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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.

## 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 immunodiagnostics.

**[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), PDCC6IP (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), RAB5A (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.

**[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), PDCC6IP (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), RAB5A (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), PDCC6IP (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), RAB5A (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), RAB5A (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, 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), TFCEP2 (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  $^{33}\text{P}$ ,  $^{32}\text{P}$ ,  $^{35}\text{S}$ ,  $^3\text{H}$ , and  $^{125}\text{I}$ . 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), RAB5A (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. 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), TFCP2 (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), PDCC6IP (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), MYO22 (SEQ ID NO: 33), EIF3E (SEQ ID NO: 39), BAT4 (SEQ ID NO: 5), ATF3 (SEQ ID NO: 19), BMX (SEQ ID NO: 45), RAB5A (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

**[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), PDCC6IP (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), MYO22 (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 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 polynucleotides 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 NAPPA 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 SPOR 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/](http://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 $\alpha$  and grown in 1.5 mL terrific broth and ampicillin (100  $\mu$ g/mL). DNA was purified with the NucleoPrepII anion exchange resin (Mach-

erey-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 rcf for 30 minutes. The DNA pellet was washed with 200  $\mu$ L of 80% ethanol, centrifuged at 5000 rcf for 15 minutes, dried, and resuspended in dH<sub>2</sub>O. 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  $\mu$ g/ $\mu$ L) was supplemented with capture antibody (50  $\mu$ 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  $\mu$ 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 NAPPA 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. Candidate antigens from the initial 4,988 antigens were selected if they met two different criteria: 1) comparison of the 95<sup>th</sup> percentiles of the cases and controls using quantile regression and 2) comparison of the proportion of cases with intensities above the 95<sup>th</sup> percentile of controls to the expected number seen by chance, with a p-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 rescaled 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.

**[0067]** 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-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	NP_005868	SEQ ID NO: 1	SEQ ID NO: 2
splicing factor 3A subunit 1 isoform 1-full length (1-793)			
FRS3	NP_006644	SEQ ID NO: 3	SEQ ID NO: 4
fibroblast growth factor receptor substrate 3-full length (1-492)			
BAT4	NP_149417	SEQ ID NO: 5	SEQ ID NO: 6
HLA-B associated transcript-4-full length (1-356)			
HOXD1	AAH14477	SEQ ID NO: 7	SEQ ID NO: 8
homeobox protein Hox-D1 full length (1-328)			
C.SNK1E	NP_001885	SEQ ID NO: 9	SEQ ID NO: 10
casein kinase I isoform epsilon full length (1-416)			
SLC33A1	NP_004724	SEQ ID NO: 11	SEQ ID NO: 12
acetyl-coenzyme A transporter 1-full length (1-549)			
ATP6AP1	NP_001174	SEQ ID NO: 13	SEQ ID NO: 14
V-type proton ATPase subunit S1 precursor-full length (1-470)			
RAC3	NP_005043	SEQ ID NO: 15	SEQ ID NO: 16
ras-related C3 botulinum toxin substrate 3 precursor-full length (1-192)			

TABLE 1-continued

Gene Name	Accession number	Amino acid	Nucleotide
BDNF	AAA96140	SEQ ID NO: 17	SEQ ID NO: 18
brain-derived neurotrophic factor transcript variant 5-full length (1-247)			
ATF3	NP_001665	SEQ ID NO: 19	SEQ ID NO: 20
cyclic AMP-dependent transcription factor ATF-3 isoform 1-full length (1-181)			
PDCD6IP	NP_037506	SEQ ID NO: 21	SEQ ID NO: 22
programmed cell death 6-interacting protein isoform 1-full length (1-868)			
RAB5A	NP_004153	SEQ ID NO: 23	SEQ ID NO: 24
ras-related protein Rab-5A-full length (1-215)			
DBT	AAH16675	SEQ ID NO: 25	SEQ ID NO: 26
Dihydroipoamide branched chain transacylase E2-full length (1-482)			
ALG10	NP_116223	SEQ ID NO: 27	SEQ ID NO: 28
alpha-1,2-glucosyltransferase ALG10-A-full length(1-473)			
CTBP1	NP_001319	SEQ ID NO: 29	SEQ ID NO: 30
C-terminal-binding protein 1 isoform 1-full length (1-440)			
SOX2	NP_003097	SEQ ID NO: 31	SEQ ID NO: 32
transcription factor SOX-2-full length (1-317)			
MYOZ2	NP_057683	SEQ ID NO: 33	SEQ ID NO: 34
myozenin-2-full length (1-264)			
C15orf48	NP_115789	SEQ ID NO: 35	SEQ ID NO: 36
normal mucosa of esophagus-specific gene 1 protein-full length (1-83)			
TRIM32	NP_001093149	SEQ ID NO: 37	SEQ ID NO: 38
E3 ubiquitin-protein ligase TRIM32-full length (1-653)			
EIF3E	NP_001559	SEQ ID NO: 39	SEQ ID NO: 40
eukaryotic translation initiation factor 3 subunit E-full length (1-445)			
ZMYM6	AAP35781	SEQ ID NO: 41	SEQ ID NO: 42
zinc finger, MYM-type 6, isoform CRA_b-partial (1-156/163)			
GPR157	EAW71612	SEQ ID NO: 43	SEQ ID NO: 44
probable G-protein coupled receptor 157-partial (1-155/335)			



TABLE 1-continued

Gene Name	Accession number	Amino acid	Nucleotide
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> ),	AAH36890	SEQ ID NO: 49	SEQ ID NO: 50

TABLE 1-continued

Gene Name	Accession number	Amino acid	Nucleotide
isoform CRA_d-full length (1-555)			
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
SELL L-selectin precursor-full length (1-375)	AAH20758	SEQ ID NO: 55	SEQ ID NO: 56

SEQUENCE LISTING

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35 40 45

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

Pro Glu Phe Glu Ala Arg Ile Arg Gln Asn Glu Ile Asn Asn Pro Lys  
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Phe Asn Phe Leu Asn Pro Asn Asp Pro Tyr His Ala Tyr Tyr Arg His  
85 90 95

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Ile Pro Lys Val Met Gln Gln Gln Gln Gln Thr Thr Gln Gln Gln Leu  
115 120 125

Pro Gln Lys Val Gln Ala Gln Val Ile Gln Glu Thr Ile Val Pro Lys  
130 135 140

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165 170 175

Asn Gly Arg Gln Phe Leu Thr Gln Leu Met Gln Lys Glu Gln Arg Asn  
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Tyr Gln Phe Asp Phe Leu Arg Pro Gln His Ser Leu Phe Asn Tyr Phe  
195 200 205

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

Leu Phe Ser Lys Leu Lys Lys Glu Ala Glu Asn Pro Arg Glu Val Leu



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Pro Val Ala Pro Val Pro Ala Pro Ala Pro Met Pro Pro Val His Pro  
 660 665 670

Pro Pro Pro Met Glu Asp Glu Pro Thr Ser Lys Lys Leu Lys Thr Glu  
 675 680 685

Asp Ser Leu Met Pro Glu Glu Phe Leu Arg Arg Asn Lys Gly Pro  
 690 695 700

Val Ser Ile Lys Val Gln Val Pro Asn Met Gln Asp Lys Thr Glu Trp  
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Lys Leu Asn Gly Gln Val Leu Val Phe Thr Leu Pro Leu Thr Asp Gln  
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50          55          60
Tyr Gly Tyr Asp Ser Asn Leu Phe Ser Phe Glu Ser Gly Arg Arg Cys
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gccctcattg ctctgatga gcagtcccac acctatgtca acacaccggc cagtgaagat 600
gaccaccgca ggggcccga ctgctgcag ccctgctctg agggctcagg acccttctc 660
ccgcaggccc ggggacctga ccaacgggac ccacaggtgt tcttgagacc aggccaggtg 720
aagtttgtgt tgggcccgc ccctgctcgg cggcacatgg tgaagtgcca gggcctctgt 780
cccagcctgc atgaccccc acaccacaat aataacaatg agggcccttc tgagtgtcca 840
gcccagccca agtgacccta cgagaacgtc accggggggc tgtggcgagg ggctggctgg 900
agactgagcc cagaggagcc gggctggaat ggccttgccc accgccgggc cgcctgctg 960
cactatgaga acctgcccc actgcccct gtgtgggaaa gccaagccca gcagctggga 1020
ggggagctg gggatgatgg ggaactcaggg gatgggtca caccctcttc caatggcttc 1080
cctgatggtg agggaggcga gacccactg cagaagccca ccagcaccgg gccgcccac 1140
cgcagccacg gcagctttcc tgtgccactg acccgcccgc gcggctcccc aagggtcttc 1200
aactttgatt tccgccggcc ggggcccag cccccaaggc agcttaacta catccagggtg 1260
gagctaaagg gctgggggtg agaccgccct aaggggcccc agaaccctc gagcccccaa 1320
gccccatgc ccaccacca ccctgccga agctcagact cctacgccgt gattgacctc 1380
aaaaagaccg tggccatgct caacctgcag agagctctgc cccgagacga tggcaccgcc 1440
aggaaaaacc ggcacaacag caccgacctg cctctg 1476

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<210> SEQ ID NO 5
<211> LENGTH: 356
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

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<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

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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  
 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  
 225 230 235 240  
 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  
 305 310 315 320  
 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 ccttgctcat caccttcacc ccagccactg accccagcga cctctggaag 60  
 gatgggcagc agcagccaca gcccgagaag ccagagtcca ccttggatgg ggctgcagcc 120  
 cgagctttct atgaggccct gattggggat gagagcagcg ctcctgactc ccagagatct 180  
 cagactgaac ctgccagaga aagaaagaga aagaaaagaa gaataatgaa ggcaccagca 240  
 gcagaagcag tggcagaagg agcatcagga agacatggac aagggagatc ccttgaggct 300  
 gaggataaga tgactcaccg gatactgagg gcagcccagg agggggacct gccagaactt 360  
 aggagactgc tggaaccgca tgaggcagga ggagctgggg ggaatatcaa cgcccgggat 420  
 gccttctggt ggaccccact gatgtgtgct gctcgagcgg gccagggggc agctgtgagc 480  
 tatctcctgg gccgtggggc tgccctgggtg ggggtctgtg agctgagtgg cagggatgag 540  
 gctcagctcg ctgaagaagc tggttcctct gaggtagccc gcatggtcag ggagagccat 600  
 ggagagacaa ggagcccgga aaaccggtct cctactecct cectccagta ctgccgagaac 660  
 tgtgacaccc acttccaaga ttccaaccac cgcacatcca ctgctcactc gctgtcactg 720

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tcgcagggtc ctcagcctcc caaccttcca cttgggggtgc ccatctccag cccgggcttc 780
aaactgctgc tgaggggggg ctgggagcca ggaatggggc tgggaccccg gggtaggggc 840
cgtgccaatc ccatccccac tgtcctcaag agggaccagg aaggactagg ctacagatca 900
gcaccccagc cccgagtgc acatttocca gcttgggata cccgagctgt ggctgggagg 960
gagagacccc ctccgggtgc cacactgagc tggagggagg agagaaggag ggaggagaaa 1020
gacagggctt gggagcggga tctaaggact tacatgaacc tcgagttc 1068

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&lt;210&gt; SEQ ID NO 7

&lt;211&gt; LENGTH: 328

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Homo sapiens

&lt;400&gt; 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

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Pro Leu Ser Gly Thr Thr Pro Thr Lys Phe Ile Lys Asn Pro Gly Ser  
 305 310 315 320  
 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  
 ctgagcttgg caccaagtt ctgccctcc gacgccggc cegtggctct gcagcccgcc 120  
 ttccctctgg gcaacggcga cggcgccttc gtcagctgtc tgcccttggc cggcccccga 180  
 ccctgcctt cccccccggc cccccccggc cggccgtccg tacgcctcc ggccgcgccc 240  
 cagtacgcgc agtgcacct ggaggggggc tacgaacctg gtgccgcacc tgccgcggca 300  
 gctggggggc cgaactacgg ctctctgggg tccggggcgg cgtacgactt cccgggctgt 360  
 ctggggcggg cggccgacga cggcgggtct cacgtccact acgccacctt ggccgtcttc 420  
 tcggggcggc gctctttctt cctcagcggc caggtggatt acgcccctt cggcgaacct 480  
 ggcccttttt cggtttgtct caaagcgtca gccgacggcc accctggtgc tttccagacc 540  
 gcacccccgg cccagggcac ctaccccaag tccgtctctc ccgcctccgg cctccctgcc 600  
 gccttcagca cgttcgagtg gatgaaagt aagaggaatg cctctaagaa aggcaaaact 660  
 gccgagtatg gggccgctag ccctccagc gccatccgca cgaatttcag caccaagcaa 720  
 ctgacagaac tggaaaaaga gtttcatttc aataagtact taactcgagc ccggcgcctc 780  
 gagatagcca actgcttga cctgaatgac acgcaagtca aaatctggtt ccagaaccgc 840  
 aggatgaaac agaagaaaag ggaacgagaa gggcttctgg ccacggccat tctgtggct 900  
 cccctccaac tccccctctc tggaacaacc cccactaagt ttatcaagaa ccccggcagc 960  
 cttctcagt cccaagagcc ttcg 984

<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

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Ile Ser Arg Ile Glu Tyr Ile His Ser Lys Asn Phe Ile His Arg Asp  
 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 gtgtgggaa caagtaccgc ctgggacgga agatcgggag cgggtccttc 60  
 ggagatatct acctgggtgc caacatcgcc tctggtgagg aagtcgcat caagctggag 120  
 tgtgtgaaga caaagcacc ccagctgcac atcgagagca agttctaaa gatgatgcag 180  
 ggtggcgtgg ggateccgtc catcaagtgg tgcggagctg agggcgacta caacgtgatg 240  
 gtcatggagc tgctggggcc tagcctcgag gacctgttca acttctgttc ccgcaaatc 300  
 agcctcaaga cgggtgtgct cttggccgac cagatgatca gccgcatcga gtatatccac 360

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tccaagaact tcattccaccg ggacgtcaag cccgacaact tctcatggg gctggggaag 420
aagggcaacc tgggtacat catcgacttc ggcctggcca agaagtaccg ggacgcccgc 480
accaccagc acattcccta ccgggaaaac aagaacctga ccggcacggc ccgctacgct 540
tccatcaaca cgcacctggg cattgagcaa agccgtcgag atgacctgga gagcctgggc 600
tacgtgtca tgtaactcaa cctgggctcc ctgccctggc aggggctcaa agcagccacc 660
aagcgcaga agtatgaacg gatcagcgag aagaagatgt caacgcccac cgaggtcctc 720
tgcaaaggct atccctccga attctcaaca tacctcaact tctgccctc cctgcggttt 780
gacgacaagc ccgactactc ttacctacgt cagctcttcc gcaacctctt ccaccggcag 840
ggcttctcct atgactacgt ctttgactgg aacatgctga aattcggtgc agcccggaat 900
cccgaggatg tggaccggga gcggcgagaa cacgaacgcg aggagaggat ggggcagcta 960
cgggggtccg cgaccggagc cctgccccct ggcccacca cggggggcac tgccaaccgg 1020
ctccgcagtg ccgccgagcc cgtggcttcc acgccagcct cccgcaccca gccggctggc 1080
aatactctc ccagagcgat ctgcggggtc gaccgggaga ggaaggtgag tatgaggctg 1140
cacaggggtg cccccccaa cgtctctccc tcagacctca ctggggcgga agaggtctcc 1200
cggatcccag cctcacagac aagtgtgcca tttgaccatc tcgggaag 1248

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&lt;210&gt; SEQ ID NO 11

&lt;211&gt; LENGTH: 549

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Homo sapiens

&lt;400&gt; SEQUENCE: 11

```

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

atgtcacccca ccattctccca caaggacagc agccggcaac ggcggccagg gaatttcagt 60

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cactctctgg atatgaagag cggccccctg ccgccaggcg gttgggatga cagtcatttg 120
gactcagcgg gccgggaagg ggacagagaa gctcttctgg gggataccgg cactggcgac 180
ttcttaaaag cccacagag cttccgggccc gaactaagca gcattttgct actactcttt 240
ctttacgtgc ttcagggtat tcccctgggc ttggcgggaa gcateccact cattttgcaa 300
agcaaaaatg ttagctatac agaccaagct ttcttcagtt ttgtcttttg gcccttcagt 360
ctcaaattac tctgggcccc gttggttgat gcggtctacg ttaagaactt cggctcgtcgc 420
aaatcttggc ttgtcccgac acagtatata ctaggactct tcatgatcta tttatccact 480
cagggtggacc gtttgcttgg gaataccgat gacagaacac ccgacgtgat tgctctcact 540
gtggcgttct ttttgtttga attcttggcc gccactcagg acattgccgt cgatggttgg 600
gcgttaacta tgttatccag ggaaaatgtg ggttatgctt ctacttgcaa ttcggtgggc 660
caaacagcgg gttacttttt gggcaatggt ttgtttttgg cccctgaate tgccgacttt 720
tgtaacaaat atttcggggt tcagcctcaa cccagaggaa tcgtaactct ttcagatttc 780
ctttttttct ggggaactgt attttaata acaacaacat tgggtgcctt tctgaaaaaa 840
gaaaacgaag tadcagtagt aaaagaagaa acacaaggga tcacagatac ttacaagctg 900
ctttttgcaa ttataaaaat gccagcagtt ctgacatttt gcctctctgat tctaactgca 960
aagattgggt tttcagcagc agatgctgta acaggactga aattggtaga agagggagta 1020
cccaaagaac atttagcctt attggcagtt ccaatggttc ctttgcatag aatactgcct 1080
ctgattatca gcaaatcac tgcaggctcc cagccattaa acacatttta caaagccatg 1140
ccctacagat tattgcttgg gttagaatat gccctactgg tttggtggac tcctaaagta 1200
gaacatcaag ggggattccc tatatattac tatatcgtag tctgctgag ttatgcttta 1260
catcaggtta cagtgtacag catgtatggt tctataatgg ctttcaatgc aaaggttagt 1320
gatccactta ttggaggaac atacatgacc cttttaaata ccgtgtccaa tctgggagga 1380
aactggcctt ctacagtagc tctttggcct gtagatcccc tcacagtaaa agagtgtgta 1440
ggagcatcaa accagaattg tcgaacacct gatgctgttg agctttgcaa aaaactgggt 1500
ggctcatgtg ttacagcctt ggatggttat tatgtggagt ccattatttg tgttttcatt 1560
ggatttgggt ggtggttctt tcttggcca aaatttaaaa agttacagga tgaaggatca 1620
tcttcgtgga aatgcaaaa gaaacaat 1647

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&lt;210&gt; SEQ ID NO 13

&lt;211&gt; LENGTH: 470

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Homo sapiens

&lt;400&gt; SEQUENCE: 13

```

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 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
65          70          75          80

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Ala	Leu	Glu	Leu	Gly	Pro	Arg	Asn	Val	Leu	Leu	Phe	Leu	Gln	Asp	Lys
				85					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
					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
						215					220				
Arg	Pro	Ser	Arg	Val	Ala	Arg	Asp	Val	Ala	Val	Val	Ala	Gly	Gly	Leu
					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
						295					300				
Ser	Phe	Ala	Arg	Leu	Ser	Leu	Thr	Tyr	Glu	Arg	Leu	Phe	Gly	Thr	Thr
					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
						360						365			
Phe	His	Cys	Glu	Tyr	Val	Ser	Ser	Leu	Ser	Lys	Lys	Gly	Ser	Leu	Leu
						375						380			
Val	Ala	Arg	Thr	Gln	Pro	Ser	Pro	Trp	Gln	Met	Met	Leu	Gln	Asp	Phe
					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										
					470										

&lt;210&gt; SEQ ID NO 14

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<211> LENGTH: 1410
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 14
atgatggcgg ccatggcgac ggctcgagtg cggatggggc cgcggtgcgc ccaggcgctc    60
tggcgcgatgc cgtggctgcc ggtgtttttg tcgttggcgg cggcggcggc ggcggcagcg    120
gcbgagcagc aggtcccctt ggtgctgtgg tcgagtgacc gggacttctg ggctcctgcg    180
gccgacactc atgaaggcca catcaccagc gacttgcagc tctctaccta cttagatccc    240
gccctggagc tgggtcccag gaatgtgctg ctgttcctgc aggacaagct gagcattgag    300
gatttcacag catatggcgg tgtgtttgga aacaagcagg acagcgcctt ttctaaccta    360
gagaatgccc tggacctggc cccctcctca ctggtgcttc ctgcccgcga ctggtatgca    420
gtcagcactc tgaccactta cctgcaggag aagctcgggg ccagcccctt gcatgtggac    480
ctggccaccc tgcgggagct gaagctcaat gccagcctcc ctgctctgct gctcattcgc    540
ctgccctaca cagccagctc tggctgtgat gcacccaggg aagtctctac aggcaacgat    600
gaggtcatcg ggcaggctct gagcacactc aagtccgaag atgtcccata cacagcggcc    660
ctcacagcgg tcgcccttc caggggtggcc cgtgatgtag ccgtggtggc cggaggggcta    720
ggtcgccagc tgctacaaaa acagccagta tcacctgtga tccatctccc tgtgagttac    780
aatgacaccg ctccccgat cctgttctgg gcccaaaact tctctgtggc gtacaaggac    840
cagtgggagg acctgactcc cctcactttt ggggtgcagg aactcaacct gactggctcc    900
ttctggaatg actcctttgc caggctctca ctgacctatg aacgactctt tggtagccaca    960
gtgacattca agttcattct ggccaaccgc ctctaccagc tgtctgcccg gcaactggtt    1020
accatggagc gcctcgaagt ccacagcaat ggctccgtcg cctacttcaa tgcttcccag    1080
gtcacagggc ccagcatcta ctcttccac tgcgagtatg tcagcagcct gagcaagaag    1140
ggtagtctcc tcgtggcccg cagcagccc cctccctggc agatgatgct tcaggacttc    1200
cagatccagg ctttcaacgt aatggggggag cagttctcct acgccagcga ctgtgccagc    1260
ttcttctccc ccggcatctg gatggggctg ctcacctccc tgttcatgct ctctcatctc    1320
acctatggcc tgcacatgat cctcagcctc aagaccatgg atcgctttga 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

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

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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 gactacatcc ccaccgtttt tgacaactac 120  
 tctgccaacg tgatggtgga cgggaaacca gtcaacttgg ggctgtggga cacagcgggt 180  
 caggaggact acgatcggct gcggccactc tcctaccccc aaactgacgt ctttctgatc 240  
 tgcttctctc tggtagagccc ggcctccttc gagaatgttc gtgccaagtg gtaccggag 300  
 gtgcggcacc actgccccca cacgcccac ctcctggtgg gcaccaagct ggacctccgc 360  
 gacgacaagg acaccattga gcggtgcgg gacaagaagc tggcaccat cacctacca 420  
 cagggcctgg ccatggcccg ggagattggc tctgtgaaat acctggagtg ctcagccctg 480  
 acccagcggg gcctgaagac agtgtttgac gaggcgatcc gcgcggtgct ctgccgccc 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

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



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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

atgacatcc ttttcttac tatggttatt tcatactttg gttgcatgaa ggctgcccc 60  
 atgaaagaag caaacatccg aggacaaggt ggcttggcct acccaggtgt gcggaccat 120  
 gggactctgg agagcgtgaa tgggccaag gcaggttcaa gagccttgac atcattggct 180  
 gacactttcg aacacatgat agaagagctg ttggatgagg accagaaagt tcggccaat 240  
 gaagaaaaca ataaggagc agacttgac acgtccaggg tgatgctcag tagtcaagt 300  
 cctttggagc ctctcttct ttttctgctg gaggaatata aaaattacct agacgctgca 360  
 aacatgtcca tgagggtccg gcgccactct gacctgccc gccgagggga gctgagcgtg 420  
 tgtgacagta ttagtgagtg ggtaacggcg gcagacaaaa agactgcagt ggacatgctg 480  
 ggcgggacgg tcacagtct tgaagggtc cctgtatcaa aaggccaact gaagcaatac 540  
 ttctacgaga ccaagtgcaa tcccatgggt tacacaaaag aaggctgcag gggcatagac 600  
 aaaaggcatt ggaactccca gtgccgaact acccagtcgt acgtgctggc cttaccatg 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  
 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

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	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					80				
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				
					150						155				160				
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

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atgatgcttc aacacccagg ccaggtctct gcctcggaag tgagtgttc tgccatcgtc    60
cctgacctgt cccctcctgg gtcactggtg tttgaggatt ttgctaacct gaagcccttt    120
gtcaaggaag agctgaggtt tgccatccag aacaagcacc tctgccaccg gatgtcctct    180
gcgctggaat cagtcactgt cagcgacaga cccctcgggg tgtccatcac aaaagccgag    240
gtagcccttg aagaagatga aaggaaaaag aggcgacgag aaagaaataa gattgcagct    300
gcaaaagtgc gaaacaagaa gaaggagaag acggagtgcc tgcagaagaa gtcggagaag    360
ctggaagtgt tgaatgctga actgaaggct cagattgagg agctcaagaa cgagaagcag    420
catttgatat acatgctcaa ccttcacggg 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				
			5						10					15					
Leu	Ala	Lys	Pro	Leu	Val	Lys	Phe	Ile	Gln	Gln	Thr	Tyr	Pro	Ser	Gly				
			20					25						30					
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								

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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  
 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

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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  
 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

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<210> SEQ ID NO 22

<211> LENGTH: 2604

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 22

atggcgacat tcactcgggt gcagctgaaa aagacctcag aggtggacct ggccaagccg 60  
ctggtgaagt tcattccagca gacttaccga agcggcgggg aagagcaggc ccagtactgc 120  
cgcgcggggg aggagctcag caagctgcgc cgcgccgcag tcggtcgtcc gctggacaag 180  
cacgagggcg cgctcgagac gctcctgaga tattatgac agattgttc tattgaacct 240  
aaattcccat tttctgaaaa tcagatctgc ttgacattta cctggaagga tgctttcgat 300  
aaaggttcac tttttggagg ctctgtaaaa ctggctcttg caagcttagg atatgaaaag 360  
agctgtgtgt tgttcaattg tgcagcctta gctagccaaa ttgcagcaga acagaacctg 420  
gataatgatg aaggattgaa aatcgctgct aaacattacc agtttgctag tgggtccttt 480  
ttacatatta aagagacggt tttatctgcc ttaagtcgag agccgacctg ggacatatct 540  
ccagatactg ttgggacctc cagtcttatt atgctggcac aggctcaaga agtatttttt 600  
ttaaagcca caagagataa aatgaaagat gccatcatag ctaaattggc taatcaggct 660  
gcagattatt ttggtgatgc ttcaaacag tgcataaca aagatactct cccaaggag 720  
gtgttccctg tcttggctgc aaagcactgt atcatgcagg ccaatgctga gtaccatcag 780  
tctatcctgg caaacacgca gaagaaattt ggagaagaaa ttgcaaggtt acagcatgca 840  
gcagaactga ttaaaacagt ggcactctgc tatgatgaat atgttaatgt gaaggathtt 900  
tctgacaaaa tcaatcgtgc ccttgctgca gcaagaagg ataatgactt catttatcat 960  
gatcgagttc cagaccttaa agatctagat cctattggca aagccacctt tgtgaaatct 1020  
accccggtca atgtacctc cagtcagaaa tttactgatc tgtttgagaa gatggttccc 1080  
gtgtcagtac agcagctctt ggctgctat aatcagagga aagccgattt ggttaacaga 1140  
tcaattgctc agatgagaga agccaccact ttggcaaatg ggggtgctagc ttccctaat 1200  
cttcacgag caattgaaga tgtgtctgga gacactgtac ctcagtttat attgactaaa 1260  
tcagatctg tgattgaaca gggaggcctc cagactgttg atcagttgat taaagaactg 1320  
cctgaattac tgcaacgaaa tagagaaatc ctatagtagt cattaaggtt gttggatgaa 1380  
gaagaagcaa ccgataatga ttaagagca aaatttaag aacgttggca aaggacacca 1440  
tccaatgaac tgtataagcc ttaagagca gagggaacca acttcagaac agtttttagat 1500  
aaagctgtgc aggcagatgg acaagtgaaa gaatgttacc agtctcatcg tgacaccatc 1560  
gtgcttttgt gtaagccaga gcctgagctg aatgctgcca tccctctgce taatccagca 1620  
aagaccatgc agggcagtg ggttgtaaat gtcttaaaat ccttattgtc aaatcttgat 1680  
gaagtaaaga aggaaagaga gggctctggag aatgacttga aatctgtgaa ttttgacatg 1740  
acaagcaagt ttttgacagc cctggctcaa gatgggtgta taaatgaaga agctctttct 1800  
gttactgaac tagatcgagt ctatggaggt cttacaacta aagccaaga atctctaag 1860  
aaacaggagg gacttcttaa aaatattcag gtctcacatc aggaattttc aaaaatgaaa 1920  
caatctaata atgaagctaa cttaagagaa gaagttttga agaatttagc tactgcatat 1980  
gacaactttg ttgaaactgt agctaatttg aaggaaggca caaagtttta caatgagttg 2040  
actgaaatcc tggtcagggt ccagaacaaa tgcagtgata tagtttttgc acggaagaca 2100

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gaaagagatg aactcttaaa ggacttgcaa caaagcattg ccagagaacc tagtgctcct 2160
tcaattccta cacctgcgta tcagtcctca ccagcaggag gacatgcacc aactcctcca 2220
actccagcgc caagaacctat gccgcctact aagccccagc cccagccag gcctccacca 2280
cctgtgcttc cagcaaatcg agctccttct gctactgctc catctccagt gggggctggg 2340
actgctgcgc cagctccatc acaaacgcct ggctcagctc ctctccaca ggcgcaggga 2400
ccaccctatc ccacctatcc aggatatcct gggtattgcc aaatgcccc gcccatgggc 2460
tataatcctt atgcgatgg ccagtataat atgcatatc caccagtgtg tcaccagagt 2520
cctggacagg ctccataccc gggaccccag cagccttcat accccttccc tcagcccca 2580
cagcagtctt actatccaca gcag 2604

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<210> SEQ ID NO 23
<211> LENGTH: 215
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 23

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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
210         215

```

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

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<400> SEQUENCE: 24

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```

atggctagtc gaggcgcaac aagacccaac gggccaataa ctggaaataa aatatgccag 60

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ttcaaactag tacttctggg agagtccgct gttggcaaat caagcctagt gcttcgtttt 120
gtgaaaggcc aatttcacga atttcaagag agtaccattg gggctgcttt tctaaccctaa 180
actgtatgtc ttgatgacac tacagtaaag tttgaaatat gggatacagc tggtaacagaa 240
cgataccata gcttagcacc aatgtactac agaggagcac aagcagccat agttgtatat 300
gatatcacia atgaggagtc ctttgcaaga gcaaaaaatt gggttaaaga acttcagagg 360
caagcaagtc ctaacattgt aatagcttta tcgggaaaca aggccagcct agcaataaaa 420
agagcagtag atttccagga agcacagtcc tatgcagatg acaatagttt attattcatg 480
gagacatccg ctaaaacatc aatgaatgta aatgaaatat tcatggcaat agctaaaaaa 540
ttgcaaaaga atgaaccaca aaatccagga gcaaatctcg ccagaggaag aggagtagac 600
cttaccgaac ccacacaacc aaccaggaat cagtgttgta gtaac 645

```

&lt;210&gt; SEQ ID NO 25

&lt;211&gt; LENGTH: 492

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Homo sapiens

&lt;400&gt; 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
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

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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

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 gatttggtt    60
cgctattttc aaacatgtgg taatgttcat gtttgaagc caaattatgt gtgtttcttt    120
ggttatcctt 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
ctctattata atctagacga tattgcctat gtggggaagc cattagtaga catagaaacg    420
gaagctttaa aagattcaga agaagatggt gttgaaactc ctgcagtgtc tcatgatgaa    480
catacacacc aagagataaa gggccgaaaa aacttgcaa ctctctcagt tcgccgtctg    540
gcaatggaaa acaatattaa gctgagtgaa gttgttggtc caggaaga tggcagaata    600
cttaaagaag atactctcaa ctatttgtaa aagcagacag gagctatatt gcctccttca    660
cccaaagttg aaattatgcc acctccacca aagccaaaag acatgactgt tcctatacta    720
gtatcaaaac ctccggtatt cacaggcaaa gacaaaacag aaccataaaa aggcctttcaa    780
    
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aaagcaatgg tcaagactat gtctgcagcc ctgaagatac ctcattttgg ttattgtgat      840
gagattgacc ttaactgaact ggtaagctc cgagaagaat taaaacccat tgcatttgct      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 tgaaccgcct ccagaattg     1140
ggctctgtgg gtcagctcag caccactgat cttacaggag gaacatttac tctttccaac     1200
attggatcaa ttggtgttac ctttgccaaa ccagtgataa tgccacctga agtagccatt     1260
ggggcccttg gatcaattaa ggccattccc cgatttaacc agaaaggaga agtatataag     1320
gcacagataa tgaatgtgag ctggtcagct gatcacagag ttattgatgg tgctacaatg     1380
tcacgcttct ccaatttggg gaaatcctat ttagaaaacc cagcttttat gctactagat     1440
ctgaaa                                           1446

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&lt;210&gt; SEQ ID NO 27

&lt;211&gt; LENGTH: 473

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Homo sapiens

&lt;400&gt; 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
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

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Ser Met Ser Phe Lys Asn Leu Ser Met Leu 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

&lt;210&gt; SEQ ID NO 28

&lt;211&gt; LENGTH: 1419

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Homo sapiens

&lt;400&gt; SEQUENCE: 28

```

atggcgcagc tggaagggtta ctatttctcg gccgccttga gctgtacctt ttagtatccc    60
tgcctcctct tctccgcctt cagccggggc ttgcgagagc cctacatgga cgagatcttc    120
cacctgcctc aggcgcagcg ctactgtgag ggccatttct ccttttccca gtgggatccc    180
atgattacta cattacctgg cttgtacctg gtgtcaattg gagtgatcaa acctgccatt    240
tggatctttg gatggtctga acatgttgtc tgctccattg ggatgctcag atttgttaat    300
cttctcttca gtgttggcaa cttctattta ctatatttgc ttttctgcaa ggtacaaccc    360
agaaaacaagg ctgcctcaag tatocagaga gtcttgtcaa cattaacact agcagtattt    420
ccaacacttt atttttttaa cttcctttat tatacagaag caggatctat gttttttact    480
ctttttgogt atttgatgtg tctttatgga aatcataaaa cttcagcctt ccttggattt    540
tgtggcttca tgtttcgcca aacaaatata atctgggctg tcttctgtgc aggaaatgtc    600
attgcacaaa agttaaaccgga ggcttggaaa actgagctac aaaagaagga agacagactt    660
ccacctatta aaggaccatt tgcagaattc agaaaaattc ttcagtttct tttggcttat    720

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tccatgtcct ttaaaaactt gagtatgctt ttgcttctga cttggccta catccttctg 780
ggatttctgt tttgtgcttt ttagtagtatt aatgggtggaa ttgttattgg cgateggagt 840
agtcataaag cctgtcttca ttttctctca ctattctact ttttttctatt tactctcttt 900
ttttctcttc ctcctctcct gtctcctagc aaaattaaga cttttctcttc cttagtttgg 960
aaacgtagaa ttctgttttt tgtggttacc ttagtctctg tgttttttag ttggaaattc 1020
acttatgctc ataaatactt gctagcagac aatagacatt atactttcta tgtgtggaaa 1080
agagtttttc aaagatatga aactgtaaaa tattgttttag ttccagccta tatatttgct 1140
ggttggagta tagctgactc attgaaatca aagtcaattt ttggaattt aatgtttttc 1200
atagcttctg tcaactgtat agttcctcag aaactgctgg aatttcgtta ctccatttta 1260
ccttatgtca tttataggtt taacatacct ctgctctcca catccagact catttgtaga 1320
ctgagctgct atgcagttgt taatttcata acttttttca tctttctgaa caagactttt 1380
cagtggccaa atagtcagga cattcaaagg tttatgtgg 1419

```

&lt;210&gt; SEQ ID NO 29

&lt;211&gt; LENGTH: 440

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Homo sapiens

&lt;400&gt; 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
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       240

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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  
 305 310 315 320  
 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  
 385 390 395 400  
 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 cgcaacttgct caacaagggc ctgccgcttg gcgtccgacc tccgatcatg 60  
 aacgggcccc tgcaccccgcg gcccttggtg gcattgctgg atggcgggga ctgcacagtg 120  
 gagatgccca tectgaagga cgtggccact gtggccttct gcgacgcgca gtccacgcag 180  
 gagatccatg agaaggtcct gaacgaggct gtgggggccc tgatgtacca caccatcact 240  
 ctaccagggg aggacctgga gaagttcaaa gccctccgca tcatcgctcg gattggcagt 300  
 ggttttgaca acatcgacat caagtcggcc ggggatttag gcattgccgt ctgcaacgtg 360  
 cccgcggcgt ctgtggagga gacggccgac tcgacgctgt gccacatcct gaacctgtac 420  
 cggcgggcca cctggtgca ccaggcgtg cgggagggca cagcagtgca gacgctcgag 480  
 cagatccgcg aggtggcgtc cggcgctgcc aggatccgcg gggagacctt gggcatcatc 540  
 ggacttggtc gcgtggggca ggcagtgggc ctgcggggcca aggccttcgg cttcaacgtg 600  
 ctcttctacg acccttactt gtcggatggc gtggagcggg cgctggggct gcagcgtgtc 660  
 agcaccctgc aggacctgct cttccacagc gactgcgtga cctgcaactg cggcctcaac 720  
 gagcacaacc accacctcat caacgacttc accgtcaagc agatgagaca aggggccttc 780  
 ctggtgaaca cagcccgggg tggcctggtg gatgagaagg cgctgggcca ggcctgaag 840  
 gagggcggga tccgcggcgc ggcctggat gtgcacgagt cggaaacctt cagctttagc 900

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cagggccctc tgaaggatgc acccaacctc atctgcaccc cccatgctgc atggtacagc    960
gagcagcgc atccatgagat gcgagaggag gcggcacggg agatccgcag agccatcaca    1020
ggccggatcc cagacagcct gaagaactgt gtcaacaagg accatctgac agccgccacc    1080
cactgggcca gcatggaccc cgccgtogtg caccttgagc tcaatggggc tgctatagg    1140
tacctccgg gcgtggtggg cgtggccccc actggcatcc cagctgctgt ggaaggtatc    1200
gtccccagcg ccatgtccct gtcccacggc ctgccccctg tggccccacc gccccacgcc    1260
ccttctctct gccaaccctg caagcccagc gcggatagag accacgccag tgaccagtgt    1320

```

&lt;210&gt; SEQ ID NO 31

&lt;211&gt; LENGTH: 317

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Homo sapiens

&lt;400&gt; 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
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

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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 ccgccgggcc cgcagcaaac ttcggggggc 60
ggcggcgcca actccaccgc ggcggcggcc ggcggcaacc agaaaaacac cccggaccgc 120
gtcaagcggc ccatgaatgc ctccatggtg tggccccgcg ggcagcggcg caagatggcc 180
caggagaacc ccaagatgca caactcggag atcagcaagc gcctggggcg cgagtggaaa 240
cttttgtcgg agacggagaa gcggccgctc atcgacgagg ctaagcggct gcgagcgtg 300
cacatgaagg agcaccgcga ttataaatac cggccccggc ggaaaaacca gacgctcatg 360
aagaagata agtacacgct gcccgcgggg ctgctggccc ccggcggcaa tagcatggcg 420
agcggggtcg ggttggggcg 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 ctgcgacgag ggcaccctcg gcatggctct tggtcccatg 720
ggttcggtgg tcaagtccga ggccagctcc agccccctg tggttacctc ttctcccac 780
tccagggcgc cctgccaggc cggggacctc cgggacatga tcagcatgta tctccccggc 840
gccgaggtgc cggaaaccgc cggccccagc agacttcaca tgtcccagca ctaccagagc 900
ggccccgtgc ccggcagcgc 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
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
    
```

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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 ataatactat gatgaagcag agaaaacagc aagcaacagc catcatgaag 60  
 gaagtccatg gaaatgatgt tgatggcatg gacctgggca aaaaggtcag catccccaga 120  
 gacatcatgt tggaagaatt atcccatctc agtaaccgtg gtgccaggct atttaagatg 180  
 cgtcaaagaa gatctgacaa atacacattt gaaaatttcc agtatcaatc tagagcacia 240  
 ataaatcaca gtattgctat gcagaatggg aaagtggatg gaagtaactt ggaaggtggt 300  
 tcgcagcaag cccccttgac tctcccac accccagatc cacgaagccc tccaaatcca 360  
 gacaacattg ctccaggata ttctggacca ctgaaggaaa ttcctcctga aaaattcaac 420  
 accacagctg tcctaagta ctatcaatct ccctgggaac aagccattag caatgatccg 480  
 gagcttttag aggtttata tcctaaactt ttcaagcctg aaggaaggc agaactgcct 540  
 gattacagga gctttaacag ggttgccaca ccatttgag gttttgaaa agcatcaaga 600  
 atggttaaat ttaaagtcc agattttgag ctactattgc taacagatcc caggtttatg 660  
 tcctttgtca atccccttc 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

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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 ttcccttggt ggtgttcattg 60  
 actgtggcgg cgggtggagc ctcatcttcc gctgtgtatt ctctttggaa aaccgatgtg 120  
 atccttgatc gaaaaaaaaa tccagaacct tgggaaactg tggaccctac tgtacctcaa 180  
 aagcttataa caatcaacca acaatggaaa cccattgaag agttgcaaaa tgtccaaagg 240  
 gtgaccaaaa 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  
 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



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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
			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



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 ggcatagccc taactcctaa ggggcagctg ctggtcttgg actgttggga tcattgcac 1920

aagatctaca gctaccatct gagaagatat tccacccca 1959

&lt;210&gt; SEQ ID NO 39

&lt;211&gt; LENGTH: 445

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Homo sapiens

&lt;400&gt; 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

 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

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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

&lt;210&gt; SEQ ID NO 40

&lt;211&gt; LENGTH: 1335

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Homo sapiens

&lt;400&gt; SEQUENCE: 40

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atggcggagt acgacttgac tactcgcatc ggcactttt tggatcgga tctagtcttt    60
ccgcttcttg aattctctc tgtaaaggag atatataatg aaaaggaatt attacaaggt    120
aaattggacc ttcttagtga taccacatg gtagactttg ctatggatgt atacaaaaac    180
ctttattctg atgatattcc tcatgctttg agagagaaaa gaaccacagt ggttgcaaaa    240
ctgaaacagc ttcaggcaga aacagaacca attgtgaaga tgtttgaaga tccagaaact    300
acaaggcaaa tgcagtcaac cagggatggt aggatgctct ttgactacct ggcggacaag    360
catggtttta ggcaggaata tttagataca ctctacagat atgcaaaatt ccagtagcaa    420
tgtgggaatt actcaggagc agcagaatat ctttattttt ttagagtgtc ggttccagca    480
acagatagaa atgctttaag ttcactctgg ggaaagctgg cctctgaaat cttaatgcag    540
aattgggatg cagccatgga agaccttaca cggttaaaag agaccataga taataattct    600
gtgagttctc cacttcagtc tcttcagcag agaacatggc tcattcactg gtctctgttt    660
gttttcttca atcaccctaa aggtcgcgat aatattattg acctcttctt ttatcagcca    720
caatatctta atgcaattca gacaatgtgt ccacacattc ttcgtattt gactacagca    780
gtcatacaaa acaaggatgt tcgaaaacgt cggcaggttc taaaagatct agttaaagtt    840
attcaacagg agtctttcac atataaagac ccaattacag aatttgttga atgtttatat    900
gttaactttg actttgatgg ggctcagaaa aagctgaggg aatgtgaatc agtgcttgtg    960
aatgacttct tcttggtggc ttgtcttgag gatttcattg aaaatgcccg tctcttcata   1020
tttgagactt tctgtcgcac ccaccagtgt atcagcatta acatgttggc agataaattg   1080
aacatgactc cagaagaagc tgaagggtgg attgtaaatt tgattagaaa tgcaagactg   1140
gatccaaga ttgattctaa attaggatcat gtggttatgg gtaacaatgc agtctcacc   1200
tatcagcaag tgattgaaaa gacaaaagc ctttccttta gaagccagat gttggccatg   1260
aatattgaga agaaacttaa tcagaatagc aggtcagagg ctcttaactg ggcaactcaa   1320
gattctggct tetac                                     1335

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&lt;210&gt; SEQ ID NO 41

&lt;211&gt; LENGTH: 156

&lt;212&gt; TYPE: PRT

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<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 ctttggatgg tgaatgtggc aaagcagtgg taccacagca ggagcttctg 60  
 gacaaaatta aagaagaacc agacaatgct caagagtatg gatgtgtcca acagccaaaa 120  
 actcaagaaa gtaaattgaa aattggtggg gtgtcttcag ttaatgagag acctattgcc 180  
 cagcagttga acccaggett tcagctttct tttgcatcat ctggcccaag tgtgttgctt 240  
 ccttcagttc cagctgttgc tattaaggtt ttttgttctg gttgtaaaaa aatgctttat 300  
 aaggggccaaa ctgcatatca taagacagga tctactcagc tcttctgctc cacacgatgc 360  
 atcaccagac attcttcacc tgcttgctg ccacctctc ccaagaaaaa ctgcacaaac 420  
 tgctcgaagt ataaaattct taacatccct 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

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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 tetcgcgct cggtcgggc ctgctggtgg ccaecgacgc cctgtggccc 120  
 gacctgcgca gccgggcaag gcgcctgctg ctcttctctg cgetggccga cctgctctcg 180  
 gccgectect acttetaagg agtgtgcag aacttcgagg gccctgctg ggactgcgtg 240  
 ctgcagggcg cgtgtgccac cttcgccaac accagctcct tcttctggac cgtggccatt 300  
 gcgcttact tgtacctcag catcgtccgc gccgcgcgcg gccctcgcac agatgcctg 360  
 ctttgggect tccatgtcgt cagggtgggtg gcggtggcgc tgcttttcca ggagcccccg 420  
 acacagcccg acccctcccg gtcttgcct cccagaggcc gcgctc 465

<210> SEQ ID NO 45  
 <211> LENGTH: 675  
 <212> TYPE: PRT  
 <213> ORGANISM: Homo sapiens  
 <400> SEQUENCE: 45

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

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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  
 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

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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
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

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atggatacaa aatctattct agaagaactt cttctcaaaa gatcacagca aaagaagaaa    60
atgtcaccaa ataattacaa agaacggctt tttgttttga ccaaaacaaa cctttcctac    120
tatgaatgat acaaaaatgaa agggggcagc agaaaaggat ccattgaaat taagaaaatc    180
agatgtgtgg agaaagtaaa tctcgaggag cagacgcctg tagagagaca gtaccattt    240
cagattgtct ataaagatgg gcttctctat gtctatgcat caaatgaaga gagccgaagt    300
cagtgggtga aagcattaca aaaagagata aggggtaacc cccacctgct ggtcaagtac    360
catagtgggt tcttctgtga cgggaagtgc ctgtgttgcc agcagagctg taaagcagcc    420
ccaggatgta cctctgtgga agcatatgct aatctgcata ctgcagctca tgaagagaaa    480
cacagagtgc ccaccttccc agacagagtg ctgaagatac ctggggcagt tctgttctc    540
aaaatggatg caccatcttc aagtaccact ctagcccaat atgacaacga atcaaagaaa    600
aactatggct cccagccacc atcttcaagt accagtctag cgcaatatga cagcaactca    660
aagaaaatct atggctccca gccaaacttc aacatgcagt atattccaag ggaagacttc    720
cctgactggg ggcaagtaag aaaactgaaa agtagcagca gcagtgaaga tgttgcaagc    780
agtaacccaa aagaagaaa tgtgaatcac accacctcaa agatttcatg ggaattccct    840
gagtcaagtt catctgaaga agaggaaaac ctggatgatt atgactgggt tgctggtaac    900
atctccagat cacaatctga acagttactc agacaaaagg gaaaagaagg agcatttatg    960
gttagaaatt cgagccaagt gggaaatgtac acagtgcctt tatttagtaa ggctgtgaa    1020
gataaaaaag gaactgtcaa acattaccac gtgcatacaa atgctgagaa caaattatac    1080
ctggcagaaa actactgttt tgattccatt ccaaagetta ttcattatca tcaacacaat    1140
tcagcaggca tgatcacagc gctccgccac cctgtgtcaa caaaggccaa caaggtcccc    1200
gactctgtgt ccttgggaaa tggaatctgg gaactgaaaa gagaagagat taccttgttg    1260
aaggagctgg gaagtggcca gtttgagtg gtccagctgg gcaagtggaa ggggcagtat    1320
    
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gatgttgctg ttaagatgat caaggagggc tccatgtcag aagatgaatt ctttcaggag 1380
gcccagacta tgatgaaact cagccatccc aagctgggta aattctatgg agtgtgttca 1440
aaggaatacc ccatatacat agtgactgaa tatataagca atggctgctt gctgaattac 1500
ctgaggagtc acggaaaagg acttgaacct tcccagctct tagaaatgtg ctacgatgtc 1560
tgtgaaggca tggcctcttt ggagagtcac caattcatac accgggactt ggctgctcgt 1620
aactgcttgg tggacagaga tctctgtgtg aaagtatctg actttggaat gacaaggat 1680
gttcttgatg atcagtatgt cagttcagtc ggaacaaagt ttccagtaa gtggtcagct 1740
ccagaggtgt ttcattactt caaatacagc agcaagtcag acgtatgggc atttgggatc 1800
ctgatgtggg aggtgttcag cctggggaag cagccctatg acttgatga caactcccag 1860
gtggttctga aggtctccca ggccacagc ctttaccggc cccactggc atcggacacc 1920
atctaccaga tcagtgtacg ctgctggcac gagcttcag aaaagcgtcc cacatttcag 1980
caactcctgt cttccattga accacttcgg gaaaaagaca agcat 2025

```

&lt;210&gt; SEQ ID NO 47

&lt;211&gt; LENGTH: 502

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Homo sapiens

&lt;400&gt; 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
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

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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  
 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

atggtctcta agaagtggg tgcagat ttt catgggactt tcagttacct tgatgatgtc 60  
 ccatttaaga caggagacaa attcaaaaca ccagctaaag ttggcttacc tattggcttc 120  
 tccttgctg attgtttgca ggttgtcaga gaagtacagt atgacttctc tttgaaaag 180  
 aaaaccattg agtgggctga agagattaag aaaatcgaag aagccgagcg ggaagcagag 240  
 tgcaaaattg cggaagcaga agctaaagtg aattctaaga gtggcccaga gggcgatagc 300  
 aaaatgagct tctccaagac tcacagtaca gccacaatgc cacctcctat taaccccatc 360  
 ctcgccagct tgcagcacia cagcatcctc acaccaactc gggtcagcag tagtgccacg 420  
 aaacagaaag ttctcagccc acctcacata aaggcggatt tcaatcttgc tgactttgag 480  
 tgtgaagaag acccatttga taatctggag ttaaaaacta ttgatgagaa ggaagagctg 540

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agaaatattc tggtaggaac cactggaccc attatggctc agttattgga caataacttg 600
cccaggggag gctctgggtc tgtgttacag gatgaggagg tctctggcatc cttggaacgg 660
gcaaccctag atttcaagcc tcttcataaa cccaatggct ttataacctt accacagtgg 720
ggcaactgtg aaaagatgtc actgtcttcc aaagtgtccc tccccctat acctgcagta 780
agcaatatca aatccctgtc ttccccaaa cttgactctg atgacagcaa tcagaagaca 840
gccaagctgg cgagcacttt ccatagcaca tctgcctcc gcaatggcac gttccagaat 900
tccctaaagc cttccaccca aagcagtgcc agtgagctca atgggcatca cactcttggg 960
ctttcagctt tgaacttggg cagtggcaca gagatgccag ccttgacatc ctcccagatg 1020
ccttccctct ctgttttgtc tgtgtgcaca gaggaatcat cacctccaaa tactggtecc 1080
acggtacccc ctactaattt ctcagtgtca caagtgtcca acatgcccag ctgtccccag 1140
gcctattctg aactgcagat gctgtccccc agcgagcggc agtgtgtgga gacgggtgtc 1200
aacatgggct actcgtacga gtgtgtcctc agagccatga agaagaaagg agagaatatt 1260
gagcagattc tcgactatct ctttgacat ggacagcttt gtgagaaggg cttcgaccct 1320
cttttagtgg aagaggctct ggaatgcac cagtgttcag aagaaaagat gatggagttt 1380
cttcagttaa tgagcaaatt taaggagatg ggctttgagc tgaagacat taaggaagt 1440
ttgctattac acaacaatga ccaggacaat gctttggaag acctcatggc tcgggcagga 1500
gccagc 1506

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&lt;210&gt; SEQ ID NO 49

&lt;211&gt; LENGTH: 555

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Homo sapiens

&lt;400&gt; SEQUENCE: 49

```

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

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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	
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					

&lt;210&gt; SEQ ID NO 50

&lt;211&gt; LENGTH: 1665

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Homo sapiens

-continued

&lt;400&gt; SEQUENCE: 50

```

atgagagtca atggagatga tgacagtgtt gcggccttga gcttctctta tgattactac   60
atgggtccca aggagaagcg gatattgtcc tccagcactg ggggcaggaa tgaccaagga   120
aagaggtact accatggcat ggaatatgag acggacctca ctccccttga aagccccaca   180
cacctcatga aattcctgac agagaacgtg tctggaaccc cagagtaccc agatttgtct   240
aagaagaata acctgatgag cttggagggg gccttgccca cccctggcaa ggcagctccc   300
ctccctgcag gccccagcaa gctggaggcc ggctctgtgg acagctacct gttaccacc   360
actgatatgt atgataatgg ctccctcaac tccttgtttg agagcattca tggggtgccg   420
ccccacacagc gctggcagcc agacagcacc ttcaaagatg acccacagga gtcgatgctc   480
ttcccagata tctgaaaac ctcccggaa ccccatgtc cagaggacta ccccagcctc   540
aaaagtgact ttgaatacac cctgggctcc cccaaagcca tccacatcaa gtcaggcgag   600
tcacccatgg ctaactcaa caaaggccag ttctaccccg tcacctgcg gaccccagca   660
ggtgggcaaag gccttgcctt gtctccaac aaagtcaaga gttgtgtgat ggttgtctt   720
gacaatgaga aggtcccagt agagcagctg cgcttctgga agcactggca tccccggcaa   780
cccactgcca agcagcgggt cattgacgtg gctgactgca aagaaaact caacactgtg   840
gagcacattg aggaggtggc ctataatgca ctgtcctttg tgtggaacct gaatgaagag   900
gccaaggtgt tcactggcgt aaactgtctg agcacagact ttctctcaca aaagggggtg   960
aaggggtgtc cctgaacct gcagattgac acctatgact gtggcttggg cactgagcgc  1020
ctggtacacc gtgctgtctg ccagatcaag atcttctgtg acaagggagc tgagaggaag  1080
atgctcgatg acgagcggaa gcagttccgg aggaaggtca agtgccctga ctccagcaac  1140
agtggcgtca agggctgcct gctgtcgggc ttcaggggca atgagacgac ctaccttcgg  1200
ccagagactg acctggagac gccaccctgt ctgttcatcc ccaatgtgca cttctccagc  1260
ctgcagcgtc ctggaggggc agcccctcg gcaggaccca gcagctcca caggctgcct  1320
ctgaagcgtg cctgctgcc cttcactgag gagtttgagc ctctgcctc caagcaggcc  1380
aaggaagcgc accttcagag agttctgctg tatgtgcgga gggagactga ggaggtgttt  1440
gacgcgctca tgttgaagac cccagacctg aaggggctga ggaatgcgat ctctgagaag  1500
tatgggttcc ctgaagagaa catttcaaaa gtctacaaga aatgcaagcg aggaatctta  1560
gtcaacatgg acaacaacat cattcagcat tacagcaacc acgtgcctt cctgctggac  1620
atgggggagc tggacggcaa aattcagatc atccttaagg agctg   1665

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&lt;210&gt; SEQ ID NO 51

&lt;211&gt; LENGTH: 418

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Homo sapiens

&lt;400&gt; SEQUENCE: 51

```

Met Arg Ser 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 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

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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  
 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

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atgcgctccc tctgcttct cagcgccttc tgcctcctgg aggcggccct ggccgcccag 60
gtgaagaaac ctgcagccgc agcagctcct ggcaactcgg agaagttgag ccccaaggcg 120
gccacgcttg ccgagcgcag cgcggcctg gccttcagct tgtaccaggc catggccaag 180
gaccaggcag tggagaacat cctgggtgca cccgtggtgg tggcctcgtc gctggggctc 240
gtgtcgctgg gcggcaaggc gaccacggcg tcgcaggcca aggcagtgtc gagcgcggag 300
cagctgcgcg acgaggaggt gcacgcggcg ctggggcagc tgctgcgctc actcagcaac 360
tccacggcgc gcaactgtac ctggaagctg ggcagccgac tgtacggacc cagctcagtg 420
agcttcgctg atgacttctg gcgcagcagc aagcagcact acaactgcga gcaactccaag 480
atcaacttcc gcgacaagcg cagcgcgctg cagtccatca acgagtgggc cgcgcagacc 540
accgacggca agctgcccga ggtoaccaag gacgtggagc gcacggacgg cgcctgttta 600
gtcaacgcca tgttcttcaa gccacactgg gatgagaaat tccaccaca gatggtggac 660
aaccgtggct tcatggtgac tcggtcctat accgtgggtg tcatgatgat gcaccggaca 720
ggcctctaca actactacga cgcgcagaag gaaaagctgc aaatcgtgga gatgcccctg 780
gcccacaagc tctccagcct catcatcctc atgccccatc acgtggagcc tctcagcgc 840
cttgaaaagc tgctaaccaa agagcagctg aagatctgga tggggaagat gcagaagaag 900
gctgttgcca tctccttgcc caaggggtgtg gtggaggtga cccatgacct gcagaaacac 960
ctggctgggc tgggctgac tgaggccatt gacaagaaca aggcgcgact gtcacgcatg 1020
tcaggcaaga aggacctgta cctggccagc gtgttccacg ccaccgcctt tgagttggac 1080
acagatggca accccttga ccaggacatc tacgggcgcg aggagctcgc cagccccaag 1140
ctgttctacg ccgaccacc cttcatcttc ctagtgcggg acacccaag cggtccctg 1200
ctattcattg ggcgcctggt ccggcctaag ggtgacaaga tgcgagacga gtta 1254

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&lt;210&gt; SEQ ID NO 53

&lt;211&gt; LENGTH: 636

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Homo sapiens

&lt;400&gt; 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

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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			180				185						190		
Asn	Arg	Asn	Tyr	Ser	Thr	Lys	Lys	Ile	Gly	Cys	Gly	Asn	Val	Cys	Glu
195			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
		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
450						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



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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 aactctttc aggagcagca gaaaatgaac 120  
 atatctcagg catcagtgtc attcaaggac gtgactatag aattcaccca ggaggagtgg 180  
 cagcaaatgg cccctgttca gaagaatctg tacagagatg tgatgctgga gaactacagc 240  
 aacctcgtct cagtggggta ctgctgttcc aaaccagagg tgatcttcaa gttggagcaa 300  
 ggagaggagc ctgtgttctc agaggaggaa ttctcaaacc agagtcaccc aaaagattac 360  
 agagggtgatg acctgatcaa gcagaacaag aaaatcaaag acaaacactt ggagcaagca 420  
 atatgtatca ataataaaa attgactaca gaggaagaga aagttttggg gaaaccattt 480  
 actctgcatg tagctgctgt tcttcaaca aaaatgtcct gcaaatgcaa ctcatgggaa 540  
 gtgaatttgc aaagtattc tgaatttacc attaataata gaaactattc acaaaagaaa 600  
 ataggttgctg gtaattgatg tgagaattca cctttcaaaa ttaactttga gaaaactcag 660  
 actggagaga aattttatga acataataaa aacatgaaag ctctcaatta taatgaaat 720  
 ctcccaagc atccaaagtt tcaaaccttg gagcaagcct ttgaatgtaa taaaattgga 780  
 aaagccttta atgataaggc taactgtgtt aaacataaca gttctcacac aggagaaaca 840  
 tcctctaag atgatgaatt taggaaaaat tgtgataaga aaactctctt tgaccacagc 900  
 agaactggca caggaagaaa acacctgcat cttaatcaat gtgggaaatc ctttgagaag 960  
 tcaactgtgg aggaatataa taaacttaat atgggtataa aacattatga attaaatcca 1020  
 agtggaaata atttcaacag aaaggcacac ctactgac ctcaaacagc tgtcatagaa 1080  
 gaaacccat tggtaagtaa tgacagaaca cagactggg ttaaatcctc tgaatatcat 1140  
 gaaaataaga aactctacca gacgtcgggt cacagagttc gccgaagaag tcaactcaatg 1200  
 atgaaacctc ataaatgtaa tgaatgtggg aaatccttct gtcagaaagg acatctcatt 1260  
 caacatcaga gaactcacac aggagagaaa ccatttgaat gtagtgaatg tggaaaaact 1320  
 ttctcccaga agtcacacct cagtactcat cagagaattc atacagcaga aaaacctat 1380  
 aatgtaatg aatgtggaaa aacatttgtc cagaagtcaa cctcagggg acatcaaaaga 1440  
 attcacacag gagaaaaacc ctatgaatgt agtgaatgtg ggaaaacttt tgttcagaag 1500  
 tccacctca gagatcatca cagaattcac acaggggaga aatcctttca atgcaatcaa 1560  
 tgtggaaaaa catttgccca gaagtcaaac ctcaagaatac atcagagaac tcactctggg 1620

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gagaaaaactt accagtgtaa tgaatgtgaa aaatccttct gccgaaaaga tcattctcatt 1680
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tttgcccga catcaacct cagagtgcac caaagaattc acactgggga gaaaccattt 1800
aaatgtaacg aatgtgggaa gaaatttgc cggaaagcaa tccttagtga tcacagaga 1860
attcacacag gggagaaacc ctttcagtgt aataaatgtg ggaaaaact 1908

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&lt;210&gt; SEQ ID NO 55

&lt;211&gt; LENGTH: 375

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Homo sapiens

&lt;400&gt; 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
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 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

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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	

&lt;210&gt; SEQ ID NO 56

&lt;211&gt; LENGTH: 1125

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Homo sapiens

&lt;400&gt; SEQUENCE: 56

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atgggctgca gaagaactag agaaggacca agcaaagcca tgatatttcc atggaaatgt    60
cagagcaccc agaggggactt atggaacatc ttcaagtgtt ggggggtggac aatgctctgt    120
tgtgatttcc tggcacatca tggaaacgac tgctggactt accattattc tgaaaaaccc    180
atgaactggc aaagggctag aagattctgc cgagacaatt acacagattt agttgccata    240
caaaaacaag cggaaattga gtatctggag aagactctgc ctttcagtcg ttcttactac    300
tggataggaa tccggaagat aggaggaata tggacgtggg tgggaaccaa caaatctctt    360
actgaagaag cagagaactg gggagatggt gagcccaaca acaagaagaa caaggaggac    420
tgcgtggaga tctatatcaa gagaaacaaa gatgcaggca aatggaacga tgacgcctgc    480
cacaaactaa aggcagcctc ctgttacaca gcttcttgcc agccctggtc atgcagtggc    540
catggagaat gtgtagaaat catcaataat tacacctgca actgtgatgt ggggtactat    600
gggccccagt gtcagtttgt gattcagtgat gagcctttgg aggccccaga gctgggtacc    660
atggactgta ctcacccttt gggaaacttc agcttcagct cacagtgtgc cttcagctgc    720
tctgaaggaa caaacttaac tgggattgaa gaaaccacct gtggaccatt tggaaactgg    780
tcatctccag aaccaacctg tcaagtgatt cagtgtgagc ctctatcagc accagatttg    840
gggatcatga actgtagcca tcccctggcc agcttcagct ttacctctgc atgtaacctc    900
atctgctcag aaggaactga gtaattggg aagaagaaaa ccatttgtga atcatctgga    960
atctgggcaa atcctagtc aatatgtcaa aaattggaca aaagtttctc aatgattaag   1020
gagggtgatt ataaccocct cttcattcca gtggcagtea tggttactgc attctctggg   1080
ttggcattta tcatttgctt ggcaaggaga ttaaaaaaag gtatg                               1125

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- 1.** A method for detecting breast cancer, comprising:
- (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), RAB5A (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), 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 contacting occurs under conditions suitable for selective binding of antibodies in the bodily fluid sample to the one or more polypeptides; and
- (b) detecting presence of antibodies to the polypeptides in the bodily fluid sample;
- wherein the presence of antibodies to the one or more polypeptides indicates a likelihood of breast cancer in the subject.
- 2.** The method of claim 1, wherein the one or more isolated polypeptides comprises ATP6AP1 (SEQ ID NO: 13), or an antigenic fragment thereof.
- 3.** The method of claim 1 wherein the subject has one or more of a lump in the 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 the subject is a carrier of a mutation in the BRCA or other gene that predisposes the subject to breast cancer.
- 4.** The method of claim 1 wherein the method results in an accurate diagnosis of breast cancer in at least 70% of cases.
- 5.** The method of claim 1 wherein the likelihood of breast cancer is a likelihood of Stage I or Stage II breast cancer.
- 6.** The method of claim 1 wherein the bodily fluid comprises serum or plasma.
- 7.** The method of claim 1 wherein those patients with a likelihood of breast cancer are further tested for the presence of breast cancer using a technique selected from the group consisting of mammography, biopsy, or magnetic resonance imaging.
- 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

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