn Asp Leu Asn Thr Thr Glu Lys Arg Ala Ala Glu Arg
                245                 250                 255

His Pro Glu Lys Tyr Gln Gly Ser Ser Val Ser Asn Leu His Val Glu
            260                 265                 270
```

```
Pro Cys Gly Thr Asn Thr His Ala Ser Ser Leu Gln His Glu Asn Ser
        275                 280                 285

Ser Leu Leu Leu Thr Lys Asp Arg Met Asn Val Glu Lys Ala Glu Phe
    290                 295                 300

Cys Asn Lys Ser Lys Gln Pro Gly Leu Ala Arg Ser Gln His Asn Arg
305                 310                 315                 320

Trp Ala Gly Ser Lys Glu Thr Cys Asn Asp Arg Arg Thr Pro Ser Thr
                325                 330                 335

Glu Lys Lys Val Asp Leu Asn Ala Asp Pro Leu Cys Glu Arg Lys Glu
            340                 345                 350

Trp Asn Lys Gln Lys Leu Pro Cys Ser Glu Asn Pro Arg Asp Thr Glu
        355                 360                 365

Asp Val Pro Trp Ile Thr Leu Asn Ser Ser Ile Gln Lys Val Asn Glu
    370                 375                 380

Trp Phe Ser Arg Ser Asp Glu Leu Leu Gly Ser Asp Asp Ser His Asp
385                 390                 395                 400

Gly Glu Ser Glu Ser Asn Ala Lys Val Ala Asp Val Leu Asp Val Leu
                405                 410                 415

Asn Glu Val Asp Glu Tyr Ser Gly Ser Ser Glu Lys Ile Asp Leu Leu
            420                 425                 430

Ala Ser Asp Pro His Glu Ala Leu Ile Cys Lys Ser Glu Arg Val His
        435                 440                 445

Ser Lys Ser Val Glu Ser Asn Ile Glu Asp Lys Ile Phe Gly Lys Thr
    450                 455                 460

Tyr Arg Lys Lys Ala Ser Leu Pro Asn Leu Ser His Val Thr Glu Asn
465                 470                 475                 480

Leu Ile Ile Gly Ala Phe Val Thr Glu Pro Gln Ile Ile Gln Glu Arg
                485                 490                 495
```

```
Pro Leu Thr Asn Lys Leu Lys Arg Lys Arg Arg Pro Thr Ser Gly Leu
            500                 505                 510

His Pro Glu Asp Phe Ile Lys Lys Ala Asp Leu Ala Val Gln Lys Thr
        515                 520                 525

Pro Glu Met Ile Asn Gln Gly Thr Asn Gln Thr Glu Gln Asn Gly Gln
    530                 535                 540

Val Met Asn Ile Thr Asn Ser Gly His Glu Asn Lys Thr Lys Gly Asp
545                 550                 555                 560

Ser Ile Gln Asn Glu Lys Asn Pro Asn Pro Ile Glu Ser Leu Glu Lys
                565                 570                 575

Glu Ser Ala Phe Lys Thr Lys Ala Glu Pro Ile Ser Ser Ser Ile Ser
            580                 585                 590

Asn Met Glu Leu Glu Leu Asn Ile His Asn Ser Lys Ala Pro Lys Lys
        595                 600                 605

Asn Arg Leu Arg Arg Lys Ser Ser Thr Arg His Ile His Ala Leu Glu
    610                 615                 620

Leu Val Val Ser Arg Asn Leu Ser Pro Pro Asn Cys Thr Glu Leu Gln
625                 630                 635                 640

Ile Asp Ser Cys Ser Ser Ser Glu Glu Ile Lys Lys Lys Lys Tyr Asn
                645                 650                 655

Gln Met Pro Val Arg His Ser Arg Asn Leu Gln Leu Met Glu Gly Lys
            660                 665                 670

Glu Pro Ala Thr Gly Ala Lys Lys Ser Asn Lys Pro Asn Glu Gln Thr
        675                 680                 685

Ser Lys Arg His Asp Ser Asp Thr Phe Pro Glu Leu Lys Leu Thr Asn
    690                 695                 700

Ala Pro Gly Ser Phe Thr Lys Cys Ser Asn Thr Ser Glu Leu Lys Glu
705                 710                 715                 720
```

```
Phe Val Asn Pro Ser Leu Pro Arg Glu Glu Lys Glu Glu Lys Leu Glu
                725                 730                 735

Thr Val Lys Val Ser Asn Asn Ala Glu Asp Pro Lys Asp Leu Met Leu
            740                 745                 750

Ser Gly Glu Arg Val Leu Gln Thr Glu Arg Ser Val Glu Ser Ser Ser
        755                 760                 765

Ile Ser Leu Val Pro Gly Thr Asp Tyr Gly Thr Gln Glu Ser Ile Ser
    770                 775                 780

Leu Leu Glu Val Ser Thr Leu Gly Lys Ala Lys Thr Glu Pro Asn Lys
785                 790                 795                 800

Cys Val Ser Gln Cys Ala Ala Phe Glu Asn Pro Lys Gly Leu Ile His
                805                 810                 815

Gly Cys Ser Lys Asp Asn Arg Asn Asp Thr Glu Gly Phe Lys Tyr Pro
            820                 825                 830

Leu Gly His Glu Val Asn His Ser Arg Glu Thr Ser Ile Glu Met Glu
        835                 840                 845

Glu Ser Glu Leu Asp Ala Gln Tyr Leu Gln Asn Thr Phe Lys Val Ser
    850                 855                 860

Lys Arg Gln Ser Phe Ala Pro Phe Ser Asn Pro Gly Asn Ala Glu Glu
865                 870                 875                 880

Glu Cys Ala Thr Phe Ser Ala His Ser Gly Ser Leu Lys Lys Gln Ser
                885                 890                 895

Pro Lys Val Thr Phe Glu Cys Glu Gln Lys Glu Glu Asn Gln Gly Lys
            900                 905                 910

Asn Glu Ser Asn Ile Lys Pro Val Gln Thr Val Asn Ile Thr Ala Gly
        915                 920                 925

Phe Pro Val Val Gly Gln Lys Asp Lys Pro Val Asp Asn Ala Lys Cys
    930                 935                 940
```

```
Ser Ile Lys Gly Gly Ser Arg Phe Cys Leu Ser Ser Gln Phe Arg Gly
945                 950                 955                 960

Asn Glu Thr Gly Leu Ile Thr Pro Asn Lys His Gly Leu Leu Gln Asn
                965                 970                 975

Pro Tyr Arg Ile Pro Pro Leu Phe Pro Ile Lys Ser Phe Val Lys Thr
            980                 985                 990

Lys Cys Lys Lys Asn Leu Leu Glu  Glu Asn Phe Glu Glu  His Ser Met
        995                 1000                1005

Ser Pro  Glu Arg Glu Met Gly  Asn Glu Asn Ile Pro  Ser Thr Val
    1010                1015                1020

Ser Thr  Ile Ser Arg Asn Asn  Ile Arg Glu Asn Val  Phe Lys Glu
    1025                1030                1035

Ala Ser  Ser Ser Asn Ile Asn  Glu Val Gly Ser Ser  Thr Asn Glu
    1040                1045                1050

Val Gly  Ser Ser Ile Asn Glu  Ile Gly Ser Ser Asp  Glu Asn Ile
    1055                1060                1065

Gln Ala  Glu Leu Gly Arg Asn  Arg Gly Pro Lys Leu  Asn Ala Met
    1070                1075                1080

Leu Arg  Leu Gly Val Leu Gln  Pro Glu Val Tyr Lys  Gln Ser Leu
    1085                1090                1095

Pro Gly  Ser Asn Cys Lys His  Pro Glu Ile Lys Lys  Gln Glu Tyr
    1100                1105                1110

Glu Glu  Val Val Gln Thr Val  Asn Thr Asp Phe Ser  Pro Tyr Leu
    1115                1120                1125

Ile Ser  Asp Asn Leu Glu Gln  Pro Met Gly Ser Ser  His Ala Ser
    1130                1135                1140

Gln Val  Cys Ser Glu Thr Pro  Asp Asp Leu Leu Asp  Asp Gly Glu
    1145                1150                1155
```

```
Ile Lys  Glu Asp Thr Ser Phe  Ala Glu Asn Asp Ile  Lys Glu Ser
    1160                1165                1170

Ser Ala  Val Phe Ser Lys Ser  Val Gln Lys Gly Glu  Leu Ser Arg
    1175                1180                1185

Ser Pro  Ser Pro Phe Thr His  Thr His Leu Ala Gln  Gly Tyr Arg
    1190                1195                1200

Arg Gly  Ala Lys Lys Leu Glu  Ser Ser Glu Glu Asn  Leu Ser Ser
    1205                1210                1215

Glu Asp  Glu Glu Leu Pro Cys  Phe Gln His Leu Leu  Phe Gly Lys
    1220                1225                1230

Val Asn  Asn Ile Pro Ser Gln  Ser Thr Arg His Ser  Thr Val Ala
    1235                1240                1245

Thr Glu  Cys Leu Ser Lys Asn  Thr Glu Glu Asn Leu  Leu Ser Leu
    1250                1255                1260

Lys Asn  Ser Leu Asn Asp Cys  Ser Asn Gln Val Ile  Leu Ala Lys
    1265                1270                1275

Ala Ser  Gln Glu His His Leu  Ser Glu Glu Thr Lys  Cys Ser Ala
    1280                1285                1290

Ser Leu  Phe Ser Ser Gln Cys  Ser Glu Leu Glu Asp  Leu Thr Ala
    1295                1300                1305

Asn Thr  Asn Thr Gln Asp Pro  Phe Leu Ile Gly Ser  Ser Lys Gln
    1310                1315                1320

Met Arg  His Gln Ser Glu Ser  Gln Gly Val Gly Leu  Ser Asp Lys
    1325                1330                1335

Glu Leu  Val Ser Asp Asp Glu  Glu Arg Gly Thr Gly  Leu Glu Glu
    1340                1345                1350

Asn Asn  Gln Glu Glu Gln Ser  Met Asp Ser Asn Leu  Gly Glu Ala
    1355                1360                1365
```

```
Ala Ser  Gly Cys Glu Ser Glu  Thr Ser Val Ser Glu  Asp Cys Ser
    1370                 1375                 1380

Gly Leu  Ser Ser Gln Ser Asp  Ile Leu Thr Thr Gln  Gln Arg Asp
    1385                 1390                 1395

Thr Met  Gln His Asn Leu Ile  Lys Leu Gln Gln Glu  Met Ala Glu
    1400                 1405                 1410

Leu Glu  Ala Val Leu Glu Gln  His Gly Ser Gln Pro  Ser Asn Ser
    1415                 1420                 1425

Tyr Pro  Ser Ile Ile Ser Asp  Ser Ser Ala Leu Glu  Asp Leu Arg
    1430                 1435                 1440

Asn Pro  Glu Gln Ser Thr Ser  Glu Lys Ala Val Leu  Thr Ser Gln
    1445                 1450                 1455

Lys Ser  Ser Glu Tyr Pro Ile  Ser Gln Asn Pro Glu  Gly Leu Ser
    1460                 1465                 1470

Ala Asp  Lys Phe Glu Val Ser  Ala Asp Ser Ser Thr  Ser Lys Asn
    1475                 1480                 1485

Lys Glu  Pro Gly Val Glu Arg  Ser Ser Pro Ser Lys  Cys Pro Ser
    1490                 1495                 1500

Leu Asp  Asp Arg Trp Tyr Met  His Ser Cys Ser Gly  Ser Leu Gln
    1505                 1510                 1515

Asn Arg  Asn Tyr Pro Ser Gln  Glu Glu Leu Ile Lys  Val Val Asp
    1520                 1525                 1530

Val Glu  Glu Gln Gln Leu Glu  Glu Ser Gly Pro His  Asp Leu Thr
    1535                 1540                 1545

Glu Thr  Ser Tyr Leu Pro Arg  Gln Asp Leu Glu Gly  Thr Pro Tyr
    1550                 1555                 1560

Leu Glu  Ser Gly Ile Ser Leu  Phe Ser Asp Asp Pro  Glu Ser Asp
    1565                 1570                 1575
```

```
Pro Ser  Glu Asp Arg Ala Pro  Glu Ser Ala Arg Val  Gly Asn Ile
    1580                 1585                 1590

Pro Ser  Ser Thr Ser Ala Leu  Lys Val Pro Gln Leu  Lys Val Ala
    1595                 1600                 1605

Glu Ser  Ala Gln Ser Pro Ala  Ala Ala His Thr Thr  Asp Thr Ala
    1610                 1615                 1620

Gly Tyr  Asn Ala Met Glu Glu  Ser Val Ser Arg Glu  Lys Pro Glu
    1625                 1630                 1635

Leu Thr  Ala Ser Thr Glu Arg  Val Asn Lys Arg Met  Ser Met Val
    1640                 1645                 1650

Val Ser  Gly Leu Thr Pro Glu  Glu Phe Met Leu Val  Tyr Lys Phe
    1655                 1660                 1665

Ala Arg  Lys His His Ile Thr  Leu Thr Asn Leu Ile  Thr Glu Glu
    1670                 1675                 1680

Thr Thr  His Val Val Met Lys  Thr Asp Ala Glu Phe  Val Cys Glu
    1685                 1690                 1695

Arg Thr  Leu Lys Tyr Phe Leu  Gly Ile Ala Gly Gly  Lys Trp Val
    1700                 1705                 1710

Val Ser  Tyr Phe Trp Val Thr  Gln Ser Ile Lys Glu  Arg Lys Met
    1715                 1720                 1725

Leu Asn  Glu His Asp Phe Glu  Val Arg Glu Asp Val  Val Asn Gly
    1730                 1735                 1740

Arg Asn  His Gln Gly Pro Lys  Arg Ala Arg Glu Ser  Gln Asp Arg
    1745                 1750                 1755

Lys Ile  Phe Arg Gly Leu Glu  Ile Cys Cys Tyr Gly  Pro Phe Thr
    1760                 1765                 1770

Asn Met  Pro Thr Asp Gln Leu  Glu Trp Met Val Gln  Leu Cys Gly
    1775                 1780                 1785
```

```
Ala Ser  Val Val Lys Glu Leu  Ser Ser Phe Thr Leu  Gly Thr Gly
    1790                 1795                 1800

Val His  Pro Ile Val Val Val  Gln Pro Asp Ala Trp  Thr Glu Asp
    1805                 1810                 1815

Asn Gly  Phe His Ala Ile Gly  Gln Met Cys Glu Ala  Pro Val Val
    1820                 1825                 1830

Thr Arg  Glu Trp Val Leu Asp  Ser Val Ala Leu Tyr  Gln Cys Gln
    1835                 1840                 1845

Glu Leu  Asp Thr Tyr Leu Ile  Pro Gln Ile Pro His  Ser His Tyr
    1850                 1855                 1860
```

<210> 18
<211> 1863
<212> PRT
<213> Homo sapiens

<400> 18

```
Met Asp Leu Ser Ala Leu Arg Val Glu Glu Val Gln Asn Val Ile Asn
1               5                  10                  15

Ala Met Gln Lys Ile Leu Glu Cys Pro Ile Cys Leu Glu Leu Ile Lys
            20                  25                  30

Glu Pro Val Ser Thr Lys Cys Asp His Ile Phe Cys Lys Phe Cys Met
        35                  40                  45

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

Lys Asn Asp Ile Thr Lys Arg Ser Leu Gln Glu Ser Thr Arg Phe Ser
65                  70                  75                  80

Gln Leu Val Glu Glu Leu Leu Lys Ile Ile Cys Ala Phe Gln Leu Asp
                85                  90                  95

Thr Gly Leu Glu Tyr Ala Asn Ser Tyr Asn Phe Ala Lys Lys Glu Asn
            100                 105                 110

Asn Ser Pro Glu His Leu Lys Asp Glu Val Ser Ile Ile Gln Ser Met
```

115 120 125

Gly Tyr Arg Asn Arg Ala Lys Arg Leu Leu Gln Ser Glu Pro Glu Asn
130 135 140

Pro Ser Leu Gln Glu Thr Ser Leu Ser Val Gln Leu Ser Asn Leu Gly
145 150 155 160

Thr Val Arg Thr Leu Arg Thr Lys Gln Arg Ile Gln Pro Gln Lys Thr
165 170 175

Ser Val Tyr Ile Glu Leu Gly Ser Asp Ser Ser Glu Asp Thr Val Asn
180 185 190

Lys Ala Thr Tyr Cys Ser Val Gly Asp Gln Glu Leu Leu Gln Ile Thr
195 200 205

Pro Gln Gly Thr Arg Asp Glu Ile Ser Leu Asp Ser Ala Lys Lys Ala
210 215 220

Ala Cys Glu Phe Ser Glu Thr Asp Val Thr Asn Thr Glu His His Gln
225 230 235 240

Pro Ser Asn Asn Asp Leu Asn Thr Thr Glu Lys Arg Ala Ala Glu Arg
245 250 255

His Pro Glu Lys Tyr Gln Gly Ser Ser Val Ser Asn Leu His Val Glu
260 265 270

Pro Cys Gly Thr Asn Thr His Ala Ser Ser Leu Gln His Glu Asn Ser
275 280 285

Ser Leu Leu Leu Thr Lys Asp Arg Met Asn Val Glu Lys Ala Glu Phe
290 295 300

Cys Asn Lys Ser Lys Gln Pro Gly Leu Ala Arg Ser Gln His Asn Arg
305 310 315 320

Trp Ala Gly Ser Lys Glu Thr Cys Asn Asp Arg Arg Thr Pro Ser Thr
325 330 335

Glu Lys Lys Val Asp Leu Asn Ala Asp Pro Leu Cys Glu Arg Lys Glu

```
            340                 345                 350

Trp Asn Lys Gln Lys Leu Pro Cys Ser Glu Asn Pro Arg Asp Thr Glu
        355                 360                 365

Asp Val Pro Trp Ile Thr Leu Asn Ser Ser Ile Gln Lys Val Asn Glu
    370                 375                 380

Trp Phe Ser Arg Ser Asp Glu Leu Leu Gly Ser Asp Asp Ser His Asp
385                 390                 395                 400

Gly Glu Ser Glu Ser Asn Ala Lys Val Ala Asp Val Leu Asp Val Leu
                405                 410                 415

Asn Glu Val Asp Glu Tyr Ser Gly Ser Ser Glu Lys Ile Asp Leu Leu
            420                 425                 430

Ala Ser Asp Pro His Glu Ala Leu Ile Cys Lys Ser Glu Arg Val His
        435                 440                 445

Ser Lys Ser Val Glu Ser Asn Ile Glu Asp Lys Ile Phe Gly Lys Thr
    450                 455                 460

Tyr Arg Lys Lys Ala Ser Leu Pro Asn Leu Ser His Val Thr Glu Asn
465                 470                 475                 480

Leu Ile Ile Gly Ala Phe Val Thr Glu Pro Gln Ile Ile Gln Glu Arg
                485                 490                 495

Pro Leu Thr Asn Lys Leu Lys Arg Lys Arg Arg Pro Thr Ser Gly Leu
            500                 505                 510

His Pro Glu Asp Phe Ile Lys Lys Ala Asp Leu Ala Val Gln Lys Thr
        515                 520                 525

Pro Glu Met Ile Asn Gln Gly Thr Asn Gln Thr Glu Gln Asn Gly Gln
    530                 535                 540

Val Met Asn Ile Thr Asn Ser Gly His Glu Asn Lys Thr Lys Gly Asp
545                 550                 555                 560

Ser Ile Gln Asn Glu Lys Asn Pro Asn Pro Ile Glu Ser Leu Glu Lys
```

565 570 575

Glu Ser Ala Phe Lys Thr Lys Ala Glu Pro Ile Ser Ser Ser Ile Ser
580 585 590

Asn Met Glu Leu Glu Leu Asn Ile His Asn Ser Lys Ala Pro Lys Lys
595 600 605

Asn Arg Leu Arg Arg Lys Ser Ser Thr Arg His Ile His Ala Leu Glu
610 615 620

Leu Val Val Ser Arg Asn Leu Ser Pro Pro Asn Cys Thr Glu Leu Gln
625 630 635 640

Ile Asp Ser Cys Ser Ser Ser Glu Glu Ile Lys Lys Lys Lys Tyr Asn
645 650 655

Gln Met Pro Val Arg His Ser Arg Asn Leu Gln Leu Met Glu Gly Lys
660 665 670

Glu Pro Ala Thr Gly Ala Lys Lys Ser Asn Lys Pro Asn Glu Gln Thr
675 680 685

Ser Lys Arg His Asp Ser Asp Thr Phe Pro Glu Leu Lys Leu Thr Asn
690 695 700

Ala Pro Gly Ser Phe Thr Lys Cys Ser Asn Thr Ser Glu Leu Lys Glu
705 710 715 720

Phe Val Asn Pro Ser Leu Pro Arg Glu Glu Lys Glu Glu Lys Leu Glu
725 730 735

Thr Val Lys Val Ser Asn Asn Ala Glu Asp Pro Lys Asp Leu Met Leu
740 745 750

Ser Gly Glu Arg Val Leu Gln Thr Glu Arg Ser Val Glu Ser Ser Ser
755 760 765

Ile Ser Leu Val Pro Gly Thr Asp Tyr Gly Thr Gln Glu Ser Ile Ser
770 775 780

Leu Leu Glu Val Ser Thr Leu Gly Lys Ala Lys Thr Glu Pro Asn Lys

785 790 795 800

Cys Val Ser Gln Cys Ala Ala Phe Glu Asn Pro Lys Gly Leu Ile His
805 810 815

Gly Cys Ser Lys Asp Asn Arg Asn Asp Thr Glu Gly Phe Lys Tyr Pro
820 825 830

Leu Gly His Glu Val Asn His Ser Arg Glu Thr Ser Ile Glu Met Glu
835 840 845

Glu Ser Glu Leu Asp Ala Gln Tyr Leu Gln Asn Thr Phe Lys Val Ser
850 855 860

Lys Arg Gln Ser Phe Ala Pro Phe Ser Asn Pro Gly Asn Ala Glu Glu
865 870 875 880

Glu Cys Ala Thr Phe Ser Ala His Ser Gly Ser Leu Lys Lys Gln Ser
885 890 895

Pro Lys Val Thr Phe Glu Cys Glu Gln Lys Glu Glu Asn Gln Gly Lys
900 905 910

Asn Glu Ser Asn Ile Lys Pro Val Gln Thr Val Asn Ile Thr Ala Gly
915 920 925

Phe Pro Val Val Gly Gln Lys Asp Lys Pro Val Asp Asn Ala Lys Cys
930 935 940

Ser Ile Lys Gly Gly Ser Arg Phe Cys Leu Ser Ser Gln Phe Arg Gly
945 950 955 960

Asn Glu Thr Gly Leu Ile Thr Pro Asn Lys His Gly Leu Leu Gln Asn
965 970 975

Pro Tyr Arg Ile Pro Pro Leu Phe Pro Ile Lys Ser Phe Val Lys Thr
980 985 990

Lys Cys Lys Lys Asn Leu Leu Glu Glu Asn Phe Glu Glu His Ser Met
995 1000 1005

Ser Pro Glu Arg Glu Met Gly Asn Glu Asn Ile Pro Ser Thr Val

1010 1015 1020

Ser Thr Ile Ser Arg Asn Asn Ile Arg Glu Asn Val Phe Lys Glu
1025 1030 1035

Ala Ser Ser Ser Asn Ile Asn Glu Val Gly Ser Ser Thr Asn Glu
1040 1045 1050

Val Gly Ser Ser Ile Asn Glu Ile Gly Ser Ser Asp Glu Asn Ile
1055 1060 1065

Gln Ala Glu Leu Gly Arg Asn Arg Gly Pro Lys Leu Asn Ala Met
1070 1075 1080

Leu Arg Leu Gly Val Leu Gln Pro Glu Val Tyr Lys Gln Ser Leu
1085 1090 1095

Pro Gly Ser Asn Cys Lys His Pro Glu Ile Lys Lys Gln Glu Tyr
1100 1105 1110

Glu Glu Val Val Gln Thr Val Asn Thr Asp Phe Ser Pro Tyr Leu
1115 1120 1125

Ile Ser Asp Asn Leu Glu Gln Pro Met Gly Ser Ser His Ala Ser
1130 1135 1140

Gln Val Cys Ser Glu Thr Pro Asp Asp Leu Leu Asp Asp Gly Glu
1145 1150 1155

Ile Lys Glu Asp Thr Ser Phe Ala Glu Asn Asp Ile Lys Glu Ser
1160 1165 1170

Ser Ala Val Phe Ser Lys Ser Val Gln Lys Gly Glu Leu Ser Arg
1175 1180 1185

Ser Pro Ser Pro Phe Thr His Thr His Leu Ala Gln Gly Tyr Arg
1190 1195 1200

Arg Gly Ala Lys Lys Leu Glu Ser Ser Glu Glu Asn Leu Ser Ser
1205 1210 1215

Glu Asp Glu Glu Leu Pro Cys Phe Gln His Leu Leu Phe Gly Lys

1220 1225 1230

Val Asn Asn Ile Pro Ser Gln Ser Thr Arg His Ser Thr Val Ala
1235 1240 1245

Thr Glu Cys Leu Ser Lys Asn Thr Glu Glu Asn Leu Leu Ser Leu
1250 1255 1260

Lys Asn Ser Leu Asn Asp Cys Ser Asn Gln Val Ile Leu Ala Lys
1265 1270 1275

Ala Ser Gln Glu His His Leu Ser Glu Glu Thr Lys Cys Ser Ala
1280 1285 1290

Ser Leu Phe Ser Ser Gln Cys Ser Glu Leu Glu Asp Leu Thr Ala
1295 1300 1305

Asn Thr Asn Thr Gln Asp Pro Phe Leu Ile Gly Ser Ser Lys Gln
1310 1315 1320

Met Arg His Gln Ser Glu Ser Gln Gly Val Gly Leu Ser Asp Lys
1325 1330 1335

Glu Leu Val Ser Asp Asp Glu Glu Arg Gly Thr Gly Leu Glu Glu
1340 1345 1350

Asn Asn Gln Glu Glu Gln Ser Met Asp Ser Asn Leu Gly Glu Ala
1355 1360 1365

Ala Ser Gly Cys Glu Ser Glu Thr Ser Val Ser Glu Asp Cys Ser
1370 1375 1380

Gly Leu Ser Ser Gln Ser Asp Ile Leu Thr Thr Gln Gln Arg Asp
1385 1390 1395

Thr Met Gln His Asn Leu Ile Lys Leu Gln Gln Glu Met Ala Glu
1400 1405 1410

Leu Glu Ala Val Leu Glu Gln His Gly Ser Gln Pro Ser Asn Ser
1415 1420 1425

Tyr Pro Ser Ile Ile Ser Asp Ser Ser Ala Leu Glu Asp Leu Arg

```
    1430                1435                1440

Asn Pro  Glu Gln Ser Thr Ser  Glu Lys Ala Val Leu  Thr Ser Gln
    1445                1450                1455

Lys Ser  Ser Glu Tyr Pro Ile  Ser Gln Asn Pro Glu  Gly Leu Ser
    1460                1465                1470

Ala Asp  Lys Phe Glu Val Ser  Ala Asp Ser Ser Thr  Ser Lys Asn
    1475                1480                1485

Lys Glu  Pro Gly Val Glu Arg  Ser Ser Pro Ser Lys  Cys Pro Ser
    1490                1495                1500

Leu Asp  Asp Arg Trp Tyr Met  His Ser Cys Ser Gly  Ser Leu Gln
    1505                1510                1515

Asn Arg  Asn Tyr Pro Ser Gln  Glu Glu Leu Ile Lys  Val Val Asp
    1520                1525                1530

Val Glu  Glu Gln Gln Leu Glu  Glu Ser Gly Pro His  Asp Leu Thr
    1535                1540                1545

Glu Thr  Ser Tyr Leu Pro Arg  Gln Asp Leu Glu Gly  Thr Pro Tyr
    1550                1555                1560

Leu Glu  Ser Gly Ile Ser Leu  Phe Ser Asp Asp Pro  Glu Ser Asp
    1565                1570                1575

Pro Ser  Glu Asp Arg Ala Pro  Glu Ser Ala Arg Val  Gly Asn Ile
    1580                1585                1590

Pro Ser  Ser Thr Ser Ala Leu  Lys Val Pro Gln Leu  Lys Val Ala
    1595                1600                1605

Glu Ser  Ala Gln Ser Pro Ala  Ala Ala His Thr Thr  Asp Thr Ala
    1610                1615                1620

Gly Tyr  Asn Ala Met Glu Glu  Ser Val Ser Arg Glu  Lys Pro Glu
    1625                1630                1635

Leu Thr  Ala Ser Thr Glu Arg  Val Asn Lys Arg Met  Ser Met Val
```

1640 1645 1650

Val Ser Gly Leu Thr Pro Glu Glu Phe Met Leu Val Tyr Lys Phe
1655 1660 1665

Ala Arg Lys His His Ile Thr Leu Thr Asn Leu Ile Thr Glu Glu
1670 1675 1680

Thr Thr His Val Val Met Lys Thr Asp Ala Glu Phe Val Cys Glu
1685 1690 1695

Arg Thr Leu Lys Tyr Phe Leu Gly Ile Ala Gly Gly Lys Trp Val
1700 1705 1710

Val Ser Tyr Phe Trp Val Thr Gln Ser Ile Lys Glu Arg Lys Met
1715 1720 1725

Leu Asn Glu His Asp Phe Glu Val Arg Gly Asp Val Val Asn Gly
1730 1735 1740

Arg Asn His Gln Gly Arg Lys Arg Ala Arg Glu Ser Gln Asp Arg
1745 1750 1755

Lys Ile Phe Arg Gly Leu Glu Ile Cys Cys Tyr Gly Pro Phe Thr
1760 1765 1770

Asn Met Pro Thr Asp Gln Leu Glu Trp Met Val Gln Leu Cys Gly
1775 1780 1785

Ala Ser Val Val Lys Glu Leu Ser Ser Phe Thr Leu Gly Thr Gly
1790 1795 1800

Val His Pro Ile Val Val Val Gln Pro Asp Ala Trp Thr Glu Asp
1805 1810 1815

Asn Gly Phe His Ala Ile Gly Gln Met Cys Glu Ala Pro Val Val
1820 1825 1830

Thr Arg Glu Trp Val Leu Asp Ser Val Ala Leu Tyr Gln Cys Gln
1835 1840 1845

Glu Leu Asp Thr Tyr Leu Ile Pro Gln Ile Pro His Ser His Tyr

1850 1855 1860

<210> 19
<211> 1863
<212> PRT
<213> Homo sapiens

<400> 19

Met Asp Leu Ser Ala Leu Arg Val Glu Glu Val Gln Asn Val Ile Asn
1 5 10 15

Ala Met Gln Lys Ile Leu Glu Cys Pro Ile Cys Leu Glu Leu Ile Lys
20 25 30

Glu Pro Val Ser Thr Lys Cys Asp His Ile Phe Cys Lys Phe Cys Met
35 40 45

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

Lys Asn Asp Ile Thr Lys Arg Ser Leu Gln Glu Ser Thr Arg Phe Ser
65 70 75 80

Gln Leu Val Glu Glu Leu Leu Lys Ile Ile Cys Ala Phe Gln Leu Asp
85 90 95

Thr Gly Leu Glu Tyr Ala Asn Ser Tyr Asn Phe Ala Lys Lys Glu Asn
100 105 110

Asn Ser Pro Glu His Leu Lys Asp Glu Val Ser Ile Ile Gln Ser Met
115 120 125

Gly Tyr Arg Asn Arg Ala Lys Arg Leu Leu Gln Ser Glu Pro Glu Asn
130 135 140

Pro Ser Leu Gln Glu Thr Ser Leu Ser Val Gln Leu Ser Asn Leu Gly
145 150 155 160

Thr Val Arg Thr Leu Arg Thr Lys Gln Arg Ile Gln Pro Gln Lys Thr
165 170 175

Ser Val Tyr Ile Glu Leu Gly Ser Asp Ser Ser Glu Asp Thr Val Asn
180 185 190

```
Lys Ala Thr Tyr Cys Ser Val Gly Asp Gln Glu Leu Leu Gln Ile Thr
        195                 200                 205

Pro Gln Gly Thr Arg Asp Glu Ile Ser Leu Asp Ser Ala Lys Lys Ala
    210                 215                 220

Ala Cys Glu Phe Ser Glu Thr Asp Val Thr Asn Thr Glu His His Gln
225                 230                 235                 240

Pro Ser Asn Asn Asp Leu Asn Thr Thr Glu Lys Arg Ala Ala Glu Arg
                245                 250                 255

His Pro Glu Lys Tyr Gln Gly Ser Ser Val Ser Asn Leu His Val Glu
            260                 265                 270

Pro Cys Gly Thr Asn Thr His Ala Ser Ser Leu Gln His Glu Asn Ser
        275                 280                 285

Ser Leu Leu Leu Thr Lys Asp Arg Met Asn Val Glu Lys Ala Glu Phe
    290                 295                 300

Cys Asn Lys Ser Lys Gln Pro Gly Leu Ala Arg Ser Gln His Asn Arg
305                 310                 315                 320

Trp Ala Gly Ser Lys Glu Thr Cys Asn Asp Arg Arg Thr Pro Ser Thr
                325                 330                 335

Glu Lys Lys Val Asp Leu Asn Ala Asp Pro Leu Cys Glu Arg Lys Glu
            340                 345                 350

Trp Asn Lys Gln Lys Leu Pro Cys Ser Glu Asn Pro Arg Asp Thr Glu
        355                 360                 365

Asp Val Pro Trp Ile Thr Leu Asn Ser Ser Ile Gln Lys Val Asn Glu
    370                 375                 380

Trp Phe Ser Arg Ser Asp Glu Leu Leu Gly Ser Asp Asp Ser His Asp
385                 390                 395                 400

Gly Glu Ser Glu Ser Asn Ala Lys Val Ala Asp Val Leu Asp Val Leu
                405                 410                 415
```

```
Asn Glu Val Asp Glu Tyr Ser Gly Ser Ser Glu Lys Ile Asp Leu Leu
            420                 425                 430

Ala Ser Asp Pro His Glu Ala Leu Ile Cys Lys Ser Glu Arg Val His
        435                 440                 445

Ser Lys Ser Val Glu Ser Asn Ile Glu Asp Lys Ile Phe Gly Lys Thr
    450                 455                 460

Tyr Arg Lys Lys Ala Ser Leu Pro Asn Leu Ser His Val Thr Glu Asn
465                 470                 475                 480

Leu Ile Ile Gly Ala Phe Val Thr Glu Pro Gln Ile Ile Gln Glu Arg
                485                 490                 495

Pro Leu Thr Asn Lys Leu Lys Arg Lys Arg Arg Pro Thr Ser Gly Leu
            500                 505                 510

His Pro Glu Asp Phe Ile Lys Lys Ala Asp Leu Ala Val Gln Lys Thr
        515                 520                 525

Pro Glu Met Ile Asn Gln Gly Thr Asn Gln Thr Glu Gln Asn Gly Gln
    530                 535                 540

Val Met Asn Ile Thr Asn Ser Gly His Glu Asn Lys Thr Lys Gly Asp
545                 550                 555                 560

Ser Ile Gln Asn Glu Lys Asn Pro Asn Pro Ile Glu Ser Leu Glu Lys
                565                 570                 575

Glu Ser Ala Phe Lys Thr Lys Ala Glu Pro Ile Ser Ser Ser Ile Ser
            580                 585                 590

Asn Met Glu Leu Glu Leu Asn Ile His Asn Ser Lys Ala Pro Lys Lys
        595                 600                 605

Asn Arg Leu Arg Arg Lys Ser Ser Thr Arg His Ile His Ala Leu Glu
    610                 615                 620

Leu Val Val Ser Arg Asn Leu Ser Pro Pro Asn Cys Thr Glu Leu Gln
625                 630                 635                 640
```

Ile Asp Ser Cys Ser Ser Ser Glu Glu Ile Lys Lys Lys Lys Tyr Asn
645 650 655

Gln Met Pro Val Arg His Ser Arg Asn Leu Gln Leu Met Glu Gly Lys
660 665 670

Glu Pro Ala Thr Gly Ala Lys Lys Ser Asn Lys Pro Asn Glu Gln Thr
675 680 685

Ser Lys Arg His Asp Ser Asp Thr Phe Pro Glu Leu Lys Leu Thr Asn
690 695 700

Ala Pro Gly Ser Phe Thr Lys Cys Ser Asn Thr Ser Glu Leu Lys Glu
705 710 715 720

Phe Val Asn Pro Ser Leu Pro Arg Glu Glu Lys Glu Glu Lys Leu Glu
725 730 735

Thr Val Lys Val Ser Asn Asn Ala Glu Asp Pro Lys Asp Leu Met Leu
740 745 750

Ser Gly Glu Arg Val Leu Gln Thr Glu Arg Ser Val Glu Ser Ser Ser
755 760 765

Ile Ser Leu Val Pro Gly Thr Asp Tyr Gly Thr Gln Glu Ser Ile Ser
770 775 780

Leu Leu Glu Val Ser Thr Leu Gly Lys Ala Lys Thr Glu Pro Asn Lys
785 790 795 800

Cys Val Ser Gln Cys Ala Ala Phe Glu Asn Pro Lys Gly Leu Ile His
805 810 815

Gly Cys Ser Lys Asp Asn Arg Asn Asp Thr Glu Gly Phe Lys Tyr Pro
820 825 830

Leu Gly His Glu Val Asn His Ser Arg Glu Thr Ser Ile Glu Met Glu
835 840 845

Glu Ser Glu Leu Asp Ala Gln Tyr Leu Gln Asn Thr Phe Lys Val Ser
850 855 860

```
Lys Arg Gln Ser Phe Ala Pro Phe Ser Asn Pro Gly Asn Ala Glu Glu
865                 870                 875                 880

Glu Cys Ala Thr Phe Ser Ala His Ser Gly Ser Leu Lys Lys Gln Ser
                885                 890                 895

Pro Lys Val Thr Phe Glu Cys Glu Gln Lys Glu Glu Asn Gln Gly Lys
            900                 905                 910

Asn Glu Ser Asn Ile Lys Pro Val Gln Thr Val Asn Ile Thr Ala Gly
        915                 920                 925

Phe Pro Val Val Gly Gln Lys Asp Lys Pro Val Asp Asn Ala Lys Cys
    930                 935                 940

Ser Ile Lys Gly Gly Ser Arg Phe Cys Leu Ser Ser Gln Phe Arg Gly
945                 950                 955                 960

Asn Glu Thr Gly Leu Ile Thr Pro Asn Lys His Gly Leu Leu Gln Asn
                965                 970                 975

Pro Tyr Arg Ile Pro Pro Leu Phe Pro Ile Lys Ser Phe Val Lys Thr
            980                 985                 990

Lys Cys Lys Lys Asn Leu Leu Glu  Glu Asn Phe Glu Glu  His Ser Met
        995                 1000                1005

Ser Pro  Glu Arg Glu Met Gly  Asn Glu Asn Ile Pro  Ser Thr Val
    1010                1015                1020

Ser Thr  Ile Ser Arg Asn Asn  Ile Arg Glu Asn Val  Phe Lys Glu
    1025                1030                1035

Ala Ser  Ser Ser Asn Ile Asn  Glu Val Gly Ser Ser  Thr Asn Glu
    1040                1045                1050

Val Gly  Ser Ser Ile Asn Glu  Ile Gly Ser Ser Asp  Glu Asn Ile
    1055                1060                1065

Gln Ala  Glu Leu Gly Arg Asn  Arg Gly Pro Lys Leu  Asn Ala Met
    1070                1075                1080
```

```
Leu Arg  Leu Gly Val Leu Gln  Pro Glu Val Tyr Lys  Gln Ser Leu
    1085                1090                1095

Pro Gly  Ser Asn Cys Lys His  Pro Glu Ile Lys Lys  Gln Glu Tyr
    1100                1105                1110

Glu Glu  Val Val Gln Thr Val  Asn Thr Asp Phe Ser  Pro Tyr Leu
    1115                1120                1125

Ile Ser  Asp Asn Leu Glu Gln  Pro Met Gly Ser Ser  His Ala Ser
    1130                1135                1140

Gln Val  Cys Ser Glu Thr Pro  Asp Asp Leu Leu Asp  Asp Gly Glu
    1145                1150                1155

Ile Lys  Glu Asp Thr Ser Phe  Ala Glu Asn Asp Ile  Lys Glu Ser
    1160                1165                1170

Ser Ala  Val Phe Ser Lys Ser  Val Gln Lys Gly Glu  Leu Ser Arg
    1175                1180                1185

Ser Pro  Ser Pro Phe Thr His  Thr His Leu Ala Gln  Gly Tyr Arg
    1190                1195                1200

Arg Gly  Ala Lys Lys Leu Glu  Ser Ser Glu Glu Asn  Leu Ser Ser
    1205                1210                1215

Glu Asp  Glu Glu Leu Pro Cys  Phe Gln His Leu Leu  Phe Gly Lys
    1220                1225                1230

Val Asn  Asn Ile Pro Ser Gln  Ser Thr Arg His Ser  Thr Val Ala
    1235                1240                1245

Thr Glu  Cys Leu Ser Lys Asn  Thr Glu Glu Asn Leu  Leu Ser Leu
    1250                1255                1260

Lys Asn  Ser Leu Asn Asp Cys  Ser Asn Gln Val Ile  Leu Ala Lys
    1265                1270                1275

Ala Ser  Gln Glu His His Leu  Ser Glu Glu Thr Lys  Cys Ser Ala
    1280                1285                1290
```

Ser Leu Phe Ser Ser Gln Cys Ser Glu Leu Glu Asp Leu Thr Ala
1295 1300 1305

Asn Thr Asn Thr Gln Asp Pro Phe Leu Ile Gly Ser Ser Lys Gln
1310 1315 1320

Met Arg His Gln Ser Glu Ser Gln Gly Val Gly Leu Ser Asp Lys
1325 1330 1335

Glu Leu Val Ser Asp Asp Glu Glu Arg Gly Thr Gly Leu Glu Glu
1340 1345 1350

Asn Asn Gln Glu Glu Gln Ser Met Asp Ser Asn Leu Gly Glu Ala
1355 1360 1365

Ala Ser Gly Cys Glu Ser Glu Thr Ser Val Ser Glu Asp Cys Ser
1370 1375 1380

Gly Leu Ser Ser Gln Ser Asp Ile Leu Thr Thr Gln Gln Arg Asp
1385 1390 1395

Thr Met Gln His Asn Leu Ile Lys Leu Gln Gln Glu Met Ala Glu
1400 1405 1410

Leu Glu Ala Val Leu Glu Gln His Gly Ser Gln Pro Ser Asn Ser
1415 1420 1425

Tyr Pro Ser Ile Ile Ser Asp Ser Ser Ala Leu Glu Asp Leu Arg
1430 1435 1440

Asn Pro Glu Gln Ser Thr Ser Glu Lys Ala Val Leu Thr Ser Gln
1445 1450 1455

Lys Ser Ser Glu Tyr Pro Ile Ser Gln Asn Pro Glu Gly Leu Ser
1460 1465 1470

Ala Asp Lys Phe Glu Val Ser Ala Asp Ser Ser Thr Ser Lys Asn
1475 1480 1485

Lys Glu Pro Gly Val Glu Arg Ser Ser Pro Ser Lys Cys Pro Ser
1490 1495 1500

```
Leu Asp  Asp Arg Trp Tyr Met  His Ser Cys Ser Gly  Ser Leu Gln
    1505                 1510                 1515

Asn Arg  Asn Tyr Pro Ser Gln  Glu Glu Leu Ile Lys  Val Val Asp
    1520                 1525                 1530

Val Glu  Glu Gln Gln Leu Glu  Glu Ser Gly Pro His  Asp Leu Thr
    1535                 1540                 1545

Glu Thr  Ser Tyr Leu Pro Arg  Gln Asp Leu Glu Gly  Thr Pro Tyr
    1550                 1555                 1560

Leu Glu  Ser Gly Ile Ser Leu  Phe Ser Asp Asp Pro  Glu Ser Asp
    1565                 1570                 1575

Pro Ser  Glu Asp Arg Ala Pro  Glu Ser Ala Arg Val  Gly Asn Ile
    1580                 1585                 1590

Pro Ser  Ser Thr Ser Ala Leu  Lys Val Pro Gln Leu  Lys Val Ala
    1595                 1600                 1605

Glu Ser  Ala Gln Ser Pro Ala  Ala Ala His Thr Thr  Asp Thr Ala
    1610                 1615                 1620

Gly Tyr  Asn Ala Met Glu Glu  Ser Val Ser Arg Glu  Lys Pro Glu
    1625                 1630                 1635

Leu Thr  Ala Ser Thr Glu Arg  Val Asn Lys Arg Met  Ser Met Val
    1640                 1645                 1650

Val Ser  Gly Leu Thr Pro Glu  Glu Phe Met Leu Val  Tyr Lys Phe
    1655                 1660                 1665

Ala Arg  Lys His His Ile Thr  Leu Thr Asn Leu Ile  Thr Glu Glu
    1670                 1675                 1680

Thr Thr  His Val Val Met Lys  Thr Asp Ala Glu Phe  Val Cys Glu
    1685                 1690                 1695

Arg Thr  Leu Met Tyr Phe Leu  Gly Ile Ala Gly Gly  Lys Trp Val
    1700                 1705                 1710
```

```
Val Ser  Tyr Phe Trp Val Thr  Gln Ser Ile Lys Glu  Arg Lys Met
    1715                 1720                 1725

Leu Asn  Glu His Asp Phe Glu  Val Arg Gly Asp Val  Val Asn Gly
    1730                 1735                 1740

Arg Asn  His Gln Gly Pro Lys  Arg Ala Arg Glu Ser  Gln Asp Arg
    1745                 1750                 1755

Lys Ile  Phe Arg Gly Leu Glu  Ile Cys Cys Tyr Gly  Pro Phe Thr
    1760                 1765                 1770

Asn Met  Pro Thr Asp Gln Leu  Glu Trp Met Val Gln  Leu Cys Gly
    1775                 1780                 1785

Ala Ser  Val Val Lys Glu Leu  Ser Ser Phe Thr Leu  Gly Thr Gly
    1790                 1795                 1800

Val His  Pro Ile Val Val Val  Gln Pro Asp Ala Trp  Thr Glu Asp
    1805                 1810                 1815

Asn Gly  Phe His Ala Ile Gly  Gln Met Cys Glu Ala  Pro Val Val
    1820                 1825                 1830

Thr Arg  Glu Trp Val Leu Asp  Ser Val Ala Leu Tyr  Gln Cys Gln
    1835                 1840                 1845

Glu Leu  Asp Thr Tyr Leu Ile  Pro Gln Ile Pro His  Ser His Tyr
    1850                 1855                 1860
```

<210> 20
<211> 1863
<212> PRT
<213> Homo sapiens

<400> 20

```
Met Asp Leu Ser Ala Leu Arg Val Glu Glu Val Gln Asn Val Ile Asn
1               5                  10                  15

Ala Met Gln Lys Ile Leu Glu Cys Pro Ile Cys Leu Glu Leu Ile Lys
            20                  25                  30
```

```
Glu Pro Val Ser Thr Lys Cys Asp His Ile Phe Cys Lys Phe Cys Met
        35                  40                  45

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

Lys Asn Asp Ile Thr Lys Arg Ser Leu Gln Glu Ser Thr Arg Phe Ser
65                  70                  75                  80

Gln Leu Val Glu Glu Leu Leu Lys Ile Ile Cys Ala Phe Gln Leu Asp
                85                  90                  95

Thr Gly Leu Glu Tyr Ala Asn Ser Tyr Asn Phe Ala Lys Lys Glu Asn
            100                 105                 110

Asn Ser Pro Glu His Leu Lys Asp Glu Val Ser Ile Ile Gln Ser Met
        115                 120                 125

Gly Tyr Arg Asn Arg Ala Lys Arg Leu Leu Gln Ser Glu Pro Glu Asn
    130                 135                 140

Pro Ser Leu Gln Glu Thr Ser Leu Ser Val Gln Leu Ser Asn Leu Gly
145                 150                 155                 160

Thr Val Arg Thr Leu Arg Thr Lys Gln Arg Ile Gln Pro Gln Lys Thr
                165                 170                 175

Ser Val Tyr Ile Glu Leu Gly Ser Asp Ser Ser Glu Asp Thr Val Asn
            180                 185                 190

Lys Ala Thr Tyr Cys Ser Val Gly Asp Gln Glu Leu Leu Gln Ile Thr
        195                 200                 205

Pro Gln Gly Thr Arg Asp Glu Ile Ser Leu Asp Ser Ala Lys Lys Ala
    210                 215                 220

Ala Cys Glu Phe Ser Glu Thr Asp Val Thr Asn Thr Glu His His Gln
225                 230                 235                 240

Pro Ser Asn Asn Asp Leu Asn Thr Thr Glu Lys Arg Ala Ala Glu Arg
                245                 250                 255
```

His Pro Glu Lys Tyr Gln Gly Ser Ser Val Ser Asn Leu His Val Glu
260 265 270

Pro Cys Gly Thr Asn Thr His Ala Ser Ser Leu Gln His Glu Asn Ser
275 280 285

Ser Leu Leu Leu Thr Lys Asp Arg Met Asn Val Glu Lys Ala Glu Phe
290 295 300

Cys Asn Lys Ser Lys Gln Pro Gly Leu Ala Arg Ser Gln His Asn Arg
305 310 315 320

Trp Ala Gly Ser Lys Glu Thr Cys Asn Asp Arg Arg Thr Pro Ser Thr
325 330 335

Glu Lys Lys Val Asp Leu Asn Ala Asp Pro Leu Cys Glu Arg Lys Glu
340 345 350

Trp Asn Lys Gln Lys Leu Pro Cys Ser Glu Asn Pro Arg Asp Thr Glu
355 360 365

Asp Val Pro Trp Ile Thr Leu Asn Ser Ser Ile Gln Lys Val Asn Glu
370 375 380

Trp Phe Ser Arg Ser Asp Glu Leu Leu Gly Ser Asp Asp Ser His Asp
385 390 395 400

Gly Glu Ser Glu Ser Asn Ala Lys Val Ala Asp Val Leu Asp Val Leu
405 410 415

Asn Glu Val Asp Glu Tyr Ser Gly Ser Ser Glu Lys Ile Asp Leu Leu
420 425 430

Ala Ser Asp Pro His Glu Ala Leu Ile Cys Lys Ser Glu Arg Val His
435 440 445

Ser Lys Ser Val Glu Ser Asn Ile Glu Asp Lys Ile Phe Gly Lys Thr
450 455 460

Tyr Arg Lys Lys Ala Ser Leu Pro Asn Leu Ser His Val Thr Glu Asn
465 470 475 480

Leu Ile Ile Gly Ala Phe Val Thr Glu Pro Gln Ile Ile Gln Glu Arg
485 490 495

Pro Leu Thr Asn Lys Leu Lys Arg Lys Arg Arg Pro Thr Ser Gly Leu
500 505 510

His Pro Glu Asp Phe Ile Lys Lys Ala Asp Leu Ala Val Gln Lys Thr
515 520 525

Pro Glu Met Ile Asn Gln Gly Thr Asn Gln Thr Glu Gln Asn Gly Gln
530 535 540

Val Met Asn Ile Thr Asn Ser Gly His Glu Asn Lys Thr Lys Gly Asp
545 550 555 560

Ser Ile Gln Asn Glu Lys Asn Pro Asn Pro Ile Glu Ser Leu Glu Lys
565 570 575

Glu Ser Ala Phe Lys Thr Lys Ala Glu Pro Ile Ser Ser Ser Ile Ser
580 585 590

Asn Met Glu Leu Glu Leu Asn Ile His Asn Ser Lys Ala Pro Lys Lys
595 600 605

Asn Arg Leu Arg Arg Lys Ser Ser Thr Arg His Ile His Ala Leu Glu
610 615 620

Leu Val Val Ser Arg Asn Leu Ser Pro Pro Asn Cys Thr Glu Leu Gln
625 630 635 640

Ile Asp Ser Cys Ser Ser Ser Glu Glu Ile Lys Lys Lys Lys Tyr Asn
645 650 655

Gln Met Pro Val Arg His Ser Arg Asn Leu Gln Leu Met Glu Gly Lys
660 665 670

Glu Pro Ala Thr Gly Ala Lys Lys Ser Asn Lys Pro Asn Glu Gln Thr
675 680 685

Ser Lys Arg His Asp Ser Asp Thr Phe Pro Glu Leu Lys Leu Thr Asn
690 695 700

```
Ala Pro Gly Ser Phe Thr Lys Cys Ser Asn Thr Ser Glu Leu Lys Glu
705                 710                 715                 720

Phe Val Asn Pro Ser Leu Pro Arg Glu Glu Lys Glu Glu Lys Leu Glu
                725                 730                 735

Thr Val Lys Val Ser Asn Asn Ala Glu Asp Pro Lys Asp Leu Met Leu
            740                 745                 750

Ser Gly Glu Arg Val Leu Gln Thr Glu Arg Ser Val Glu Ser Ser Ser
        755                 760                 765

Ile Ser Leu Val Pro Gly Thr Asp Tyr Gly Thr Gln Glu Ser Ile Ser
    770                 775                 780

Leu Leu Glu Val Ser Thr Leu Gly Lys Ala Lys Thr Glu Pro Asn Lys
785                 790                 795                 800

Cys Val Ser Gln Cys Ala Ala Phe Glu Asn Pro Lys Gly Leu Ile His
                805                 810                 815

Gly Cys Ser Lys Asp Asn Arg Asn Asp Thr Glu Gly Phe Lys Tyr Pro
            820                 825                 830

Leu Gly His Glu Val Asn His Ser Arg Glu Thr Ser Ile Glu Met Glu
        835                 840                 845

Glu Ser Glu Leu Asp Ala Gln Tyr Leu Gln Asn Thr Phe Lys Val Ser
    850                 855                 860

Lys Arg Gln Ser Phe Ala Pro Phe Ser Asn Pro Gly Asn Ala Glu Glu
865                 870                 875                 880

Glu Cys Ala Thr Phe Ser Ala His Ser Gly Ser Leu Lys Lys Gln Ser
                885                 890                 895

Pro Lys Val Thr Phe Glu Cys Glu Gln Lys Glu Glu Asn Gln Gly Lys
            900                 905                 910

Asn Glu Ser Asn Ile Lys Pro Val Gln Thr Val Asn Ile Thr Ala Gly
        915                 920                 925
```

```
Phe Pro Val Val Gly Gln Lys Asp Lys Pro Val Asp Asn Ala Lys Cys
    930                 935                 940

Ser Ile Lys Gly Gly Ser Arg Phe Cys Leu Ser Ser Gln Phe Arg Gly
945                 950                 955                 960

Asn Glu Thr Gly Leu Ile Thr Pro Asn Lys His Gly Leu Leu Gln Asn
                965                 970                 975

Pro Tyr Arg Ile Pro Pro Leu Phe Pro Ile Lys Ser Phe Val Lys Thr
            980                 985                 990

Lys Cys Lys Lys Asn Leu Leu Glu  Glu Asn Phe Glu Glu  His Ser Met
        995                 1000                1005

Ser Pro  Glu Arg Glu Met Gly  Asn Glu Asn Ile Pro  Ser Thr Val
    1010                1015                1020

Ser Thr  Ile Ser Arg Asn Asn  Ile Arg Glu Asn Val  Phe Lys Glu
    1025                1030                1035

Ala Ser  Ser Ser Asn Ile Asn  Glu Val Gly Ser Ser  Thr Asn Glu
    1040                1045                1050

Val Gly  Ser Ser Ile Asn Glu  Ile Gly Ser Ser Asp  Glu Asn Ile
    1055                1060                1065

Gln Ala  Glu Leu Gly Arg Asn  Arg Gly Pro Lys Leu  Asn Ala Met
    1070                1075                1080

Leu Arg  Leu Gly Val Leu Gln  Pro Glu Val Tyr Lys  Gln Ser Leu
    1085                1090                1095

Pro Gly  Ser Asn Cys Lys His  Pro Glu Ile Lys Lys  Gln Glu Tyr
    1100                1105                1110

Glu Glu  Val Val Gln Thr Val  Asn Thr Asp Phe Ser  Pro Tyr Leu
    1115                1120                1125

Ile Ser  Asp Asn Leu Glu Gln  Pro Met Gly Ser Ser  His Ala Ser
    1130                1135                1140
```

```
Gln Val  Cys Ser Glu Thr Pro  Asp Asp Leu Leu Asp  Asp Gly Glu
    1145                 1150                 1155

Ile Lys  Glu Asp Thr Ser Phe  Ala Glu Asn Asp Ile  Lys Glu Ser
    1160                 1165                 1170

Ser Ala  Val Phe Ser Lys Ser  Val Gln Lys Gly Glu  Leu Ser Arg
    1175                 1180                 1185

Ser Pro  Ser Pro Phe Thr His  Thr His Leu Ala Gln  Gly Tyr Arg
    1190                 1195                 1200

Arg Gly  Ala Lys Lys Leu Glu  Ser Ser Glu Glu Asn  Leu Ser Ser
    1205                 1210                 1215

Glu Asp  Glu Glu Leu Pro Cys  Phe Gln His Leu Leu  Phe Gly Lys
    1220                 1225                 1230

Val Asn  Asn Ile Pro Ser Gln  Ser Thr Arg His Ser  Thr Val Ala
    1235                 1240                 1245

Thr Glu  Cys Leu Ser Lys Asn  Thr Glu Glu Asn Leu  Leu Ser Leu
    1250                 1255                 1260

Lys Asn  Ser Leu Asn Asp Cys  Ser Asn Gln Val Ile  Leu Ala Lys
    1265                 1270                 1275

Ala Ser  Gln Glu His His Leu  Ser Glu Glu Thr Lys  Cys Ser Ala
    1280                 1285                 1290

Ser Leu  Phe Ser Ser Gln Cys  Ser Glu Leu Glu Asp  Leu Thr Ala
    1295                 1300                 1305

Asn Thr  Asn Thr Gln Asp Pro  Phe Leu Ile Gly Ser  Ser Lys Gln
    1310                 1315                 1320

Met Arg  His Gln Ser Glu Ser  Gln Gly Val Gly Leu  Ser Asp Lys
    1325                 1330                 1335

Glu Leu  Val Ser Asp Asp Glu  Glu Arg Gly Thr Gly  Leu Glu Glu
    1340                 1345                 1350
```

```
Asn Asn  Gln Glu Glu Gln Ser  Met Asp Ser Asn Leu  Gly Glu Ala
    1355                 1360                 1365

Ala Ser  Gly Cys Glu Ser Glu  Thr Ser Val Ser Glu  Asp Cys Ser
    1370                 1375                 1380

Gly Leu  Ser Ser Gln Ser Asp  Ile Leu Thr Thr Gln  Gln Arg Asp
    1385                 1390                 1395

Thr Met  Gln His Asn Leu Ile  Lys Leu Gln Gln Glu  Met Ala Glu
    1400                 1405                 1410

Leu Glu  Ala Val Leu Glu Gln  His Gly Ser Gln Pro  Ser Asn Ser
    1415                 1420                 1425

Tyr Pro  Ser Ile Ile Ser Asp  Ser Ser Ala Leu Glu  Asp Leu Arg
    1430                 1435                 1440

Asn Pro  Glu Gln Ser Thr Ser  Glu Lys Ala Val Leu  Thr Ser Gln
    1445                 1450                 1455

Lys Ser  Ser Glu Tyr Pro Ile  Ser Gln Asn Pro Glu  Gly Leu Ser
    1460                 1465                 1470

Ala Asp  Lys Phe Glu Val Ser  Ala Asp Ser Ser Thr  Ser Lys Asn
    1475                 1480                 1485

Lys Glu  Pro Gly Val Glu Arg  Ser Ser Pro Ser Lys  Cys Pro Ser
    1490                 1495                 1500

Leu Asp  Asp Arg Trp Tyr Met  His Ser Cys Ser Gly  Ser Leu Gln
    1505                 1510                 1515

Asn Arg  Asn Tyr Pro Ser Gln  Glu Glu Leu Ile Lys  Val Val Asp
    1520                 1525                 1530

Val Glu  Glu Gln Gln Leu Glu  Glu Ser Gly Pro His  Asp Leu Thr
    1535                 1540                 1545

Glu Thr  Ser Tyr Leu Pro Arg  Gln Asp Leu Glu Gly  Thr Pro Tyr
    1550                 1555                 1560
```

```
Leu Glu  Ser Gly Ile Ser Leu  Phe Ser Asp Asp Pro  Glu Ser Asp
    1565                 1570                 1575

Pro Ser  Glu Asp Arg Ala Pro  Glu Ser Ala Arg Val  Gly Asn Ile
    1580                 1585                 1590

Pro Ser  Ser Thr Ser Ala Leu  Lys Val Pro Gln Leu  Lys Val Ala
    1595                 1600                 1605

Glu Ser  Ala Gln Ser Pro Ala  Ala Ala His Thr Thr  Asp Thr Ala
    1610                 1615                 1620

Gly Tyr  Asn Ala Met Glu Glu  Ser Val Ser Arg Glu  Lys Pro Glu
    1625                 1630                 1635

Leu Thr  Ala Ser Thr Glu Arg  Val Asn Lys Arg Met  Ser Met Val
    1640                 1645                 1650

Val Ala  Gly Leu Thr Pro Glu  Glu Phe Met Leu Val  Tyr Lys Phe
    1655                 1660                 1665

Ala Arg  Lys His His Ile Thr  Leu Thr Asn Leu Ile  Thr Glu Glu
    1670                 1675                 1680

Thr Thr  His Val Val Met Lys  Thr Asp Ala Glu Phe  Val Cys Glu
    1685                 1690                 1695

Arg Thr  Leu Met Tyr Phe Leu  Gly Ile Ala Gly Gly  Lys Trp Val
    1700                 1705                 1710

Val Ser  Tyr Phe Trp Val Thr  Gln Ser Ile Lys Glu  Arg Lys Met
    1715                 1720                 1725

Leu Asn  Glu His Asp Phe Glu  Val Arg Gly Asp Val  Val Asn Gly
    1730                 1735                 1740

Arg Asn  His Gln Gly Pro Lys  Arg Ala Arg Glu Ser  Gln Asp Arg
    1745                 1750                 1755

Lys Ile  Phe Arg Gly Leu Glu  Ile Cys Cys Tyr Gly  Pro Phe Thr
    1760                 1765                 1770
```

Asn Met Pro Thr Asp Gln Leu Glu Trp Met Val Gln Leu Cys Gly
1775 1780 1785

Ala Ser Val Val Lys Glu Leu Ser Ser Phe Thr Leu Gly Thr Gly
1790 1795 1800

Val His Pro Ile Val Val Val Gln Pro Asp Ala Trp Thr Glu Asp
1805 1810 1815

Asn Gly Phe His Ala Ile Gly Gln Met Cys Glu Ala Pro Val Val
1820 1825 1830

Thr Arg Glu Trp Val Leu Asp Ser Val Ala Leu Tyr Gln Cys Gln
1835 1840 1845

Glu Leu Asp Thr Tyr Leu Ile Pro Gln Ile Pro His Ser His Tyr
1850 1855 1860

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Ala Met Gln Lys Ile Leu Glu Cys Pro Ile Cys Leu Glu Leu Ile Lys
20 25 30

Glu Pro Val Ser Thr Lys Cys Asp His Ile Phe Cys Lys Phe Cys Met
35 40 45

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

Lys Asn Asp Ile Thr Lys Arg Ser Leu Gln Glu Ser Thr Arg Phe Ser
65 70 75 80

Gln Leu Val Glu Glu Leu Leu Lys Ile Ile Cys Ala Phe Gln Leu Asp
85 90 95

```
Thr Gly Leu Glu Tyr Ala Asn Ser Tyr Asn Phe Ala Lys Lys Glu Asn
            100                 105                 110

Asn Ser Pro Glu His Leu Lys Asp Glu Val Ser Ile Ile Gln Ser Met
        115                 120                 125

Gly Tyr Arg Asn Arg Ala Lys Arg Leu Leu Gln Ser Glu Pro Glu Asn
    130                 135                 140

Pro Ser Leu Gln Glu Thr Ser Leu Ser Val Gln Leu Ser Asn Leu Gly
145                 150                 155                 160

Thr Val Arg Thr Leu Arg Thr Lys Gln Arg Ile Gln Pro Gln Lys Thr
                165                 170                 175

Ser Val Tyr Ile Glu Leu Gly Ser Asp Ser Ser Glu Asp Thr Val Asn
            180                 185                 190

Lys Ala Thr Tyr Cys Ser Val Gly Asp Gln Glu Leu Leu Gln Ile Thr
        195                 200                 205

Pro Gln Gly Thr Arg Asp Glu Ile Ser Leu Asp Ser Ala Lys Lys Ala
    210                 215                 220

Ala Cys Glu Phe Ser Glu Thr Asp Val Thr Asn Thr Glu His His Gln
225                 230                 235                 240

Pro Ser Asn Asn Asp Leu Asn Thr Thr Glu Lys Arg Ala Ala Glu Arg
                245                 250                 255

His Pro Glu Lys Tyr Gln Gly Ser Ser Val Ser Asn Leu His Val Glu
            260                 265                 270

Pro Cys Gly Thr Asn Thr His Ala Ser Ser Leu Gln His Glu Asn Ser
        275                 280                 285

Ser Leu Leu Leu Thr Lys Asp Arg Met Asn Val Glu Lys Ala Glu Phe
    290                 295                 300

Cys Asn Lys Ser Lys Gln Pro Gly Leu Ala Arg Ser Gln His Asn Arg
305                 310                 315                 320
```

```
Trp Ala Gly Ser Lys Glu Thr Cys Asn Asp Arg Arg Thr Pro Ser Thr
                325                 330                 335

Glu Lys Lys Val Asp Leu Asn Ala Asp Pro Leu Cys Glu Arg Lys Glu
            340                 345                 350

Trp Asn Lys Gln Lys Leu Pro Cys Ser Glu Asn Pro Arg Asp Thr Glu
        355                 360                 365

Asp Val Pro Trp Ile Thr Leu Asn Ser Ser Ile Gln Lys Val Asn Glu
    370                 375                 380

Trp Phe Ser Arg Ser Asp Glu Leu Leu Gly Ser Asp Asp Ser His Asp
385                 390                 395                 400

Gly Glu Ser Glu Ser Asn Ala Lys Val Ala Asp Val Leu Asp Val Leu
                405                 410                 415

Asn Glu Val Asp Glu Tyr Ser Gly Ser Ser Glu Lys Ile Asp Leu Leu
            420                 425                 430

Ala Ser Asp Pro His Glu Ala Leu Ile Cys Lys Ser Glu Arg Val His
        435                 440                 445

Ser Lys Ser Val Glu Ser Asn Ile Glu Asp Lys Ile Phe Gly Lys Thr
    450                 455                 460

Tyr Arg Lys Lys Ala Ser Leu Pro Asn Leu Ser His Val Thr Glu Asn
465                 470                 475                 480

Leu Ile Ile Gly Ala Phe Val Thr Glu Pro Gln Ile Ile Gln Glu Arg
                485                 490                 495

Pro Leu Thr Asn Lys Leu Lys Arg Lys Arg Arg Pro Thr Ser Gly Leu
            500                 505                 510

His Pro Glu Asp Phe Ile Lys Lys Ala Asp Leu Ala Val Gln Lys Thr
        515                 520                 525

Pro Glu Met Ile Asn Gln Gly Thr Asn Gln Thr Glu Gln Asn Gly Gln
    530                 535                 540
```

```
Val Met Asn Ile Thr Asn Ser Gly His Glu Asn Lys Thr Lys Gly Asp
545                 550                 555                 560

Ser Ile Gln Asn Glu Lys Asn Pro Asn Pro Ile Glu Ser Leu Glu Lys
                565                 570                 575

Glu Ser Ala Phe Lys Thr Lys Ala Glu Pro Ile Ser Ser Ser Ile Ser
            580                 585                 590

Asn Met Glu Leu Glu Leu Asn Ile His Asn Ser Lys Ala Pro Lys Lys
        595                 600                 605

Asn Arg Leu Arg Arg Lys Ser Ser Thr Arg His Ile His Ala Leu Glu
    610                 615                 620

Leu Val Val Ser Arg Asn Leu Ser Pro Pro Asn Cys Thr Glu Leu Gln
625                 630                 635                 640

Ile Asp Ser Cys Ser Ser Ser Glu Glu Ile Lys Lys Lys Lys Tyr Asn
                645                 650                 655

Gln Met Pro Val Arg His Ser Arg Asn Leu Gln Leu Met Glu Gly Lys
            660                 665                 670

Glu Pro Ala Thr Gly Ala Lys Lys Ser Asn Lys Pro Asn Glu Gln Thr
        675                 680                 685

Ser Lys Arg His Asp Ser Asp Thr Phe Pro Glu Leu Lys Leu Thr Asn
    690                 695                 700

Ala Pro Gly Ser Phe Thr Lys Cys Ser Asn Thr Ser Glu Leu Lys Glu
705                 710                 715                 720

Phe Val Asn Pro Ser Leu Pro Arg Glu Glu Lys Glu Glu Lys Leu Glu
                725                 730                 735

Thr Val Lys Val Ser Asn Asn Ala Glu Asp Pro Lys Asp Leu Met Leu
            740                 745                 750

Ser Gly Glu Arg Val Leu Gln Thr Glu Arg Ser Val Glu Ser Ser Ser
        755                 760                 765
```

```
Ile Ser Leu Val Pro Gly Thr Asp Tyr Gly Thr Gln Glu Ser Ile Ser
    770                 775                 780

Leu Leu Glu Val Ser Thr Leu Gly Lys Ala Lys Thr Glu Pro Asn Lys
785                 790                 795                 800

Cys Val Ser Gln Cys Ala Ala Phe Glu Asn Pro Lys Gly Leu Ile His
                805                 810                 815

Gly Cys Ser Lys Asp Asn Arg Asn Asp Thr Glu Gly Phe Lys Tyr Pro
            820                 825                 830

Leu Gly His Glu Val Asn His Ser Arg Glu Thr Ser Ile Glu Met Glu
        835                 840                 845

Glu Ser Glu Leu Asp Ala Gln Tyr Leu Gln Asn Thr Phe Lys Val Ser
    850                 855                 860

Lys Arg Gln Ser Phe Ala Pro Phe Ser Asn Pro Gly Asn Ala Glu Glu
865                 870                 875                 880

Glu Cys Ala Thr Phe Ser Ala His Ser Gly Ser Leu Lys Lys Gln Ser
                885                 890                 895

Pro Lys Val Thr Phe Glu Cys Glu Gln Lys Glu Glu Asn Gln Gly Lys
            900                 905                 910

Asn Glu Ser Asn Ile Lys Pro Val Gln Thr Val Asn Ile Thr Ala Gly
        915                 920                 925

Phe Pro Val Val Gly Gln Lys Asp Lys Pro Val Asp Asn Ala Lys Cys
    930                 935                 940

Ser Ile Lys Gly Gly Ser Arg Phe Cys Leu Ser Ser Gln Phe Arg Gly
945                 950                 955                 960

Asn Glu Thr Gly Leu Ile Thr Pro Asn Lys His Gly Leu Leu Gln Asn
                965                 970                 975

Pro Tyr Arg Ile Pro Pro Leu Phe Pro Ile Lys Ser Phe Val Lys Thr
            980                 985                 990
```

```
Lys Cys Lys Lys Asn Leu Leu Glu  Glu Asn Phe Glu Glu  His Ser Met
        995                 1000                1005

Ser Pro  Glu Arg Glu Met Gly  Asn Glu Asn Ile Pro  Ser Thr Val
    1010                1015                1020

Ser Thr  Ile Ser Arg Asn Asn  Ile Arg Glu Asn Val  Phe Lys Glu
    1025                1030                1035

Ala Ser  Ser Ser Asn Ile Asn  Glu Val Gly Ser Ser  Thr Asn Glu
    1040                1045                1050

Val Gly  Ser Ser Ile Asn Glu  Ile Gly Ser Ser Asp  Glu Asn Ile
    1055                1060                1065

Gln Ala  Glu Leu Gly Arg Asn  Arg Gly Pro Lys Leu  Asn Ala Met
    1070                1075                1080

Leu Arg  Leu Gly Val Leu Gln  Pro Glu Val Tyr Lys  Gln Ser Leu
    1085                1090                1095

Pro Gly  Ser Asn Cys Lys His  Pro Glu Ile Lys Lys  Gln Glu Tyr
    1100                1105                1110

Glu Glu  Val Val Gln Thr Val  Asn Thr Asp Phe Ser  Pro Tyr Leu
    1115                1120                1125

Ile Ser  Asp Asn Leu Glu Gln  Pro Met Gly Ser Ser  His Ala Ser
    1130                1135                1140

Gln Val  Cys Ser Glu Thr Pro  Asp Asp Leu Leu Asp  Asp Gly Glu
    1145                1150                1155

Ile Lys  Glu Asp Thr Ser Phe  Ala Glu Asn Asp Ile  Lys Glu Ser
    1160                1165                1170

Ser Ala  Val Phe Ser Lys Ser  Val Gln Lys Gly Glu  Leu Ser Arg
    1175                1180                1185

Ser Pro  Ser Pro Phe Thr His  Thr His Leu Ala Gln  Gly Tyr Arg
    1190                1195                1200
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Arg Gly Ala Lys Lys Leu Glu Ser Ser Glu Glu Asn Leu Ser Ser
1205 1210 1215

Glu Asp Glu Glu Leu Pro Cys Phe Gln His Leu Leu Phe Gly Lys
1220 1225 1230

Val Asn Asn Ile Pro Ser Gln Ser Thr Arg His Ser Thr Val Ala
1235 1240 1245

Thr Glu Cys Leu Ser Lys Asn Thr Glu Glu Asn Leu Leu Ser Leu
1250 1255 1260

Lys Asn Ser Leu Asn Asp Cys Ser Asn Gln Val Ile Leu Ala Lys
1265 1270 1275

Ala Ser Gln Glu His His Leu Ser Glu Glu Thr Lys Cys Ser Ala
1280 1285 1290

Ser Leu Phe Ser Ser Gln Cys Ser Glu Leu Glu Asp Leu Thr Ala
1295 1300 1305

Asn Thr Asn Thr Gln Asp Pro Phe Leu Ile Gly Ser Ser Lys Gln
1310 1315 1320

Met Arg His Gln Ser Glu Ser Gln Gly Val Gly Leu Ser Asp Lys
1325 1330 1335

Glu Leu Val Ser Asp Asp Glu Glu Arg Gly Thr Gly Leu Glu Glu
1340 1345 1350

Asn Asn Gln Glu Glu Gln Ser Met Asp Ser Asn Leu Gly Glu Ala
1355 1360 1365

Ala Ser Gly Cys Glu Ser Glu Thr Ser Val Ser Glu Asp Cys Ser
1370 1375 1380

Gly Leu Ser Ser Gln Ser Asp Ile Leu Thr Thr Gln Gln Arg Asp
1385 1390 1395

Thr Met Gln His Asn Leu Ile Lys Leu Gln Gln Glu Met Ala Glu
1400 1405 1410

```
Leu Glu  Ala Val Leu Glu Gln  His Gly Ser Gln Pro  Ser Asn Ser
    1415                 1420                 1425

Tyr Pro  Ser Ile Ile Ser Asp  Ser Ser Ala Leu Glu  Asp Leu Arg
    1430                 1435                 1440

Asn Pro  Glu Gln Ser Thr Ser  Glu Lys Ala Val Leu  Thr Ser Gln
    1445                 1450                 1455

Lys Ser  Ser Glu Tyr Pro Ile  Ser Gln Asn Pro Glu  Gly Leu Ser
    1460                 1465                 1470

Ala Asp  Lys Phe Glu Val Ser  Ala Asp Ser Ser Thr  Ser Lys Asn
    1475                 1480                 1485

Lys Glu  Pro Gly Val Glu Arg  Ser Ser Pro Ser Lys  Cys Pro Ser
    1490                 1495                 1500

Leu Asp  Asp Arg Trp Tyr Met  His Ser Cys Ser Gly  Ser Leu Gln
    1505                 1510                 1515

Asn Arg  Asn Tyr Pro Ser Gln  Glu Glu Leu Ile Lys  Val Val Asp
    1520                 1525                 1530

Val Glu  Glu Gln Gln Leu Glu  Glu Ser Gly Pro His  Asp Leu Thr
    1535                 1540                 1545

Glu Thr  Ser Tyr Leu Pro Arg  Gln Asp Leu Glu Gly  Thr Pro Tyr
    1550                 1555                 1560

Leu Glu  Ser Gly Ile Ser Leu  Phe Ser Asp Asp Pro  Glu Ser Asp
    1565                 1570                 1575

Pro Ser  Glu Asp Arg Ala Pro  Glu Ser Ala Arg Val  Gly Asn Ile
    1580                 1585                 1590

Pro Ser  Ser Thr Ser Ala Leu  Lys Val Pro Gln Leu  Lys Val Ala
    1595                 1600                 1605

Glu Ser  Ala Gln Ser Pro Ala  Ala Ala His Thr Thr  Asp Thr Ala
    1610                 1615                 1620
```

```
Gly Tyr  Asn Ala Met Glu Glu  Ser Val Ser Arg Glu  Lys Pro Glu
    1625                1630                1635

Leu Thr  Ala Ser Thr Glu Arg  Val Asn Lys Arg Met  Ser Met Val
    1640                1645                1650

Val Ser  Gly Leu Thr Pro Glu  Glu Phe Met Leu Val  Tyr Lys Phe
    1655                1660                1665

Ala Arg  Lys His His Ile Thr  Leu Thr Asn Leu Ile  Thr Glu Glu
    1670                1675                1680

Thr Thr  His Val Val Met Lys  Thr Asp Ala Glu Phe  Val Cys Glu
    1685                1690                1695

Arg Thr  Leu Lys Tyr Phe Leu  Gly Ile Ala Gly Gly  Lys Trp Val
    1700                1705                1710

Val Ser  Tyr Phe Trp Val Thr  Gln Ser Ile Lys Glu  Arg Lys Met
    1715                1720                1725

Leu Asn  Glu His Asp Phe Glu  Val Arg Gly Asp Val  Val Asn Gly
    1730                1735                1740

Arg Asn  His Gln Gly Pro Lys  Arg Ala Arg Glu Ser  Gln Asp Arg
    1745                1750                1755

Lys Ile  Phe Arg Gly Leu Glu  Ile Cys Cys Tyr Gly  Pro Phe Thr
    1760                1765                1770

Asn Met  Pro Thr Asp Gln Leu  Glu Trp Met Val Gln  Leu Cys Gly
    1775                1780                1785

Ala Ser  Val Val Lys Glu Leu  Ser Ser Phe Thr Leu  Gly Thr Gly
    1790                1795                1800

Val His  Pro Ile Val Val Val  Gln Pro Asp Ala Trp  Thr Glu Asp
    1805                1810                1815

Asn Gly  Phe His Ala Ile Gly  Gln Met Cys Glu Ala  Pro Val Val
    1820                1825                1830
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Thr Arg  Glu Trp Val Leu Asp  Ser Val Ala Leu Tyr  Gln Cys Gln
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Glu Leu  Asp Thr
    1850


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1               5                   10                  15

gct atg cag aaa atc tta gag tgt ccc atc tgt ctg gag ttg atc aag       96
Ala Met Gln Lys Ile Leu Glu Cys Pro Ile Cys Leu Glu Leu Ile Lys
            20                  25                  30

gaa cct gtc tcc aca aag tgt gac cac ata ttt tgc aaa ttt tgc atg      144
Glu Pro Val Ser Thr Lys Cys Asp His Ile Phe Cys Lys Phe Cys Met
        35                  40                  45

ctg aaa ctt ctc aac cag aag aaa ggg cct tca cag tgt cct tta tgt      192
Leu Lys Leu Leu Asn Gln Lys Lys Gly Pro Ser Gln Cys Pro Leu Cys
    50                  55                  60

aag aat gat ata acc aaa agg agc cta caa gaa agt acg aga ttt agt      240
Lys Asn Asp Ile Thr Lys Arg Ser Leu Gln Glu Ser Thr Arg Phe Ser
65                  70                  75                  80

caa ctt gtt gaa gag cta ttg aaa atc att tgt gct ttt cag ctt gac      288
Gln Leu Val Glu Glu Leu Leu Lys Ile Ile Cys Ala Phe Gln Leu Asp
                85                  90                  95

aca ggt ttg gag tat gca aac agc tat aat ttt gca aaa aag gaa aat      336
Thr Gly Leu Glu Tyr Ala Asn Ser Tyr Asn Phe Ala Lys Lys Glu Asn
            100                 105                 110

aac tct cct gaa cat cta aaa gat gaa gtt tct atc atc caa agt atg      384
Asn Ser Pro Glu His Leu Lys Asp Glu Val Ser Ile Ile Gln Ser Met
        115                 120                 125

ggc tac aga aac cgt gcc aaa aga ctt cta cag agt gaa ccc gaa aat      432
Gly Tyr Arg Asn Arg Ala Lys Arg Leu Leu Gln Ser Glu Pro Glu Asn
    130                 135                 140

cct tcc ttg cag gaa acc agt ctc agt gtc caa ctc tct aac ctt gga      480
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```
Pro Ser Leu Gln Glu Thr Ser Leu Ser Val Gln Leu Ser Asn Leu Gly
145                 150                 155                 160

act gtg aga act ctg agg aca aag cag cgg ata caa cct caa aag acg      528
Thr Val Arg Thr Leu Arg Thr Lys Gln Arg Ile Gln Pro Gln Lys Thr
                165                 170                 175

tct gtc tac att gaa ttg gga tct gat tct tct gaa gat acc gtt aat      576
Ser Val Tyr Ile Glu Leu Gly Ser Asp Ser Ser Glu Asp Thr Val Asn
            180                 185                 190

aag gca act tat tgc agt gtg gga gat caa gaa ttg tta caa atc acc      624
Lys Ala Thr Tyr Cys Ser Val Gly Asp Gln Glu Leu Leu Gln Ile Thr
        195                 200                 205

cct caa gga acc agg gat gaa atc agt ttg gat tct gca aaa aag gct      672
Pro Gln Gly Thr Arg Asp Glu Ile Ser Leu Asp Ser Ala Lys Lys Ala
    210                 215                 220

gct tgt gaa ttt tct gag acg gat gta aca aat act gaa cat cat caa      720
Ala Cys Glu Phe Ser Glu Thr Asp Val Thr Asn Thr Glu His His Gln
225                 230                 235                 240

ccc agt aat aat gat ttg aac acc act gag aag cgt gca gct gag agg      768
Pro Ser Asn Asn Asp Leu Asn Thr Thr Glu Lys Arg Ala Ala Glu Arg
                245                 250                 255

cat cca gaa aag tat cag ggt agt tct gtt tca aac ttg cat gtg gag      816
His Pro Glu Lys Tyr Gln Gly Ser Ser Val Ser Asn Leu His Val Glu
            260                 265                 270

cca tgt ggc aca aat act cat gcc agc tca tta cag cat gag aac agc      864
Pro Cys Gly Thr Asn Thr His Ala Ser Ser Leu Gln His Glu Asn Ser
        275                 280                 285

agt tta tta ctc act aaa gac aga atg aat gta gaa aag gct gaa ttc      912
Ser Leu Leu Leu Thr Lys Asp Arg Met Asn Val Glu Lys Ala Glu Phe
    290                 295                 300

tgt aat aaa agc aaa cag cct ggc tta gca agg agc caa cat aac aga      960
Cys Asn Lys Ser Lys Gln Pro Gly Leu Ala Arg Ser Gln His Asn Arg
305                 310                 315                 320

tgg gct gga agt aag gaa aca tgt aat gat agg cgg act ccc agc aca     1008
Trp Ala Gly Ser Lys Glu Thr Cys Asn Asp Arg Arg Thr Pro Ser Thr
                325                 330                 335

gaa aaa aag gta gat ctg aat gct gat ccc ctg tgt gag aga aaa gaa     1056
Glu Lys Lys Val Asp Leu Asn Ala Asp Pro Leu Cys Glu Arg Lys Glu
            340                 345                 350

tgg aat aag cag aaa ctg cca tgc tca gag aat cct aga gat act gaa     1104
Trp Asn Lys Gln Lys Leu Pro Cys Ser Glu Asn Pro Arg Asp Thr Glu
        355                 360                 365

gat gtt cct tgg ata aca cta aat agc agc att cag aaa gtt aat gag     1152
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Asp Val Pro Trp Ile Thr Leu Asn Ser Ser Ile Gln Lys Val Asn Glu
    370                 375                 380

tgg ttt tcc aga agt gat gaa ctg tta ggt tct gat gac tca cat gat     1200
Trp Phe Ser Arg Ser Asp Glu Leu Leu Gly Ser Asp Asp Ser His Asp
385                 390                 395                 400

ggg gag tct gaa tca aat gcc aaa gta gct gat gta ttg gac gtt cta     1248
Gly Glu Ser Glu Ser Asn Ala Lys Val Ala Asp Val Leu Asp Val Leu
                405                 410                 415

aat gag gta gat gaa tat tct ggt tct tca gag aaa ata gac tta ctg     1296
Asn Glu Val Asp Glu Tyr Ser Gly Ser Ser Glu Lys Ile Asp Leu Leu
            420                 425                 430

gcc agt gat cct cat gag gct tta ata tgt aaa agt gaa aga gtt cac     1344
Ala Ser Asp Pro His Glu Ala Leu Ile Cys Lys Ser Glu Arg Val His
        435                 440                 445

tcc aaa tca gta gag agt aat att gaa gac aaa ata ttt ggg aaa acc     1392
Ser Lys Ser Val Glu Ser Asn Ile Glu Asp Lys Ile Phe Gly Lys Thr
    450                 455                 460

tat cgg aag aag gca agc ctc ccc aac tta agc cat gta act gaa aat     1440
Tyr Arg Lys Lys Ala Ser Leu Pro Asn Leu Ser His Val Thr Glu Asn
465                 470                 475                 480

cta att ata gga gca ttt gtt act gag cca cag ata ata caa gag cgt     1488
Leu Ile Ile Gly Ala Phe Val Thr Glu Pro Gln Ile Ile Gln Glu Arg
                485                 490                 495

ccc ctc aca aat aaa tta aag cgt aaa agg aga cct aca tca ggc ctt     1536
Pro Leu Thr Asn Lys Leu Lys Arg Lys Arg Arg Pro Thr Ser Gly Leu
            500                 505                 510

cat cct gag gat ttt atc aag aaa gca gat ttg gca gtt caa aag act     1584
His Pro Glu Asp Phe Ile Lys Lys Ala Asp Leu Ala Val Gln Lys Thr
        515                 520                 525

cct gaa atg ata aat cag gga act aac caa acg gag cag aat ggt caa     1632
Pro Glu Met Ile Asn Gln Gly Thr Asn Gln Thr Glu Gln Asn Gly Gln
    530                 535                 540

gtg atg aat att act aat agt ggt cat gag aat aaa aca aaa ggt gat     1680
Val Met Asn Ile Thr Asn Ser Gly His Glu Asn Lys Thr Lys Gly Asp
545                 550                 555                 560

tct att cag aat gag aaa aat cct aac cca ata gaa tca ctc gaa aaa     1728
Ser Ile Gln Asn Glu Lys Asn Pro Asn Pro Ile Glu Ser Leu Glu Lys
                565                 570                 575

gaa tct gct ttc aaa acg aaa gct gaa cct ata agc agc agt ata agc     1776
Glu Ser Ala Phe Lys Thr Lys Ala Glu Pro Ile Ser Ser Ser Ile Ser
            580                 585                 590

aat atg gaa ctc gaa tta aat atc cac aat tca aaa gca cct aaa aag     1824
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Asn Met Glu Leu Glu Leu Asn Ile His Asn Ser Lys Ala Pro Lys Lys
        595                 600                 605

aat agg ctg agg agg aag tct tct acc agg cat att cat gcg ctt gaa     1872
Asn Arg Leu Arg Arg Lys Ser Ser Thr Arg His Ile His Ala Leu Glu
    610                 615                 620

cta gta gtc agt aga aat cta agc cca cct aat tgt act gaa ttg caa     1920
Leu Val Val Ser Arg Asn Leu Ser Pro Pro Asn Cys Thr Glu Leu Gln
625                 630                 635                 640

att gat agt tgt tct agc agt gaa gag ata aag aaa aaa aag tac aac     1968
Ile Asp Ser Cys Ser Ser Ser Glu Glu Ile Lys Lys Lys Lys Tyr Asn
                645                 650                 655

caa atg cca gtc agg cac agc aga aac cta caa ctc atg gaa ggt aaa     2016
Gln Met Pro Val Arg His Ser Arg Asn Leu Gln Leu Met Glu Gly Lys
            660                 665                 670

gaa cct gca act gga gcc aag aag agt aac aag cca aat gaa cag aca     2064
Glu Pro Ala Thr Gly Ala Lys Lys Ser Asn Lys Pro Asn Glu Gln Thr
        675                 680                 685

agt aaa aga cat gac agc gat act ttc cca gag ctg aag tta aca aat     2112
Ser Lys Arg His Asp Ser Asp Thr Phe Pro Glu Leu Lys Leu Thr Asn
    690                 695                 700

gca cct ggt tct ttt act aag tgt tca aat acc agt gaa ctt aaa gaa     2160
Ala Pro Gly Ser Phe Thr Lys Cys Ser Asn Thr Ser Glu Leu Lys Glu
705                 710                 715                 720

ttt gtc aat cct agc ctt cca aga gaa gaa aaa gaa gag aaa cta gaa     2208
Phe Val Asn Pro Ser Leu Pro Arg Glu Glu Lys Glu Glu Lys Leu Glu
                725                 730                 735

aca gtt aaa gtg tct aat aat gct gaa gac ccc aaa gat ctc atg tta     2256
Thr Val Lys Val Ser Asn Asn Ala Glu Asp Pro Lys Asp Leu Met Leu
            740                 745                 750

agt gga gaa agg gtt ttg caa act gaa aga tct gta gag agt agc agt     2304
Ser Gly Glu Arg Val Leu Gln Thr Glu Arg Ser Val Glu Ser Ser Ser
        755                 760                 765

att tca ttg gta cct ggt act gat tat ggc act cag gaa agt atc tcg     2352
Ile Ser Leu Val Pro Gly Thr Asp Tyr Gly Thr Gln Glu Ser Ile Ser
    770                 775                 780

tta ctg gaa gtt agc act cta ggg aag gca aaa aca gaa cca aat aaa     2400
Leu Leu Glu Val Ser Thr Leu Gly Lys Ala Lys Thr Glu Pro Asn Lys
785                 790                 795                 800

tgt gtg agt cag tgt gca gca ttt gaa aac ccc aag gga cta att cat     2448
Cys Val Ser Gln Cys Ala Ala Phe Glu Asn Pro Lys Gly Leu Ile His
                805                 810                 815

ggt tgt tcc aaa gat aat aga aat gac aca gaa ggc ttt aag tat cca     2496
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Gly Cys Ser Lys Asp Asn Arg Asn Asp Thr Glu Gly Phe Lys Tyr Pro
            820                 825                 830

ttg gga cat gaa gtt aac cac agt cgg gaa aca agc ata gaa atg gaa     2544
Leu Gly His Glu Val Asn His Ser Arg Glu Thr Ser Ile Glu Met Glu
        835                 840                 845

gaa agt gaa ctt gat gct cag tat ttg cag aat aca ttc aag gtt tca     2592
Glu Ser Glu Leu Asp Ala Gln Tyr Leu Gln Asn Thr Phe Lys Val Ser
    850                 855                 860

aag cgc cag tca ttt gct ccg ttt tca aat cca gga aat gca gaa gag     2640
Lys Arg Gln Ser Phe Ala Pro Phe Ser Asn Pro Gly Asn Ala Glu Glu
865                 870                 875                 880

gaa tgt gca aca ttc tct gcc cac tct ggg tcc tta aag aaa caa agt     2688
Glu Cys Ala Thr Phe Ser Ala His Ser Gly Ser Leu Lys Lys Gln Ser
                885                 890                 895

cca aaa gtc act ttt gaa tgt gaa caa aag gaa gaa aat caa gga aag     2736
Pro Lys Val Thr Phe Glu Cys Glu Gln Lys Glu Glu Asn Gln Gly Lys
            900                 905                 910

aat gag tct aat atc aag cct gta cag aca gtt aat atc act gca ggc     2784
Asn Glu Ser Asn Ile Lys Pro Val Gln Thr Val Asn Ile Thr Ala Gly
        915                 920                 925

ttt cct gtg gtt ggt cag aaa gat aag cca gtt gat aat gcc aaa tgt     2832
Phe Pro Val Val Gly Gln Lys Asp Lys Pro Val Asp Asn Ala Lys Cys
    930                 935                 940

agt atc aaa gga ggc tct agg ttt tgt cta tca tct cag ttc aga ggc     2880
Ser Ile Lys Gly Gly Ser Arg Phe Cys Leu Ser Ser Gln Phe Arg Gly
945                 950                 955                 960

aac gaa act gga ctc att act cca aat aaa cat gga ctt tta caa aac     2928
Asn Glu Thr Gly Leu Ile Thr Pro Asn Lys His Gly Leu Leu Gln Asn
                965                 970                 975

cca tat cgt ata cca cca ctt ttt ccc atc aag tca ttt gtt aaa act     2976
Pro Tyr Arg Ile Pro Pro Leu Phe Pro Ile Lys Ser Phe Val Lys Thr
            980                 985                 990

aaa tgt aag aaa aat ctg cta gag  gaa aac ttt gag gaa  cat tca atg   3024
Lys Cys Lys Lys Asn Leu Leu Glu  Glu Asn Phe Glu Glu  His Ser Met
        995                 1000                1005

tca cct  gaa aga gaa atg gga  aat gag aac att cca  agt aca gtg      3069
Ser Pro  Glu Arg Glu Met Gly  Asn Glu Asn Ile Pro  Ser Thr Val
    1010                1015                1020

agc aca  att agc cgt aat aac  att aga gaa aat gtt  ttt aaa gaa.     3114
Ser Thr  Ile Ser Arg Asn Asn  Ile Arg Glu Asn Val  Phe Lys Glu
    1025                1030                1035

gcc agc  tca agc aat att aat  gaa gta ggt tcc agt  act aat gaa      3159
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Ala Ser  Ser Ser Asn Ile Asn  Glu Val Gly Ser Ser  Thr Asn Glu
    1040                 1045                 1050

gtg ggc  tcc agt att aat gaa  ata ggt tcc agt gat  gaa aac att      3204
Val Gly  Ser Ser Ile Asn Glu  Ile Gly Ser Ser Asp  Glu Asn Ile
    1055                 1060                 1065

caa gca  gaa cta ggt aga aac  aga ggg cca aaa ttg  aat gct atg      3249
Gln Ala  Glu Leu Gly Arg Asn  Arg Gly Pro Lys Leu  Asn Ala Met
    1070                 1075                 1080

ctt aga  tta ggg gtt ttg caa  cct gag gtc tat aaa  caa agt ctt      3294
Leu Arg  Leu Gly Val Leu Gln  Pro Glu Val Tyr Lys  Gln Ser Leu
    1085                 1090                 1095

cct gga  agt aat tgt aag cat  cct gaa ata aaa aag  caa gaa tat      3339
Pro Gly  Ser Asn Cys Lys His  Pro Glu Ile Lys Lys  Gln Glu Tyr
    1100                 1105                 1110

gaa gaa  gta gtt cag act gtt  aat aca gat ttc tct  cca tat ctg      3384
Glu Glu  Val Val Gln Thr Val  Asn Thr Asp Phe Ser  Pro Tyr Leu
    1115                 1120                 1125

att tca  gat aac tta gaa cag  cct atg gga agt agt  cat gca tct      3429
Ile Ser  Asp Asn Leu Glu Gln  Pro Met Gly Ser Ser  His Ala Ser
    1130                 1135                 1140

cag gtt  tgt tct gag aca cct  gat gac ctg tta gat  gat ggt gaa      3474
Gln Val  Cys Ser Glu Thr Pro  Asp Asp Leu Leu Asp  Asp Gly Glu
    1145                 1150                 1155

ata aag  gaa gat act agt ttt  gct gaa aat gac att  aag gaa agt      3519
Ile Lys  Glu Asp Thr Ser Phe  Ala Glu Asn Asp Ile  Lys Glu Ser
    1160                 1165                 1170

tct gct  gtt ttt agc aaa agc  gtc cag aaa gga gag  ctt agc agg      3564
Ser Ala  Val Phe Ser Lys Ser  Val Gln Lys Gly Glu  Leu Ser Arg
    1175                 1180                 1185

agt cct  agc cct ttc acc cat  aca cat ttg gct cag  ggt tac cga      3609
Ser Pro  Ser Pro Phe Thr His  Thr His Leu Ala Gln  Gly Tyr Arg
    1190                 1195                 1200

aga ggg  gcc aag aaa tta gag  tcc tca gaa gag aac  tta tct agt      3654
Arg Gly  Ala Lys Lys Leu Glu  Ser Ser Glu Glu Asn  Leu Ser Ser
    1205                 1210                 1215

gag gat  gaa gag ctt ccc tgc  ttc caa cac ttg tta  ttt ggt aaa      3699
Glu Asp  Glu Glu Leu Pro Cys  Phe Gln His Leu Leu  Phe Gly Lys
    1220                 1225                 1230

gta aac  aat ata cct tct cag  tct act agg cat agc  acc gtt gct      3744
Val Asn  Asn Ile Pro Ser Gln  Ser Thr Arg His Ser  Thr Val Ala
    1235                 1240                 1245

acc gag  tgt ctg tct aag aac  aca gag gag aat tta  tta tca ttg      3789
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Thr Glu  Cys Leu Ser Lys Asn  Thr Glu Glu Asn Leu  Leu Ser Leu
    1250                 1255                 1260

aag aat  agc tta aat gac tgc  agt aac cag gta ata  ttg gca aag      3834
Lys Asn  Ser Leu Asn Asp Cys  Ser Asn Gln Val Ile  Leu Ala Lys
    1265                 1270                 1275

gca tct  cag gaa cat cac ctt  agt gag gaa aca aaa  tgt tct gct      3879
Ala Ser  Gln Glu His His Leu  Ser Glu Glu Thr Lys  Cys Ser Ala
    1280                 1285                 1290

agc ttg  ttt tct tca cag tgc  agt gaa ttg gaa gac  ttg act gca      3924
Ser Leu  Phe Ser Ser Gln Cys  Ser Glu Leu Glu Asp  Leu Thr Ala
    1295                 1300                 1305

aat aca  aac acc cag gat cct  ttc ttg att ggt tct  tcc aaa caa      3969
Asn Thr  Asn Thr Gln Asp Pro  Phe Leu Ile Gly Ser  Ser Lys Gln
    1310                 1315                 1320

atg agg  cat cag tct gaa agc  cag gga gtt ggt ctg  agt gac aag      4014
Met Arg  His Gln Ser Glu Ser  Gln Gly Val Gly Leu  Ser Asp Lys
    1325                 1330                 1335

gaa ttg  gtt tca gat gat gaa  gaa aga gga acg ggc  ttg gaa gaa      4059
Glu Leu  Val Ser Asp Asp Glu  Glu Arg Gly Thr Gly  Leu Glu Glu
    1340                 1345                 1350

aat aat  caa gaa gag caa agc  atg gat tca aac tta  ggt gaa gca      4104
Asn Asn  Gln Glu Glu Gln Ser  Met Asp Ser Asn Leu  Gly Glu Ala
    1355                 1360                 1365

gca tct  ggg tgt gag agt gaa  aca agc gtc tct gaa  gac tgc tca      4149
Ala Ser  Gly Cys Glu Ser Glu  Thr Ser Val Ser Glu  Asp Cys Ser
    1370                 1375                 1380

ggg cta  tcc tct cag agt gac  att tta acc act cag  cag agg gat      4194
Gly Leu  Ser Ser Gln Ser Asp  Ile Leu Thr Thr Gln  Gln Arg Asp
    1385                 1390                 1395

acc atg  caa cat aac ctg ata  aag ctc cag cag gaa  atg gct gaa      4239
Thr Met  Gln His Asn Leu Ile  Lys Leu Gln Gln Glu  Met Ala Glu
    1400                 1405                 1410

cta gaa  gct gtg tta gaa cag  cat ggg agc cag cct  tct aac agc      4284
Leu Glu  Ala Val Leu Glu Gln  His Gly Ser Gln Pro  Ser Asn Ser
    1415                 1420                 1425

tac cct  tcc atc ata agt gac  tct tct gcc ctt gag  gac ctg cga      4329
Tyr Pro  Ser Ile Ile Ser Asp  Ser Ser Ala Leu Glu  Asp Leu Arg
    1430                 1435                 1440

aat cca  gaa caa agc aca tca  gaa aaa gca gta tta  act tca cag      4374
Asn Pro  Glu Gln Ser Thr Ser  Glu Lys Ala Val Leu  Thr Ser Gln
    1445                 1450                 1455

aaa agt  agt gaa tac cct ata  agc cag aat cca gaa  ggc ctt tct      4419
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Lys Ser  Ser Glu Tyr Pro Ile  Ser Gln Asn Pro Glu  Gly Leu Ser
    1460                 1465                 1470

gct gac  aag ttt gag gtg tct  gca gat agt tct acc  agt aaa aat      4464
Ala Asp  Lys Phe Glu Val Ser  Ala Asp Ser Ser Thr  Ser Lys Asn
    1475                 1480                 1485

aaa gaa  cca gga gtg gaa agg  tca tcc cct tct aaa  tgc cca tca      4509
Lys Glu  Pro Gly Val Glu Arg  Ser Ser Pro Ser Lys  Cys Pro Ser
    1490                 1495                 1500

tta gat  gat agg tgg tac atg  cac agt tgc tct ggg  agt ctt cag      4554
Leu Asp  Asp Arg Trp Tyr Met  His Ser Cys Ser Gly  Ser Leu Gln
    1505                 1510                 1515

aat aga  aac tac cca tct caa  gag gag ctc att aag  gtt gtt gat      4599
Asn Arg  Asn Tyr Pro Ser Gln  Glu Glu Leu Ile Lys  Val Val Asp
    1520                 1525                 1530

gtg gag  gag caa cag ctg gaa  gag tct ggg cca cac  gat ttg acg      4644
Val Glu  Glu Gln Gln Leu Glu  Glu Ser Gly Pro His  Asp Leu Thr
    1535                 1540                 1545

gaa aca  tct tac ttg cca agg  caa gat cta gag gga  acc cct tac      4689
Glu Thr  Ser Tyr Leu Pro Arg  Gln Asp Leu Glu Gly  Thr Pro Tyr
    1550                 1555                 1560

ctg gaa  tct gga atc agc ctc  ttc tct gat gac cct  gaa tct gat      4734
Leu Glu  Ser Gly Ile Ser Leu  Phe Ser Asp Asp Pro  Glu Ser Asp
    1565                 1570                 1575

cct tct  gaa gac aga gcc cca  gag tca gct cgt gtt  ggc aac ata      4779
Pro Ser  Glu Asp Arg Ala Pro  Glu Ser Ala Arg Val  Gly Asn Ile
    1580                 1585                 1590

cca tct  tca acc tct gca ttg  aaa gtt ccc caa ttg  aaa gtt gca      4824
Pro Ser  Ser Thr Ser Ala Leu  Lys Val Pro Gln Leu  Lys Val Ala
    1595                 1600                 1605

gaa tct  gcc cag agt cca gct  gct gct cat act act  gat act gct      4869
Glu Ser  Ala Gln Ser Pro Ala  Ala Ala His Thr Thr  Asp Thr Ala
    1610                 1615                 1620

ggg tat  aat gca atg gaa gaa  agt gtg agc agg gag  aag cca gaa      4914
Gly Tyr  Asn Ala Met Glu Glu  Ser Val Ser Arg Glu  Lys Pro Glu
    1625                 1630                 1635

ttg aca  gct tca aca gaa agg  gtc aac aaa aga atg  tcc atg gtg      4959
Leu Thr  Ala Ser Thr Glu Arg  Val Asn Lys Arg Met  Ser Met Val
    1640                 1645                 1650

gtg tct  ggc ctg acc cca gaa  gaa ttt atg ctc gtg  tac aag ttt      5004
Val Ser  Gly Leu Thr Pro Glu  Glu Phe Met Leu Val  Tyr Lys Phe
    1655                 1660                 1665

gcc aga  aaa cac cac atc act  tta act aat cta att  act gaa gag      5049
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Ala Arg  Lys His His Ile Thr  Leu Thr Asn Leu Ile  Thr Glu Glu
    1670                 1675                 1680

act act  cat gtt gtt atg aaa  aca gat gct gag ttt  gtg tgt gaa      5094
Thr Thr  His Val Val Met Lys  Thr Asp Ala Glu Phe  Val Cys Glu
    1685                 1690                 1695

cgg aca  ctg aaa tat ttt cta  gga att gcg gga gga  aaa tgg gta      5139
Arg Thr  Leu Lys Tyr Phe Leu  Gly Ile Ala Gly Gly  Lys Trp Val
    1700                 1705                 1710

gtt agc  tat ttc tgg gtg acc  cag tct att aaa gaa  aga aaa atg      5184
Val Ser  Tyr Phe Trp Val Thr  Gln Ser Ile Lys Glu  Arg Lys Met
    1715                 1720                 1725

ctg aat  gag cat gat ttt gaa  gtc aga gga gat gtg  gtc aat gga      5229
Leu Asn  Glu His Asp Phe Glu  Val Arg Gly Asp Val  Val Asn Gly
    1730                 1735                 1740

aga aac  cac caa ggt cca aag  cga gca aga gaa tcc  cag gac aga      5274
Arg Asn  His Gln Gly Pro Lys  Arg Ala Arg Glu Ser  Gln Asp Arg
    1745                 1750                 1755

aag atc  ttc agg ggg cta gaa  atc tgt tgc tat ggg  ccc ttc acc      5319
Lys Ile  Phe Arg Gly Leu Glu  Ile Cys Cys Tyr Gly  Pro Phe Thr
    1760                 1765                 1770

aac atg  ccc aca gat caa ctg  gaa tgg atg gta cag  ctg tgt ggt      5364
Asn Met  Pro Thr Asp Gln Leu  Glu Trp Met Val Gln  Leu Cys Gly
    1775                 1780                 1785

gct tct  gtg gtg aag gag cct  ttc atc att cac cct  tgg cac agg      5409
Ala Ser  Val Val Lys Glu Pro  Phe Ile Ile His Pro  Trp His Arg
    1790                 1795                 1800

tgt cca  ccc aat tgt ggt tgt  gca gcc aga tgc ctg  gac aga gga      5454
Cys Pro  Pro Asn Cys Gly Cys  Ala Ala Arg Cys Leu  Asp Arg Gly
    1805                 1810                 1815

caa tgg  ctt cca tgc aat tgg  gca gat gtg tga                      5487
Gln Trp  Leu Pro Cys Asn Trp  Ala Asp Val
    1820                 1825
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<210> 23
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<212> PRT
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<400> 23

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1               5                  10                  15

Ala Met Gln Lys Ile Leu Glu Cys Pro Ile Cys Leu Glu Leu Ile Lys
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            20                  25                  30

Glu Pro Val Ser Thr Lys Cys Asp His Ile Phe Cys Lys Phe Cys Met
        35                  40                  45

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

Lys Asn Asp Ile Thr Lys Arg Ser Leu Gln Glu Ser Thr Arg Phe Ser
65                  70                  75                  80

Gln Leu Val Glu Glu Leu Leu Lys Ile Ile Cys Ala Phe Gln Leu Asp
                85                  90                  95

Thr Gly Leu Glu Tyr Ala Asn Ser Tyr Asn Phe Ala Lys Lys Glu Asn
            100                 105                 110

Asn Ser Pro Glu His Leu Lys Asp Glu Val Ser Ile Ile Gln Ser Met
        115                 120                 125

Gly Tyr Arg Asn Arg Ala Lys Arg Leu Leu Gln Ser Glu Pro Glu Asn
    130                 135                 140

Pro Ser Leu Gln Glu Thr Ser Leu Ser Val Gln Leu Ser Asn Leu Gly
145                 150                 155                 160

Thr Val Arg Thr Leu Arg Thr Lys Gln Arg Ile Gln Pro Gln Lys Thr
                165                 170                 175

Ser Val Tyr Ile Glu Leu Gly Ser Asp Ser Ser Glu Asp Thr Val Asn
            180                 185                 190

Lys Ala Thr Tyr Cys Ser Val Gly Asp Gln Glu Leu Leu Gln Ile Thr
        195                 200                 205

Pro Gln Gly Thr Arg Asp Glu Ile Ser Leu Asp Ser Ala Lys Lys Ala
    210                 215                 220

Ala Cys Glu Phe Ser Glu Thr Asp Val Thr Asn Thr Glu His His Gln
225                 230                 235                 240

Pro Ser Asn Asn Asp Leu Asn Thr Thr Glu Lys Arg Ala Ala Glu Arg
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245 250 255

His Pro Glu Lys Tyr Gln Gly Ser Ser Val Ser Asn Leu His Val Glu
260 265 270

Pro Cys Gly Thr Asn Thr His Ala Ser Ser Leu Gln His Glu Asn Ser
275 280 285

Ser Leu Leu Leu Thr Lys Asp Arg Met Asn Val Glu Lys Ala Glu Phe
290 295 300

Cys Asn Lys Ser Lys Gln Pro Gly Leu Ala Arg Ser Gln His Asn Arg
305 310 315 320

Trp Ala Gly Ser Lys Glu Thr Cys Asn Asp Arg Arg Thr Pro Ser Thr
325 330 335

Glu Lys Lys Val Asp Leu Asn Ala Asp Pro Leu Cys Glu Arg Lys Glu
340 345 350

Trp Asn Lys Gln Lys Leu Pro Cys Ser Glu Asn Pro Arg Asp Thr Glu
355 360 365

Asp Val Pro Trp Ile Thr Leu Asn Ser Ser Ile Gln Lys Val Asn Glu
370 375 380

Trp Phe Ser Arg Ser Asp Glu Leu Leu Gly Ser Asp Asp Ser His Asp
385 390 395 400

Gly Glu Ser Glu Ser Asn Ala Lys Val Ala Asp Val Leu Asp Val Leu
405 410 415

Asn Glu Val Asp Glu Tyr Ser Gly Ser Ser Glu Lys Ile Asp Leu Leu
420 425 430

Ala Ser Asp Pro His Glu Ala Leu Ile Cys Lys Ser Glu Arg Val His
435 440 445

Ser Lys Ser Val Glu Ser Asn Ile Glu Asp Lys Ile Phe Gly Lys Thr
450 455 460

Tyr Arg Lys Lys Ala Ser Leu Pro Asn Leu Ser His Val Thr Glu Asn

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465                 470                 475                 480

Leu Ile Ile Gly Ala Phe Val Thr Glu Pro Gln Ile Ile Gln Glu Arg
                485                 490                 495

Pro Leu Thr Asn Lys Leu Lys Arg Lys Arg Arg Pro Thr Ser Gly Leu
            500                 505                 510

His Pro Glu Asp Phe Ile Lys Lys Ala Asp Leu Ala Val Gln Lys Thr
        515                 520                 525

Pro Glu Met Ile Asn Gln Gly Thr Asn Gln Thr Glu Gln Asn Gly Gln
    530                 535                 540

Val Met Asn Ile Thr Asn Ser Gly His Glu Asn Lys Thr Lys Gly Asp
545                 550                 555                 560

Ser Ile Gln Asn Glu Lys Asn Pro Asn Pro Ile Glu Ser Leu Glu Lys
                565                 570                 575

Glu Ser Ala Phe Lys Thr Lys Ala Glu Pro Ile Ser Ser Ser Ile Ser
            580                 585                 590

Asn Met Glu Leu Glu Leu Asn Ile His Asn Ser Lys Ala Pro Lys Lys
        595                 600                 605

Asn Arg Leu Arg Arg Lys Ser Ser Thr Arg His Ile His Ala Leu Glu
    610                 615                 620

Leu Val Val Ser Arg Asn Leu Ser Pro Pro Asn Cys Thr Glu Leu Gln
625                 630                 635                 640

Ile Asp Ser Cys Ser Ser Ser Glu Glu Ile Lys Lys Lys Lys Tyr Asn
                645                 650                 655

Gln Met Pro Val Arg His Ser Arg Asn Leu Gln Leu Met Glu Gly Lys
            660                 665                 670

Glu Pro Ala Thr Gly Ala Lys Lys Ser Asn Lys Pro Asn Glu Gln Thr
        675                 680                 685

Ser Lys Arg His Asp Ser Asp Thr Phe Pro Glu Leu Lys Leu Thr Asn
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690 695 700

Ala Pro Gly Ser Phe Thr Lys Cys Ser Asn Thr Ser Glu Leu Lys Glu
705 710 715 720

Phe Val Asn Pro Ser Leu Pro Arg Glu Glu Lys Glu Glu Lys Leu Glu
725 730 735

Thr Val Lys Val Ser Asn Asn Ala Glu Asp Pro Lys Asp Leu Met Leu
740 745 750

Ser Gly Glu Arg Val Leu Gln Thr Glu Arg Ser Val Glu Ser Ser Ser
755 760 765

Ile Ser Leu Val Pro Gly Thr Asp Tyr Gly Thr Gln Glu Ser Ile Ser
770 775 780

Leu Leu Glu Val Ser Thr Leu Gly Lys Ala Lys Thr Glu Pro Asn Lys
785 790 795 800

Cys Val Ser Gln Cys Ala Ala Phe Glu Asn Pro Lys Gly Leu Ile His
805 810 815

Gly Cys Ser Lys Asp Asn Arg Asn Asp Thr Glu Gly Phe Lys Tyr Pro
820 825 830

Leu Gly His Glu Val Asn His Ser Arg Glu Thr Ser Ile Glu Met Glu
835 840 845

Glu Ser Glu Leu Asp Ala Gln Tyr Leu Gln Asn Thr Phe Lys Val Ser
850 855 860

Lys Arg Gln Ser Phe Ala Pro Phe Ser Asn Pro Gly Asn Ala Glu Glu
865 870 875 880

Glu Cys Ala Thr Phe Ser Ala His Ser Gly Ser Leu Lys Lys Gln Ser
885 890 895

Pro Lys Val Thr Phe Glu Cys Glu Gln Lys Glu Glu Asn Gln Gly Lys
900 905 910

Asn Glu Ser Asn Ile Lys Pro Val Gln Thr Val Asn Ile Thr Ala Gly

915 920 925

Phe Pro Val Val Gly Gln Lys Asp Lys Pro Val Asp Asn Ala Lys Cys
930 935 940

Ser Ile Lys Gly Gly Ser Arg Phe Cys Leu Ser Ser Gln Phe Arg Gly
945 950 955 960

Asn Glu Thr Gly Leu Ile Thr Pro Asn Lys His Gly Leu Leu Gln Asn
965 970 975

Pro Tyr Arg Ile Pro Pro Leu Phe Pro Ile Lys Ser Phe Val Lys Thr
980 985 990

Lys Cys Lys Lys Asn Leu Leu Glu Glu Asn Phe Glu Glu His Ser Met
995 1000 1005

Ser Pro Glu Arg Glu Met Gly Asn Glu Asn Ile Pro Ser Thr Val
1010 1015 1020

Ser Thr Ile Ser Arg Asn Asn Ile Arg Glu Asn Val Phe Lys Glu
1025 1030 1035

Ala Ser Ser Ser Asn Ile Asn Glu Val Gly Ser Ser Thr Asn Glu
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Val Gly Ser Ser Ile Asn Glu Ile Gly Ser Ser Asp Glu Asn Ile
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Gln Ala Glu Leu Gly Arg Asn Arg Gly Pro Lys Leu Asn Ala Met
1070 1075 1080

Leu Arg Leu Gly Val Leu Gln Pro Glu Val Tyr Lys Gln Ser Leu
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Pro Gly Ser Asn Cys Lys His Pro Glu Ile Lys Lys Gln Glu Tyr
1100 1105 1110

Glu Glu Val Val Gln Thr Val Asn Thr Asp Phe Ser Pro Tyr Leu
1115 1120 1125

Ile Ser Asp Asn Leu Glu Gln Pro Met Gly Ser Ser His Ala Ser

1130 1135 1140

Gln Val Cys Ser Glu Thr Pro Asp Asp Leu Leu Asp Asp Gly Glu
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Ile Lys Glu Asp Thr Ser Phe Ala Glu Asn Asp Ile Lys Glu Ser
1160 1165 1170

Ser Ala Val Phe Ser Lys Ser Val Gln Lys Gly Glu Leu Ser Arg
1175 1180 1185

Ser Pro Ser Pro Phe Thr His Thr His Leu Ala Gln Gly Tyr Arg
1190 1195 1200

Arg Gly Ala Lys Lys Leu Glu Ser Ser Glu Glu Asn Leu Ser Ser
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Glu Asp Glu Glu Leu Pro Cys Phe Gln His Leu Leu Phe Gly Lys
1220 1225 1230

Val Asn Asn Ile Pro Ser Gln Ser Thr Arg His Ser Thr Val Ala
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Thr Glu Cys Leu Ser Lys Asn Thr Glu Glu Asn Leu Leu Ser Leu
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Lys Asn Ser Leu Asn Asp Cys Ser Asn Gln Val Ile Leu Ala Lys
1265 1270 1275

Ala Ser Gln Glu His His Leu Ser Glu Glu Thr Lys Cys Ser Ala
1280 1285 1290

Ser Leu Phe Ser Ser Gln Cys Ser Glu Leu Glu Asp Leu Thr Ala
1295 1300 1305

Asn Thr Asn Thr Gln Asp Pro Phe Leu Ile Gly Ser Ser Lys Gln
1310 1315 1320

Met Arg His Gln Ser Glu Ser Gln Gly Val Gly Leu Ser Asp Lys
1325 1330 1335

Glu Leu Val Ser Asp Asp Glu Glu Arg Gly Thr Gly Leu Glu Glu

1340 1345 1350

Asn Asn Gln Glu Glu Gln Ser Met Asp Ser Asn Leu Gly Glu Ala
1355 1360 1365

Ala Ser Gly Cys Glu Ser Glu Thr Ser Val Ser Glu Asp Cys Ser
1370 1375 1380

Gly Leu Ser Ser Gln Ser Asp Ile Leu Thr Thr Gln Gln Arg Asp
1385 1390 1395

Thr Met Gln His Asn Leu Ile Lys Leu Gln Gln Glu Met Ala Glu
1400 1405 1410

Leu Glu Ala Val Leu Glu Gln His Gly Ser Gln Pro Ser Asn Ser
1415 1420 1425

Tyr Pro Ser Ile Ile Ser Asp Ser Ser Ala Leu Glu Asp Leu Arg
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Asn Pro Glu Gln Ser Thr Ser Glu Lys Ala Val Leu Thr Ser Gln
1445 1450 1455

Lys Ser Ser Glu Tyr Pro Ile Ser Gln Asn Pro Glu Gly Leu Ser
1460 1465 1470

Ala Asp Lys Phe Glu Val Ser Ala Asp Ser Ser Thr Ser Lys Asn
1475 1480 1485

Lys Glu Pro Gly Val Glu Arg Ser Ser Pro Ser Lys Cys Pro Ser
1490 1495 1500

Leu Asp Asp Arg Trp Tyr Met His Ser Cys Ser Gly Ser Leu Gln
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Asn Arg Asn Tyr Pro Ser Gln Glu Glu Leu Ile Lys Val Val Asp
1520 1525 1530

Val Glu Glu Gln Gln Leu Glu Glu Ser Gly Pro His Asp Leu Thr
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Glu Thr Ser Tyr Leu Pro Arg Gln Asp Leu Glu Gly Thr Pro Tyr

1550 1555 1560

Leu Glu Ser Gly Ile Ser Leu Phe Ser Asp Asp Pro Glu Ser Asp
1565 1570 1575

Pro Ser Glu Asp Arg Ala Pro Glu Ser Ala Arg Val Gly Asn Ile
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Pro Ser Ser Thr Ser Ala Leu Lys Val Pro Gln Leu Lys Val Ala
1595 1600 1605

Glu Ser Ala Gln Ser Pro Ala Ala Ala His Thr Thr Asp Thr Ala
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Gly Tyr Asn Ala Met Glu Glu Ser Val Ser Arg Glu Lys Pro Glu
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Leu Thr Ala Ser Thr Glu Arg Val Asn Lys Arg Met Ser Met Val
1640 1645 1650

Val Ser Gly Leu Thr Pro Glu Glu Phe Met Leu Val Tyr Lys Phe
1655 1660 1665

Ala Arg Lys His His Ile Thr Leu Thr Asn Leu Ile Thr Glu Glu
1670 1675 1680

Thr Thr His Val Val Met Lys Thr Asp Ala Glu Phe Val Cys Glu
1685 1690 1695

Arg Thr Leu Lys Tyr Phe Leu Gly Ile Ala Gly Gly Lys Trp Val
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Val Ser Tyr Phe Trp Val Thr Gln Ser Ile Lys Glu Arg Lys Met
1715 1720 1725

Leu Asn Glu His Asp Phe Glu Val Arg Gly Asp Val Val Asn Gly
1730 1735 1740

Arg Asn His Gln Gly Pro Lys Arg Ala Arg Glu Ser Gln Asp Arg
1745 1750 1755

Lys Ile Phe Arg Gly Leu Glu Ile Cys Cys Tyr Gly Pro Phe Thr

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    1760                1765                1770

Asn Met  Pro Thr Asp Gln Leu  Glu Trp Met Val Gln  Leu Cys Gly
    1775                1780                1785

Ala Ser  Val Val Lys Glu Pro  Phe Ile Ile His Pro  Trp His Arg
    1790                1795                1800

Cys Pro  Pro Asn Cys Gly Cys  Ala Ala Arg Cys Leu  Asp Arg Gly
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Gln Trp  Leu Pro Cys Asn Trp  Ala Asp Val
    1820                1825
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ttt cct tat aaa gct tac ccg tca cag ctt gct atg atg aat tct att      96
Phe Pro Tyr Lys Ala Tyr Pro Ser Gln Leu Ala Met Met Asn Ser Ile
            20                  25                  30

ctc aga gga tta aac agc aag caa cat tgt ttg ttg gag agt ccc aca     144
Leu Arg Gly Leu Asn Ser Lys Gln His Cys Leu Leu Glu Ser Pro Thr
        35                  40                  45

gga agt gga aaa agc tta gcc tta ctt tgt tct gct tta gca tgg caa     192
Gly Ser Gly Lys Ser Leu Ala Leu Leu Cys Ser Ala Leu Ala Trp Gln
    50                  55                  60

caa tct ctt agt ggg aaa cca gca gat gag ggc gta agt gaa aaa gct     240
Gln Ser Leu Ser Gly Lys Pro Ala Asp Glu Gly Val Ser Glu Lys Ala
65                  70                  75                  80

gaa gta caa ttg tca tgt tgt tgt gca tgc cat tca aag gat ttt aca     288
Glu Val Gln Leu Ser Cys Cys Cys Ala Cys His Ser Lys Asp Phe Thr
                85                  90                  95

aac aat gac atg aac caa gga act tca cgt cat ttc aac tat cca agc     336
Asn Asn Asp Met Asn Gln Gly Thr Ser Arg His Phe Asn Tyr Pro Ser
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                100                 105                 110

aca cca cct tct gaa aga aat ggc act tca tca act tgt caa gac tcc      384
Thr Pro Pro Ser Glu Arg Asn Gly Thr Ser Ser Thr Cys Gln Asp Ser
        115                 120                 125

cct gaa aaa acc act ctg gct gca aag tta tct gct aag aaa cag gca      432
Pro Glu Lys Thr Thr Leu Ala Ala Lys Leu Ser Ala Lys Lys Gln Ala
    130                 135                 140

tcc ata tac aga gat gaa aat gat gat ttt caa gta gag aag aaa aga      480
Ser Ile Tyr Arg Asp Glu Asn Asp Asp Phe Gln Val Glu Lys Lys Arg
145                 150                 155                 160

att cga ccc tta gaa act aca cag cag att aga aaa cgt cat tgc ttt      528
Ile Arg Pro Leu Glu Thr Thr Gln Gln Ile Arg Lys Arg His Cys Phe
                165                 170                 175

gga aca gaa gta cac aat ttg gat gca aaa gtt gat tca gga aag act      576
Gly Thr Glu Val His Asn Leu Asp Ala Lys Val Asp Ser Gly Lys Thr
            180                 185                 190

gta aaa ctc aac tct cca ctg gaa aag ata aac tcc ttt tcg cca cag      624
Val Lys Leu Asn Ser Pro Leu Glu Lys Ile Asn Ser Phe Ser Pro Gln
        195                 200                 205

aaa ccc cct ggc cac tgt tct agg tgc tgt tgt tct act aaa caa gga      672
Lys Pro Pro Gly His Cys Ser Arg Cys Cys Cys Ser Thr Lys Gln Gly
    210                 215                 220

aac agt caa gag tca tcg aat acc att aag aag gat cat aca ggg aaa      720
Asn Ser Gln Glu Ser Ser Asn Thr Ile Lys Lys Asp His Thr Gly Lys
225                 230                 235                 240

tcc aag ata ccc aaa ata tat ttt ggg aca cgc aca cac aag cag att      768
Ser Lys Ile Pro Lys Ile Tyr Phe Gly Thr Arg Thr His Lys Gln Ile
                245                 250                 255

gct cag att act aga gag ctc cgg agg acg gca tat tca ggg gtt cca      816
Ala Gln Ile Thr Arg Glu Leu Arg Arg Thr Ala Tyr Ser Gly Val Pro
            260                 265                 270

atg act att ctt tcc agc agg gat cat act tgt gtc cat cct gag gta      864
Met Thr Ile Leu Ser Ser Arg Asp His Thr Cys Val His Pro Glu Val
        275                 280                 285

gtc ggt aac ttc aac aga aat gag aag tgc atg gaa ttg cta gat ggg      912
Val Gly Asn Phe Asn Arg Asn Glu Lys Cys Met Glu Leu Leu Asp Gly
    290                 295                 300

aaa aac gga aaa tcc tgc tat ttt tat cat gga gtt cat aaa att agt      960
Lys Asn Gly Lys Ser Cys Tyr Phe Tyr His Gly Val His Lys Ile Ser
305                 310                 315                 320

gat cag cac aca tta cag act ttc caa ggg atg tgc aaa gcc tgg gat     1008
Asp Gln His Thr Leu Gln Thr Phe Gln Gly Met Cys Lys Ala Trp Asp
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                325                 330                 335

ata gaa gaa ctt gtc agc ctg ggg aag aaa cta aag gcc tgt cca tat     1056
Ile Glu Glu Leu Val Ser Leu Gly Lys Lys Leu Lys Ala Cys Pro Tyr
            340                 345                 350

tac aca gcc cga gaa cta ata caa gat gct gac atc ata ttt tgt ccc     1104
Tyr Thr Ala Arg Glu Leu Ile Gln Asp Ala Asp Ile Ile Phe Cys Pro
        355                 360                 365

tac aac tat ctt cta gat gca caa ata agg gaa agt atg gat tta aat     1152
Tyr Asn Tyr Leu Leu Asp Ala Gln Ile Arg Glu Ser Met Asp Leu Asn
    370                 375                 380

ctg aaa gaa cag gtt gtc att tta gat gaa gct cat aac atc gag gac     1200
Leu Lys Glu Gln Val Val Ile Leu Asp Glu Ala His Asn Ile Glu Asp
385                 390                 395                 400

tgt gct cgg gaa tca gca agt tac agt gta aca gaa gtt cag ctt cgg     1248
Cys Ala Arg Glu Ser Ala Ser Tyr Ser Val Thr Glu Val Gln Leu Arg
                405                 410                 415

ttt gct cgg gat gaa cta gat agt atg gtc aac aat aat ata agg aag     1296
Phe Ala Arg Asp Glu Leu Asp Ser Met Val Asn Asn Asn Ile Arg Lys
            420                 425                 430

aaa gat cat gaa ccc cta cga gct gtg tgc tgt agc ctc att aat tgg     1344
Lys Asp His Glu Pro Leu Arg Ala Val Cys Cys Ser Leu Ile Asn Trp
        435                 440                 445

tta gaa gca aac gct gaa tat ctt gta gaa aga gat tat gaa tca gct     1392
Leu Glu Ala Asn Ala Glu Tyr Leu Val Glu Arg Asp Tyr Glu Ser Ala
    450                 455                 460

tgt aaa ata tgg agt gga aat gaa atg ctc tta act tta cac aaa atg     1440
Cys Lys Ile Trp Ser Gly Asn Glu Met Leu Leu Thr Leu His Lys Met
465                 470                 475                 480

ggt atc acc act gct act ttt ccc att ttg cag gga cat ttt tct gct     1488
Gly Ile Thr Thr Ala Thr Phe Pro Ile Leu Gln Gly His Phe Ser Ala
                485                 490                 495

gtt ctt caa aaa gag gaa aaa atc tca cca att tat ggt aaa gag gag     1536
Val Leu Gln Lys Glu Glu Lys Ile Ser Pro Ile Tyr Gly Lys Glu Glu
            500                 505                 510

gca aga gaa gta cct gtt att agt gca tca act caa ata atg ctt aaa     1584
Ala Arg Glu Val Pro Val Ile Ser Ala Ser Thr Gln Ile Met Leu Lys
        515                 520                 525

gga ctt ttt atg gta ctt gac tat ctt ttt agg caa aat agc aga ttt     1632
Gly Leu Phe Met Val Leu Asp Tyr Leu Phe Arg Gln Asn Ser Arg Phe
    530                 535                 540

gca gat gat tat aaa att gcg att caa cag act tac tcc tgg aca aat     1680
Ala Asp Asp Tyr Lys Ile Ala Ile Gln Gln Thr Tyr Ser Trp Thr Asn
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545                 550                 555                 560

cag att gat att tca gac aaa aat ggg ttg ttg gtt cta cca aaa aat     1728
Gln Ile Asp Ile Ser Asp Lys Asn Gly Leu Leu Val Leu Pro Lys Asn
                565                 570                 575

aag aaa cgt tca cga cag aaa act gca gtt cat gtg cta aac ttt tgg     1776
Lys Lys Arg Ser Arg Gln Lys Thr Ala Val His Val Leu Asn Phe Trp
            580                 585                 590

tgc tta aat cca gct gtg gcc ttt tca gat att aat ggc aaa gtt cag     1824
Cys Leu Asn Pro Ala Val Ala Phe Ser Asp Ile Asn Gly Lys Val Gln
        595                 600                 605

acc att gtt ttg aca tct ggt aca tta tca cca atg aaa tcc ttt tcg     1872
Thr Ile Val Leu Thr Ser Gly Thr Leu Ser Pro Met Lys Ser Phe Ser
    610                 615                 620

tca gaa ctt ggt gtt aca ttt act atc cag ctg gag gct aat cat atc     1920
Ser Glu Leu Gly Val Thr Phe Thr Ile Gln Leu Glu Ala Asn His Ile
625                 630                 635                 640

att aaa aat tca cag gtt tgg gtt ggt acc att ggg tca ggc ccc aag     1968
Ile Lys Asn Ser Gln Val Trp Val Gly Thr Ile Gly Ser Gly Pro Lys
                645                 650                 655

ggt cgg aat ctc tgt gct acc ttc cag aat act gaa aca ttt gag ttc     2016
Gly Arg Asn Leu Cys Ala Thr Phe Gln Asn Thr Glu Thr Phe Glu Phe
            660                 665                 670

caa gat gaa gtg gga gca ctt ttg tta tct gtg tgc cag act gtg agc     2064
Gln Asp Glu Val Gly Ala Leu Leu Leu Ser Val Cys Gln Thr Val Ser
        675                 680                 685

caa gga att ttg tgt ttc ttg cca tct tac aag tta tta gaa aaa tta     2112
Gln Gly Ile Leu Cys Phe Leu Pro Ser Tyr Lys Leu Leu Glu Lys Leu
    690                 695                 700

aaa gaa cgt tgg ctc tct act ggt tta tgg cat aat ctg gag ttg gtg     2160
Lys Glu Arg Trp Leu Ser Thr Gly Leu Trp His Asn Leu Glu Leu Val
705                 710                 715                 720

aag aca gtc att gta gaa cca cag gga gga gaa aaa aca aat ttt gat     2208
Lys Thr Val Ile Val Glu Pro Gln Gly Gly Glu Lys Thr Asn Phe Asp
                725                 730                 735

gaa tta ctg cag gtg tac tat gac gca atc aaa tac aaa gga gag aaa     2256
Glu Leu Leu Gln Val Tyr Tyr Asp Ala Ile Lys Tyr Lys Gly Glu Lys
            740                 745                 750

gat gga gct ctc ctg gta gca gtt tgt cgt ggt aaa gtg agt gag ggt     2304
Asp Gly Ala Leu Leu Val Ala Val Cys Arg Gly Lys Val Ser Glu Gly
        755                 760                 765

ctg gat ttc tca gat gac aat gcc cgt gct gtc ata aca ata gga att     2352
Leu Asp Phe Ser Asp Asp Asn Ala Arg Ala Val Ile Thr Ile Gly Ile
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    770                 775                 780

cct ttt cca aat gtg aaa gat cta cag gtt gaa cta aaa cga caa tac     2400
Pro Phe Pro Asn Val Lys Asp Leu Gln Val Glu Leu Lys Arg Gln Tyr
785                 790                 795                 800

aat gac cac cat tca aaa ttg aga ggt ctt cta cct ggc cgt cag tgg     2448
Asn Asp His His Ser Lys Leu Arg Gly Leu Leu Pro Gly Arg Gln Trp
                805                 810                 815

tat gaa att caa gca tac agg gcc tta aac cag gcc ctt ggt aga tgt     2496
Tyr Glu Ile Gln Ala Tyr Arg Ala Leu Asn Gln Ala Leu Gly Arg Cys
            820                 825                 830

att aga cac aga aat gat tgg gga gct ctt att cta gtg gat gat cgc     2544
Ile Arg His Arg Asn Asp Trp Gly Ala Leu Ile Leu Val Asp Asp Arg
        835                 840                 845

ttt agg aat aac cca agt cgc tat ata tct gga ctt tct aaa tgg gta     2592
Phe Arg Asn Asn Pro Ser Arg Tyr Ile Ser Gly Leu Ser Lys Trp Val
    850                 855                 860

cgg cag cag att cag cac cat tca acc ttt gaa agt gca ctg gag tcc     2640
Arg Gln Gln Ile Gln His His Ser Thr Phe Glu Ser Ala Leu Glu Ser
865                 870                 875                 880

ttg gct gaa ttt tcc aaa aag cat caa aaa gtt ctt aat gta tcc ata     2688
Leu Ala Glu Phe Ser Lys Lys His Gln Lys Val Leu Asn Val Ser Ile
                885                 890                 895

aag gac aga acc aat ata cag gac aat gag tct aca ctt gaa gtg acc     2736
Lys Asp Arg Thr Asn Ile Gln Asp Asn Glu Ser Thr Leu Glu Val Thr
            900                 905                 910

tct tta aag tac agt acc cca cct tat tta ctg gaa gca gca agt cat     2784
Ser Leu Lys Tyr Ser Thr Pro Pro Tyr Leu Leu Glu Ala Ala Ser His
        915                 920                 925

cta tca cca gaa aat ttt gtg gaa gat gaa gca aag ata tgt gtc cag     2832
Leu Ser Pro Glu Asn Phe Val Glu Asp Glu Ala Lys Ile Cys Val Gln
    930                 935                 940

gaa cta cag tgt cct aaa att att acc aaa aat tca cct cta cca agt     2880
Glu Leu Gln Cys Pro Lys Ile Ile Thr Lys Asn Ser Pro Leu Pro Ser
945                 950                 955                 960

agc att atc tcc aga aag gag aaa aat gat cca gta ttc ctg gaa gaa     2928
Ser Ile Ile Ser Arg Lys Glu Lys Asn Asp Pro Val Phe Leu Glu Glu
                965                 970                 975

gca ggg aaa gca gaa aaa att gtg att tcc aga tcc aca agc cca act     2976
Ala Gly Lys Ala Glu Lys Ile Val Ile Ser Arg Ser Thr Ser Pro Thr
            980                 985                 990

ttc aac aaa caa aca aag aga gtt  agc tgg tca agc ttt  aat tct ttg   3024
Phe Asn Lys Gln Thr Lys Arg Val  Ser Trp Ser Ser Phe  Asn Ser Leu
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        995                 1000                1005

gga cag  tat ttt act ggt aaa  ata ccg aag gca aca  cct gag ctc      3069
Gly Gln  Tyr Phe Thr Gly Lys  Ile Pro Lys Ala Thr  Pro Glu Leu
    1010                1015                1020

ggg tca  tca gag aat agt gcc  tct agt cct ccc cgt  ttc aaa aca      3114
Gly Ser  Ser Glu Asn Ser Ala  Ser Ser Pro Pro Arg  Phe Lys Thr
    1025                1030                1035

gag aag  atg gaa agt aaa act  gtt ttg ccc ttc act  gat aaa tgt      3159
Glu Lys  Met Glu Ser Lys Thr  Val Leu Pro Phe Thr  Asp Lys Cys
    1040                1045                1050

gaa tcc  tca aat ctg aca gta  aac aca tcg ttt gga  tca tgc cct      3204
Glu Ser  Ser Asn Leu Thr Val  Asn Thr Ser Phe Gly  Ser Cys Pro
    1055                1060                1065

caa tca  gaa acc att att tca  tca tta aag att gat  gcc acc ctt      3249
Gln Ser  Glu Thr Ile Ile Ser  Ser Leu Lys Ile Asp  Ala Thr Leu
    1070                1075                1080

act aga  aaa aat cat tct gaa  cat ccg ctc tgt tct  gaa gaa gcc      3294
Thr Arg  Lys Asn His Ser Glu  His Pro Leu Cys Ser  Glu Glu Ala
    1085                1090                1095

ctg gat  cca gac att gaa ttg  tct cta gta agt gaa  gaa gat aaa      3339
Leu Asp  Pro Asp Ile Glu Leu  Ser Leu Val Ser Glu  Glu Asp Lys
    1100                1105                1110

cag tcc  act tca aat aga gat  ttt gaa aca gaa gca  gaa gat gaa      3384
Gln Ser  Thr Ser Asn Arg Asp  Phe Glu Thr Glu Ala  Glu Asp Glu
    1115                1120                1125

tct atc  tat ttt aca cct gaa  ctt tac gat cct gaa  gat aca gat      3429
Ser Ile  Tyr Phe Thr Pro Glu  Leu Tyr Asp Pro Glu  Asp Thr Asp
    1130                1135                1140

gaa gaa  aaa aat gac cta gct  gaa act gat aga gga  aat aga ttg      3474
Glu Glu  Lys Asn Asp Leu Ala  Glu Thr Asp Arg Gly  Asn Arg Leu
    1145                1150                1155

gct aac  aat tca gat tgc att  tta gct aaa gac ctt  ttt gaa att      3519
Ala Asn  Asn Ser Asp Cys Ile  Leu Ala Lys Asp Leu  Phe Glu Ile
    1160                1165                1170

aga act  ata aaa gaa gta gat  tca gcc aga gaa gtg  aaa gct gag      3564
Arg Thr  Ile Lys Glu Val Asp  Ser Ala Arg Glu Val  Lys Ala Glu
    1175                1180                1185

gat tgc  ata gat aca aag ttg  aat gga att ctg cat  att gaa gaa      3609
Asp Cys  Ile Asp Thr Lys Leu  Asn Gly Ile Leu His  Ile Glu Glu
    1190                1195                1200

agt aaa  att gat gac att gat  ggt aat gta aaa aca  act tgg ata      3654
Ser Lys  Ile Asp Asp Ile Asp  Gly Asn Val Lys Thr  Thr Trp Ile
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    1205                1210                1215

aat gaa  ctg gaa ctg gga aaa  act cat gaa ata gaa  ata aag aac      3699
Asn Glu  Leu Glu Leu Gly Lys  Thr His Glu Ile Glu  Ile Lys Asn
    1220                1225                1230

ttt aaa  cca tct cct tcc aaa  aat aaa ggc atg ttt  cct ggt ttt      3744
Phe Lys  Pro Ser Pro Ser Lys  Asn Lys Gly Met Phe  Pro Gly Phe
    1235                1240                1245

aag taa                                                          3750
Lys
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            20                  25                  30

Leu Arg Gly Leu Asn Ser Lys Gln His Cys Leu Leu Glu Ser Pro Thr
        35                  40                  45

Gly Ser Gly Lys Ser Leu Ala Leu Leu Cys Ser Ala Leu Ala Trp Gln
    50                  55                  60

Gln Ser Leu Ser Gly Lys Pro Ala Asp Glu Gly Val Ser Glu Lys Ala
65                  70                  75                  80

Glu Val Gln Leu Ser Cys Cys Cys Ala Cys His Ser Lys Asp Phe Thr
                85                  90                  95

Asn Asn Asp Met Asn Gln Gly Thr Ser Arg His Phe Asn Tyr Pro Ser
            100                 105                 110

Thr Pro Pro Ser Glu Arg Asn Gly Thr Ser Ser Thr Cys Gln Asp Ser
        115                 120                 125

Pro Glu Lys Thr Thr Leu Ala Ala Lys Leu Ser Ala Lys Lys Gln Ala
    130                 135                 140
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Ser Ile Tyr Arg Asp Glu Asn Asp Asp Phe Gln Val Glu Lys Lys Arg
145 150 155 160

Ile Arg Pro Leu Glu Thr Thr Gln Gln Ile Arg Lys Arg His Cys Phe
165 170 175

Gly Thr Glu Val His Asn Leu Asp Ala Lys Val Asp Ser Gly Lys Thr
180 185 190

Val Lys Leu Asn Ser Pro Leu Glu Lys Ile Asn Ser Phe Ser Pro Gln
195 200 205

Lys Pro Pro Gly His Cys Ser Arg Cys Cys Cys Ser Thr Lys Gln Gly
210 215 220

Asn Ser Gln Glu Ser Ser Asn Thr Ile Lys Lys Asp His Thr Gly Lys
225 230 235 240

Ser Lys Ile Pro Lys Ile Tyr Phe Gly Thr Arg Thr His Lys Gln Ile
245 250 255

Ala Gln Ile Thr Arg Glu Leu Arg Arg Thr Ala Tyr Ser Gly Val Pro
260 265 270

Met Thr Ile Leu Ser Ser Arg Asp His Thr Cys Val His Pro Glu Val
275 280 285

Val Gly Asn Phe Asn Arg Asn Glu Lys Cys Met Glu Leu Leu Asp Gly
290 295 300

Lys Asn Gly Lys Ser Cys Tyr Phe Tyr His Gly Val His Lys Ile Ser
305 310 315 320

Asp Gln His Thr Leu Gln Thr Phe Gln Gly Met Cys Lys Ala Trp Asp
325 330 335

Ile Glu Glu Leu Val Ser Leu Gly Lys Lys Leu Lys Ala Cys Pro Tyr
340 345 350

Tyr Thr Ala Arg Glu Leu Ile Gln Asp Ala Asp Ile Ile Phe Cys Pro
355 360 365

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Tyr Asn Tyr Leu Leu Asp Ala Gln Ile Arg Glu Ser Met Asp Leu Asn
    370                 375                 380

Leu Lys Glu Gln Val Val Ile Leu Asp Glu Ala His Asn Ile Glu Asp
385                 390                 395                 400

Cys Ala Arg Glu Ser Ala Ser Tyr Ser Val Thr Glu Val Gln Leu Arg
                405                 410                 415

Phe Ala Arg Asp Glu Leu Asp Ser Met Val Asn Asn Asn Ile Arg Lys
            420                 425                 430

Lys Asp His Glu Pro Leu Arg Ala Val Cys Cys Ser Leu Ile Asn Trp
        435                 440                 445

Leu Glu Ala Asn Ala Glu Tyr Leu Val Glu Arg Asp Tyr Glu Ser Ala
    450                 455                 460

Cys Lys Ile Trp Ser Gly Asn Glu Met Leu Leu Thr Leu His Lys Met
465                 470                 475                 480

Gly Ile Thr Thr Ala Thr Phe Pro Ile Leu Gln Gly His Phe Ser Ala
                485                 490                 495

Val Leu Gln Lys Glu Glu Lys Ile Ser Pro Ile Tyr Gly Lys Glu Glu
            500                 505                 510

Ala Arg Glu Val Pro Val Ile Ser Ala Ser Thr Gln Ile Met Leu Lys
        515                 520                 525

Gly Leu Phe Met Val Leu Asp Tyr Leu Phe Arg Gln Asn Ser Arg Phe
    530                 535                 540

Ala Asp Asp Tyr Lys Ile Ala Ile Gln Gln Thr Tyr Ser Trp Thr Asn
545                 550                 555                 560

Gln Ile Asp Ile Ser Asp Lys Asn Gly Leu Leu Val Leu Pro Lys Asn
                565                 570                 575

Lys Lys Arg Ser Arg Gln Lys Thr Ala Val His Val Leu Asn Phe Trp
            580                 585                 590
```

```
Cys Leu Asn Pro Ala Val Ala Phe Ser Asp Ile Asn Gly Lys Val Gln
        595                 600                 605

Thr Ile Val Leu Thr Ser Gly Thr Leu Ser Pro Met Lys Ser Phe Ser
    610                 615                 620

Ser Glu Leu Gly Val Thr Phe Thr Ile Gln Leu Glu Ala Asn His Ile
625                 630                 635                 640

Ile Lys Asn Ser Gln Val Trp Val Gly Thr Ile Gly Ser Gly Pro Lys
                645                 650                 655

Gly Arg Asn Leu Cys Ala Thr Phe Gln Asn Thr Glu Thr Phe Glu Phe
            660                 665                 670

Gln Asp Glu Val Gly Ala Leu Leu Leu Ser Val Cys Gln Thr Val Ser
        675                 680                 685

Gln Gly Ile Leu Cys Phe Leu Pro Ser Tyr Lys Leu Leu Glu Lys Leu
    690                 695                 700

Lys Glu Arg Trp Leu Ser Thr Gly Leu Trp His Asn Leu Glu Leu Val
705                 710                 715                 720

Lys Thr Val Ile Val Glu Pro Gln Gly Gly Glu Lys Thr Asn Phe Asp
                725                 730                 735

Glu Leu Leu Gln Val Tyr Tyr Asp Ala Ile Lys Tyr Lys Gly Glu Lys
            740                 745                 750

Asp Gly Ala Leu Leu Val Ala Val Cys Arg Gly Lys Val Ser Glu Gly
        755                 760                 765

Leu Asp Phe Ser Asp Asp Asn Ala Arg Ala Val Ile Thr Ile Gly Ile
    770                 775                 780

Pro Phe Pro Asn Val Lys Asp Leu Gln Val Glu Leu Lys Arg Gln Tyr
785                 790                 795                 800

Asn Asp His His Ser Lys Leu Arg Gly Leu Leu Pro Gly Arg Gln Trp
                805                 810                 815
```

Tyr Glu Ile Gln Ala Tyr Arg Ala Leu Asn Gln Ala Leu Gly Arg Cys
820 825 830

Ile Arg His Arg Asn Asp Trp Gly Ala Leu Ile Leu Val Asp Asp Arg
835 840 845

Phe Arg Asn Asn Pro Ser Arg Tyr Ile Ser Gly Leu Ser Lys Trp Val
850 855 860

Arg Gln Gln Ile Gln His His Ser Thr Phe Glu Ser Ala Leu Glu Ser
865 870 875 880

Leu Ala Glu Phe Ser Lys Lys His Gln Lys Val Leu Asn Val Ser Ile
885 890 895

Lys Asp Arg Thr Asn Ile Gln Asp Asn Glu Ser Thr Leu Glu Val Thr
900 905 910

Ser Leu Lys Tyr Ser Thr Pro Pro Tyr Leu Leu Glu Ala Ala Ser His
915 920 925

Leu Ser Pro Glu Asn Phe Val Glu Asp Glu Ala Lys Ile Cys Val Gln
930 935 940

Glu Leu Gln Cys Pro Lys Ile Ile Thr Lys Asn Ser Pro Leu Pro Ser
945 950 955 960

Ser Ile Ile Ser Arg Lys Glu Lys Asn Asp Pro Val Phe Leu Glu Glu
965 970 975

Ala Gly Lys Ala Glu Lys Ile Val Ile Ser Arg Ser Thr Ser Pro Thr
980 985 990

Phe Asn Lys Gln Thr Lys Arg Val Ser Trp Ser Ser Phe Asn Ser Leu
995 1000 1005

Gly Gln Tyr Phe Thr Gly Lys Ile Pro Lys Ala Thr Pro Glu Leu
1010 1015 1020

Gly Ser Ser Glu Asn Ser Ala Ser Ser Pro Pro Arg Phe Lys Thr
1025 1030 1035

```
Glu Lys  Met Glu Ser Lys Thr  Val Leu Pro Phe Thr  Asp Lys Cys
    1040                1045                1050

Glu Ser  Ser Asn Leu Thr Val  Asn Thr Ser Phe Gly  Ser Cys Pro
    1055                1060                1065

Gln Ser  Glu Thr Ile Ile Ser  Ser Leu Lys Ile Asp  Ala Thr Leu
    1070                1075                1080

Thr Arg  Lys Asn His Ser Glu  His Pro Leu Cys Ser  Glu Glu Ala
    1085                1090                1095

Leu Asp  Pro Asp Ile Glu Leu  Ser Leu Val Ser Glu  Glu Asp Lys
    1100                1105                1110

Gln Ser  Thr Ser Asn Arg Asp  Phe Glu Thr Glu Ala  Glu Asp Glu
    1115                1120                1125

Ser Ile  Tyr Phe Thr Pro Glu  Leu Tyr Asp Pro Glu  Asp Thr Asp
    1130                1135                1140

Glu Glu  Lys Asn Asp Leu Ala  Glu Thr Asp Arg Gly  Asn Arg Leu
    1145                1150                1155

Ala Asn  Asn Ser Asp Cys Ile  Leu Ala Lys Asp Leu  Phe Glu Ile
    1160                1165                1170

Arg Thr  Ile Lys Glu Val Asp  Ser Ala Arg Glu Val  Lys Ala Glu
    1175                1180                1185

Asp Cys  Ile Asp Thr Lys Leu  Asn Gly Ile Leu His  Ile Glu Glu
    1190                1195                1200

Ser Lys  Ile Asp Asp Ile Asp  Gly Asn Val Lys Thr  Thr Trp Ile
    1205                1210                1215

Asn Glu  Leu Glu Leu Gly Lys  Thr His Glu Ile Glu  Ile Lys Asn
    1220                1225                1230

Phe Lys  Pro Ser Pro Ser Lys  Asn Lys Gly Met Phe  Pro Gly Phe
    1235                1240                1245
```

Lys

<210> 26
<211> 528
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (1)..(528)

<400> 26

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cat caa aaa gtt ctt aat gta tcc ata aag gac aga acc aat ata cag       48
His Gln Lys Val Leu Asn Val Ser Ile Lys Asp Arg Thr Asn Ile Gln
1               5                   10                  15

gac aat gag tct aca ctt gaa gtg acc tct tta aag tac agt acc cca       96
Asp Asn Glu Ser Thr Leu Glu Val Thr Ser Leu Lys Tyr Ser Thr Pro
            20                  25                  30

cct tat tta ctg gaa gca gca agt cat cta tca cca gaa aat ttt gtg      144
Pro Tyr Leu Leu Glu Ala Ala Ser His Leu Ser Pro Glu Asn Phe Val
        35                  40                  45

gaa gat gaa gca aag ata tgt gtc cag gaa cta cag tgt cct aaa att      192
Glu Asp Glu Ala Lys Ile Cys Val Gln Glu Leu Gln Cys Pro Lys Ile
    50                  55                  60

att acc aaa aat tca cct cta cca agt agc att atc tcc aga aag gag      240
Ile Thr Lys Asn Ser Pro Leu Pro Ser Ser Ile Ile Ser Arg Lys Glu
65                  70                  75                  80

aaa aat gat cca gta ttc ctg gaa gaa gca ggg aaa gca gaa aaa att      288
Lys Asn Asp Pro Val Phe Leu Glu Glu Ala Gly Lys Ala Glu Lys Ile
                85                  90                  95

gtg att tcc aga tcc aca agc cca act ttc aac aaa caa aca aag aga      336
Val Ile Ser Arg Ser Thr Ser Pro Thr Phe Asn Lys Gln Thr Lys Arg
            100                 105                 110

gtt agc tgg tca agc ttt aat tct ttg gga cag tat ttt act ggt aaa      384
Val Ser Trp Ser Ser Phe Asn Ser Leu Gly Gln Tyr Phe Thr Gly Lys
        115                 120                 125

ata ccg aag gca aca cct gag ctc ggg tca tca gag aat agt gcc tct      432
Ile Pro Lys Ala Thr Pro Glu Leu Gly Ser Ser Glu Asn Ser Ala Ser
    130                 135                 140

agt cct ccc cgt ttc aaa aca gag aag atg gaa agt aaa act gtt ttg      480
Ser Pro Pro Arg Phe Lys Thr Glu Lys Met Glu Ser Lys Thr Val Leu
145                 150                 155                 160
```

```
ccc ttc act gat aaa tgt gaa tcc tca aat ctg aca gta aac aca tcg      528
Pro Phe Thr Asp Lys Cys Glu Ser Ser Asn Leu Thr Val Asn Thr Ser
                165                 170                 175
```

<210> 27
<211> 176
<212> PRT
<213> Homo sapiens

<400> 27

```
His Gln Lys Val Leu Asn Val Ser Ile Lys Asp Arg Thr Asn Ile Gln
1               5                   10                  15

Asp Asn Glu Ser Thr Leu Glu Val Thr Ser Leu Lys Tyr Ser Thr Pro
            20                  25                  30

Pro Tyr Leu Leu Glu Ala Ala Ser His Leu Ser Pro Glu Asn Phe Val
        35                  40                  45

Glu Asp Glu Ala Lys Ile Cys Val Gln Glu Leu Gln Cys Pro Lys Ile
    50                  55                  60

Ile Thr Lys Asn Ser Pro Leu Pro Ser Ser Ile Ile Ser Arg Lys Glu
65                  70                  75                  80

Lys Asn Asp Pro Val Phe Leu Glu Glu Ala Gly Lys Ala Glu Lys Ile
                85                  90                  95

Val Ile Ser Arg Ser Thr Ser Pro Thr Phe Asn Lys Gln Thr Lys Arg
            100                 105                 110

Val Ser Trp Ser Ser Phe Asn Ser Leu Gly Gln Tyr Phe Thr Gly Lys
        115                 120                 125

Ile Pro Lys Ala Thr Pro Glu Leu Gly Ser Ser Glu Asn Ser Ala Ser
    130                 135                 140

Ser Pro Pro Arg Phe Lys Thr Glu Lys Met Glu Ser Lys Thr Val Leu
145                 150                 155                 160

Pro Phe Thr Asp Lys Cys Glu Ser Ser Asn Leu Thr Val Asn Thr Ser
                165                 170                 175
```

<210> 28
<211> 30
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (1)..(30)

<400> 28
tcc aga tcc aca agc cca act ttc aac aaa 30
Ser Arg Ser Thr Ser Pro Thr Phe Asn Lys
1 5 10

<210> 29
<211> 10
<212> PRT
<213> Homo sapiens

<400> 29

Ser Arg Ser Thr Ser Pro Thr Phe Asn Lys
1 5 10

<210> 30
<211> 1249
<212> PRT
<213> Homo sapiens

<400> 30

Met Ser Ser Met Trp Ser Glu Tyr Thr Ile Gly Gly Val Lys Ile Tyr
1 5 10 15

Phe Pro Tyr Lys Ala Tyr Pro Ser Gln Leu Ala Met Met Asn Ser Ile
20 25 30

Leu Arg Gly Leu Asn Ser Lys Gln His Cys Leu Leu Glu Ser Pro Thr
35 40 45

Gly Ser Gly Lys Ser Leu Ala Leu Leu Cys Ser Ala Leu Ala Trp Gln
50 55 60

Gln Ser Leu Ser Gly Lys Pro Ala Asp Glu Gly Val Ser Glu Lys Ala
65 70 75 80

Glu Val Gln Leu Ser Cys Cys Cys Ala Cys His Ser Lys Asp Phe Thr

85 90 95

Asn Asn Asp Met Asn Gln Gly Thr Ser Arg His Phe Asn Tyr Pro Ser
100 105 110

Thr Pro Pro Ser Glu Arg Asn Gly Thr Ser Ser Thr Cys Gln Asp Ser
115 120 125

Pro Glu Lys Thr Thr Leu Ala Ala Lys Leu Ser Ala Lys Lys Gln Ala
130 135 140

Ser Ile Tyr Arg Asp Glu Asn Asp Asp Phe Gln Val Glu Lys Lys Arg
145 150 155 160

Ile Arg Pro Leu Glu Thr Thr Gln Gln Ile Arg Lys Arg His Cys Phe
165 170 175

Gly Thr Glu Val His Asn Leu Asp Ala Lys Val Asp Ser Gly Lys Thr
180 185 190

Val Lys Leu Asn Ser Pro Leu Glu Lys Ile Asn Ser Phe Ser Pro Gln
195 200 205

Lys Pro Pro Gly His Cys Ser Arg Cys Cys Cys Ser Thr Lys Gln Gly
210 215 220

Asn Ser Gln Glu Ser Ser Asn Thr Ile Lys Lys Asp His Thr Gly Lys
225 230 235 240

Ser Lys Ile Pro Lys Ile Tyr Phe Gly Thr Arg Thr His Lys Gln Ile
245 250 255

Ala Gln Ile Thr Arg Glu Leu Arg Arg Thr Ala Tyr Ser Gly Val Pro
260 265 270

Met Thr Ile Leu Ser Ser Arg Asp His Thr Cys Val His Pro Glu Val
275 280 285

Val Gly Asn Phe Asn Arg Asn Glu Lys Cys Met Glu Leu Leu Asp Gly
290 295 300

Lys Asn Gly Lys Ser Cys Tyr Phe Tyr His Gly Val His Lys Ile Ser

305 310 315 320

Asp Gln His Thr Leu Gln Thr Phe Gln Gly Met Cys Lys Ala Trp Asp
325 330 335

Ile Glu Glu Leu Val Ser Leu Gly Lys Lys Leu Lys Ala Cys Pro Tyr
340 345 350

Tyr Thr Ala Arg Glu Leu Ile Gln Asp Ala Asp Ile Ile Phe Cys Pro
355 360 365

Tyr Asn Tyr Leu Leu Asp Ala Gln Ile Arg Glu Ser Met Asp Leu Asn
370 375 380

Leu Lys Glu Gln Val Val Ile Leu Asp Glu Ala His Asn Ile Glu Asp
385 390 395 400

Cys Ala Arg Glu Ser Ala Ser Tyr Ser Val Thr Glu Val Gln Leu Arg
405 410 415

Phe Ala Arg Asp Glu Leu Asp Ser Met Val Asn Asn Asn Ile Arg Lys
420 425 430

Lys Asp His Glu Pro Leu Arg Ala Val Cys Cys Ser Leu Ile Asn Trp
435 440 445

Leu Glu Ala Asn Ala Glu Tyr Leu Val Glu Arg Asp Tyr Glu Ser Ala
450 455 460

Cys Lys Ile Trp Ser Gly Asn Glu Met Leu Leu Thr Leu His Lys Met
465 470 475 480

Gly Ile Thr Thr Ala Thr Phe Pro Ile Leu Gln Gly His Phe Ser Ala
485 490 495

Val Leu Gln Lys Glu Glu Lys Ile Ser Pro Ile Tyr Gly Lys Glu Glu
500 505 510

Ala Arg Glu Val Pro Val Ile Ser Ala Ser Thr Gln Ile Met Leu Lys
515 520 525

Gly Leu Phe Met Val Leu Asp Tyr Leu Phe Arg Gln Asn Ser Arg Phe

530 535 540

Ala Asp Asp Tyr Lys Ile Ala Ile Gln Gln Thr Tyr Ser Trp Thr Asn
545 550 555 560

Gln Ile Asp Ile Ser Asp Lys Asn Gly Leu Leu Val Leu Pro Lys Asn
565 570 575

Lys Lys Arg Ser Arg Gln Lys Thr Ala Val His Val Leu Asn Phe Trp
580 585 590

Cys Leu Asn Pro Ala Val Ala Phe Ser Asp Ile Asn Gly Lys Val Gln
595 600 605

Thr Ile Val Leu Thr Ser Gly Thr Leu Ser Pro Met Lys Ser Phe Ser
610 615 620

Ser Glu Leu Gly Val Thr Phe Thr Ile Gln Leu Glu Ala Asn His Ile
625 630 635 640

Ile Lys Asn Ser Gln Val Trp Val Gly Thr Ile Gly Ser Gly Pro Lys
645 650 655

Gly Arg Asn Leu Cys Ala Thr Phe Gln Asn Thr Glu Thr Phe Glu Phe
660 665 670

Gln Asp Glu Val Gly Ala Leu Leu Leu Ser Val Cys Gln Thr Val Ser
675 680 685

Gln Gly Ile Leu Cys Phe Leu Pro Ser Tyr Lys Leu Leu Glu Lys Leu
690 695 700

Lys Glu Arg Trp Leu Ser Thr Gly Leu Trp His Asn Leu Glu Leu Val
705 710 715 720

Lys Thr Val Ile Val Glu Pro Gln Gly Gly Glu Lys Thr Asn Phe Asp
725 730 735

Glu Leu Leu Gln Val Tyr Tyr Asp Ala Ile Lys Tyr Lys Gly Glu Lys
740 745 750

Asp Gly Ala Leu Leu Val Ala Val Cys Arg Gly Lys Val Ser Glu Gly

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        755                 760                 765

Leu Asp Phe Ser Asp Asp Asn Ala Arg Ala Val Ile Thr Ile Gly Ile
    770                 775                 780

Pro Phe Pro Asn Val Lys Asp Leu Gln Val Glu Leu Lys Arg Gln Tyr
785                 790                 795                 800

Asn Asp His His Ser Lys Leu Arg Gly Leu Leu Pro Gly Arg Gln Trp
                805                 810                 815

Tyr Glu Ile Gln Ala Tyr Arg Ala Leu Asn Gln Ala Leu Gly Arg Cys
            820                 825                 830

Ile Arg His Arg Asn Asp Trp Gly Ala Leu Ile Leu Val Asp Asp Arg
        835                 840                 845

Phe Arg Asn Asn Pro Ser Arg Tyr Ile Ser Gly Leu Ser Lys Trp Val
    850                 855                 860

Arg Gln Gln Ile Gln His His Ser Thr Phe Glu Ser Ala Leu Glu Ser
865                 870                 875                 880

Leu Ala Glu Phe Ser Lys Lys His Gln Lys Val Leu Asn Val Ser Ile
                885                 890                 895

Lys Asp Arg Thr Asn Ile Gln Asp Asn Glu Ser Thr Leu Glu Val Thr
            900                 905                 910

Ser Leu Lys Tyr Ser Thr Pro Pro Tyr Leu Leu Glu Ala Ala Ser His
        915                 920                 925

Leu Ser Pro Glu Asn Phe Val Glu Asp Glu Ala Lys Ile Cys Val Gln
    930                 935                 940

Glu Leu Gln Cys Pro Lys Ile Ile Thr Lys Asn Ser Pro Leu Pro Ser
945                 950                 955                 960

Ser Ile Ile Ser Arg Lys Glu Lys Asn Asp Pro Val Phe Leu Glu Glu
                965                 970                 975

Ala Gly Lys Ala Glu Lys Ile Val Ile Ser Arg Ser Thr Ser Pro Thr
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980 985 990

Ala Asn Lys Gln Thr Lys Arg Val Ser Trp Ser Ser Phe Asn Ser Leu
995 1000 1005

Gly Gln Tyr Phe Thr Gly Lys Ile Pro Lys Ala Thr Pro Glu Leu
1010 1015 1020

Gly Ser Ser Glu Asn Ser Ala Ser Ser Pro Pro Arg Phe Lys Thr
1025 1030 1035

Glu Lys Met Glu Ser Lys Thr Val Leu Pro Phe Thr Asp Lys Cys
1040 1045 1050

Glu Ser Ser Asn Leu Thr Val Asn Thr Ser Phe Gly Ser Cys Pro
1055 1060 1065

Gln Ser Glu Thr Ile Ile Ser Ser Leu Lys Ile Asp Ala Thr Leu
1070 1075 1080

Thr Arg Lys Asn His Ser Glu His Pro Leu Cys Ser Glu Glu Ala
1085 1090 1095

Leu Asp Pro Asp Ile Glu Leu Ser Leu Val Ser Glu Glu Asp Lys
1100 1105 1110

Gln Ser Thr Ser Asn Arg Asp Phe Glu Thr Glu Ala Glu Asp Glu
1115 1120 1125

Ser Ile Tyr Phe Thr Pro Glu Leu Tyr Asp Pro Glu Asp Thr Asp
1130 1135 1140

Glu Glu Lys Asn Asp Leu Ala Glu Thr Asp Arg Gly Asn Arg Leu
1145 1150 1155

Ala Asn Asn Ser Asp Cys Ile Leu Ala Lys Asp Leu Phe Glu Ile
1160 1165 1170

Arg Thr Ile Lys Glu Val Asp Ser Ala Arg Glu Val Lys Ala Glu
1175 1180 1185

Asp Cys Ile Asp Thr Lys Leu Asn Gly Ile Leu His Ile Glu Glu

1190 1195 1200

Ser Lys Ile Asp Asp Ile Asp Gly Asn Val Lys Thr Thr Trp Ile
1205 1210 1215

Asn Glu Leu Glu Leu Gly Lys Thr His Glu Ile Glu Ile Lys Asn
1220 1225 1230

Phe Lys Pro Ser Pro Ser Lys Asn Lys Gly Met Phe Pro Gly Phe
1235 1240 1245

Lys

<210> 31
<211> 2274
<212> DNA
<213> HOMO SAPIENS

<220>
<221> CDS
<222> (1)..(2274)

<400> 31
atg gct gct gga caa aac ctc caa agt tct gaa aga tca gaa atg ata 48
Met Ala Ala Gly Gln Asn Leu Gln Ser Ser Glu Arg Ser Glu Met Ile
1 5 10 15

gct acc tgg agt cca gct gta cgg aca ctg agg aat att act aat aat 96
Ala Thr Trp Ser Pro Ala Val Arg Thr Leu Arg Asn Ile Thr Asn Asn
20 25 30

gct gac att cag cag atg aac cgg cca tca aat gta gca cat atc tta 144
Ala Asp Ile Gln Gln Met Asn Arg Pro Ser Asn Val Ala His Ile Leu
35 40 45

cag act ctt tca gca cct acg aaa aat tta gaa cag cag gtg aat cac 192
Gln Thr Leu Ser Ala Pro Thr Lys Asn Leu Glu Gln Gln Val Asn His
50 55 60

agc cag cag gga cat aca aat gcc aat gca gtg ctg ttt agc caa gtg 240
Ser Gln Gln Gly His Thr Asn Ala Asn Ala Val Leu Phe Ser Gln Val
65 70 75 80

aaa gtg act cca gag aca cac atg cta cag cag cag cag cag gcc cag 288
Lys Val Thr Pro Glu Thr His Met Leu Gln Gln Gln Gln Gln Ala Gln
85 90 95

cag cag cag cag cag cac ccg gtt tta cac ctt cag ccc cag cag ata 336
Gln Gln Gln Gln Gln His Pro Val Leu His Leu Gln Pro Gln Gln Ile

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                100                 105                 110

atg cag ctc cag cag cag cag cag cag cag atc tct cag caa cct tac      384
Met Gln Leu Gln Gln Gln Gln Gln Gln Gln Ile Ser Gln Gln Pro Tyr
        115                 120                 125

ccc cag cag ccg ccg cat cca ttt tca cag caa cag cag cag cag cag      432
Pro Gln Gln Pro Pro His Pro Phe Ser Gln Gln Gln Gln Gln Gln Gln
    130                 135                 140

caa gcc cat ccg cat cag ttt tca cag caa cag cta cag ttt cca cag      480
Gln Ala His Pro His Gln Phe Ser Gln Gln Gln Leu Gln Phe Pro Gln
145                 150                 155                 160

caa cag ttg cat cct cca cag cag ctg cat cgc cct cag cag cag ctc      528
Gln Gln Leu His Pro Pro Gln Gln Leu His Arg Pro Gln Gln Gln Leu
                165                 170                 175

cag ccc ttt cag cag cag cat gcc ctg cag cag cag ttc cat cag ctg      576
Gln Pro Phe Gln Gln Gln His Ala Leu Gln Gln Gln Phe His Gln Leu
            180                 185                 190

cag cag cac cag ctc cag cag cag cag ctc gcc cag ctc cag cag cag      624
Gln Gln His Gln Leu Gln Gln Gln Gln Leu Ala Gln Leu Gln Gln Gln
        195                 200                 205

cac agc ctg ctc cag cag cag cag caa cag cag att cag cag cag cag      672
His Ser Leu Leu Gln Gln Gln Gln Gln Gln Gln Ile Gln Gln Gln Gln
    210                 215                 220

ctc cag cgc atg cac cag cag cag cag cag cag cag atg caa agt cag      720
Leu Gln Arg Met His Gln Gln Gln Gln Gln Gln Gln Met Gln Ser Gln
225                 230                 235                 240

aca gcg cca cac ttg agt cag acg tca cag gcg ctg cag cat cag gtt      768
Thr Ala Pro His Leu Ser Gln Thr Ser Gln Ala Leu Gln His Gln Val
                245                 250                 255

cca cct cag cag ccc ccg cag cag cag cag caa cag cag cca cca cca      816
Pro Pro Gln Gln Pro Pro Gln Gln Gln Gln Gln Gln Gln Pro Pro Pro
            260                 265                 270

tcg cct cag cag cat cag ctt ttt gga cat gat cca gca gtg gag att      864
Ser Pro Gln Gln His Gln Leu Phe Gly His Asp Pro Ala Val Glu Ile
        275                 280                 285

cca gaa gaa ggc ttc tta ttg gga tgt gtg ttt gca att gcg gat tat      912
Pro Glu Glu Gly Phe Leu Leu Gly Cys Val Phe Ala Ile Ala Asp Tyr
    290                 295                 300

cca gag cag atg tct gat aag caa ctg ctg gcc acc tgg aaa agg ata      960
Pro Glu Gln Met Ser Asp Lys Gln Leu Leu Ala Thr Trp Lys Arg Ile
305                 310                 315                 320

atc cag gca cat ggc ggc act gtt gac ccc acc ttc acg agt cga tgc     1008
Ile Gln Ala His Gly Gly Thr Val Asp Pro Thr Phe Thr Ser Arg Cys
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                325                 330                 335

acg cac ctt ctc tgt gag agt caa gtc agc agc gcg tat gca cag gca     1056
Thr His Leu Leu Cys Glu Ser Gln Val Ser Ser Ala Tyr Ala Gln Ala
            340                 345                 350

ata aga gaa aga aag aga tgt gtt act gca cac tgg tta aac aca gtc     1104
Ile Arg Glu Arg Lys Arg Cys Val Thr Ala His Trp Leu Asn Thr Val
        355                 360                 365

tta aag aag aag aaa atg gta ccg ccg cac cga gcc ctt cac ttc cca     1152
Leu Lys Lys Lys Lys Met Val Pro Pro His Arg Ala Leu His Phe Pro
    370                 375                 380

gtg gcc ttc cca cca gga gga aag cca tgt tca cag cat att att tct     1200
Val Ala Phe Pro Pro Gly Gly Lys Pro Cys Ser Gln His Ile Ile Ser
385                 390                 395                 400

gtg act gga ttt gtt gat agt gac aga gat gac cta aaa tta atg gct     1248
Val Thr Gly Phe Val Asp Ser Asp Arg Asp Asp Leu Lys Leu Met Ala
                405                 410                 415

tat ttg gca ggt gcc aaa tat acg ggt tat cta tgc cgc agc aac aca     1296
Tyr Leu Ala Gly Ala Lys Tyr Thr Gly Tyr Leu Cys Arg Ser Asn Thr
            420                 425                 430

gtc ctc atc tgt aaa gaa cca act ggt tta aag tat gaa aaa gcc aaa     1344
Val Leu Ile Cys Lys Glu Pro Thr Gly Leu Lys Tyr Glu Lys Ala Lys
        435                 440                 445

gag tgg agg ata ccc tgt gtc aac gcc cag tgg ctt ggc gac att ctt     1392
Glu Trp Arg Ile Pro Cys Val Asn Ala Gln Trp Leu Gly Asp Ile Leu
    450                 455                 460

ctg gga aac ttt gag gca ctg agg cag att cag tat agt cgc tac acg     1440
Leu Gly Asn Phe Glu Ala Leu Arg Gln Ile Gln Tyr Ser Arg Tyr Thr
465                 470                 475                 480

gca ttc agt ctg cag gat cca ttt gcc cct acc cag cat tta gtt tta     1488
Ala Phe Ser Leu Gln Asp Pro Phe Ala Pro Thr Gln His Leu Val Leu
                485                 490                 495

aat ctt tta gat gct tgg aga gtt ccc tta aaa gtg tct gca gag ttg     1536
Asn Leu Leu Asp Ala Trp Arg Val Pro Leu Lys Val Ser Ala Glu Leu
            500                 505                 510

ttg atg agt ata aga cta cct ccc aaa ctg aaa cag aat gaa gta gct     1584
Leu Met Ser Ile Arg Leu Pro Pro Lys Leu Lys Gln Asn Glu Val Ala
        515                 520                 525

aat gtc cag cct tct tcc aaa aga gcc aga att gaa gac gta cca cct     1632
Asn Val Gln Pro Ser Ser Lys Arg Ala Arg Ile Glu Asp Val Pro Pro
    530                 535                 540

ccc act aaa aag cta act cca gaa ttg acc cct ttt gtg ctt ttc act     1680
Pro Thr Lys Lys Leu Thr Pro Glu Leu Thr Pro Phe Val Leu Phe Thr
```

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545                 550                 555                 560

gga ttc gag cct gtc cag gtt caa cag tat att aag aag ctc tac att     1728
Gly Phe Glu Pro Val Gln Val Gln Gln Tyr Ile Lys Lys Leu Tyr Ile
                565                 570                 575

ctt ggt gga gag gtt gcg gag tct gca cag aag tgc aca cac ctc att     1776
Leu Gly Gly Glu Val Ala Glu Ser Ala Gln Lys Cys Thr His Leu Ile
            580                 585                 590

gcc agc aaa gtg act cgc acc gtg aag ttc ctg acg gcg att tct gtc     1824
Ala Ser Lys Val Thr Arg Thr Val Lys Phe Leu Thr Ala Ile Ser Val
        595                 600                 605

gtg aag cac ata gtg acg cca gag tgg ctg gaa gaa tgc ttc agg tgt     1872
Val Lys His Ile Val Thr Pro Glu Trp Leu Glu Glu Cys Phe Arg Cys
    610                 615                 620

cag aag ttc att gat gag cag aac tac att ctc cga gat gct gag gca     1920
Gln Lys Phe Ile Asp Glu Gln Asn Tyr Ile Leu Arg Asp Ala Glu Ala
625                 630                 635                 640

gaa gta ctt ttc tct ttc agc ttg gaa gaa tcc tta aaa cgg gca cac     1968
Glu Val Leu Phe Ser Phe Ser Leu Glu Glu Ser Leu Lys Arg Ala His
                645                 650                 655

gtt tct cca ctc ttt aag gca aaa tat ttt tac atc aca cct gga atc     2016
Val Ser Pro Leu Phe Lys Ala Lys Tyr Phe Tyr Ile Thr Pro Gly Ile
            660                 665                 670

tgc cca agt ctt tcc act atg aag gca atc gta gag tgt gca gga gga     2064
Cys Pro Ser Leu Ser Thr Met Lys Ala Ile Val Glu Cys Ala Gly Gly
        675                 680                 685

aag gtg tta tcc aag cag cca tct ttc cgg aag ctc atg gag cac aag     2112
Lys Val Leu Ser Lys Gln Pro Ser Phe Arg Lys Leu Met Glu His Lys
    690                 695                 700

cag aac tcg agt ttg tcg gaa ata att tta ata tcc tgt gaa aat gac     2160
Gln Asn Ser Ser Leu Ser Glu Ile Ile Leu Ile Ser Cys Glu Asn Asp
705                 710                 715                 720

ctt cat tta tgc cga gaa tat ttt gcc aga ggc ata gat gtt cac aat     2208
Leu His Leu Cys Arg Glu Tyr Phe Ala Arg Gly Ile Asp Val His Asn
                725                 730                 735

gca gag ttc gtt ctg act gga gtg ctc act caa acg ctg gac tat gaa     2256
Ala Glu Phe Val Leu Thr Gly Val Leu Thr Gln Thr Leu Asp Tyr Glu
            740                 745                 750

tca tat aag ttt aac tga                                             2274
Ser Tyr Lys Phe Asn
        755
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<210> 32

<211> 757
<212> PRT
<213> HOMO SAPIENS

<400> 32

Met Ala Ala Gly Gln Asn Leu Gln Ser Ser Glu Arg Ser Glu Met Ile
1 5 10 15

Ala Thr Trp Ser Pro Ala Val Arg Thr Leu Arg Asn Ile Thr Asn Asn
20 25 30

Ala Asp Ile Gln Gln Met Asn Arg Pro Ser Asn Val Ala His Ile Leu
35 40 45

Gln Thr Leu Ser Ala Pro Thr Lys Asn Leu Glu Gln Gln Val Asn His
50 55 60

Ser Gln Gln Gly His Thr Asn Ala Asn Ala Val Leu Phe Ser Gln Val
65 70 75 80

Lys Val Thr Pro Glu Thr His Met Leu Gln Gln Gln Gln Gln Ala Gln
85 90 95

Gln Gln Gln Gln Gln His Pro Val Leu His Leu Gln Pro Gln Gln Ile
100 105 110

Met Gln Leu Gln Gln Gln Gln Gln Gln Gln Ile Ser Gln Gln Pro Tyr
115 120 125

Pro Gln Gln Pro Pro His Pro Phe Ser Gln Gln Gln Gln Gln Gln Gln
130 135 140

Gln Ala His Pro His Gln Phe Ser Gln Gln Gln Leu Gln Phe Pro Gln
145 150 155 160

Gln Gln Leu His Pro Pro Gln Gln Leu His Arg Pro Gln Gln Gln Leu
165 170 175

Gln Pro Phe Gln Gln Gln His Ala Leu Gln Gln Gln Phe His Gln Leu
180 185 190

Gln Gln His Gln Leu Gln Gln Gln Gln Leu Ala Gln Leu Gln Gln Gln
195 200 205

His Ser Leu Leu Gln Gln Gln Gln Gln Gln Gln Ile Gln Gln Gln Gln
210 215 220

Leu Gln Arg Met His Gln Gln Gln Gln Gln Gln Gln Met Gln Ser Gln
225 230 235 240

Thr Ala Pro His Leu Ser Gln Thr Ser Gln Ala Leu Gln His Gln Val
245 250 255

Pro Pro Gln Gln Pro Pro Gln Gln Gln Gln Gln Gln Gln Pro Pro Pro
260 265 270

Ser Pro Gln Gln His Gln Leu Phe Gly His Asp Pro Ala Val Glu Ile
275 280 285

Pro Glu Glu Gly Phe Leu Leu Gly Cys Val Phe Ala Ile Ala Asp Tyr
290 295 300

Pro Glu Gln Met Ser Asp Lys Gln Leu Leu Ala Thr Trp Lys Arg Ile
305 310 315 320

Ile Gln Ala His Gly Gly Thr Val Asp Pro Thr Phe Thr Ser Arg Cys
325 330 335

Thr His Leu Leu Cys Glu Ser Gln Val Ser Ser Ala Tyr Ala Gln Ala
340 345 350

Ile Arg Glu Arg Lys Arg Cys Val Thr Ala His Trp Leu Asn Thr Val
355 360 365

Leu Lys Lys Lys Lys Met Val Pro Pro His Arg Ala Leu His Phe Pro
370 375 380

Val Ala Phe Pro Pro Gly Gly Lys Pro Cys Ser Gln His Ile Ile Ser
385 390 395 400

Val Thr Gly Phe Val Asp Ser Asp Arg Asp Asp Leu Lys Leu Met Ala
405 410 415

Tyr Leu Ala Gly Ala Lys Tyr Thr Gly Tyr Leu Cys Arg Ser Asn Thr
420 425 430

Val Leu Ile Cys Lys Glu Pro Thr Gly Leu Lys Tyr Glu Lys Ala Lys
435 440 445

Glu Trp Arg Ile Pro Cys Val Asn Ala Gln Trp Leu Gly Asp Ile Leu
450 455 460

Leu Gly Asn Phe Glu Ala Leu Arg Gln Ile Gln Tyr Ser Arg Tyr Thr
465 470 475 480

Ala Phe Ser Leu Gln Asp Pro Phe Ala Pro Thr Gln His Leu Val Leu
485 490 495

Asn Leu Leu Asp Ala Trp Arg Val Pro Leu Lys Val Ser Ala Glu Leu
500 505 510

Leu Met Ser Ile Arg Leu Pro Pro Lys Leu Lys Gln Asn Glu Val Ala
515 520 525

Asn Val Gln Pro Ser Ser Lys Arg Ala Arg Ile Glu Asp Val Pro Pro
530 535 540

Pro Thr Lys Lys Leu Thr Pro Glu Leu Thr Pro Phe Val Leu Phe Thr
545 550 555 560

Gly Phe Glu Pro Val Gln Val Gln Gln Tyr Ile Lys Lys Leu Tyr Ile
565 570 575

Leu Gly Gly Glu Val Ala Glu Ser Ala Gln Lys Cys Thr His Leu Ile
580 585 590

Ala Ser Lys Val Thr Arg Thr Val Lys Phe Leu Thr Ala Ile Ser Val
595 600 605

Val Lys His Ile Val Thr Pro Glu Trp Leu Glu Glu Cys Phe Arg Cys
610 615 620

Gln Lys Phe Ile Asp Glu Gln Asn Tyr Ile Leu Arg Asp Ala Glu Ala
625 630 635 640

Glu Val Leu Phe Ser Phe Ser Leu Glu Glu Ser Leu Lys Arg Ala His
645 650 655

Val Ser Pro Leu Phe Lys Ala Lys Tyr Phe Tyr Ile Thr Pro Gly Ile
660 665 670

Cys Pro Ser Leu Ser Thr Met Lys Ala Ile Val Glu Cys Ala Gly Gly
675 680 685

Lys Val Leu Ser Lys Gln Pro Ser Phe Arg Lys Leu Met Glu His Lys
690 695 700

Gln Asn Ser Ser Leu Ser Glu Ile Ile Leu Ile Ser Cys Glu Asn Asp
705 710 715 720

Leu His Leu Cys Arg Glu Tyr Phe Ala Arg Gly Ile Asp Val His Asn
725 730 735

Ala Glu Phe Val Leu Thr Gly Val Leu Thr Gln Thr Leu Asp Tyr Glu
740 745 750

Ser Tyr Lys Phe Asn
755

<210> 33
<211> 603
<212> PRT
<213> HOMO SAPIENS

<400> 33

Met Ser Ala Ala Val Thr Ala Gly Lys Leu Ala Arg Ala Pro Ala Asp
1 5 10 15

Pro Gly Lys Ala Gly Val Pro Gly Val Ala Ala Pro Gly Ala Pro Ala
20 25 30

Ala Ala Pro Pro Ala Lys Glu Ile Pro Glu Val Leu Val Asp Pro Arg
35 40 45

Ser Arg Arg Arg Tyr Val Arg Gly Arg Phe Leu Gly Lys Gly Gly Phe
50 55 60

Ala Lys Cys Phe Glu Ile Ser Asp Ala Asp Thr Lys Glu Val Phe Ala
65 70 75 80

Gly Lys Ile Val Pro Lys Ser Leu Leu Leu Lys Pro His Gln Arg Glu
85 90 95

Lys Met Ser Met Glu Ile Ser Ile His Arg Ser Leu Ala His Gln His
100 105 110

Val Val Gly Phe His Gly Phe Phe Glu Asp Asn Asp Phe Val Phe Val
115 120 125

Val Leu Glu Leu Cys Arg Arg Arg Ser Leu Leu Glu Leu His Lys Arg
130 135 140

Arg Lys Ala Leu Thr Glu Pro Glu Ala Arg Tyr Tyr Leu Arg Gln Ile
145 150 155 160

Val Leu Gly Cys Gln Tyr Leu His Arg Asn Arg Val Ile His Arg Asp
165 170 175

Leu Lys Leu Gly Asn Leu Phe Leu Asn Glu Asp Leu Glu Val Lys Ile
180 185 190

Gly Asp Phe Gly Leu Ala Thr Lys Val Glu Tyr Asp Gly Glu Arg Lys
195 200 205

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

Lys Lys Gly His Ser Phe Glu Val Asp Val Trp Ser Ile Gly Cys Ile
225 230 235 240

Met Tyr Thr Leu Leu Val Gly Lys Pro Pro Phe Glu Thr Ser Cys Leu
245 250 255

Lys Glu Thr Tyr Leu Arg Ile Lys Lys Asn Glu Tyr Ser Ile Pro Lys
260 265 270

His Ile Asn Pro Val Ala Ala Ser Leu Ile Gln Lys Met Leu Gln Thr
275 280 285

Asp Pro Thr Ala Arg Pro Thr Ile Asn Glu Leu Leu Asn Asp Glu Phe
290 295 300

Phe Thr Ser Gly Tyr Ile Pro Ala Arg Leu Pro Ile Thr Cys Leu Thr
305 310 315 320

Ile Pro Pro Arg Phe Ser Ile Ala Pro Ser Ser Leu Asp Pro Ser Asn
325 330 335

Arg Lys Pro Leu Thr Val Leu Asn Lys Gly Leu Glu Asn Pro Leu Pro
340 345 350

Glu Arg Pro Arg Glu Lys Glu Glu Pro Val Val Arg Glu Thr Gly Glu
355 360 365

Val Val Asp Cys His Leu Ser Asp Met Leu Gln Gln Leu His Ser Val
370 375 380

Asn Ala Ser Lys Pro Ser Glu Arg Gly Leu Val Arg Gln Glu Glu Ala
385 390 395 400

Glu Asp Pro Ala Cys Ile Pro Ile Phe Trp Val Ser Lys Trp Val Asp
405 410 415

Tyr Ser Asp Lys Tyr Gly Leu Gly Tyr Gln Leu Cys Asp Asn Ser Val
420 425 430

Gly Val Leu Phe Asn Asp Ser Thr Arg Leu Ile Leu Tyr Asn Asp Gly
435 440 445

Asp Ser Leu Gln Tyr Ile Glu Arg Asp Gly Thr Glu Ser Tyr Leu Thr
450 455 460

Val Ser Ser His Pro Asn Ser Leu Met Lys Lys Ile Thr Leu Leu Lys
465 470 475 480

Tyr Phe Arg Asn Tyr Met Ser Glu His Leu Leu Lys Ala Gly Ala Asn
485 490 495

Ile Thr Pro Arg Glu Gly Asp Glu Leu Ala Arg Leu Pro Tyr Leu Arg
500 505 510

Thr Trp Phe Arg Thr Arg Ser Ala Ile Ile Leu His Leu Ser Asn Gly
515 520 525

Ser Val Gln Ile Asn Phe Phe Gln Asp His Thr Lys Leu Ile Leu Cys
530 535 540

Pro Leu Met Ala Ala Val Thr Tyr Ile Asp Glu Lys Arg Asp Phe Arg
545 550 555 560

Thr Tyr Arg Leu Ser Leu Leu Glu Glu Tyr Gly Cys Cys Lys Glu Leu
565 570 575

Ala Ser Arg Leu Arg Tyr Ala Arg Thr Met Val Asp Lys Leu Leu Ser
580 585 590

Ser Arg Ser Ala Ser Asn Arg Leu Lys Ala Ser
595 600

<210> 34
<211> 685
<212> PRT
<213> HOMO SAPIENS

<400> 34

Met Glu Leu Leu Arg Thr Ile Thr Tyr Gln Pro Ala Ala Ser Thr Lys
1 5 10 15

Met Cys Glu Gln Ala Leu Gly Lys Gly Cys Gly Gly Asp Ser Lys Lys
20 25 30

Lys Arg Pro Pro Gln Pro Pro Glu Glu Ser Gln Pro Pro Gln Ser Gln
35 40 45

Ala Gln Val Pro Pro Ala Ala Pro His His His His His His Ser His
50 55 60

Ser Gly Pro Glu Ile Ser Arg Ile Ile Val Asp Pro Thr Thr Gly Lys
65 70 75 80

Arg Tyr Cys Arg Gly Lys Val Leu Gly Lys Gly Gly Phe Ala Lys Cys
85 90 95

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

Ile Pro His Ser Arg Val Ala Lys Pro His Gln Arg Glu Lys Ile Asp
115 120 125

Lys Glu Ile Glu Leu His Arg Ile Leu His His Lys His Val Val Gln
130 135 140

Phe Tyr His Tyr Phe Glu Asp Lys Glu Asn Ile Tyr Ile Leu Leu Glu
145 150 155 160

Tyr Cys Ser Arg Arg Ser Met Ala His Ile Leu Lys Ala Arg Lys Val
165 170 175

Leu Thr Glu Pro Glu Val Arg Tyr Tyr Leu Arg Gln Ile Val Ser Gly
180 185 190

Leu Lys Tyr Leu His Glu Gln Glu Ile Leu His Arg Asp Leu Lys Leu
195 200 205

Gly Asn Phe Phe Ile Asn Glu Ala Met Glu Leu Lys Val Gly Asp Phe
210 215 220

Gly Leu Ala Ala Arg Leu Glu Pro Leu Glu His Arg Arg Arg Thr Ile
225 230 235 240

Cys Gly Thr Pro Asn Tyr Leu Ser Pro Glu Val Leu Asn Lys Gln Gly
245 250 255

His Gly Cys Glu Ser Asp Ile Trp Ala Leu Gly Cys Val Met Tyr Thr
260 265 270

Met Leu Leu Gly Arg Pro Pro Phe Glu Thr Thr Asn Leu Lys Glu Thr
275 280 285

Tyr Arg Cys Ile Arg Glu Ala Arg Tyr Thr Met Pro Ser Ser Leu Leu
290 295 300

Ala Pro Ala Lys His Leu Ile Ala Ser Met Leu Ser Lys Asn Pro Glu
305 310 315 320

Asp Arg Pro Ser Leu Asp Asp Ile Ile Arg His Asp Phe Phe Leu Gln
325 330 335

```
Gly Phe Thr Pro Asp Arg Leu Ser Ser Ser Cys Cys His Thr Val Pro
            340                 345                 350

Asp Phe His Leu Ser Ser Pro Ala Lys Asn Phe Phe Lys Lys Ala Ala
        355                 360                 365

Ala Ala Leu Phe Gly Gly Lys Lys Asp Lys Ala Arg Tyr Ile Asp Thr
    370                 375                 380

His Asn Arg Val Ser Lys Glu Asp Glu Asp Ile Tyr Lys Leu Arg His
385                 390                 395                 400

Asp Leu Lys Lys Thr Ser Ile Thr Gln Gln Pro Ser Lys His Arg Thr
                405                 410                 415

Asp Glu Glu Leu Gln Pro Pro Thr Thr Thr Val Ala Arg Ser Gly Thr
            420                 425                 430

Pro Ala Val Glu Asn Lys Gln Gln Ile Gly Asp Ala Ile Arg Met Ile
        435                 440                 445

Val Arg Gly Thr Leu Gly Ser Cys Ser Ser Ser Ser Glu Cys Leu Glu
    450                 455                 460

Asp Ser Thr Met Gly Ser Val Ala Asp Thr Val Ala Arg Val Leu Arg
465                 470                 475                 480

Gly Cys Leu Glu Asn Met Pro Glu Ala Asp Cys Ile Pro Lys Glu Gln
                485                 490                 495

Leu Ser Thr Ser Phe Gln Trp Val Thr Lys Trp Val Asp Tyr Ser Asn
            500                 505                 510

Lys Tyr Gly Phe Gly Tyr Gln Leu Ser Asp His Thr Val Gly Val Leu
        515                 520                 525

Phe Asn Asn Gly Ala His Met Ser Leu Leu Pro Asp Lys Lys Thr Val
    530                 535                 540

His Tyr Tyr Ala Glu Leu Gly Gln Cys Ser Val Phe Pro Ala Thr Asp
545                 550                 555                 560
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Ala Pro Glu Gln Phe Ile Ser Gln Val Thr Val Leu Lys Tyr Phe Ser
565 570 575

His Tyr Met Glu Glu Asn Leu Met Asp Gly Gly Asp Leu Pro Ser Val
580 585 590

Thr Asp Ile Arg Arg Pro Arg Leu Tyr Leu Leu Gln Trp Leu Lys Ser
595 600 605

Asp Lys Ala Leu Met Met Leu Phe Asn Asp Gly Thr Phe Gln Val Asn
610 615 620

Phe Tyr His Asp His Thr Lys Ile Ile Ile Cys Ser Gln Asn Glu Glu
625 630 635 640

Tyr Leu Leu Thr Tyr Ile Asn Glu Asp Arg Ile Ser Thr Thr Phe Arg
645 650 655

Leu Thr Thr Leu Leu Met Ser Gly Cys Ser Ser Glu Leu Lys Asn Arg
660 665 670

Met Glu Tyr Ala Leu Asn Met Leu Leu Gln Arg Cys Asn
675 680 685

<210> 35
<211> 646
<212> PRT
<213> HOMO SAPIENS

<400> 35

Met Glu Pro Ala Ala Gly Phe Leu Ser Pro Arg Pro Phe Gln Arg Ala
1 5 10 15

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

Leu Arg Gly Pro Glu Leu Glu Met Leu Ala Gly Leu Pro Thr Ser Asp
35 40 45

Pro Gly Arg Leu Ile Thr Asp Pro Arg Ser Gly Arg Thr Tyr Leu Lys
50 55 60

Gly Arg Leu Leu Gly Lys Gly Gly Phe Ala Arg Cys Tyr Glu Ala Thr

65 70 75 80

Asp Thr Glu Thr Gly Ser Ala Tyr Ala Val Lys Val Ile Pro Gln Ser
85 90 95

Arg Val Ala Lys Pro His Gln Arg Glu Lys Ile Leu Asn Glu Ile Glu
100 105 110

Leu His Arg Asp Leu Gln His Arg His Ile Val Arg Phe Ser His His
115 120 125

Phe Glu Asp Ala Asp Asn Ile Tyr Ile Phe Leu Glu Leu Cys Ser Arg
130 135 140

Lys Ser Leu Ala His Ile Trp Lys Ala Arg His Thr Leu Leu Glu Pro
145 150 155 160

Glu Val Arg Tyr Tyr Leu Arg Gln Ile Leu Ser Gly Leu Lys Tyr Leu
165 170 175

His Gln Arg Gly Ile Leu His Arg Asp Leu Lys Leu Gly Asn Phe Phe
180 185 190

Ile Thr Glu Asn Met Glu Leu Lys Val Gly Asp Phe Gly Leu Ala Ala
195 200 205

Arg Leu Glu Pro Pro Glu Gln Arg Lys Lys Thr Ile Cys Gly Thr Pro
210 215 220

Asn Tyr Val Ala Pro Glu Val Leu Leu Arg Gln Gly His Gly Pro Glu
225 230 235 240

Ala Asp Val Trp Ser Leu Gly Cys Val Met Tyr Thr Leu Leu Cys Gly
245 250 255

Ser Pro Pro Phe Glu Thr Ala Asp Leu Lys Glu Thr Tyr Arg Cys Ile
260 265 270

Lys Gln Val His Tyr Thr Leu Pro Ala Ser Leu Ser Leu Pro Ala Arg
275 280 285

Gln Leu Leu Ala Ala Ile Leu Arg Ala Ser Pro Arg Asp Arg Pro Ser

290 295 300

Ile Asp Gln Ile Leu Arg His Asp Phe Phe Thr Lys Gly Tyr Thr Pro
305 310 315 320

Asp Arg Leu Pro Ile Ser Ser Cys Val Thr Val Pro Asp Leu Thr Pro
325 330 335

Pro Asn Pro Ala Arg Ser Leu Phe Ala Lys Val Thr Lys Ser Leu Phe
340 345 350

Gly Arg Lys Lys Lys Ser Lys Asn His Ala Gln Glu Arg Asp Glu Val
355 360 365

Ser Gly Leu Val Ser Gly Leu Met Arg Thr Ser Val Gly His Gln Asp
370 375 380

Ala Arg Pro Glu Ala Pro Ala Ala Ser Gly Pro Ala Pro Val Ser Leu
385 390 395 400

Val Glu Thr Ala Pro Glu Asp Ser Ser Pro Arg Gly Thr Leu Ala Ser
405 410 415

Ser Gly Asp Gly Phe Glu Glu Gly Leu Thr Val Ala Thr Val Val Glu
420 425 430

Ser Ala Leu Cys Ala Leu Arg Asn Cys Ile Ala Phe Met Pro Pro Ala
435 440 445

Glu Gln Asn Pro Ala Pro Leu Ala Gln Pro Glu Pro Leu Val Trp Val
450 455 460

Ser Lys Trp Val Asp Tyr Ser Asn Lys Phe Gly Phe Gly Tyr Gln Leu
465 470 475 480

Ser Ser Arg Arg Val Ala Val Leu Phe Asn Asp Gly Thr His Met Ala
485 490 495

Leu Ser Ala Asn Arg Lys Thr Val His Tyr Asn Pro Thr Ser Thr Lys
500 505 510

His Phe Ser Phe Ser Val Gly Ala Val Pro Arg Ala Leu Gln Pro Gln

515 520 525

Leu Gly Ile Leu Arg Tyr Phe Ala Ser Tyr Met Glu Gln His Leu Met
530 535 540

Lys Gly Gly Asp Leu Pro Ser Val Glu Glu Val Glu Val Pro Ala Pro
545 550 555 560

Pro Leu Leu Leu Gln Trp Val Lys Thr Asp Gln Ala Leu Leu Met Leu
565 570 575

Phe Ser Asp Gly Thr Val Gln Val Asn Phe Tyr Gly Asp His Thr Lys
580 585 590

Leu Ile Leu Ser Gly Trp Glu Pro Leu Leu Val Thr Phe Val Ala Arg
595 600 605

Asn Arg Ser Ala Cys Thr Tyr Leu Ala Ser His Leu Arg Gln Leu Gly
610 615 620

Cys Ser Pro Asp Leu Arg Gln Arg Leu Arg Tyr Ala Leu Arg Leu Leu
625 630 635 640

Arg Asp Arg Ser Pro Ala
645

<210> 36
<211> 603
<212> PRT
<213> HOMO SAPIENS

<400> 36

Met Ser Ala Ala Val Thr Ala Gly Lys Leu Ala Arg Ala Pro Ala Asp
1 5 10 15

Pro Gly Lys Ala Gly Val Pro Gly Val Ala Ala Pro Gly Ala Pro Ala
20 25 30

Ala Ala Pro Pro Ala Lys Glu Ile Pro Glu Val Leu Val Asp Pro Arg
35 40 45

Ser Arg Arg Arg Tyr Val Arg Gly Arg Phe Leu Gly Lys Gly Gly Phe
50 55 60

Ala Lys Cys Phe Glu Ile Ser Asp Ala Asp Thr Lys Glu Val Phe Ala
65 70 75 80

Gly Lys Ile Val Pro Lys Ser Leu Leu Leu Lys Pro His Gln Arg Glu
85 90 95

Lys Met Ser Met Glu Ile Ser Ile His Arg Ser Leu Ala His Gln His
100 105 110

Val Val Gly Phe His Gly Phe Phe Glu Asp Asn Asp Phe Val Phe Val
115 120 125

Val Leu Glu Leu Cys Arg Arg Arg Ser Leu Leu Glu Leu His Lys Arg
130 135 140

Arg Lys Ala Leu Thr Glu Pro Glu Ala Arg Tyr Tyr Leu Arg Gln Ile
145 150 155 160

Val Leu Gly Cys Gln Tyr Leu His Arg Asn Arg Val Ile His Arg Asp
165 170 175

Leu Lys Leu Gly Asn Leu Phe Leu Asn Glu Asp Leu Glu Val Lys Ile
180 185 190

Gly Asp Phe Gly Leu Ala Thr Lys Val Glu Tyr Asp Gly Glu Arg Lys
195 200 205

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

Lys Lys Gly His Ser Phe Glu Val Asp Val Trp Ser Ile Gly Cys Ile
225 230 235 240

Met Tyr Thr Leu Leu Val Gly Lys Pro Pro Phe Glu Thr Ser Cys Leu
245 250 255

Lys Glu Thr Tyr Leu Arg Ile Lys Lys Asn Glu Tyr Ser Ile Pro Lys
260 265 270

His Ile Asn Pro Val Ala Ala Ser Leu Ile Gln Lys Met Leu Gln Thr
275 280 285

Asp Pro Thr Ala Arg Pro Thr Ile Asn Glu Leu Leu Asn Asp Glu Phe
290 295 300

Phe Thr Ser Gly Tyr Ile Pro Ala Arg Leu Pro Ile Thr Cys Leu Thr
305 310 315 320

Ile Pro Pro Arg Phe Ser Ile Ala Pro Ser Ser Leu Asp Pro Ser Asn
325 330 335

Arg Lys Pro Leu Thr Val Leu Asn Lys Gly Leu Glu Asn Pro Leu Pro
340 345 350

Glu Arg Pro Arg Glu Lys Glu Glu Pro Val Val Arg Glu Thr Gly Glu
355 360 365

Val Val Asp Cys His Leu Ser Asp Met Leu Gln Gln Leu His Ser Val
370 375 380

Asn Ala Ser Lys Pro Ser Glu Arg Gly Leu Val Arg Gln Glu Glu Ala
385 390 395 400

Glu Asp Pro Ala Cys Ile Pro Ile Phe Trp Val Ser Lys Trp Val Asp
405 410 415

Tyr Ser Asp Lys Tyr Gly Leu Gly Tyr Gln Leu Cys Asp Asn Ser Val
420 425 430

Gly Val Leu Phe Asn Asp Ser Thr Arg Leu Ile Leu Tyr Asn Asp Gly
435 440 445

Asp Ser Leu Gln Tyr Ile Glu Arg Asp Gly Thr Glu Ser Tyr Leu Thr
450 455 460

Val Ser Ser His Pro Asn Ser Leu Met Lys Lys Ile Thr Leu Leu Lys
465 470 475 480

Tyr Phe Arg Asn Tyr Met Ser Glu His Leu Leu Lys Ala Gly Ala Asn
485 490 495

Ile Thr Pro Arg Glu Gly Asp Glu Leu Ala Arg Leu Pro Tyr Leu Arg
500 505 510

Thr Trp Phe Arg Thr Arg Ser Ala Ile Ile Leu His Leu Ser Asn Gly
515 520 525

Ser Val Gln Ile Asn Phe Phe Gln Asp His Thr Lys Leu Ile Leu Cys
530 535 540

Pro Leu Met Ala Ala Val Thr Tyr Ile Asp Glu Lys Arg Asp Phe Arg
545 550 555 560

Thr Tyr Arg Leu Ser Leu Leu Glu Glu Tyr Gly Cys Cys Lys Glu Leu
565 570 575

Ala Ser Arg Leu Arg Tyr Ala Arg Thr Met Val Asp Lys Leu Leu Ser
580 585 590

Ser Arg Ser Ala Ser Asn Arg Leu Lys Ala Ser
595 600

<210> 37
<211> 603
<212> PRT
<213> HOMO SAPIENS

<400> 37

Met Asn Ala Ala Ala Lys Ala Gly Lys Leu Ala Arg Ala Pro Ala Asp
1 5 10 15

Leu Gly Lys Gly Gly Val Pro Gly Asp Ala Val Pro Gly Ala Pro Val
20 25 30

Ala Ala Pro Leu Ala Lys Glu Ile Pro Glu Val Leu Val Asp Pro Arg
35 40 45

Ser Arg Arg Gln Tyr Val Arg Gly Arg Phe Leu Gly Lys Gly Gly Phe
50 55 60

Ala Lys Cys Phe Glu Ile Ser Asp Ala Asp Thr Lys Glu Val Phe Ala
65 70 75 80

Gly Lys Ile Val Pro Lys Ser Leu Leu Leu Lys Pro His Gln Lys Glu
85 90 95

```
Lys Met Ser Met Glu Ile Ser Ile His Arg Ser Leu Ala His Gln His
            100                 105                 110

Val Val Gly Phe His Asp Phe Phe Glu Asp Ser Asp Phe Val Phe Val
        115                 120                 125

Val Leu Glu Leu Cys Arg Arg Arg Ser Leu Leu Glu Leu His Lys Arg
    130                 135                 140

Arg Lys Ala Leu Thr Glu Pro Glu Ala Arg Tyr Tyr Leu Arg Gln Ile
145                 150                 155                 160

Val Leu Gly Cys Gln Tyr Leu His Arg Asn Gln Val Ile His Arg Asp
                165                 170                 175

Leu Lys Leu Gly Asn Leu Phe Leu Asn Glu Asp Leu Glu Val Lys Ile
            180                 185                 190

Gly Asp Phe Gly Leu Ala Thr Lys Val Glu Tyr Glu Gly Glu Arg Lys
        195                 200                 205

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

Lys Lys Gly His Ser Phe Glu Val Asp Val Trp Ser Ile Gly Cys Ile
225                 230                 235                 240

Met Tyr Thr Leu Leu Val Gly Lys Pro Pro Phe Glu Thr Ser Cys Leu
                245                 250                 255

Lys Glu Thr Tyr Leu Arg Ile Lys Lys Asn Glu Tyr Ser Ile Pro Lys
            260                 265                 270

His Ile Asn Pro Val Ala Ala Ser Leu Ile Gln Lys Met Leu Gln Thr
        275                 280                 285

Asp Pro Thr Ala Arg Pro Thr Ile His Glu Leu Leu Asn Asp Glu Phe
    290                 295                 300

Phe Thr Ser Gly Tyr Ile Pro Ala Arg Leu Pro Ile Thr Cys Leu Thr
305                 310                 315                 320
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```
Ile Pro Pro Arg Phe Ser Ile Ala Pro Ser Ser Leu Asp Pro Ser Ser
                325                 330                 335

Arg Lys Pro Leu Lys Val Leu Asn Lys Gly Val Glu Asn Pro Leu Pro
            340                 345                 350

Asp Arg Pro Arg Glu Lys Glu Glu Pro Val Val Arg Glu Thr Asn Glu
        355                 360                 365

Ala Ile Glu Cys His Leu Ser Asp Leu Leu Gln Gln Leu Thr Ser Val
    370                 375                 380

Asn Ala Ser Lys Pro Ser Glu Arg Gly Leu Val Arg Gln Glu Glu Ala
385                 390                 395                 400

Glu Asp Pro Ala Cys Ile Pro Ile Phe Trp Val Ser Lys Trp Val Asp
                405                 410                 415

Tyr Ser Asp Lys Tyr Gly Leu Gly Tyr Gln Leu Cys Asp Asn Ser Val
            420                 425                 430

Gly Val Leu Phe Asn Asp Ser Thr Arg Leu Ile Leu Tyr Asn Asp Gly
        435                 440                 445

Asp Ser Leu Gln Tyr Ile Glu Arg Asp Gly Thr Glu Ser Tyr Leu Thr
    450                 455                 460

Val Ser Ser His Pro Asn Ser Leu Met Lys Lys Ile Thr Leu Leu Asn
465                 470                 475                 480

Tyr Phe Arg Asn Tyr Met Ser Glu His Leu Leu Lys Ala Gly Ala Asn
                485                 490                 495

Ile Thr Pro Arg Glu Gly Asp Glu Leu Ala Arg Leu Pro Tyr Leu Arg
            500                 505                 510

Thr Trp Phe Arg Thr Arg Ser Ala Ile Ile Leu His Leu Ser Asn Gly
        515                 520                 525

Thr Val Gln Ile Asn Phe Phe Gln Asp His Thr Lys Leu Ile Leu Cys
    530                 535                 540
```

```
Pro Leu Met Ala Ala Val Thr Tyr Ile Asn Glu Lys Arg Asp Phe Gln
545                 550                 555                 560

Thr Tyr Arg Leu Ser Leu Leu Glu Glu Tyr Gly Cys Cys Lys Glu Leu
                565                 570                 575

Ala Ser Arg Leu Arg Tyr Ala Arg Thr Met Val Asp Lys Leu Leu Ser
            580                 585                 590

Ser Arg Ser Ala Ser Asn Arg Leu Lys Ala Ser
        595                 600
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<210> 38
<211> 1731
<212> DNA
<213> DROSOPHILA MELANOGASTER

<220>
<221> CDS
<222> (1)..(1731)

<400> 38

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atg gcc gcg aag ccc gag gat aag agc acg gat att ccg gat cgc ctc      48
Met Ala Ala Lys Pro Glu Asp Lys Ser Thr Asp Ile Pro Asp Arg Leu
1               5                   10                  15

gtc gac atc aac cag cgg aaa acc tac aag cgc atg cgg ttc ttc ggc      96
Val Asp Ile Asn Gln Arg Lys Thr Tyr Lys Arg Met Arg Phe Phe Gly
            20                  25                  30

aag ggc ggg ttt gca aaa tgt tac gag atc atc gat gtg gaa acc gac     144
Lys Gly Gly Phe Ala Lys Cys Tyr Glu Ile Ile Asp Val Glu Thr Asp
        35                  40                  45

gac gtc ttc gcc ggc aag atc gta tcc aag aag ctg atg atc aaa cac     192
Asp Val Phe Ala Gly Lys Ile Val Ser Lys Lys Leu Met Ile Lys His
    50                  55                  60

aat cag aag gag aag acc gcc cag gag ata act att cac cgc agc ctt     240
Asn Gln Lys Glu Lys Thr Ala Gln Glu Ile Thr Ile His Arg Ser Leu
65                  70                  75                  80

aac cat ccg aac att gtc aag ttt cac aac tac ttt gaa gat tcg cag     288
Asn His Pro Asn Ile Val Lys Phe His Asn Tyr Phe Glu Asp Ser Gln
                85                  90                  95

aat atc tac att gtg ctg gag ctg tgc aag aaa aga tcc atg atg gag     336
Asn Ile Tyr Ile Val Leu Glu Leu Cys Lys Lys Arg Ser Met Met Glu
            100                 105                 110
```

```
ctg cac aaa cgt agg aaa agc att acg gag ttc gaa tgc cgc tac tac      384
Leu His Lys Arg Arg Lys Ser Ile Thr Glu Phe Glu Cys Arg Tyr Tyr
        115                 120                 125

att tac cag ata atc cag ggc gtt aag tac ttg cac gat aac cgc att      432
Ile Tyr Gln Ile Ile Gln Gly Val Lys Tyr Leu His Asp Asn Arg Ile
    130                 135                 140

atc cat cga gat ctg aag ctg ggc aat ctc ttc ctc aac gat ttg ttg      480
Ile His Arg Asp Leu Lys Leu Gly Asn Leu Phe Leu Asn Asp Leu Leu
145                 150                 155                 160

cac gtg aag atc ggg gat ttc ggg ttg gcc acg cgc att gag tat gag      528
His Val Lys Ile Gly Asp Phe Gly Leu Ala Thr Arg Ile Glu Tyr Glu
                165                 170                 175

ggc gag cga aaa aag acc tta tgc gga acg ccc aac tat ata gcc ccg      576
Gly Glu Arg Lys Lys Thr Leu Cys Gly Thr Pro Asn Tyr Ile Ala Pro
            180                 185                 190

gag atc ctc acc aag aag ggc cac tcc ttc gag gtg gac atc tgg tcg      624
Glu Ile Leu Thr Lys Lys Gly His Ser Phe Glu Val Asp Ile Trp Ser
        195                 200                 205

att ggc tgc gtc atg tac aca ctg ctt gtg ggc cag ccg ccg ttc gaa      672
Ile Gly Cys Val Met Tyr Thr Leu Leu Val Gly Gln Pro Pro Phe Glu
    210                 215                 220

acc aag act ctg aag gat acg tac tcg aaa atc aag aag tgc gag tac      720
Thr Lys Thr Leu Lys Asp Thr Tyr Ser Lys Ile Lys Lys Cys Glu Tyr
225                 230                 235                 240

cgc gtg ccc agc tac tta agg aaa ccg gcg gcg gat atg gtc atc gcc      768
Arg Val Pro Ser Tyr Leu Arg Lys Pro Ala Ala Asp Met Val Ile Ala
                245                 250                 255

atg ctg cag cca aat ccg gag agc cgc ccg gca att ggt cag ctg ctg      816
Met Leu Gln Pro Asn Pro Glu Ser Arg Pro Ala Ile Gly Gln Leu Leu
            260                 265                 270

aac ttt gag ttc ctc aag ggc tca aag gtg ccc atg ttc ttg ccc agc      864
Asn Phe Glu Phe Leu Lys Gly Ser Lys Val Pro Met Phe Leu Pro Ser
        275                 280                 285

tct tgt ctg aca atg gcg ccg cgt atc ggc agc aac gac acc atc gag      912
Ser Cys Leu Thr Met Ala Pro Arg Ile Gly Ser Asn Asp Thr Ile Glu
    290                 295                 300

gat tcg atg cac cgc aag cca ctg atg gag atg aac ggc atc agg ccc      960
Asp Ser Met His Arg Lys Pro Leu Met Glu Met Asn Gly Ile Arg Pro
305                 310                 315                 320

gac gac act cgt ctg gag tcg acc ttc ctc aag gcc aat ctg cac gac     1008
Asp Asp Thr Arg Leu Glu Ser Thr Phe Leu Lys Ala Asn Leu His Asp
                325                 330                 335
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gcc att acc gcg tca gcg cag gtg tgc cgc cac agc gag gac tat cgc     1056
Ala Ile Thr Ala Ser Ala Gln Val Cys Arg His Ser Glu Asp Tyr Arg
            340                 345                 350

agc gat atc gag agc ctg tac cag cag ctc act aat ctt atc aac gga     1104
Ser Asp Ile Glu Ser Leu Tyr Gln Gln Leu Thr Asn Leu Ile Asn Gly
        355                 360                 365

aag ccg cga att ctg caa ggc aat ctg ggc gac gag aac aca gat cct     1152
Lys Pro Arg Ile Leu Gln Gly Asn Leu Gly Asp Glu Asn Thr Asp Pro
    370                 375                 380

gca gcg cag ccg ctc ttc tgg ata tcc aag tgg gtt gac tac agc gac     1200
Ala Ala Gln Pro Leu Phe Trp Ile Ser Lys Trp Val Asp Tyr Ser Asp
385                 390                 395                 400

aag tac gga ttt ggt tac cag ctg tgc gat gag ggc atc ggc gtg atg     1248
Lys Tyr Gly Phe Gly Tyr Gln Leu Cys Asp Glu Gly Ile Gly Val Met
                405                 410                 415

ttc aac gac acc aca aag ctg atc ctg ctg ccg aat cag atc aac gta     1296
Phe Asn Asp Thr Thr Lys Leu Ile Leu Leu Pro Asn Gln Ile Asn Val
            420                 425                 430

cac ttc atc gac aag gat ggc aag gag acg tac atg acc acc acg gat     1344
His Phe Ile Asp Lys Asp Gly Lys Glu Thr Tyr Met Thr Thr Thr Asp
        435                 440                 445

tac tgc aag tcg ctt gac aag aag atg aag ctg ctg tcg tac ttt aag     1392
Tyr Cys Lys Ser Leu Asp Lys Lys Met Lys Leu Leu Ser Tyr Phe Lys
    450                 455                 460

cgc tac atg atc gag cac ctg gtg aag gca ggt gcc aac aat gtg aac     1440
Arg Tyr Met Ile Glu His Leu Val Lys Ala Gly Ala Asn Asn Val Asn
465                 470                 475                 480

att gag agc gat caa atc tcg cgt atg ccc cat tta cac tcc tgg ttc     1488
Ile Glu Ser Asp Gln Ile Ser Arg Met Pro His Leu His Ser Trp Phe
                485                 490                 495

cgt aca aca tgt gcc gta gtt atg cat ttg acc aac ggt tct gtg cag     1536
Arg Thr Thr Cys Ala Val Val Met His Leu Thr Asn Gly Ser Val Gln
            500                 505                 510

cta aac ttc tca gat cac atg aag ctc atc ctc tgc ccg cgc atg agt     1584
Leu Asn Phe Ser Asp His Met Lys Leu Ile Leu Cys Pro Arg Met Ser
        515                 520                 525

gct ata acc tat atg gac cag gag aag aac ttc cgc acc tac cga ttt     1632
Ala Ile Thr Tyr Met Asp Gln Glu Lys Asn Phe Arg Thr Tyr Arg Phe
    530                 535                 540

tcg acc att gtg gag aac ggc gtg tct aaa gac ttg tac cag aag atc     1680
Ser Thr Ile Val Glu Asn Gly Val Ser Lys Asp Leu Tyr Gln Lys Ile
545                 550                 555                 560
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cga tat gcc cag gag aaa ctt agg aaa atg ctg gag aag atg ttc aca 1728
Arg Tyr Ala Gln Glu Lys Leu Arg Lys Met Leu Glu Lys Met Phe Thr
565 570 575

taa 1731

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Val Asp Ile Asn Gln Arg Lys Thr Tyr Lys Arg Met Arg Phe Phe Gly
20 25 30

Lys Gly Gly Phe Ala Lys Cys Tyr Glu Ile Ile Asp Val Glu Thr Asp
35 40 45

Asp Val Phe Ala Gly Lys Ile Val Ser Lys Lys Leu Met Ile Lys His
50 55 60

Asn Gln Lys Glu Lys Thr Ala Gln Glu Ile Thr Ile His Arg Ser Leu
65 70 75 80

Asn His Pro Asn Ile Val Lys Phe His Asn Tyr Phe Glu Asp Ser Gln
85 90 95

Asn Ile Tyr Ile Val Leu Glu Leu Cys Lys Lys Arg Ser Met Met Glu
100 105 110

Leu His Lys Arg Arg Lys Ser Ile Thr Glu Phe Glu Cys Arg Tyr Tyr
115 120 125

Ile Tyr Gln Ile Ile Gln Gly Val Lys Tyr Leu His Asp Asn Arg Ile
130 135 140

Ile His Arg Asp Leu Lys Leu Gly Asn Leu Phe Leu Asn Asp Leu Leu
145 150 155 160

His Val Lys Ile Gly Asp Phe Gly Leu Ala Thr Arg Ile Glu Tyr Glu
165 170 175

Gly Glu Arg Lys Lys Thr Leu Cys Gly Thr Pro Asn Tyr Ile Ala Pro
180 185 190

Glu Ile Leu Thr Lys Lys Gly His Ser Phe Glu Val Asp Ile Trp Ser
195 200 205

Ile Gly Cys Val Met Tyr Thr Leu Leu Val Gly Gln Pro Pro Phe Glu
210 215 220

Thr Lys Thr Leu Lys Asp Thr Tyr Ser Lys Ile Lys Lys Cys Glu Tyr
225 230 235 240

Arg Val Pro Ser Tyr Leu Arg Lys Pro Ala Ala Asp Met Val Ile Ala
245 250 255

Met Leu Gln Pro Asn Pro Glu Ser Arg Pro Ala Ile Gly Gln Leu Leu
260 265 270

Asn Phe Glu Phe Leu Lys Gly Ser Lys Val Pro Met Phe Leu Pro Ser
275 280 285

Ser Cys Leu Thr Met Ala Pro Arg Ile Gly Ser Asn Asp Thr Ile Glu
290 295 300

Asp Ser Met His Arg Lys Pro Leu Met Glu Met Asn Gly Ile Arg Pro
305 310 315 320

Asp Asp Thr Arg Leu Glu Ser Thr Phe Leu Lys Ala Asn Leu His Asp
325 330 335

Ala Ile Thr Ala Ser Ala Gln Val Cys Arg His Ser Glu Asp Tyr Arg
340 345 350

Ser Asp Ile Glu Ser Leu Tyr Gln Gln Leu Thr Asn Leu Ile Asn Gly
355 360 365

Lys Pro Arg Ile Leu Gln Gly Asn Leu Gly Asp Glu Asn Thr Asp Pro
370 375 380

Ala Ala Gln Pro Leu Phe Trp Ile Ser Lys Trp Val Asp Tyr Ser Asp
385 390 395 400

Lys Tyr Gly Phe Gly Tyr Gln Leu Cys Asp Glu Gly Ile Gly Val Met
405 410 415

Phe Asn Asp Thr Thr Lys Leu Ile Leu Leu Pro Asn Gln Ile Asn Val
420 425 430

His Phe Ile Asp Lys Asp Gly Lys Glu Thr Tyr Met Thr Thr Thr Asp
435 440 445

Tyr Cys Lys Ser Leu Asp Lys Lys Met Lys Leu Leu Ser Tyr Phe Lys
450 455 460

Arg Tyr Met Ile Glu His Leu Val Lys Ala Gly Ala Asn Asn Val Asn
465 470 475 480

Ile Glu Ser Asp Gln Ile Ser Arg Met Pro His Leu His Ser Trp Phe
485 490 495

Arg Thr Thr Cys Ala Val Val Met His Leu Thr Asn Gly Ser Val Gln
500 505 510

Leu Asn Phe Ser Asp His Met Lys Leu Ile Leu Cys Pro Arg Met Ser
515 520 525

Ala Ile Thr Tyr Met Asp Gln Glu Lys Asn Phe Arg Thr Tyr Arg Phe
530 535 540

Ser Thr Ile Val Glu Asn Gly Val Ser Lys Asp Leu Tyr Gln Lys Ile
545 550 555 560

Arg Tyr Ala Gln Glu Lys Leu Arg Lys Met Leu Glu Lys Met Phe Thr
565 570 575

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domain) protein 1 (PAXIP1), mRNA.

<400> 40

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ggaggtcaag tattacgcgg tgggcgacat cgacccgcag gttattcagc ttctcaaggc     120

tggaaaagcg aaggaagttt cctacaatgc actagcctca cacataatct cagaggatgg     180

ggacaatcca gaggtgggag aagctcggga agtctttgac ttacctgttg taaagccttc     240

ttgggtgatt ctgtccgttc agtgtggaac tcttctgcca gtaa atg gtt ttt ctc      296
                                                  Met Val Phe Leu
                                                  1

cag aat cat gtc aga ttt ttt ttg gaa tca ctg cct gcc ttt ctc agg       344
Gln Asn His Val Arg Phe Phe Leu Glu Ser Leu Pro Ala Phe Leu Arg
5                   10                  15                  20

gtg ttg ata caa gct gga gct ctt tgt tgg agt ctt cca gag ctc tcc       392
Val Leu Ile Gln Ala Gly Ala Leu Cys Trp Ser Leu Pro Glu Leu Ser
                25                  30                  35

cag gga gag gta ggg aag gga gct tgt cca gca gaa gtt ggg aag cac       440
Gln Gly Glu Val Gly Lys Gly Ala Cys Pro Ala Glu Val Gly Lys His
            40                  45                  50

aga gat cat ctg cct tct tct gac ccg gta ttg atg cag gct gag gcc       488
Arg Asp His Leu Pro Ser Ser Asp Pro Val Leu Met Gln Ala Glu Ala
        55                  60                  65

tct gtt gta atg tgc tgg gtg tca tct gaa gac aga agt gcc ctg tgg       536
Ser Val Val Met Cys Trp Val Ser Ser Glu Asp Arg Ser Ala Leu Trp
    70                  75                  80

gct ttg gtt acg ttc tat ggg gga gat tgc cag cta acc ctc aat aag       584
Ala Leu Val Thr Phe Tyr Gly Gly Asp Cys Gln Leu Thr Leu Asn Lys
85                  90                  95                  100

aaa tgc acg cat ttg att gtt cca gag cca aag ggg gag aaa tac gaa       632
Lys Cys Thr His Leu Ile Val Pro Glu Pro Lys Gly Glu Lys Tyr Glu
                105                 110                 115

tgt gct tta aag cga gca agt att aaa att gtg act cct gac tgg gtt       680
Cys Ala Leu Lys Arg Ala Ser Ile Lys Ile Val Thr Pro Asp Trp Val
            120                 125                 130

ctg gat tgc gta tca gag aaa acc aaa aag gac gaa gca ttt tat cat       728
Leu Asp Cys Val Ser Glu Lys Thr Lys Lys Asp Glu Ala Phe Tyr His
        135                 140                 145

cct cgt ctg att att tat gaa gag gaa gaa gag gaa gag gaa gag gag       776
Pro Arg Leu Ile Ile Tyr Glu Glu Glu Glu Glu Glu Glu Glu Glu Glu
    150                 155                 160

gag gaa gta gaa aat gag gaa caa gat tct cag aat gag ggt agt aca       824
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Glu Glu Val Glu Asn Glu Glu Gln Asp Ser Gln Asn Glu Gly Ser Thr
165                 170                 175                 180

gat gag aag tca agc cct gcc agc tct caa gaa ggg tct cct tca ggt      872
Asp Glu Lys Ser Ser Pro Ala Ser Ser Gln Glu Gly Ser Pro Ser Gly
                185                 190                 195

gac cag cag ttt tca cct aaa tcc aac act gaa aaa tct aaa ggg gaa      920
Asp Gln Gln Phe Ser Pro Lys Ser Asn Thr Glu Lys Ser Lys Gly Glu
            200                 205                 210

tta atg ttt gat gat tct tca gat tca tca ccg gaa aaa cag gag aga      968
Leu Met Phe Asp Asp Ser Ser Asp Ser Ser Pro Glu Lys Gln Glu Arg
        215                 220                 225

aat tta aac tgg acc ccg gcc gaa gtc cca cag tta gct gca gca aaa     1016
Asn Leu Asn Trp Thr Pro Ala Glu Val Pro Gln Leu Ala Ala Ala Lys
    230                 235                 240

cgc agg ctg cct cag gga aag gag cct ggg ttg att aac ttg tgt gcc     1064
Arg Arg Leu Pro Gln Gly Lys Glu Pro Gly Leu Ile Asn Leu Cys Ala
245                 250                 255                 260

aat gtc cca ccc gtc cca ggt aac att ttg ccc cct gag gtc cgg ggt     1112
Asn Val Pro Pro Val Pro Gly Asn Ile Leu Pro Pro Glu Val Arg Gly
                265                 270                 275

aat tta atg gct gct gga caa aac ctc caa agt tct gaa aga tca gaa     1160
Asn Leu Met Ala Ala Gly Gln Asn Leu Gln Ser Ser Glu Arg Ser Glu
            280                 285                 290

atg ata gct acc tgg agt cca gct gta cgg aca ctg agg aat att act     1208
Met Ile Ala Thr Trp Ser Pro Ala Val Arg Thr Leu Arg Asn Ile Thr
        295                 300                 305

aat aat gct gac att cag cag atg aac cgg cca tca aat gta gca cat     1256
Asn Asn Ala Asp Ile Gln Gln Met Asn Arg Pro Ser Asn Val Ala His
    310                 315                 320

atc tta cag act ctt tca gca cct acg aaa aat tta gaa cag cag gtg     1304
Ile Leu Gln Thr Leu Ser Ala Pro Thr Lys Asn Leu Glu Gln Gln Val
325                 330                 335                 340

aat cac agc cag cag gga cat aca aat gcc aat gca gtg ctg ttt agc     1352
Asn His Ser Gln Gln Gly His Thr Asn Ala Asn Ala Val Leu Phe Ser
                345                 350                 355

caa gtg aaa gtg act cca gag aca cac atg cta cag cag cag cag cag     1400
Gln Val Lys Val Thr Pro Glu Thr His Met Leu Gln Gln Gln Gln Gln
            360                 365                 370

gcc cag cag cag cag cag cag cac ccg gtt tta cac ctt cag ccc cag     1448
Ala Gln Gln Gln Gln Gln Gln His Pro Val Leu His Leu Gln Pro Gln
        375                 380                 385

cag ata atg cag ctc cag cag cag cag cag cag cag atc tct cag caa     1496
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Gln Ile Met Gln Leu Gln Gln Gln Gln Gln Gln Ile Ser Gln Gln
    390                 395                 400

cct tac ccc cag cag ccg ccg cat cca ttt tca cag caa cag cag cag      1544
Pro Tyr Pro Gln Gln Pro Pro His Pro Phe Ser Gln Gln Gln Gln Gln
405                 410                 415                 420

cag cag caa gcc cat ccg cat cag ttt tca cag caa cag cta cag ttt      1592
Gln Gln Gln Ala His Pro His Gln Phe Ser Gln Gln Gln Leu Gln Phe
                425                 430                 435

cca cag caa cag ttg cat cct cca cag cag ctg cat cgc cct cag cag      1640
Pro Gln Gln Gln Leu His Pro Pro Gln Gln Leu His Arg Pro Gln Gln
            440                 445                 450

cag ctc cag ccc ttt cag cag cag cat gcc ctg cag cag cag ttc cat      1688
Gln Leu Gln Pro Phe Gln Gln Gln His Ala Leu Gln Gln Gln Phe His
        455                 460                 465

cag ctg cag cag cac cag ctc cag cag cag cag ctt gcc cag ctc cag      1736
Gln Leu Gln Gln His Gln Leu Gln Gln Gln Gln Leu Ala Gln Leu Gln
    470                 475                 480

cag cag cac agc ctg ctc cag cag cag cag caa cag cag att cag cag      1784
Gln Gln His Ser Leu Leu Gln Gln Gln Gln Gln Gln Gln Ile Gln Gln
485                 490                 495                 500

cag cag ctc cag cgc atg cac cag cag cag cag cag cag cag atg caa      1832
Gln Gln Leu Gln Arg Met His Gln Gln Gln Gln Gln Gln Gln Met Gln
                505                 510                 515

agt cag aca gcg cca cac ttg agt cag acg tca cag gcg ctg cag cat      1880
Ser Gln Thr Ala Pro His Leu Ser Gln Thr Ser Gln Ala Leu Gln His
            520                 525                 530

cag gtt cca cct cag cag ccc ccg cag cag cag cag caa cag cag cca      1928
Gln Val Pro Pro Gln Gln Pro Pro Gln Gln Gln Gln Gln Gln Gln Pro
        535                 540                 545

cca cca tcg cct cag cag cat cag ctt ttt gga cat gat cca gca gtg      1976
Pro Pro Ser Pro Gln Gln His Gln Leu Phe Gly His Asp Pro Ala Val
    550                 555                 560

gag att cca gaa gaa ggc ttc tta ttg gga tgt gtg ttt gca att gcg      2024
Glu Ile Pro Glu Glu Gly Phe Leu Leu Gly Cys Val Phe Ala Ile Ala
565                 570                 575                 580

gat tat cca gag cag atg tct gat aag caa ctg ctg gcc acc tgg aaa      2072
Asp Tyr Pro Glu Gln Met Ser Asp Lys Gln Leu Leu Ala Thr Trp Lys
                585                 590                 595

agg ata atc cag gca cat ggc ggc act gtt gac ccc acc ttc acg agt      2120
Arg Ile Ile Gln Ala His Gly Gly Thr Val Asp Pro Thr Phe Thr Ser
            600                 605                 610

cga tgc acg cac ctt ctc tgt gag agt caa gtc agc agc gcg tat gca      2168
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Arg Cys Thr His Leu Leu Cys Glu Ser Gln Val Ser Ser Ala Tyr Ala
        615                 620                 625

cag gca ata aga gaa aga aag aga tgt gtt act gca cac tgg tta aac     2216
Gln Ala Ile Arg Glu Arg Lys Arg Cys Val Thr Ala His Trp Leu Asn
    630                 635                 640

aca gtc tta aag aag aag aaa atg gta ccg ccg cac cga gcc ctt cac     2264
Thr Val Leu Lys Lys Lys Lys Met Val Pro Pro His Arg Ala Leu His
645                 650                 655                 660

ttc cca gtg gcc ttc cca cca gga gga aag cca tgt tca cag cat att     2312
Phe Pro Val Ala Phe Pro Pro Gly Gly Lys Pro Cys Ser Gln His Ile
                665                 670                 675

att tct gtg act gga ttt gtt gat agt gac aga gat gac cta aaa tta     2360
Ile Ser Val Thr Gly Phe Val Asp Ser Asp Arg Asp Asp Leu Lys Leu
            680                 685                 690

atg gct tat ttg gca ggt gcc aaa tat acg ggt tat cta tgc cgc agc     2408
Met Ala Tyr Leu Ala Gly Ala Lys Tyr Thr Gly Tyr Leu Cys Arg Ser
        695                 700                 705

aac aca gtc ctc atc tgt aaa gaa cca act ggt tta aag tat gaa aaa     2456
Asn Thr Val Leu Ile Cys Lys Glu Pro Thr Gly Leu Lys Tyr Glu Lys
    710                 715                 720

gcc aaa gag tgg agg ata ccc tgt gtc aac gcc cag tgg ctt ggc gac     2504
Ala Lys Glu Trp Arg Ile Pro Cys Val Asn Ala Gln Trp Leu Gly Asp
725                 730                 735                 740

att ctt ctg gga aac ttt gag gca ctg agg cag att cag tat agt cgc     2552
Ile Leu Leu Gly Asn Phe Glu Ala Leu Arg Gln Ile Gln Tyr Ser Arg
                745                 750                 755

tac acg gca ttc agt ctg cag gat cca ttt gcc cct acc cag cat tta     2600
Tyr Thr Ala Phe Ser Leu Gln Asp Pro Phe Ala Pro Thr Gln His Leu
            760                 765                 770

gtt tta aat ctt tta gat gct tgg aga gtt ccc tta aaa gtg tct gca     2648
Val Leu Asn Leu Leu Asp Ala Trp Arg Val Pro Leu Lys Val Ser Ala
        775                 780                 785

gag ttg ttg atg agt ata aga cta cct ccc aaa ctg aaa cag aat gaa     2696
Glu Leu Leu Met Ser Ile Arg Leu Pro Pro Lys Leu Lys Gln Asn Glu
    790                 795                 800

gta gct aat gtc cag cct tct tcc aaa aga gcc aga att gaa gac gta     2744
Val Ala Asn Val Gln Pro Ser Ser Lys Arg Ala Arg Ile Glu Asp Val
805                 810                 815                 820

cca cct ccc act aaa aag cta act cca gaa ttg acc cct ttt gtg ctt     2792
Pro Pro Pro Thr Lys Lys Leu Thr Pro Glu Leu Thr Pro Phe Val Leu
                825                 830                 835

ttc act gga ttc gag cct gtc cag gtt caa cag tat att aag aag ctc     2840
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Phe Thr Gly Phe Glu Pro Val Gln Val Gln Gln Tyr Ile Lys Lys Leu
            840                 845                 850

tac att ctt ggt gga gag gtt gcg gag tct gca cag aag tgc aca cac      2888
Tyr Ile Leu Gly Gly Glu Val Ala Glu Ser Ala Gln Lys Cys Thr His
        855                 860                 865

ctc att gcc agc aaa gtg act cgc acc gtg aag ttc ctg acg gcg att      2936
Leu Ile Ala Ser Lys Val Thr Arg Thr Val Lys Phe Leu Thr Ala Ile
    870                 875                 880

tct gtc gtg aag cac ata gtg acg cca gag tgg ctg gaa gaa tgc ttc      2984
Ser Val Val Lys His Ile Val Thr Pro Glu Trp Leu Glu Glu Cys Phe
885                 890                 895                 900

agg tgt cag aag ttc att gat gag cag aac tac att ctc cga gat gct      3032
Arg Cys Gln Lys Phe Ile Asp Glu Gln Asn Tyr Ile Leu Arg Asp Ala
                905                 910                 915

gag gca gaa gta ctt ttc tct ttc agc ttg gaa gaa tcc tta aaa cgg      3080
Glu Ala Glu Val Leu Phe Ser Phe Ser Leu Glu Glu Ser Leu Lys Arg
            920                 925                 930

gca cac gtt tct cca ctc ttt aag gca aaa tat ttt tac atc aca cct      3128
Ala His Val Ser Pro Leu Phe Lys Ala Lys Tyr Phe Tyr Ile Thr Pro
        935                 940                 945

gga atc tgc cca agt ctt tcc act atg aag gca atc gta gag tgt gca      3176
Gly Ile Cys Pro Ser Leu Ser Thr Met Lys Ala Ile Val Glu Cys Ala
    950                 955                 960

gga gga aag gtg tta tcc aag cag cca tct ttc cgg aag ctc atg gag      3224
Gly Gly Lys Val Leu Ser Lys Gln Pro Ser Phe Arg Lys Leu Met Glu
965                 970                 975                 980

cac aag cag aac tcg agt ttg tcg gaa ata att tta ata tcc tgt gaa      3272
His Lys Gln Asn Ser Ser Leu Ser Glu Ile Ile Leu Ile Ser Cys Glu
                985                 990                 995

aat gac ctt cat  tta tgc cga gaa tat  ttt gcc aga ggc ata  gat       3317
Asn Asp Leu His  Leu Cys Arg Glu Tyr  Phe Ala Arg Gly Ile  Asp
            1000                1005                1010

gtt cac aat gca  gag ttc gtt ctg act  gga gtg ctc act caa  acg       3362
Val His Asn Ala  Glu Phe Val Leu Thr  Gly Val Leu Thr Gln  Thr
            1015                1020                1025

ctg gac tat gaa  tca tat aag ttt aac  tga tggcgtctag gctgccgtgc      3412
Leu Asp Tyr Glu  Ser Tyr Lys Phe Asn
            1030                1035

atgtcgactc ctgcggtgcg gggctggctg tctggctggc gaggagctgc tgcgcttcct   3472

tcacatgctc ttgttttcca gctgctttcc tgggggatca gactgtgaag caggaagaca   3532

gatataataa atatactgca tctttttaag atgtgcaatt ttattctgag gaaacataaa   3592
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ttatgttttg tattatatga ctttaagagc ccacattagg ttttatgatt catttgccag 3652

gtttttaaat gttttcacaa aactgttacg ggacttcaac tagaaataaa atggtgtaaa 3712

taaagacctt gctatctcta aattatggat gttaaagatt tgaaatgttt tgtactttga 3772

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Ala Phe Leu Arg Val Leu Ile Gln Ala Gly Ala Leu Cys Trp Ser Leu
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Pro Glu Leu Ser Gln Gly Glu Val Gly Lys Gly Ala Cys Pro Ala Glu
35 40 45

Val Gly Lys His Arg Asp His Leu Pro Ser Ser Asp Pro Val Leu Met
50 55 60

Gln Ala Glu Ala Ser Val Val Met Cys Trp Val Ser Ser Glu Asp Arg
65 70 75 80

Ser Ala Leu Trp Ala Leu Val Thr Phe Tyr Gly Gly Asp Cys Gln Leu
85 90 95

Thr Leu Asn Lys Lys Cys Thr His Leu Ile Val Pro Glu Pro Lys Gly
100 105 110

Glu Lys Tyr Glu Cys Ala Leu Lys Arg Ala Ser Ile Lys Ile Val Thr
115 120 125

Pro Asp Trp Val Leu Asp Cys Val Ser Glu Lys Thr Lys Lys Asp Glu
130 135 140

Ala Phe Tyr His Pro Arg Leu Ile Ile Tyr Glu Glu Glu Glu Glu Glu

145 150 155 160

Glu Glu Glu Glu Glu Glu Val Glu Asn Glu Glu Gln Asp Ser Gln Asn
165 170 175

Glu Gly Ser Thr Asp Glu Lys Ser Ser Pro Ala Ser Ser Gln Glu Gly
180 185 190

Ser Pro Ser Gly Asp Gln Gln Phe Ser Pro Lys Ser Asn Thr Glu Lys
195 200 205

Ser Lys Gly Glu Leu Met Phe Asp Asp Ser Ser Asp Ser Ser Pro Glu
210 215 220

Lys Gln Glu Arg Asn Leu Asn Trp Thr Pro Ala Glu Val Pro Gln Leu
225 230 235 240

Ala Ala Ala Lys Arg Arg Leu Pro Gln Gly Lys Glu Pro Gly Leu Ile
245 250 255

Asn Leu Cys Ala Asn Val Pro Pro Val Pro Gly Asn Ile Leu Pro Pro
260 265 270

Glu Val Arg Gly Asn Leu Met Ala Ala Gly Gln Asn Leu Gln Ser Ser
275 280 285

Glu Arg Ser Glu Met Ile Ala Thr Trp Ser Pro Ala Val Arg Thr Leu
290 295 300

Arg Asn Ile Thr Asn Asn Ala Asp Ile Gln Gln Met Asn Arg Pro Ser
305 310 315 320

Asn Val Ala His Ile Leu Gln Thr Leu Ser Ala Pro Thr Lys Asn Leu
325 330 335

Glu Gln Gln Val Asn His Ser Gln Gln Gly His Thr Asn Ala Asn Ala
340 345 350

Val Leu Phe Ser Gln Val Lys Val Thr Pro Glu Thr His Met Leu Gln
355 360 365

Gln Gln Gln Gln Ala Gln Gln Gln Gln Gln Gln His Pro Val Leu His

370 375 380

Leu Gln Pro Gln Gln Ile Met Gln Leu Gln Gln Gln Gln Gln Gln Gln
385 390 395 400

Ile Ser Gln Gln Pro Tyr Pro Gln Gln Pro Pro His Pro Phe Ser Gln
405 410 415

Gln Gln Gln Gln Gln Gln Gln Ala His Pro His Gln Phe Ser Gln Gln
420 425 430

Gln Leu Gln Phe Pro Gln Gln Gln Leu His Pro Pro Gln Gln Leu His
435 440 445

Arg Pro Gln Gln Gln Leu Gln Pro Phe Gln Gln Gln His Ala Leu Gln
450 455 460

Gln Gln Phe His Gln Leu Gln Gln His Gln Leu Gln Gln Gln Gln Leu
465 470 475 480

Ala Gln Leu Gln Gln Gln His Ser Leu Leu Gln Gln Gln Gln Gln Gln
485 490 495

Gln Ile Gln Gln Gln Gln Leu Gln Arg Met His Gln Gln Gln Gln Gln
500 505 510

Gln Gln Met Gln Ser Gln Thr Ala Pro His Leu Ser Gln Thr Ser Gln
515 520 525

Ala Leu Gln His Gln Val Pro Pro Gln Gln Pro Pro Gln Gln Gln Gln
530 535 540

Gln Gln Gln Pro Pro Pro Ser Pro Gln Gln His Gln Leu Phe Gly His
545 550 555 560

Asp Pro Ala Val Glu Ile Pro Glu Glu Gly Phe Leu Leu Gly Cys Val
565 570 575

Phe Ala Ile Ala Asp Tyr Pro Glu Gln Met Ser Asp Lys Gln Leu Leu
580 585 590

Ala Thr Trp Lys Arg Ile Ile Gln Ala His Gly Gly Thr Val Asp Pro

595 600 605

Thr Phe Thr Ser Arg Cys Thr His Leu Leu Cys Glu Ser Gln Val Ser
610 615 620

Ser Ala Tyr Ala Gln Ala Ile Arg Glu Arg Lys Arg Cys Val Thr Ala
625 630 635 640

His Trp Leu Asn Thr Val Leu Lys Lys Lys Lys Met Val Pro Pro His
645 650 655

Arg Ala Leu His Phe Pro Val Ala Phe Pro Pro Gly Gly Lys Pro Cys
660 665 670

Ser Gln His Ile Ile Ser Val Thr Gly Phe Val Asp Ser Asp Arg Asp
675 680 685

Asp Leu Lys Leu Met Ala Tyr Leu Ala Gly Ala Lys Tyr Thr Gly Tyr
690 695 700

Leu Cys Arg Ser Asn Thr Val Leu Ile Cys Lys Glu Pro Thr Gly Leu
705 710 715 720

Lys Tyr Glu Lys Ala Lys Glu Trp Arg Ile Pro Cys Val Asn Ala Gln
725 730 735

Trp Leu Gly Asp Ile Leu Leu Gly Asn Phe Glu Ala Leu Arg Gln Ile
740 745 750

Gln Tyr Ser Arg Tyr Thr Ala Phe Ser Leu Gln Asp Pro Phe Ala Pro
755 760 765

Thr Gln His Leu Val Leu Asn Leu Leu Asp Ala Trp Arg Val Pro Leu
770 775 780

Lys Val Ser Ala Glu Leu Leu Met Ser Ile Arg Leu Pro Pro Lys Leu
785 790 795 800

Lys Gln Asn Glu Val Ala Asn Val Gln Pro Ser Ser Lys Arg Ala Arg
805 810 815

Ile Glu Asp Val Pro Pro Pro Thr Lys Lys Leu Thr Pro Glu Leu Thr

820 825 830

Pro Phe Val Leu Phe Thr Gly Phe Glu Pro Val Gln Val Gln Gln Tyr
835 840 845

Ile Lys Lys Leu Tyr Ile Leu Gly Gly Glu Val Ala Glu Ser Ala Gln
850 855 860

Lys Cys Thr His Leu Ile Ala Ser Lys Val Thr Arg Thr Val Lys Phe
865 870 875 880

Leu Thr Ala Ile Ser Val Val Lys His Ile Val Thr Pro Glu Trp Leu
885 890 895

Glu Glu Cys Phe Arg Cys Gln Lys Phe Ile Asp Glu Gln Asn Tyr Ile
900 905 910

Leu Arg Asp Ala Glu Ala Glu Val Leu Phe Ser Phe Ser Leu Glu Glu
915 920 925

Ser Leu Lys Arg Ala His Val Ser Pro Leu Phe Lys Ala Lys Tyr Phe
930 935 940

Tyr Ile Thr Pro Gly Ile Cys Pro Ser Leu Ser Thr Met Lys Ala Ile
945 950 955 960

Val Glu Cys Ala Gly Gly Lys Val Leu Ser Lys Gln Pro Ser Phe Arg
965 970 975

Lys Leu Met Glu His Lys Gln Asn Ser Ser Leu Ser Glu Ile Ile Leu
980 985 990

Ile Ser Cys Glu Asn Asp Leu His Leu Cys Arg Glu Tyr Phe Ala Arg
995 1000 1005

Gly Ile Asp Val His Asn Ala Glu Phe Val Leu Thr Gly Val Leu
1010 1015 1020

Thr Gln Thr Leu Asp Tyr Glu Ser Tyr Lys Phe Asn
1025 1030 1035