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(54) **AUTOANTIBODY SIGNATURE FOR THE EARLY DETECTION OF OVARIAN CANCER**

(71) Applicants: **Karen ANDERSON**, Scottsdlae, AZ (US); **Joshua LABAER**, Chandler, AZ (US); **Garrick WALLSTROM**, Mesa, AZ (US); **Daniel CRAMER**, Chestnut Hill, MA (US); **ARIZONA BOARD OF REGENTS, A BODY CORPRATE OF THE S TATE OF ARIZONA, ACTING FOR AND BEHALF OF ARI**, Scottsdale, AZ (US)

(72) Inventors: **Karen Anderson**, Scottsdale, AZ (US); **Joshua LaBaer**, Chandler, AZ (US); **Garrick Wallstrom**, Mesa, AZ (US); **Daniel Cramer**, Chestnut Hill, AZ (US)

(73) Assignee: **Arizona Board of Regents on behalf of Arizona Stat State University**, Scottsdale, AZ (US)

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(57) **ABSTRACT**

Methods for identifying antigens as potential biomarkers for the early detection of ovarian cancer, as well as kits for utilizing said antigens as biomarkers and in personalized medicine/therapeutics assessment. Protein microarrays displaying full-length candidate antigens were developed and sequentially screening to select candidate autoantibody biomarkers to limit the false discovery rate inherent to large-scale proteomic screening.

# AUTOANTIBODY SIGNATURE FOR THE EARLY DETECTION OF OVARIAN CANCER

## CROSS-REFERENCE TO RELATED APPLICATION

**[0001]** This application claims priority to U.S. provisional patent Application No. 61/759,047 filed on Jan. 31, 2013, which is incorporated by reference herein in its entirety.

## STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT

**[0002]** This invention was made with government support under CA117374 awarded by The National Institutes of Health. The U.S. government has certain rights in the invention.

## BACKGROUND OF THE INVENTION

**[0003]** Ovarian cancer is the fifth leading cause of cancer-related mortality of women in the U.S., with over 15,000 deaths per year. Early diagnosis is associated with improved overall survival; however, the majority of patients are currently diagnosed with advanced disease. The five-year survival rate for late-stage ovarian cancer remains less than 30%.

**[0004]** Despite the identification of serum CA 125 as a biomarker for ovarian cancer in 1983, there are currently no screening biomarkers recommended for use for the general population. The utility of CA 125 as a screening test is limited by a low sensitivity of 50% for early stage disease at 99% specificity.

**[0005]** Combining CA 125 with transvaginal ultrasound (TVUS) increased the specificity of detection in the UKCTOCS large-scale screening trial. In a recent joint validation study of 28 potential markers for detecting ovarian cancer in blood, the most accurate marker remains CA 125, followed closely by HE4. Panels of markers demonstrated only marginal improvements over CA 125 alone for the early detection of disease.

**[0006]** A recent study showed that the addition of CEA and VCAM-1 to CA 125 and HE4 increased the sensitivity of detection of stage I and II ovarian cancer to 86% at 98% specificity, but this remains to be confirmed in a blinded validation study using prediagnostic sera.

**[0007]** Protein overexpression or mutation can also lead to the spontaneous development of autoantibodies (AAb) in the sera of patients with cancer. Tumor antigen-specific AAb have been identified in the sera of patients with cancer, including patients with early-stage disease. p53-specific AAb, which are associated with p53 mutation and resultant protein stabilization, have been detected in early-stage ovarian cancer. p53-specific AAb have also been detected in 41.7% of patients with serous ovarian cancer at 91.7% specificity. Unlike CA 125 and HE4, p53-AAb were associated with improved survival.

**[0008]** However, identification and utilization of other biomarkers for detection of early stage ovarian cancer remains elusive.

## SUMMARY OF THE INVENTION

**[0009]** Methods to identify antibody signatures in early-stage breast cancer using Nucleic Acid Protein Programmable Arrays (NAPPA) have been developed. Diagnostic test kits and personalized medicine determinations, such as the identification of biomarkers for the early detection of ovarian cancer, also are disclosed.

**[0010]** A novel protein microarray technology NAPPA, which are generated by printing full-length cDNAs encoding the target proteins at each feature of the array, was used. The proteins are then transcribed and translated by a cell-free system and immobilized in situ using epitope tags fused to the proteins. Sera are added, and bound IgG is detected by standard secondary reagents.

**[0011]** These and other aspects of the invention will be apparent upon reference to the following detailed description and figures. To that end, any patent and other documents cited herein are hereby incorporated by reference in their entirety.

## DETAILED DESCRIPTION OF THE INVENTION

**[0012]** Embodiments described herein relate to methods for identifying autoantibodies as potential biomarkers for the early detection of ovarian cancer, as well as to kits for utilizing said autoantibodies as diagnostic biomarkers and for personalized medicine/therapeutics assessment.

**[0013]** Protein microarrays displaying full-length candidate antigens have been developed and sequentially screened to select candidate autoantibody biomarkers. Sera from patients with ovarian cancer were found to contain autoantibodies (AAb) to tumor-derived proteins. Thus, to detect AAb, high-density programmable protein microarrays (NAPPA) expressing 5,177 candidate tumor antigens are probed with sera from patients with serous ovarian cancer and healthy controls, bound IgG measured.

**[0014]** In one embodiment, a set of 741 antigens was selected and probed with an independent set of sera from serous ovarian cancer patients and matched controls. Twelve potential autoantigens were identified with sensitivities ranging from 13-22% at >93% specificity. Surprisingly, many of these twelve autoantigens are not known to previously have been associated with ovarian cancer.

### Non-Limiting Examples

**[0015]** The objective of this study was to identify novel AAb biomarkers for the detection of serous ovarian cancer. To profile the ovarian cancer immune response, NAPPA microarrays displaying 5,177 full-length candidate antigens were generated using cDNAs derived from the DNASU Plasmid Repository at Arizona State University. These cDNAs were all sequence-verified, full length, wild-type genes fused in frame with either a C-terminal GST tag or N-terminal FLAG tag in a vector optimized for mammalian protein expression.

**[0016]** The cDNAs were printed on amine-treated glass slides with anti-tag antibodies at a high density (up to 2300 antigens/slide; 3 slides/gene set) using a Genetix QArray2 with 300 pm solid tungsten pins. Proteins were expressed and captured in situ on the arrays using a coupled in vitro transcription-translation system derived from rabbit reticulocyte lysate. Protein expression was confirmed by probing the arrays with anti-tag antibodies. For detecting antibodies, the arrays were incubated with serum diluted in 5% PBS mile with 0.2% Tween 20 overnight and detected with anti-human IgG-HRP with Tyramide. Slides were scanned with a Perkin Elmer ProScanArray HT and the images quantitated using ArrayPro software.

**[0017]** A sequential screening strategy was used to select candidate AAb biomarkers to limit the false discovery rate inherent to large-scale proteomic screening.

**[0018]** First, 34 cases of serous ovarian cancer and 30 age-matched healthy controls (Cohort 1) were screened on 5,177 candidate tumor antigens. 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.

**[0019]** Candidate antigens from the initial 5,177 antigens were selected if they met two different criteria: 1) comparison of the 95th percentiles of the cases and controls using quantile regression and 2) comparison of the proportion of cases with intensities above the 95th percentile of controls to the expected number seen by chance using binomial tests. Using these criteria, 741 antigens were selected for further testing.

**[0020]** Second, 60 cases and 60 healthy controls (Cohort 2) were screened on the 741 antigens, which were printed in duplicate on the arrays. Following the use of spot-level quality control procedures, the arrays were similarly normalized and analyzed using receiver operator characteristic (ROC) curve analysis. Specifically, we tested the hypothesis that the partial area under the ROC curve (PAUC) in the region where the specificity >95% exceeds 0.00125, which is the PAUC for a non-informative diagnostic test. We computed q-values and identified 12 potential AAb biomarkers that were statistically significant with a false discovery rate threshold of 15% (Table 1).

**[0021]** Descriptions of these biomarkers, their amino acid sequences and their nucleic acid sequences are provided in Table 2. Third, an independent assay (Luminex bead array) was used to display these autoantigens, and sera from women in Cohort 2 was re-screened. Finally, a smaller set of 7 autoantigens was displayed and screened with sera from an independent set (Cohort 3) of non-serous cancers (n=30), false-negative CA 125 (n=20), benign ovarian disease (n=30), and healthy controls (n=30).

TABLE 1

NAPPA Results for 12 Potential Biomarkers for Ovarian Cancer

| Protein | PAUC P-Value | Sensitivity | Specificity |
|---|---|---|---|
| ACSBG1 | 0.0020 | 15.5% | 93.3% |
| AFP | 0.0040 | 15.5% | 93.3% |
| CSNK1A1L | 0.0047 | 13.8% | 93.3% |
| DHFR | 0.0057 | 17.2% | 93.3% |
| MBNL1 | 0.0067 | 13.8% | 93.3% |
| p53 | 0.0067 | 21.4% | 93.1% |
| PRL | 0.0026 | 17.2% | 93.3% |
| PSMC1 | 0.0057 | 15.5% | 93.3% |
| PTGFR | 0.0070 | 15.5% | 93.3% |
| PTPRA | 0.0004 | 22.4% | 93.3% |
| RAB7L1 | 0.0034 | 20.7% | 93.3% |
| SCYL3 | 0.0063 | 19.0% | 93.3 |

**[0022]** The twelve biomarkers for ovarian cancer can be utilized on an array or other substrate as a diagnostic test in which sera from a patient is tested for ovarian cancer autoantibodies.

TABLE 2

Candidate Biomarkers

ACSBG1 NP_055977 acyl-CoA synthetase bubblegum family member 1 full length (1-724), M633V
Amino acid sequence

(SEQ ID NO: 1)

MPRNSGAGYGCPHGDPSMLDSRETPQESRQDMIVRTTQEKLKTSSLTDRQPLSKESLNHALELSVPEKVNN
AQWDAPEEALWTTRADGRVRLRIDPSCPQLPYTVHRMFYEALDKYGDLIALGFKRQDKWEHISYSQYYLLA
RRAAKGFLKLGLKQAHSVAILGFNSPEWFFSAVGTVFAGGIVTGIYTTSSPEACQYIAYDCCANVIMVDTQ
KQLEKILKIWKQLPHLKAVVIYKEPPPNKMANVYTMEEFMELGNEVPEEALDAIIDTQQPNQCCVLVYTSG
TTGNPKGVMLSQDNITWTARYGSQAGDIRPAEVQQEVVVSYLPLSHIAAQIYDLWTGIQWGAQVCFAEPDA
LKGSLVNTLREVEPTSHMGVPRVWEKIMERIQEVAAQSGFIRRKMLLWAMSVTLEQNLTCPGSDLKPFTTR
LADYLVLAKVRQALGFAKCQKNFYGAAPMMAETQHFFLGLNIRLYAGYGLSETSGPHFMSSPYNYRLYSSG
KLVPGCRVKLVNQDAEGIGEICLWGRTIFMGYLNMEDKTCEAIDEEGWLHTGDAGRLDADGFLYITGRLKE
LIITAGGENVPPVPIEEAVKMELPIISNAMLIGDQRKFLSMLLTLKCTLDPDTSDQTDNLTEQAVEFCQRV
GSRATTVSEIIEKKDEAVYQAIEEGIRRVNMNAAARPYHIQKWAILERDFSISGGELGPTMKLKRLTVLEK
YKGIIDSFYQEQKM

Encoding nucleotide sequence

(SEQ ID NO: 2)

ATGCCACGCAATTCTGGAGCTGGATACGGCTGCCCACACGGGGACCCCAGCATGCTGGACAGCAGAGAGAC
CCCACAGGAGAGCCGGCAGGACATGATTGTGAGGACCACCCAAGAAAAATTGAAAACCAGCTCACTGACTG
ACAGGCAGCCACTCTCCAAAGAGTCCCTGAACCATGCTCTCGAGCTCTCAGTGCCAGAGAAGGTGAATAAT
GCCCAGTGGGATGCTCCAGAGGAGGCGCTGTGGACGACTCGGGCCGATGGGCGGGTGCGCCTGCGCATAGA
CCCCAGCTGCCCACAGCTTCCCTACACTGTGCATCGGATGTTCTACGAGGCCCTGGATAAGTATGGGGACC
TCATCGCTTTGGGCTTCAAGCGCCAGGACAAGTGGGAACACATCTCCTACTCCCAATACTACCTGCTCGCC
CGCAGAGCCGCCAAGGGCTTCCTGAAGCTCGGCCTGAAGCAGGCCCACAGTGTGGCCATCCTCGGCTTCAA
CTCCCCGGAGTGGTTCTTCTCGGCAGTGGGCACAGTATTTGCAGGTGGCATCGTCACTGGCATCTACACCA
CCAGCTCCCCAGAGGCCTGCCAGTACATCGCTTATGACTGCTGCGCCAATGTCATCATGGTCGACACGCAG
AAGCAGCTGGAAAAGATCCTGAAGATCTGGAAACAGTTGCCACATCTAAAGGCAGTCGTGATATATAAAGA
ACCTCCTCCAAACAAGATGGCCAATGTGTACACGATGGAGGAATTCATGGAGCTGGGGAATGAAGTGCCTG
AGGAAGCCCTGGACGCCATCATTGACACCCAGCAGCCCAACCAGTGCTGTGTGCTAGTCTACACTTCCGGC
ACCACTGGGAACCCCAAGGGCGTGATGCTGAGTCAAGACAATATCACGTGGACGGCACGGTACGGCAGCCA
GGCCGGTGACATCCGGCCGGCAGAAGTCCAGCAGGAGGTGGTAGTCAGCTACCTGCCCCTCAGCCATATTG
CCGCCCAGATCTACGACCTGTGGACAGGCATCCAGTGGGGGGCCCAGGTTTGCTTTGCCGAACCCGACGCC
CTGAAGGGGAGCCTGGTGAACACGCTGCGGGAGGTGGAGCCCACATCACACATGGGGGTGCCCCGGGTATG
GGAGAAGATCATGGAGCGCATCCAGGAGGTGGCGGCTCAGTCTGGCTTCATCCGGCGGAAGATGCTGCTGT
GGGCCATGTCGGTGACCTTGGAGCAGAACCTCACCTGCCCCGGCAGCGACCTGAAGCCCTTCACAACCAGA
CTGGCAGATTACCTGGTGCTAGCCAAGGTTCGCCAGGCACTGGGATTTGCCAAGTGTCAAAAGAACTTCTA

TABLE 2-continued

Candidate Biomarkers

TGGAGCGGCCCCCATGATGGCAGAGACACAGCACTTCTTCCTGGGTCTCAACATCCGCTTGTATGCGGGCT
ATGGCCTCAGTGAGACCTCAGGCCCCCACTTCATGTCCAGTCCCTACAACTACCGGCTGTACAGCTCAGGC
AAGTTGGTGCCCGGCTGTCGGGTGAAGCTGGTGAACCAGGACGCAGAGGGCATTGGTGAGATCTGCCTGTG
GGGCCGCACCATATTCATGGGCTACCTGAACATGGAGGACAAGACTTGTGAGGCCATCGACGAGGAAGGCT
GGCTGCACACGGGTGATGCTGGCCGCCTGGACGCCGATGGCTTCCTCTACATCACTGGGCGCCTCAAAGAA
TTAATCATCACAGCTGGTGGGGAGAATGTGCCCCCTGTGCCCATCGAGGAGGCCGTGAAGATGGAGCTGCC
CATCATCAGCAATGCCATGCTCATTGGGGACCAGAGGAAGTTCCTGTCCATGCTGCTCACCTTGAAGTGCA
CTCTGGACCCAGACACCTCTGACCAGACTGATAATCTGACTGAACAAGCTGTGGAGTTCTGCCAGAGGGTG
GGCAGCAGAGCCACCACAGTGTCCGAGATCATAGAGAAGAAGGATGAGGCCGTGTACCAGGCCATCGAAGA
GGGGATCCGGAGGGTCAACATGAACGCGGCGGCCCGGCCCTACCACATCCAGAAGTGGGCCATTCTCGAGA
GAGACTTCTCCATTTCGGGTGGAGAGTTGGGTCCCACGATGAAACTGAAACGGCTCACAGTTTTGGAGAAG
TACAAAGGTATCATTGACTCCTTTTACCAAGAGCAAAAAATG

AFP NP_001125 alpha-fetoprotein full length (1-609)
Amino acid sequence
(SEQ ID NO: 3)
MKWVESIFLIFLLNFTESRTLHRNEYGIASILDSYQCTAEISLADLATIFFAQFVQEATYKEVSKMVKDAL
TAIEKPTGDEQSSGCLENQLPAFLEELCHEKEILEKYGHSDCCSQSEEGRHNCFLAHKKPTPASIPLFQVP
EPVTSCEAYEEDRETFMNKFIYEIARRHPFLYAPTILLWAARYDKIIPSCCKAENAVECFQTKAATVTKEL
RESSLLNQHACAVMKNFGTRTFQAITVTKLSQKFTKVNFTEIQKLVLDVAHVHEHCCRGDVLDCLQDGEKI
MSYICSQQDTLSNKITECCKLTTLERGQCIIHAENDEKPEGLSPNLNRFLGDRDFNQFSSGEKNIFLASFV
HEYSRRHPQLAVSVILRVAKGYQELLEKCFQTENPLECQDKGEEELQKYIQESQALAKRSCGLFQKLGEYY
LQNAFLVAYTKKAPQLTSSELMAITRKMAATAATCCQLSEDKLLACGEGAADIIIGHLCIRHEMTPVNPGV
GQCCTSSYANRRPCFSSLVVDETYVPPAFSDDKFIFHKDLCQAQGVALQTMKQEFLINLVKQKPQITEEQL
EAVIADFSGLLEKCCQGQEQEVCFAEEGQKLISKTRAALGV

Encoding nucleotide sequence
(SEQ ID NO: 4)
ATGAAGTGGGTGGAATCAATTTTTTTAATTTTCCTACTAAATTTTACTGAATCCAGAACACTGCATAGAAA
TGAATATGGAATAGCTTCCATATTGGATTCTTACCAATGTACTGCAGAGATAAGTTTAGCTGACCTGGCTA
CCATATTTTTTGCCCAGTTTGTTCAAGAAGCCACTTACAAGGAAGTAAGCAAAATGGTGAAAGATGCATTG
ACTGCAATTGAGAAACCCACTGGAGATGAACAGTCTTCAGGGTGTTTAGAAAACCAGCTACCTGCCTTTCT
GGAAGAACTTTGCCATGAGAAAGAAATTTTGGAGAAGTACGGACATTCAGACTGCTGCAGCCAAAGTGAAG
AGGGAAGACATAACTGTTTTCTTGCACACAAAAAGCCCACTCCAGCATCGATCCCACTTTTCCAAGTTCCA
GAACCTGTCACAAGCTGTGAAGCATATGAAGAAGACAGGGAGACATTCATGAACAAATTCATTTATGAGAT
AGCAAGAAGGCATCCCTTCCTGTATGCACCTACAATTCTTCTTTGGGCTGCTCGCTATGACAAAATAATTC
CATCTTGCTGCAAAGCTGAAAATGCAGTTGAATGCTTCCAAACAAAGGCAGCAACAGTTACAAAAGAATTA
AGAGAAAGCAGCTTGTTAAATCAACATGCATGTGCAGTAATGAAAAATTTTGGGACCCGAACTTTCCAAGC
CATAACTGTTACTAAACTGAGTCAGAAGTTTACCAAAGTTAATTTTACTGAAATCCAGAAACTAGTCCTGG
ATGTGGCCCATGTACATGAGCACTGTTGCAGAGGAGATGTGCTGGATTGTCTGCAGGATGGGGAAAAAATC
ATGTCCTACATATGTTCTCAACAAGACACTCTGTCAAACAAAATAACAGAATGCTGCAAACTGACCACGCT
GGAACGTGGTCAATGTATAATTCATGCAGAAAATGATGAAAAACCTGAAGGTCTATCTCCAAATCTAAACA
GGTTTTTAGGAGATAGAGATTTTAACCAATTTTCTTCAGGGGAAAAAAATATCTTCTTGGCAAGTTTTGTT
CATGAATATTCAAGAAGACATCCTCAGCTTGCTGTCTCAGTAATTCTAAGAGTTGCTAAAGGATACCAGGA
GTTATTGGAGAAGTGTTTCCAGACTGAAAACCCTCTTGAATGCCAAGATAAAGGAGAAGAAGAATTACAGA
AATACATCCAGGAGAGCCAAGCATTGGCAAAGCGAAGCTGCGGCCTCTTCCAGAAACTAGGAGAATATTAC
TTACAAAATGCGTTTCTCGTTGCTTACACAAAGAAAGCCCCCCAGCTGACCTCGTCGGAGCTGATGGCCAT
CACCAGAAAAATGGCAGCCACAGCAGCCACTTGTTGCCAACTCAGTGAGGACAAACTATTGGCCTGTGGCG
AGGGAGCGGCTGACATTATTATCGGACACTTATGTATCAGACATGAAATGACTCCAGTAAACCCTGGTGTT
GGCCAGTGCTGCACTTCTTCATATGCCAACAGGAGGCCATGCTTCAGCAGCTTGGTGGTGGATGAAACATA
TGTCCCTCCTGCATTCTCTGATGACAAGTTCATTTTCCATAAGGATCTGTGCCAAGCTCAGGGTGTAGCGC
TGCAAACGATGAAGCAAGAGTTTCTCATTAACCTTGTGAAGCAAAAGCCACAAATAACAGAGGAACAACTT
GAGGCTGTCATTGCAGATTTCTCAGGCCTGTTGGAGAAATGCTGCCAAGGCCAGGAACAGGAAGTCTGCTT
TGCTGAAGAGGGACAAAAACTGATTTCAAAAACTCGTGCTGCTTTGGGAGTT

CSNK1A1L NP_660204 casein kinase 1, alpha 1-like full length
(1-337), R224K
Amino acid sequence
(SEQ ID NO: 5)
MTNNSGSKAELVVGGKYKLVRKIGSGSFGDVYLGITTTNGEEVAVKLESQKVKHPQLLYESKLYTILQGGV
GIPHMHWYGQEKDNNVLVMDLLGPSLEDLFNFCSRRFTMKTVLMLADQMISRIEYVHTKNFLHRDIKPDNF
LMGTGRHCNKLFLIDFGLAKKYRDNRTRQHIPYREDKHLIGTVRYASINAHLGIEQSRRDDMESLGYVFMY
FNRTSLPWQGLKAMTKKQKYEKISEKKMSTPVEVLCKGFPAEFAMYLNYCRGLRFEEVPDYMYLRQLFRIL
FRTLNHQYDYTFDWTMLKQKAAQQAASSSGQGQQAQTQTGKQTEKNKNNVKDN

Encoding nucleotide sequence
(SEQ ID NO: 6)
ATGACAAACAACAGCGGCTCCAAAGCCGAACTCGTTGTGGGAGGGAAATACAAACTGGTGCGGAAGATCGG
GTCTGGCTCCTTTGGAGACGTTTATCTGGGCATCACCACCACCAACGGCGAGGAAGTAGCAGTGAAGCTGG
AATCTCAGAAGGTCAAGCACCCCCAGTTGCTGTATGAGAGCAAACTCTACACGATTCTTCAAGGTGGGGTT
GGCATCCCCCACATGCACTGGTATGGTCAGGAAAAAGACAACAATGTGCTAGTCATGGACCTTCTGGGACC
CAGCCTCGAAGACCTCTTTAATTTCTGTTCAAGAAGGTTCACCATGAAAACTGTACTTATGTTAGCCGACC
AGATGATCAGCAGAATTGAATACGTGCATACAAAGAATTTTCTACACCGAGACATTAAACCAGATAACTTC
CTGATGGGTACTGGGCGTCACTGTAATAAGTTGTTCCTTATTGATTTTGGTTTGGCCAAAAAGTACAGAGA
CAACAGGACCAGGCAACACATACCGTACAGAGAAGATAAACACCTCATTGGCACTGTCCGATATGCCAGCA

TABLE 2-continued

Candidate Biomarkers

TCAATGCACATCTTGGTATTGAGCAGAGCCGCCGAGATGACATGGAATCCTTAGGCTACGTTTTCATGTAT
TTTAATAGAACCAGCCTGCCGTGGCAAGGACTAAAGGCTATGACAAAAAAACAAAAATATGAAAAGATTAG
TGAGAAGAAGATGTCCACCCCTGTTGAAGTTTTATGTAAGGGGTTTCCTGCAGAATTCGCCATGTACTTGA
ACTACTGTCGTGGGCTGCGCTTTGAGGAAGTCCCAGATTACATGTATCTGAGGCAGCTATTCCGCATTCTT
TTCAGGACCCTGAACCACCAATATGACTACACATTTGATTGGACGATGTTAAAGCAGAAAGCAGCACAGCA
GGCAGCCTCTTCCAGTGGGCAGGGTCAGCAGGCCCAAACCCAGACAGGCAAGCAAACTGAAAAAAACAAGA
ATAATGTGAAAGATAAC

DHFR NP_000782 dihydrofolate reductase full length (1-187)
Amino acid sequence
(SEQ ID NO: 7)
MVGSLNCIVAVSQNMGIGKNGDLPWPPLRNEFRYFQRMTTTSSVEGKQNLVIMGKKTWFSIPEKNRPLKGR
INLVLSRELKEPPQGAHFLSRSLDDALKLTEQPELANKVDMVWIVGGSSVYKEAMNHPGHLKLFVTRIMQD
FESDTFFPEIDLEKYKLLPEYPGVLSDVQEEKGIKYKFEVYEKND

Encoding nucleotide sequence
(SEQ ID NO: 8)
ATGGTTGGTTCGCTAAACTGCATCGTCGCTGTGTCCCAGAACATGGGCATCGGCAAGAACGGGGACCTGCC
CTGGCCACCGCTCAGGAATGAATTCAGATATTTCCAGAGAATGACCACAACCTCTTCAGTAGAAGGTAAAC
AGAATCTGGTGATTATGGGTAAGAAGACCTGGTTCTCCATTCCTGAGAAGAATCGACCTTTAAAGGGTAGA
ATTAATTTAGTTCTCAGCAGAGAACTCAAGGAACCTCCACAAGGAGCTCATTTTCTTTCCAGAAGTCTAGA
TGATGCCTTAAAACTTACTGAACAACCAGAATTAGCAAATAAAGTAGACATGGTCTGGATAGTTGGTGGCA
GTTCTGTTTATAAGGAAGCCATGAATCACCCAGGCCATCTTAAACTATTTGTGACAAGGATCATGCAAGAC
TTTGAAAGTGACACGTTTTTTCCAGAAATTGATTTGGAGAAATATAAACTTCTGCCAGAATACCCAGGTGT
TCTCTCTGATGTCCAGGAGGAGAAAGGCATTAAGTACAAATTTGAAGTATATGAGAAGAATGAT

MBNL1 NP_066368 muscleblind-like (*Drosophila*) full length (1-382)
Amino acid sequence
(SEQ ID NO: 9)
MAVSVTPIRDTKWLTLEVCREFQRGTCSRPDTECKFAHPSKSCQVENGRVIACFDSLKGRCSRENCKYLHP
PPHLKTQLEINGRNNLIQQKNMAMLAQQMQLANAMMPGAPLQPVPMFSVAPSLATNASAAAFNPYLGPVSP
SLVPAEILPTAPMLVTGNPGVPVPAAAAAAAQKLMRTDRLEVCREYQRGNCNRGENDCRFAHPADSTMIDT
NDNTVTVCMDYIKGRCSREKCKYFHPPAHLQAKIKAAQYQVNQAAAAQAAATAAAMGIPQAVLPPLPKRPA
LEKTNGATAVFNTGIFQYQQALANMQLQQHTAFLPPGSILCMTPATSVVPMVHGATPATVSAATTSATSVP
FAATATANQIPIISAEHLTSHKYVTQM

Encoding nucleotide sequence
(SEQ ID NO: 10)
ATGGCTGTTAGTGTCACACCAATTCGGGACACAAAATGGCTAACACTGGAAGTATGTAGAGAGTTCCAGAG
GGGGACTTGCTCACGGCCAGACACGGAATGTAAATTTGCACATCCTTCGAAAAGCTGCCAAGTTGAAAATG
GACGAGTAATCGCCTGCTTTGATTCATTGAAAGGCCGTTGCTCCAGGGAGAACTGCAAATATCTTCATCCA
CCCCCACATTTAAAAACGCAGTTGGAGATAAATGGACGCAATAACTTGATTCAGCAGAAGAACATGGCCAT
GTTGGCCCAGCAAATGCAACTAGCCAATGCCATGATGCCTGGTGCCCCATTACAACCCGTGCCAATGTTTT
CAGTTGCACCAAGCTTAGCCACCAATGCATCAGCAGCCGCCTTTAATCCCTATCTGGGACCTGTTTCTCCA
AGCCTGGTCCCGGCAGAGATCTTGCCGACTGCACCAATGTTGGTTACAGGGAATCCGGGTGTCCCTGTACC
TGCAGCTGCTGCAGCTGCTGCACAGAAATTAATGCGAACAGACAGACTTGAGGTATGTCGAGAGTACCAAC
GTGGCAATTGCAACCGAGGAGAAAATGATTGTCGGTTTGCTCATCCTGCTGACAGCACAATGATTGACACC
AATGACAACACAGTCACTGTGTGTATGGATTACATCAAAGGGAGATGCTCTCGGGAAAAGTGCAAATACTT
TCATCCCCCTGCACATTTGCAAGCCAAGATCAAGGCTGCCCAATACCAGGTCAACCAGGCTGCAGCTGCAC
AGGCTGCAGCCACCGCAGCTGCCATGGGAATTCCTCAAGCTGTACTTCCCCCATTACCAAAGAGGCCTGCT
CTTGAAAAAACCAACGGTGCCACCGCAGTCTTTAACACTGGTATTTTCCAATACCAACAGGCTCTAGCCAA
CATGCAGTTACAACAGCATACAGCATTTCTCCCACCAGGCTCAATATTGTGCATGACACCCGCTACAAGTG
TTGTTCCCATGGTGCACGGTGCTACGCCAGCCACTGTGTCCGCAGCAACAACATCTGCCACAAGTGTTCCC
TTCGCTGCAACAGCCACAGCCAACCAGATACCCATAATATCTGCCGAACATCTGACTAGCCACAAGTATGT
TACCCAGATG

TP53 ABM86630 tumor protein p53 full length (1-393)
Amino acid sequence
(SEQ ID NO: 11)
MEEPQSDPSVEPPLSQETFSDLWKLLPENNVLSPLPSQAMDDLMLSPDDIEQWFTEDPGPDEAPRMPEAAP
RVAPAPAAPTPAAPAPAPSWPLSSSVPSQKTYQGSYGFRLGFLHSGTAKSVTCTYSPALNKMFCQLAKTCP
VQLWVDSTPPPGTRVRAMAIYKQSQHMTEVVRRCPHHERCSDSDGLAPPQHLIRVEGNLRVEYLDDRNTFR
HSVVVPYEPPEVGSDCTTIHYNYMCNSSCMGGMNRRPILTIITLEDSSGNLLGRNSFEVRVCACAGRDRRT
EEENLRKKGEPHHELPSGSTKRALPNNTSSSPQPKKKPLDGEYFTLQIRGRERFEMFRELNEALELKDAQA
GKEPGGSRAHSSHLKSKKGQSTSRHKKLMFKTEGPDSD

Encoding nucleotide sequence
(SEQ ID NO: 12)
ATGGAGGAGCCGCAGTCAGATCCTAGCGTCGAGCCCCCTCTGAGTCAGGAAACATTTTCAGACCTATGGAA
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CGCGTGGCCCCTGCACCAGCAGCTCCTACACCGGCGGCCCCTGCACCAGCCCCCTCCTGGCCCCTGTCATC
TTCTGTCCCTTCCCAGAAAACCTACCAGGGCAGCTACGGTTTCCGTCTGGGCTTCTTGCATTCTGGGACAG
CCAAGTCTGTGACTTGCACGTACTCCCCTGCCCTCAACAAGATGTTTTGCCAACTGGCCAAGACCTGCCCT
GTGCAGCTGTGGGTTGATTCCACACCCCCGCCCGGCACCCGCGTCCGCGCCATGGCCATCTACAAGCAGTC

TABLE 2-continued

Candidate Biomarkers

ACAGCACATGACGGAGGTTGTGAGGCGCTGCCCCCACCATGAGCGCTGCTCAGATAGCGATGGTCTGGCCC
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CATAGTGTGGTGGTGCCCTATGAGCCGCCTGAGGTTGGCTCTGACTGTACCACCATCCACTACAACTACAT
GTGTAACAGTTCCTGCATGGGCGGCATGAACCGGAGGCCCATCCTCACCATCATCACACTGGAAGACTCCA
GTGGTAATCTACTGGGACGGAACAGCTTTGAGGTGCGTGTTTGTGCCTGTGCTGGGAGAGACCGGCGCACA
GAGGAAGAGAATCTCCGCAAGAAAGGGGAGCCTCACCACGAGCTGCCCTCAGGGAGCACTAAGCGAGCACT
GCCCAACAACACCAGCTCCTCTCCCCAGCCAAAGAAGAAACCACTGGATGGAGAATATTTCACCCTTCAGA
TCCGTGGGCGTGAGCGCTTCGAGATGTTCCGAGAGCTGAATGAGGCCTTGGAACTCAAGGATGCCCAGGCT
GGGAAGGAGCCAGGGGGGAGCAGGGCTCACTCCAGCCACCTGAAGTCCAAAAAGGGTCAGTCTACCTCCCG
CCATAAAAAACTCATGTTCAAGACAGAAGGGCCTGACTCAGAC

PRL NP_000939 prolactin full length (1-227)
Amino acid sequence
(SEQ ID NO: 13)
MNIKGSPWKGSLLLLLVSNLLLCQSVAPLPICPGGAARCQVTLRDLFDRAVVLSHYIHNLSSEMFSEFDKR
YTHGRGFITKAINSCHTSSLATPEDKEQAQQMNQKDFLSLIVSILRSWNEPLYHLVTEVRGMQEAPEAILS
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LKLLKCRIIHNNNC

Encoding nucleotide sequence
(SEQ ID NO: 14)
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ACCGCGCCGTCGTCCTGTCCCACTACATCCATAACCTCTCCTCAGAAATGTTCAGCGAATTCGATAAACGG
TATACCCATGGCCGGGGGTTCATTACCAAGGCCATCAACAGCTGCCACACTTCTTCCCTTGCCACCCCCGA
AGACAAGGAGCAAGCCCAACAGATGAATCAAAAAGACTTTCTGAGCCTGATAGTCAGCATATTGCGATCCT
GGAATGAGCCTCTGTATCATCTGGTCACGGAAGTACGTGGTATGCAAGAAGCCCCGGAGGCTATCCTATCC
AAAGCTGTAGAGATTGAGGAGCAAACCAAACGGCTTCTAGAGGGCATGGAGCTGATAGTCAGCCAGGTTCA
TCCTGAAACCAAAGAAAATGAGATCTACCCTGTCTGGTCGGGACTTCCATCCCTGCAGATGGCTGATGAAG
AGTCTCGCCTTTCTGCTTATTATAACCTGCTCCACTGCCTACGCAGGGATTCACATAAAATCGACAATTAT
CTCAAGCTCCTGAAGTGCCGAATCATCCACAACAACAACTGCTTG

PSMC1 NP_032973 proteasome (prosome, macropain) 26S subunit, ATPase,
1 full length (1-440)
Amino acid sequence
(SEQ ID NO: 15)
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LLMEEEFIRNQEQMKPLEEKQEEERSKVDDLRGTPMSVGTLEEIIDDNHAIVSTSVGSEHYVSILSFVDKD
LLEPGCSVLLNHKVHAVIGVLMDDTDPLVTVMKVEKAPQETYADIGGLDNQIQEIKESVELPLTHPEYYEE
MGIKPPKGVILYGPPGTGKTLLAKAVANQTSATFLRVVGSELIQKYLGDGPKLVRELFRVAEEHAPSIVFI
DEIDAIGTKRYDSNSGGEREIQRTMLELLNQLDGFDSRGDVKVIMATNRIETLDPALIRPGRIDRKIEFPL
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LYKKQEGTPEGLYL

Encoding nucleotide sequence
(SEQ ID NO: 16)
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AACTGCCACTGGTGACACCTCACACTCAGTGCCGGTTAAAATTACTGAAGTTAGAGAGAATTAAAGACTAT
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CTGCTGGAACCTGGCTGCTCGGTCCTGCTCAACCACAAGGTGCATGCCGTGATAGGGGTGCTGATGGATGA
CACGGATCCCCTGGTCACAGTGATGAAGGTAGAAAAGGCCCCCCAGGAGACCTATGCAGATATTGGGGGGT
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GTGATGGGCCCAAACTCGTACGGGAATTGTTCCGAGTTGCTGAAGAACATGCACCGTCCATCGTGTTTATT
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AATGTTGGAACTGCTGAACCAGTTGGATGGATTTGATTCTAGGGGAGATGTGAAAGTTATCATGGCCACAA
ACCGAATAGAAACTTTGGATCCAGCACTTATCAGACCAGGCCGCATTGACAGGAAGATTGAGTTCCCCCTG
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CCTGGACGACCTGATCATGGCTAAAGATGACCTCTCTGGTGCTGACATCAAGGCAATCTGTACAGAAGCTG
GTCTGATGGCCTTAAGAGAACGTAGAATGAAAGTAACAAATGAAGACTTCAAAAAATCTAAAGAAAATGTT
CTTTATAAGAAACAGGAAGGCACCCCTGAGGGGCTGTATCTC

PTGFR NP_000950 prostaglandin F receptor (FP) full length (1-359)
Amino acid sequence
(SEQ ID NO: 17)
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GLVITDFFGHLINGAIAVFVYASDKEWIRFDQSNVLCSIFGICMVFSGLCPLLLGSVMAIERCIGVTKPIF
HSTKITSKHVKMMLSGVCLFAVFIALLPILGHRDYKIQASRTWCFYNTEDIKDWEDRFYLLLFSFLGLLAL

TABLE 2-continued

Candidate Biomarkers

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SAST

Encoding nucleotide sequence

(SEQ ID NO: 18)

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TCGCCATTCTCATGAAGGCATATCAGAGATTTAGACAGAAGTCCAAGGCATCGTTTCTGCTTTTGGCCAGT
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TAAAGAATGGATCCGCTTTGACCAATCAAATGTCCTTTGCAGTATTTTTGGTATCTGCATGGTGTTTTCTG
GTCTGTGCCCACTTCTTCTAGGCAGTGTGATGGCCATTGAGCGGTGTATTGGAGTCACAAAACCAATATTT
CATTCTACGAAAATTACATCCAAACATGTGAAAATGATGTTAAGTGGTGTGTGCTTGTTTGCTGTTTTCAT
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CAGAAGACATCAAAGACTGGGAAGATAGATTTTATCTTCTACTTTTTTCTTTTCTGGGGCTCTTAGCCCTT
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AAAGGCTGTCCTTAAGAATCTCTATAAGCTTGCCAGTCAATGCTGTGGAGTGCATGTCATCAGCTTACATA
TTTGGGAGCTTAGTTCCATTAAAAATTCCTTAAAGGTTGCTGCTATTTCTGAGTCACCAGTTGCAGAGAAA
TCAGCAAGCACC

PTPRA NP_543030 protein tyrosine phosphatase, receptor type, A full length (1-793)
Amino acid sequence

(SEQ ID NO: 19)

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VDKLEEEINRRMADDNKLFREEFNALPACPIQATCEAASKEENKEKNRYVNILPYDHSRVHLTPVEGVPDS
DYINASFINGYQEKNKFIAAQGPKEETVNDFWRMIWEQNTATIVMVTNLKERKECKCAQYWPDQGCWTYGN
IRVSVEDVTVLVDYTVRKFCIQQVGDMTNRKPQRLITQFHFTSWPDFGVPFTPIGMLKFLKKVKACNPQYA
GAIVVHCSAGVGRTGTFVVIDAMLDMMHTERKVDVYGFVSRIRAQRCQMVQTDMQYVFIYQALLEHYLYGD
TELEVTSLETHLQKIYNKIPGTSNNGLEEEFKKLTSIKIQNDKMRTGNLPANMKKNRVLQIIPYEFNRVII
PVKRGEENTDYVNASFIDGYRQKDSYIASQGPLLHTIEDFWRMIWEWKSCSIVMLTELEERGQEKCAQYWP
SDGLVSYGDITVELKKEEECESYTVRDLLVTNTRENKSRQIRQFHFHGWPEVGIPSDGKGMISIIAAVQKQ
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YIDAFSDYANFK

Encoding nucleotide sequence

(SEQ ID NO: 20)

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GTGGACAAGCTGGAAGAGGAAATTAACCGGAGAATGGCAGACGACAATAAGCTCTTCAGGGAGGAATTCAA
CGCTCTCCCTGCATGTCCTATCCAGGCCACCTGTGAGGCTGCTTCCAAGGAGGAAAACAAGGAAAAAAATC
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GATTACATCAATGCTTCATTCATCAACGGTTACCAAGAAAAGAACAAATTCATTGCTGCACAAGGACCAAA
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GGGCGACATGACCAACAGAAAGCCACAGCGCCTCATCACTCAGTTCCACTTTACCAGCTGGCCAGACTTTG
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CTCCTATATCGCCAGCCAGGGCCCTCTTCTCCACACAATTGAGGACTTCTGGCGAATGATCTGGGAGTGGA
AATCCTGCTCTATCGTGATGCTAACAGAACTGGAGGAGAGAGGCCAGGAGAAGTGTGCCCAGTACTGGCCA
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TABLE 2-continued

| Candidate Biomarkers |
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| CGTCCGAGACCTCCTGGTCACCAACACCAGGGAGAATAAGAGCCGGCAGATCCGGCAGTTCCACTTCCATG<br>GCTGGCCTGAAGTGGGCATCCCCAGTGACGGAAAGGGCATGATCAGCATCATCGCCGCCGTGCAGAAGCAG<br>CAGCAGCAGTCAGGGAACCACCCCATCACCGTGCACTGCAGCGCCGGGGCAGGAAGGACGGGGACCTTCTG<br>TGCCCTGAGCACCGTCCTGGAGCGTGTGAAAGCAGAGGGGATTTTGGATGTCTTCCAGACTGTCAAGAGCC<br>TGCGGCTACAGAGGCCACACATGGTCCAGACACTGGAACAGTATGAGTTCTGCTACAAGGTGGTGCAGGAG<br>TATATTGATGCATTCTCAGATTATGCCAACTTCAAG |
| RAB7L1 NP_003920 RAB7, member RAS oncogene family-like 1 full<br>length (1-203)<br>Amino acid sequence<br>(SEQ ID NO: 21)<br>MGSRDHLFKVLVVGDAAVGKTSLVQRYSQDSFSKHYKSTVGVDFALKVLQWSDYEIVRLQLWDIAGQERFT<br>SMTRLYYRDASACVIMFDVTNATTFSNSQRWKQDLDSKLTLPNGEPVPCLLLANKCDLSPWAVSRDQIDRF<br>SKENGFTGWTETSVKENKNINEAMRVLIEKMMRNSTEDIMSLSTQGDYINLQTKSSSWSCC |
| Encoding nucleotide sequence<br>(SEQ ID NO: 22)<br>ATGGGCAGCCGCGACCACCTGTTCAAAGTGCTGGTGGTGGGGGACGCCGCAGTGGGCAAGACGTCGCTGGT<br>GCAGCGATATTCCCAGGACAGCTTCAGCAAACACTACAAGTCCACGGTGGGAGTGGATTTTGCTCTGAAGG<br>TTCTCCAGTGGTCTGACTACGAGATAGTGCGGCTTCAGCTGTGGGATATTGCAGGGCAGGAGCGCTTCACC<br>TCTATGACACGATTGTATTATCGGGATGCCTCTGCCTGTGTTATTATGTTTGACGTTACCAATGCCACTAC<br>CTTCAGCAACAGCCAGAGGTGGAAACAGGACCTAGACAGCAAGCTCACACTACCCAATGGAGAGCCGGTGC<br>CCTGCCTGCTCTTGGCCAACAAGTGTGATCTGTCCCCTTGGGCAGTGAGCCGGGACCAGATTGACCGGTTC<br>AGTAAAGAGAACGGTTTCACAGGTTGGACAGAAACATCAGTCAAGGAGAACAAAAATATTAATGAGGCTAT<br>GAGAGTCCTCATTGAAAAGATGATGAGAAATTCCACAGAAGATATCATGTCTTTGTCCACCCAAGGGGACT<br>ACATCAATCTACAAACCAAGTCCTCCAGCTGGTCCTGCTGC |
| SCYL3 NP_065156 SCY1-like 3 (*S. cerevisiae*) full length (1-688), G543A<br>Amino acid sequence<br>(SEQ ID NO: 23)<br>MGSENSALKSYTLREPPFTLPSGLAVYPAVLQDGKFASVFVYKRENEDKVNKAAKHLKTLRHPCLLRFLSC<br>TVEADGIHLVTERVQPLEVALETLSSAEVCAGIYDILLALIFLHDRGHLTHNNVCLSSVFVSEDGHWKLGG<br>METVCKVSQATPEFLRSIQSIRDPASIPPEEMSPEFTTLPECHGHARDAFSFGTLVESLLTILNEQVSADV<br>LSSFQQTLHSTLLNPIPKCRPALCTLLSHDFFRNDFLEVVNFLKSLTLKSEEEKTEFFKFLLDRVSCLSEE<br>LIASRLVPLLLNQLVFAEPVAVKSFLPYLLGPKKDHAQGETPCLLSPALFQSRVIPVLLQLFEVHEEHVRM<br>VLLSHIEAYVEHFTQEQLKKVILPQVLLGLRDTSDSIVAITLHSLAVLVSLLGPEVVVGGERTKIFKRTAP<br>SFTKNTDLSLEGDPFSQPIKFPINGLSDVKNTSEDSENFPSSSKKSEEWPDWSEPEEPENQTVNIQIWPRE<br>PCDDVKSQCTTLDVEESSWDDCEPSSLDTKVNPGGGITATKPVTSAEQKPIPALLSLTEESMPWKSSLPQK<br>ISLVQRGDDADQIEPPKVSSQERPLKVPSELGLGEEFTIQVKKKPVKDPEMDWFADMIPEIKPSAAFLILP<br>ELRTEMVPKKDDVSPVMQFSSKFAAAEITEGEAEGWEEEGELNWEDNNW |
| Encoding nucleotide sequence<br>(SEQ ID NO: 24)<br>ATGGGATCAGAGAACAGTGCTTTAAAGAGCTATACACTGAGAGAACCACCATTTACCTTACCCTCTGGACT<br>TGCTGTTTATCCCGCTGTACTGCAAGATGGCAAATTTGCTTCAGTTTTTGTGTATAAGAGAGAAAATGAAG<br>ACAAGGTTAATAAAGCTGCCAAGCATTTGAAGACACTTCGTCACCCTTGCTTGCTAAGATTTTTATCTTGT<br>ACTGTGGAAGCGGATGGCATTCATCTTGTCACTGAGCGAGTACAGCCCCTGGAAGTGGCTTTGGAAACATT<br>GTCTTCTGCAGAGGTCTGTGCTGGGATCTATGACATATTGCTGGCTCTTATCTTCCTTCATGACAGAGGAC<br>ACCTAACACACAATAATGTCTGTTTATCATCTGTGTTTGTGAGTGAAGATGGACACTGGAAGCTAGGAGGA<br>ATGGAAACTGTTTGTAAAGTTTCTCAGGCCACACCAGAGTTTCTGAGGAGTATTCAGTCAATAAGAGACCC<br>AGCATCTATCCCTCCTGAAGAGATGTCTCCAGAATTCACAACTCTCCCAGAGTGTCATGGACATGCCCGGG<br>ATGCCTTTTCATTTGGAACATTGGTGGAAAGTTTGCTCACAATCTTAAATGAACAGGTTTCAGCGGATGTT<br>CTCTCCAGCTTTCAACAGACCTTGCACTCAACTTTGCTGAATCCCATTCCAAAATGTCGGCCAGCGCTCTG<br>CACCTTACTATCTCATGACTTCTTCAGAAATGATTTTCTGGAAGTTGTGAATTTCTTGAAAAGTTTAACAT<br>TGAAGAGTGAAGAGGAGAAAACGGAATTCTTTAAATTTCTGCTGGACAGAGTCAGCTGCTTGTCAGAGGAA<br>TTGATAGCTTCAAGGTTGGTGCCTCTTCTGCTTAATCAGTTGGTGTTTGCAGAGCCAGTGGCTGTTAAGAG<br>TTTTCTTCCTTATCTGCTTGGCCCCAAAAAAGATCATGCGCAGGGAGAAACTCCTTGCTTGCTCTCACCAG<br>CCCTGTTCCAGTCACGGGTGATCCCCGTGCTTCTCCAGTTGTTTGAAGTTCATGAAGAGCATGTGCGGATG<br>GTGCTGCTGTCTCACATCGAGGCCTACGTGGAGCACTTCACTCAGGAGCAGCTGAAGAAAGTCATCTTGCC<br>ACAGGTTTTGCTGGGCCTGCGTGATACTAGTGATTCCATTGTGGCAATTACTCTGCATAGCCTAGCAGTGC<br>TGGTCTCTCTGCTTGGACCAGAGGTGGTTGTGGGAGGAGAACGAACCAAGATCTTCAAACGCACTGCCCCA<br>AGTTTTACTAAAAATACTGACCTTTCTCTAGAAGGTGATCCATTTTCTCAGCCTATTAAATTTCCCATAAA<br>CGGACTCTCAGATGTAAAAAATACTTCGGAGGACAGTGAAAACTTCCCATCAAGTTCTAAAAAGTCTGAGG<br>AGTGGCCTGACTGGAGTGAACCTGAGGAGCCTGAAAATCAAACTGTCAACATACAGATTTGGCCTAGAGAA<br>CCTTGTGATGATGTCAAGTCCCAGTGCACTACCTTGGATGTGGAAGAGTCATCTTGGGATGACTGCGAGCC<br>CAGCAGCTTAGATACTAAAGTAAACCCAGGAGGTGGAATCACTGCTACAAAACCTGTTACCTCAGCGGAGC<br>AGAAGCCTATTCCTGCTTTGCTTTCACTCACTGAAGAGTCTATGCCTTGGAAATCAAGCTTACCCCAAAAG<br>ATTAGCCTTGTACAAAGGGGGGATGACGCAGACCAAATCGAGCCGCCAAAAGTGTCATCACAAGAAAGGCC<br>CCTTAAGGTTCCATCAGAACTTGGTTTAGGAGAGGAATTCACCATTCAAGTAAAAAAGAAGCCAGTAAAAG<br>ATCCTGAGATGGATTGGTTTGCTGATATGATCCCAGAAATTAAGCCTTCTGCTGCTTTTCTTATATTACCT<br>GAACTGAGGACAGAAATGGTCCCAAAAAAGGATGATGTCTCCCCAGTGATGCAGTTTTCCTCAAAATTTGC<br>TGCAGCAGAAATTACTGAGGGAGAGGCTGAAGGCTGGGAAGAAGAAGGGGAGCTGAACTGGGAAGATAATA<br>ACTGG |

The claims are not meant to be limited to the materials and methods, embodiments, and examples described herein.

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                               SEQUENCE LISTING


<160> NUMBER OF SEQ ID NOS: 24

<210> SEQ ID NO 1
<211> LENGTH: 724
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 1

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Ile Val Arg Thr Thr Gln Glu Lys Leu Lys Thr Ser Ser Leu Thr Asp
        35                  40                  45

Arg Gln Pro Leu Ser Lys Glu Ser Leu Asn His Ala Leu Glu Leu Ser
    50                  55                  60

Val Pro Glu Lys Val Asn Asn Ala Gln Trp Asp Ala Pro Glu Glu Ala
65                  70                  75                  80

Leu Trp Thr Thr Arg Ala Asp Gly Arg Val Arg Leu Arg Ile Asp Pro
                85                  90                  95

Ser Cys Pro Gln Leu Pro Tyr Thr Val His Arg Met Phe Tyr Glu Ala
            100                 105                 110

Leu Asp Lys Tyr Gly Asp Leu Ile Ala Leu Gly Phe Lys Arg Gln Asp
        115                 120                 125

Lys Trp Glu His Ile Ser Tyr Ser Gln Tyr Tyr Leu Leu Ala Arg Arg
    130                 135                 140

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

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                165                 170                 175

Thr Val Phe Ala Gly Gly Ile Val Thr Gly Ile Tyr Thr Thr Ser Ser
            180                 185                 190

Pro Glu Ala Cys Gln Tyr Ile Ala Tyr Asp Cys Cys Ala Asn Val Ile
        195                 200                 205

Met Val Asp Thr Gln Lys Gln Leu Glu Lys Ile Leu Lys Ile Trp Lys
    210                 215                 220

Gln Leu Pro His Leu Lys Ala Val Val Ile Tyr Lys Glu Pro Pro Pro
225                 230                 235                 240

Asn Lys Met Ala Asn Val Tyr Thr Met Glu Glu Phe Met Glu Leu Gly
                245                 250                 255

Asn Glu Val Pro Glu Glu Ala Leu Asp Ala Ile Ile Asp Thr Gln Gln
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Pro Asn Gln Cys Cys Val Leu Val Tyr Thr Ser Gly Thr Thr Gly Asn
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Pro Lys Gly Val Met Leu Ser Gln Asp Asn Ile Thr Trp Thr Ala Arg
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Tyr Gly Ser Gln Ala Gly Asp Ile Arg Pro Ala Glu Val Gln Gln Glu
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Val Val Val Ser Tyr Leu Pro Leu Ser His Ile Ala Ala Gln Ile Tyr
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Pro Thr Ser His Met Gly Val Pro Arg Val Trp Glu Lys Ile Met Glu
    370                 375                 380

Arg Ile Gln Glu Val Ala Ala Gln Ser Gly Phe Ile Arg Arg Lys Met
385                 390                 395                 400

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Phe Tyr Gly Ala Ala Pro Met Met Ala Glu Thr Gln His Phe Phe Leu
    450                 455                 460

Gly Leu Asn Ile Arg Leu Tyr Ala Gly Tyr Gly Leu Ser Glu Thr Ser
465                 470                 475                 480

Gly Pro His Phe Met Ser Ser Pro Tyr Asn Tyr Arg Leu Tyr Ser Ser
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Gly Lys Leu Val Pro Gly Cys Arg Val Lys Leu Val Asn Gln Asp Ala
            500                 505                 510

Glu Gly Ile Gly Glu Ile Cys Leu Trp Gly Arg Thr Ile Phe Met Gly
        515                 520                 525

Tyr Leu Asn Met Glu Asp Lys Thr Cys Glu Ala Ile Asp Glu Glu Gly
    530                 535                 540

Trp Leu His Thr Gly Asp Ala Gly Arg Leu Asp Ala Asp Gly Phe Leu
545                 550                 555                 560

Tyr Ile Thr Gly Arg Leu Lys Glu Leu Ile Ile Thr Ala Gly Gly Glu
                565                 570                 575

Asn Val Pro Pro Val Pro Ile Glu Glu Ala Val Lys Met Glu Leu Pro
            580                 585                 590

Ile Ile Ser Asn Ala Met Leu Ile Gly Asp Gln Arg Lys Phe Leu Ser
        595                 600                 605

Met Leu Leu Thr Leu Lys Cys Thr Leu Asp Pro Asp Thr Ser Asp Gln
    610                 615                 620

Thr Asp Asn Leu Thr Glu Gln Ala Val Glu Phe Cys Gln Arg Val Gly
625                 630                 635                 640

Ser Arg Ala Thr Thr Val Ser Glu Ile Ile Glu Lys Lys Asp Glu Ala
                645                 650                 655

Val Tyr Gln Ala Ile Glu Glu Gly Ile Arg Arg Val Asn Met Asn Ala
            660                 665                 670

Ala Ala Arg Pro Tyr His Ile Gln Lys Trp Ala Ile Leu Glu Arg Asp
        675                 680                 685

Phe Ser Ile Ser Gly Gly Glu Leu Gly Pro Thr Met Lys Leu Lys Arg
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Glu Gln Lys Met


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<213> ORGANISM: Homo Sapiens

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ttgaaaacca gctcactgac tgacaggcag ccactctcca aagagtccct gaaccatgct 180

ctcgagctct cagtgccaga gaaggtgaat aatgcccagt gggatgctcc agaggaggcg 240

ctgtggacga ctcgggccga tgggcgggtg cgcctgcgca tagaccccag ctgcccacag 300

cttccctaca ctgtgcatcg gatgttctac gaggccctgg ataagtatgg ggacctcatc 360

gctttgggct tcaagcgcca ggacaagtgg gaacacatct cctactccca atactacctg 420

ctcgcccgca gagccgccaa gggcttcctg aagctcggcc tgaagcaggc ccacagtgtg 480

gccatcctcg gcttcaactc cccggagtgg ttcttctcgg cagtgggcac agtatttgca 540

ggtggcatcg tcactggcat ctacaccacc agctccccag aggcctgcca gtacatcgct 600

tatgactgct gcgccaatgt catcatggtc gacacgcaga agcagctgga aaagatcctg 660

aagatctgga aacagttgcc acatctaaag gcagtcgtga tatataaaga acctcctcca 720

aacaagatgg ccaatgtgta cacgatggag gaattcatgg agctggggaa tgaagtgcct 780

gaggaagccc tggacgccat cattgacacc cagcagccca accagtgctg tgtgctagtc 840

tacacttccg gcaccactgg gaaccccaag ggcgtgatgc tgagtcaaga caatatcacg 900

tggacggcac ggtacggcag ccaggccggt gacatccggc cggcagaagt ccagcaggag 960

gtggtagtca gctacctgcc cctcagccat attgccgccc agatctacga cctgtggaca 1020

ggcatccagt gggggcccca ggtttgcttt gccgaacccg acgccctgaa ggggagcctg 1080

gtgaacacgc tgcgggaggt ggagcccaca tcacacatgg gggtgccccg ggtatgggag 1140

aagatcatgg agcgcatcca ggaggtggcg gctcagtctg gcttcatccg gcggaagatg 1200

ctgctgtggg ccatgtcggt gaccttggag cagaacctca cctgccccgg cagcgacctg 1260

aagcccttca caaccagact ggcagattac ctggtgctag ccaaggttcg ccaggcactg 1320

ggatttgcca agtgtcaaaa gaacttctat ggagcggccc ccatgatggc agagacacag 1380

cacttcttcc tgggtctcaa catccgcttg tatgcgggct atggcctcag tgagacctca 1440

ggcccccact tcatgtccag tccctacaac taccggctgt acagctcagg caagttggtg 1500

cccggctgtc gggtgaagct ggtgaaccag gacgcagagg gcattggtga gatctgcctg 1560

tggggccgca ccatattcat gggctacctg aacatggagg acaagacttg tgaggccatc 1620

gacgaggaag gctggctgca cacgggtgat gctggccgcc tggacgccga tggcttcctc 1680

tacatcactg ggcgcctcaa agaattaatc atcacagctg gtggggagaa tgtgcccccct 1740

gtgcccatcg aggaggccgt gaagatggag ctgcccatca tcagcaatgc catgctcatt 1800

ggggaccaga ggaagttcct gtccatgctg ctcaccttga agtgcactct ggacccagac 1860

acctctgacc agactgataa tctgactgaa caagctgtgg agttctgcca gagggtgggc 1920

agcagagcca ccacagtgtc cgagatcata gagaagaagg atgaggccgt gtaccaggcc 1980

atcgaagagg ggatccggag ggtcaacatg aacgcggcgg cccggcccta ccacatccag 2040

aagtgggcca ttctcgagag agacttctcc atttcgggtg gagagttggg tcccacgatg 2100

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aaactgaaac ggctcacagt tttggagaag tacaaaggta tcattgactc cttttaccaa   2160

gagcaaaaaa tg                                                       2172


<210> SEQ ID NO 3
<211> LENGTH: 609
<212> TYPE: PRT
<213> ORGANISM: Homo Sapiens

<400> SEQUENCE: 3

Met Lys Trp Val Glu Ser Ile Phe Leu Ile Phe Leu Leu Asn Phe Thr
1               5                   10                  15

Glu Ser Arg Thr Leu His Arg Asn Glu Tyr Gly Ile Ala Ser Ile Leu
            20                  25                  30

Asp Ser Tyr Gln Cys Thr Ala Glu Ile Ser Leu Ala Asp Leu Ala Thr
        35                  40                  45

Ile Phe Phe Ala Gln Phe Val Gln Glu Ala Thr Tyr Lys Glu Val Ser
    50                  55                  60

Lys Met Val Lys Asp Ala Leu Thr Ala Ile Glu Lys Pro Thr Gly Asp
65                  70                  75                  80

Glu Gln Ser Ser Gly Cys Leu Glu Asn Gln Leu Pro Ala Phe Leu Glu
                85                  90                  95

Glu Leu Cys His Glu Lys Glu Ile Leu Glu Lys Tyr Gly His Ser Asp
            100                 105                 110

Cys Cys Ser Gln Ser Glu Glu Gly Arg His Asn Cys Phe Leu Ala His
        115                 120                 125

Lys Lys Pro Thr Pro Ala Ser Ile Pro Leu Phe Gln Val Pro Glu Pro
    130                 135                 140

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

Lys Phe Ile Tyr Glu Ile Ala Arg Arg His Pro Phe Leu Tyr Ala Pro
                165                 170                 175

Thr Ile Leu Leu Trp Ala Ala Arg Tyr Asp Lys Ile Ile Pro Ser Cys
            180                 185                 190

Cys Lys Ala Glu Asn Ala Val Glu Cys Phe Gln Thr Lys Ala Ala Thr
        195                 200                 205

Val Thr Lys Glu Leu Arg Glu Ser Ser Leu Leu Asn Gln His Ala Cys
    210                 215                 220

Ala Val Met Lys Asn Phe Gly Thr Arg Thr Phe Gln Ala Ile Thr Val
225                 230                 235                 240

Thr Lys Leu Ser Gln Lys Phe Thr Lys Val Asn Phe Thr Glu Ile Gln
                245                 250                 255

Lys Leu Val Leu Asp Val Ala His Val His Glu His Cys Cys Arg Gly
            260                 265                 270

Asp Val Leu Asp Cys Leu Gln Asp Gly Glu Lys Ile Met Ser Tyr Ile
        275                 280                 285

Cys Ser Gln Gln Asp Thr Leu Ser Asn Lys Ile Thr Glu Cys Cys Lys
    290                 295                 300

Leu Thr Thr Leu Glu Arg Gly Gln Cys Ile Ile His Ala Glu Asn Asp
305                 310                 315                 320

Glu Lys Pro Glu Gly Leu Ser Pro Asn Leu Asn Arg Phe Leu Gly Asp
                325                 330                 335

Arg Asp Phe Asn Gln Phe Ser Ser Gly Glu Lys Asn Ile Phe Leu Ala
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            340                 345                 350

Ser Phe Val His Glu Tyr Ser Arg Arg His Pro Gln Leu Ala Val Ser
        355                 360                 365

Val Ile Leu Arg Val Ala Lys Gly Tyr Gln Glu Leu Leu Glu Lys Cys
    370                 375                 380

Phe Gln Thr Glu Asn Pro Leu Glu Cys Gln Asp Lys Gly Glu Glu Glu
385                 390                 395                 400

Leu Gln Lys Tyr Ile Gln Glu Ser Gln Ala Leu Ala Lys Arg Ser Cys
                405                 410                 415

Gly Leu Phe Gln Lys Leu Gly Glu Tyr Tyr Leu Gln Asn Ala Phe Leu
            420                 425                 430

Val Ala Tyr Thr Lys Lys Ala Pro Gln Leu Thr Ser Ser Glu Leu Met
        435                 440                 445

Ala Ile Thr Arg Lys Met Ala Ala Thr Ala Ala Thr Cys Cys Gln Leu
    450                 455                 460

Ser Glu Asp Lys Leu Leu Ala Cys Gly Glu Gly Ala Ala Asp Ile Ile
465                 470                 475                 480

Ile Gly His Leu Cys Ile Arg His Glu Met Thr Pro Val Asn Pro Gly
                485                 490                 495

Val Gly Gln Cys Cys Thr Ser Ser Tyr Ala Asn Arg Arg Pro Cys Phe
            500                 505                 510

Ser Ser Leu Val Val Asp Glu Thr Tyr Val Pro Pro Ala Phe Ser Asp
        515                 520                 525

Asp Lys Phe Ile Phe His Lys Asp Leu Cys Gln Ala Gln Gly Val Ala
    530                 535                 540

Leu Gln Thr Met Lys Gln Glu Phe Leu Ile Asn Leu Val Lys Gln Lys
545                 550                 555                 560

Pro Gln Ile Thr Glu Glu Gln Leu Glu Ala Val Ile Ala Asp Phe Ser
                565                 570                 575

Gly Leu Leu Glu Lys Cys Cys Gln Gly Gln Glu Gln Glu Val Cys Phe
            580                 585                 590

Ala Glu Glu Gly Gln Lys Leu Ile Ser Lys Thr Arg Ala Ala Leu Gly
        595                 600                 605

Val


<210> SEQ ID NO 4
<211> LENGTH: 1827
<212> TYPE: DNA
<213> ORGANISM: Homo Sapiens

<400> SEQUENCE: 4

atgaagtggg tggaatcaat ttttttaatt ttcctactaa attttactga atccagaaca      60

ctgcatagaa atgaatatgg aatagcttcc atattggatt cttaccaatg tactgcagag     120

ataagtttag ctgacctggc taccatattt tttgcccagt ttgttcaaga agccacttac     180

aaggaagtaa gcaaaatggt gaaagatgca ttgactgcaa ttgagaaacc cactggagat     240

gaacagtctt cagggtgttt agaaaaccag ctacctgcct ttctggaaga actttgccat     300

gagaaagaaa ttttggagaa gtacggacat tcagactgct gcagccaaag tgaagaggga     360

agacataact gttttcttgc acacaaaaag cccactccag catcgatccc acttttccaa     420

gttccagaac ctgtcacaag ctgtgaagca tatgaagaag acagggagac attcatgaac     480
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aaattcattt atgagatagc aagaaggcat cccttcctgt atgcacctac aattcttctt    540

tgggctgctc gctatgacaa aataattcca tcttgctgca aagctgaaaa tgcagttgaa    600

tgcttccaaa caaaggcagc aacagttaca aaagaattaa gagaaagcag cttgttaaat    660

caacatgcat gtgcagtaat gaaaaatttt gggacccgaa ctttccaagc cataactgtt    720

actaaactga gtcagaagtt taccaaagtt aattttactg aaatccagaa actagtcctg    780

gatgtggccc atgtacatga gcactgttgc agaggagatg tgctggattg tctgcaggat    840

ggggaaaaaa tcatgtccta catatgttct caacaagaca ctctgtcaaa caaaataaca    900

gaatgctgca aactgaccac gctggaacgt ggtcaatgta taattcatgc agaaaatgat    960

gaaaaacctg aaggtctatc tccaaatcta aacaggtttt taggagatag agattttaac   1020

caattttctt caggggaaaa aaatatcttc ttggcaagtt ttgttcatga atattcaaga   1080

agacatcctc agcttgctgt ctcagtaatt ctaagagttg ctaaaggata ccaggagtta   1140

ttggagaagt gtttccagac tgaaaaccct cttgaatgcc aagataaagg agaagaagaa   1200

ttacagaaat acatccagga gagccaagca ttggcaaagc gaagctgcgg cctcttccag   1260

aaactaggag aatattactt acaaaatgcg tttctcgttg cttacacaaa gaaagccccc   1320

cagctgacct cgtcggagct gatggccatc accagaaaaa tggcagccac agcagccact   1380

tgttgccaac tcagtgagga caaactattg gcctgtggcg agggagcggc tgacattatt   1440

atcggacact tatgtatcag acatgaaatg actccagtaa accctggtgt tggccagtgc   1500

tgcacttctt catatgccaa caggaggcca tgcttcagca gcttggtggt ggatgaaaca   1560

tatgtccctc ctgcattctc tgatgacaag ttcattttcc ataaggatct gtgccaagct   1620

cagggtgtag cgctgcaaac gatgaagcaa gagtttctca ttaaccttgt gaagcaaaag   1680

ccacaaataa cagaggaaca acttgaggct gtcattgcag atttctcagg cctgttggag   1740

aaatgctgcc aaggccagga acaggaagtc tgctttgctg aagagggaca aaaactgatt   1800

tcaaaaactc gtgctgcttt gggagtt                                        1827
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<210> SEQ ID NO 5
<211> LENGTH: 337
<212> TYPE: PRT
<213> ORGANISM: Homo Sapiens

<400> SEQUENCE: 5

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

Tyr Lys Leu Val Arg Lys Ile Gly Ser Gly Ser Phe Gly Asp Val Tyr
            20                  25                  30

Leu Gly Ile Thr Thr Thr Asn Gly Glu Glu Val Ala Val Lys Leu Glu
        35                  40                  45

Ser Gln Lys Val Lys His Pro Gln Leu Leu Tyr Glu Ser Lys Leu Tyr
    50                  55                  60

Thr Ile Leu Gln Gly Gly Val Gly Ile Pro His Met His Trp Tyr Gly
65                  70                  75                  80

Gln Glu Lys Asp Asn Asn Val Leu Val Met Asp Leu Leu Gly Pro Ser
                85                  90                  95

Leu Glu Asp Leu Phe Asn Phe Cys Ser Arg Arg Phe Thr Met Lys Thr
            100                 105                 110

Val Leu Met Leu Ala Asp Gln Met Ile Ser Arg Ile Glu Tyr Val His
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        115                 120                 125

Thr Lys Asn Phe Leu His Arg Asp Ile Lys Pro Asp Asn Phe Leu Met
    130                 135                 140

Gly Thr Gly Arg His Cys Asn Lys Leu Phe Leu Ile Asp Phe Gly Leu
145                 150                 155                 160

Ala Lys Lys Tyr Arg Asp Asn Arg Thr Arg Gln His Ile Pro Tyr Arg
                165                 170                 175

Glu Asp Lys His Leu Ile Gly Thr Val Arg Tyr Ala Ser Ile Asn Ala
            180                 185                 190

His Leu Gly Ile Glu Gln Ser Arg Arg Asp Asp Met Glu Ser Leu Gly
        195                 200                 205

Tyr Val Phe Met Tyr Phe Asn Arg Thr Ser Leu Pro Trp Gln Gly Leu
    210                 215                 220

Lys Ala Met Thr Lys Lys Gln Lys Tyr Glu Lys Ile Ser Glu Lys Lys
225                 230                 235                 240

Met Ser Thr Pro Val Glu Val Leu Cys Lys Gly Phe Pro Ala Glu Phe
                245                 250                 255

Ala Met Tyr Leu Asn Tyr Cys Arg Gly Leu Arg Phe Glu Glu Val Pro
            260                 265                 270

Asp Tyr Met Tyr Leu Arg Gln Leu Phe Arg Ile Leu Phe Arg Thr Leu
        275                 280                 285

Asn His Gln Tyr Asp Tyr Thr Phe Asp Trp Thr Met Leu Lys Gln Lys
    290                 295                 300

Ala Ala Gln Gln Ala Ala Ser Ser Ser Gly Gln Gly Gln Gln Ala Gln
305                 310                 315                 320

Thr Gln Thr Gly Lys Gln Thr Glu Lys Asn Lys Asn Asn Val Lys Asp
                325                 330                 335

Asn


<210> SEQ ID NO 6
<211> LENGTH: 1011
<212> TYPE: DNA
<213> ORGANISM: Homo Sapiens

<400> SEQUENCE: 6

atgacaaaca acagcggctc caaagccgaa ctcgttgtgg gagggaaata caaactggtg     60

cggaagatcg ggtctggctc ctttggagac gtttatctgg gcatcaccac caccaacggc    120

gaggaagtag cagtgaagct ggaatctcag aaggtcaagc acccccagtt gctgtatgag    180

agcaaactct acacgattct tcaaggtggg gttggcatcc cccacatgca ctggtatggt    240

caggaaaaag acaacaatgt gctagtcatg gaccttctgg gacccagcct cgaagacctc    300

tttaatttct gttcaagaag gttcaccatg aaaactgtac ttatgttagc cgaccagatg    360

atcagcagaa ttgaatacgt gcatacaaag aattttctac accgagacat taaaccagat    420

aacttcctga tgggtactgg gcgtcactgt aataagttgt tccttattga ttttggtttg    480

gccaaaaagt acagagacaa caggaccagg caacacatac cgtacagaga agataaacac    540

ctcattggca ctgtccgata tgccagcatc aatgcacatc ttggtattga gcagagccgc    600

cgagatgaca tggaatcctt aggctacgtt ttcatgtatt ttaatagaac cagcctgccg    660

tggcaaggac taaaggctat gacaaaaaaa caaaaatatg aaaagattag tgagaagaag    720

atgtccaccc ctgttgaagt tttatgtaag ggtttcctg cagaattcgc catgtacttg     780
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aactactgtc gtgggctgcg ctttgaggaa gtcccagatt acatgtatct gaggcagcta    840

ttccgcattc ttttcaggac cctgaaccac caatatgact acacatttga ttggacgatg    900

ttaaagcaga aagcagcaca gcaggcagcc tcttccagtg ggcagggtca gcaggcccaa    960

acccagacag gcaagcaaac tgaaaaaaac aagaataatg tgaaagataa c            1011


<210> SEQ ID NO 7
<211> LENGTH: 187
<212> TYPE: PRT
<213> ORGANISM: Homo Sapiens

<400> SEQUENCE: 7

Met Val Gly Ser Leu Asn Cys Ile Val Ala Val Ser Gln Asn Met Gly
1               5                   10                  15

Ile Gly Lys Asn Gly Asp Leu Pro Trp Pro Pro Leu Arg Asn Glu Phe
            20                  25                  30

Arg Tyr Phe Gln Arg Met Thr Thr Thr Ser Ser Val Glu Gly Lys Gln
        35                  40                  45

Asn Leu Val Ile Met Gly Lys Lys Thr Trp Phe Ser Ile Pro Glu Lys
    50                  55                  60

Asn Arg Pro Leu Lys Gly Arg Ile Asn Leu Val Leu Ser Arg Glu Leu
65                  70                  75                  80

Lys Glu Pro Pro Gln Gly Ala His Phe Leu Ser Arg Ser Leu Asp Asp
                85                  90                  95

Ala Leu Lys Leu Thr Glu Gln Pro Glu Leu Ala Asn Lys Val Asp Met
            100                 105                 110

Val Trp Ile Val Gly Gly Ser Ser Val Tyr Lys Glu Ala Met Asn His
        115                 120                 125

Pro Gly His Leu Lys Leu Phe Val Thr Arg Ile Met Gln Asp Phe Glu
    130                 135                 140

Ser Asp Thr Phe Phe Pro Glu Ile Asp Leu Glu Lys Tyr Lys Leu Leu
145                 150                 155                 160

Pro Glu Tyr Pro Gly Val Leu Ser Asp Val Gln Glu Glu Lys Gly Ile
                165                 170                 175

Lys Tyr Lys Phe Glu Val Tyr Glu Lys Asn Asp
            180                 185


<210> SEQ ID NO 8
<211> LENGTH: 561
<212> TYPE: DNA
<213> ORGANISM: Homo Sapiens

<400> SEQUENCE: 8

atggttggtt cgctaaactg catcgtcgct gtgtcccaga acatgggcat cggcaagaac     60

ggggacctgc cctggccacc gctcaggaat gaattcagat atttccagag aatgaccaca    120

acctcttcag tagaaggtaa acagaatctg gtgattatgg gtaagaagac ctggttctcc    180

attcctgaga agaatcgacc tttaaagggt agaattaatt tagttctcag cagagaactc    240

aaggaacctc cacaaggagc tcattttctt tccagaagtc tagatgatgc cttaaaactt    300

actgaacaac cagaattagc aaataaagta gacatggtct ggatagttgg tggcagttct    360

gtttataagg aagccatgaa tcacccaggc catcttaaac tatttgtgac aaggatcatg    420

caagactttg aaagtgacac gtttttttcca gaaattgatt tggagaaata taaacttctg    480
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ccagaatacc caggtgttct ctctgatgtc caggaggaga aaggcattaa gtacaaattt    540

gaagtatatg agaagaatga t                                               561


<210> SEQ ID NO 9
<211> LENGTH: 382
<212> TYPE: PRT
<213> ORGANISM: Homo Sapiens

<400> SEQUENCE: 9

Met Ala Val Ser Val Thr Pro Ile Arg Asp Thr Lys Trp Leu Thr Leu
1               5                   10                  15

Glu Val Cys Arg Glu Phe Gln Arg Gly Thr Cys Ser Arg Pro Asp Thr
            20                  25                  30

Glu Cys Lys Phe Ala His Pro Ser Lys Ser Cys Gln Val Glu Asn Gly
        35                  40                  45

Arg Val Ile Ala Cys Phe Asp Ser Leu Lys Gly Arg Cys Ser Arg Glu
    50                  55                  60

Asn Cys Lys Tyr Leu His Pro Pro Pro His Leu Lys Thr Gln Leu Glu
65                  70                  75                  80

Ile Asn Gly Arg Asn Asn Leu Ile Gln Gln Lys Asn Met Ala Met Leu
                85                  90                  95

Ala Gln Gln Met Gln Leu Ala Asn Ala Met Met Pro Gly Ala Pro Leu
            100                 105                 110

Gln Pro Val Pro Met Phe Ser Val Ala Pro Ser Leu Ala Thr Asn Ala
        115                 120                 125

Ser Ala Ala Ala Phe Asn Pro Tyr Leu Gly Pro Val Ser Pro Ser Leu
    130                 135                 140

Val Pro Ala Glu Ile Leu Pro Thr Ala Pro Met Leu Val Thr Gly Asn
145                 150                 155                 160

Pro Gly Val Pro Val Pro Ala Ala Ala Ala Ala Ala Ala Gln Lys Leu
                165                 170                 175

Met Arg Thr Asp Arg Leu Glu Val Cys Arg Glu Tyr Gln Arg Gly Asn
            180                 185                 190

Cys Asn Arg Gly Glu Asn Asp Cys Arg Phe Ala His Pro Ala Asp Ser
        195                 200                 205

Thr Met Ile Asp Thr Asn Asp Asn Thr Val Thr Val Cys Met Asp Tyr
    210                 215                 220

Ile Lys Gly Arg Cys Ser Arg Glu Lys Cys Lys Tyr Phe His Pro Pro
225                 230                 235                 240

Ala His Leu Gln Ala Lys Ile Lys Ala Ala Gln Tyr Gln Val Asn Gln
                245                 250                 255

Ala Ala Ala Ala Gln Ala Ala Ala Thr Ala Ala Ala Met Gly Ile Pro
            260                 265                 270

Gln Ala Val Leu Pro Pro Leu Pro Lys Arg Pro Ala Leu Glu Lys Thr
        275                 280                 285

Asn Gly Ala Thr Ala Val Phe Asn Thr Gly Ile Phe Gln Tyr Gln Gln
    290                 295                 300

Ala Leu Ala Asn Met Gln Leu Gln Gln His Thr Ala Phe Leu Pro Pro
305                 310                 315                 320

Gly Ser Ile Leu Cys Met Thr Pro Ala Thr Ser Val Val Pro Met Val
                325                 330                 335
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His Gly Ala Thr Pro Ala Thr Val Ser Ala Ala Thr Thr Ser Ala Thr
            340                 345                 350

Ser Val Pro Phe Ala Ala Thr Ala Thr Ala Asn Gln Ile Pro Ile Ile
        355                 360                 365

Ser Ala Glu His Leu Thr Ser His Lys Tyr Val Thr Gln Met
    370                 375                 380


<210> SEQ ID NO 10
<211> LENGTH: 1146
<212> TYPE: DNA
<213> ORGANISM: Homo Sapiens

<400> SEQUENCE: 10

atggctgtta gtgtcacacc aattcgggac acaaaatggc taacactgga agtatgtaga      60

gagttccaga gggggacttg ctcacggcca gacacggaat gtaaatttgc acatccttcg     120

aaaagctgcc aagttgaaaa tggacgagta atcgcctgct ttgattcatt gaaaggccgt     180

tgctccaggg agaactgcaa atatcttcat ccacccccac atttaaaaac gcagttggag     240

ataaatggac gcaataactt gattcagcag aagaacatgg ccatgttggc ccagcaaatg     300

caactagcca atgccatgat gcctggtgcc ccattacaac ccgtgccaat gttttcagtt     360

gcaccaagct tagccaccaa tgcatcagca gccgccttta atccctatct gggacctgtt     420

tctccaagcc tggtcccggc agagatcttg ccgactgcac caatgttggt tacagggaat     480

ccgggtgtcc ctgtacctgc agctgctgca gctgctgcac agaaattaat gcgaacagac     540

agacttgagg tatgtcgaga gtaccaacgt ggcaattgca accgaggaga aaatgattgt     600

cggtttgctc atcctgctga cagcacaatg attgacacca atgacaacac agtcactgtg     660

tgtatggatt acatcaaagg gagatgctct cgggaaaagt gcaaatactt tcatccccct     720

gcacatttgc aagccaagat caaggctgcc caataccagg tcaaccaggc tgcagctgca     780

caggctgcag ccaccgcagc tgccatggga attcctcaag ctgtacttcc cccattacca     840

aagaggcctg ctcttgaaaa aaccaacggt gccaccgcag tctttaacac tggtattttc     900

caataccaac aggctctagc caacatgcag ttacaacagc atacagcatt tctcccacca     960

ggctcaatat tgtgcatgac acccgctaca agtgttgttc ccatggtgca cggtgctacg    1020

ccagccactg tgtccgcagc aacaacatct gccacaagtg ttcccttcgc tgcaacagcc    1080

acagccaacc agatacccat aatatctgcc gaacatctga ctagccacaa gtatgttacc    1140

cagatg                                                               1146


<210> SEQ ID NO 11
<211> LENGTH: 393
<212> TYPE: PRT
<213> ORGANISM: Homo Sapiens

<400> SEQUENCE: 11

Met Glu Glu Pro Gln Ser Asp Pro Ser Val Glu Pro Pro Leu Ser Gln
1               5                   10                  15

Glu Thr Phe Ser Asp Leu Trp Lys Leu Leu Pro Glu Asn Asn Val Leu
            20                  25                  30

Ser Pro Leu Pro Ser Gln Ala Met Asp Asp Leu Met Leu Ser Pro Asp
        35                  40                  45

Asp Ile Glu Gln Trp Phe Thr Glu Asp Pro Gly Pro Asp Glu Ala Pro
    50                  55                  60
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Arg Met Pro Glu Ala Ala Pro Arg Val Ala Pro Ala Pro Ala Ala Pro
65                  70                  75                  80

Thr Pro Ala Ala Pro Ala Pro Ala Pro Ser Trp Pro Leu Ser Ser Ser
                85                  90                  95

Val Pro Ser Gln Lys Thr Tyr Gln Gly Ser Tyr Gly Phe Arg Leu Gly
            100                 105                 110

Phe Leu His Ser Gly Thr Ala Lys Ser Val Thr Cys Thr Tyr Ser Pro
        115                 120                 125

Ala Leu Asn Lys Met Phe Cys Gln Leu Ala Lys Thr Cys Pro Val Gln
    130                 135                 140

Leu Trp Val Asp Ser Thr Pro Pro Pro Gly Thr Arg Val Arg Ala Met
145                 150                 155                 160

Ala Ile Tyr Lys Gln Ser Gln His Met Thr Glu Val Val Arg Arg Cys
                165                 170                 175

Pro His His Glu Arg Cys Ser Asp Ser Asp Gly Leu Ala Pro Pro Gln
            180                 185                 190

His Leu Ile Arg Val Glu Gly Asn Leu Arg Val Glu Tyr Leu Asp Asp
        195                 200                 205

Arg Asn Thr Phe Arg His Ser Val Val Val Pro Tyr Glu Pro Pro Glu
    210                 215                 220

Val Gly Ser Asp Cys Thr Thr Ile His Tyr Asn Tyr Met Cys Asn Ser
225                 230                 235                 240

Ser Cys Met Gly Gly Met Asn Arg Arg Pro Ile Leu Thr Ile Ile Thr
                245                 250                 255

Leu Glu Asp Ser Ser Gly Asn Leu Leu Gly Arg Asn Ser Phe Glu Val
            260                 265                 270

Arg Val Cys Ala Cys Ala Gly Arg Asp Arg Arg Thr Glu Glu Glu Asn
        275                 280                 285

Leu Arg Lys Lys Gly Glu Pro His His Glu Leu Pro Ser Gly Ser Thr
    290                 295                 300

Lys Arg Ala Leu Pro Asn Asn Thr Ser Ser Ser Pro Gln Pro Lys Lys
305                 310                 315                 320

Lys Pro Leu Asp Gly Glu Tyr Phe Thr Leu Gln Ile Arg Gly Arg Glu
                325                 330                 335

Arg Phe Glu Met Phe Arg Glu Leu Asn Glu Ala Leu Glu Leu Lys Asp
            340                 345                 350

Ala Gln Ala Gly Lys Glu Pro Gly Gly Ser Arg Ala His Ser Ser His
        355                 360                 365

Leu Lys Ser Lys Lys Gly Gln Ser Thr Ser Arg His Lys Lys Leu Met
    370                 375                 380

Phe Lys Thr Glu Gly Pro Asp Ser Asp
385                 390


<210> SEQ ID NO 12
<211> LENGTH: 1179
<212> TYPE: DNA
<213> ORGANISM: Homo Sapiens

<400> SEQUENCE: 12

atggaggagc cgcagtcaga tcctagcgtc gagccccctc tgagtcagga aacattttca      60

gacctatgga aactacttcc tgaaaacaac gttctgtccc ccttgccgtc ccaagcaatg     120
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gatgatttga tgctgtcccc ggacgatatt gaacaatggt tcactgaaga cccaggtcca     180

gatgaagctc ccagaatgcc agaggctgct ccccgcgtgg cccctgcacc agcagctcct     240

acaccggcgg cccctgcacc agccccctcc tggcccctgt catcttctgt cccttcccag     300

aaaacctacc agggcagcta cggtttccgt ctgggcttct tgcattctgg gacagccaag     360

tctgtgactt gcacgtactc ccctgccctc aacaagatgt tttgccaact ggccaagacc     420

tgccctgtgc agctgtgggt tgattccaca cccccgcccg gcacccgcgt ccgcgccatg     480

gccatctaca agcagtcaca gcacatgacg gaggttgtga ggcgctgccc ccaccatgag     540

cgctgctcag atagcgatgg tctggcccct cctcagcatc ttatccgagt ggaaggaaat     600

ttgcgtgtgg agtatttgga tgacagaaac acttttcgac atagtgtggt ggtgccctat     660

gagccgcctg aggttggctc tgactgtacc accatccact acaactacat gtgtaacagt     720

tcctgcatgg gcggcatgaa ccggaggccc atcctcacca tcatcacact ggaagactcc     780

agtggtaatc tactgggacg gaacagcttt gaggtgcgtg tttgtgcctg tgctgggaga     840

gaccggcgca cagaggaaga gaatctccgc aagaaagggg agcctcacca cgagctgccc     900

tcagggagca ctaagcgagc actgcccaac aacaccagct cctctcccca gccaaagaag     960

aaaccactgg atggagaata tttcaccctt cagatccgtg ggcgtgagcg cttcgagatg    1020

ttccgagagc tgaatgaggc cttggaactc aaggatgccc aggctgggaa ggagccaggg    1080

gggagcaggg ctcactccag ccacctgaag tccaaaaagg gtcagtctac ctcccgccat    1140

aaaaaactca tgttcaagac agaagggcct gactcagac                           1179


<210> SEQ ID NO 13
<211> LENGTH: 227
<212> TYPE: PRT
<213> ORGANISM: Homo Sapiens

<400> SEQUENCE: 13

Met Asn Ile Lys Gly Ser Pro Trp Lys Gly Ser Leu Leu Leu Leu Leu
1               5                   10                  15

Val Ser Asn Leu Leu Leu Cys Gln Ser Val Ala Pro Leu Pro Ile Cys
            20                  25                  30

Pro Gly Gly Ala Ala Arg Cys Gln Val Thr Leu Arg Asp Leu Phe Asp
        35                  40                  45

Arg Ala Val Val Leu Ser His Tyr Ile His Asn Leu Ser Ser Glu Met
    50                  55                  60

Phe Ser Glu Phe Asp Lys Arg Tyr Thr His Gly Arg Gly Phe Ile Thr
65                  70                  75                  80

Lys Ala Ile Asn Ser Cys His Thr Ser Ser Leu Ala Thr Pro Glu Asp
                85                  90                  95

Lys Glu Gln Ala Gln Gln Met Asn Gln Lys Asp Phe Leu Ser Leu Ile
            100                 105                 110

Val Ser Ile Leu Arg Ser Trp Asn Glu Pro Leu Tyr His Leu Val Thr
        115                 120                 125

Glu Val Arg Gly Met Gln Glu Ala Pro Glu Ala Ile Leu Ser Lys Ala
    130                 135                 140

Val Glu Ile Glu Glu Gln Thr Lys Arg Leu Leu Glu Gly Met Glu Leu
145                 150                 155                 160

Ile Val Ser Gln Val His Pro Glu Thr Lys Glu Asn Glu Ile Tyr Pro
                165                 170                 175
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Val Trp Ser Gly Leu Pro Ser Leu Gln Met Ala Asp Glu Glu Ser Arg
            180                 185                 190

Leu Ser Ala Tyr Tyr Asn Leu Leu His Cys Leu Arg Arg Asp Ser His
        195                 200                 205

Lys Ile Asp Asn Tyr Leu Lys Leu Leu Lys Cys Arg Ile Ile His Asn
    210                 215                 220

Asn Asn Cys
225


<210> SEQ ID NO 14
<211> LENGTH: 684
<212> TYPE: DNA
<213> ORGANISM: Homo Sapiens

<400> SEQUENCE: 14

atgaacatca aaggatcgcc atggaaaggg tccctcctgc tgctgctggt gtcaaacctg      60

ctcctgtgcc agagcgtggc cccttgccc atctgtcccg gcggggctgc ccgatgccag     120

gtgacccttc gagacctgtt tgaccgcgcc gtcgtcctgt cccactacat ccataacctc     180

tcctcagaaa tgttcagcga attcgataaa cggtataccc atggccgggg gttcattacc     240

aaggccatca acagctgcca cacttcttcc cttgccaccc ccgaagacaa ggagcaagcc     300

caacagatga atcaaaaaga ctttctgagc ctgatagtca gcatattgcg atcctggaat     360

gagcctctgt atcatctggt cacggaagta cgtggtatgc aagaagcccc ggaggctatc     420

ctatccaaag ctgtagagat tgaggagcaa accaaacggc ttctagaggg catggagctg     480

atagtcagcc aggttcatcc tgaaaccaaa gaaaatgaga tctaccctgt ctggtcggga     540

cttccatccc tgcagatggc tgatgaagag tctcgccttt ctgcttatta taacctgctc     600

cactgcctac gcagggattc acataaaatc gacaattatc tcaagctcct gaagtgccga     660

atcatccaca acaacaactg cttg                                            684


<210> SEQ ID NO 15
<211> LENGTH: 440
<212> TYPE: PRT
<213> ORGANISM: Homo Sapiens

<400> SEQUENCE: 15

Met Gly Gln Ser Gln Ser Gly Gly His Gly Pro Gly Gly Gly Lys Lys
1               5                   10                  15

Asp Asp Lys Asp Lys Lys Lys Lys Tyr Glu Pro Pro Val Pro Thr Arg
            20                  25                  30

Val Gly Lys Lys Lys Lys Lys Thr Lys Gly Pro Asp Ala Ala Ser Lys
        35                  40                  45

Leu Pro Leu Val Thr Pro His Thr Gln Cys Arg Leu Lys Leu Leu Lys
    50                  55                  60

Leu Glu Arg Ile Lys Asp Tyr Leu Leu Met Glu Glu Glu Phe Ile Arg
65                  70                  75                  80

Asn Gln Glu Gln Met Lys Pro Leu Glu Glu Lys Gln Glu Glu Glu Arg
                85                  90                  95

Ser Lys Val Asp Asp Leu Arg Gly Thr Pro Met Ser Val Gly Thr Leu
            100                 105                 110

Glu Glu Ile Ile Asp Asp Asn His Ala Ile Val Ser Thr Ser Val Gly
        115                 120                 125
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Ser Glu His Tyr Val Ser Ile Leu Ser Phe Val Asp Lys Asp Leu Leu
    130                 135                 140

Glu Pro Gly Cys Ser Val Leu Leu Asn His Lys Val His Ala Val Ile
145                 150                 155                 160

Gly Val Leu Met Asp Asp Thr Asp Pro Leu Val Thr Val Met Lys Val
                165                 170                 175

Glu Lys Ala Pro Gln Glu Thr Tyr Ala Asp Ile Gly Gly Leu Asp Asn
            180                 185                 190

Gln Ile Gln Glu Ile Lys Glu Ser Val Glu Leu Pro Leu Thr His Pro
        195                 200                 205

Glu Tyr Tyr Glu Glu Met Gly Ile Lys Pro Pro Lys Gly Val Ile Leu
    210                 215                 220

Tyr Gly Pro Pro Gly Thr Gly Lys Thr Leu Leu Ala Lys Ala Val Ala
225                 230                 235                 240

Asn Gln Thr Ser Ala Thr Phe Leu Arg Val Val Gly Ser Glu Leu Ile
                245                 250                 255

Gln Lys Tyr Leu Gly Asp Gly Pro Lys Leu Val Arg Glu Leu Phe Arg
            260                 265                 270

Val Ala Glu Glu His Ala Pro Ser Ile Val Phe Ile Asp Glu Ile Asp
        275                 280                 285

Ala Ile Gly Thr Lys Arg Tyr Asp Ser Asn Ser Gly Gly Glu Arg Glu
    290                 295                 300

Ile Gln Arg Thr Met Leu Glu Leu Leu Asn Gln Leu Asp Gly Phe Asp
305                 310                 315                 320

Ser Arg Gly Asp Val Lys Val Ile Met Ala Thr Asn Arg Ile Glu Thr
                325                 330                 335

Leu Asp Pro Ala Leu Ile Arg Pro Gly Arg Ile Asp Arg Lys Ile Glu
            340                 345                 350

Phe Pro Leu Pro Asp Glu Lys Thr Lys Lys Arg Ile Phe Gln Ile His
        355                 360                 365

Thr Ser Arg Met Thr Leu Ala Asp Asp Val Thr Leu Asp Asp Leu Ile
    370                 375                 380

Met Ala Lys Asp Asp Leu Ser Gly Ala Asp Ile Lys Ala Ile Cys Thr
385                 390                 395                 400

Glu Ala Gly Leu Met Ala Leu Arg Glu Arg Arg Met Lys Val Thr Asn
                405                 410                 415

Glu Asp Phe Lys Lys Ser Lys Glu Asn Val Leu Tyr Lys Lys Gln Glu
            420                 425                 430

Gly Thr Pro Glu Gly Leu Tyr Leu
        435                 440


<210> SEQ ID NO 16
<211> LENGTH: 1320
<212> TYPE: DNA
<213> ORGANISM: Homo Sapiens

<400> SEQUENCE: 16

atgggtcaaa gtcagagtgg tggtcatggt cctggaggtg gcaagaagga tgacaaggac      60

aagaaaaaga aatatgaacc tcctgtacca actagagtgg ggaaaaagaa gaagaaaaca     120

aagggaccag atgctgccag caaactgcca ctggtgacac ctcacactca gtgccggtta     180

aaattactga agttagagag aattaaagac tatcttctca tggaggaaga attcattaga     240
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aatcaggaac aaatgaaacc attagaagaa aagcaagagg aggaaagatc aaaagtggat    300

gatctgaggg ggaccccgat gtcagtagga accttggaag agattattga tgacaatcat    360

gccatcgtgt ctacatctgt gggctcagaa cactacgtca gcattctttc atttgtagac    420

aaggatctgc tggaacctgg ctgctcggtc ctgctcaacc acaaggtgca tgccgtgata    480

ggggtgctga tggatgacac ggatcccctg gtcacagtga tgaaggtaga aaaggccccc    540

caggagacct atgcagatat tgggggggttg gacaaccaaa ttcaggaaat taaggaatct    600

gtggagcttc ctctcaccca tcctgaatat tatgaagaga tgggtataaa gcctcctaag    660

gggtcattc tctatggtcc acctggcaca ggtaaaacct tgttagccaa agcagtagca    720

aaccaaacct cagccacttt cttgagagtg gttggctctg aacttattca gaagtaccta    780

ggtgatgggc ccaaactcgt acgggaattg ttccgagttg ctgaagaaca tgcaccgtcc    840

atcgtgttta ttgatgaaat tgacgccatt gggacaaaaa gatatgactc caattctggt    900

ggtgagagag aaattcagcg aacaatgttg gaactgctga accagttgga tggatttgat    960

tctaggggag atgtgaaagt tatcatggcc acaaaccgaa tagaaacttt ggatccagca   1020

cttatcagac caggccgcat tgacaggaag attgagttcc ccctgcctga tgaaaagacg   1080

aagaagcgca tctttcagat tcacacaagc aggatgacgc tggctgatga tgtaaccctg   1140

gacgacctga tcatggctaa agatgacctc tctggtgctg acatcaaggc aatctgtaca   1200

gaagctggtc tgatggcctt aagagaacgt agaatgaaag taacaaatga agacttcaaa   1260

aaatctaaag aaaatgttct ttataagaaa caggaaggca cccctgaggg gctgtatctc   1320
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<210> SEQ ID NO 17
<211> LENGTH: 359
<212> TYPE: PRT
<213> ORGANISM: Homo Sapiens

<400> SEQUENCE: 17

Met Ser Met Asn Asn Ser Lys Gln Leu Val Ser Pro Ala Ala Ala Leu
1               5                   10                  15

Leu Ser Asn Thr Thr Cys Gln Thr Glu Asn Arg Leu Ser Val Phe Phe
            20                  25                  30

Ser Val Ile Phe Met Thr Val Gly Ile Leu Ser Asn Ser Leu Ala Ile
        35                  40                  45

Ala Ile Leu Met Lys Ala Tyr Gln Arg Phe Arg Gln Lys Ser Lys Ala
    50                  55                  60

Ser Phe Leu Leu Leu Ala Ser Gly Leu Val Ile Thr Asp Phe Phe Gly
65                  70                  75                  80

His Leu Ile Asn Gly Ala Ile Ala Val Phe Val Tyr Ala Ser Asp Lys
                85                  90                  95

Glu Trp Ile Arg Phe Asp Gln Ser Asn Val Leu Cys Ser Ile Phe Gly
            100                 105                 110

Ile Cys Met Val Phe Ser Gly Leu Cys Pro Leu Leu Leu Gly Ser Val
        115                 120                 125

Met Ala Ile Glu Arg Cys Ile Gly Val Thr Lys Pro Ile Phe His Ser
    130                 135                 140

Thr Lys Ile Thr Ser Lys His Val Lys Met Met Leu Ser Gly Val Cys
145                 150                 155                 160

Leu Phe Ala Val Phe Ile Ala Leu Leu Pro Ile Leu Gly His Arg Asp
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                165                 170                 175

Tyr Lys Ile Gln Ala Ser Arg Thr Trp Cys Phe Tyr Asn Thr Glu Asp
            180                 185                 190

Ile Lys Asp Trp Glu Asp Arg Phe Tyr Leu Leu Leu Phe Ser Phe Leu
        195                 200                 205

Gly Leu Leu Ala Leu Gly Val Ser Leu Leu Cys Asn Ala Ile Thr Gly
    210                 215                 220

Ile Thr Leu Leu Arg Val Lys Phe Lys Ser Gln Gln His Arg Gln Gly
225                 230                 235                 240

Arg Ser His His Leu Glu Met Val Ile Gln Leu Leu Ala Ile Met Cys
                245                 250                 255

Val Ser Cys Ile Cys Trp Ser Pro Phe Leu Val Thr Met Ala Asn Ile
            260                 265                 270

Gly Ile Asn Gly Asn His Ser Leu Glu Thr Cys Glu Thr Thr Leu Phe
        275                 280                 285

Ala Leu Arg Met Ala Thr Trp Asn Gln Ile Leu Asp Pro Trp Val Tyr
    290                 295                 300

Ile Leu Leu Arg Lys Ala Val Leu Lys Asn Leu Tyr Lys Leu Ala Ser
305                 310                 315                 320

Gln Cys Cys Gly Val His Val Ile Ser Leu His Ile Trp Glu Leu Ser
                325                 330                 335

Ser Ile Lys Asn Ser Leu Lys Val Ala Ala Ile Ser Glu Ser Pro Val
            340                 345                 350

Ala Glu Lys Ser Ala Ser Thr
        355


<210> SEQ ID NO 18
<211> LENGTH: 1077
<212> TYPE: DNA
<213> ORGANISM: Homo Sapiens

<400> SEQUENCE: 18

atgtccatga acaattccaa acagctagtg tctcctgcag ctgcgcttct ttcaaacaca      60

acctgccaga cggaaaaccg gctttccgta tttttttcag taatcttcat gacagtggga     120

atcttgtcaa acagccttgc catcgccatt ctcatgaagg catatcagag atttagacag     180

aagtccaagg catcgtttct gcttttggcc agtggcctgg taatcactga tttctttggc     240

catctcatca atggagccat agcagtattt gtatatgctt ctgataaaga atggatccgc     300

tttgaccaat caaatgtcct ttgcagtatt tttggtatct gcatggtgtt ttctggtctg     360

tgcccacttc ttctaggcag tgtgatggcc attgagcggt gtattggagt cacaaaacca     420

atatttcatt ctacgaaaat tacatccaaa catgtgaaaa tgatgttaag tggtgtgtgc     480

ttgtttgctg ttttcatagc tttgctgccc atccttggac atcgagacta taaaattcag     540

gcgtcgagga cctggtgttt ctacaacaca gaagacatca aagactggga agatagattt     600

tatcttctac tttttttcttt tctggggctc ttagcccttg gtgtttcatt gttgtgcaat     660

gcaatcacag gaattacact tttaagagtt aaatttaaaa gtcagcagca cagacaaggc     720

agatctcatc atttggaaat ggtaatccag ctcctggcga taatgtgtgt ctcctgtatt     780

tgttggagcc catttctggt tacaatggcc aacattggaa taaatggaaa tcattctctg     840

gaaacctgtg aaacaacact tttgctctcc cgaatggcaa catggaatca aatcttagat     900
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ccttgggtat atattcttct acgaaaggct gtccttaaga atctctataa gcttgccagt    960

caatgctgtg gagtgcatgt catcagctta catatttggg agcttagttc cattaaaaat   1020

tccttaaagg ttgctgctat ttctgagtca ccagttgcag agaaatcagc aagcacc      1077


<210> SEQ ID NO 19
<211> LENGTH: 793
<212> TYPE: PRT
<213> ORGANISM: Homo Sapiens

<400> SEQUENCE: 19

Met Asp Ser Trp Phe Ile Leu Val Leu Leu Gly Ser Gly Leu Ile Cys
1               5                   10                  15

Val Ser Ala Asn Asn Ala Thr Thr Val Ala Pro Ser Val Gly Ile Thr
            20                  25                  30

Arg Leu Ile Asn Ser Ser Thr Ala Glu Pro Val Lys Glu Glu Ala Lys
        35                  40                  45

Thr Ser Asn Pro Thr Ser Ser Leu Thr Ser Leu Ser Val Ala Pro Thr
    50                  55                  60

Phe Ser Pro Asn Ile Thr Leu Gly Pro Thr Tyr Leu Thr Thr Val Asn
65                  70                  75                  80

Ser Ser Asp Ser Asp Asn Gly Thr Thr Arg Thr Ala Ser Thr Asn Ser
                85                  90                  95

Ile Gly Ile Thr Ile Ser Pro Asn Gly Thr Trp Leu Pro Asp Asn Gln
            100                 105                 110

Phe Thr Asp Ala Arg Thr Glu Pro Trp Glu Gly Asn Ser Ser Thr Ala
        115                 120                 125

Ala Thr Thr Pro Glu Thr Phe Pro Pro Ser Asp Glu Thr Pro Ile Ile
    130                 135                 140

Ala Val Met Val Ala Leu Ser Ser Leu Leu Val Ile Val Phe Ile Ile
145                 150                 155                 160

Ile Val Leu Tyr Met Leu Arg Phe Lys Lys Tyr Lys Gln Ala Gly Ser
                165                 170                 175

His Ser Asn Ser Phe Arg Leu Ser Asn Gly Arg Thr Glu Asp Val Glu
            180                 185                 190

Pro Gln Ser Val Pro Leu Leu Ala Arg Ser Pro Ser Thr Asn Arg Lys
        195                 200                 205

Tyr Pro Pro Leu Pro Val Asp Lys Leu Glu Glu Glu Ile Asn Arg Arg
    210                 215                 220

Met Ala Asp Asp Asn Lys Leu Phe Arg Glu Glu Phe Asn Ala Leu Pro
225                 230                 235                 240

Ala Cys Pro Ile Gln Ala Thr Cys Glu Ala Ala Ser Lys Glu Glu Asn
                245                 250                 255

Lys Glu Lys Asn Arg Tyr Val Asn Ile Leu Pro Tyr Asp His Ser Arg
            260                 265                 270

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

Ala Ser Phe Ile Asn Gly Tyr Gln Glu Lys Asn Lys Phe Ile Ala Ala
    290                 295                 300

Gln Gly Pro Lys Glu Glu Thr Val Asn Asp Phe Trp Arg Met Ile Trp
305                 310                 315                 320

Glu Gln Asn Thr Ala Thr Ile Val Met Val Thr Asn Leu Lys Glu Arg
                325                 330                 335
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Lys Glu Cys Lys Cys Ala Gln Tyr Trp Pro Asp Gln Gly Cys Trp Thr
            340                 345                 350

Tyr Gly Asn Ile Arg Val Ser Val Glu Asp Val Thr Val Leu Val Asp
        355                 360                 365

Tyr Thr Val Arg Lys Phe Cys Ile Gln Gln Val Gly Asp Met Thr Asn
    370                 375                 380

Arg Lys Pro Gln Arg Leu Ile Thr Gln Phe His Phe Thr Ser Trp Pro
385                 390                 395                 400

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

Lys Val Lys Ala Cys Asn Pro Gln Tyr Ala Gly Ala Ile Val Val His
            420                 425                 430

Cys Ser Ala Gly Val Gly Arg Thr Gly Thr Phe Val Val Ile Asp Ala
        435                 440                 445

Met Leu Asp Met Met His Thr Glu Arg Lys Val Asp Val Tyr Gly Phe
    450                 455                 460

Val Ser Arg Ile Arg Ala Gln Arg Cys Gln Met Val Gln Thr Asp Met
465                 470                 475                 480

Gln Tyr Val Phe Ile Tyr Gln Ala Leu Leu Glu His Tyr Leu Tyr Gly
                485                 490                 495

Asp Thr Glu Leu Glu Val Thr Ser Leu Glu Thr His Leu Gln Lys Ile
            500                 505                 510

Tyr Asn Lys Ile Pro Gly Thr Ser Asn Asn Gly Leu Glu Glu Glu Phe
        515                 520                 525

Lys Lys Leu Thr Ser Ile Lys Ile Gln Asn Asp Lys Met Arg Thr Gly
    530                 535                 540

Asn Leu Pro Ala Asn Met Lys Lys Asn Arg Val Leu Gln Ile Ile Pro
545                 550                 555                 560

Tyr Glu Phe Asn Arg Val Ile Ile Pro Val Lys Arg Gly Glu Glu Asn
                565                 570                 575

Thr Asp Tyr Val Asn Ala Ser Phe Ile Asp Gly Tyr Arg Gln Lys Asp
            580                 585                 590

Ser Tyr Ile Ala Ser Gln Gly Pro Leu Leu His Thr Ile Glu Asp Phe
        595                 600                 605

Trp Arg Met Ile Trp Glu Trp Lys Ser Cys Ser Ile Val Met Leu Thr
    610                 615                 620

Glu Leu Glu Glu Arg Gly Gln Glu Lys Cys Ala Gln Tyr Trp Pro Ser
625                 630                 635                 640

Asp Gly Leu Val Ser Tyr Gly Asp Ile Thr Val Glu Leu Lys Lys Glu
                645                 650                 655

Glu Glu Cys Glu Ser Tyr Thr Val Arg Asp Leu Leu Val Thr Asn Thr
            660                 665                 670

Arg Glu Asn Lys Ser Arg Gln Ile Arg Gln Phe His Phe His Gly Trp
        675                 680                 685

Pro Glu Val Gly Ile Pro Ser Asp Gly Lys Gly Met Ile Ser Ile Ile
    690                 695                 700

Ala Ala Val Gln Lys Gln Gln Gln Gln Ser Gly Asn His Pro Ile Thr
705                 710                 715                 720

Val His Cys Ser Ala Gly Ala Gly Arg Thr Gly Thr Phe Cys Ala Leu
                725                 730                 735
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Ser Thr Val Leu Glu Arg Val Lys Ala Glu Gly Ile Leu Asp Val Phe
            740                 745                 750

Gln Thr Val Lys Ser Leu Arg Leu Gln Arg Pro His Met Val Gln Thr
        755                 760                 765

Leu Glu Gln Tyr Glu Phe Cys Tyr Lys Val Val Gln Glu Tyr Ile Asp
    770                 775                 780

Ala Phe Ser Asp Tyr Ala Asn Phe Lys
785                 790


<210> SEQ ID NO 20
<211> LENGTH: 2379
<212> TYPE: DNA
<213> ORGANISM: Homo Sapiens

<400> SEQUENCE: 20

atggattcct ggttcattct tgttctgctc ggcagtggtc tgatatgtgt cagtgccaac     60

aatgctacca cagttgcacc ttctgtagga attacaagat taattaactc atcaacggca    120

gaaccagtta aagaagaggc caaaacttca aatccaactt cttcactaac ttctctttct    180

gtggcaccaa cattcagccc aaatataact ctgggaccca cctatttaac cactgtcaat    240

tcttcagact ctgacaatgg gaccacaaga acagcaagca ccaattctat aggcattaca    300

atttcaccaa atggaacgtg gcttccagat aaccagttca cggatgccag aacagaaccc    360

tgggaggggga attccagcac cgcagcaacc actccagaaa ctttccctcc ttcagatgag    420

acaccaatta ttgcggtgat ggtggccctg tcctctctgc tagtgatcgt gtttattatc    480

atagttttgt acatgttaag gtttaagaaa tacaagcaag ctgggagcca ttccaattct    540

ttccgcttat ccaacggccg cactgaggat gtggagcccc agagtgtgcc acttctggcc    600

agatccccaa gcaccaacag gaaataccca cccctgcccg tggacaagct ggaagaggaa    660

attaaccgga gaatggcaga cgacaataag ctcttcaggg aggaattcaa cgctctccct    720

gcatgtccta tccaggccac ctgtgaggct gcttccaagg aggaaaacaa ggaaaaaaat    780

cgatatgtaa acatcttgcc ttatgaccac tctagagtcc acctgacacc ggttgaaggg    840

gttccagatt ctgattacat caatgcttca ttcatcaacg gttaccaaga aaagaacaaa    900

ttcattgctg cacaaggacc aaaagaagaa acggtgaatg atttctggcg gatgatctgg    960

gaacaaaaca cagccaccat cgtcatggtt accaacctga aggagagaaa ggagtgcaag   1020

tgcgcccagt actggccaga ccaaggctgc tggacctatg ggaatattcg ggtgtctgta   1080

gaggatgtga ctgtcctggt ggactacaca gtacggaagt tctgcatcca gcaggtgggc   1140

gacatgacca acagaaagcc acagcgcctc atcactcagt tccactttac cagctggcca   1200

gactttgggg tgccttttac cccgatcggc atgctcaagt tcctcaagaa ggtgaaggcc   1260

tgtaaccctc agtatgcagg ggccatcgtg gtccactgca gtgcaggtgt agggcgtaca   1320

ggtacctttg tcgtcattga tgccatgctg gacatgatgc atacagaacg gaaggtggac   1380

gtgtatggct ttgtgagccg gatccgggca cagcgctgcc agatggtgca aaccgatatg   1440

cagtatgtct tcatatacca agcccttctg gagcattatc tctatggaga tacagaactg   1500

gaagtgacct ctctagaaac ccacctgcag aaaatttaca acaaaatccc agggaccagc   1560

aacaatggat tagaggagga gtttaagaag ttaacatcaa tcaaaatcca gaatgacaag   1620

atgcggactg gaaaccttcc agccaacatg aagaagaacc gtgttttaca gatcattcca   1680
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tatgaattca acagagtgat cattccagtt aagcggggcg aagagaatac agactatgtg   1740

aacgcatcct ttattgatgg ctaccggcag aaggactcct atatcgccag ccagggccct   1800

cttctccaca caattgagga cttctggcga atgatctggg agtggaaatc ctgctctatc   1860

gtgatgctaa cagaactgga ggagagaggc caggagaagt gtgcccagta ctggccatct   1920

gatggactgg tgtcctatgg agatattaca gtggaactga agaaggagga ggaatgtgag   1980

agctacaccg tccgagacct cctggtcacc aacaccaggg agaataagag ccggcagatc   2040

cggcagttcc acttccatgg ctggcctgaa gtgggcatcc ccagtgacgg aaagggcatg   2100

atcagcatca tcgccgccgt gcagaagcag cagcagcagt cagggaacca ccccatcacc   2160

gtgcactgca gcgccggggc aggaaggacg gggaccttct gtgccctgag caccgtcctg   2220

gagcgtgtga aagcagaggg gattttggat gtcttccaga ctgtcaagag cctgcggcta   2280

cagaggccac acatggtcca gacactggaa cagtatgagt tctgctacaa ggtggtgcag   2340

gagtatattg atgcattctc agattatgcc aacttcaag                          2379


<210> SEQ ID NO 21
<211> LENGTH: 203
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 21

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

Ala Val Gly Lys Thr Ser Leu Val Gln Arg Tyr Ser Gln Asp Ser Phe
            20                  25                  30

Ser Lys His Tyr Lys Ser Thr Val Gly Val Asp Phe Ala Leu Lys Val
        35                  40                  45

Leu Gln Trp Ser Asp Tyr Glu Ile Val Arg Leu Gln Leu Trp Asp Ile
    50                  55                  60

Ala Gly Gln Glu Arg Phe Thr Ser Met Thr Arg Leu Tyr Tyr Arg Asp
65                  70                  75                  80

Ala Ser Ala Cys Val Ile Met Phe Asp Val Thr Asn Ala Thr Thr Phe
                85                  90                  95

Ser Asn Ser Gln Arg Trp Lys Gln Asp Leu Asp Ser Lys Leu Thr Leu
            100                 105                 110

Pro Asn Gly Glu Pro Val Pro Cys Leu Leu Leu Ala Asn Lys Cys Asp
        115                 120                 125

Leu Ser Pro Trp Ala Val Ser Arg Asp Gln Ile Asp Arg Phe Ser Lys
    130                 135                 140

Glu Asn Gly Phe Thr Gly Trp Thr Glu Thr Ser Val Lys Glu Asn Lys
145                 150                 155                 160

Asn Ile Asn Glu Ala Met Arg Val Leu Ile Glu Lys Met Met Arg Asn
                165                 170                 175

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

Leu Gln Thr Lys Ser Ser Ser Trp Ser Cys Cys
        195                 200


<210> SEQ ID NO 22
<211> LENGTH: 609
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens
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<400> SEQUENCE: 22

atgggcagcc gcgaccacct gttcaaagtg ctggtggtgg gggacgccgc agtgggcaag      60

acgtcgctgg tgcagcgata ttcccaggac agcttcagca aacactacaa gtccacggtg     120

ggagtggatt ttgctctgaa ggttctccag tggtctgact acgagatagt gcggcttcag     180

ctgtgggata ttgcagggca ggagcgcttc acctctatga cacgattgta ttatcgggat     240

gcctctgcct gtgttattat gtttgacgtt accaatgcca ctaccttcag caacagccag     300

aggtggaaac aggacctaga cagcaagctc acactaccca atggagagcc ggtgccctgc     360

ctgctcttgg ccaacaagtg tgatctgtcc ccttgggcag tgagccggga ccagattgac     420

cggttcagta aagagaacgg tttcacaggt tggacagaaa catcagtcaa ggagaacaaa     480

aatattaatg aggctatgag agtcctcatt gaaaagatga tgagaaattc cacagaagat     540

atcatgtctt tgtccaccca aggggactac atcaatctac aaaccaagtc ctccagctgg     600

tcctgctgc                                                             609


<210> SEQ ID NO 23
<211> LENGTH: 688
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 23

Met Gly Ser Glu Asn Ser Ala Leu Lys Ser Tyr Thr Leu Arg Glu Pro
1               5                   10                  15

Pro Phe Thr Leu Pro Ser Gly Leu Ala Val Tyr Pro Ala Val Leu Gln
            20                  25                  30

Asp Gly Lys Phe Ala Ser Val Phe Val Tyr Lys Arg Glu Asn Glu Asp
        35                  40                  45

Lys Val Asn Lys Ala Ala Lys His Leu Lys Thr Leu Arg His Pro Cys
    50                  55                  60

Leu Leu Arg Phe Leu Ser Cys Thr Val Glu Ala Asp Gly Ile His Leu
65                  70                  75                  80

Val Thr Glu Arg Val Gln Pro Leu Glu Val Ala Leu Glu Thr Leu Ser
                85                  90                  95

Ser Ala Glu Val Cys Ala Gly Ile Tyr Asp Ile Leu Leu Ala Leu Ile
            100                 105                 110

Phe Leu His Asp Arg Gly His Leu Thr His Asn Asn Val Cys Leu Ser
        115                 120                 125

Ser Val Phe Val Ser Glu Asp Gly His Trp Lys Leu Gly Gly Met Glu
    130                 135                 140

Thr Val Cys Lys Val Ser Gln Ala Thr Pro Glu Phe Leu Arg Ser Ile
145                 150                 155                 160

Gln Ser Ile Arg Asp Pro Ala Ser Ile Pro Pro Glu Glu Met Ser Pro
                165                 170                 175

Glu Phe Thr Thr Leu Pro Glu Cys His Gly His Ala Arg Asp Ala Phe
            180                 185                 190

Ser Phe Gly Thr Leu Val Glu Ser Leu Leu Thr Ile Leu Asn Glu Gln
        195                 200                 205

Val Ser Ala Asp Val Leu Ser Ser Phe Gln Gln Thr Leu His Ser Thr
    210                 215                 220

Leu Leu Asn Pro Ile Pro Lys Cys Arg Pro Ala Leu Cys Thr Leu Leu
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225                 230                 235                 240

Ser His Asp Phe Phe Arg Asn Asp Phe Leu Glu Val Val Asn Phe Leu
                245                 250                 255

Lys Ser Leu Thr Leu Lys Ser Glu Glu Glu Lys Thr Glu Phe Phe Lys
            260                 265                 270

Phe Leu Leu Asp Arg Val Ser Cys Leu Ser Glu Glu Leu Ile Ala Ser
        275                 280                 285

Arg Leu Val Pro Leu Leu Leu Asn Gln Leu Val Phe Ala Glu Pro Val
    290                 295                 300

Ala Val Lys Ser Phe Leu Pro Tyr Leu Leu Gly Pro Lys Lys Asp His
305                 310                 315                 320

Ala Gln Gly Glu Thr Pro Cys Leu Leu Ser Pro Ala Leu Phe Gln Ser
                325                 330                 335

Arg Val Ile Pro Val Leu Leu Gln Leu Phe Glu Val His Glu Glu His
            340                 345                 350

Val Arg Met Val Leu Leu Ser His Ile Glu Ala Tyr Val Glu His Phe
        355                 360                 365

Thr Gln Glu Gln Leu Lys Lys Val Ile Leu Pro Gln Val Leu Leu Gly
    370                 375                 380

Leu Arg Asp Thr Ser Asp Ser Ile Val Ala Ile Thr Leu His Ser Leu
385                 390                 395                 400

Ala Val Leu Val Ser Leu Leu Gly Pro Glu Val Val Val Gly Gly Glu
                405                 410                 415

Arg Thr Lys Ile Phe Lys Arg Thr Ala Pro Ser Phe Thr Lys Asn Thr
            420                 425                 430

Asp Leu Ser Leu Glu Gly Asp Pro Phe Ser Gln Pro Ile Lys Phe Pro
        435                 440                 445

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

Phe Pro Ser Ser Ser Lys Lys Ser Glu Glu Trp Pro Asp Trp Ser Glu
465                 470                 475                 480

Pro Glu Glu Pro Glu Asn Gln Thr Val Asn Ile Gln Ile Trp Pro Arg
                485                 490                 495

Glu Pro Cys Asp Asp Val Lys Ser Gln Cys Thr Thr Leu Asp Val Glu
            500                 505                 510

Glu Ser Ser Trp Asp Asp Cys Glu Pro Ser Ser Leu Asp Thr Lys Val
        515                 520                 525

Asn Pro Gly Gly Gly Ile Thr Ala Thr Lys Pro Val Thr Ser Ala Glu
    530                 535                 540

Gln Lys Pro Ile Pro Ala Leu Leu Ser Leu Thr Glu Glu Ser Met Pro
545                 550                 555                 560

Trp Lys Ser Ser Leu Pro Gln Lys Ile Ser Leu Val Gln Arg Gly Asp
                565                 570                 575

Asp Ala Asp Gln Ile Glu Pro Pro Lys Val Ser Ser Gln Glu Arg Pro
            580                 585                 590

Leu Lys Val Pro Ser Glu Leu Gly Leu Gly Glu Glu Phe Thr Ile Gln
        595                 600                 605

Val Lys Lys Lys Pro Val Lys Asp Pro Glu Met Asp Trp Phe Ala Asp
    610                 615                 620

Met Ile Pro Glu Ile Lys Pro Ser Ala Ala Phe Leu Ile Leu Pro Glu
625                 630                 635                 640
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Leu Arg Thr Glu Met Val Pro Lys Lys Asp Asp Val Ser Pro Val Met
                645                 650                 655

Gln Phe Ser Ser Lys Phe Ala Ala Ala Glu Ile Thr Glu Gly Glu Ala
            660                 665                 670

Glu Gly Trp Glu Glu Glu Gly Glu Leu Asn Trp Glu Asp Asn Asn Trp
        675                 680                 685


<210> SEQ ID NO 24
<211> LENGTH: 2064
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 24

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ccctctggac ttgctgttta tcccgctgta ctgcaagatg gcaaatttgc ttcagttttt     120

gtgtataaga gagaaaatga agacaaggtt aataaagctg ccaagcattt gaagacactt     180

cgtcaccctt gcttgctaag atttttatct tgtactgtgg aagcggatgg cattcatctt     240

gtcactgagc gagtacagcc cctggaagtg gctttggaaa cattgtcttc tgcagaggtc     300

tgtgctggga tctatgacat attgctggct cttatcttcc ttcatgacag aggacaccta     360

acacacaata atgtctgttt atcatctgtg tttgtgagtg aagatggaca ctggaagcta     420

ggaggaatgg aaactgtttg taaagtttct caggccacac cagagtttct gaggagtatt     480

cagtcaataa gagacccagc atctatccct cctgaagaga tgtctccaga attcacaact     540

ctcccagagt gtcatggaca tgcccgggat gccttttcat ttggaacatt ggtggaaagt     600

ttgctcacaa tcttaaatga acaggtttca gcggatgttc tctccagctt tcaacagacc     660

ttgcactcaa ctttgctgaa tcccattcca aaatgtcggc cagcgctctg caccttacta     720

tctcatgact tcttcagaaa tgattttctg gaagttgtga atttcttgaa aagtttaaca     780

ttgaagagtg aagaggagaa aacggaattc tttaaatttc tgctggacag agtcagctgc     840

ttgtcagagg aattgatagc ttcaaggttg gtgcctcttc tgcttaatca gttggtgttt     900

gcagagccag tggctgttaa gagttttctt ccttatctgc ttggccccaa aaaagatcat     960

gcgcagggag aaactccttg cttgctctca ccagccctgt tccagtcacg ggtgatcccc    1020

gtgcttctcc agttgtttga agttcatgaa gagcatgtgc ggatggtgct gctgtctcac    1080

atcgaggcct acgtggagca cttcactcag gagcagctga agaaagtcat cttgccacag    1140

gttttgctgg gcctgcgtga tactagtgat tccattgtgg caattactct gcatagccta    1200

gcagtgctgg tctctctgct tggaccagag gtggttgtgg gaggagaacg aaccaagatc    1260

ttcaaacgca ctgccccaag ttttactaaa aatactgacc tttctctaga aggtgatcca    1320

ttttctcagc ctattaaatt tcccataaac ggactctcag atgtaaaaaa tacttcggag    1380

gacagtgaaa acttcccatc aagttctaaa aagtctgagg agtggcctga ctggagtgaa    1440

cctgaggagc ctgaaaatca aactgtcaac atacagattt ggcctagaga accttgtgat    1500

gatgtcaagt cccagtgcac taccttggat gtggaagagt catcttggga tgactgcgag    1560

cccagcagct tagatactaa agtaaaccca ggaggtggaa tcactgctac aaaacctgtt    1620

acctcagcgg agcagaagcc tattcctgct ttgctttcac tcactgaaga gtctatgcct    1680

tggaaatcaa gcttacccca aaagattagc cttgtacaaa ggggggatga cgcagaccaa    1740
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atcgagccgc caaaagtgtc atcacaagaa aggcccctta aggttccatc agaacttggt   1800

ttaggagagg aattcaccat tcaagtaaaa aagaagccag taaaagatcc tgagatggat   1860

tggtttgctg atatgatccc agaaattaag ccttctgctg cttttcttat attacctgaa   1920

ctgaggacag aaatggtccc aaaaaaggat gatgtctccc cagtgatgca gttttcctca   1980

aaatttgctg cagcagaaat tactgaggga gaggctgaag gctgggaaga agaaggggag   2040

ctgaactggg aagataataa ctgg                                          2064
```

**1**. A method for detecting ovarian cancer onset, comprising the steps of:

contacting a fluid from a patient that contains immunoglobulins with a substrate having one or more biomarkers selected from the group consisting of ACSBG1, AFP, CSNK1A1L, DHFR, MBNL1, TP53, PRL, PSMC1, PTGFR, PTPRA, RAB7L1, and SCYL3; and

detecting whether one or more of said biomarkers is bound by said immunoglobulins.

**2**. The method of claim **1**, wherein said substrate one or more biomarkers comprises a Nucleic Acid Protein Programmable Array (NAPPA).

**3**. A diagnostic test kit for ovarian cancer, comprising a substrate including one or more biomarkers selected from the group consisting of ACSBG1, AFP, CSNK1A1L, DHFR, MBNL1, P53, PRL, PSMC1, PTGFR, PTPRA, RAB7L1, and SCYL3.

**4**. A diagnostic test kit for ovarian cancer, comprising a substrate including biomarkers ACSBG1, AFP, CSNK1A1L, DHFR, MBNL1, P53, PRL, PSMC1, PTGFR, PTPRA, RAB7L1, and SCYL3.

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