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(54) **BIOMARKERS FOR THE EARLY
DETECTION OF BREAST CANCER**

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(57) **ABSTRACT**

The present invention provides reagents and methods for breast cancer detection.

Specification includes a Sequence Listing.

BIOMARKERS FOR THE EARLY DETECTION OF BREAST CANCER

CROSS-REFERENCE

[0001] This application claims priority to U.S. Provisional Patent Application Ser. No. 61/373,359 filed Aug. 13, 2010, incorporated by reference herein in its entirety.

STATEMENT OF U.S. GOVERNMENT INTEREST

[0002] This work was funded in part by grant number 7U01CA117374 awarded by the Early Detection Research Network (NIH/NCI 7U01CA117374). The U.S. government has certain rights in the invention.

SEQUENCE LISTING STATEMENT

[0003] The sequence listing is filed in this application in electronic format only and is incorporated by reference herein. The sequence listing text file "10-294-PCT_SeqList.txt" was created on Aug. 1, 2011, and is 54,649 byte in size.

BACKGROUND

[0004] Despite recent advances in early detection and treatment, breast cancer remains a common and significant health problem in the United States. Women diagnosed with stage II and III breast cancer have a high-risk for distant recurrence and up to half of these women will develop metastatic disease, which remains incurable with current therapy. In this setting, there is intense effort in the search for biomarkers that can detect early disease, and to monitor for disease progression and recurrence. With the advent of molecularly-targeted therapeutics, biomarkers that are associated with biological subtypes of cancer may be useful for predicting responses to therapeutic interventions.

[0005] Proteomics-based approaches to distinguish cancer-bearing patient sera from healthy control sera have been challenged by the difficulty in identifying small quantities of protein fragments within complex protein mixtures, protein instability, and natural variations in protein content within patient populations. Autoantibodies (AAb) to tumor antigens have advantages over other serum proteins as potential cancer biomarkers as they are stable, highly specific, easily purified from serum, and are readily detected with well-validated secondary reagents. Although they have high specificities to distinguish cancer from control sera, most tumor AAb demonstrate poor sensitivities. Testing multiple antigens in parallel may serve to increase the predictive value of tumor-specific antibodies for use as immunodiagnosics.

[0006] Protein microarrays offer an emerging platform to present tumor antigens to screen for immune responses. In comparison to traditional ELISAs, protein microarrays are capable of presenting and assessing hundreds of tumor antigens simultaneously. The responses are rapidly identified because the address of each protein is known in advance and there are no representation issues; all proteins, even rare ones, are represented equally (usually in duplicate). The proteins are arrayed on a single microscope slide requiring only a few microliters of serum per assay. Known tumor antigens as well as predicted tumor antigens can be included to generate a comprehensive protein tumor antigen array. Despite some early demonstrations of feasibility, protein microarrays are not yet widely used, due to the labor and

technical issues associated with production, purification, and quality control of proteins for spotting on the array, as well as difficulties with downstream validation assays of target AAb.

SUMMARY OF THE INVENTION

[0007] In a first aspect, the present invention provides polypeptide probe sets comprising:

[0008] at least 2 different isolated polypeptides selected from the group consisting of ATP6AP1 (SEQ ID NO: 13), PDCD6IP (SEQ ID NO: 21), DBT (SEQ ID NO: 25), CSNK1E (SEQ TD NO: 9), FRS3 (SEQ TD NO: 3), RAC3 (SEQ TD NO: 15), HOXD1 (SEQ ID NO: 7), SF3A1 (SEQ ID NO: 1), CTBP1 (SEQ ID NO: 29), C15orf48 (SEQ ID NO: 35), MYOZ2 (SEQ ID NO: 33), EIF3E (SEQ ID NO: 39), BAT4 (SEQ ID NO: 5), ATF3 (SEQ ID NO: 19), BMX (SEQ TD NO: 45), RAB5A (SEQ TD NO: 23), UBAP1 (SEQ TD NO: 47), SOX2 (SEQ ID NO: 31), GPR157 (SEQ ID NO: 43), BDNF (SEQ ID NO: 17), ZMYM6 (SEQ ID NO: 41), SLC33A1 (SEQ ID NO: 11), TRIM32 (SEQ ID NO: 37), ALG10 (SEQ ID NO: 27), TFCP2 (SEQ ID NO: 49), SERPINH1 (SEQ ID NO: 51), SELL (SEQ TD NO: 55), ZNF510 (SEQ TD NO: 53), or antigenic fragments thereof, attached to the support.

[0009] In a second aspect, the present invention provides polynucleotide arrays comprising:

[0010] (a) a support; and

[0011] (b) at least 2 different isolated nucleic acids encoding polypeptides selected from the group consisting of ATP6AP1 (SEQ ID NO: 14), PDCD6IP (SEQ TD NO: 22), DBT (SEQ TD NO: 26), CSNK1E (SEQ ID NO: 10), FRS3 (SEQ ID NO: 4), RAC3 (SEQ ID NO: 16), HOXD1 (SEQ ID NO: 8), SF3A1 (SEQ ID NO: 2), CTBP1 (SEQ ID NO: 30), C15orf48 (SEQ ID NO: 36), MYOZ2 (SEQ ID NO: 34), EIF3E (SEQ ID NO: 40), BAT4 (SEQ ID NO: 6), ATF3 (SEQ ID NO: 20), BMX (SEQ ID NO: 46), RABSA (SEQ ID NO: 24), UBAP1 (SEQ ID NO: 48), SOX2 (SEQ ID NO: 32), GPR157 (SEQ ID NO: 44), BDNF (SEQ ID NO: 18), ZMYM6 (SEQ ID NO: 42), SLC33A1 (SEQ ID NO: 12), TRIM32 (SEQ ID NO: 38), ALG10 (SEQ ID NO: 28), TFCP2 (SEQ ID NO: 50), SERPINH1 (SEQ ID NO: 52), SELL (SEQ ID NO: 56), ZNF510 (SEQ ID NO: 54), or antigenic fragments thereof, attached to the support.

[0012] In a third aspect, the present invention provides methods for detecting breast cancer, comprising:

[0013] (a) contacting a suitable bodily fluid sample obtained from a subject at risk of breast cancer with one or more isolated polypeptides selected from the group consisting of ATP6AP1 (SEQ ID NO: 13), PDCD6IP (SEQ ID NO: 21), DBT (SEQ ID NO: 25), CSNK1E (SEQ ID NO: 9), FRS3 (SEQ ID NO: 3), RAC3 (SEQ ID NO: 15), HOXD1 (SEQ ID NO: 7), SF3A1 (SEQ ID NO: 1), CTBP1 (SEQ ID NO: 29), C15orf48 (SEQ ID NO: 35), MYOZ2 (SEQ ID NO: 33), EIF3E (SEQ ID NO: 39), BAT4 (SEQ ID NO: 5), ATF3 (SEQ ID NO: 19), BMX (SEQ ID NO: 45), RABSA (SEQ ID NO: 23), UBAP1 (SEQ ID NO: 47), SOX2 (SEQ ID NO: 31), GPR157 (SEQ ID NO: 43), BDNF (SEQ ID NO: 17), ZMYM6 (SEQ ID NO: 41), SLC33A1 (SEQ ID NO: 11), TRIM32 (SEQ ID NO: 37), ALG10 (SEQ ID NO: 27), TFCP2 (SEQ ID NO: 49), SERPINH1 (SEQ ID NO: 51), SELL (SEQ ID NO: 55), ZNF510 (SEQ ID NO: 53), or

antigenic fragments thereof; wherein the contacting occurs under conditions suitable for selective binding of antibodies in the bodily fluid sample to the one or more polypeptides; and

[0014] (b) detecting presence of antibodies to the polypeptides in the bodily fluid sample;

[0015] wherein the presence of antibodies to the one or more polypeptides indicates a likelihood of breast cancer in the subject.

DETAILED DESCRIPTION OF THE INVENTION

[0016] In a first aspect, the present invention provides polypeptide probe sets comprising:

[0017] (a) at least 2 different isolated polypeptides selected from the group consisting of ATP6AP1 (SEQ ID NO: 13), PDCD6IP (SEQ ID NO: 21), DBT (SEQ ID NO: 25), CSNK1E (SEQ ID NO: 9), FRS3 (SEQ ID NO: 3), RAC3 (SEQ ID NO: 15), HOXD1 (SEQ ID NO: 7), SF3A1 (SEQ ID NO: 1), CTBP1 (SEQ ID NO: 29), C15orf48 (SEQ ID NO: 35), MYOZ2 (SEQ ID NO: 33), EIF3E (SEQ ID NO: 39), BAT4 (SEQ ID NO: 5), ATF3 (SEQ ID NO: 19), BMX (SEQ ID NO: 45), RABSA (SEQ ID NO: 23), UBAP1 (SEQ ID NO: 47), SOX2 (SEQ ID NO: 31), GPR157 (SEQ ID NO: 43), BDNF (SEQ ID NO: 17), ZMYM6 (SEQ ID NO: 41), SLC33A1 (SEQ ID NO: 11), TRIM32 (SEQ ID NO: 37), ALG10 (SEQ ID NO: 27), TFCP2 (SEQ ID NO: 49), SERPINH1 (SEQ ID NO: 51), SELL (SEQ ID NO: 55), ZNF510 (SEQ ID NO: 53), or antigenic fragments thereof, attached to the support.

[0018] Using a sequential screening strategy to select antigen-specific antibodies (AAb) from 4988 tumor antigens, 119 AAb potential novel biomarkers for the early detection of breast cancer were identified. A blinded validation study produced supporting evidence for 28 of these potential biomarkers, recited above. Thus, the polypeptide probe sets of the invention can be used, for example, to detect tumor antigen-specific autoantibodies in a bodily fluid sample from patients with breast cancer, such as early stage breast cancer. Descriptions of the polypeptides, their amino acid sequences and their nucleic acid sequences are provided in Table 1.

[0019] In various embodiments, the polypeptide probe sets comprise at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, or all 28 of the recited polypeptides, or antigenic portions thereof.

[0020] In a preferred embodiment, the at least 2 different isolated polypeptides in the probe sets are selected from the group consisting of ATP6AP1 (SEQ ID NO: 13), PDCD6IP (SEQ ID NO: 21), DBT (SEQ ID NO: 25), CSNK1E (SEQ ID NO: 9), FRS3 (SEQ ID NO: 3), HOXD1 (SEQ ID NO: 7), SF3A1 (SEQ ID NO: 1), C15orf48 (SEQ ID NO: 35), MYOZ2 (SEQ ID NO: 33), BAT4 (SEQ ID NO: 5), BMX (SEQ ID NO: 45), RAB5A (SEQ ID NO: 23), UBAP1 (SEQ ID NO: 47), GPR157 (SEQ ID NO: 43), ZMYM6 (SEQ ID NO: 41), SLC33A1 (SEQ ID NO: 11), TRIM32 (SEQ ID NO: 37), ALG10 (SEQ ID NO: 27), TFCP2 (SEQ ID NO: 49), SERPINH1 (SEQ ID NO: 51), SELL (SEQ ID NO: 55), ZNF510 (SEQ ID NO: 53), or antigenic fragments thereof. Thus, in various embodiments, the polypeptide probe sets comprise at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, or all 22 of the recited polypeptides, or antigenic portions thereof. In a further preferred embodiment the probe sets comprise ATP6AP1 (SEQ ID NO: 13)

and at least one other of the recited polypeptides, or antigenic portions thereof. Thus, in various embodiments, the polypeptide arrays comprise at least ATP6AP1 and 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, or all 27 of the other recited polypeptides, or antigenic portions thereof.

[0021] In a preferred embodiment, the probe sets comprise at least 2, 3, 4, 5, or all 6 of ATP6AP1 (SEQ ID NO: 13), CTBP1 (SEQ ID NO: 29), EIF3E (SEQ ID NO: 39), ATF3 (SEQ ID NO: 19), SOX2 (SEQ ID NO: 31), and BDNF (SEQ ID NO: 17), or antigenic portions thereof. The term “polypeptide” is used in its broadest sense to refer to a polymer of subunit amino acids, amino acid analogs, or peptidomimetics, including proteins and peptoids. The polypeptides may be naturally occurring full length proteins or fragments thereof, processed forms of naturally occurring polypeptides (such as by enzymatic digestion), chemically synthesized polypeptides, or recombinantly expressed polypeptides. The polypeptides may comprise D- and/or L-amino acids, as well as any other synthetic amino acid subunit, and may contain any other type of suitable modification, including but not limited to peptidomimetic bonds and reduced peptide bonds.

[0022] As used herein, an “antigenic fragment” is any portion of at least 4 amino acids of the recited polypeptide that can give rise to an immune response. In various preferred embodiments, the antigenic fragments are at least 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 35, 40, 45, 50, 75, 100, 150, 200, 250, 300, or the full amino acid sequence of the recited polypeptide.

[0023] In various further preferred embodiments, that can be combined with any other embodiments, the polypeptide probe sets comprise no more than 20,000 different polypeptides, or antigenic portions thereof and preferably comprise no more than 10,000; 5,000; 1,000; 500; 250; 100; 75; 50; 45; 40; 35; 30; 28, 27, 26, 25, 24, 23, 22, 21, 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, or 2 different polypeptides. In this and other embodiments, two or more antigenic portions of the same polypeptide in the probe set count only as 1 polypeptide or antigenic portion thereof.

[0024] As will be appreciated by those of skill in the art, it may be desirable to include further polypeptides or other molecules in the probe sets as references, controls, positional markers, or as additional markers. Any suitable such further polypeptide or other molecule can be used. Exemplary additional polypeptide markers include but are not limited to p53, CTBP1, RAC3, and activating transcription factor-3 (ATF3). Exemplary analytical controls include human IgG and empty spots (when the probe set is present on a support). Any portion or the entirety of the recited polypeptides may be used in the probe set, so long as it is capable of binding to autoantibodies against the polypeptide.

[0025] The polypeptide probe sets can be present in any form useful for a given purpose. In various preferred embodiments, they can be present in solution, lyophilized, frozen, or immobilized on a substrate.

[0026] In one preferred embodiment, the polypeptides are immobilized on a substrate. Any suitable technique for immobilizing the polypeptides on the support can be used. In one embodiment, Nucleic Acid Protein Programmable Array (NAPPA) technology can be used. NAPPA arrays are generated by printing full-length cDNAs encoding the target proteins at each feature of the array. The proteins are then

transcribed and translated by a cell-free system and immobilized in situ using epitope tags fused to the proteins. Other suitable immobilization methods include, but are not limited to luciferase immunoprecipitation systems (LIPS), Luminex™ beads, wells of a 96 well dish, standard immune dipstick assays, standard ELISA assays,

[0027] As used herein, an array may be any arrangement or disposition of the polypeptides. In one embodiment, the polypeptides are at specific and identifiable locations on the array. Those of skill in the art will recognize that many such permutations of the polypeptides on the array are possible. In another non-limiting embodiment, each distinct location on the array comprises a distinct polypeptide.

[0028] Any suitable support may be used. Examples of such supports include, but are not limited to, microarrays, beads, columns, optical fibers, wipes, nitrocellulose, nylon, glass, quartz, diazotized membranes (paper or nylon), silicones, polyformaldehyde, cellulose, cellulose acetate, paper, ceramics, metals, metalloids, semiconductive materials, coated beads, magnetic particles; plastics such as polyethylene, polypropylene, and polystyrene; and gel-forming materials, such as proteins (e.g., gelatins), lipopolysaccharides, silicates, agarose, polyacrylamides, methylmethacrylate polymers; sol gels; porous polymer hydrogels; nanostructured surfaces; nanotubes (such as carbon nanotubes), and nanoparticles (such as gold nanoparticles or quantum dots).

[0029] In one embodiment, the support is a solid support. Any suitable "solid support" may be used to which the polypeptides can be attached including but not limited to dextrans, hydrogels, silicon, quartz, other piezoelectric materials such as langasite ($\text{La}_3\text{Ga}_5\text{SiO}_{14}$), nitrocellulose, nylon, glass, diazotized membranes (paper or nylon), polyformaldehyde, cellulose, cellulose acetate, paper, ceramics, metals, metalloids, semiconductive materials, coated beads, magnetic particles; plastics such as polyethylene, polypropylene, and polystyrene; and gel-forming materials, such as proteins (e.g., gelatins), lipopolysaccharides, silicates, agarose and polyacrylamides.

[0030] Any suitably sized solid support can be used. In one non-limiting example, the solid support comprises slides with dimensions of approximately 3 inches by 1 inch.

[0031] In all embodiments of the invention, the polypeptides of the probe set may further comprise a tag, such as a detectable moiety. This is particularly preferred when the polypeptide probe sets or in solution, or in any other format where different polypeptides in the probe set cannot be distinguished by differential positions on a support. In such embodiments, it is particularly preferred that the different polypeptides, or antigenic fragments thereof, that are present in the probe set are distinguishable, through the use of differentially detectable tags, using techniques known to those of skill in the art. The tag(s) can be linked to the polypeptide through covalent bonding, including, but not limited to, disulfide bonding, hydrogen bonding, electrostatic bonding, recombinant fusion and conformational bonding. Alternatively, the tag(s) can be linked to the polypeptide by means of one or more linking compounds. Techniques for conjugating tags to polypeptides are well known to the skilled artisan. The polypeptides of the probe set, comprising a detectable tag can be used diagnostically to, for example, assess the presence of antibodies to the polypeptides in a sample; and thereby detect the presence of breast cancer, or monitor the development or progression of

breast cancer as part of a clinical testing procedure. Any suitable detection tag can be used, including but not limited to enzymes, prosthetic groups, fluorescent materials, luminescent materials, bioluminescent materials, radioactive materials, positron emitting metals, and nonradioactive paramagnetic metal ions. The tag used will depend on the specific detection/analysis/diagnosis techniques and/or methods used such as immunohistochemical staining of (tissue) samples, flow cytometric detection, scanning laser cytometric detection, fluorescent immunoassays, enzyme-linked immunosorbent assays (ELISAs), radioimmunoassays (RIAs), bioassays (e.g., neutralization assays), Western blotting applications, etc. For immunohistochemical staining of tissue samples preferred tags are enzymes that catalyze production and local deposition of a detectable product. Enzymes typically conjugated to polypeptides to permit their immunohistochemical visualization are well known and include, but are not limited to, acetylcholinesterase, alkaline phosphatase, beta-galactosidase, glucose oxidase, horseradish peroxidase, and urease. Typical substrates for production and deposition of visually detectable products are also well known to the skilled person in the art. The polypeptides can be labeled using colloidal gold or they can be labeled with radioisotopes, such as ^{33}P , ^{32}P , ^{35}S , ^3H , and ^{125}I . Polypeptides of the probe set can be attached to radionuclides directly or indirectly via a chelating agent by methods well known in the art.

[0032] In a second aspect, the present invention provides polynucleotide arrays comprising:

[0033] (a) a support; and

[0034] (b) at least 2 different isolated nucleic acids encoding polypeptides selected from the group consisting of ATP6AP1 (SEQ ID NO: 14), PDCD6IP (SEQ ID NO: 22), DBT (SEQ ID NO: 26), CSNK1E (SEQ ID NO: 10), FRS3 (SEQ ID NO: 4), RAC3 (SEQ ID NO: 16), HOXD1 (SEQ ID NO: 8), SF3A1 (SEQ ID NO: 2), CTBP1 (SEQ ID NO: 30), C15orf48 (SEQ ID NO: 36), MYOZ2 (SEQ ID NO: 34), EIF3E (SEQ ID NO: 40), BAT4 (SEQ ID NO: 6), ATF3 (SEQ ID NO: 20), BMX (SEQ ID NO: 46), RABSA (SEQ ID NO: 24), UBAP1 (SEQ ID NO: 48), SOX2 (SEQ ID NO: 32), GPR157 (SEQ ID NO: 44), BDNF (SEQ ID NO: 18), ZMYM6 (SEQ ID NO: 42), SLC33A1 (SEQ ID NO: 12), TRIM32 (SEQ ID NO: 38), ALG10 (SEQ ID NO: 28), TFPC2 (SEQ ID NO: 50), SERPINH1 (SEQ ID NO: 52), SELL (SEQ ID NO: 56), ZNF510 (SEQ ID NO: 54), or antigenic fragments thereof, attached to the support. In this aspect, the arrays can also be used for example, to detect tumor antigen-specific autoantibodies in patients with breast cancer, such as early stage breast cancer. Any suitable technique can be used for attaching the nucleic acids to the support. In one embodiment, NAPPA arrays are generated by printing cDNAs encoding the target proteins, or antigenic fragments thereof, at features of the support. Other techniques for printing nucleic acids on a support can be used and are well known in the art.

[0035] In various embodiments, the arrays comprise at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, or all 28 of the recited nucleic acids, attached to the support.

[0036] In a preferred embodiment the at least 2 different isolated nucleic acids encode polypeptides selected from the group consisting of ATP6AP1 (SEQ ID NO: 14), PDCD6IP (SEQ ID NO: 22), DBT (SEQ ID NO: 26), CSNK1E (SEQ ID NO: 10), FRS3 (SEQ ID NO: 4), HOXD1 (SEQ ID NO:

8), SF3A1 (SEQ ID NO: 2), C15orf48 (SEQ ID NO: 36), MYOZ2 (SEQ ID NO: 34), BAT4 (SEQ ID NO: 6), BMX (SEQ ID NO: 46), RAB5A (SEQ ID NO: 24), UBAP1 (SEQ ID NO: 48), GPR157 (SEQ ID NO: 44), ZMYM6 (SEQ ID NO: 42), SLC33A1 (SEQ ID NO: 12), TRIM32 (SEQ ID NO: 38), ALG10 (SEQ ID NO: 28), TFCEP2 (SEQ ID NO: 50), SERPINH1 (SEQ ID NO: 52), SELL (SEQ ID NO: 56), ZNF510 (SEQ ID NO: 54), or antigenic fragments thereof. Thus, in various embodiments, the polynucleotide arrays comprise at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, or all 22 of the recited nucleic acids, or antigenic portions thereof, attached to the support.

[0037] In a further preferred embodiment the at least 2 different isolated nucleic acids encode ATP6AP1 (SEQ ID NO: 14) and at least one other of the recited nucleic acids, or antigenic portions thereof. Thus, in various embodiments, the polynucleotide arrays comprise at least ATP6AP1 and 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, or all 27 of the other recited nucleic acids, or antigenic portions thereof, attached to the support.

[0038] In another preferred embodiment, the at least isolated nucleic acids encode 2, 3, 4, 5, or all 6 of ATP6AP1 (SEQ ID NO: 13), CTBP1 (SEQ ID NO: 29), EIF3E (SEQ ID NO: 39), ATF3 (SEQ ID NO: 19), SOX2 (SEQ ID NO: 31), and BDNF (SEQ ID NO: 17), or antigenic portions thereof.

[0039] In various further preferred embodiments, that can be combined with any other embodiments, the arrays comprise no more than 20,000 different nucleic acids, and preferably comprise no more than 10,000; 5,000; 1,000; 500; 250; 100; 75; 50; 45; 40; 35; 30; 28, 27, 26, 25, 24, 23, 22, 21, 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, or 2 different nucleic acids.

[0040] As will be appreciated by those of skill in the art, it may be desirable to place nucleic acids encoding other polypeptides on the support as controls, positional markers, or as additional markers, including but not limited to p53, CTBP1, RAC3, and activating transcription factor-3 (ATF3).

[0041] Any portion or the entirety of the recited nucleic acid may be attached to the support, so long as it encodes a polypeptide, or antigenic fragment thereof, capable of binding to autoantibodies against the polypeptide.

[0042] The definitions and all embodiments disclosed in the first aspect apply to this second aspect.

[0043] In a third aspect, the present invention provides methods for detecting breast cancer, comprising:

[0044] (a) contacting a suitable bodily fluid sample obtained from a subject at risk of breast cancer with one or more isolated polypeptides selected from the group consisting of ATP6AP1 (SEQ ID NO: 13), PDCE6IP (SEQ ID NO: 21), DBT (SEQ ID NO: 25), CSNK1E (SEQ ID NO: 9), FRS3 (SEQ ID NO: 3), RAC3 (SEQ ID NO: 15), HOXD1 (SEQ ID NO: 7), SF3A1 (SEQ ID NO: 1), CTBP1 (SEQ ID NO: 29), C15orf48 (SEQ ID NO: 35), MYOZ2 (SEQ ID NO: 33), EIF3E (SEQ ID NO: 39), BAT4 (SEQ ID NO: 5), ATF3 (SEQ ID NO: 19), BMX (SEQ ID NO: 45), RABSA (SEQ ID NO: 23), UBAP1 (SEQ ID NO: 47), SOX2 (SEQ ID NO: 31), GPR157 (SEQ ID NO: 43), BDNF (SEQ ID NO: 17), ZMYM6 (SEQ ID NO: 41), SLC33A1 (SEQ ID NO: 11), TRIM32 (SEQ ID NO: 37), ALG10 (SEQ ID NO: 27), TFCEP2 (SEQ ID NO: 49), SERPINH1 (SEQ ID NO: 51), SELL (SEQ ID NO: 55), ZNF510 (SEQ ID NO: 53), or

antigenic fragments thereof; wherein the contacting occurs under conditions suitable for selective binding of antibodies in the bodily fluid sample to the one or more polypeptides; and

[0045] (b) detecting presence of antibodies to the polypeptides in the bodily fluid sample;

[0046] wherein the presence of antibodies in the bodily fluid sample to the one or more polypeptides indicates a likelihood of breast cancer in the subject.

[0047] The inventors have discovered that the presence of autoantibodies to one or more of the recited polypeptides is a positive predictor of breast cancer, and thus the methods of the invention provide valuable diagnostic and prognostic information to an attending physician.

[0048] As used herein a subject “at risk of breast cancer” is any human considered to be in a risk group for breast cancer. In one embodiment, the subject is a woman. In other embodiments, the subject has one or more of a lump in their breast tissue, lymph nodes, or armpit; changes in breast size or shape; skin dimpling; nipple inversion; spontaneous single-nipple discharge; a family/personal history of breast cancer; or is a carrier of a mutation in the BRCA or other gene that predisposes one to breast cancer.

[0049] Suitable bodily fluid samples include serum, plasma, CSF, pleural fluid, joint fluid, nipple discharge, saliva. In a preferred embodiment, the bodily fluid sample is serum or plasma.

[0050] In one embodiment, the presence of any amount of antibodies to the polypeptides in a sample from a subject at risk of breast cancer can indicate a likelihood of breast cancer in the subject. In another embodiment, if antibodies to the polypeptides are present in a sample from a subject at risk of breast cancer, at levels which are higher than that of a control sample (i.e. a sample from a subject who does not have breast cancer) than the subject at risk of breast cancer has a likelihood of breast cancer. Subjects with a likelihood of breast cancer can then be tested for the actual presence of breast cancer using standard diagnostic techniques known to the skilled artisan, including mammography, biopsy, or breast MRI. In various embodiments, the method results in an accurate diagnosis in at least 70% of cases; more preferably of at least 75%, 80%, 85%, 90%, or more of the cases. In a preferred embodiment, the likelihood of breast cancer is a likelihood of Stage I or Stage II breast cancer.

[0051] In various embodiments, the methods comprise contacting a bodily fluid sample, such as serum, obtained from a subject at risk of breast cancer with 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, or all 28 of the recited polypeptides, or antigenic fragments thereof. In various embodiments, the presence of antibodies in the bodily fluid sample to 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, or all 28 of the recited polypeptides, or antigenic fragments thereof, indicates a likelihood of breast cancer in the subject.

[0052] In a preferred embodiment, the one or more isolated polypeptides are selected from the group consisting of ATP6AP1 (SEQ ID NO: 13), PDCE6IP (SEQ ID NO: 21), DBT (SEQ ID NO: 25), CSNK1E (SEQ ID NO: 9), FRS3 (SEQ ID NO: 3), HOXD1 (SEQ ID NO: 7), SF3A1 (SEQ ID NO: 1), C15orf48 (SEQ ID NO: 35), MYOZ2 (SEQ ID NO: 33), BAT4 (SEQ ID NO: 5), BMX (SEQ ID NO: 45), RABSA (SEQ ID NO: 23), UBAP1 (SEQ ID NO: 47), GPR157 (SEQ ID NO: 43), ZMYM6 (SEQ ID NO: 41),

SLC33A1 (SEQ ID NO: 11), TRIM32 (SEQ ID NO: 37), ALG10 (SEQ TD NO: 27), TFCEP2 (SEQ TD NO: 49), SERPINH1 (SEQ TD NO: 51), SELL (SEQ ID NO: 55), ZNF510 (SEQ ID NO: 53), or antigenic fragments thereof. Thus, in various embodiments, the methods comprise contacting a serum sample obtained from a subject at risk of breast cancer with 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, or all 22 of the recited polypeptides, or antigenic fragments thereof.

[0053] In a further preferred embodiment, the methods comprise contacting a bodily fluid sample, such as a serum sample, obtained from a subject at risk of breast cancer with ATP6AP1 (SEQ ID NO: 13), or an antigenic fragment thereof. In this embodiment, the method may further comprise contacting the serum sample with 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, or all 27 of the other recited polypeptides, or antigenic portions thereof.

[0054] In a preferred embodiment, the methods comprise contacting a bodily fluid sample, such as a serum sample, obtained from a subject at risk of breast cancer with 2, 3, 4, 5, or all 6 of ATP6AP1 (SEQ ID NO: 13), CTBP1 (SEQ ID NO: 29), EIF3E (SEQ ID NO: 39), ATF3 (SEQ ID NO: 19), SOX2 (SEQ ID NO: 31), and BDNF (SEQ ID NO: 17), or antigenic portions thereof.

[0055] In one preferred embodiment, the method comprises contacting the bodily fluid sample, such as a serum sample, to a polypeptide array of any embodiment of the first aspect of the invention, or to an array according to any embodiment of the second aspect of the invention after the encoded proteins are then transcribed and translated by a cell-free system and immobilized in situ using epitope tags fused to the proteins.

[0056] As will be appreciated by those of skill in the art, it may be desirable to test for autoantibodies to other polypeptides, and so the method may comprise testing for such further autoantibodies, such as antibodies to p53, CTBP1, RAC3, and activating transcription factor-3 (ATF3).

[0057] The "binding" may comprise any detectable interaction of an antibody with an antigen (polypeptide or polynucleotide molecule), including without limitation a covalent bond, ionic bond, salt bridge, hydrogen bond, van der Waals interaction, hydrophobic/hydrophilic interaction, electrostatic interaction, steric interaction, other associations, or any combination of any of the foregoing. As will be understood by those of skill in the art, array interactions do not require chemical binding.

[0058] In one embodiment, a probe set, such as an array according to any embodiment of the invention are contacted with the bodily fluid, such as a serum sample, under conditions suitable for binding of antibodies in the fluid to antigens in the probe set; unbound antibodies are washed and bound antibodies are detected by labeled secondary reagents, such as labeled secondary antibodies. Suitable conditions and reagents to promote binding of specific antibody types to antigens (polypeptides or polynucleotide molecules) is well within the level of those of skill in the art. Thus, the methods of the invention are not limited by any specific type of binding conditions employed. Such conditions will vary depending on the type of sample, desired stringency of the binding interaction, and nature of the competing materials in the binding solution, the type of molecules (polypeptide or polynucleotide) in the probe set,

the type of probe set, and, for embodiments in which the probe set is present on a support, the type of support, and the density of the molecules arrayed on the support. In a preferred embodiment, the conditions comprise a step to remove unbound antibodies. Determining the need for such a step, and appropriate conditions for such a step, are well within the level of skill in the art.

[0059] Any type of labeled secondary reagents label can be used in the methods of the present invention, including but not limited to radioisotope labels, fluorescent labels, luminescent labels, and electrochemical labels (ie: antibody labels with different electrode mid-point potential, where detection comprises detecting electric potential of the label). In a preferred embodiment, fluorescent or electrochemical labels are used. Detection of signal from detectable labels is well within the level of skill in the art. For example, fluorescent array readers are well known in the art, as are instruments to record electric potentials on a substrate (For electrochemical detection see, for example, J. Wang (2000) *Analytical Electrochemistry*, Vol., 2nd ed., Wiley-VCH, New York). In a further embodiment, the detectable labels comprise quantum dots. In one embodiment, secondary labels can be used, including but not limited to secondary antibodies or ligands that bind to the antibodies. In embodiments where multiple polypeptides are used as probes, it is preferable that they are differentially distinguishable, as discussed above. In a further embodiment, antibodies bound to each polypeptide are quantified by staining with anti-fusion tag antibodies and measurement of the fluorescence intensity signal generated from secondary antibodies. Detecting presence of antibodies to the polypeptides in the bodily fluid sample can be accomplished by standard methods in the art. Suitable conditions and reagents will be understood by those of skill in the art based on the teachings herein. The presence of antibodies to the polypeptides may be determined by immunoassay methods utilizing the antibodies described above. Such immunoassay methods include, but are not limited to, direct or indirect immunoassay such as for example a competitive binding assay, a non-competitive binding assay, a radioimmunoassay, immunohistochemistry, an enzyme-linked immunosorbent assay (ELISA), a sandwich assay, a gel diffusion immunodiffusion assay, an agglutination assay, dot blotting, a fluorescent immunoassay such as fluorescence-activated cell sorting (FACS), chemiluminescence immunoassay, immunoPCR immunoassay, a protein A or protein G immunoassay, and an immunoelectrophoresis assay such as western blotting and others commonly used and widely described in scientific and patent literature, and many employed commercially.

[0060] In the case of an enzyme immunoassay, an enzyme is conjugated to the second antibody, usually by means of glutaraldehyde or periodate. As will be readily recognized, however, a wide variety of different ligation techniques exist which are well-known to the skilled artisan. Commonly used enzymes include horseradish peroxidase, glucose oxidase, beta-galactosidase and alkaline phosphatase, among others. The substrates to be used with the specific enzymes are generally chosen for the production, upon hydrolysis by the corresponding enzyme, of a detectable color change. For example, p-nitrophenyl phosphate is suitable for use with alkaline phosphatase conjugates; for peroxidase conjugates, 1,2-phenylenediamine or toluidine are commonly used. It is also possible to employ fluorogenic substrates, which yield a fluorescent product, rather than the chromogenic substrates

noted above. A solution containing the appropriate substrate is then added to the tertiary complex. The substrate reacts with the enzyme linked to the second antibody, giving a qualitative visual signal, which may be further quantitated, usually spectrophotometrically, to give an evaluation of the amount of secreted protein or fragment thereof. Alternately, fluorescent compounds, such as fluorescein and rhodamine, may be chemically coupled to antibodies without altering their binding capacity. When activated by illumination with light of a particular wavelength, the fluorochrome-labeled antibody absorbs the light energy, inducing a state of excitability in the molecule, followed by emission of the light at a characteristic longer wavelength. The emission appears as a characteristic color visually detectable with a light microscope. Immunofluorescence and EIA techniques are both very well established in the art and are particularly preferred for the present method. However, other reporter molecules, such as radioisotopes, chemiluminescent or bioluminescent molecules may also be employed.

[0061] In a further embodiment, the presence of antibodies to the polypeptides may be determined by using Western blot analysis. The technique generally comprises separating sample antibody proteins by gel electrophoresis on the basis of molecular weight and transferring the antibody proteins to a suitable solid support, such as nitrocellulose filter, a nylon filter, or derivatized nylon filter. The sample is incubated with the polypeptides or antigenic fragments thereof that specifically bind the sample antibodies and the resulting complex is detected. The polypeptides may be directly labeled or alternatively may be subsequently detected using labeled secondary antibodies that specifically bind to the polypeptide-antibody complex. Antibody binding reagents may be, for example, protein A, or other antibodies. Antibody binding reagents may be radiolabeled or enzyme linked. Detection may be by autoradiography, calorimetric reaction or chemiluminescence. This method allows both quantitation of an amount of sample antibody and determination of its identity by a relative position on the membrane which is indicative of a migration distance in the acrylamide gel during electrophoresis. The definitions and all embodiments disclosed in the first and second aspects apply to this third aspect.

Examples

[0062] Custom NAPP protein microarrays were used to detect tumor antigen-specific AAb in the sera of patients with early-stage breast cancer. Using a sequential screening strategy to select AAb from 4988 tumor antigens, we identified 119 AAb potential biomarkers for the early detection of breast cancer. A blinded validation study produced supporting evidence for 28 of these potential biomarkers.

[0063] Sera used in these analyses were obtained from Fox Chase Cancer Center (FCCC) and the Duke University Medical Center (DUMC) with support from the NCI Early Detection Research Network and the NCI Breast SPORE program. Sera were derived from early-stage breast cancer patients from FCCC (53 cases/53 controls); control sera were sex- and age-matched (+/-2 yrs). All samples were obtained at the time of routine mammography, prior to the diagnosis of cancer, and were selected retrospectively. To control for benign breast disease, we obtained an independent set of sera of early-stage invasive breast cancer patients and age-matched (+/-3 yrs) benign breast disease controls from DUMC (102 cases/102 controls). These samples were

collected using a standardized sample collection protocol and stored at -80° C. until use. Cases and matched controls were processed simultaneously. Written consent was obtained from all subjects under institutional review board approval.

[0064] Sequence-verified, full-length cDNA expression plasmids in flexible donor vector systems were obtained from the Harvard Institute of Proteomics and are publicly available (see web site dnasu.asu.edu/DNASU/). These were converted to the T7-based mammalian expression vector pANT7_GST using LR recombinase (Invitrogen, Carlsbad, Calif.). Expression plasmids were transformed into *E. coli* DH5 α , and grown in 1.5 mL terrific broth and ampicillin (100 μ g/mL). DNA was purified with the NucleoPrepII anion exchange resin (Macherey-Nagel Inc., Bethlehem, Pa.) using a Biomek FX (Beckman Coulter, Inc., Fullerton, Calif.) automated laboratory workstation. Automated addition of all solutions was accomplished using a Matrix WellMate™ (Thermo Scientific, Hudson, N.H.) rapid bulk liquid-dispensing instrument. Purified DNA was precipitated by addition of 0.6 volumes isopropanol, followed by centrifugation at 5000 ref for 30 minutes. The DNA pellet was washed with 200 μ L of 80% ethanol, centrifuged at 5000 ref for 15 minutes, dried, and resuspended in dH₂O. For bead array ELISAs, larger quantities of DNA were prepared using standard Nucleobond™ preparation methods (Macherey-Nagel Inc., Bethlehem, Pa.).

[0065] Plasmid DNA (1.5 μ g/ μ L) was supplemented with capture antibody (50 μ g/mL, anti-GST antibody, GE Healthcare Biosciences, Piscataway, N.J.) or anti-FLAG antibody (Sigma-Aldrich, St. Louis, Mo.), protein crosslinker (2 mM, BS3, Pierce, Rockford, Ill.) and BSA (3 mg/mL, Sigma-Aldrich) to the DNA prior to printing onto the array surface. All samples were printed using a Genetix QArray2™ with 300 μ m solid tungsten pins on amine-treated glass slides. Arrays were stored in an air-tight container at room temperature, protected from light. The printed DNA was transcribed and translated in situ using previously published protocols. Protein expression was detected using anti-GST MAb (Cell Signaling, Danvers, Mass.) diluted at 1:200. For detecting serum antibodies, the arrays were incubated with serum diluted 1:300-1:600 in 5% PBS milk with 0.2% Tween 20. All incubations were carried out at 4° C. overnight with mixing (Corning hybridization chambers) unless indicated otherwise. Detection on the array was carried out using an anti-human IgG (Jackson ImmunoResearch Labs, West Grove, Pa.) conjugated with HRP. The slides were developed for fluorescent detection using the Tyramide Signal Amplification reagent (PerkinElmer, Waltham, Mass.) per manufacturer's instructions. Slides were scanned with a Perkin Elmer ProScanArray HT and the images were quantitated using MicroVigene software (Vigene Tech version 2.9.9.2). The highly immunogenic EBV-derived antigen, EBNA-1, was included as N- and C-terminal fragments for positive control antigens. Negative controls included empty vectors and no DNA controls. Registration spots for array alignment were printed purified human IgG proteins.

[0066] For the first screening stage, 53 cases and 53 control sera from FCCC were screened on 4,988 antigens displayed in NAPP protein array format. Each array was normalized by first removing the background signal estimated by the first quartile of the non-spots and then log-

transforming the median-scaled raw intensities to bring the data to the same scale and stabilize the variance across the range of signals.

[0067] Candidate antigens from the initial 4,988 antigens were selected if they met two different criteria: 1) comparison of the 9.5th percentiles of the cases and controls using quantile regression and 2) comparison of the proportion of cases with intensities above the 95th percentile of controls to the expected number seen by chance, with a $p\text{-value} \leq 0.05$ ($n=217$). Additional antigens ($n=544$) were ranked based on intensity and decreasing specificity (cases/controls). Independent arrays of these 761 candidate antigens were screened with a fully independent set of age-matched sera consisting of 76 controls with benign breast disease and 102 patient sera from DUMC, randomly divided into training and validation sets. We normalized these arrays as follows. First, we removed differences in intensity associated with plates and pins by consecutively multiplying the raw intensities by three factors: the median intensity of all antigens divided by the median intensity of antigens from the same plate, the median intensity of all antigens divided by the median intensity of antigens printed at the same within-pin

position, and the median intensity of all antigens divided by the median intensity of antigens printed with the same pin. These scalings yielded a median reduction in variance of 9%. We removed any duplicate antigen pairs that differed by more than 3 times the median absolute deviation, resulting in removal of 0.5% of spots. Third, we resealed the raw intensities as above and averaged duplicate antigen pairs. Finally, we removed background signal by subtracting the first quartile of control spot (no DNA) intensity and divided the excess intensity by the median excess intensity.

[0068] We used the partial area under the receiver operating characteristic curve (pAUC) as the basis for comparing the normalized intensities of cases and controls for each antigen. Specifically, we used the pAUC where the false positive rate is at most 5%. For each antigen we tested the hypothesis that the pAUC was greater than 0.00125, which is the same partial area under the 45 degree line receiver operating characteristic curve that represents no difference between cases and controls. We used the training set to identify 119 potential antigen biomarkers with $p\text{-values}$ less than 0.05 and confirmed 28 of these using the validation set ($p < 0.05$). Training and validation statistics for the 28 breast cancer biomarkers is provided in Table 1.

TABLE 1

Gene Name	Accession number	Amino acid	Nucleotide
SF3A1 splicing factor 3A subunit 1 isoform 1- full length (1-793)	NP_005868	SEQ ID NO: 1	SEQ ID NO: 2
FRS3 fibroblast growth factor receptor substrate 3-full length (1-492)	NP_006644	SEQ ID NO: 3	SEQ ID NO: 4
BAT4 HLA-B associated transcript-4-full length (1-356)	NP_149417	SEQ ID NO: 5	SEQ ID NO: 6
HOXD1 homeobox protein Hox-D1 full length (1-328)	AAH14477	SEQ ID NO: 7	SEQ ID NO: 8
CSNK1E casein kinase I isoform epsilon full length (1-416)	NP_001885	SEQ ID NO: 9	SEQ ID NO: 10
SLC33A1 acetyl-coenzyme A transporter 1-full length (1-549)	NP_004724	SEQ ID NO: 11	SEQ ID NO: 12
ATP6AP1 V-type proton ATPase subunit S1 precursor-full length (1-470)	NP_001174	SEQ ID NO: 13	SEQ ID NO: 14
RAC3 ras-related C3 botulinum toxin substrate 3 precursor-full length (1-192)	NP_005043	SEQ ID NO: 15	SEQ ID NO: 16
BDNF brain-derived neurotrophic factor transcript variant 5- full length (1-247)	AAA96140	SEQ ID NO: 17	SEQ ID NO: 18
ATF3 cyclic AMP- dependent transcription factor ATF-3 isoform 1-full length (1-181)	NP_001665	SEQ ID NO: 19	SEQ ID NO: 20

TABLE 1-continued

Gene Name	Accession number	Amino acid	Nucleotide
PDCD6IP programmed cell death 6-interacting protein isoform 1- full length (1-868)	NP_037506	SEQ ID NO: 21	SEQ ID NO: 22
RAB5A ras-related protein Rab-5A-full length (1-215)	NP_004153	SEQ ID NO: 23	SEQ ID NO: 24
DBT Dihydrolipoamide branched chain transacylase E2-full length (1-482)	AAH16675	SEQ ID NO: 25	SEQ ID NO: 26
ALG10 alpha-1,2- glucosyltransferase ALG10-A-full length (1-473)	NP_116223	SEQ ID NO: 27	SEQ ID NO: 28
CTBP1 C-terminal-binding protein 1 isoform 1- full length (1-440)	NP_001319	SEQ ID NO: 29	SEQ ID NO: 30
SOX2 transcription factor SOX-2-full length (1- 317)	NP_003097	SEQ ID NO: 31	SEQ ID NO: 32
MYOZ2 myozenin-2-full length (1-264)	NP_057683	SEQ ID NO: 33	SEQ ID NO: 34
C15orf48 normal mucosa of esophagus-specific gene 1 protein-full length (1-83)	NP_115789	SEQ ID NO: 35	SEQ ID NO: 36
TRIM32 E3 ubiquitin-protein ligase TRIM32-full length (1-653)	NP_001093149	SEQ ID NO: 37	SEQ ID NO: 38
EIF3E eukaryotic translation initiation factor 3 subunit E- full length (1-445)	NP_001559	SEQ ID NO: 39	SEQ ID NO: 40
ZMYM6 zinc finger, MYM- type 6, isoform CRA_b-partial (1- 156/163)	AAP35781	SEQ ID NO: 41	SEQ ID NO: 42
GPR157 probable G-protein coupled receptor 157-partial (1- 155/335)	EAW71612	SEQ ID NO: 43	SEQ ID NO: 44
BMX cytoplasmic tyrosine-protein kinase BMX-full length (1-675)	NP_001712	SEQ ID NO: 45	SEQ ID NO: 46
UBAP1 ubiquitin-associated protein 1 isoform 1- full length (1-502)	NP_057609	SEQ ID NO: 47	SEQ ID NO: 48
TFCP2 grainyhead-like 3 (<i>Drosophila</i>), isoform CRA_d-full length (1-555)	AAH36890	SEQ ID NO: 49	SEQ ID NO: 50
SERPINH1 serpin H1 precursor- full length (1-418)	NP_001226	SEQ ID NO: 51	SEQ ID NO: 52
ZNF510 zinc finger protein 510-partial (1- 636/683)	AAH68587	SEQ ID NO: 53	SEQ ID NO: 54

TABLE 1-continued

Gene Name	Accession number	Amino acid	Nucleotide
SELL L-selectin precursor-full length (1-375)	AAH20758	SEQ ID NO: 55	SEQ ID NO: 56

SEQUENCE LISTING

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Val Arg Asn Ile Val Asp Lys Thr Ala Ser Phe Val Ala Arg Asn Gly
50 55 60

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Phe Asn Phe Leu Asn Pro Asn Asp Pro Tyr His Ala Tyr Tyr Arg His
85 90 95

Lys Val Ser Glu Phe Lys Glu Gly Lys Ala Gln Glu Pro Ser Ala Ala
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Tyr Gln Phe Asp Phe Leu Arg Pro Gln His Ser Leu Phe Asn Tyr Phe
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Thr Lys Leu Val Glu Gln Tyr Thr Lys Ile Leu Ile Pro Pro Lys Gly
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Leu Phe Ser Lys Leu Lys Lys Glu Ala Glu Asn Pro Arg Glu Val Leu
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Asp Gln Val Cys Tyr Arg Val Glu Trp Ala Lys Phe Gln Glu Arg Glu
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Gly Ala Arg Ile Leu Ile Gln Glu Arg Tyr Glu Lys Phe Gly Glu Ser
 305 310 315 320

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 325 330 335

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 340 345 350

Gln Asp Met Asp Glu Gly Ser Asp Asp Glu Glu Glu Gly Gln Lys Val
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Pro Pro Pro Pro Glu Thr Pro Met Pro Pro Pro Leu Pro Pro Thr Pro
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 420 425 430

Leu Leu Asp Pro Arg Trp Leu Glu Gln Arg Asp Arg Ser Ile Arg Glu
 435 440 445

Lys Gln Ser Asp Asp Glu Val Tyr Ala Pro Gly Leu Asp Ile Glu Ser
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Glu Thr Ala Ile Gly Lys Lys Ile Gly Glu Glu Glu Ile Gln Lys Pro
 485 490 495

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 530 535 540

Ile Gly Pro Ser Lys Pro Asn Glu Ile Pro Gln Gln Pro Pro Pro Pro
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 740 745 750

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

<210> SEQ ID NO 4

<211> LENGTH: 1476

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 4

```

atggggagct gctgcagctg cctgaacaga gacagcgttc cagacaacca ccccaccaag    60
ttcaagtgta caaatgtgga tgatgagggg gtggagctgg gctctggggg gatggagctg    120
acgcagagtg agctggtgct gcacctgcat cggcgtgagg ccgtccgctg gccttatctc    180
tgcttgcggc gctatggcta cgactccaac ctcttctect ttgagagtgg ccgccgatgt    240
cagacaggcc agggaatatt tgcatttaag tgttcccggg ctgaggaaat cttcaacctc    300

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cttcaggatc tgatgcagtg caacagcadc aatgtgatgg aagagcctgt catcatcacc 360
cgcaatagcc accccgctga gcttgacctc cctcgagccc cccagccacc caatgctcta 420
ggctacactg tctccagctt ttccaatggc tgccttgagg agggcccacg attctcagct 480
ccccggcgge tctcgacaag cagcctgcgg caccctcgc ttggggaaga gtccacccat 540
gcccctcattg ctctgatga gcagtcacc acctatgtca acacaccggc cagtgaagat 600
gaccacgcga ggggcccga ctgctgcag cccctgctg agggtcaggc acccttctc 660
ccgcaggccc ggggacctga ccaacgggac ccacaggtgt tcttgacgcc aggccaggtg 720
aagtttgtgt tgggcccgc cctgctcgg cggcacatgg tgaagtgcc gggcctctgt 780
cccagcctgc atgaccccc acaccacaat aataacaatg agggcccttc tgagtgtcca 840
gcccagccca agtgcaccta cgagaacgtc accggggggc tgtggcgagg ggctggctgg 900
agactgagcc cagaggagcc gggctggaat ggccttgccc accgcccggc cgccctgctg 960
cactatgaga acctgcccc actgccccct gtgtgggaaa gccaaagcca gcagctggga 1020
ggggaggctg gggatgatgg ggactogagg gatgggctca caccctcttc caatggcttc 1080
cctgatgggtg agggagcaga gacccactg cagaagccca ccagcacccg ggcgcccac 1140
cgagccacg gcagctttcc tgtgccactg acccgccgcc gggctcccc aagggtcttc 1200
aactttgatt tccgccggcc ggggcccag ccccaaggc agcttaacta catccaggtg 1260
gagctaaagg gctgggggtg agaccgccct aaggggcccc agaaccctc gagcccccaa 1320
gcccccatg ccaccaccca cctgcccga agctcagact cctacgccgt gattgacctc 1380
aaaaagaccg tggccatgtc caactgcag agagctctgc cccgagacga tggcaccgcc 1440
aggaaaaccc ggcacaacag caccgacctg cctctg 1476

```

<210> SEQ ID NO 5

<211> LENGTH: 356

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 5

```

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

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145	150	155	160
Tyr Leu Leu Gly Arg Gly Ala Ala Trp Val Gly Val Cys Glu Leu Ser	165	170	175
Gly Arg Asp Ala Ala Gln Leu Ala Glu Glu Ala Gly Phe Pro Glu Val	180	185	190
Ala Arg Met Val Arg Glu Ser His Gly Glu Thr Arg Ser Pro Glu Asn	195	200	205
Arg Ser Pro Thr Pro Ser Leu Gln Tyr Cys Glu Asn Cys Asp Thr His	210	215	220
Phe Gln Asp Ser Asn His Arg Thr Ser Thr Ala His Leu Leu Ser Leu	225	230	235
Ser Gln Gly Pro Gln Pro Pro Asn Leu Pro Leu Gly Val Pro Ile Ser	245	250	255
Ser Pro Gly Phe Lys Leu Leu Leu Arg Gly Gly Trp Glu Pro Gly Met	260	265	270
Gly Leu Gly Pro Arg Gly Glu Gly Arg Ala Asn Pro Ile Pro Thr Val	275	280	285
Leu Lys Arg Asp Gln Glu Gly Leu Gly Tyr Arg Ser Ala Pro Gln Pro	290	295	300
Arg Val Thr His Phe Pro Ala Trp Asp Thr Arg Ala Val Ala Gly Arg	305	310	315
Glu Arg Pro Pro Arg Val Ala Thr Leu Ser Trp Arg Glu Glu Arg Arg	325	330	335
Arg Glu Glu Lys Asp Arg Ala Trp Glu Arg Asp Leu Arg Thr Tyr Met	340	345	350
Asn Leu Glu Phe	355		

<210> SEQ ID NO 6
 <211> LENGTH: 1068
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 6

```

atgtcccggc ccttgetcat caccttcacc ccagccactg accccagcga cctctggaag    60
gatgggcagc agcagccaca gcccgagaag ccagagtcca ccttggatgg ggctgcagcc    120
cgagctttct atgaggccct gattggggat gagagcagcg ctcttgactc ccagagatct    180
cagactgaac ctgccagaga aagaaagaga aagaaaagaa gaataatgaa ggcaccagca    240
gcagaagcag tggcagaagg agcatcagga agacatggac aaggagatc ccttgaggct    300
gaggataaga tgactcaccg gatactgagg gcagcccagg agggggacct gccagaactt    360
aggagactgc tggaaaccga tgaggcagga ggagctgggg ggaatatcaa cgcccgggat    420
gccttctggt ggaccccact gatgtgtgct gctcgagcgg gccagggggc agctgtgagc    480
tatctctctg gccgtggggc tgcctgggtg ggggtctgtg agctgagtgg cagggatgcg    540
gctcagctcg ctgaagaagc tggcttcctt gaggtagccc gcatggtcag ggagagccat    600
ggagagacaa ggagcccgga aaaccggtct cctactcctt ccctccagta ctgcgagaac    660
tgtgacacce acttccaaga ttccaaccac cgcacateca ctgctcaact getgtcactg    720
tcgcagggtc ctcagcctcc caaccttcca cttgggggtg ccatctccag cccgggcttc    780
aaactgctgc tgaggggggg ctgggagcca ggaatggggc tgggaccocg gggtgagggc    840
    
```


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cgtgccaate ccatcccccac tgctctcaag agggaccagg aaggactagg ctacagatca    900
gcaccccagc cccgagtgac acatttccca gottgggata cccgagctgt ggctggggagg    960
gagagacccc ctccgggtggc cacactgagc tggagggagg agagaaggag ggaggagaaa    1020
gacagggctt gggagcggga tctaaggact tacatgaacc tcgagttc                    1068

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<210> SEQ ID NO 7
<211> LENGTH: 328
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 7

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```

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

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Pro Ser Gln Ser Gln Glu Pro Ser
325

<210> SEQ ID NO 8
<211> LENGTH: 984
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 8

```

atgagctcct acctggagta cgtgtcatgc agcagcagcg gcggggtcgg cggcgacgtg    60
ctcagcttgg cacccaagtt ctgccgctcc gacgcccggc ccgtggctct gcagcccgcc    120
ttccctctgg gcaacggcga cggcgcttc gtcagctgtc tgcccctggc cgccgcccga    180
ccctcgcttt ccccccggc cgcccccgcg cggccgtccg taccgctcc gcccgcgccc    240
cagtacgcgc agtgcacct ggagggggcc tacgaacctg gtgccgcacc tgccgcgga    300
gtggggggcg cggactacgg ctctctgggg tccgggcccg cgtacgactt cccgggctgt    360
ctggggcggg cggccgacga cggcgggtct cacgtccact acgccacctc ggcgctcttc    420
tcgggcccgg gctctttcct cctcagcgcc caggtggatt acgcccctt cggcgaacct    480
ggcctttttt cggttgtct caaagcgtca gccgacggcc acctgggtgc tttccagacc    540
gcatccccgg ccccaggcac ctacccaag tccgtctctc ccgctccgg cctccctgcc    600
gccttcagca cgttcgagt gatgaaagt aagaggaatg cctctaagaa aggcaaactc    660
gccgagtatg gggccgctag cccctccagc gcgatccgca cgaatttcag caccaagcaa    720
ctgacagaac tgaaaaaaga gtttcatttc aataagtact taactcgagc ccggcgcatc    780
gagatagcca actgcttgca cctgaatgac acgcaagtca aaatctgggt ccagaaccgc    840
aggatgaaac agaagaaaag ggaacgagaa gggcttctgg ccacggccat tctgtgggt    900
ccctccaac ttcccctctc tggaacaacc cccactaagt ttatcaagaa ccccgcgagc    960
ccttctcagt cccaagagcc ttcg                                     984

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<210> SEQ ID NO 9
<211> LENGTH: 416
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 9

```

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

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

<210> SEQ ID NO 10
 <211> LENGTH: 1248
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens
 <400> SEQUENCE: 10

```

atggagctac gtgtggggaa caagtaccgc ctgggacgga agatcgggag cgggtccttc    60
ggagatatct acctgggtgc caacatcgcc tctggtgagg aagtcgcat caagctggag    120
tgtgtgaaga caaagcacc ccagctgcac atcgagagca agttctacaa gatgatgcag    180
ggtggcgtgg ggatcccgtc catcaagtgg tgcggagctg agggcgacta caacgtgatg    240
gtcatggagc tgctggggcc tagcctcgag gacctgttca acttctgttc cgcgaaattc    300
agcctcaaga cgggtgctgct cttggccgac cagatgatca gccgcatcga gtatatccac    360
    
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tccaagaact tcattccaccg ggacgtcaag cccgacaact tcctcatggg gctggggaag 420
aagggaacc tgggtctacat catcgacttc ggctggcca agaagtaccg ggacgcccgc 480
accaccagc acattcccta cgggaaaac aagaacctga cggcacggc cegctacgct 540
tccatcaaca cgcacctggg cattgagcaa agccgtcgag atgacctgga gagcctgggc 600
tacgtgctca tgtacttcaa cctgggctcc ctgcctggc aggggctcaa agcagccacc 660
aagcgcaga agtatgaacg gatcagcgag aagaagatgt caacgcccac cgaggctctc 720
tgcaaaggct atccctccga attctcaaca tacctcaact tctgccgctc cctgcggttt 780
gacgacaagc ccgactactc ttacctactg cagctcttcc gcaacctctt ccaccggcag 840
ggcttctct atgactactg ctttgactgg aacatgctga aattcggtgc agcccgaat 900
cccaggatg tggaccggga gcggcgagaa cacgaacgcg aggagaggat ggggcagcta 960
cgggggtccg cgaccggagc cctgccccct ggcccaccca cgggggcccac tgccaaccgg 1020
ctccgcagtg ccgcccagcc cgtggcttcc acgccagcct cccgcatcca gccggctggc 1080
aatacttctc ccagagcgat ctgcggggtc gaccgggaga ggaaggtgag tatgaggctg 1140
cacaggggtg cgcccccaa cgtctcctcc tcagacctca ctgggcccga agaggtctcc 1200
cggatcccag cctcacagac aagtgtgcca tttgaccatc tcgggaag 1248

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<210> SEQ ID NO 11
<211> LENGTH: 549
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 11

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```

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

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Asn Val Gly Tyr Ala Ser Thr Cys Asn Ser Val Gly Gln Thr Ala Gly
 210 215 220
 Tyr Phe Leu Gly Asn Val Leu Phe Leu Ala Leu Glu Ser Ala Asp Phe
 225 230 235 240
 Cys Asn Lys Tyr Leu Arg Phe Gln Pro Gln Pro Arg Gly Ile Val Thr
 245 250 255
 Leu Ser Asp Phe Leu Phe Phe Trp Gly Thr Val Phe Leu Ile Thr Thr
 260 265 270
 Thr Leu Val Ala Leu Leu Lys Lys Glu Asn Glu Val Ser Val Val Lys
 275 280 285
 Glu Glu Thr Gln Gly Ile Thr Asp Thr Tyr Lys Leu Leu Phe Ala Ile
 290 295 300
 Ile Lys Met Pro Ala Val Leu Thr Phe Cys Leu Leu Ile Leu Thr Ala
 305 310 315 320
 Lys Ile Gly Phe Ser Ala Ala Asp Ala Val Thr Gly Leu Lys Leu Val
 325 330 335
 Glu Glu Gly Val Pro Lys Glu His Leu Ala Leu Leu Ala Val Pro Met
 340 345 350
 Val Pro Leu Gln Ile Ile Leu Pro Leu Ile Ile Ser Lys Tyr Thr Ala
 355 360 365
 Gly Pro Gln Pro Leu Asn Thr Phe Tyr Lys Ala Met Pro Tyr Arg Leu
 370 375 380
 Leu Leu Gly Leu Glu Tyr Ala Leu Leu Val Trp Trp Thr Pro Lys Val
 385 390 395 400
 Glu His Gln Gly Gly Phe Pro Ile Tyr Tyr Tyr Ile Val Val Leu Leu
 405 410 415
 Ser Tyr Ala Leu His Gln Val Thr Val Tyr Ser Met Tyr Val Ser Ile
 420 425 430
 Met Ala Phe Asn Ala Lys Val Ser Asp Pro Leu Ile Gly Gly Thr Tyr
 435 440 445
 Met Thr Leu Leu Asn Thr Val Ser Asn Leu Gly Gly Asn Trp Pro Ser
 450 455 460
 Thr Val Ala Leu Trp Leu Val Asp Pro Leu Thr Val Lys Glu Cys Val
 465 470 475 480
 Gly Ala Ser Asn Gln Asn Cys Arg Thr Pro Asp Ala Val Glu Leu Cys
 485 490 495
 Lys Lys Leu Gly Gly Ser Cys Val Thr Ala Leu Asp Gly Tyr Tyr Val
 500 505 510
 Glu Ser Ile Ile Cys Val Phe Ile Gly Phe Gly Trp Trp Phe Phe Leu
 515 520 525
 Gly Pro Lys Phe Lys Lys Leu Gln Asp Glu Gly Ser Ser Ser Trp Lys
 530 535 540
 Cys Lys Arg Asn Asn
 545

<210> SEQ ID NO 12
 <211> LENGTH: 1647
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens

 <400> SEQUENCE: 12

atgtcaccca ccattccca caaggacagc agccggcaac ggcggccagg gaatttcagt 60

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cactctctgg atatgaagag cggtcocctg cggccaggcg gttgggatga cagtcatttg 120
gactcagcgg gccgggaagg ggacagagaa gctcttctgg gggataccgg cactggcgac 180
ttcttaaaag ccccacagag cttccggggc gaactaagca gcattttgct actactcttt 240
ctttacgtgc ttcagggtat tcccctgggc ttggcgggaa gcaccccact cattttgcaa 300
agcaaaaatg ttagctatac agaccaagct ttcttcagtt ttgtcttttg gcccttcagt 360
ctcaaaattac tctgggcccc gttggttgat gcggtctacg ttaagaactt cggtcgtcgc 420
aaatcttgge ttgtcccgac acagtatata ctaggactct tcatgatcta tttatccact 480
caggtggacc gtttgcttgg gaataccgat gacagaacac ccgacgtgat tgctctcact 540
gtggcgttct ttttgtttga attcttgccc gccactcagg acattgccgt cgatggttgg 600
gcgtaacta tgttatccag ggaaaatgtg ggttatgctt ctacttgcaa ttcggtgggc 660
caaacagcgg gttacttttt gggcaatggt ttgttttttg cccttgaatc tgccgacttt 720
tgtaacaaat atttgcggtt tcagcctcaa cccagaggaa tcgttactct ttcagatttc 780
ctttttttct ggggaactgt atttttaata acaacaacat tggttgccct tctgaaaaaa 840
gaaaacgaag tatcagtagt aaaagaagaa acacaagggg tcacagatac ttacaagctg 900
ctttttgcaa ttataaaaat gccagcagtt ctgacatttt gccttctgat tctaactgca 960
aagattgggt tttcagcagc agatgctgta acaggactga aattggtaga agagggagta 1020
cccaaagaac atttagcctt attggcagtt ccaatggttc ctttgcagat aatctgcct 1080
ctgattatca gaaatacac tgcaggtccc cagccattaa acacatttta caaagccatg 1140
ccctacagat tattgcttgg gttagaatat gccctactgg tttgggtggc tcttaaagta 1200
gaacatcaag ggggattccc tatatattac tatatcgtag tctgtctgag ttatgcttta 1260
catcagggta cagtgtagac catgtatggt tctataatgg ctttcaatgc aaagggttagt 1320
gatccactta ttggaggaac atacatgacc cttttaaata ccgtgtccaa tctgggagga 1380
aactggcctt ctacagtage tctttggcct gtagatcccc tcacagtaaa agagtgtgta 1440
ggagcatcaa accagaattg tcgaacacct gatgctgttg agctttgcaa aaaactgggt 1500
ggctcatgtg ttacagccct ggatgggtat tatgtggagt ccattatttg tgttttcatt 1560
ggatttggtt ggtggttctt tcttgggtcca aaatttaaaa agttacagga tgaaggatca 1620
tcttcgtgga aatgcaaaaag gaacaat 1647

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<210> SEQ ID NO 13
<211> LENGTH: 470
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 13

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```

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

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-continued

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

-continued

<210> SEQ ID NO 14
 <211> LENGTH: 1410
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 14

```

atgatggcgg ccatggcgac ggctcgagtg cggatggggc cgcggtgcgc ccagggcgtc   60
tggcgc atgc cgtggctgcc ggtgtttttg tegtggcgg cggcggcggc ggcggcagcg   120
gcggagcagc aggtcccgtt ggtgctgtgg tcgagtgacc gggacttggt ggtcctgag   180
gccgacactc atgaaggcca catcaccagc gacttgacgc tctctaccta cttagatccc   240
gccctggagc tgggtcccag gaatgtgctg ctgttcctgc aggacaagct gagcattgag   300
gatttcacag catatggcgg tgtgttttga aacaagcagg acagcgcctt ttctaaccta   360
gagaatgccc tggacctggc cccctcctca ctggtgcttc ctgccgtcga ctggtatgca   420
gtcagcactc tgaccactta cctgcaggag aagctcgggg ccagcccctt gcatgtggac   480
ctggccaccc tgcgggagct gaagctcaat gccagcctcc ctgctctgct gctcattcgc   540
ctgccctaca cagccagctc tggctctgat gcacccaggg aagtccctcac aggcaacgat   600
gagggtcatcg ggcaggctct gagcacactc aagtccgaag atgtcccata cacagcggcc   660
ctcacagcgg tccgcccttc caggggtggc cgtgatgtag ccgtgggtggc cggaggggcta   720
ggtgccagc tgcatacaaaa acagccagta tcacctgtga tccatcctcc tgtgagttac   780
aatgacaccg ctccccggat cctgttctgg gcccaaaact tctctgtggc gtacaaggac   840
cagtgggagg acctgactcc cctcaacttt ggggtgcagg aactcaacct gactggtccc   900
ttctggaatg actcctttgc caggctctca ctgacctatg aacgactctt tggtagcaca   960
gtgacattca agttcattct ggccaaccgc ctctaccagc tgtctgcccg gcaactggttt  1020
accatggagc gcctcgaagt ccacagcaat ggctccgtcg cctacttcaa tgettcccag  1080
gtcacagggc ccagcatcta ctcctccac tgcgagtatg tcagcagcct gagcaagaag  1140
ggtagtctcc tegtggcccc cacgcagccc tctccctggc agatgatgct tcaggacttc  1200
cagatccagg ctttcaacgt aatgggggag cagttctcct acgccagcga ctgtgccagc  1260
ttctctccc ccggcatctg gatggggctg ctcacctccc tgttcatgct cttcatcttc  1320
acctatggcc tgcacatgat cctcagcctc aagacatgg atcgcttga tgaccacaag  1380
ggccccacta tttctttgac ccagattgtg                                     1410

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<210> SEQ ID NO 15
 <211> LENGTH: 192
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 15

```

Met Gln Ala Ile Lys Cys Val Val Val Gly Asp Gly Ala Val Gly Lys
1           5           10           15

Thr Cys Leu Leu Ile Ser Tyr Thr Thr Asn Ala Phe Pro Gly Glu Tyr
          20           25           30

Ile Pro Thr Val Phe Asp Asn Tyr Ser Ala Asn Val Met Val Asp Gly
          35           40           45

Lys Pro Val Asn Leu Gly Leu Trp Asp Thr Ala Gly Gln Glu Asp Tyr
          50           55           60

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Asp Arg Leu Arg Pro Leu Ser Tyr Pro Gln Thr Asp Val Phe Leu Ile
 65 70 75 80

Cys Phe Ser Leu Val Ser Pro Ala Ser Phe Glu Asn Val Arg Ala Lys
 85 90 95

Trp Tyr Pro Glu Val Arg His His Cys Pro His Thr Pro Ile Leu Leu
 100 105 110

Val Gly Thr Lys Leu Asp Leu Arg Asp Asp Lys Asp Thr Ile Glu Arg
 115 120 125

Leu Arg Asp Lys Lys Leu Ala Pro Ile Thr Tyr Pro Gln Gly Leu Ala
 130 135 140

Met Ala Arg Glu Ile Gly Ser Val Lys Tyr Leu Glu Cys Ser Ala Leu
 145 150 155 160

Thr Gln Arg Gly Leu Lys Thr Val Phe Asp Glu Ala Ile Arg Ala Val
 165 170 175

Leu Cys Pro Pro Pro Val Lys Lys Pro Gly Lys Lys Cys Thr Val Phe
 180 185 190

<210> SEQ ID NO 16
 <211> LENGTH: 576
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 16

```

atgcaggcca tcaagtgcgt ggtggtcggc gacggcgccg tggggaagac atgcttgctg    60
atcagctaca cgaccaacgc cttccccgga gagtacatcc ccaccgtttt tgacaactac    120
tctgccaaac tgatggtgga cgggaaacca gtcaacttgg ggctgtggga cacagcgggt    180
caggaggact acgatcggct gcggcactc tcctaccccc aaactgacgt ctttctgatc    240
tgcttctctc tggtgagccc ggcctccttc gagaatgttc gtgccaagtg gtacceggag    300
gtgcggcacc actgccccca cagcoccac ctcctggtgg gcaccaagct ggacctccgc    360
gacgacaagg acaccattga gcggctgcgg gacaagaagc tggcacccat cacctacca    420
cagggcctgg ccatggcccc ggagattggc tctgtgaaat acctggagtg ctcagccctg    480
accagcggg gcctgaagac agtgtttgac gaggcgatcc gcgcggtgct ctgcccgccc    540
ccagtgaaga agccggggaa gaagtgcacc gtcttc                                576
    
```

<210> SEQ ID NO 17
 <211> LENGTH: 247
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 17

Met Thr Ile Leu Phe Leu Thr Met Val Ile Ser Tyr Phe Gly Cys Met
 1 5 10 15

Lys Ala Ala Pro Met Lys Glu Ala Asn Ile Arg Gly Gln Gly Gly Leu
 20 25 30

Ala Tyr Pro Gly Val Arg Thr His Gly Thr Leu Glu Ser Val Asn Gly
 35 40 45

Pro Lys Ala Gly Ser Arg Gly Leu Thr Ser Leu Ala Asp Thr Phe Glu
 50 55 60

His Met Ile Glu Glu Leu Leu Asp Glu Asp Gln Lys Val Arg Pro Asn
 65 70 75 80

-continued

Glu Glu Asn Asn Lys Asp Ala Asp Leu Tyr Thr Ser Arg Val Met Leu
 85 90 95

Ser Ser Gln Val Pro Leu Glu Pro Pro Leu Leu Phe Leu Leu Glu Glu
 100 105 110

Tyr Lys Asn Tyr Leu Asp Ala Ala Asn Met Ser Met Arg Val Arg Arg
 115 120 125

His Ser Asp Pro Ala Arg Arg Gly Glu Leu Ser Val Cys Asp Ser Ile
 130 135 140

Ser Glu Trp Val Thr Ala Ala Asp Lys Lys Thr Ala Val Asp Met Ser
 145 150 155 160

Gly Gly Thr Val Thr Val Leu Glu Lys Val Pro Val Ser Lys Gly Gln
 165 170 175

Leu Lys Gln Tyr Phe Tyr Glu Thr Lys Cys Asn Pro Met Gly Tyr Thr
 180 185 190

Lys Glu Gly Cys Arg Gly Ile Asp Lys Arg His Trp Asn Ser Gln Cys
 195 200 205

Arg Thr Thr Gln Ser Tyr Val Arg Ala Leu Thr Met Asp Ser Lys Lys
 210 215 220

Arg Ile Gly Trp Arg Phe Ile Arg Ile Asp Thr Ser Cys Val Cys Thr
 225 230 235 240

Leu Thr Ile Lys Arg Gly Arg
 245

<210> SEQ ID NO 18
 <211> LENGTH: 741
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 18

```

atgaccatcc ttttccttac tatggttatt tcatactttg gttgcatgaa ggetgcccc 60
atgaaagaag caaacatccg aggacaaggt ggcttgccct acccaggtgt gcggaccat 120
gggactctgg agagcgtgaa tgggcccagg gcaggttcaa gagccttgac atcattggct 180
gacactttcg aacacatgat agaagagctg ttggatgagg accagaaagt tcggcccaat 240
gaagaaaaca ataaggacgc agacttgtag acgtccaggg tgatgctcag tagtcaagtg 300
cctttggagc ctctcttct ctttctgctg gaggaataca aaaattacct agacgtgca 360
aacatgtcca tgagggtccg gcgccactct gacctgccc gccgagggga gctgagcgtg 420
tgtgacagta ttagtgagtg ggtaacggcg gcagacaaaa agactgcagt ggacatgtcg 480
ggcgggacgg tcacagtcct tgaaaaggtc cctgtatcaa aaggccaact gaagcaatac 540
ttctacgaga ccaagtgcaa tcccatgggt tacacaaaag aaggctgcag gggcatagac 600
aaaaggcatt ggaactccca gtgccgaact acccagtcgt acgtgcgggc ccttaccatg 660
gatagcaaaa agagaattgg ctggcgattc ataaggatag acacttcttg tgtatgtaca 720
ttgaccatta aaaggggaag a 741
    
```

<210> SEQ ID NO 19
 <211> LENGTH: 181
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 19

Met Met Leu Gln His Pro Gly Gln Val Ser Ala Ser Glu Val Ser Ala

-continued

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

<210> SEQ ID NO 20

<211> LENGTH: 543

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 20

```

atgatgcttc aacaccccagg ccaggctctc gctcgggaag tgagtgettc tgccatcgtc      60
ccctgcctgt cccctcctgg gtcactgggtg tttgaggatt ttgctaacct gacgcccttt    120
gtcaaggaag agctgagggtt tgccatccag aacaagcacc tctgccaccg gatgtcctct    180
gcgctggaat cagtcactgt cagcgacaga cccctcgggg tgtccatcac aaaagccgag    240
gtagcccctg aagaagatga aaggaaaaag aggcgacgag aaagaaataa gattgcagct    300
gcaaagtgcc gaaacaagaa gaaggagaag acggagtgcc tgcagaaaga gtcggagaag    360
ctggaaaagt tgaatgctga actgaaggct cagattgagg agctcaagaa cgagaagcag    420
catttgatat acatgctcaa ccttcacggtg cccacgtgta ttgtccgggc tcagaatggg    480
aggactccag aagatgagag aaacctcttt atccaacaga taaaagaagg aacattgcag    540
agc                                                                                   543

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<210> SEQ ID NO 21

<211> LENGTH: 868

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 21

Met Ala Thr Phe Ile Ser Val Gln Leu Lys Lys Thr Ser Glu Val Asp	1	5	10	15
Leu Ala Lys Pro Leu Val Lys Phe Ile Gln Gln Thr Tyr Pro Ser Gly	20	25	30	

-continued

Gly Glu Glu Gln Ala Gln Tyr Cys Arg Ala Ala Glu Glu Leu Ser Lys
35 40 45

Leu Arg Arg Ala Ala Val Gly Arg Pro Leu Asp Lys His Glu Gly Ala
50 55 60

Leu Glu Thr Leu Leu Arg Tyr Tyr Asp Gln Ile Cys Ser Ile Glu Pro
65 70 75 80

Lys Phe Pro Phe Ser Glu Asn Gln Ile Cys Leu Thr Phe Thr Trp Lys
85 90 95

Asp Ala Phe Asp Lys Gly Ser Leu Phe Gly Gly Ser Val Lys Leu Ala
100 105 110

Leu Ala Ser Leu Gly Tyr Glu Lys Ser Cys Val Leu Phe Asn Cys Ala
115 120 125

Ala Leu Ala Ser Gln Ile Ala Ala Glu Gln Asn Leu Asp Asn Asp Glu
130 135 140

Gly Leu Lys Ile Ala Ala Lys His Tyr Gln Phe Ala Ser Gly Ala Phe
145 150 155 160

Leu His Ile Lys Glu Thr Val Leu Ser Ala Leu Ser Arg Glu Pro Thr
165 170 175

Val Asp Ile Ser Pro Asp Thr Val Gly Thr Leu Ser Leu Ile Met Leu
180 185 190

Ala Gln Ala Gln Glu Val Phe Phe Leu Lys Ala Thr Arg Asp Lys Met
195 200 205

Lys Asp Ala Ile Ile Ala Lys Leu Ala Asn Gln Ala Ala Asp Tyr Phe
210 215 220

Gly Asp Ala Phe Lys Gln Cys Gln Tyr Lys Asp Thr Leu Pro Lys Glu
225 230 235 240

Val Phe Pro Val Leu Ala Ala Lys His Cys Ile Met Gln Ala Asn Ala
245 250 255

Glu Tyr His Gln Ser Ile Leu Ala Lys Gln Gln Lys Lys Phe Gly Glu
260 265 270

Glu Ile Ala Arg Leu Gln His Ala Ala Glu Leu Ile Lys Thr Val Ala
275 280 285

Ser Arg Tyr Asp Glu Tyr Val Asn Val Lys Asp Phe Ser Asp Lys Ile
290 295 300

Asn Arg Ala Leu Ala Ala Ala Lys Lys Asp Asn Asp Phe Ile Tyr His
305 310 315 320

Asp Arg Val Pro Asp Leu Lys Asp Leu Asp Pro Ile Gly Lys Ala Thr
325 330 335

Leu Val Lys Ser Thr Pro Val Asn Val Pro Ile Ser Gln Lys Phe Thr
340 345 350

Asp Leu Phe Glu Lys Met Val Pro Val Ser Val Gln Gln Ser Leu Ala
355 360 365

Ala Tyr Asn Gln Arg Lys Ala Asp Leu Val Asn Arg Ser Ile Ala Gln
370 375 380

Met Arg Glu Ala Thr Thr Leu Ala Asn Gly Val Leu Ala Ser Leu Asn
385 390 395 400

Leu Pro Ala Ala Ile Glu Asp Val Ser Gly Asp Thr Val Pro Gln Ser
405 410 415

Ile Leu Thr Lys Ser Arg Ser Val Ile Glu Gln Gly Gly Ile Gln Thr
420 425 430

-continued

Val Asp Gln Leu Ile Lys Glu Leu Pro Glu Leu Leu Gln Arg Asn Arg
 435 440 445

Glu Ile Leu Asp Glu Ser Leu Arg Leu Leu Asp Glu Glu Glu Ala Thr
 450 455 460

Asp Asn Asp Leu Arg Ala Lys Phe Lys Glu Arg Trp Gln Arg Thr Pro
 465 470 475 480

Ser Asn Glu Leu Tyr Lys Pro Leu Arg Ala Glu Gly Thr Asn Phe Arg
 485 490 495

Thr Val Leu Asp Lys Ala Val Gln Ala Asp Gly Gln Val Lys Glu Cys
 500 505 510

Tyr Gln Ser His Arg Asp Thr Ile Val Leu Leu Cys Lys Pro Glu Pro
 515 520 525

Glu Leu Asn Ala Ala Ile Pro Ser Ala Asn Pro Ala Lys Thr Met Gln
 530 535 540

Gly Ser Glu Val Val Asn Val Leu Lys Ser Leu Leu Ser Asn Leu Asp
 545 550 555 560

Glu Val Lys Lys Glu Arg Glu Gly Leu Glu Asn Asp Leu Lys Ser Val
 565 570 575

Asn Phe Asp Met Thr Ser Lys Phe Leu Thr Ala Leu Ala Gln Asp Gly
 580 585 590

Val Ile Asn Glu Glu Ala Leu Ser Val Thr Glu Leu Asp Arg Val Tyr
 595 600 605

Gly Gly Leu Thr Thr Lys Val Gln Glu Ser Leu Lys Lys Gln Glu Gly
 610 615 620

Leu Leu Lys Asn Ile Gln Val Ser His Gln Glu Phe Ser Lys Met Lys
 625 630 635 640

Gln Ser Asn Asn Glu Ala Asn Leu Arg Glu Glu Val Leu Lys Asn Leu
 645 650 655

Ala Thr Ala Tyr Asp Asn Phe Val Glu Leu Val Ala Asn Leu Lys Glu
 660 665 670

Gly Thr Lys Phe Tyr Asn Glu Leu Thr Glu Ile Leu Val Arg Phe Gln
 675 680 685

Asn Lys Cys Ser Asp Ile Val Phe Ala Arg Lys Thr Glu Arg Asp Glu
 690 695 700

Leu Leu Lys Asp Leu Gln Gln Ser Ile Ala Arg Glu Pro Ser Ala Pro
 705 710 715 720

Ser Ile Pro Thr Pro Ala Tyr Gln Ser Ser Pro Ala Gly Gly His Ala
 725 730 735

Pro Thr Pro Pro Thr Pro Ala Pro Arg Thr Met Pro Pro Thr Lys Pro
 740 745 750

Gln Pro Pro Ala Arg Pro Pro Pro Pro Val Leu Pro Ala Asn Arg Ala
 755 760 765

Pro Ser Ala Thr Ala Pro Ser Pro Val Gly Ala Gly Thr Ala Ala Pro
 770 775 780

Ala Pro Ser Gln Thr Pro Gly Ser Ala Pro Pro Pro Gln Ala Gln Gly
 785 790 795 800

Pro Pro Tyr Pro Thr Tyr Pro Gly Tyr Pro Gly Tyr Cys Gln Met Pro
 805 810 815

Met Pro Met Gly Tyr Asn Pro Tyr Ala Tyr Gly Gln Tyr Asn Met Pro
 820 825 830

Tyr Pro Pro Val Tyr His Gln Ser Pro Gly Gln Ala Pro Tyr Pro Gly

-continued

835	840	845	
Pro Gln Gln Pro Ser Tyr	Pro Phe Pro Gln Pro	Pro Gln Gln Ser Tyr	
850	855	860	
Tyr Pro Gln Gln			
865			
<210> SEQ ID NO 22			
<211> LENGTH: 2604			
<212> TYPE: DNA			
<213> ORGANISM: Homo sapiens			
<400> SEQUENCE: 22			
atggcgacat tcatctcggg gcagctgaaa aagacctcag aggtggacct ggccaagccg			60
ctggtgaagt tcatccagca gacttaccca agcggcgggg aagagcaggc ccagtactgc			120
cgcgcggcgg aggagctcag caagtgcgc cgcgccgag tcggtcgtcc gctggacaag			180
cacgagggcg cgctcgagac gctcctgaga tattatgac agatttggtc tattgaacct			240
aaattcccat tttctgaaaa tcagatctgc ttgacattta cctggaagga tgctttcgat			300
aaaggttcac tttttggagg ctctgtaaaa ctggctcttg caagcttagg atatgaaaag			360
agctgtgtgt tgttcaattg tgcagcetta gctagccaaa ttgcagcaga acagaacctg			420
gataatgatg aaggattgaa aatcgctgct aaacattacc agtttgctag tggcgccttt			480
ttacatatta aagagacggt tttatctgcc ttaagtcgag agccgaccgt ggacatatct			540
ccagatactg ttgggacct cagtcttatt atgctggcac aggcctcaaga agtatttttt			600
ttaaagcca caagagataa aatgaaagat gccatcatag ctaaattggc taatcaggct			660
gcagattatt ttggtgatgc tttcaaacag tgtcaataca aagatactct cccaaggag			720
gtgttcctg tcttggtgct aaagcactgt atcatgcagg ccaatgctga gtaccatcag			780
tctatcctgg caaacacgca gaagaaatgt ggagaagaaa ttgcaagggt acagcatgca			840
gcagaactga ttaaacagct gccatctcgc tatgatgaat atgttaatgt gaaggatgtt			900
tctgacaaaa tcaatcgtgc ccttgctgca gcaaagaagg ataatgactt cattttatcat			960
gatcgagttc cagaccttaa agatctagat cctattggca aagccacct tgtgaaatct			1020
accccggtca atgtaccat cagtcagaaa tttactgac tgtttgagaa gatggttccc			1080
gtgtcagtac agcagctctt ggctgctat aatcagagga aagccgattt ggttaacaga			1140
tcaattgctc agatgagaga agccaccact ttggcaaatg gggctgctagc tcccttaat			1200
cttcagcag caattgaaga tgtgtctgga gacctgtac ctcagctat attgactaaa			1260
tccagatctg tgattgaaca gggaggcatc cagactgttg atcagttgat taaagaactg			1320
cctgaattac tgcaacgaaa tagagaaatc ctatagatg cattaagggt gttggatgaa			1380
gaagaagcaa ccgataatga ttaagagca aaatttaagg aacgttggca aaggacacca			1440
tccaatgaac tgtataagcc ttaagagca gagggaacca acttcagaac agtttttagat			1500
aaagctgtgc aggcagatgg acaagtgaaa gaatgttacc agtctcatcg tgacaccatc			1560
gtgcttttgt gtaagccaga gcctgagctg aatgctgcca tcccttctgc taatccagca			1620
aagaccatgc agggcagtg ggttgtaaat gtcttaaaat ccttattgct aaatcttgat			1680
gaagtaaaga aggaaagaga gggctcggag aatgacttga aatctgtgaa ttttgacatg			1740
acaagcaagt ttttgacagc cctggctcaa gatggtgtga taaatgaaga agctctttct			1800

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gttactgaac tagatcagat ctatggaggt cttacaacta aagtccaaga atctctaaag 1860
aacacaggagg gacttcttaa aatatctcag gtctcacatc aggaattttc aaaatgaaa 1920
caatctaata atgaagctaa cttaaagaaa gaagttttga agaatttagc tactgcatat 1980
gacaactttg ttgaacttgt agctaatttg aaggaaggca caaagtttta caatgagttg 2040
actgaaatcc tggtcagggt ccagaacaaa tgcagtgata tagtttttgc acggaagaca 2100
gaaagagatg aactcttaaa ggacttgcaa caaagcattg ccagagaacc tagtgctcct 2160
tcaattccta cacctgcgta tcagtcctca ccagcaggag gacatgcacc aactcctcca 2220
actccagcgc caagaacat gccgcctact aagccccagc cccagccag gcctccacca 2280
cctgtgcttc cagcaaatcg agctccttct gctactgctc catctccagt gggggctggg 2340
actgctgctc cagctccatc acaaacgctt ggctcagctc ctctccaca ggcgcagggg 2400
ccaccctatc ccacctatcc aggatatcct gggatttggc aaatgcccac gcccatgggg 2460
tataatcctt atgctgatgg ccagtataat atgccatc caccagtgtg tcaccagagt 2520
cctggacagg ctccatacc gggaccccag cagccttcat accccttccc tcagcccca 2580
cagcagctct actatccaca gcag 2604

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<210> SEQ ID NO 23

<211> LENGTH: 215

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 23

```

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

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-continued

210 215

<210> SEQ ID NO 24
 <211> LENGTH: 645
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 24

atggctagtc gaggcgcaac aagacccaac gggccaaata ctggaaataa aatatgccag 60
 ttcaaactag tacttctggg agagtcgct gttggcaaat caagcctagt gcttcgtttt 120
 gtgaaaggcc aatttcatga atttcaagag agtaccattg gggctgcttt tctaaccctaa 180
 actgtatgtc ttgatgacac tacagtaaag tttgaaatat gggatacagc tggtaagaa 240
 cgataccata gcctagcacc aatgtactac agaggagcac aagcagccat agttgtatat 300
 gatatcacia atgaggagtc ctttgaaga gcaaaaaatt gggttaaaga acttcagagg 360
 caagcaagtc ctaacattgt aatagcttta tcgggaaaca aggccgacct agcaataaa 420
 agagcagtag atttccagga agcacagtcc tatgcagatg acaatagttt attattcatg 480
 gagacatccg ctaaaacatc aatgaatgta aatgaaatat tcatggcaat agctaaaaaa 540
 ttgcaaaga atgaaccaca aatccagga gcaaattctg ccagaggaag aggagtagac 600
 cttaccgaac ccacacaacc aaccaggaat cagtgttgta gtaac 645

<210> SEQ ID NO 25
 <211> LENGTH: 482
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 25

Met Ala Ala Val Arg Met Leu Arg Thr Trp Ser Arg Asn Ala Gly Lys
 1 5 10 15

Leu Ile Cys Val Arg Tyr Phe Gln Thr Cys Gly Asn Val His Val Leu
 20 25 30

Lys Pro Asn Tyr Val Cys Phe Phe Gly Tyr Pro Ser Phe Lys Tyr Ser
 35 40 45

His Pro His His Phe Leu Lys Thr Thr Ala Ala Leu Arg Gly Gln Val
 50 55 60

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

Val Lys Glu Trp Tyr Val Lys Glu Gly Asp Thr Val Ser Gln Phe Asp
 85 90 95

Ser Ile Cys Glu Val Gln Ser Asp Lys Ala Ser Val Thr Ile Thr Ser
 100 105 110

Arg Tyr Asp Gly Val Ile Lys Lys Leu Tyr Tyr Asn Leu Asp Asp Ile
 115 120 125

Ala Tyr Val Gly Lys Pro Leu Val Asp Ile Glu Thr Glu Ala Leu Lys
 130 135 140

Asp Ser Glu Glu Asp Val Val Glu Thr Pro Ala Val Ser His Asp Glu
 145 150 155 160

His Thr His Gln Glu Ile Lys Gly Arg Lys Thr Leu Ala Thr Pro Ala
 165 170 175

Val Arg Arg Leu Ala Met Glu Asn Asn Ile Lys Leu Ser Glu Val Val
 180 185 190

-continued

Gly Ser Gly Lys Asp Gly Arg Ile Leu Lys Glu Asp Ile Leu Asn Tyr
 195 200 205

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

Ile Met Pro Pro Pro Pro Lys Pro Lys Asp Met Thr Val Pro Ile Leu
 225 230 235 240

Val Ser Lys Pro Pro Val Phe Thr Gly Lys Asp Lys Thr Glu Pro Ile
 245 250 255

Lys Gly Phe Gln Lys Ala Met Val Lys Thr Met Ser Ala Ala Leu Lys
 260 265 270

Ile Pro His Phe Gly Tyr Cys Asp Glu Ile Asp Leu Thr Glu Leu Val
 275 280 285

Lys Leu Arg Glu Glu Leu Lys Pro Ile Ala Phe Ala Arg Gly Ile Lys
 290 295 300

Leu Ser Phe Met Pro Phe Phe Leu Lys Ala Ala Ser Leu Gly Leu Leu
 305 310 315 320

Gln Phe Pro Ile Leu Asn Ala Ser Val Asp Glu Asn Cys Gln Asn Ile
 325 330 335

Thr Tyr Lys Ala Ser His Asn Ile Gly Ile Ala Met Asp Thr Glu Gln
 340 345 350

Gly Leu Ile Val Pro Asn Val Lys Asn Val Gln Ile Cys Ser Ile Phe
 355 360 365

Asp Ile Ala Thr Glu Leu Asn Arg Leu Gln Lys Leu Gly Ser Val Gly
 370 375 380

Gln Leu Ser Thr Thr Asp Leu Thr Gly Gly Thr Phe Thr Leu Ser Asn
 385 390 395 400

Ile Gly Ser Ile Gly Gly Thr Phe Ala Lys Pro Val Ile Met Pro Pro
 405 410 415

Glu Val Ala Ile Gly Ala Leu Gly Ser Ile Lys Ala Ile Pro Arg Phe
 420 425 430

Asn Gln Lys Gly Glu Val Tyr Lys Ala Gln Ile Met Asn Val Ser Trp
 435 440 445

Ser Ala Asp His Arg Val Ile Asp Gly Ala Thr Met Ser Arg Phe Ser
 450 455 460

Asn Leu Trp Lys Ser Tyr Leu Glu Asn Pro Ala Phe Met Leu Leu Asp
 465 470 475 480

Leu Lys

<210> SEQ ID NO 26
 <211> LENGTH: 1446
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 26

```

atggctgcag tccgtatgct gagaacctgg agcaggaatg cggggaagct gatttgtggt      60
cgctattttc aaacatgtgg taatgttcat gttttgaagc caaattatgt gtgtttcttt      120
ggttatccct cattcaagta tagtcatcca catcacttcc tgaaaacaac tgctgctctc      180
cgtggacagg ttgttcagtt caagctctca gacattggag aagggattag agaagtaact      240
gttaaagaat ggtatgtaaa agaaggagat acagtgtctc agtttgatag catctgtgaa      300
gttcaaagtg ataaagcttc tgttaccatc actagtcggt atgatggagt cattaaaaaa      360
    
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ctctattata atctagacga tattgcctat gtggggaagc cattagtaga catagaaacg 420
gaagctttaa aagattcaga agaagatggt gttgaaactc ctgcagtgtc tcatgatgaa 480
catacacacc aagagataaa gggccgaaaa aactggcaa ctctgcagt tgcgcgtctg 540
gcaatggaaa acaatattaa gctgagttaa gttgttggt caggaaaaga tggcagaata 600
cttaaagaag atatcctcaa ctatttgaa aagcagacag gagctatatt gcctccttca 660
cccaaagttg aaattatgcc acctccacca aagccaaaag acatgactgt tcctatacta 720
gtatcaaac ctccgttatt cacaggcaaa gacaaaacag aaccataaa aggctttcaa 780
aaagcaatgg tcaagactat gtctgcagcc ctgaagatac ctcattttgg ttattgtgat 840
gagattgacc ttactgaact ggttaagctc cgagaagaat taaaacccat tgcatttget 900
cgtggaatta aactctcctt tatgccttcc ttcttaaagg ctgcttcctt gggattacta 960
cagtttccta tccttaacgc ttctgtggat gaaaactgcc agaataaac atataaggct 1020
tctcataaca ttgggatagc aatggatact gagcagggtt tgattgtccc taatgtgaaa 1080
aatgttcaga tctgctctat atttgacatc gccactgaac tgaaccgctt ccagaaattg 1140
ggctctgtgg gtcagctcag caccactgat cttacaggag gaacatttac tctttccaac 1200
attggatcaa ttggtggtac ctttgccaaa ccagtataaa tgccacctga agtagccatt 1260
ggggcccttg gatcaattaa ggccattccc cgatttaacc agaaggaga agtatataag 1320
gcacagataa tgaatgtgag ctggctcagct gatcacagag ttattgatgg tgctacaatg 1380
tcacgcttct ccaatttggt gaaatcctat ttagaaaacc cagcttttat gctactagat 1440
ctgaaa 1446

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<210> SEQ ID NO 27

<211> LENGTH: 473

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 27

```

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

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Leu Phe Ala Tyr Leu Met Cys Leu Tyr Gly Asn His Lys Thr Ser Ala
 165 170 175
 Phe Leu Gly Phe Cys Gly Phe Met Phe Arg Gln Thr Asn Ile Ile Trp
 180 185 190
 Ala Val Phe Cys Ala Gly Asn Val Ile Ala Gln Lys Leu Thr Glu Ala
 195 200 205
 Trp Lys Thr Glu Leu Gln Lys Lys Glu Asp Arg Leu Pro Pro Ile Lys
 210 215 220
 Gly Pro Phe Ala Glu Phe Arg Lys Ile Leu Gln Phe Leu Leu Ala Tyr
 225 230 235 240
 Ser Met Ser Phe Lys Asn Leu Ser Met Leu Leu Leu Thr Trp Pro
 245 250 255
 Tyr Ile Leu Leu Gly Phe Leu Phe Cys Ala Phe Val Val Val Asn Gly
 260 265 270
 Gly Ile Val Ile Gly Asp Arg Ser Ser His Glu Ala Cys Leu His Phe
 275 280 285
 Pro Gln Leu Phe Tyr Phe Phe Ser Phe Thr Leu Phe Phe Ser Phe Pro
 290 295 300
 His Leu Leu Ser Pro Ser Lys Ile Lys Thr Phe Leu Ser Leu Val Trp
 305 310 315 320
 Lys Arg Arg Ile Leu Phe Phe Val Val Thr Leu Val Ser Val Phe Leu
 325 330 335
 Val Trp Lys Phe Thr Tyr Ala His Lys Tyr Leu Leu Ala Asp Asn Arg
 340 345 350
 His Tyr Thr Phe Tyr Val Trp Lys Arg Val Phe Gln Arg Tyr Glu Thr
 355 360 365
 Val Lys Tyr Leu Leu Val Pro Ala Tyr Ile Phe Ala Gly Trp Ser Ile
 370 375 380
 Ala Asp Ser Leu Lys Ser Lys Ser Ile Phe Trp Asn Leu Met Phe Phe
 385 390 395 400
 Ile Cys Leu Phe Thr Val Ile Val Pro Gln Lys Leu Leu Glu Phe Arg
 405 410 415
 Tyr Phe Ile Leu Pro Tyr Val Ile Tyr Arg Leu Asn Ile Pro Leu Pro
 420 425 430
 Pro Thr Ser Arg Leu Ile Cys Glu Leu Ser Cys Tyr Ala Val Val Asn
 435 440 445
 Phe Ile Thr Phe Phe Ile Phe Leu Asn Lys Thr Phe Gln Trp Pro Asn
 450 455 460
 Ser Gln Asp Ile Gln Arg Phe Met Trp
 465 470

<210> SEQ ID NO 28

<211> LENGTH: 1419

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 28

```

atggcgagc tggaggta ctatttctg gccgcttga gctgtacct tttagtatcc 60
tgctcctct tctccgctt cagccgggagc ttgcgagagc cctacatgga cgagatcttc 120
cacctgcctc aggcgcagcg ctactgtgag ggccatttct ccctttccca gtgggatccc 180
atgattacta cattacctg cttgtacctg gtgtcaattg gaggatcaa acctgccatt 240

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tggatctttg gatggtctga acatgttgtc tgctccattg ggatgctcag atttgtaat 300
cttctcttca gtggtggcaa cttctattta ctatatttgc tttctgcaa ggtacaaccc 360
agaaacaagg ctgcctcaag tatccagaga gtcttgctca cattaacact agcagtattt 420
ccaacacttt atttttttaa cttcctttat tatacagaag caggatctat gttttttact 480
ctttttgcgt atttgatgtg tctttatgga aatcataaaa cttcagcctt ccttgattt 540
tgtgcttca tgtttcgga aacaaatc atctggctg tctctgtgc aggaaatgc 600
attgcacaaa agttaacgga ggcttgaaa actgagctac aaaagaagga agacagactt 660
ccacctatta aaggaccatt tgcagaattc agaaaaattc ttcagtttct tttggcttat 720
tccatgtcct ttaaaaaact gagtatgctt ttgcttctga cttggccta catcctctg 780
ggatttctgt tttgtgctt tgtagtagtt aatggtgaa ttgttattgg cgatcggagt 840
agtcatgaag cctgtcttca ttttctcaa ctattctact ttttttctt tactctctt 900
ttttctctt ctcactcct gtctcctagc aaaattaaga ctttctctt cttagtttg 960
aaacgtagaa ttctgtttt tgtggttacc ttagtctctg tgttttagt ttggaaattc 1020
acttatgctc ataaactct gctagcagac aatagacatt atactttcta tgtgtggaaa 1080
agagttttc aaagatatga aactgtaaaa tatttgtag ttccagccta tatatttgc 1140
ggttgagta tagctgactc attgaaatca aagtcaattt tttggaattt aatgttttc 1200
atatgcttgt tcaactgtat agttcctcag aaactgctgg aatttcgtta cttcatttta 1260
ccttatgtca tttatagct taacatacct ctgcctccca catccagact catttgtgaa 1320
ctgagctgct atgcagttgt taatttcata acttttttca tctttctgaa caagactttt 1380
cagtggccaa atagtcagga cattcaaagg tttatgtgg 1419

```

<210> SEQ ID NO 29

<211> LENGTH: 440

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 29

```

Met Gly Ser Ser His Leu Leu Asn Lys Gly Leu Pro Leu Gly Val Arg
1          5          10          15

Pro Pro Ile Met Asn Gly Pro Leu His Pro Arg Pro Leu Val Ala Leu
20        25        30

Leu Asp Gly Arg Asp Cys Thr Val Glu Met Pro Ile Leu Lys Asp Val
35        40        45

Ala Thr Val Ala Phe Cys Asp Ala Gln Ser Thr Gln Glu Ile His Glu
50        55        60

Lys Val Leu Asn Glu Ala Val Gly Ala Leu Met Tyr His Thr Ile Thr
65        70        75        80

Leu Thr Arg Glu Asp Leu Glu Lys Phe Lys Ala Leu Arg Ile Ile Val
85        90        95

Arg Ile Gly Ser Gly Phe Asp Asn Ile Asp Ile Lys Ser Ala Gly Asp
100       105       110

Leu Gly Ile Ala Val Cys Asn Val Pro Ala Ala Ser Val Glu Glu Thr
115      120      125

Ala Asp Ser Thr Leu Cys His Ile Leu Asn Leu Tyr Arg Arg Ala Thr
130      135      140

Trp Leu His Gln Ala Leu Arg Glu Gly Thr Arg Val Gln Ser Val Glu

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

<210> SEQ ID NO 30
 <211> LENGTH: 1320
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 30

atgggcagct cgcaacttgc caacaagggc ctgccgcttg gcgtccgacc tccgatcatg	60
aacgggcccc tgcacccgcg gccctgggtg gcattgctgg atggccggga ctgcacagtg	120
gagatgcccc tcttgaagga cgtggccact gtggccttct gcgacgcgca gtccacgcag	180
gagatccatg agaaggtcct gaacgaggct gtgggggccc tgatgtacca caccatcact	240
ctcaccaggg aggacctgga gaagtcaaa gccctccgca tcatcgtcgg gattggcagt	300
ggttttgaca acatcgacat caagtcggcc ggggatttag gcattgacct ctgcaactg	360

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ccccggcgct ctgtggagga gacggccgac tgcagcgtgt gccacatcct gaacctgtac 420
cggcggggcca cctggctgca ccaggcgctg cgggagggca cagcagtcga gagcgtcgag 480
cagatccgcg aggtggcgct cggcgctgcc aggatccgcg gggagacctt gggcatcate 540
ggacttggtc gcgtggggca ggcagtggcg ctgcggggcca aggccttcgg cttcaactgt 600
ctcttctacg acccttactt gtcggatggc gtggagcggg cgctggggct gcagcgtgtc 660
agcaccctgc aggacctgct cttccacagc gactgcgtga ccctgcaact cggcctcaac 720
gagcacaacc accacctcat caacgacttc accgtcaagc agatgagaca aggggccttc 780
ctggtgaaca cagccccggg tggcctggtg gatgagaagg cgctgggcca ggcctgaag 840
gagggcggga tccgcgcgcc ggccctggat gtgcacgagt cggaaacctt cagctttagc 900
cagggccctc tgaaggatgc acccaacctc atctgcaccc cccatgctgc atggtacagc 960
gagcaggcat ccatcgagat gcgagaggag gcggcacggg agatccgcag agccatcaca 1020
ggcgggatcc cagacagcct gaagaactgt gtcaacaagg accatctgac agccgccacc 1080
cactggggca gcatggacce cgccgtcgtg caccctgagc tcaatggggc tgcctatagg 1140
taccctccgg gcgtggtggg cgtggccccc actggcatcc cagctgctgt ggaaggtatc 1200
gtccccagcg ccatgtcctt gtccccagcc ctgccccctg tgccccacce gccccagcc 1260
ccttctcctg gccaaacctg caagcccagc gcggatagag accacgccag tgaccagtgt 1320

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<210> SEQ ID NO 31

<211> LENGTH: 317

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 31

```

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

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Gln Met Gln Pro Met His Arg Tyr Asp Val Ser Ala Leu Gln Tyr Asn
 195 200 205

Ser Met Thr Ser Ser Gln Thr Tyr Met Asn Gly Ser Pro Thr Tyr Ser
 210 215 220

Met Ser Tyr Ser Gln Gln Gly Thr Pro Gly Met Ala Leu Gly Ser Met
 225 230 235 240

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

Ser Ser Ser His Ser Arg Ala Pro Cys Gln Ala Gly Asp Leu Arg Asp
 260 265 270

Met Ile Ser Met Tyr Leu Pro Gly Ala Glu Val Pro Glu Pro Ala Ala
 275 280 285

Pro Ser Arg Leu His Met Ser Gln His Tyr Gln Ser Gly Pro Val Pro
 290 295 300

Gly Thr Ala Ile Asn Gly Thr Leu Pro Leu Ser His Met
 305 310 315

<210> SEQ ID NO 32
 <211> LENGTH: 951
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 32

```

atgtacaaca tgatggagac ggagctgaag cgcggggccc cgcagcaaac ttcggggggc 60
ggcggcggca actccaccgc ggccggggcc ggcggcaacc agaaaaacag cccggaccgc 120
gtcaagcggc ccatgaatgc cttcatggtg tgggtcccgcg ggcagcggcg caagatggcc 180
caggagaacc ccaagatgca caactcggag atcagcaagc gcctggggcg cgagtggaaa 240
cttttgtcgg agacggagaa ggcggcgttc atcgacgagg ctaagcggct gcgagcgtg 300
cacatgaagg agcaccggga ttataaatc cggccccggc ggaaaaccaa gacgctcatg 360
aagaaggata agtacacgct gcccgggggg ctgctggccc cggcgggcaa tagcatggcg 420
agcgggggtcg ggggtggggcg cggcctgggc gcgggcgtga accagcgcac ggacagttac 480
gcgcacatga acggctggag caacggcagc tacagcatga tgcaggacca gctgggctac 540
ccgcagcacc cgggcctcaa tgcgcacggc gcagcgcaga tgcagcccat gcaccgctac 600
gacgtgagcg ccctgcagta caactccatg accagctcgc agacctacat gaacggctcg 660
cccacctaca gcatgtccta ctcgcagcag ggcaccctg gcatggctct tggetccatg 720
ggttcgggtg tcaagtccga ggccagctcc agccccctg tggttaacctc ttectcccac 780
tccaggggcg cctgccaggc cggggacctc cgggacatga tcagcatgta tctcccggc 840
gccgaggtgc cggaacccgc cgcgccagc agacttcaca tgtcccagca ctaccagagc 900
ggcccgggtg cgggcacggc cattaacggc aactgcccc tctcacacat g 951
    
```

<210> SEQ ID NO 33
 <211> LENGTH: 264
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 33

Met Leu Ser His Asn Thr Met Met Lys Gln Arg Lys Gln Gln Ala Thr
 1 5 10 15

Ala Ile Met Lys Glu Val His Gly Asn Asp Val Asp Gly Met Asp Leu

-continued

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

<210> SEQ ID NO 34
 <211> LENGTH: 792
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 34

```

atgctatcac ataactat gatgaagcag agaaaacagc aagcaacagc catcatgaag      60
gaagtccatg gaaatgatgt tgatggcatg gacctgggca aaaaggtcag catccccaga    120
gacatcatgt tggagaat atcccatctc agtaaccgtg gtgccaggct atttaagatg    180
cgtcaaagaa gatctgacaa atacacattt gaaaatttcc agtatcaatc tagagcaciaa   240
ataaatcaca gtattgctat gcagaatggg aaagtggatg gaagtaactt ggaaggtggt   300
tcgcagcaag ccccttgac tcctcccaac accccagatc cacgaagccc tccaaatcca   360
gacaacattg ctccaggata ttctggacca ctgaaggaaa ttctcctga aaaattcaac   420
accacagctg tcctaaagta ctatcaatct ccctgggaac aagccattag caatgatccg   480
gagcttttag aggctttata tcctaaactt ttcaagcctg aaggaaagc agaactgcct   540
gattacagga gctttaacag ggttgccaca ccatttgag gtttgaaaa agcatcaaga   600
atggttaaat ttaaagttcc agattttgag ctactattgc taacagatcc caggtttatg   660
    
```


-continued

```

tcctttgtca atcccccttc tggcagacgg tcctttaata ggactcctaa gggatggata 720
tctgagaata ttctatagt gataacaacc gaacctacag atgataccac tgtaccagaa 780
tcagaagacc ta 792

```

```

<210> SEQ ID NO 35
<211> LENGTH: 83
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

```

```

<400> SEQUENCE: 35

```

```

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

```

```

<210> SEQ ID NO 36
<211> LENGTH: 249
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

```

```

<400> SEQUENCE: 36

```

```

atgagctttt tccaactcct gatgaaaagg aaggaactca ttcccttggg ggtgttcctg 60
actgtggcgg cgggtggagc ctcatctttc gctgtgtatt ctctttggaa aaccgatgtg 120
atccttgatc gaaaaaaaa tccagaacct tgggaaactg tggaccctac tgtacctcaa 180
aagcttataa caatcaacca acaatggaaa ccattgaag agttgcaaaa tgtccaaagg 240
gtgaccaaa 249

```

```

<210> SEQ ID NO 37
<211> LENGTH: 653
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

```

```

<400> SEQUENCE: 37

```

```

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

```

-continued

Leu Leu Met Cys Arg Ser Cys Gly Arg Arg Leu Pro Arg Gln Phe Cys
 100 105 110

Arg Ser Cys Gly Leu Val Leu Cys Glu Pro Cys Arg Glu Ala Asp His
 115 120 125

Gln Pro Pro Gly His Cys Thr Leu Pro Val Lys Glu Ala Ala Glu Glu
 130 135 140

Arg Arg Arg Asp Phe Gly Glu Lys Leu Thr Arg Leu Arg Glu Leu Met
 145 150 155 160

Gly Glu Leu Gln Arg Arg Lys Ala Ala Leu Glu Gly Val Ser Lys Asp
 165 170 175

Leu Gln Ala Arg Tyr Lys Ala Val Leu Gln Glu Tyr Gly His Glu Glu
 180 185 190

Arg Arg Val Gln Asp Glu Leu Ala Arg Ser Arg Lys Phe Phe Thr Gly
 195 200 205

Ser Leu Ala Glu Val Glu Lys Ser Asn Ser Gln Val Val Glu Glu Gln
 210 215 220

Ser Tyr Leu Leu Asn Ile Ala Glu Val Gln Ala Val Ser Arg Cys Asp
 225 230 235 240

Tyr Phe Leu Ala Lys Ile Lys Gln Ala Asp Val Ala Leu Leu Glu Glu
 245 250 255

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

Leu Thr Leu Gln Asp Val Glu Leu Leu Lys Val Gly His Val Gly Pro
 275 280 285

Leu Gln Ile Gly Gln Ala Val Lys Lys Pro Arg Thr Val Asn Val Glu
 290 295 300

Asp Ser Trp Ala Met Glu Ala Thr Ala Ser Ala Ala Ser Thr Ser Val
 305 310 315 320

Thr Phe Arg Glu Met Asp Met Ser Pro Glu Glu Val Val Ala Ser Pro
 325 330 335

Arg Ala Ser Pro Ala Lys Gln Arg Gly Pro Glu Ala Ala Ser Asn Ile
 340 345 350

Gln Gln Cys Leu Phe Leu Lys Lys Met Gly Ala Lys Gly Ser Thr Pro
 355 360 365

Gly Met Phe Asn Leu Pro Val Ser Leu Tyr Val Thr Ser Gln Gly Glu
 370 375 380

Val Leu Val Ala Asp Arg Gly Asn Tyr Arg Ile Gln Val Phe Thr Arg
 385 390 395 400

Lys Gly Phe Leu Lys Glu Ile Arg Arg Ser Pro Ser Gly Ile Asp Ser
 405 410 415

Phe Val Leu Ser Phe Leu Gly Ala Asp Leu Pro Asn Leu Thr Pro Leu
 420 425 430

Ser Val Ala Met Asn Cys Gln Gly Leu Ile Gly Val Thr Asp Ser Tyr
 435 440 445

Asp Asn Ser Leu Lys Val Tyr Thr Leu Asp Gly His Cys Val Ala Cys
 450 455 460

His Arg Ser Gln Leu Ser Lys Pro Trp Gly Ile Thr Ala Leu Pro Ser
 465 470 475 480

Gly Gln Phe Val Val Thr Asp Val Glu Gly Gly Lys Leu Trp Cys Phe
 485 490 495

Thr Val Asp Arg Gly Ser Gly Val Val Lys Tyr Ser Cys Leu Cys Ser

-continued

	500		505		510										
Ala Val Arg Pro Lys Phe Val Thr Cys Asp Ala Glu Gly Thr Val Tyr															
	515					520					525				
Phe Thr Gln Gly Leu Gly Leu Asn Leu Glu Asn Arg Gln Asn Glu His															
	530					535					540				
His Leu Glu Gly Gly Phe Ser Ile Gly Ser Val Gly Pro Asp Gly Gln															
	545				550				555						560
Leu Gly Arg Gln Ile Ser His Phe Phe Ser Glu Asn Glu Asp Phe Arg															
				565				570							575
Cys Ile Ala Gly Met Cys Val Asp Ala Arg Gly Asp Leu Ile Val Ala															
	580							585							590
Asp Ser Ser Arg Lys Glu Ile Leu His Phe Pro Lys Gly Gly Gly Tyr															
	595					600					605				
Ser Val Leu Ile Arg Glu Gly Leu Thr Cys Pro Val Gly Ile Ala Leu															
	610					615					620				
Thr Pro Lys Gly Gln Leu Leu Val Leu Asp Cys Trp Asp His Cys Ile															
	625				630					635					640
Lys Ile Tyr Ser Tyr His Leu Arg Arg Tyr Ser Thr Pro															
				645					650						

<210> SEQ ID NO 38
 <211> LENGTH: 1959
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 38

```

atggctgcag cagcagcttc tcacctgaac ctggatgccc tccgggaagt gctagaatgc    60
cccactctgca tggagtcctt cacagaagag cagctgcgtc ccaagcttct gcaactgtggc    120
cataccatct gcgcaccatg cctggagaag ctattggcca gtagcatcaa tgggtgtccgc    180
tgtccctttt gcagcaagat taccgcgata accagcttga cccagctgac agacaatctg    240
acagtgctaa agatcattga tacagctggg ctcagcgagg ctgtggggct gctcatgtgt    300
cggctcctgt ggcggcgtct gccccggcaa ttctgccgga gctgtggttt ggtgttatgt    360
gagccctgcc gggaggcaga ccatacagcct cctggccact gtacactccc tgtcaaagaa    420
gcagctgagg agcggcgtcg ggactttgga gagaagttaa ctctctgcg ggaacttatg    480
ggggagctgc agcggcgcaa ggcagccttg gaaggtgtct ccaaggacct tcaggcaagg    540
tataaagcag ttctccagga gtatgggcat gaggagcgca ggggccagga tgagctggct    600
cgctctcgga agttcttcac aggctctttg gctgaagttg agaagtcaa tagtcaagtg    660
gtagaggagc agagttacct gcttaacatt gcagaggtgc aggctgtgtc tcgctgtgac    720
tacttctcgg ccaagatcaa gcaggcagat gtagcactac tggaggagac agctgatgag    780
gaggagccag agctcactgc cagcttgctt cgggagctca ccctgcaaga tgtggagctc    840
cttaaggtag gtcattgttg cccccccaa attggacaag ctgttaagaa gccccggaca    900
gttaacgtgg aagattcctg ggccatggag gccacagcgt ctgctgctc tacctctgtt    960
acttttagag agatggacat gagcccggag gaagtggttg ccagccctag ggcctcacct   1020
gctaaacagc ggggtctctg gccagcctcc aatatccagc agtgcctctt tctcaagaag   1080
atgggggcca aaggcagcac tccaggaatg ttcaatcttc cagtcagtct ctacgtgacc   1140
agtcaaggtg aagtactagt cgctgaccgt ggtaactatc gtatacaagt ctttaccggc   1200
    
```

-continued

```

aaaggctttt tgaaggaaat ccgccgcagc cccagtgcca ttgatagctt tgtgctaagc 1260
ttccttgggg cagatctacc caacctcact cctctctcag tggcaatgaa ctgccagggg 1320
ctgattgggtg tgactgacag ctatgataac tocctcaagg tatatacctt ggatggccac 1380
tgcgtggcct gtcacaggag ccagctgagc aaaccatggg gtatcacagc cttgccatct 1440
ggccagtttg tagtaaccga tgtggaaggt ggaaagcttt ggtgtttcac agttgatcga 1500
ggatcagggg tggtaaata cagctgccta tgtagtctg tgcggcccaa atttgtcacc 1560
tgtgatgctg agggcacctg ctacttcacc cagggcttag gcctcaatct ggagaatcgg 1620
cagaatgagc accacctgga ggggtgcttt tccattgget ctgtaggccc tgatgggcag 1680
ctgggtcgcc agattagcca cttcttctcg gagaatgagg atttccgctg cattgtggc 1740
atgtgtgtgg atgctctggt tgatctcctc gtggtgaca gtatgcgcaa ggaattctc 1800
cattttccta aggggtgggg ctatagtctc cttattcgag agggacttac ctgtccggtg 1860
ggcatagccc taactcctaa ggggcagctg ctggtcttgg actgttggga tcattgcatc 1920
aagatctaca gctaccatct gagaagatat tccacccca 1959

```

<210> SEQ ID NO 39

<211> LENGTH: 445

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 39

```

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

```

-continued

His Pro Lys Gly Arg Asp Asn Ile Ile Asp Leu Phe Leu Tyr Gln Pro
 225 230 235 240

Gln Tyr Leu Asn Ala Ile Gln Thr Met Cys Pro His Ile Leu Arg Tyr
 245 250 255

Leu Thr Thr Ala Val Ile Thr Asn Lys Asp Val Arg Lys Arg Arg Gln
 260 265 270

Val Leu Lys Asp Leu Val Lys Val Ile Gln Gln Glu Ser Tyr Thr Tyr
 275 280 285

Lys Asp Pro Ile Thr Glu Phe Val Glu Cys Leu Tyr Val Asn Phe Asp
 290 295 300

Phe Asp Gly Ala Gln Lys Lys Leu Arg Glu Cys Glu Ser Val Leu Val
 305 310 315 320

Asn Asp Phe Phe Leu Val Ala Cys Leu Glu Asp Phe Ile Glu Asn Ala
 325 330 335

Arg Leu Phe Ile Phe Glu Thr Phe Cys Arg Ile His Gln Cys Ile Ser
 340 345 350

Ile Asn Met Leu Ala Asp Lys Leu Asn Met Thr Pro Glu Glu Ala Glu
 355 360 365

Arg Trp Ile Val Asn Leu Ile Arg Asn Ala Arg Leu Asp Ala Lys Ile
 370 375 380

Asp Ser Lys Leu Gly His Val Val Met Gly Asn Asn Ala Val Ser Pro
 385 390 395 400

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

Met Leu Ala Met Asn Ile Glu Lys Lys Leu Asn Gln Asn Ser Arg Ser
 420 425 430

Glu Ala Pro Asn Trp Ala Thr Gln Asp Ser Gly Phe Tyr
 435 440 445

<210> SEQ ID NO 40
 <211> LENGTH: 1335
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 40

```

atggcggagt acgacttgac tactcgcac cgcactttt tggatcggca tctagtcttt    60
ccgcttcttg aatttctctc tgtaaaggag atatataatg aaaaggaatt attacaaggt    120
aaattggacc ttcttagtga taccaacatg gtagactttg ctatggatgt atacaaaaac    180
ctttattctg atgatattcc tcatgctttg agagagaaaa gaaccacagt ggttgacaaa    240
ctgaaacagc ttcaggcaga aacagaacca attgtgaaga tgtttgaaga tccagaaact    300
acaaggcaaa tgcagctaac cagggatggg aggatgctct ttgactacct ggcggacaag    360
catggtttta ggcaggaata tttagatata ctctacagat atgcaaaatt ccagtagcaa    420
tgtgggaatt actcaggagc agcagaatat ctttattttt ttagagtgct ggttccagca    480
acagatagaa atgctttaag ttcactctgg ggaaagctgg cctctgaaat cttaatgcag    540
aattgggatg cagccatgga agaccttaca cggttaaaag agaccataga taataattct    600
gtgagttctc cacttcagtc tcttcagcag agaacatggc tcattcactg gtctctgttt    660
gttttcttca atcaccocaa aggtcgggat aatattattg acctcttctt ttatcagcca    720
caatatctta atgcaattca gacaatgtgt ccacacattc ttcgctatth gactacagca    780
    
```

-continued

```

gtcataacaa acaaggatgt tcgaaaacgt cggcaggttc taaaagatct agttaaagtt 840
attcaacagg agtcttacac atataaagac ccaattacag aatttggtga atgtttatat 900
gttaactttg actttgatgg ggctcagaaa aagctgaggg aatgtgaatc agtgcttggtg 960
aatgacttct tcttggtggc ttgtcttgag gatttcattg aaaatgcccg tctcttcata 1020
tttgagactt tctgtcgcac ccaccagtgt atcagcatta acatggtggc agataaattg 1080
aacatgactc cagaagaagc tgaaagggtg attgtaaatt tgattagaaa tgcaagactg 1140
gatgccaaga ttgattctaa attaggtcat gtggttatgg gtaacaatgc agtctcaccc 1200
tatcagcaag tgattgaaaa gacccaaaagc ctttccttta gaagccagat gttggccatg 1260
aatattgaga agaaacttaa tcagaatagc aggtcagagg ctccctaactg ggcaactcaa 1320
gattctggct tctac 1335

```

```

<210> SEQ ID NO 41
<211> LENGTH: 156
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

```

```

<400> SEQUENCE: 41

```

```

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

```

```

<210> SEQ ID NO 42
<211> LENGTH: 468
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

```

```

<400> SEQUENCE: 42

```

```

atgaaagaac ctttgatggg tgaatgtggc aaagcagtgg taccacagca ggagcttctg 60
gacaaaatta aagaagaacc agacaatgct caagagtatg gatgtgtcca acagccaaaa 120
actcaagaaa gtaaattgaa aattgggtgg gtgtcttcag ttaatgagag acctattgcc 180
cagcagttga acccaggctt tcagctttct tttgcatcat ctggcccaag tgtgttgctt 240
ccttcagttc cagctgttgc tattaaggtt tttgttctg gttgtaaaaa aatgctttat 300

```

-continued

```

aagggccaaa ctgcatatca taagacagga tctactcagc tcttctgctc cacacgatgc 360
atcaccagac attcttcacc tgctgctg ccacctctc ccaagaaaac ctgcacaaac 420
tgctcgaagt ataaaattct taacatcct ttttacttta cctttttt 468

```

```

<210> SEQ ID NO 43
<211> LENGTH: 155
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

```

```

<400> SEQUENCE: 43

```

```

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

```

```

<210> SEQ ID NO 44
<211> LENGTH: 465
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

```

```

<400> SEQUENCE: 44

```

```

atgcagccgt ccccgccgcc caccgagctg gtgccgtcgg agcgcgccgt ggtgctgctg 60
tcgtgcgcac tctccgcgct cggctcgggc ctgctggtgg ccacgcacgc cctgtggccc 120
gacctgcgca gccgggcaag gcgcctgctg ctcttctctg cgtggccga cctgctctcg 180
gccgcctcct acttctacgg agtgetgcag aacttcgcgg gcccgctgtg ggactgcgtg 240
ctgcaggggc cgctgtccac cttcgccaac accagctcct tcttctggac cgtggccatt 300
gcgctctact tgtacctcag catcgtccgc gccgcgcgcg ggctcgcac agatgcctg 360
ctttggcct tccatgtcgt caggtgggtg gcggtggcgc tgcttttcca ggagcccccg 420
acacaggccg acccctcccg gtcttgcct cccagaggcc gcgtc 465

```

```

<210> SEQ ID NO 45
<211> LENGTH: 675
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

```

```

<400> SEQUENCE: 45

```

-continued

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

-continued

Asp Ser Val Ser Leu Gly Asn Gly Ile Trp Glu Leu Lys Arg Glu Glu
 405 410 415

Ile Thr Leu Leu Lys Glu Leu Gly Ser Gly Gln Phe Gly Val Val Gln
 420 425 430

Leu Gly Lys Trp Lys Gly Gln Tyr Asp Val Ala Val Lys Met Ile Lys
 435 440 445

Glu Gly Ser Met Ser Glu Asp Glu Phe Phe Gln Glu Ala Gln Thr Met
 450 455 460

Met Lys Leu Ser His Pro Lys Leu Val Lys Phe Tyr Gly Val Cys Ser
 465 470 475 480

Lys Glu Tyr Pro Ile Tyr Ile Val Thr Glu Tyr Ile Ser Asn Gly Cys
 485 490 495

Leu Leu Asn Tyr Leu Arg Ser His Gly Lys Gly Leu Glu Pro Ser Gln
 500 505 510

Leu Leu Glu Met Cys Tyr Asp Val Cys Glu Gly Met Ala Phe Leu Glu
 515 520 525

Ser His Gln Phe Ile His Arg Asp Leu Ala Ala Arg Asn Cys Leu Val
 530 535 540

Asp Arg Asp Leu Cys Val Lys Val Ser Asp Phe Gly Met Thr Arg Tyr
 545 550 555 560

Val Leu Asp Asp Gln Tyr Val Ser Ser Val Gly Thr Lys Phe Pro Val
 565 570 575

Lys Trp Ser Ala Pro Glu Val Phe His Tyr Phe Lys Tyr Ser Ser Lys
 580 585 590

Ser Asp Val Trp Ala Phe Gly Ile Leu Met Trp Glu Val Phe Ser Leu
 595 600 605

Gly Lys Gln Pro Tyr Asp Leu Tyr Asp Asn Ser Gln Val Val Leu Lys
 610 615 620

Val Ser Gln Gly His Arg Leu Tyr Arg Pro His Leu Ala Ser Asp Thr
 625 630 635 640

Ile Tyr Gln Ile Met Tyr Ser Cys Trp His Glu Leu Pro Glu Lys Arg
 645 650 655

Pro Thr Phe Gln Gln Leu Leu Ser Ser Ile Glu Pro Leu Arg Glu Lys
 660 665 670

Asp Lys His
 675

<210> SEQ ID NO 46
 <211> LENGTH: 2025
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 46

```

atggatacaa aatctattct agaagaactt cttctcaaaa gatcacagca aaagaagaaa    60
atgtcaccaa ataattacaa agaacggctt tttgttttga ccaaaacaaa cttttcctac    120
tatgaatatg acaaaatgaa aaggggcagc agaaaaggat ccattgaaat taagaaaatc    180
agatgtgtgg agaaagtaaa tctcaggagag cagacgcctg tagagagaca gtaccattt    240
cagattgtct ataaagatgg gcttctctat gtctatgcat caaatgaaga gagccgaagt    300
cagtggttga aagcattaca aaaagagata aggggtaacc cccacctgct ggtcaagtac    360
catagtgggt tcttcgtgga cgggaagttc ctgtgttgcc agcagagctg taaagcagcc    420
    
```

-continued

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ccaggatgta ccctctggga agcatatgct aatctgcata ctgcagtcaa tgaagagaaa 480
cacagagttc ccaccttccc agacagagtg ctgaagatac ctcgggcagt tctgttctc 540
aaaaatggatg caccatcttc aagtaccact ctageccaat atgacaacga atcaaagaaa 600
aactatggct cccagccacc atcttcaagt accagtctag cgcaatatga cagcaactca 660
aagaaaaatct atggctccca gccaaacttc aacatgcagt atattccaag ggaagacttc 720
cctgactggt ggcaagtaag aaaactgaaa agtagcagca gcagtgaaga tgttgcaagc 780
agtaaccaa aagaaagaaa tgtgaatcac accacctcaa agatttcag ggaattccct 840
gagtcaagtt catctgaaga agaggaaaac ctggatgatt atgactggtt tgctgtaac 900
atctccagat cacaatctga acagttactc agacaaaagg gaaaagaagg agcatttatg 960
gttagaatt cgagccaagt gggaatgtac acagtgtcct tatttagtaa ggctgtgaat 1020
gataaaaaag gaactgtcaa acattaccac gtgcatacaa atgctgagaa caaattatac 1080
ctggcagaaa actactgttt tgattocatt ccaaagctta ttcattatca tcaacacaat 1140
tcagcaggca tgatcacacg gctccgccac cctgtgtcaa caaaggccaa caaggctccc 1200
gactctgtgt ccctgggaaa tggaatctgg gaactgaaaa gagaagagat taccttgttg 1260
aaggagctgg gaagtggcca gtttgagtg gtccagctgg gcaagtggaa ggggcagtat 1320
gatgttgctg ttaagatgat caaggagggc tccatgtcag aagatgaatt cttcaggag 1380
gcccagacta tgatgaaact cagccatccc aagctgggta aattctatgg agtgtgttca 1440
aaggaatacc ccatatacat agtgactgaa tatataagca atggctgctt gctgaattac 1500
ctgaggagtc acgaaaaagg acttgaacct tcccagctct tagaaatgtg ctacgatgtc 1560
tgtgaaggca tggccttctt ggagagtcac caattcatac accgggactt ggctgctcgt 1620
aactgcttg tggacagaga tctctgtgtg aaagtatctg actttggaat gacaaggat 1680
gttcttgatg atcagtatgt cagttcagtc ggaacaaagt tccagtcaa gtggtcagct 1740
ccagaggtgt ttcattactt caaatcacgc agcaagtcag acgtatgggc atttgggac 1800
ctgatgtggg aggtgttcag cctggggaag cagccctatg acttgatga caactcccag 1860
gtggttctga aggtctccca gggccacag ctttaccggc cccacctggc atcggacacc 1920
atctaccaga tcatgtacag ctgctggcac gagcttcag aaaagcgtcc cacatttcag 1980
caactcctgt cttccattga accacttcgg gaaaaagaca agcat 2025

```

<210> SEQ ID NO 47

<211> LENGTH: 502

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 47

```

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

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-continued

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

-continued

Leu Leu Leu His Asn Asn Asp Gln Asp Asn Ala Leu Glu Asp Leu Met
485 490 495

Ala Arg Ala Gly Ala Ser
500

<210> SEQ ID NO 48
<211> LENGTH: 1506
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 48

```

atggcttcta agaagttggg tgcagathtt catgggactt tcagttacct tgatgatgtc    60
ccatttaaga caggagacaa attcaaaaca ccagctaaag ttggtctacc tattggcttc    120
tccttgcttg attgtttgca ggttgcaga gaagtacagt atgacttctc tttggaaaag    180
aaaaccattg agtgggctga agagattaag aaaatcgaag aagccgagcg ggaagcagag    240
tgcaaaattg cggaagcaga agctaaagtg aattctaaga gtggcccaga gggcgatagc    300
aaaatgagct tctccaagac tcacagtaca gccacaatgc cacctcctat taaccccatc    360
ctcgccagct tgcagacaaa cagcctcctc acaccaatc gggtcagcag tagtgccacg    420
aaacagaaag ttctcagccc acctcacata aaggcggatt tcaatcttgc tgactttgag    480
tgtgaagaag acccatttga taatctggag ttaaaaacta ttgatgagaa ggaagagctg    540
agaaatattc tggtaggaac cactggaccc attatggctc agttattgga caataacttg    600
cccaggggag gctctgggct tgtgttacag gatgaggagg tcctggcctc cttggaacgg    660
gcaaccctag atttcaagcc tcttcataaa cccaatggct ttataacctt accacagttg    720
ggcaactgtg aaaagatgtc actgtcttcc aaagtgtccc tccccctat acctgcagta    780
agcaatatca aatcctgtgc tttccccaaa cttgactctg atgacagcaa tcagaagaca    840
gccaaagctgg cgagcacttt ccatagcaca tcctgcctcc gcaatggcac gttccagaat    900
tcctaaagc cttccaccca aagcagtgcc agtgagctca atgggcatca cactcttggg    960
ctttcagctt tgaacttggg cagtggcaca gagatgccag ccctgacatc ctcccagatg   1020
ccttccctct ctgttttgtc tgtgtgcaca gaggaatcat cacctccaaa tactgggtccc   1080
acggteaccc ctccaatatt ctcaagtgtc caagtgccca acatgccccag ctgtccccag   1140
gcctattctg aactgcagat gctgtcccc agcgagcggc agtgtgtgga gacgggtggtc   1200
aacatgggct actcgtacga gtgtgtcctc agagccatga agaagaaagg agagaatatt   1260
gagcagattc tcgactatct ctttgccat ggacagcttt gtgagaaggg cttcgaccct   1320
cttttagtgg aagaggtctc ggaaatgcac cagtgttcag aagaaaagat gatggagttt   1380
cttcagttaa tgagcaaatt taaggagatg ggctttgagc tgaagacat taaggaagtt   1440
ttgctattac acaacaatga ccaggacaat gctttggaag acctcatggc tcgggcagga   1500
gccagc                                           1506

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<210> SEQ ID NO 49
<211> LENGTH: 555
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 49

Met Arg Val Asn Gly Asp Asp Asp Ser Val Ala Ala Leu Ser Phe Leu
1 5 10 15

-continued

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

-continued

His Phe Ser Ser Leu Gln Arg Ser Gly Gly Ala Ala Pro Ser Ala Gly
 420 425 430

Pro Ser Ser Ser Asn Arg Leu Pro Leu Lys Arg Thr Cys Ser Pro Phe
 435 440 445

Thr Glu Glu Phe Glu Pro Leu Pro Ser Lys Gln Ala Lys Glu Gly Asp
 450 455 460

Leu Gln Arg Val Leu Leu Tyr Val Arg Arg Glu Thr Glu Glu Val Phe
 465 470 475 480

Asp Ala Leu Met Leu Lys Thr Pro Asp Leu Lys Gly Leu Arg Asn Ala
 485 490 495

Ile Ser Glu Lys Tyr Gly Phe Pro Glu Glu Asn Ile Tyr Lys Val Tyr
 500 505 510

Lys Lys Cys Lys Arg Gly Ile Leu Val Asn Met Asp Asn Asn Ile Ile
 515 520 525

Gln His Tyr Ser Asn His Val Ala Phe Leu Leu Asp Met Gly Glu Leu
 530 535 540

Asp Gly Lys Ile Gln Ile Ile Leu Lys Glu Leu
 545 550 555

<210> SEQ ID NO 50
 <211> LENGTH: 1665
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens
 <400> SEQUENCE: 50

```

atgagagtca atggagatga tgacagtgtt gcggccttga gcttcctcta tgattactac      60
atgggtccca aggagaagcg gatattgtcc tocagcactg ggggcaggaa tgaccaagga      120
aagaggtact accatggcat ggaatatgag acggacctca ctcccctga aagccccaca      180
cacctcatga aattcctgac agagaacgtg tctggaacct cagagtacct agatttgctc      240
aagaagaata acctgatgag cttggagggg gccttgccca ccctggcaa ggcagctccc      300
ctccctgcag gccccagcaa gctggaggcc ggctctgtgg acagctacct gttaccacc      360
actgatatgt atgataatgg ctccctcaac tccttgttg agagcattca tggggtgccg      420
cccacacagc gctggcagcc agacagcacc ttcaaagatg acccacagga gtcgatgctc      480
ttcccagata tcctgaaaac ctccccggaa ccccatgtc cagaggacta cccagcctc      540
aaaagtgact ttgaatacac cctgggctcc cccaaagcca tccacatcaa gtcaggcgag      600
tcacctatgg cctacctcaa caaaggccag ttctaccccg tcacctgcg gaccccagca      660
ggtggcaaaag gccttgccct gtcctccaac aaagtcaaga gtgtggtgat ggttgtcttc      720
gacaatgaga aggtcccagt agagcagctg cgcttctgga agcactggca tccccggcaa      780
cccactgcca agcagcgggt cattgacgtg gctgactgca aagaaaactt caaactgtg      840
gagcacattg aggaggtggc ctataatgca ctgtcctttg tgtggaacct gaatgaagag      900
gccaaggtgt tcacggcgt aaactgtctg agcacagact ttcctcaca aaagggggtg      960
aaggggtgtcc ccctgaacct gcagattgac acctatgact gtggcttggg cactgagcgc      1020
ctggtacacc gtgctgtctg ccagatcaag atcttctgtg acaaggggagc tgagaggaag      1080
atgcgcgatg acgagcggaa gcagtcccg aggaaggtca agtgccctga ctccagcaac      1140
agtggcgtca agggctgcct gctgtcgggc ttcaggggca atgagacgac ctaccttcgg      1200
ccagagactg acctggagac gccaccctgt ctgttcatcc ccaatgtgca cttctccagc      1260
    
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-continued

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ctgcagcgcct ctggaggggc agccccctcg gcaggaccca gcagctccaa caggtgcct 1320
ctgaagcgta cctgctcgcc ctcaactgag gagtttgagc ctctgccctc caagcaggcc 1380
aaggaaggcg accttcagag agttctgctg tatgtgcgga gggagactga ggaggtgttt 1440
gacgcgctca tgttgaagac cccagacctg aaggggctga ggaatgcgat ctctgagaag 1500
tatgggttcc ctgaagagaa catttacaaa gtctacaaga aatgcaagcg aggaatctta 1560
gtcaacatgg acaacaacat cattcagcat tacagcaacc acgtcgcctt cctgctggac 1620
atgggggagc tggacggcaa aattcagatc atccttaagg agctg 1665

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<210> SEQ ID NO 51
<211> LENGTH: 418
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 51

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

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-continued

Gln Leu Lys Ile Trp Met Gly Lys Met Gln Lys Lys Ala Val Ala Ile
 290 295 300

Ser Leu Pro Lys Gly Val Val Glu Val Thr His Asp Leu Gln Lys His
 305 310 315 320

Leu Ala Gly Leu Gly Leu Thr Glu Ala Ile Asp Lys Asn Lys Ala Asp
 325 330 335

Leu Ser Arg Met Ser Gly Lys Lys Asp Leu Tyr Leu Ala Ser Val Phe
 340 345 350

His Ala Thr Ala Phe Glu Leu Asp Thr Asp Gly Asn Pro Phe Asp Gln
 355 360 365

Asp Ile Tyr Gly Arg Glu Glu Leu Arg Ser Pro Lys Leu Phe Tyr Ala
 370 375 380

Asp His Pro Phe Ile Phe Leu Val Arg Asp Thr Gln Ser Gly Ser Leu
 385 390 395 400

Leu Phe Ile Gly Arg Leu Val Arg Pro Lys Gly Asp Lys Met Arg Asp
 405 410 415

Glu Leu

<210> SEQ ID NO 52
 <211> LENGTH: 1254
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 52

```

atgcgctccc tctgtcttct cagcgccctc tgcctcctgg aggcggccct ggccgcccag 60
gtgaagaaac ctgcagccgc agcagctcct ggcaactgagg agaagttgag ccccaaggcg 120
gccacgcttg ccgagcgccg cgccggcctg gccttcagct tgtaccaggc catggccaag 180
gaccaggcag tggagaacat cctggtgtca cccgtggtgg tggcctcgtc gctggggctc 240
gtgtcgctgg gcggcaaggc gaccacggcg tcgcaggcca aggcagtgct gagcgccgag 300
cagctgcgcg acgaggaggc gcacgccggc ctggggcagc tgctgcgctc actcagcaac 360
tccacggcgc gcaacgtgac ctggaagctg ggcagccgac tgtacggacc cagctcagtg 420
agcttcgctg atgacttcgt gcgcagcagc aagcagcact acaactgcga gcaactccaag 480
atcaacttcc gcgacaagcg cagcgcgctg cagtccatca acgagtgggc cgcgcagacc 540
accgacggca agctgcccga ggtcaccaag gacgtggagc gcacggacgg cgcctctgta 600
gtcaacgcca tgttcttcaa gccacactgg gatgagaaat tccaccacia gatggtggac 660
aaccgtggct tcatggtgac tcggtcctat accgtgggtg tcatgatgat gcaccggaca 720
ggcctctaca actactacga cgacgagaag gaaaagctgc aaatcgtgga gatgccctg 780
gcccacaage tctccagcct catcctcctc atgccccatc acgtggagcc tctcgagcgc 840
cttgaaaagc tgctaacca agagcagctg aagatctgga tggggaagat gcagaagaag 900
gctgttgcca tctccttgcc caagggtgtg gtggaggtga cccatgacct gcagaaacac 960
ctggctgggc tgggcctgac tgaggccatt gacaagaaca aggccgactt gtcacgcatg 1020
tcaggcaaga aggacctgta cctggccagc gtgttccacg ccaccgcctt tgagttggac 1080
acagatggca acccctttga ccaggacatc tacgggcgcg aggagctgcg cagccccaag 1140
ctgttctacg ccgaccacc cttcatcttc ctagtgcggg acacccaag cggctccctg 1200
ctattcattg ggcgctggt cgggcctaag ggtgacaaga tgcgagacga gttta 1254
    
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<210> SEQ ID NO 53
<211> LENGTH: 636
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 53

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

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-continued

355				360				365							
Arg	Thr	Gln	Thr	Trp	Val	Lys	Ser	Ser	Glu	Tyr	His	Glu	Asn	Lys	Lys
370						375					380				
Ser	Tyr	Gln	Thr	Ser	Val	His	Arg	Val	Arg	Arg	Arg	Ser	His	Ser	Met
385					390					395					400
Met	Lys	Pro	Tyr	Lys	Cys	Asn	Glu	Cys	Gly	Lys	Ser	Phe	Cys	Gln	Lys
				405					410					415	
Gly	His	Leu	Ile	Gln	His	Gln	Arg	Thr	His	Thr	Gly	Glu	Lys	Pro	Phe
			420					425					430		
Glu	Cys	Ser	Glu	Cys	Gly	Lys	Thr	Phe	Ser	Gln	Lys	Ser	His	Leu	Ser
		435					440					445			
Thr	His	Gln	Arg	Ile	His	Thr	Ala	Glu	Lys	Pro	Tyr	Lys	Cys	Asn	Glu
						455					460				
Cys	Gly	Lys	Thr	Phe	Val	Gln	Lys	Ser	Thr	Leu	Arg	Gly	His	Gln	Arg
465					470						475				480
Ile	His	Thr	Gly	Glu	Lys	Pro	Tyr	Glu	Cys	Ser	Glu	Cys	Gly	Lys	Thr
			485						490					495	
Phe	Val	Gln	Lys	Ser	Thr	Leu	Arg	Asp	His	His	Arg	Ile	His	Thr	Gly
			500					505					510		
Glu	Lys	Ser	Phe	Gln	Cys	Asn	Gln	Cys	Gly	Lys	Thr	Phe	Gly	Gln	Lys
		515					520					525			
Ser	Asn	Leu	Arg	Ile	His	Gln	Arg	Thr	His	Thr	Gly	Glu	Lys	Thr	Tyr
		530				535					540				
Gln	Cys	Asn	Glu	Cys	Glu	Lys	Ser	Phe	Trp	Arg	Lys	Asp	His	Leu	Ile
545					550					555					560
Gln	His	Gln	Lys	Thr	His	Thr	Gly	Glu	Lys	Pro	Phe	Lys	Cys	Asn	Glu
			565						570					575	
Cys	Gly	Lys	Thr	Phe	Ala	Arg	Thr	Ser	Thr	Leu	Arg	Val	His	Gln	Arg
			580					585					590		
Ile	His	Thr	Gly	Glu	Lys	Pro	Phe	Lys	Cys	Asn	Glu	Cys	Gly	Lys	Lys
		595				600						605			
Phe	Val	Arg	Lys	Ala	Ile	Leu	Ser	Asp	His	Gln	Arg	Ile	His	Thr	Gly
		610				615					620				
Glu	Lys	Pro	Phe	Gln	Cys	Asn	Lys	Cys	Gly	Lys	Thr				
625					630					635					

<210> SEQ ID NO 54
 <211> LENGTH: 1908
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 54

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gcagaagggtg gttatccttt acggttctcc acactctttc aggagcagca gaaatgaac    120
atatctcagg catcagtgtc attcaaggac gtgactatag aattcaccca ggaggagtgg    180
cagcaaatgg ccctgtttca gaagaatctg tacagagatg tgatgctgga gaactacagc    240
aacctcgtct cagtggggta ctgctgtttc aaaccagagg tgatcttcaa gttggagcaa    300
ggagagggagc cttggttctc agaggaggaa ttctcaaacc agagtcaccc aaaagattac    360
agaggatgatg acctgatcaa gcagaacaag aaaatcaaag acaaactt ggagcaagca    420
atatgtatca ataataaac attgactaca gaggaagaga aagttttggg gaaaccattt    480
    
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actctgcatg tagctgctgt tgcttcaaca aaaatgtcct gcaaatgcaa ctcatgggaa 540
gtgaatttgc aaagtatttc tgaatttadc attaataata gaaactattc aacaaagaaa 600
ataggttgcg gtaatgtatg tgagaattca cctttcaaaa ttaactttga gaaaactcag 660
actggagaga aattttatga acataataaa aacatgaaag ctctcaatta taatgaaaat 720
cttccaagc atccaaagt tcaaactttg gagcaagctt ttgaatgtaa taaaattgga 780
aaagccttta atgataaggc taactgtggt aaacataaca gttctcacac aggagaaaca 840
tcctctaag atgatgaatt taggaaaaat tgtgataaga aaactctctt tgaccacagg 900
agaactggca caggaagaa acacctgcat cttaatcaat gtgggaaatc ctttgagaag 960
tcaactgtgg aggaatataa taaacttaat atgggtataa aacattatga attaaatcca 1020
agtggaaata atttcaacag aaaggcacac ctcaactgac ctcaaacagc tgtcatagaa 1080
gagaacccat tggaagtaa tgacagaaca cagacttggg ttaaatcctc tgaatatcat 1140
gaaaataaga aatcctacca gacgtcgggt cacagagttc gccgaagaag tcaactcaatg 1200
atgaaacct ataaatgtaa tgaatgtggg aaatccttct gtcagaaagg acatctcatt 1260
caacatcaga gaactcacac aggagagaaa ccatttgaat gtagtgaatg tggaaaaact 1320
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tccacctca gagatcatca cagaattcac acaggggaga aatccttca atgcaatcaa 1560
tgtggaaaaa catttggcca gaagtcaaac ctcaagaatac atcagagaac tcacactggg 1620
gagaaaactt accagtgtaa tgaatgtgaa aaatccttct ggcgaaaaga tcatctcatt 1680
caacatcaga aaactcacac gggagagaaa ccattcaaat gtaacgaatg tgggaaaact 1740
tttgccgga catcaacct cagagtgcac caaagaattc aactgggga gaaaccattt 1800
aaatgtaacg aatgtgggaa gaaatttgtc cggaaagcaa tccttagtga tcatcagaga 1860
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<210> SEQ ID NO 55

<211> LENGTH: 375

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 55

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

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100			105			110		
Trp Val Gly	Thr Asn Lys	Ser Leu Thr	Glu Glu Ala	Glu Asn Trp	Gly			
	115		120		125			
Asp Gly Glu	Pro Asn Asn	Lys Lys Asn	Lys Glu Asp	Cys Val Glu	Ile			
	130		135		140			
Tyr Ile Lys	Arg Asn Lys	Asp Ala Gly	Lys Trp Asn	Asp Asp Ala	Cys			
	145		150		155			160
His Lys Leu	Lys Ala Ala	Leu Cys Tyr	Thr Ala Ser	Cys Gln Pro	Trp			
		165		170				175
Ser Cys Ser	Gly His Gly	Glu Cys Val	Glu Ile Ile	Asn Asn Tyr	Thr			
	180			185				190
Cys Asn Cys	Asp Val Gly	Tyr Tyr Gly	Pro Gln Cys	Gln Phe Val	Ile			
	195		200		205			
Gln Cys Glu	Pro Leu Glu	Ala Pro Glu	Leu Gly Thr	Met Asp Cys	Thr			
	210		215		220			
His Pro Leu	Gly Asn Phe	Ser Phe Ser	Ser Ser Gln	Cys Ala Phe	Ser Cys			
	225		230		235			240
Ser Glu Gly	Thr Asn Leu	Thr Gly Ile	Glu Glu Thr	Thr Cys Gly	Pro			
	245		250		255			
Phe Gly Asn	Trp Ser Ser	Pro Glu Pro	Thr Cys Gln	Val Ile Gln	Cys			
	260		265		270			
Glu Pro Leu	Ser Ala Pro	Asp Leu Gly	Ile Met Asn	Cys Ser His	Pro			
	275		280		285			
Leu Ala Ser	Phe Ser Phe	Thr Ser Ala	Cys Thr Phe	Ile Cys Ser	Glu			
	290		295		300			
Gly Thr Glu	Leu Ile Gly	Lys Lys Lys	Thr Ile Cys	Glu Ser Ser	Gly			
	305		310		315			320
Ile Trp Ser	Asn Pro Ser	Pro Ile Cys	Gln Lys Leu	Asp Lys Ser	Phe			
	325		330		335			
Ser Met Ile	Lys Glu Gly	Asp Tyr Asn	Pro Leu Phe	Ile Pro Val	Ala			
	340		345		350			
Val Met Val	Thr Ala Phe	Ser Gly Leu	Ala Phe Ile	Ile Trp Leu	Ala			
	355		360		365			
Arg Arg Leu	Lys Lys Gly	Met						
	370		375					

<210> SEQ ID NO 56

<211> LENGTH: 1125

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 56

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tgtgatttc tggcacatca tggaaaccgac tgctggactt accattattc tgaaaaacc    180
atgaactggc aaaggctag aagattctgc cgagacaatt acacagattt agttgccata    240
caaaacaagg cggaaattga gtatctggag aagactctgc ctttcagtcg ttcttactac    300
tggatagga tccggaagat aggaggaata tggacgtggg tgggaaccaa caaatctctt    360
actgaagaag cagagaactg ggggatggt gagccaaca acaagaagaa caaggaggac    420
tgcgtggaga tctatatcaa gagaaacaaa gatgcaggca aatggaacga tgacgctgac    480

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cacaaactaa aggcagccct ctgttacaca gcttcttgcc agccctggtc atgcagtgge	540
catggagaat gtgtagaaat catcaataat tacacctgea actgtgatgt ggggtactat	600
gggccccagt gtcagtttgt gattcagtggt gagcctttgg aggccccaga gctgggtacc	660
atggactgta ctcacccttt gggaaacttc agcttcagct cacagtggtc cttcagctgc	720
tctgaaggaa caaacttaac tgggattgaa gaaaccacct gtggaccatt tggaaactgg	780
tcattctccag aaccaacctg tcaagtgatt cagtgtgagc ctctatcagc accagatttg	840
gggatcatga actgtagcca tccccggcc agcttcagct ttacctctgc atgtaccttc	900
atctgctcag aaggaactga gttaattggg aagaagaaaa ccatttgtga atcatctgga	960
atctggtcaa atcctagtcc aatatgtcaa aaattggaca aaagtttctc aatgattaag	1020
gagggtgatt ataacccect cttcattcca gtggcagtc tggttactgc attctctggg	1080
ttggcattta tcatttggct ggcaaggaga ttaaaaaag gtatg	1125

1-7. (canceled)

8. A polypeptide probe set comprising:

at least 2 different isolated polypeptides selected from the group consisting of ATP6AP1 (SEQ ID NO: 13), PDCD6IP (SEQ ID NO: 21), DBT (SEQ ID NO: 25), CSNK1E (SEQ ID NO: 9), FRS3 (SEQ ID NO: 3), HOXD1 (SEQ ID NO: 7), SF3A1 (SEQ ID NO: 1), C15orf48 (SEQ ID NO: 35), MYOZ2 (SEQ ID NO: 33), BAT4 (SEQ ID NO: 5), BMX (SEQ ID NO: 45), RAB5A (SEQ ID NO: 23), UBAP1 (SEQ ID NO: 47), GPR157 (SEQ ID NO: 43), ZMYM6 (SEQ ID NO: 41), SLC33A1 (SEQ ID NO: 11), TRIM32 (SEQ ID NO: 37), ALG10 (SEQ ID NO: 27), TFPC2 (SEQ ID NO: 49), SERPINH1 (SEQ ID NO: 51), SELL (SEQ ID NO: 55), ZNF510 (SEQ ID NO: 53), or antigenic fragments thereof; wherein the probe set comprise no more than 100 different polypeptides.

9. The polypeptide probe set of claim 8 wherein the at least 2 different isolated polypeptides comprise ATP6AP1 (SEQ ID NO: 13), or an antigenic fragment thereof.

10. The polypeptide probe set of claim 8, wherein the probe set is present on a support.

11. The polypeptide probe set of claim 8, wherein the probe set is present in solution.

12. The polypeptide probe set of claim 8, wherein the probe set comprise no more than 50 different polypeptides.

13. The polypeptide probe set of claim 8, wherein the probe set comprise no more than 25 different polypeptides.

14. A polynucleotide array comprising:

(a) a support; and

(b) at least 2 different isolated nucleic acids encoding polypeptides selected from the group consisting of ATP6AP1 (SEQ ID NO: 14), PDCD6IP (SEQ ID NO: 22), DBT (SEQ ID NO: 26), CSNK1E (SEQ ID NO: 10), FRS3 (SEQ ID NO: 4), HOXD1 (SEQ ID NO: 8), SF3A1 (SEQ ID NO: 2), C15orf48 (SEQ ID NO: 36), MYOZ2 (SEQ ID NO: 34), BAT4 (SEQ ID NO: 6), BMX (SEQ ID NO: 46), RAB5A (SEQ ID NO: 24), UBAP1 (SEQ ID NO: 48), GPR157 (SEQ ID NO: 44), ZMYM6 (SEQ ID NO: 42), SLC33A1 (SEQ ID NO: 12), TRIM32 (SEQ ID NO: 38), ALG10 (SEQ ID NO: 28), TFPC2 (SEQ ID NO: 50), SERPINH1 (SEQ ID NO: 52), SELL (SEQ ID NO: 56), ZNF510 (SEQ ID NO: 54), or antigenic fragments thereof, attached to the support wherein the array comprise no more than 100 different isolated nucleic acids.

15. The polynucleotide array of claim 14 wherein the at least 2 different isolated nucleic acids encoding ATP6AP1 (SEQ ID NO: 14), or an antigenic fragment thereof.

16. The polynucleotide array of claim 14 wherein the array is a Nucleic Acid Protein Programmable Array.

17. The polynucleotide array of claim 14, wherein the array comprise no more than 50 different isolated nucleic acids.

18. The polynucleotide array of claim 14, wherein the array comprise no more than 25 different isolated nucleic acids

* * * * *