US 20100190652A1

(19) **United States**

(12) **Patent Application Publication**

Nagalla et al.

(10) **Pub. No.: US 2010/0190652 A1**

(43) **Pub. Date: Jul. 29, 2010**

(54) **BIOMARKERS FOR DETECTION OF NEONATAL SEPSIS IN BIOLOGICAL FLUID**

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(21) Appl. No.: **12/693,387**

(22) Filed: **Jan. 25, 2010**

Related U.S. Application Data

(60) Provisional application No. 61/147,635, filed on Jan. 27, 2009.

Publication Classification

(51) **Int. Cl.**

C40B 30/00	(2006.01)
G01N 33/53	(2006.01)
G01N 33/573	(2006.01)

(52) **U.S. Cl.** **506/7**; 435/7.1; 435/7.4

(57) **ABSTRACT**

The present invention concerns the identification and detection of biological fluid biomarkers of neonatal sepsis using global proteomic approaches.

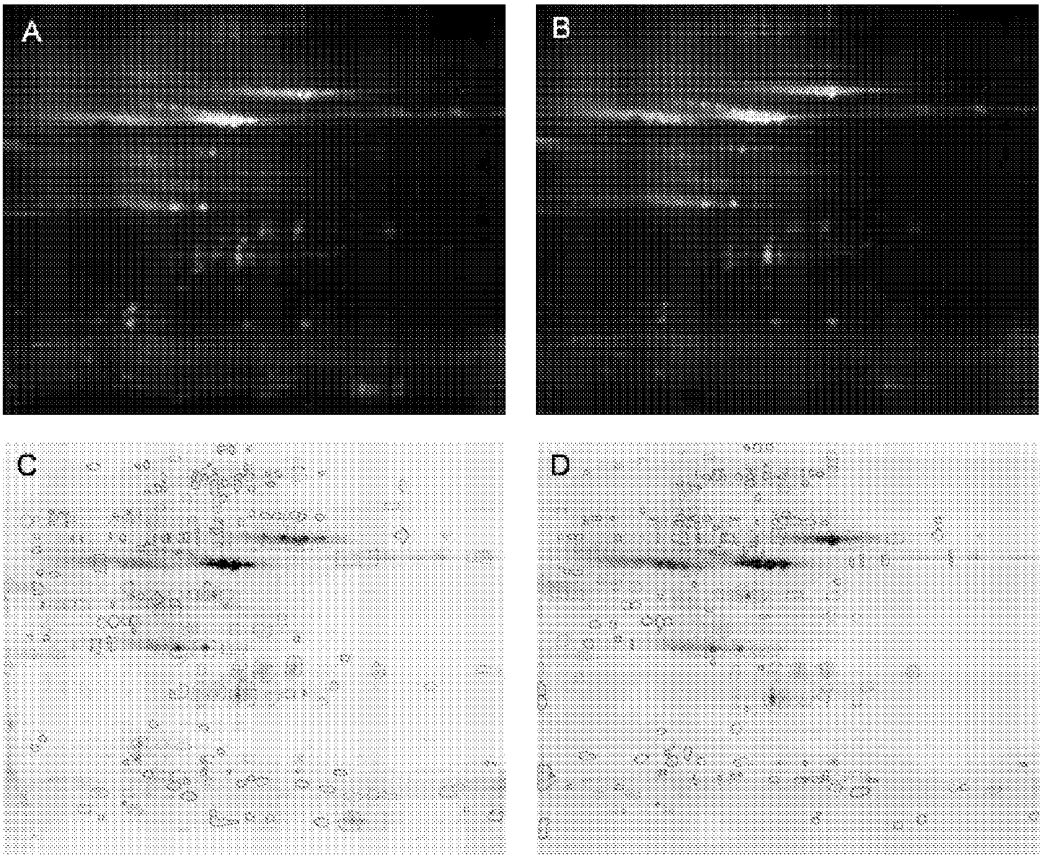


Figure 1

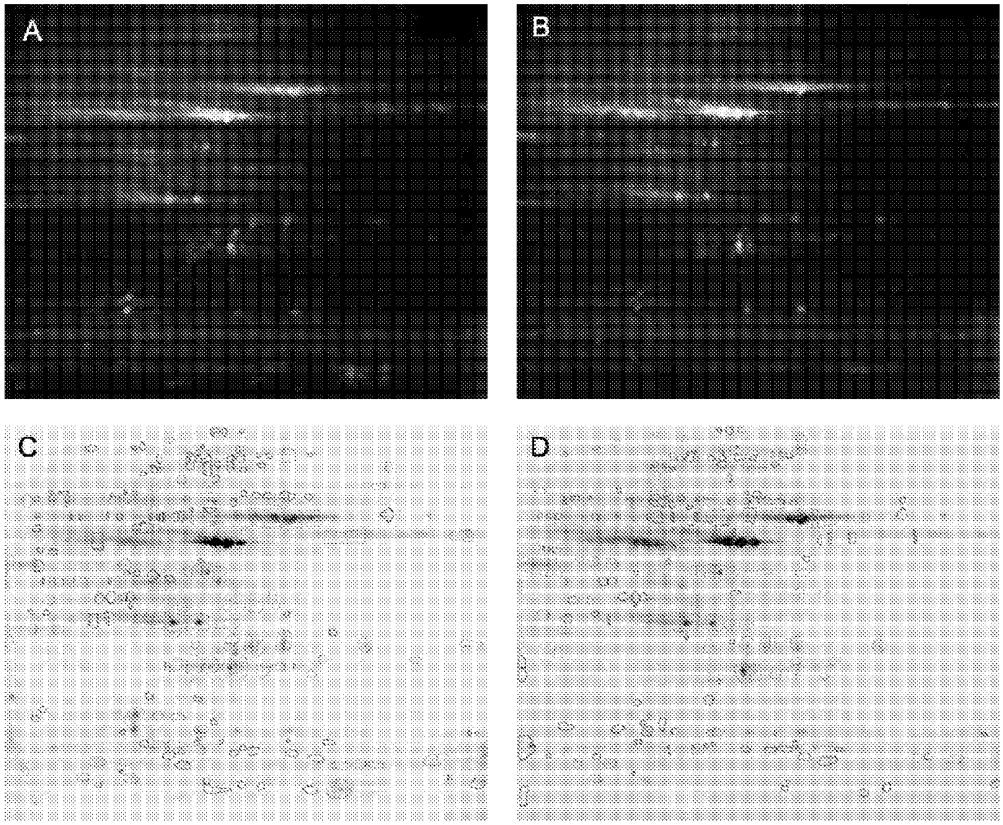


Figure 2A

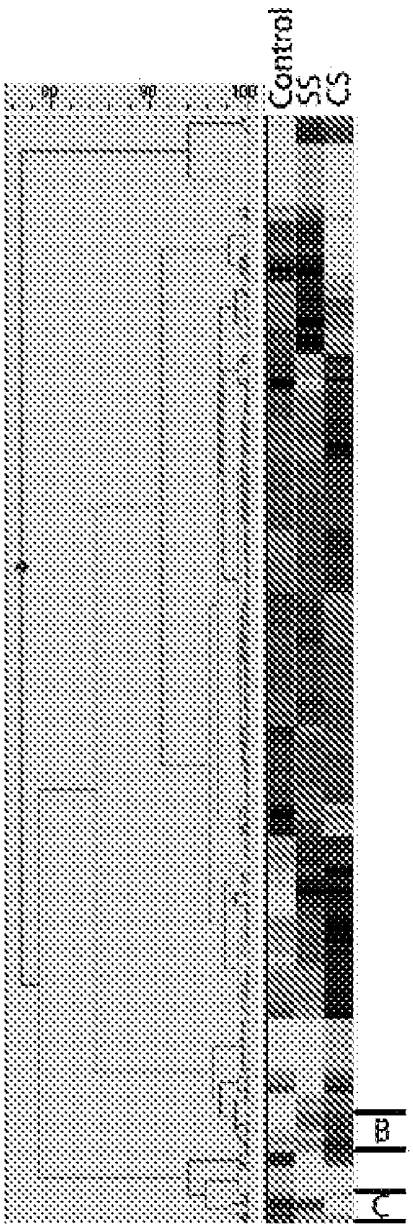


Figure 2B

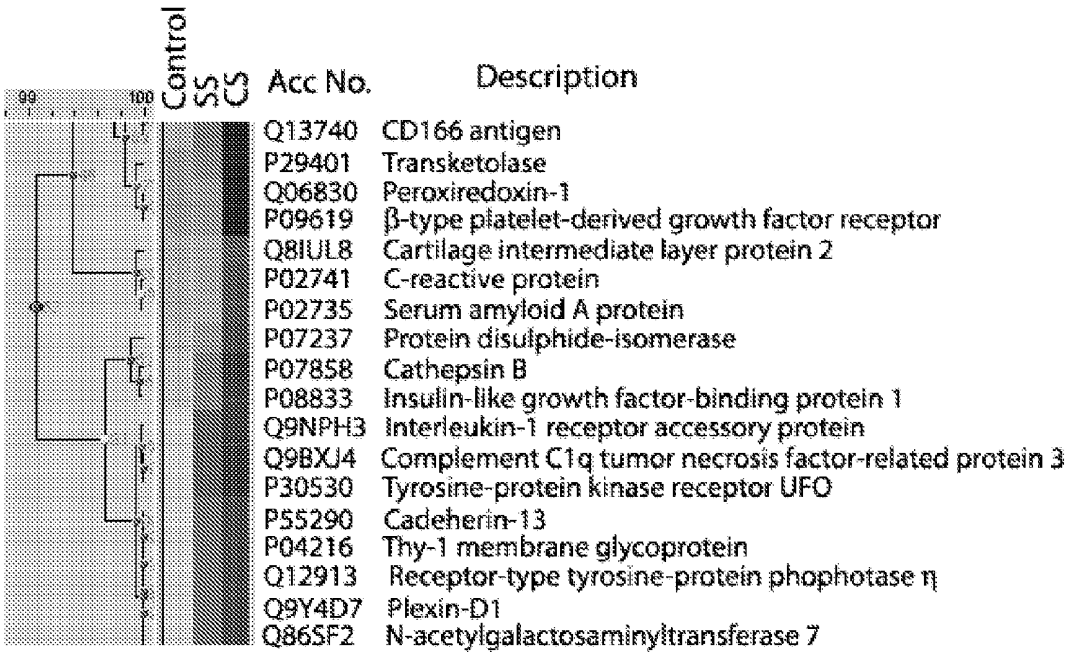
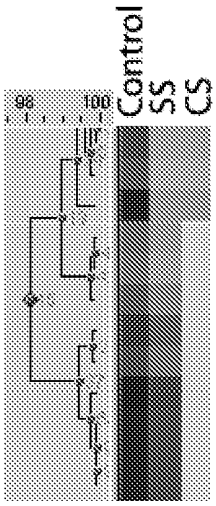

Control
SS
CS
Acc No.
Description
99
100
Q13740 CD166 antigen
P29401 Transketolase
Q06830 Peroxiredoxin-1
P09619 β-type platelet-derived growth factor receptor
Q8IUL8 Cartilage intermediate layer protein 2
P02741 C-reactive protein
P02735 Serum amyloid A protein
P07237 Protein disulphide-isomerase
P07858 Cathepsin B
P08833 Insulin-like growth factor-binding protein 1
Q9NPH3 Interleukin-1 receptor accessory protein
Q9BXJ4 Complement C1q tumor necrosis factor-related protein 3
P30530 Tyrosine-protein kinase receptor UFO
P55290 Cadeherin-13
P04216 Thy-1 membrane glycoprotein
Q12913 Receptor-type tyrosine-protein phophotase η
Q9Y4D7 Plexin-D1
Q86SF2 N-acetylgalactosaminyltransferase 7

Figure 2C



Acc No.	Description
Q15149	Plectin-1
Q15942	Zyxin
P05186	Alkaline phosphatase, tissue-nonspecific isozyme
O15143	Actin-related protein 2/3 complex subunit 1B
Q9H4B7	Tubulin β-1 chain
Q9NUQ9	Protein FAM49B
P09972	Fructose-biphosphate aldolase C
P52907	F-actin-capping protein subunit α-1
Q06323	Proteasome activator complex subunit 1
Q96JB1	Ciiliary dynein heavy chain 8
P13489	Ribonuclease inhibitor
Q01082	Spectrin β chain, brain 1

BIOMARKERS FOR DETECTION OF NEONATAL SEPSIS IN BIOLOGICAL FLUID

RELATED APPLICATION

[0001] This application claims priority under 35 U.S.C. §119(e) to U.S. provisional application No. 61/147,635, filed Jan. 27, 2009, the entire contents of which are incorporated herein by reference.

BACKGROUND OF THE INVENTION

[0002] 1. Field of the Invention

[0003] The present invention concerns the identification and detection of biomarkers of neonatal sepsis and neonatal sepsis associated complications in biological fluids using global proteomic approaches.

[0004] 2. Sequence Listing

[0005] The instant application contains a Sequence Listing which has been submitted via EFS-Web and is hereby incorporated by reference in its entirety. Said ASCII copy, created on Dec. 9, 2009, is named PTX-0013PR.txt, and is 412,016 bytes in size.

[0006] 3. Description of the Related Art

[0007] Sepsis is a serious problem for neonates who are admitted for neonatal intensive care. It is associated with an increase in mortality, morbidity, and prolonged length of hospital stay. Thus, both the human and fiscal costs of these infections are high. Possible ("rule-out" or "suspected") early onset septicemia remains the most common admitting diagnosis to the neonatal intensive care unit (NICU). Although the rate of early-onset sepsis increases with the degree of both prematurity and low birth weight, no specific laboratory test has been shown to be sufficiently precise to allow the identification of patients who have a "real" blood-stream infection and, therefore, who need to be treated with a full course of antibiotics. As a result, antibiotic use is many times the rate of "proven" sepsis and overuse of these agents facilitates the growth of resistant organisms in the neonatal intensive care unit. (Clarke 2004). In addition, the prolongation of hospital stay adds immeasurably to the cost of care in the NICU and enhances the risk of nosocomial septicemia from subsequent hospital acquired micro-organisms.

[0008] The U.S. Department of Health and Human Services Centers for Disease Control and Prevention defines early-onset infection as an infection during hospitalization that occurs during the first 72 hours of life, whereas late-onset infection occurs after that period of time. (Lopez 2002). Nosocomial infection is equivalent to late-onset, or infection after the first 72 hours of life. (Craft 2001). Infection rates may be stated as a percent of admissions, percent of liveborn infants, or by the number of infections per 1000 patient days. Early onset infection rates consistently run at approximately 2 per thousand live births. As 20% to 30% of preterm neonates may have two or more nosocomial infection episodes, infection rates per patient days probably gives a more accurate idea of magnitude in late-onset infection, whereas rates per patient group (admissions, liveborn infants, birth-weight range, gestational age range) give a good idea of attack or incidence rates.

[0009] The neonatal intensive care unit (NICU) nosocomial or late onset infection rate has increased over the past decade. (Craft 2001, Zafar 2001). The total number of neonates who develop nosocomial infection per admission varies from 6.2% (Ferguson 1996) to 33% (Hentschel 1999) or, when reported as total infections per 1000 patient days, the rate varies from 4.8 (Ferguson 1996) to 22 (Drews 1995). Blood-stream infections (nosocomial sepsis) vary from 3% to 28% of admissions. (Ferguson 1996, Hentschel 1999, Berger 1998, Horbar 2001, Nagata 2002). The variability of infection rates depends on the gestational age, the distribution of the infants surveyed for the report, and on the specific environment and care practices. (Gaynes 1996).

[0010] The gold standard for the diagnosis of true early-onset sepsis remains the finding of a positive blood culture for a known pathogen. Commonly, early onset sepsis will be considered present when a neonate has at least two of the following features in the clinical course, and a positive blood culture of 1 mL or greater volume:

[0011] 1) Maternal history of fever >100.4° F., prolonged premature rupture of membranes during labor (>12 hours duration), or presumed chorioamnionitis

[0012] 2) Malodorous or purulent appearing amniotic fluid at delivery

[0013] 3) Clinical findings consistent with sepsis that may include any of the following signs: low 5 minute Apgar score (<6), pallor, cyanosis, hypotension, tachypnea, tachycardia, apnea, abdominal distension, poor feeding, or lethargy

[0014] 4) Supporting laboratory data that includes a WBC count on CBC<8000/mm3 or >35,000/mm3; I:T neutrophil count >2; CRP >8; or pneumonia on chest radiograph.

[0015] This points to the need for the identification of sepsis-associated biomarkers within biological fluid obtained at delivery able to identify subjects with early-onset neonatal sepsis and neonatal sepsis associated complications to facilitate early treatment. Reductions in the risk of neonatal sepsis and its associated morbidities may well depend upon earlier identification of patients at risk.

SUMMARY OF THE INVENTION

[0016] In one aspect, the invention provides a method for diagnosis of neonatal sepsis in a mammalian subject comprising: (a) testing in a sample of biological fluid obtained from said subject the level of one or more proteins selected from the group consisting of C-reactive protein precursor (SEQ ID NO:1), Interleukin-1 receptor accessory protein precursor (SEQ ID NO:2), Interleukin-6 precursor (SEQ ID NO:3), Interleukin-1 receptor-like 1 precursor (SEQ ID NO:4), Serum amyloid A protein precursor (SEQ ID NO:5), CD5 antigen-like precursor (SEQ ID NO:6), Beta-2-microglobulin precursor (SEQ ID NO:7), Bone-marrow proteoglycan precursor (SEQ ID NO:8), Selenium-binding protein 1 (SEQ ID NO:9), Lipopolysaccharide-binding protein precursor (SEQ ID NO:10), Chondroitin sulfate proteoglycan 4 precursor (SEQ ID NO:11), Osteopontin precursor (SEQ ID NO:12), Rho GDP-dissociation inhibitor 2 (SEQ ID NO:13), Carbonic anhydrase 2 (SEQ ID NO:14), Neutrophil gelatinase-associated lipocalin precursor (SEQ ID NO:15), Collagen alpha-5(IV) chain precursor (SEQ ID NO:16), Connective tissue growth factor precursor (SEQ ID NO:17), Macrophage colony-stimulating factor 1 precursor (SEQ ID NO:18), Protein kinase C-binding protein NELL2 precursor (SEQ ID NO:19), Neudesin precursor (SEQ ID NO:20), Protein disulfide-isomerase precursor (SEQ ID NO:21), Ribonuclease pancreatic precursor (SEQ ID NO:22), Delta-like protein precursor (SEQ ID NO:23), Chromogranin-A precursor (SEQ ID NO:24), Osteomodulin precursor (SEQ ID NO:25), Collagen alpha-2(I) chain precursor (SEQ ID NO:26), Prolow-density lipoprotein receptor-related protein 1 precursor

(SEQ ID NO:27), Laminin subunit gamma-1 precursor (SEQ ID NO:28), Laminin subunit beta-1 precursor (SEQ ID NO:29), Collagen alpha-1(II) chain precursor (SEQ ID NO:30), Metalloproteinase inhibitor 1 precursor (SEQ ID NO:31), Protein FAM3C precursor (SEQ ID NO:32), Alpha-actinin-1 (SEQ ID NO:33), F-actin-capping protein subunit alpha-1 (SEQ ID NO:34), Aminopeptidase N (SEQ ID NO:35), Insulin-like growth factor-binding protein 1 precursor (SEQ ID NO:36), Cell adhesion molecule 1 precursor (SEQ ID NO:37), Cathepsin B precursor (SEQ ID NO:38), Exostosin-2 (SEQ ID NO:39), Cathepsin D precursor (SEQ ID NO:40), Neurogenic locus notch homolog protein 3 precursor (SEQ ID NO:41), Cystatin-M precursor (SEQ ID NO:42), Noelin precursor (SEQ ID NO:43), Insulin-like growth factor-binding protein 2 precursor (SEQ ID NO:44), Endoplasmin precursor (SEQ ID NO:45), Proprotein convertase subtilisin/kexin type 9 precursor (SEQ ID NO:46), Insulin-like growth factor-binding protein complex acid labile chain precursor (SEQ ID NO:47), Ezrin (SEQ ID NO:48), Fatty acid-binding protein, liver (SEQ ID NO:49), Probable G-protein coupled receptor 116 precursor (SEQ ID NO:50), Seprase (SEQ ID NO:51), Oncoprotein-induced transcript 3 protein precursor (SEQ ID NO:52), Hypoxia up-regulated protein 1 precursor (SEQ ID NO:53), Trans-Golgi network integral membrane protein 2 precursor (SEQ ID NO:54), Transketolase (SEQ ID NO:55), Receptor-type tyrosine-protein phosphatase F precursor (SEQ ID NO:56), Intercellular adhesion molecule 1 precursor (SEQ ID NO:57), Low-density lipoprotein receptor precursor (SEQ ID NO:58), 78 kDa glucose-regulated protein precursor (SEQ ID NO:59), Neighbor of punc e11 precursor (SEQ ID NO:60), Mannosyl-oligosaccharide 1,2-alpha-mannosidase IA (SEQ ID NO:61), Pyruvate kinase isozymes M1/M2 (SEQ ID NO:62), Matrix metalloproteinase-9 (SEQ ID NO:64), Alpha-1-acid glycoprotein 1 (SEQ ID NO:65), and Stress-induced-phosphoprotein 1 (SEQ ID NO:63), relative to the level in normal biological fluid or biological fluid known to be indicative of neonatal sepsis; and (b)

[0017] diagnosing said subject with neonatal sepsis if said level shows a statistically significant difference relative to the level in said normal biological fluid, or does not show a statistically significant difference relative to the level in said biological fluid known to be indicative of neonatal sepsis.

[0018] In certain embodiments, the method includes testing the level of at least two, at least three, at least four, at least five, at least six, at least seven, and so on, of the listed proteins, in any combination.

[0019] In a specific embodiment, the subject is a human patient.

[0020] In certain embodiments, the biological fluid is selected from the group consisting of cord blood, cerebrospinal fluid, and neonatal serum. In a specific embodiment, the biological fluid is cord blood.

[0021] In another embodiment, the diagnosis is determined within 24 hours of birth.

[0022] In one embodiment, the testing is implemented using an apparatus adapted to determine the level of said proteins. In another embodiment, the testing is performed by using a software program executed by a suitable processor. In certain embodiments, the program is embodied in software stored on a tangible medium. In certain other embodiments, the tangible medium is selected from the group consisting of a CD-ROM, a floppy disk, a hard drive, a DVD, and a memory associated with the processor.

[0023] In certain embodiments, the methods of the invention further include a step of preparing a report recording the results of the testing or the diagnosis. In one embodiment, the report is recorded or stored on a tangible medium. In a specific embodiment, the tangible medium is paper. In another embodiment, the tangible medium is selected from the group consisting of a CD-ROM, a floppy disk, a hard drive, a DVD, and a memory associated with the processor.

[0024] In certain other embodiments, the methods of the invention further include a step of communicating the results of said diagnosis to an interested party. In one embodiment, the interested party is the patient or the attending physician. In another embodiment, the communication is in writing, by email, or by telephone.

[0025] In one embodiment, the method includes testing the level of proteins Insulin-like growth factor-binding protein 1 precursor (SEQ ID NO:36), Interleukin-6 precursor (SEQ ID NO:3), C-reactive protein precursor (SEQ ID NO:1), Beta-2-microglobulin precursor (SEQ ID NO:7), Cathepsin B precursor (SEQ ID NO:38), Cystatin-M precursor (SEQ ID NO:42), Insulin-like growth factor-binding protein 2 precursor (SEQ ID NO:44), Matrix metalloproteinase-9 (SEQ ID NO:64), Metalloproteinase inhibitor 1 precursor (SEQ ID NO:31), and Alpha-1-acid glycoprotein 1 (SEQ ID NO:65), and diagnosing said subject with neonatal sepsis, if one or more of said tested proteins shows a significant difference in the cord blood sample relative to normal cord blood. In a certain embodiment, the method includes diagnosing said subject with neonatal sepsis, if all of said tested proteins show a significant difference in the cord blood sample relative to normal cord blood.

[0026] In one embodiment, the method includes testing the level of proteins Insulin-like growth factor-binding protein 1 precursor (SEQ ID NO:36) and Interleukin-6 precursor (SEQ ID NO:3), and diagnosing said subject with neonatal sepsis, if one or more of said tested proteins shows a significant difference in the cord blood sample relative to normal cord blood. In other embodiments, the method includes testing the level of proteins Insulin-like growth factor-binding protein 1 precursor (SEQ ID NO:36) and C-reactive protein precursor (SEQ ID NO:1). In yet other embodiments, the method includes testing the level of proteins Insulin-like growth factor-binding protein 1 precursor (SEQ ID NO:36) and Beta-2-microglobulin precursor (SEQ ID NO:7). In still other embodiments, the method includes testing the level of proteins Insulin-like growth factor-binding protein 1 precursor (SEQ ID NO:36) and Cathepsin B precursor (SEQ ID NO:38). In still other embodiments, the method includes testing the level of proteins Insulin-like growth factor-binding protein 1 precursor (SEQ ID NO:36) and Cystatin-M precursor (SEQ ID NO:42). In still other embodiments, the method includes testing the level of proteins Insulin-like growth factor-binding protein 1 precursor (SEQ ID NO:36) and Insulin-like growth factor-binding protein 2 precursor (SEQ ID NO:44). In still other embodiments, the method includes testing the level of proteins Insulin-like growth factor-binding protein 1 precursor (SEQ ID NO:36) and Matrix metalloproteinase-9 (SEQ ID NO:64). In still other embodiments, the method includes testing the level of proteins Insulin-like growth factor-binding protein 1 precursor (SEQ ID NO:36) and Metalloproteinase inhibitor 1 precursor (SEQ ID NO:31). In still other embodiments, the method includes

testing the level of proteins Insulin-like growth factor-binding protein 1 precursor (SEQ ID NO:36) and Alpha-1-acid glycoprotein 1 (SEQ ID NO:65).

[0027] In certain embodiments, the level of the listed proteins is determined by an immunoassay, by mass spectrometry, or by using a protein array.

[0028] In another aspect, the invention provides the use of any one or more proteins selected from the group consisting of C-reactive protein precursor (SEQ ID NO:1), Interleukin-1 receptor accessory protein precursor (SEQ ID NO:2), Interleukin-6 precursor (SEQ ID NO:3), Interleukin-1 receptor-like 1 precursor (SEQ ID NO:4), Serum amyloid A protein precursor (SEQ ID NO:5), CD5 antigen-like precursor (SEQ ID NO:6), Beta-2-microglobulin precursor (SEQ ID NO:7), Bone-marrow proteoglycan precursor (SEQ ID NO:8), Selenium-binding protein 1 (SEQ ID NO:9), Lipopolysaccharide-binding protein precursor (SEQ ID NO:10), Chondroitin sulfate proteoglycan 4 precursor (SEQ ID NO:11), Osteopontin precursor (SEQ ID NO:12), Rho GDP-dissociation inhibitor 2 (SEQ ID NO:13), Carbonic anhydrase 2 (SEQ ID NO:14), Neutrophil gelatinase-associated lipocalin precursor (SEQ ID NO:15), Collagen alpha-5(IV) chain precursor (SEQ ID NO:16), Connective tissue growth factor precursor (SEQ ID NO:17), Macrophage colony-stimulating factor 1 precursor (SEQ ID NO:18), Protein kinase C-binding protein NELL2 precursor (SEQ ID NO:19), Neudesin precursor (SEQ ID NO:20), Protein disulfide-isomerase precursor (SEQ ID NO:21), Ribonuclease pancreatic precursor (SEQ ID NO:22), Delta-like protein precursor (SEQ ID NO:23), Chromogranin-A precursor (SEQ ID NO:24), Osteomodulin precursor (SEQ ID NO:25), Collagen alpha-2(I) chain precursor (SEQ ID NO:26), Prolow-density lipoprotein receptor-related protein 1 precursor (SEQ ID NO:27), Laminin subunit gamma-1 precursor (SEQ ID NO:28), Laminin subunit beta-1 precursor (SEQ ID NO:29), Collagen alpha-1(II) chain precursor (SEQ ID NO:30), Metalloproteinase inhibitor 1 precursor (SEQ ID NO:31), Protein FAM3C precursor (SEQ ID NO:32), Alpha-actinin-1 (SEQ ID NO:33), F-actin-capping protein subunit alpha-1 (SEQ ID NO:34), Aminopeptidase N (SEQ ID NO:35), Insulin-like growth factor-binding protein 1 precursor (SEQ ID NO:36), Cell adhesion molecule 1 precursor (SEQ ID NO:37), Cathepsin B precursor (SEQ ID NO:38), Exostosin-2 (SEQ ID NO:39), Cathepsin D precursor (SEQ ID NO:40), Neurogenic locus notch homolog protein 3 precursor (SEQ ID NO:41), Cystatin-M precursor (SEQ ID NO:42), Noelin precursor (SEQ ID NO:43), Insulin-like growth factor-binding protein 2 precursor (SEQ ID NO:44), Endoplasmin precursor (SEQ ID NO:45), Proprotein convertase subtilisin/kexin type 9 precursor (SEQ ID NO:46), Insulin-like growth factor-binding protein complex acid labile chain precursor (SEQ ID NO:47), Ezrin (SEQ ID NO:48), Fatty acid-binding protein, liver (SEQ ID NO:49), Probable G-protein coupled receptor 116 precursor (SEQ ID NO:50), Seprase (SEQ ID NO:51), Oncoprotein-induced transcript 3 protein precursor (SEQ ID NO:52), Hypoxia up-regulated protein 1 precursor (SEQ ID NO:53), Trans-Golgi network integral membrane protein 2 precursor (SEQ ID NO:54), Transketolase (SEQ ID NO:55), Receptor-type tyrosine-protein phosphatase F precursor (SEQ ID NO:56), Intercellular adhesion molecule 1 precursor (SEQ ID NO:57), Low-density lipoprotein receptor precursor (SEQ ID NO:58), 78 kDa glucose-regulated protein precursor (SEQ ID NO:59), Neighbor of punc e11 precursor (SEQ ID NO:60), Mannosyl-oligosaccharide 1,2-alpha-mannosidase IA (SEQ ID NO:61), Pyruvate kinase isozymes M1/M2 (SEQ ID NO:62), Matrix metalloproteinase-9 (SEQ ID NO:64), Alpha-1-acid glycoprotein 1 (SEQ ID NO:65), and Stress-induced-phosphoprotein 1 (SEQ ID NO:63), in the manufacture of a proteomic profile of a biological fluid for the early diagnosis of neonatal sepsis in a subject.

[0029] In certain embodiments, the proteomic profile comprises information of the level of at least two of said proteins, at least three, at least four, at least five, at least six, at least seven, and so on, of the listed proteins, in any combination.

[0030] In a specific embodiment, the subject is a human patient.

[0031] In certain embodiments, the biological fluid is selected from the group consisting of cord blood, neonatal serum and cerebrospinal fluid. In a specific embodiment, the biological fluid is cord blood.

[0032] In one embodiment, the proteomic profile comprises information of the level of said proteins and wherein the diagnosis of said subject with neonatal sepsis is made if one or more of said tested proteins shows a significant difference in the biological fluid sample relative to normal biological fluid.

[0033] In another embodiment, the diagnosis is determined within 24 hours of birth.

[0034] In one embodiment, the proteomic profile comprises information of the level of proteins Insulin-like growth factor-binding protein 1 precursor (SEQ ID NO:36), Interleukin-6 precursor (SEQ ID NO:3), C-reactive protein precursor (SEQ ID NO:1), Beta-2-microglobulin precursor (SEQ ID NO:7), Cathepsin B precursor (SEQ ID NO:38), Cystatin-M precursor (SEQ ID NO:42), Insulin-like growth factor-binding protein 2 precursor (SEQ ID NO:44), Matrix metalloproteinase-9 (SEQ ID NO:64), Metalloproteinase inhibitor 1 precursor (SEQ ID NO:31), and Alpha-1-acid glycoprotein 1 (SEQ ID NO:65), and wherein the diagnosis of said subject with neonatal sepsis is made if one or more of said tested proteins shows a significant difference in the biological fluid sample relative to normal biological fluid. In a specific embodiment, the diagnosis of said subject with neonatal sepsis is made if all of said tested proteins show a significant difference in the biological fluid sample relative to normal biological fluid.

[0035] In certain embodiments, the level of the listed proteins is determined by an immunoassay, by mass spectrometry, or by using a protein array.

[0036] In yet another aspect, the invention provides an immunoassay kit comprising antibodies and reagents for the detection of one or more proteins selected from the group consisting of C-reactive protein precursor (SEQ ID NO:1), Interleukin-1 receptor accessory protein precursor (SEQ ID NO:2), Interleukin-6 precursor (SEQ ID NO:3), Interleukin-1 receptor-like 1 precursor (SEQ ID NO:4), Serum amyloid A protein precursor (SEQ ID NO:5), CD5 antigen-like precursor (SEQ ID NO:6), Beta-2-microglobulin precursor (SEQ ID NO:7), Bone-marrow proteoglycan precursor (SEQ ID NO:8), Selenium-binding protein 1 (SEQ ID NO:9), Lipopolysaccharide-binding protein precursor (SEQ ID NO:10), Chondroitin sulfate proteoglycan 4 precursor (SEQ ID NO:11), Osteopontin precursor (SEQ ID NO:12), Rho GDP-dissociation inhibitor 2 (SEQ ID NO:13), Carbonic anhydrase 2 (SEQ ID NO:14), Neutrophil gelatinase-associated lipocalin precursor (SEQ ID NO:15), Collagen alpha-5 (IV) chain precursor (SEQ ID NO:16), Connective tissue growth factor precursor (SEQ ID NO:17), Macrophage

colony-stimulating factor 1 precursor (SEQ ID NO:18), Protein kinase C-binding protein NELL2 precursor (SEQ ID NO:19), Neudesin precursor (SEQ ID NO:20), Protein disulfide-isomerase precursor (SEQ ID NO:21), Ribonuclease pancreatic precursor (SEQ ID NO:22), Delta-like protein precursor (SEQ ID NO:23), Chromogranin-A precursor (SEQ ID NO:24), Osteomodulin precursor (SEQ ID NO:25), Collagen alpha-2(I) chain precursor (SEQ ID NO:26), Prolow-density lipoprotein receptor-related protein 1 precursor (SEQ ID NO:27), Laminin subunit gamma-1 precursor (SEQ ID NO:28), Laminin subunit beta-1 precursor (SEQ ID NO:29), Collagen alpha-1(II) chain precursor (SEQ ID NO:30), Metalloproteinase inhibitor 1 precursor (SEQ ID NO:31), Protein FAM3C precursor (SEQ ID NO:32), Alpha-actinin-1 (SEQ ID NO:33), F-actin-capping protein subunit alpha-1 (SEQ ID NO:34), Aminopeptidase N (SEQ ID NO:35), Insulin-like growth factor-binding protein 1 precursor (SEQ ID NO:36), Cell adhesion molecule 1 precursor (SEQ ID NO:37), Cathepsin B precursor (SEQ ID NO:38), Exostosin-2 (SEQ ID NO:39), Cathepsin D precursor (SEQ ID NO:40), Neurogenic locus notch homolog protein 3 precursor (SEQ ID NO:41), Cystatin-M precursor (SEQ ID NO:42), Noelin precursor (SEQ ID NO:43), Insulin-like growth factor-binding protein 2 precursor (SEQ ID NO:44), Endoplasmin precursor (SEQ ID NO:45), Proprotein convertase subtilisin/kexin type 9 precursor (SEQ ID NO:46), Insulin-like growth factor-binding protein complex acid labile chain precursor (SEQ ID NO:47), Ezrin (SEQ ID NO:48), Fatty acid-binding protein, liver (SEQ ID NO:49), Probable G-protein coupled receptor 116 precursor (SEQ ID NO:50), Seprase (SEQ ID NO:51), Oncoprotein-induced transcript 3 protein precursor (SEQ ID NO:52), Hypoxia up-regulated protein 1 precursor (SEQ ID NO:53), Trans-Golgi network integral membrane protein 2 precursor (SEQ ID NO:54), Transketolase (SEQ ID NO:55), Receptor-type tyrosine-protein phosphatase F precursor (SEQ ID NO:56), Intercellular adhesion molecule 1 precursor (SEQ ID NO:57), Low-density lipoprotein receptor precursor (SEQ ID NO:58), 78 kDa glucose-regulated protein precursor (SEQ ID NO:59), Neighbor of punc e11 precursor (SEQ ID NO:60), Mannosyl-oligosaccharide 1,2-alpha-mannosidase IA (SEQ ID NO:61), Pyruvate kinase isozymes M1/M2 (SEQ ID NO:62), Matrix metalloproteinase-9 (SEQ ID NO:64), Alpha-1-acid glycoprotein 1 (SEQ ID NO:65), and Stress-induced-phosphoprotein 1 (SEQ ID NO:63).

[0037] In another aspect, the invention provides an immunoassay kit comprising antibodies and reagents for the detection of one or more proteins selected from the group consisting of Insulin-like growth factor-binding protein 1 precursor (SEQ ID NO:36), Interleukin-6 precursor (SEQ ID NO:3), C-reactive protein precursor (SEQ ID NO:1), Beta-2-microglobulin precursor (SEQ ID NO:7), Cathepsin B precursor (SEQ ID NO:38), Cystatin-M precursor (SEQ ID NO:42), Insulin-like growth factor-binding protein 2 precursor (SEQ ID NO:44), Matrix metalloproteinase-9 (SEQ ID NO:64), Metalloproteinase inhibitor 1 precursor (SEQ ID NO:31), and Alpha-1-acid glycoprotein 1 (SEQ ID NO:65).

[0038] In one embodiment, the immunoassay kit includes antibodies and reagents for the detection of all of listed proteins.

[0039] In yet another aspect, the invention provides a report comprising the results of and/or diagnosis based on a test comprising (a) testing in a sample of biological fluid obtained from said subject the level of one or more proteins selected from the group consisting of C-reactive protein precursor (SEQ ID NO:1), Interleukin-1 receptor accessory protein precursor (SEQ ID NO:2), Interleukin-6 precursor (SEQ ID NO:3), Interleukin-1 receptor-like 1 precursor (SEQ ID NO:4), Serum amyloid A protein precursor (SEQ ID NO:5), CD5 antigen-like precursor (SEQ ID NO:6), Beta-2-microglobulin precursor (SEQ ID NO:7), Bone-marrow proteoglycan precursor (SEQ ID NO:8), Selenium-binding protein 1 (SEQ ID NO:9), Lipopolysaccharide-binding protein precursor (SEQ ID NO:10), Chondroitin sulfate proteoglycan 4 precursor (SEQ ID NO:11), Osteopontin precursor (SEQ ID NO:12), Rho GDP-dissociation inhibitor 2 (SEQ ID NO:13), Carbonic anhydrase 2 (SEQ ID NO:14), Neutrophil gelatinase-associated lipocalin precursor (SEQ ID NO:15), Collagen alpha-5(IV) chain precursor (SEQ ID NO:16), Connective tissue growth factor precursor (SEQ ID NO:17), Macrophage colony-stimulating factor 1 precursor (SEQ ID NO:18), Protein kinase C-binding protein NELL2 precursor (SEQ ID NO:19), Neudesin precursor (SEQ ID NO:20), Protein disulfide-isomerase precursor (SEQ ID NO:21), Ribonuclease pancreatic precursor (SEQ ID NO:22), Delta-like protein precursor (SEQ ID NO:23), Chromogranin-A precursor (SEQ ID NO:24), Osteomodulin precursor (SEQ ID NO:25), Collagen alpha-2(I) chain precursor (SEQ ID NO:26), Prolow-density lipoprotein receptor-related protein 1 precursor (SEQ ID NO:27), Laminin subunit gamma-1 precursor (SEQ ID NO:28), Laminin subunit beta-1 precursor (SEQ ID NO:29), Collagen alpha-1(II) chain precursor (SEQ ID NO:30), Metalloproteinase inhibitor 1 precursor (SEQ ID NO:31), Protein FAM3C precursor (SEQ ID NO:32), Alpha-actinin-1 (SEQ ID NO:33), F-actin-capping protein subunit alpha-1 (SEQ ID NO:34), Aminopeptidase N (SEQ ID NO:35), Insulin-like growth factor-binding protein 1 precursor (SEQ ID NO:36), Cell adhesion molecule 1 precursor (SEQ ID NO:37), Cathepsin B precursor (SEQ ID NO:38), Exostosin-2 (SEQ ID NO:39), Cathepsin D precursor (SEQ ID NO:40), Neurogenic locus notch homolog protein 3 precursor (SEQ ID NO:41), Cystatin-M precursor (SEQ ID NO:42), Noelin precursor (SEQ ID NO:43), Insulin-like growth factor-binding protein 2 precursor (SEQ ID NO:44), Endoplasmin precursor (SEQ ID NO:45), Proprotein convertase subtilisin/kexin type 9 precursor (SEQ ID NO:46), Insulin-like growth factor-binding protein complex acid labile chain precursor (SEQ ID NO:47), Ezrin (SEQ ID NO:48), Fatty acid-binding protein, liver (SEQ ID NO:49), Probable G-protein coupled receptor 116 precursor (SEQ ID NO:50), Seprase (SEQ ID NO:51), Oncoprotein-induced transcript 3 protein precursor (SEQ ID NO:52), Hypoxia up-regulated protein 1 precursor (SEQ ID NO:53), Trans-Golgi network integral membrane protein 2 precursor (SEQ ID NO:54), Transketolase (SEQ ID NO:55), Receptor-type tyrosine-protein phosphatase F precursor (SEQ ID NO:56), Intercellular adhesion molecule 1 precursor (SEQ ID NO:57), Low-density lipoprotein receptor precursor (SEQ ID NO:58), 78 kDa glucose-regulated protein precursor (SEQ ID NO:59), Neighbor of punc e11 precursor (SEQ ID NO:60), Mannosyl-oligosaccharide 1,2-alpha-mannosidase IA (SEQ ID NO:61), Pyruvate kinase isozymes M1/M2 (SEQ ID NO:62), Matrix metalloproteinase-9 (SEQ ID NO:64), Alpha-1-acid glycoprotein 1 (SEQ ID NO:65), and Stress-induced-phosphoprotein 1 (SEQ ID NO:63), relative to the level in normal biological fluid or biological fluid known to be indicative of neonatal sepsis; and (b) diagnosing said subject with neonatal sepsis if said level shows a statistically significant difference relative to the level in said normal biological fluid, or does not

show a statistically significant difference relative to the level in said biological fluid known to be indicative of neonatal sepsis.

[0040] In still another aspect, the invention provides a tangible medium storing the results of and/or diagnosis based on a test comprising (a) testing in a sample of biological fluid obtained from said subject the level of one or more proteins selected from the group consisting of C-reactive protein precursor (SEQ ID NO:1), Interleukin-1 receptor accessory protein precursor (SEQ ID NO:2), Interleukin-6 precursor (SEQ ID NO:3), Interleukin-1 receptor-like 1 precursor (SEQ ID NO:4), Serum amyloid A protein precursor (SEQ ID NO:5), CD5 antigen-like precursor (SEQ ID NO:6), Beta-2-microglobulin precursor (SEQ ID NO:7), Bone-marrow proteoglycan precursor (SEQ ID NO:8), Selenium-binding protein 1 (SEQ ID NO:9), Lipopolysaccharide-binding protein precursor (SEQ ID NO:10), Chondroitin sulfate proteoglycan 4 precursor (SEQ ID NO:11), Osteopontin precursor (SEQ ID NO:12), Rho GDP-dissociation inhibitor 2 (SEQ ID NO:13), Carbonic anhydrase 2 (SEQ ID NO:14), Neutrophil gelatinase-associated lipocalin precursor (SEQ ID NO:15), Collagen alpha-5(IV) chain precursor (SEQ ID NO:16), Connective tissue growth factor precursor (SEQ ID NO:17), Macrophage colony-stimulating factor 1 precursor (SEQ ID NO:18), Protein kinase C-binding protein NELL2 precursor (SEQ ID NO:19), Neudesin precursor (SEQ ID NO:20), Protein disulfide-isomerase precursor (SEQ ID NO:21), Ribonuclease pancreatic precursor (SEQ ID NO:22), Delta-like protein precursor (SEQ ID NO:23), Chromogranin-A precursor (SEQ ID NO:24), Osteomodulin precursor (SEQ ID NO:25), Collagen alpha-2(I) chain precursor (SEQ ID NO:26), Prolow-density lipoprotein receptor-related protein 1 precursor (SEQ ID NO:27), Laminin subunit gamma-1 precursor (SEQ ID NO:28), Laminin subunit beta-1 precursor (SEQ ID NO:29), Collagen alpha-1(II) chain precursor (SEQ ID NO:30), Metalloproteinase inhibitor 1 precursor (SEQ ID NO:31), Protein FAM3C precursor (SEQ ID NO:32), Alpha-actinin-1 (SEQ ID NO:33), F-actin-capping protein subunit alpha-1 (SEQ ID NO:34), Aminopeptidase N (SEQ ID NO:35), Insulin-like growth factor-binding protein 1 precursor (SEQ ID NO:36), Cell adhesion molecule 1 precursor (SEQ ID NO:37), Cathepsin B precursor (SEQ ID NO:38), Exostosin-2 (SEQ ID NO:39), Cathepsin D precursor (SEQ ID NO:40), Neurogenic locus notch homolog protein 3 precursor (SEQ ID NO:41), Cystatin-M precursor (SEQ ID NO:42), Noelin precursor (SEQ ID NO:43), Insulin-like growth factor-binding protein 2 precursor (SEQ ID NO:44), Endoplasmin precursor (SEQ ID NO:45), Proprotein convertase subtilisin/kexin type 9 precursor (SEQ ID NO:46), Insulin-like growth factor-binding protein complex acid labile chain precursor (SEQ ID NO:47), Ezrin (SEQ ID NO:48), Fatty acid-binding protein, liver (SEQ ID NO:49), Probable G-protein coupled receptor 116 precursor (SEQ ID NO:50), Seprase (SEQ ID NO:51), Oncoprotein-induced transcript 3 protein precursor (SEQ ID NO:52), Hypoxia up-regulated protein 1 precursor (SEQ ID NO:53), Trans-Golgi network integral membrane protein 2 precursor (SEQ ID NO:54), Transketolase (SEQ ID NO:55), Receptor-type tyrosine-protein phosphatase F precursor (SEQ ID NO:56), Intercellular adhesion molecule 1 precursor (SEQ ID NO:57), Low-density lipoprotein receptor precursor (SEQ ID NO:58), 78 kDa glucose-regulated protein precursor (SEQ ID NO:59), Neighbor of punc e11 precursor (SEQ ID NO:60), Mannosyl-oligosaccharide 1,2-alpha-mannosidase IA (SEQ ID NO:61), Pyruvate kinase isozymes M1/M2 (SEQ ID NO:62), Matrix metalloproteinase-9 (SEQ ID NO:64), Alpha-1-acid glycoprotein 1 (SEQ ID NO:65), and Stress-induced-phosphoprotein 1 (SEQ ID NO:63), relative to the level in normal biological fluid or biological fluid known to be indicative of neonatal sepsis; and (b) diagnosing said subject with neonatal sepsis if said level shows a statistically significant difference relative to the level in said normal biological fluid, or does not show a statistically significant difference relative to the level in said biological fluid known to be indicative of neonatal sepsis.

BRIEF DESCRIPTION OF THE DRAWINGS

[0041] FIG. **1** depicts Cord Blood DIGE Analysis: (A) control (red) vs. suspected sepsis (SS) (green) DIGE gel. (B) control (red) vs. confirmed sepsis (CS) (green) DIGE gel. Spots that are not differentially expressed appear yellow. (C) Differentially expressed spots between suspected sepsis (SS) vs. control. (D) Differentially expressed spots between confirmed sepsis (CS) vs. control. Spots highlighted in red were determined to be ≧2 fold down regulated and spots highlighted in green were determined to be ≧2 fold up regulated.

[0042] FIG. **2** depicts spectral counts of cord blood proteins from control, suspected sepsis (SS), and confirmed sepsis (CS) neonatal subjects are loaded into GeneMaths software for differential expression visualization. Proteins are hierarchically clustered using Euclidean distance learning in 200 iterations and shown in FIG. **2**A. Selected sub clusters of up regulated (FIG. **2**B) and down regulated proteins (FIG. **2**C) are also shown. Positions of the selected sub clusters in FIG. **2**A are marked accordingly.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

I. Definitions

[0043] Unless defined otherwise, technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. Singleton et al., Dictionary of Microbiology and Molecular Biology 2nd ed., J. Wiley & Sons (New York, N.Y. 1994) provides one skilled in the art with a general guide to many of the terms used in the present application.

[0044] The term "neonatal sepsis" is used herein to describe infection of the blood of a newborn and includes all complications associated with such infection. Neonatal sepsis associated complications include but are not limited to respiratory distress syndrome (RDS), central nervous system (CNS) complications, e.g., periventricular hemorrhage and periventricular leukomalacia, mental retardation, cerebral palsy (CP), disability and death.

[0045] The term "proteome" is used herein to describe a significant portion of proteins in a biological sample at a given time. The concept of proteome is fundamentally different from the genome. While the genome is virtually static, the proteome continually changes in response to internal and external events.

[0046] The term "proteomic profile" is used to refer to a representation of the expression pattern of a plurality of proteins in a biological sample, e.g. a biological fluid at a given time. The proteomic profile can, for example, be represented as a mass spectrum, but other representations based on any physicochemical or biochemical properties of the proteins are also included. Thus the proteomic profile may, for example,

be based on differences in the electrophoretic properties of proteins, as determined by two-dimensional gel electrophoresis, e.g. by 2-D PAGE, and can be represented, e.g. as a plurality of spots in a two-dimensional electrophoresis gel.

[0047] Differential expression profiles may have important diagnostic value, even in the absence of specifically identified proteins. Single protein spots can then be detected, for example, by immunoblotting, multiple spots or proteins using protein microarrays. The proteomic profile typically represents or contains information that could range from a few peaks to a complex profile representing 50 or more peaks. Thus, for example, the proteomic profile may contain or represent at least 2, or at least 5 or at least 10 or at least 15, or at least 20, or at least 25, or at least 30, or at least 35, or at least 40, or at least 45, or at least 50, or at least 60, or at least 65, or at least 70, or at least 75, or at least 80, or at least 85, or at least 85, or at least 90, or at least 95, or at least 100, or at least 125, or at least 150, or at least 175, or at least 200 proteins.

[0048] The term "biological fluid" as used herein refers to refers to liquid material derived from a human or other animal. Biological fluids include, but are not limited to, cord blood, neonatal serum, cerebrospinal fluid (CSF), cervical-vaginal fluid (CVF), amniotic fluid, serum, plasma, urine, cerebrospinal fluid, breast milk, mucus, saliva, and sweat.

[0049] "Patient response" can be assessed using any endpoint indicating a benefit to the patient, including, without limitation, (1) inhibition, at least to some extent, of the progression of a pathologic condition, (2) prevention of the pathologic condition, (3) relief, at least to some extent, of one or more symptoms associated with the pathologic condition; (4) increase in the length of survival following treatment; and/or (5) decreased mortality at a given point of time following treatment.

[0050] The term "treatment" refers to both therapeutic treatment and prophylactic or preventative measures, wherein the object is to prevent or slow down (lessen) the targeted pathologic condition or disorder. Those in need of treatment include those already with the disorder as well as those prone to have the disorder or those in whom the disorder is to be prevented.

[0051] The designation of any particular protein, as used herein, includes all fragments, precursors, and naturally occurring variants, such as alternatively spliced and allelic variants and isoforms, as well as soluble forms of the protein named, along with native sequence homologs (including all naturally occurring variants) in other species. Thus, for example, when it is stated that the level of haptoglobin precursor (Swiss-Prot Acc. No. P00738) is tested, the statement specifically includes testing any fragments, precursers, or naturally occurring variant of the protein listed under Swiss-Prot Acc. No. P00738, as well as its non-human homologs and naturally occurring variants thereof, if subject is non-human.

II. Detailed Description

[0052] The present invention concerns methods and means for an early, reliable and non-invasive testing of neonatal sepsis and/or neonatal sepsis associated complications by proteomic analysis of biological fluid, such as cord blood. The invention further concerns identification of biomarkers of neonatal sepsis. In another aspect, the invention concerns the use of proteins in the preparation or manufacture of proteomic profiles as a means for the early determination of neonatal sepsis. The invention utilizes proteomics techniques well known in the art, as described, for example, in the following textbooks, the contents of which are hereby expressly incorporated by reference: *Proteome Research: New Frontiers in Functional Genomics* (*Principles and Practice*), M. R. Wilkins et al., eds., Springer Verlag, 1007; *2-D Proteome Analysis Protocols*, Andrew L Link, editor, Humana Press, 1999; *Proteome Research: Two-Dimensional Gel Electrophoresis and Identification Methods* (*Principles and Practice*), T. Rabilloud editor, Springer Verlag, 2000; *Proteome Research: Mass Spectrometry* (*Principles and Practice*), P. James editor, Springer Verlag, 2001; *Introduction to Proteomics*, D. C. Liebler editor, Humana Press, 2002; *Proteomics in Practice: A Laboratory Manual of Proteome Analysis*, R. Westermeier et al., eds., John Wiley & Sons, 2002.

[0053] One skilled in the art will recognize many methods and materials similar or equivalent to those described herein, which could be used in the practice of the present invention. Indeed, the present invention is in no way limited to the methods and materials described.

[0054] 1. Identification of Proteins and Polypeptides Expressed in Biological Fluids

[0055] According to the present invention, proteomics analysis of biological fluids can be performed using a variety of methods known in the art. Biological fluids include, for example, cord blood, neonatal serum, cerebrospinal fluid (CSF), cervical-vaginal fluid (CVF), amniotic fluid, serum, plasma, urine, cerebrospinal fluid, breast milk, mucus, saliva, and sweat.

[0056] Typically, protein patterns (proteome maps) of samples from different sources, such as normal biological fluid (normal sample) and a test biological fluid (test sample), are compared to detect proteins that are up- or down-regulated in a disease. These proteins can then be excised for identification and full characterization, e.g. using peptide-mass fingerprinting and/or mass spectrometry and sequencing methods, or the normal and/or disease-specific proteome map can be used directly for the diagnosis of the disease of interest, or to confirm the presence or absence of the disease.

[0057] In comparative analysis, it is important to treat the normal and test samples exactly the same way, in order to correctly represent the relative level or abundance of proteins, and obtain accurate results. The required amount of total proteins will depend on the analytical technique used, and can be readily determined by one skilled in the art. The proteins present in the biological samples are typically separated by two-dimensional gel electrophoresis (2-DE) according to their pI and molecular weight. The proteins are first separated by their charge using isoelectric focusing (one-dimensional gel electrophoresis). This step can, for example, be carried out using immobilized pH-gradient (IPG) strips, which are commercially available. The second dimension is a normal SDS-PAGE analysis, where the focused IPG strip is used as the sample. After 2-DE separation, proteins can be visualized with conventional dyes, like Coomassie Blue or silver staining, and imaged using known techniques and equipment, such as, e.g. Bio-Rad GS800 densitometer and PDQUEST software, both of which are commercially available. Individual spots are then cut from the gel, destained, and subjected to tryptic digestion. The peptide mixtures can be analyzed by mass spectrometry (MS). Alternatively, the peptides can be separated, for example by capillary high pressure liquid chromatography (HPLC) and can be analyzed by MS either individually, or in pools.

[0058] Mass spectrometers consist of an ion source, mass analyzer, ion detector, and data acquisition unit. First, the peptides are ionized in the ion source. Then the ionized peptides are separated according to their mass-to-charge ratio in the mass analyzer and the separate ions are detected. Mass spectrometry has been widely used in protein analysis, especially since the invention of matrix-assisted laser-desorption ionisation/time-of-flight (MALDI-TOF) and electrospray ionisation (ESI) methods. There are several versions of mass analyzer, including, for example, MALDI-TOF and triple or quadrupole-TOF, or ion trap mass analyzer coupled to ESI. Thus, for example, a Q-Tof-2 mass spectrometer utilizes an orthogonal time-of-flight analyzer that allows the simultaneous detection of ions across the full mass spectrum range. For further details see, e.g. Chemusevich et al., *J. Mass Spectrom.* 36:849-865 (2001). If desired, the amino acid sequences of the peptide fragments and eventually the proteins from which they derived can be determined by techniques known in the art, such as certain variations of mass spectrometry, or Edman degradation.

[0059] 2. Early Detection of Neonatal Sepsis

[0060] Neonatal sepsis, defined as infection of the blood of a newborn, is difficult to diagnose clinically. Despite advances in neonatal care, the mortality and morbidity from neonatal sepsis remains high (Stoll 2002). Neonatal sepsis is an important contributor to neonatal morbidity including poor neurodevelopmental outcomes and neonatal death. Neonatal sepsis associated complications include, for example, respiratory distress syndrome (RDS), central nervous system (CNS) complications, cerebral palsy (CP), disability and death.

[0061] The highest rates of neonatal sepsis occur in low-birth-weight (LBW) infants, those with depressed respiratory function at birth, and those with maternal perinatal risk factors. Risk factors for early-onset neonatal sepsis include obstetric complications, including preterm delivery, premature rupture of membranes, maternal bleeding, e.g., as caused by placenta previa, abruptio placentae, infection of the amniotic fluid, placenta, urinary tract or endometrium, toxemia, precipitous delivery, and frequent vaginal examinations during delivery. Extended hospital stays and contaminated hospital equipment are common causes of late-onset neonatal sepsis. Organisms which can cause neonatal sepsis include the following non-limiting examples: Coagulase-negative staphylococci, including *S. epidermidis, S. haemolyticus, S. hominis, S. warneri, S. saprophyticus, S. cohnii*, and *S. capitis*, Group B *Streptococcus, Staphylococcus aureus, Enterococcus fecalis* and *E. faecium, Listeria monocytogenes, Escherichia coli, P. aeruginosa, Haemophilus influenzae, Streptococcus bovis*, α-hemolytic streptococci, *Streptococcus pneumoniae, Neisseria meningitides* and *N. gonorrhoeae*. Typically, the organisms which give rise to early-onset neonatal sepsis are acquired intrapartum as an ascending infection from the cervix, transplacentally from the mother or as the fetus passes through the birth canal.

[0062] Unfortunately, due to nonspecific and subtle early signs, the diagnosis of neonatal sepsis is difficult. Signs and symptoms of neonatal sepsis include, for example, body temperature changes breathing problems, diarrhea, low blood sugar, reduced movements, reduced sucking, seizures, slow heart rate, swollen belly area, vomiting, and jaundice. The gold standard for diagnosing neonatal sepsis is blood culture; however, negative blood cultures occur even when strong clinical indicators of septicemia are present and even in cases where bacterial infection is later proven by autopsy (Kaufman D, Fairchild K D, Clin Microbiol Rev. 2004 July; 17(3):638-80). Furthermore, it is often difficult to obtain a sufficient blood sample in neonates, particularly preterm neonates. Given its rapid progression and high mortality rate, rapid empiric antibiotic therapy is typically administered, pending blood culture results. Initial therapy can include ampicillin or penicillin G and an aminoglycoside, e.g., gentamicin, or cefotaxime. Given negative outcomes associated with neonatal sepsis and the lack of confidence in currently available means for detecting neonatal sepsis, use of antibiotic treatment is not only common but prolonged, which contributes to drug resistance among neonatal pathogens. Therefore, development of early, reliable and non-invasive markers for neonatal sepsis and neonatal sepsis associated complications is imperative to allow for therapy and intervention to optimize the outcome for the neonate and to minimize the use or prolonged use of potentially unnecessary antibiotics.

[0063] 3. Early Detection and Diagnosis of Neonatal Sepsis Using Biomarkers in Biological Fluids

[0064] In one aspect, the present invention provides reliable, non-invasive methods for the diagnosis of the neonatal sepsis and neonatal sepsis associated complications using biomarkers identified in biological fluid, such as cord blood, using a proteomics approach. In certain embodiment, the biomarkers associated with neonatal sepsis are predictors for early and late onset central nervous system (CNS) complications. In one embodiment, the biomarkers are predictors for periventricular hemorrhage and/or periventricular leukomalacia. In another embodiment, the biomarkers are predictors for mental retardation.

[0065] In one embodiment, the instant invention allows detection of neonatal sepsis and neonatal sepsis associated complications biomarkers within about 30 minutes and 24 hours of sample collection. In certain embodiments, early-onset neonatal sepsis and/or an associated complication is diagnosed within about 30 minutes and 48 hours of sample collection. In another embodiment, early-onset neonatal sepsis and/or an associated complication is diagnosed within about 48 hours of sample collection. In yet another embodiment, early-onset neonatal sepsis and/or an associated complication is diagnosed within about 24 hours of sample collection. In still another embodiment, early-onset neonatal sepsis and/or an associated complication is diagnosed within about 12 hours of sample collection. In another embodiment, early-onset neonatal sepsis and/or an associated complication is diagnosed within about 4 hours of sample collection. In other embodiments, early-onset neonatal sepsis and/or an associated complication is diagnosed within about 2 hours of sample collection. In one embodiment, early-onset neonatal sepsis and/or an associated complication is diagnosed within about 1 hours of sample collection. In another embodiment, early-onset neonatal sepsis and/or an associated complication is diagnosed within about 30 minutes of sample collection.

[0066] In certain other embodiments, early-onset neonatal sepsis and/or an associated complication is diagnosed within about 30 minutes and 48 hours of birth. In another embodiment, early-onset neonatal sepsis and/or an associated complication is diagnosed within about 48 hours of birth. In yet another embodiment, early-onset neonatal sepsis and/or an associated complication is diagnosed within about 24 hours of birth. In still another embodiment, early-onset neonatal sepsis and/or an associated complication is diagnosed within about 12 hours of birth. In another embodiment, early-onset

neonatal sepsis and/or an associated complication is diagnosed within about 4 hours of birth. In other embodiments, early-onset neonatal sepsis and/or an associated complication is diagnosed within about 2 hours of birth. In one embodiment, early-onset neonatal sepsis and/or an associated complication is diagnosed within about 1 hours of birth. In another embodiment, early-onset neonatal sepsis and/or an associated complication is diagnosed within about 30 minutes of birth.

[0067] As noted before, in the context of the present invention the term "proteomic profile" is used to refer to a representation of the expression pattern of a plurality of proteins in a biological sample, e.g. a biological fluid at a given time. The proteomic profile can, for example, be represented as a mass spectrum, but other representations based on any physicochemical or biochemical properties of the proteins are also included. Although it is possible to identify and sequence all or some of the proteins present in the proteome of a biological fluid, this is not necessary for the diagnostic use of the proteomic profiles generated in accordance with the present invention. Diagnosis of a particular disease can be based on characteristic differences (unique expression signatures) between a normal proteomic profile, and proteomic profile of the same biological fluid obtained under the same circumstances, when the disease or pathologic condition to be diagnosed is present. The unique expression signature can be any unique feature or motif within the proteomic profile of a test or reference biological sample that differs from the proteomic profile of a corresponding normal biological sample obtained from the same type of source, in a statistically significant manner. For example, if the proteomic profile is presented in the form of a mass spectrum, the unique expression signature is typically a peak or a combination of peaks that differ, qualitatively or quantitatively, from the mass spectrum of a corresponding normal sample. Thus, the appearance of a new peak or a combination of new peaks in the mass spectrum, or any statistically significant change in the amplitude or shape of an existing peak or combination of existing peaks, or the disappearance of an existing peak, in the mass spectrum can be considered a unique expression signature. When the proteomic profile of the test sample obtained from a mammalian subject is compared with the proteomic profile of a reference sample comprising a unique expression signature characteristic of a pathologic maternal or fetal condition, the mammalian subject is diagnosed with such pathologic condition if it shares the unique expression signature with the reference sample.

[0068] A particular pathologic maternal/fetal condition can be diagnosed by comparing the proteomic profile of a biological fluid obtained from the subject to be diagnosed with the proteomic profile of a normal biological fluid of the same kind, obtained and treated in the same manner. If the proteomic profile of the test sample is essentially the same as the proteomic profile of the normal sample, the subject is considered to be free of the subject pathologic maternal/fetal condition. If the proteomic profile of the test sample shows a unique expression signature relative to the proteomic profile of the normal sample, the subject is diagnosed with the maternal/fetal condition in question.

[0069] Alternatively or in addition, the proteomic profile of the test sample may be compared with the proteomic profile of a reference sample, obtained from a biological fluid of a subject independently diagnosed with the pathologic maternal/fetal condition ion question. In this case, the subject is diagnosed with the pathologic condition if the proteomic profile of the test sample shares at least one feature, or a combination of features representing a unique expression signature, with the proteomic profile of the reference sample.

[0070] Statistical methods for comparing proteomic profiles are well known in the art. For example, in the case of a mass spectrum, the proteomic profile is defined by the peak amplitude values at key mass/charge (M/Z) positions along the horizontal axis of the spectrum. Accordingly, a characteristic proteomic profile can, for example, be characterized by the pattern formed by the combination of spectral amplitudes at given M/Z vales. The presence or absence of a characteristic expression signature, or the substantial identity of two profiles can be determined by matching the proteomic profile (pattern) of a test sample with the proteomic profile (pattern) of a reference or normal sample, with an appropriate algorithm. A statistical method for analyzing proteomic patterns is disclosed, for example, in Petricoin III, et al., *The Lancet* 359:572-77 (2002); Issaq et al., *Biochem Biophys Commun* 292:587-92 (2002); Ball et al., *Bioinformatics* 18:395-404 (2002); and Li et al., *Clinical Chemistry Journal,* 48:1296-1304 (2002).

[0071] In a particular embodiment, the diagnostic tests of the present invention are performed in the form of protein arrays or immunoassays.

[0072] 4. Protein Arrays

[0073] In recent years, protein arrays have gained wide recognition as a powerful means to detect proteins, monitor their expression levels, and investigate protein interactions and functions. They enable high-throughput protein analysis, when large numbers of determinations can be performed simultaneously, using automated means. In the microarray or chip format, that was originally developed for DNA arrays, such determinations can be carried out with minimum use of materials while generating large amounts of data.

[0074] Although proteome analysis by 2D gel electrophoresis and mass spectrometry, as described above, is very effective, it does not always provide the needed high sensitivity and this might miss many proteins that are expressed at low abundance. Protein microarrays, in addition to their high efficiency, provide improved sensitivity. Protein arrays are formed by immobilizing proteins on a solid surface, such as glass, silicon, micro-wells, nitrocellulose, PVDF membranes, and microbeads, using a variety of covalent and non-covalent attachment chemistries well known in the art. The solid support should be chemically stable before and after the coupling procedure, allow good spot morphology, display minimal nonspecific binding, should not contribute a background in detection systems, and should be compatible with different detection systems.

[0075] In general, protein microarrays use the same detection methods commonly used for the reading of DNA arrays. Similarly, the same instrumentation as used for reading DNA microarrays is applicable to protein arrays.

[0076] Thus, capture arrays (e.g. antibody arrays) can be probed with fluorescently labeled proteins from two different sources, such as normal and diseased biological fluids. In this case, the readout is based on the change in the fluorescent signal as a reflection of changes in the expression level of a target protein. Alternative readouts include, without limitation, fluorescence resonance energy transfer, surface plasmon resonance, rolling circle DNA amplification, mass spectrometry, resonance light scattering, and atomic force microscopy.

[0077] For further details, see, for example, Zhou H, et al., *Trends Biotechnol.* 19:S34-9 (2001); Zhu et al., *Current Opin. Chem. Biol.* 5:40-45-(2001); Wilson and Nock, *Angew Chem Int Ed Engl* 42:494-500 (2003); and Schweitzer and Kingsmore, *Curr Opin Biotechnol* 13:14-9 (2002). Biomolecule arrays are also disclosed in U.S. Pat. No. 6,406,921, issued Jun. 18, 2002, the entire disclosure of which is hereby expressly incorporated by reference.

[0078] 5. Immunoassays

[0079] The diagnostic assays of the present invention can also be performed in the form of various immunoassay formats, which are well known in the art. There are two main types of immunoassays, homogenous and heterogeneous. In homogenous immunoassays, both the immunological reaction between an antigen and an antibody and the detection are carried out in a homogenous reaction. Heterogeneous immunoassays include at least one separation step, which allows the differentiation of reaction products from unreacted reagents.

[0080] ELISA is a heterogeneous immunoassay, which has been widely used in laboratory practice since the early 1970's. The assay can be used to detect antigensin various formats.

[0081] In the "sandwich" format the antigen being assayed is held between two different antibodies. In this method, a solid surface is first coated with a solid phase antibody. The test sample, containing the antigen (i.e. a diagnostic protein), or a composition containing the antigen, being measured, is then added and the antigen is allowed to react with the bound antibody. Any unbound antigen is washed away. A known amount of enzyme-labeled antibody is then allowed to react with the bound antigen. Any excess unbound enzyme-linked antibody is washed away after the reaction. The substrate for the enzyme used in the assay is then added and the reaction between the substrate and the enzyme produces a color change. The amount of visual color change is a direct measurement of specific enzyme-conjugated bound antibody, and consequently the antigen present in the sample tested.

[0082] ELISA can also be used as a competitive assay. In the competitive assay format, the test specimen containing the antigen to be determined is mixed with a precise amount of enzyme-labeled antigen and both compete for binding to an anti-antigen antibody attached to a solid surface. Excess free enzyme-labeled antigen is washed off before the substrate for the enzyme is added. The amount of color intensity resulting from the enzyme-substrate interaction is a measure of the amount of antigen in the sample tested. Homogenous immunoassays include, for example, the Enzyme Multiplied Immunoassay Technique (EMIT), which typically includes a biological sample comprising the compound or compounds to be measured, enzyme-labeled molecules of the compound (s) to be measured, specific antibody or antibodies binding the compound(s) to be measured, and a specific enzyme chromogenic substrate. In a typical EMIT excess of specific antibodies is added to a biological sample. If the biological sample contains the proteins to be detected, such proteins bind to the antibodies. A measured amount of the corresponding enzyme-labeled proteins is then added to the mixture. Antibody binding sites not occupied by molecules of the protein in the sample are occupied with molecules of the added enzyme-labeled protein. As a result, enzyme activity is reduced because only free enzyme-labeled protein can act on the substrate. The amount of substrate converted from a colorless to a colored form determines the amount of free enzyme left in the mixture. A high concentration of the protein to be detected in the sample causes higher absorbance readings. Less protein in the sample results in less enzyme activity and consequently lower absorbance readings. Inactivation of the enzyme label when the Ag-enzyme complex is Ab-bound makes the EMIT a unique system, enabling the test to be performed without a separation of bound from unbound compounds as is necessary with other immunoassay methods.

[0083] Part of this invention is also an immunoassay kit. In one aspect, the invention includes a sandwich immunoassay kit comprising a capture antibody and a detector antibody. The capture antibody and detector antibody can be monoclonal or polyclonal. In another aspect, the invention includes a diagnostic kit comprising lateral flow devices, such as immunochromatographic strip (ICS) tests, using immunoflowchromatography. The lateral flow devices employ lateral flow assay techniques as generally described in U.S. Pat. Nos. 4,943,522; 4,861,711; 4,857,453; 4,855,240; 4,775,636; 4,703,017; 4,361, 537; 4,235,601; 4,168,146; 4,094,647, the entire contents of each of which is incorporated by reference. In yet another aspect, the immunoassay kit may comprise, for example, in separate containers (a) monoclonal antibodies having binding specificity for the polypeptides used in the diagnosis of a particular maternal/fetal condition, such as neonatal sepsis; (b) and anti-antibody immunoglobulins. This immunoassay kit may be utilized for the practice of the various methods provided herein. The monoclonal antibodies and the anti-antibody immunoglobulins may be provided in an amount of about 0.001 mg to about 100 grams, and more preferably about 0.01 mg to about 1 gram. The anti-antibody immunoglobulin may be a polyclonal immunoglobulin, protein A or protein G or functional fragments thereof, which may be labeled prior to use by methods known in the art. The diagnostic kit may further include where necessary agents for reducing background interference in a test, agents for increasing signal, software and algorithms for combining and interpolating marker values to produce a prediction of clinical outcome of interest, apparatus for conducting a test, calibration curves and charts, standardization curves and charts, and the like. The test kit may be packaged in any suitable manner, typically with all elements in a single container along with a sheet of printed instructions for carrying out the test.

[0084] 6. Diagnostic and Treatment Methods

[0085] The diagnostic methods of the present invention are valuable tools for practicing physicians to make quick treatment decisions, which are often critical for the survival of the neonate. Thus, for example, if a neonate shows symptoms of neonatal sepsis, or is otherwise at risk for neonatal sepsis, it is important to take immediate steps to treat the condition and improve the chances of the survival of the neonate.

[0086] Following the measurement or obtainment of the expression levels of the proteins identified herein, the assay results, findings, diagnoses, predictions and/or treatment recommendations are typically recorded and communicated to technicians, physicians and/or patients, for example. In certain embodiments, computers will be used to communicate such information to interested parties, such as, patients and/or the attending physicians. In some embodiments, the assays will be performed or the assay results analyzed in a country or jurisdiction which differs from the country or jurisdiction to which the results or diagnoses are communicated.

[0087] In a preferred embodiment, a diagnosis, prediction and/or treatment recommendation based on the expression

level in a test subject of one or more of the biomarkers presented herein is communicated to the subject as soon as possible after the assay is completed and the diagnosis and/or prediction is generated. The one or more biomarkers identified and quantified in the methods described herein can be contained in one or more panels. The number of biomarkers comprising a panel can include 1 biomarker, 2 biomarkers, 3 biomarkers, 4 biomarkers, 5 biomarkers, 6 biomarkers, 7 biomarkers, 8 biomarkers, 9 biomarkers, 10 biomarkers, 11 biomarkers, 12 biomarkers, 13 biomarkers, 14 biomarkers, 15 biomarkers, 16 biomarkers, 17 biomarkers, 18 biomarkers, 19 biomarkers, 20 biomarkers, etc. The results and/or related information may be communicated to the subject by the subject's treating physician. Alternatively, the results may be communicated directly to a test subject by any means of communication, including writing, such as by providing a written report, electronic forms of communication, such as email, or telephone. Communication may be facilitated by use of a computer, such as in case of email communications. In certain embodiments, the communication containing results of a diagnostic test and/or conclusions drawn from and/or treatment recommendations based on the test, may be generated and delivered automatically to the subject using a combination of computer hardware and software which will be familiar to artisans skilled in telecommunications. One example of a healthcare-oriented communications system is described in U.S. Pat. No. 6,283,761, the entire contents of which are incorporated by reference herein; however, the present invention is not limited to methods which utilize this particular communications system. In certain embodiments of the methods of the invention, all or some of the method steps, including the assaying of samples, diagnosing of diseases, and communicating of assay results or diagnoses, may be carried out in diverse (e.g., foreign) jurisdictions.

[0088] To facilitate diagnosis, the reference and/or subject biomarker profiles or expression level of one or more of the biomarkers presented herein of the present invention can be displayed on a display device, contained electronically, or in a machine-readable medium, such as but not limited to, analog tapes like those readable by a VCR, CD-ROM, DVD-ROM, USB flash media, among others. Such machine-readable media can also contain additional test results, such as, without limitation, measurements of clinical parameters and traditional laboratory risk factors. Alternatively or additionally, the machine-readable media can also comprise subject information such as medical history and any relevant family history.

[0089] Further details of the invention will be apparent from the following non-limiting examples. All references cited throughout the disclosure, and the references cited therein, are expressly incorporated by reference herein.

Example 1

Identification of Cord Blood Biomarkers of Neonatal Sepsis Using Global Proteomic Approaches

Experimental Methods

[0090] Sample Collection: Umbilical cord blood samples from a prospective observational cohort of 82 women in spontaneous preterm labor at 20-34 weeks' gestation were analyzed. Early-onset neonatal sepsis was defined as a positive neonatal blood culture within 72 hours of delivery. Of 82 subjects, 71 delivered at <34 weeks and 5 of neonates had confirmed neonatal sepsis (neonatal blood culture positive) and 8 of the neonates had diagnosis of suspected sepsis (blood culture negative, clinical symptoms suggestive of infection).

[0091] Immunodepletion of cord serum: Serum samples used for 2-DLC experiments were depleted of 12 most abundant proteins (albumin, IgG, IgA, IgM, α-1-anti-trypsin, transferrin, haptoglobin, α-1-acid glycoprotein, α-2-macroglobulin, fibrinogen, apolipoproteins A-I and A-II) using IgY-12 LC2 proteome partitioning system (Beckman Coulter, Fullerton, Calif.). Appropriate fractions were collected, concentrated, and buffer exchanged with 10 mM Tris (pH 8.4). Protein concentration was determined using a DC protein assay kit (Bio-Rad, Hercules, Calif.).

[0092] Differential Gel Electrophoresis (DIGE): Following protein assay, 50 μg of protein was labeled with CyDye DIGE Fluor minimal dye (GE Lifesciences) at a concentration of 400 pm of dye. Different dyes (Cy5, Cy3, Cy2) were used to label control, suspected sepsis (SS), or confirmed sepsis (CS) cord blood serum (CBS) samples, respectively. Labeled proteins were dissolved in IEF buffer containing 0.5% ampholytes and rehydrated on to a 24 cm IPG strip (pH 4-7) for 12 h at room temperature. After rehydration, the IPG strip was subjected to isoelectric focusing for ~10 h to attain a total of 64000 volt*hours. Focused proteins in the IPG strip were first reduced by equilibrating with buffer containing 1% DTT for 15 min and then alkylated with buffer containing 2.5% IAA. After reduction and alkylation steps, the IPG strip was loaded on to a gradient (8~16%) polyacrylamide gel (24×20 cm) and the SDS-PAGE was conducted at 85 V for 18 h to resolve proteins in the second dimension. After electrophoresis, the gel was scanned in a Typhoon 9400 scanner (GE Lifesciences) using appropriate lasers and filters with PMT voltage set at 600. Images in different channels were overlaid using selected colors and differences were visualized using ImageQuant TL software (v7.0, GE Lifesciences). Raw scanned image files were loaded into Phoretix 2D Evolution (Nonlinear Dynamics), and difference maps were generated for confirmed and suspected sepsis versus control.

[0093] 2-DLC Sample Processing: Following protein assay, 1 mg portions of samples were digested with trypsin, and resulting peptides were separated with strong cation exchange (SCX) chromatography. Samples were dried and dissolved in 105 μl of digestion buffer containing 0.2 M NH4HCO3 and 0.3% Rapigest (Waters, Milford, Mass.) (pH 8.5). Cysteine residues were reduced and alkylated by incubating in 12.5 μL of 0.1 M DTT at 50° C. for 45 min followed by dark room incubation in 7 μL of 0.5 M iodoacetamide for another 30 min. Proteins were digested for 2 h at 37° C. by adding 4 μL of 0.1 M CaCl2 and sequencing grade trypsin (Trypsin Gold, Promega) at an enzyme to substrate ratio of 33:1. Digestion was stopped by adding 60 μL of 0.2 M HCl and resulting peptides were purified using C18 SepPak Plus cartridges (Waters, Milford, Mass.).

[0094] SCX chromatography was performed using a 100× 2.1 mm polysulfoethyl A column (The Nest Group, Southborough, Mass.). Mobile phase A contained 10 mM potassium phosphate (pH 3) and 25% acetonitrile (ACN). Mobile phase B was identical except that it contained 350 mM KCl. Following loading and washing in mobile phase A, peptides were eluted using a linear gradient of 0-50% B over 45 min, followed by a linear gradient of 50-100% B over 15 min, followed by a 20 min wash at 100% A. A total of 95 one-minute fractions were collected, dried by vacuum centrifugation, and re-dissolved by shaking in 100 μL of 0.1% TFA. Peptide fractions were desalted using a 96-well spin column,

Vydac C18 silica (The Nest Group, Southborough, Mass.). The desalted fractions were consolidated into 35 fractions, evaporated, and dissolved in 20 μL of 5% formic acid (FA) for LC-MS/MS analysis.

[0095] LC-MS/MS Analysis: Portions of each fraction were analyzed by LC/MS using an Agilent 1100 series capillary LC system and an LTQ ion trap mass spectrometer (Thermo Electron, San Jose, Calif., USA) with an Ion Max electrospray source fitted with a 34-gauge metal needle kit (ThermoFinnigan, San Jose, Calif.). Samples were applied at 20 μL/min to a trap cartridge, and then switched onto a 0.5× 250 mm Zorbax SB-C18 column (Agilent Technologies, Palo Alto, Calif., USA) using mobile phase A containing 0.1% FA. Mass spectra files were generated from raw data using Bioworks Browser software (version 3.1, ThermoFinnigan, San Jose, Calif.). A total of 1,195,238 tandem mass spectra were generated from all LC-MS/MS analyses.

[0096] Peptide and Protein Identification: Tandem mass spectra were searched against a composite protein database containing forward and reversed entries (decoy proteins) of Swiss-Prot (version 54.2) database selected for human subspecies. All searches were performed using X! Tandem (Fenyo 2003) search engine configured to use a mass tolerance of 1.8 Da and 0.4 Da for parent and fragment ions, trypsin enzyme specificity, fixed carbamidomethyl modification on cysteine residues, and several potential in vivo and in vitro modifications. Peptide and protein identifications in all samples were compiled together to generate a comprehensive cord blood proteome, using probabilistic protein identification algorithms (Nesvizhskii 2003) implemented in Scaffold software (version 1.6, Proteome Software, Portland, Oreg.). Peptide identifications with probability ≧0.8 are considered as likely to be present in the sample. Protein identifications with at least two unique peptide identifications are considered to be present in cord blood.

[0097] Label-Free Quantification: The total number of tandem mass spectra matched to a protein (spectral counting) is a label-free, sensitive, and semi-quantitative measure for estimating its abundance in complex mixtures. (Liu 2004). The difference of a protein's spectral counts between two complex samples was used to quantify its relative expression. (Old 2005). In this study, cord blood proteins with at least two unique peptide identifications in one sample were considered for label-free quantification. Homologous proteins (sequence homology >50%) with shared spectral counts were combined into single entry. Shared spectral counts of non-homologous were assigned to the protein with highest number of spectral matches (Occam's razor). Spectral counts of curated proteins were subjected to independent pair-wise comparisons between control and CS neonatal subjects were used to quantify the relative expression of a protein. (Gravett 2007, Nagalla 2007, Pereira 2007, Zybailov 2006). Proteins with a p-value of ≦0.05 in the pair-wise comparison were considered as significantly differentially expressed between the samples. The fold expression change (FC) of differentially expressed proteins was quantified using the equation described in Old et al. 2005).

[0098] Enzyme Linked Immunosorbent Assay (ELISA): 10 candidate biomarkers for detection of sepsis were measured with solid phase sandwich immunoassays. Available commercial antibodies and antigens were purchased from various vendors to prepare immunoassays. Standard curves were developed using known quantities of recombinant proteins or standards provided by manufacturer, to reference sample concentrations. All assays were performed in triplicate and interassay and intrasaay coefficient of variations ranged from 3-7%.

[0099] One-way analyses of variance (ANOVA) were conducted to compare log-transformed ELISA values of samples from subjects without sepsis and subjects with confirmed sepsis. For presentation, we transformed the average log value back to original units (harmonic mean), and applied the Bonferroni correction to account for multiple comparisons. Based on results from individual protein comparisons, we evaluated the classification performance of several different combinations of 2, 3 or 4 proteins using logistic regression models. Receiver operating characteristic (ROC) curves were computed based on the risk scores from each of the multiprotein models. Descriptive and inferential statistics were computed using SAS software (v9.1); ROC curves were produced and compared using customized STATA modules. (Pepe 2003).

[0100] Statistical Analysis of ELISA Data: Candidate protein biomarker concentrations in cord blood measured by ELISA experiments in control subjects without sepsis (n=77), and subjects with confirmed sepsis (n=5) were log transformed before subjecting them to statistical analysis. Independent pair-wise comparisons of log-transformed protein concentrations between control vs. sepsis were performed using one-way analysis of variance (ANOVA) test. For presentation, we transformed the average log value back to original units (harmonic mean), and applied the Bonferroni correction to account for multiple comparisons. Based on results from individual protein comparisons, we evaluated the classification performance of several different combinations of 2, 3 or 4 proteins using logistic regression models. Receiver operating characteristic (ROC) curves were computed based on the risk scores from each of the multi-protein models.

[0101] Descriptive and inferential statistics were computed using SAS software (v9.1); ROC curves were produced and compared using customized STATA modules. (Pepe 2003).

Results

[0102] Proteomic changes in cord blood proteome in neonatal sepsis: 2-dimensional gel electrophoresis analysis: Cord blood (CB) from control, suspected sepsis (SS), and confirmed sepsis (CS) subjects was subjected to affinity purification to remove high abundance serum proteins. Depleted CBS from control, SS, and CS subjects were labeled with Cy5, Cy3, and Cy2 dyes, respectively. Labeled samples were resolved on a 2D gel. FIGS. **1**A and **1**B show DIGE gel images of CBS from control (red) vs. SS (green) and control (red) vs. CS (green), respectively. Spots that are differentially expressed between SS vs. control (FIG. **1**C) and CS vs. control (FIG. **1**D) were determined using Phoretix 2D evolution software. Spot intensities in difference maps (FIGS. **1**C and **1**D) were normalized based on total spot volume. Spots in difference maps that are ≧2 fold down regulated were highlighted in red and ≧2 fold up regulated were highlighted in green.

[0103] Conclusion: 2-D gel analysis identified differential expression of multiple proteins in the cord blood of neonatal sepsis subjects.

[0104] Cord Blood Proteome: A total of 670 proteins with at least two unique peptide (p≧0.8) matches were identified from all 2-DLC mass spectrometry experiments. Cord blood proteins are ranked according to the decreasing order of spectral counts and shown in Supplemental Table 1 (column No.

5). Functional annotation of cord blood proteome was performed using Gene Ontology (GO) annotations from DAVID bioinformatics resource (Dennis 2003). Proteins with metabolic (21%), immune response (10%), transport (10%), and developmental (7%) functions constituted a majority of the cord blood proteome.

[0105] Clustering of differentially expressed proteins in cord blood proteome in neonatal sepsis: Total number of MS/MS spectra matched to a protein is directly related to its abundance in complex mixtures. (Liu 2004). Global protein expression changes in CB between control, SS, and CS subjects are visualized using GeneMaths software (version 1.5, Applied Maths, Austin, Tex.). Spectral counts of proteins with at least two peptide identifications ($p \geqq 0.8$) in one of the samples were individually mean normalized and analyzed by GeneMaths software. Proteins with similar expression changes between samples were hierarchically clustered using Euclidean distance learning method with 200 simulations (FIG. **2**A). Representative protein clusters with proteins that are up regulated in CS and control samples are shown in FIG. **2**B and FIG. **2**C, respectively.

[0106] Conclusion: Visualization of cord blood proteome using hierarchical clustering demonstrated specific clusters of proteins over expressed in neonatal sepsis subjects.

[0107] Cord blood biomarkers for neonatal sepsis identified by 2-dimensional liquid chromatography and tandem mass spectrometry (2D LC-MS-MS): CB samples from control and confirmed sepsis (CS) samples were subjected to 2-DLC based tandem mass spectrometry followed by label-free quantification. CB proteins that passed label-free quantification with a p value of $\leqq 0.05$ and a fold change of $\geqq +2.0$ were considered as significantly differentially expressed between control and neonatal sepsis subjects (Table 1). Biological function annotation for differentially expressed proteins in Table 1 was performed using Bioinformatics Harvester. Table 1 below lists differentially expressed cord blood proteins between control and neonatal sepsis samples with their Swiss-Prot accession number, description, fold change, and p-value. Proteins were grouped according to their biological function.

TABLE 1

Cord Blood Biomarkers of Neonatal Sepsis

Biological Function	Swiss-Prot Acc. No	Description	CS vs. Control Fold Change	CS vs. Control P Value
	P02741	C-reactive protein precursor (SEQ ID NO: 1)	6.6	<0.0001
	Q9NPH3	Interleukin-1 receptor accessory protein precursor (SEQ ID NO: 2)	6.4	0.0117
	P05231	Interleukin-6 precursor (SEQ ID NO: 3)	5.5	0.0246
	Q01638	Interleukin-1 receptor-like 1 precursor (SEQ ID NO: 4)	5.5	0.0246
	P02735	Serum amyloid A protein precursor (SEQ ID NO: 5)	3.8	0.0179
	O43866	CD5 antigen-like precursor (SEQ ID NO: 6)	3.4	0.0095
Inflammation	P61769	Beta-2-microglobulin precursor (SEQ ID NO: 7)	2.5	0.0001
and Immune	P13727	Bone-marrow proteoglycan precursor (SEQ ID NO: 8)	2.5	0.0039
response	Q13228	Selenium-binding protein 1 (SEQ ID NO: 9)	2.4	0.0231
modulators	P18428	Lipopolysaccharide-binding protein precursor (SEQ ID NO: 10)	2.4	<0.0001
	Q6UVK1	Chondroitin sulfate proteoglycan 4 precursor (SEQ ID NO: 11)	2.3	0.0104
	P10451	Osteopontin precursor (SEQ ID NO: 12)	2.2	0.0022
	P52566	Rho GDP-dissociation inhibitor 2 (SEQ ID NO: 13)	−2.2	0.0189
	P00918	Carbonic anhydrase 2 (SEQ ID NO: 14)	−3.1	0.0234
	P80188	Neutrophil gelatinase-associated lipocalin precursor (SEQ ID NO: 15)	−3.5	0.0087
	P29400	Collagen alpha-5(IV) chain precursor (SEQ ID NO: 16)	7.2	0.0056
	P29279	Connective tissue growth factor precursor (SEQ ID NO: 17)	7.2	0.0056
Extracellular	P09603	Macrophage colony-stimulating factor 1 precursor (SEQ ID NO: 18)	5.5	0.0246
Matrix,	Q99435	Protein kinase C-binding protein NELL2 precursor (SEQ ID NO: 19)	4.5	0.0019
Matricellular, and	Q9UMX5	Neudesin precursor (SEQ ID NO: 20)	4.5	0.0168
Cytoskeletal	P07237	Protein disulfide-isomerase precursor (SEQ ID NO: 21)	4	0.0317
	P07998	Ribonuclease pancreatic precursor (SEQ ID NO: 22)	3.9	0.0007
	P80370	Delta-like protein precursor (SEQ ID NO: 23)	3.8	0.0034
	P10645	Chromogranin-A precursor (SEQ ID NO: 24)	3.6	0.0002
	Q99983	Osteomodulin precursor (SEQ ID NO: 25)	3.5	0.0318
	P08123	Collagen alpha-2(I) chain precursor (SEQ ID NO: 26)	3.2	0.0004
	Q07954	Prolow-density lipoprotein receptor-related protein 1 precursor (SEQ ID NO: 27)	3.1	0.0005

TABLE 1-continued

Cord Blood Biomarkers of Neonatal Sepsis

Biological Function	Swiss-Prot Acc. No	Description	CS vs. Control Fold Change	CS vs. Control P Value
	P11047	Laminin subunit gamma-1 precursor (SEQ ID NO: 28)	2.8	0.0422
	P07942	Laminin subunit beta-1 precursor (SEQ ID NO: 29)	2.4	0.001
	P02458	Collagen alpha-1(II) chain precursor (SEQ ID NO: 30)	2.4	0.0231
	P01033	Metalloproteinase inhibitor 1 precursor (SEQ ID NO: 31)	2.3	0.0169
	Q92520	Protein FAM3C precursor (SEQ ID NO: 32)	2.2	0.0418
	P12814	Alpha-actinin-1 (SEQ ID NO: 33)	−3.3	0.0143
	P52907	F-actin-capping protein subunit alpha-1 (SEQ ID NO: 34)	−6.7	0.0083
	P15144	Aminopeptidase N (SEQ ID NO: 35)	13.4	<0.0001
	P08833	Insulin-like growth factor-binding protein 1 precursor (SEQ ID NO: 36)	10.1	<0.0001
	Q9BY67	Cell adhesion molecule 1 precursor (SEQ ID NO: 37)	8.1	0.0027
	P07858	Cathepsin B precursor (SEQ ID NO: 38)	5.5	0.0046
	Q93063	Exostosin-2 (SEQ ID NO: 39)	5.5	0.0246
	P07339	Cathepsin D precursor (SEQ ID NO: 40)	3.8	<0.0001
Development and Apoptosis	Q9UM47	Neurogenic locus notch homolog protein 3 precursor (SEQ ID NO: 41)	3.4	0.0095
	Q15828	Cystatin-M precursor (SEQ ID NO: 42)	2.9	0.0031
	Q99784	Noelin precursor (SEQ ID NO: 43)	2.9	0.0491
	P18065	Insulin-like growth factor-binding protein 2 precursor (SEQ ID NO: 44)	2.6	<0.0001
	P14625	Endoplasmin precursor (SEQ ID NO: 45)	2.3	0.0169
	Q8NBP7	Proprotein convertase subtilisin/kexin type 9 precursor (SEQ ID NO: 46)	2.2	0.0046
	P35858	Insulin-like growth factor-binding protein complex acid labile chain precursor (SEQ ID NO: 47)	−2.3	0.0016
ERM	P15311	Ezrin (SEQ ID NO: 48)	5.5	0.0046
	P07148	Fatty acid-binding protein, liver (SEQ ID NO: 49)	8.1	0.0027
	Q8IZF2	Probable G-protein coupled receptor 116 precursor (SEQ ID NO: 50)	6.5	0.0012
	Q12884	Seprase (SEQ ID NO: 51)	6.4	0.0117
	Q8WWZ8	Oncoprotein-induced transcript 3 protein precursor (SEQ ID NO: 52)	4.5	0.0168
	Q9Y4L1	Hypoxia up-regulated protein 1 precursor (SEQ ID NO: 53)	3.5	0.0318
	O43493	Trans-Golgi network integral membrane protein 2 precursor (SEQ ID NO: 54)	3.5	0.0318
Proteins of miscellaneous class or unknown	P29401	Transketolase (SEQ ID NO: 55)	3.4	0.0173
	P10586	Receptor-type tyrosine-protein phosphatase F precursor (SEQ ID NO: 56)	2.9	0.0491
	P05362	Intercellular adhesion molecule 1 precursor (SEQ ID NO: 57)	2.8	0.006
	P01130	Low-density lipoprotein receptor precursor (SEQ ID NO: 58)	2.8	0.006
	P11021	78 kDa glucose-regulated protein precursor (SEQ ID NO: 59)	2.6	0.0049
	Q8TDY8	Neighbor of punc e11 precursor (SEQ ID NO: 60)	2.3	0.0455
	P33908	Mannosyl-oligosaccharide 1,2-alpha-mannosidase IA (SEQ ID NO: 61)	2.2	0.0418
	P14618	Pyruvate kinase isozymes M1/M2 (SEQ ID NO: 62)	−5	0.007
	P31948	Stress-induced-phosphoprotein 1 (SEQ ID NO: 63)	−5.3	0.0323

[0108] Conclusion: 2D-LC MS-MS analysis identified differential abundance of 60 potential biomarkers of neonatal sepsis in cord blood that are statistically significant.

[0109] Validation of potential neonatal sepsis biomarkers using enzyme linked immunosorbent assays: A total of 10 significantly differentially expressed proteins from the 2-DLC study were cross validated on a cohort of 77 control and 5 neonatal sepsis subjects, using ELISA. Measured protein concentrations were log-transformed and compared in a pair-wise between control and sepsis groups, using an ANOVA test. Proteins that passed the comparison with a p-value $\leqq 0.05$ are shown in Table 2 below. The mean concentration of each protein in respective sample groups was determined by computing the harmonic mean of protein concentrations (ng/ml) measured by ELISA (shown in Table 2).

TABLE 2

Validation of potential neonatal sepsis biomarkers with ELISA

Accession (SEQ ID NO)	ID	Protein	Control, No Sepsis (n = 77) Geometric Mean ng/ml	Confirmed Sepsis (n = 5) Geometric Mean ng/ml	Confirmed Sepsis vs. Control, No Sepsis p value	AUROC
P08833 (SEQ ID NO: 36)	IBP1	Insulin-like growth factor-binding protein 1	74.3	1671.2	0.0061	0.918
P05231 (SEQ ID NO: 3)	IL6	Interleukin-6	0.7	401.1	0.0009	0.790
P02741 (SEQ ID NO: 1)	CRP	C-reactive protein	248.2	4910.4	0.0030	0.862
P61769 (SEQ ID NO: 7)	B2MG	Beta-2-microglobulin	2434.2	4410.2	0.0082	0.835
P07858 (SEQ ID NO: 38)	CATB	Cathepsin B	162.2	487.8	0.0012	0.805
Q15828 (SEQ ID NO: 42)	CYTM	Cystatin-M	154.5	211.3	0.2295	0.600
P18065 (SEQ ID NO: 44)	IBP2	Insulin-like growth factor-binding protein 2	142.5	212.7	0.0910	0.719
P14780 (SEQ ID NO: 64)	MMP9	Matrix metalloproteinase-9	178.3	54.7	0.0052	0.881
P01033 (SEQ ID NO: 31)	TIMP1	Metalloproteinase inhibitor 1	278.0	473.0	0.0131	0.761
P02763 (SEQ ID NO: 65)	A1AG1	Alpha-1-acid glycoprotein 1	32225.8	285987.5	0.0291	0.783

[0110] Conclusion: ELISA analysis of potential biomarkers on individual samples confirmed the differential expression of candidate proteins observed by 2D-LC-MS-MS analysis.

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SEQUENCE LISTING

<160> NUMBER OF SEQ ID NOS: 65

<210> SEQ ID NO 1
<211> LENGTH: 224
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 1

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Met Glu Lys Leu Leu Cys Phe Leu Val Leu Thr Ser Leu Ser His Ala
1               5                   10                  15

Phe Gly Gln Thr Asp Met Ser Arg Lys Ala Phe Val Phe Pro Lys Glu
            20                  25                  30

Ser Asp Thr Ser Tyr Val Ser Leu Lys Ala Pro Leu Thr Lys Pro Leu
        35                  40                  45

Lys Ala Phe Thr Val Cys Leu His Phe Tyr Thr Glu Leu Ser Ser Thr
    50                  55                  60

Arg Gly Tyr Ser Ile Phe Ser Tyr Ala Thr Lys Arg Gln Asp Asn Glu
65                  70                  75                  80

Ile Leu Ile Phe Trp Ser Lys Asp Ile Gly Tyr Ser Phe Thr Val Gly
                85                  90                  95

Gly Ser Glu Ile Leu Phe Glu Val Pro Glu Val Thr Val Ala Pro Val
            100                 105                 110

His Ile Cys Thr Ser Trp Glu Ser Ala Ser Gly Ile Val Glu Phe Trp
        115                 120                 125

Val Asp Gly Lys Pro Arg Val Arg Lys Ser Leu Lys Lys Gly Tyr Thr
    130                 135                 140

Val Gly Ala Glu Ala Ser Ile Ile Leu Gly Gln Glu Gln Asp Ser Phe
145                 150                 155                 160

Gly Gly Asn Phe Glu Gly Ser Gln Ser Leu Val Gly Asp Ile Gly Asn
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                165                 170                 175

Val Asn Met Trp Asp Phe Val Leu Ser Pro Asp Glu Ile Asn Thr Ile
            180                 185                 190

Tyr Leu Gly Gly Pro Phe Ser Pro Asn Val Leu Asn Trp Arg Ala Leu
        195                 200                 205

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


<210> SEQ ID NO 2
<211> LENGTH: 570
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 2

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

Gln Ser Asp Ala Ser Glu Arg Cys Asp Asp Trp Gly Leu Asp Thr Met
            20                  25                  30

Arg Gln Ile Gln Val Phe Glu Asp Glu Pro Ala Arg Ile Lys Cys Pro
        35                  40                  45

Leu Phe Glu His Phe Leu Lys Phe Asn Tyr Ser Thr Ala His Ser Ala
    50                  55                  60

Gly Leu Thr Leu Ile Trp Tyr Trp Thr Arg Gln Asp Arg Asp Leu Glu
65                  70                  75                  80

Glu Pro Ile Asn Phe Arg Leu Pro Glu Asn Arg Ile Ser Lys Glu Lys
                85                  90                  95

Asp Val Leu Trp Phe Arg Pro Thr Leu Leu Asn Asp Thr Gly Asn Tyr
            100                 105                 110

Thr Cys Met Leu Arg Asn Thr Thr Tyr Cys Ser Lys Val Ala Phe Pro
        115                 120                 125

Leu Glu Val Val Gln Lys Asp Ser Cys Phe Asn Ser Pro Met Lys Leu
    130                 135                 140

Pro Val His Lys Leu Tyr Ile Glu Tyr Gly Ile Gln Arg Ile Thr Cys
145                 150                 155                 160

Pro Asn Val Asp Gly Tyr Phe Pro Ser Ser Val Lys Pro Thr Ile Thr
                165                 170                 175

Trp Tyr Met Gly Cys Tyr Lys Ile Gln Asn Phe Asn Asn Val Ile Pro
            180                 185                 190

Glu Gly Met Asn Leu Ser Phe Leu Ile Ala Leu Ile Ser Asn Asn Gly
        195                 200                 205

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

Leu Thr Arg Thr Leu Thr Val Lys Val Val Gly Ser Pro Lys Asn Ala
225                 230                 235                 240

Val Pro Pro Val Ile His Ser Pro Asn Asp His Val Val Tyr Glu Lys
                245                 250                 255

Glu Pro Gly Glu Glu Leu Leu Ile Pro Cys Thr Val Tyr Phe Ser Phe
            260                 265                 270

Leu Met Asp Ser Arg Asn Glu Val Trp Trp Thr Ile Asp Gly Lys Lys
        275                 280                 285

Pro Asp Asp Ile Thr Ile Asp Val Thr Ile Asn Glu Ser Ile Ser His
    290                 295                 300
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Ser Arg Thr Glu Asp Glu Thr Arg Thr Gln Ile Leu Ser Ile Lys Lys
305                 310                 315                 320

Val Thr Ser Glu Asp Leu Lys Arg Ser Tyr Val Cys His Ala Arg Ser
                325                 330                 335

Ala Lys Gly Glu Val Ala Lys Ala Ala Lys Val Lys Gln Lys Val Pro
            340                 345                 350

Ala Pro Arg Tyr Thr Val Glu Leu Ala Cys Gly Phe Gly Ala Thr Val
        355                 360                 365

Leu Leu Val Val Ile Leu Ile Val Val Tyr His Val Tyr Trp Leu Glu
    370                 375                 380

Met Val Leu Phe Tyr Arg Ala His Phe Gly Thr Asp Glu Thr Ile Leu
385                 390                 395                 400

Asp Gly Lys Glu Tyr Asp Ile Tyr Val Ser Tyr Ala Arg Asn Ala Glu
                405                 410                 415

Glu Glu Glu Phe Val Leu Leu Thr Leu Arg Gly Val Leu Glu Asn Glu
            420                 425                 430

Phe Gly Tyr Lys Leu Cys Ile Phe Asp Arg Asp Ser Leu Pro Gly Gly
        435                 440                 445

Ile Val Thr Asp Glu Thr Leu Ser Phe Ile Gln Lys Ser Arg Arg Leu
    450                 455                 460

Leu Val Val Leu Ser Pro Asn Tyr Val Leu Gln Gly Thr Gln Ala Leu
465                 470                 475                 480

Leu Glu Leu Lys Ala Gly Leu Glu Asn Met Ala Ser Arg Gly Asn Ile
                485                 490                 495

Asn Val Ile Leu Val Gln Tyr Lys Ala Val Lys Glu Thr Lys Val Lys
            500                 505                 510

Glu Leu Lys Arg Ala Lys Thr Val Leu Thr Val Ile Lys Trp Lys Gly
        515                 520                 525

Glu Lys Ser Lys Tyr Pro Gln Gly Arg Phe Trp Lys Gln Leu Gln Val
    530                 535                 540

Ala Met Pro Val Lys Lys Ser Pro Arg Arg Ser Ser Ser Asp Glu Gln
545                 550                 555                 560

Gly Leu Ser Tyr Ser Ser Leu Lys Asn Val
                565                 570


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

<400> SEQUENCE: 3

Met Asn Ser Phe Ser Thr Ser Ala Phe Gly Pro Val Ala Phe Ser Leu
1               5                   10                  15

Gly Leu Leu Leu Val Leu Pro Ala Ala Phe Pro Ala Pro Val Pro Pro
            20                  25                  30

Gly Glu Asp Ser Lys Asp Val Ala Ala Pro His Arg Gln Pro Leu Thr
        35                  40                  45

Ser Ser Glu Arg Ile Asp Lys Gln Ile Arg Tyr Ile Leu Asp Gly Ile
    50                  55                  60

Ser Ala Leu Arg Lys Glu Thr Cys Asn Lys Ser Asn Met Cys Glu Ser
65                  70                  75                  80

Ser Lys Glu Ala Leu Ala Glu Asn Asn Leu Asn Leu Pro Lys Met Ala
                85                  90                  95
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Glu Lys Asp Gly Cys Phe Gln Ser Gly Phe Asn Glu Glu Thr Cys Leu
            100                 105                 110

Val Lys Ile Ile Thr Gly Leu Leu Glu Phe Glu Val Tyr Leu Glu Tyr
        115                 120                 125

Leu Gln Asn Arg Phe Glu Ser Ser Glu Glu Gln Ala Arg Ala Val Gln
    130                 135                 140

Met Ser Thr Lys Val Leu Ile Gln Phe Leu Gln Lys Lys Ala Lys Asn
145                 150                 155                 160

Leu Asp Ala Ile Thr Thr Pro Asp Pro Thr Thr Asn Ala Ser Leu Leu
                165                 170                 175

Thr Lys Leu Gln Ala Gln Asn Gln Trp Leu Gln Asp Met Thr Thr His
            180                 185                 190

Leu Ile Leu Arg Ser Phe Lys Glu Phe Leu Gln Ser Ser Leu Arg Ala
        195                 200                 205

Leu Arg Gln Met
    210


<210> SEQ ID NO 4
<211> LENGTH: 556
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 4

Met Gly Phe Trp Ile Leu Ala Ile Leu Thr Ile Leu Met Tyr Ser Thr
1               5                   10                  15

Ala Ala Lys Phe Ser Lys Gln Ser Trp Gly Leu Glu Asn Glu Ala Leu
            20                  25                  30

Ile Val Arg Cys Pro Arg Gln Gly Lys Pro Ser Tyr Thr Val Asp Trp
        35                  40                  45

Tyr Tyr Ser Gln Thr Asn Lys Ser Ile Pro Thr Gln Glu Arg Asn Arg
    50                  55                  60

Val Phe Ala Ser Gly Gln Leu Leu Lys Phe Leu Pro Ala Ala Val Ala
65                  70                  75                  80

Asp Ser Gly Ile Tyr Thr Cys Ile Val Arg Ser Pro Thr Phe Asn Arg
                85                  90                  95

Thr Gly Tyr Ala Asn Val Thr Ile Tyr Lys Lys Gln Ser Asp Cys Asn
            100                 105                 110

Val Pro Asp Tyr Leu Met Tyr Ser Thr Val Ser Gly Ser Glu Lys Asn
        115                 120                 125

Ser Lys Ile Tyr Cys Pro Thr Ile Asp Leu Tyr Asn Trp Thr Ala Pro
    130                 135                 140

Leu Glu Trp Phe Lys Asn Cys Gln Ala Leu Gln Gly Ser Arg Tyr Arg
145                 150                 155                 160

Ala His Lys Ser Phe Leu Val Ile Asp Asn Val Met Thr Glu Asp Ala
                165                 170                 175

Gly Asp Tyr Thr Cys Lys Phe Ile His Asn Glu Asn Gly Ala Asn Tyr
            180                 185                 190

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

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

Val Glu Ile Gly Lys Asn Ala Asn Leu Thr Cys Ser Ala Cys Phe Gly
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225                 230                 235                 240

Lys Gly Thr Gln Phe Leu Ala Ala Val Leu Trp Gln Leu Asn Gly Thr
                245                 250                 255

Lys Ile Thr Asp Phe Gly Glu Pro Arg Ile Gln Gln Glu Glu Gly Gln
            260                 265                 270

Asn Gln Ser Phe Ser Asn Gly Leu Ala Cys Leu Asp Met Val Leu Arg
        275                 280                 285

Ile Ala Asp Val Lys Glu Glu Asp Leu Leu Leu Gln Tyr Asp Cys Leu
    290                 295                 300

Ala Leu Asn Leu His Gly Leu Arg Arg His Thr Val Arg Leu Ser Arg
305                 310                 315                 320

Lys Asn Pro Ile Asp His His Ser Ile Tyr Cys Ile Ile Ala Val Cys
                325                 330                 335

Ser Val Phe Leu Met Leu Ile Asn Val Leu Val Ile Ile Leu Lys Met
            340                 345                 350

Phe Trp Ile Glu Ala Thr Leu Leu Trp Arg Asp Ile Ala Lys Pro Tyr
        355                 360                 365

Lys Thr Arg Asn Asp Gly Lys Leu Tyr Asp Ala Tyr Val Val Tyr Pro
    370                 375                 380

Arg Asn Tyr Lys Ser Ser Thr Asp Gly Ala Ser Arg Val Glu His Phe
385                 390                 395                 400

Val His Gln Ile Leu Pro Asp Val Leu Glu Asn Lys Cys Gly Tyr Thr
                405                 410                 415

Leu Cys Ile Tyr Gly Arg Asp Met Leu Pro Gly Glu Asp Val Val Thr
            420                 425                 430

Ala Val Glu Thr Asn Ile Arg Lys Ser Arg Arg His Ile Phe Ile Leu
        435                 440                 445

Thr Pro Gln Ile Thr His Asn Lys Glu Phe Ala Tyr Glu Gln Glu Val
    450                 455                 460

Ala Leu His Cys Ala Leu Ile Gln Asn Asp Ala Lys Val Ile Leu Ile
465                 470                 475                 480

Glu Met Glu Ala Leu Ser Glu Leu Asp Met Leu Gln Ala Glu Ala Leu
                485                 490                 495

Gln Asp Ser Leu Gln His Leu Met Lys Val Gln Gly Thr Ile Lys Trp
            500                 505                 510

Arg Glu Asp His Ile Ala Asn Lys Arg Ser Leu Asn Ser Lys Phe Trp
        515                 520                 525

Lys His Val Arg Tyr Gln Met Pro Val Pro Ser Lys Ile Pro Arg Lys
    530                 535                 540

Ala Ser Ser Leu Thr Pro Leu Ala Ala Gln Lys Gln
545                 550                 555


<210> SEQ ID NO 5
<211> LENGTH: 122
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 5

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

Ser Ser Arg Ser Phe Phe Ser Phe Leu Gly Glu Ala Phe Asp Gly Ala
            20                  25                  30
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```
Arg Asp Met Trp Arg Ala Tyr Ser Asp Met Arg Glu Ala Asn Tyr Ile
        35                  40                  45

Gly Ser Asp Lys Tyr Phe His Ala Arg Gly Asn Tyr Asp Ala Ala Lys
    50                  55                  60

Arg Gly Pro Gly Gly Val Trp Ala Ala Glu Ala Ile Ser Asp Ala Arg
65                  70                  75                  80

Glu Asn Ile Gln Arg Phe Phe Gly His Gly Ala Glu Asp Ser Leu Ala
                85                  90                  95

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

Phe Arg Pro Ala Gly Leu Pro Glu Lys Tyr
        115                 120


<210> SEQ ID NO 6
<211> LENGTH: 347
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 6

Met Ala Leu Leu Phe Ser Leu Ile Leu Ala Ile Cys Thr Arg Pro Gly
1               5                   10                  15

Phe Leu Ala Ser Pro Ser Gly Val Arg Leu Val Gly Gly Leu His Arg
            20                  25                  30

Cys Glu Gly Arg Val Glu Val Glu Gln Lys Gly Gln Trp Gly Thr Val
        35                  40                  45

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

Leu Gly Cys Gly Ala Ala Ser Gly Thr Pro Ser Gly Ile Leu Tyr Glu
65                  70                  75                  80

Pro Pro Ala Glu Lys Glu Gln Lys Val Leu Ile Gln Ser Val Ser Cys
                85                  90                  95

Thr Gly Thr Glu Asp Thr Leu Ala Gln Cys Glu Gln Glu Glu Val Tyr
            100                 105                 110

Asp Cys Ser His Asp Glu Asp Ala Gly Ala Ser Cys Glu Asn Pro Glu
        115                 120                 125

Ser Ser Phe Ser Pro Val Pro Glu Gly Val Arg Leu Ala Asp Gly Pro
    130                 135                 140

Gly His Cys Lys Gly Arg Val Glu Val Lys His Gln Asn Gln Trp Tyr
145                 150                 155                 160

Thr Val Cys Gln Thr Gly Trp Ser Leu Arg Ala Ala Lys Val Val Cys
                165                 170                 175

Arg Gln Leu Gly Cys Gly Arg Ala Val Leu Thr Gln Lys Arg Cys Asn
            180                 185                 190

Lys His Ala Tyr Gly Arg Lys Pro Ile Trp Leu Ser Gln Met Ser Cys
        195                 200                 205

Ser Gly Arg Glu Ala Thr Leu Gln Asp Cys Pro Ser Gly Pro Trp Gly
    210                 215                 220

Lys Asn Thr Cys Asn His Asp Glu Asp Thr Trp Val Glu Cys Glu Asp
225                 230                 235                 240

Pro Phe Asp Leu Arg Leu Val Gly Gly Asp Asn Leu Cys Ser Gly Arg
                245                 250                 255

Leu Glu Val Leu His Lys Gly Val Trp Gly Ser Val Cys Asp Asp Asn
            260                 265                 270
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```
Trp Gly Glu Lys Glu Asp Gln Val Val Cys Lys Gln Leu Gly Cys Gly
        275                 280                 285

Lys Ser Leu Ser Pro Ser Phe Arg Asp Arg Lys Cys Tyr Gly Pro Gly
    290                 295                 300

Val Gly Arg Ile Trp Leu Asp Asn Val Arg Cys Ser Gly Glu Glu Gln
305                 310                 315                 320

Ser Leu Glu Gln Cys Gln His Arg Phe Trp Gly Phe His Asp Cys Thr
                325                 330                 335

His Gln Glu Asp Val Ala Val Ile Cys Ser Gly
            340                 345


<210> SEQ ID NO 7
<211> LENGTH: 119
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 7

Met Ser Arg Ser Val Ala Leu Ala Val Leu Ala Leu Leu Ser Leu Ser
1               5                   10                  15

Gly Leu Glu Ala Ile Gln Arg Thr Pro Lys Ile Gln Val Tyr Ser Arg
            20                  25                  30

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

Gly Phe His Pro Ser Asp Ile Glu Val Asp Leu Leu Lys Asn Gly Glu
    50                  55                  60

Arg Ile Glu Lys Val Glu His Ser Asp Leu Ser Phe Ser Lys Asp Trp
65                  70                  75                  80

Ser Phe Tyr Leu Leu Tyr Tyr Thr Glu Phe Thr Pro Thr Glu Lys Asp
                85                  90                  95

Glu Tyr Ala Cys Arg Val Asn His Val Thr Leu Ser Gln Pro Lys Ile
            100                 105                 110

Val Lys Trp Asp Arg Asp Met
        115


<210> SEQ ID NO 8
<211> LENGTH: 222
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 8

Met Lys Leu Pro Leu Leu Leu Ala Leu Leu Phe Gly Ala Val Ser Ala
1               5                   10                  15

Leu His Leu Arg Ser Glu Thr Ser Thr Phe Glu Thr Pro Leu Gly Ala
            20                  25                  30

Lys Thr Leu Pro Glu Asp Glu Glu Thr Pro Glu Gln Glu Met Glu Glu
        35                  40                  45

Thr Pro Cys Arg Glu Leu Glu Glu Glu Glu Glu Trp Gly Ser Gly Ser
    50                  55                  60

Glu Asp Ala Ser Lys Lys Asp Gly Ala Val Glu Ser Ile Ser Val Pro
65                  70                  75                  80

Asp Met Val Asp Lys Asn Leu Thr Cys Pro Glu Glu Glu Asp Thr Val
                85                  90                  95

Lys Val Val Gly Ile Pro Gly Cys Gln Thr Cys Arg Tyr Leu Leu Val
            100                 105                 110
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```
Arg Ser Leu Gln Thr Phe Ser Gln Ala Trp Phe Thr Cys Arg Arg Cys
        115                 120                 125

Tyr Arg Gly Asn Leu Val Ser Ile His Asn Phe Asn Ile Asn Tyr Arg
    130                 135                 140

Ile Gln Cys Ser Val Ser Ala Leu Asn Gln Gly Gln Val Trp Ile Gly
145                 150                 155                 160

Gly Arg Ile Thr Gly Ser Gly Arg Cys Arg Arg Phe Gln Trp Val Asp
                165                 170                 175

Gly Ser Arg Trp Asn Phe Ala Tyr Trp Ala Ala His Gln Pro Trp Ser
            180                 185                 190

Arg Gly Gly His Cys Val Ala Leu Cys Thr Arg Gly Gly Tyr Trp Arg
        195                 200                 205

Arg Ala His Cys Leu Arg Arg Leu Pro Phe Ile Cys Ser Tyr
    210                 215                 220


<210> SEQ ID NO 9
<211> LENGTH: 472
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 9

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

Glu Ala Met Lys Gly Pro Arg Glu Glu Ile Val Tyr Leu Pro Cys Ile
            20                  25                  30

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

Val Asp Pro Lys Ser Pro Gln Tyr Cys Gln Val Ile His Arg Leu Pro
    50                  55                  60

Met Pro Asn Leu Lys Asp Glu Leu His His Ser Gly Trp Asn Thr Cys
65                  70                  75                  80

Ser Ser Cys Phe Gly Asp Ser Thr Lys Ser Arg Thr Lys Leu Val Leu
                85                  90                  95

Pro Ser Leu Ile Ser Ser Arg Ile Tyr Val Val Asp Val Gly Ser Glu
            100                 105                 110

Pro Arg Ala Pro Lys Leu His Lys Val Ile Glu Pro Lys Asp Ile His
        115                 120                 125

Ala Lys Cys Glu Leu Ala Phe Leu His Thr Ser His Cys Leu Ala Ser
    130                 135                 140

Gly Glu Val Met Ile Ser Ser Leu Gly Asp Val Lys Gly Asn Gly Lys
145                 150                 155                 160

Gly Gly Phe Val Leu Leu Asp Gly Glu Thr Phe Glu Val Lys Gly Thr
                165                 170                 175

Trp Glu Arg Pro Gly Gly Ala Ala Pro Leu Gly Tyr Asp Phe Trp Tyr
            180                 185                 190

Gln Pro Arg His Asn Val Met Ile Ser Thr Glu Trp Ala Ala Pro Asn
        195                 200                 205

Val Leu Arg Asp Gly Phe Asn Pro Ala Asp Val Glu Ala Gly Leu Tyr
    210                 215                 220

Gly Ser His Leu Tyr Val Trp Asp Trp Gln Arg His Glu Ile Val Gln
225                 230                 235                 240

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

His Asn Pro Asp Ala Ala Gln Gly Phe Val Gly Cys Ala Leu Ser Ser
           260                 265                 270

Thr Ile Gln Arg Phe Tyr Lys Asn Glu Gly Gly Thr Trp Ser Val Glu
       275                 280                 285

Lys Val Ile Gln Val Pro Pro Lys Lys Val Lys Gly Trp Leu Leu Pro
   290                 295                 300

Glu Met Pro Gly Leu Ile Thr Asp Ile Leu Leu Ser Leu Asp Asp Arg
305                 310                 315                 320

Phe Leu Tyr Phe Ser Asn Trp Leu His Gly Asp Leu Arg Gln Tyr Asp
               325                 330                 335

Ile Ser Asp Pro Gln Arg Pro Arg Leu Thr Gly Gln Leu Phe Leu Gly
           340                 345                 350

Gly Ser Ile Val Lys Gly Gly Pro Val Gln Val Leu Glu Asp Glu Glu
       355                 360                 365

Leu Lys Ser Gln Pro Glu Pro Leu Val Val Lys Gly Lys Arg Val Ala
   370                 375                 380

Gly Gly Pro Gln Met Ile Gln Leu Ser Leu Asp Gly Lys Arg Leu Tyr
385                 390                 395                 400

Ile Thr Thr Ser Leu Tyr Ser Ala Trp Asp Lys Gln Phe Tyr Pro Asp
               405                 410                 415

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

Lys Gly Gly Leu Lys Leu Asn Pro Asn Phe Leu Val Asp Phe Gly Lys
       435                 440                 445

Glu Pro Leu Gly Pro Ala Leu Ala His Glu Leu Arg Tyr Pro Gly Gly
   450                 455                 460

Asp Cys Ser Ser Asp Ile Trp Ile
465                 470


<210> SEQ ID NO 10
<211> LENGTH: 481
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 10

Met Gly Ala Leu Ala Arg Ala Leu Pro Ser Ile Leu Leu Ala Leu Leu
1               5                   10                  15

Leu Thr Ser Thr Pro Glu Ala Leu Gly Ala Asn Pro Gly Leu Val Ala
           20                  25                  30

Arg Ile Thr Asp Lys Gly Leu Gln Tyr Ala Ala Gln Glu Gly Leu Leu
       35                  40                  45

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

Asp Leu Arg Ile Pro His Val Gly Arg Gly Arg Tyr Glu Phe His Ser
65                  70                  75                  80

Leu Asn Ile His Ser Cys Glu Leu Leu His Ser Ala Leu Arg Pro Val
               85                  90                  95

Pro Gly Gln Gly Leu Ser Leu Ser Ile Ser Asp Ser Ser Ile Arg Val
           100                 105                 110

Gln Gly Arg Trp Lys Val Arg Lys Ser Phe Phe Lys Leu Gln Gly Ser
       115                 120                 125
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```
Phe Asp Val Ser Val Lys Gly Ile Ser Ile Ser Val Asn Leu Leu Leu
    130                 135                 140

Gly Ser Glu Ser Ser Gly Arg Pro Thr Val Thr Ala Ser Ser Cys Ser
145                 150                 155                 160

Ser Asp Ile Ala Asp Val Glu Val Asp Met Ser Gly Asp Leu Gly Trp
                165                 170                 175

Leu Leu Asn Leu Phe His Asn Gln Ile Glu Ser Lys Phe Gln Lys Val
            180                 185                 190

Leu Glu Ser Arg Ile Cys Glu Met Ile Gln Lys Ser Val Ser Ser Asp
        195                 200                 205

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

Phe Ala Asp Ile Asp Tyr Ser Leu Val Glu Ala Pro Arg Ala Thr Ala
225                 230                 235                 240

Gln Met Leu Glu Val Met Phe Lys Gly Glu Ile Phe His Arg Asn His
                245                 250                 255

Arg Ser Pro Val Thr Leu Leu Ala Ala Val Met Ser Leu Pro Glu Glu
            260                 265                 270

His Asn Lys Met Val Tyr Phe Ala Ile Ser Asp Tyr Val Phe Asn Thr
        275                 280                 285

Ala Ser Leu Val Tyr His Glu Glu Gly Tyr Leu Asn Phe Ser Ile Thr
    290                 295                 300

Asp Asp Met Ile Pro Pro Asp Ser Asn Ile Arg Leu Thr Thr Lys Ser
305                 310                 315                 320

Phe Arg Pro Phe Val Pro Arg Leu Ala Arg Leu Tyr Pro Asn Met Asn
                325                 330                 335

Leu Glu Leu Gln Gly Ser Val Pro Ser Ala Pro Leu Leu Asn Phe Ser
            340                 345                 350

Pro Gly Asn Leu Ser Val Asp Pro Tyr Met Glu Ile Asp Ala Phe Val
        355                 360                 365

Leu Leu Pro Ser Ser Ser Lys Glu Pro Val Phe Arg Leu Ser Val Ala
    370                 375                 380

Thr Asn Val Ser Ala Thr Leu Thr Phe Asn Thr Ser Lys Ile Thr Gly
385                 390                 395                 400

Phe Leu Lys Pro Gly Lys Val Lys Val Glu Leu Lys Glu Ser Lys Val
                405                 410                 415

Gly Leu Phe Asn Ala Glu Leu Leu Glu Ala Leu Leu Asn Tyr Tyr Ile
            420                 425                 430

Leu Asn Thr Phe Tyr Pro Lys Phe Asn Asp Lys Leu Ala Glu Gly Phe
        435                 440                 445

Pro Leu Pro Leu Leu Lys Arg Val Gln Leu Tyr Asp Leu Gly Leu Gln
    450                 455                 460

Ile His Lys Asp Phe Leu Phe Leu Gly Ala Asn Val Gln Tyr Met Arg
465                 470                 475                 480

Val


<210> SEQ ID NO 11
<211> LENGTH: 2322
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 11
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```
Met Gln Ser Gly Arg Gly Pro Pro Leu Pro Ala Pro Gly Leu Ala Leu
1               5                  10                  15

Ala Leu Thr Leu Thr Met Leu Ala Arg Leu Ala Ser Ala Ala Ser Phe
            20                  25                  30

Phe Gly Glu Asn His Leu Glu Val Pro Val Ala Thr Ala Leu Thr Asp
        35                  40                  45

Ile Asp Leu Gln Leu Gln Phe Ser Thr Ser Gln Pro Glu Ala Leu Leu
    50                  55                  60

Leu Leu Ala Ala Gly Pro Ala Asp His Leu Leu Leu Gln Leu Tyr Ser
65                  70                  75                  80

Gly Arg Leu Gln Val Arg Leu Val Leu Gly Gln Glu Glu Leu Arg Leu
                85                  90                  95

Gln Thr Pro Ala Glu Thr Leu Leu Ser Asp Ser Ile Pro His Thr Val
            100                 105                 110

Val Leu Thr Val Val Glu Gly Trp Ala Thr Leu Ser Val Asp Gly Phe
        115                 120                 125

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

Gly Leu Phe Val Gly Gly Thr Gly Thr Leu Gly Leu Pro Tyr Leu Arg
145                 150                 155                 160

Gly Thr Ser Arg Pro Leu Arg Gly Cys Leu His Ala Ala Thr Leu Asn
                165                 170                 175

Gly Arg Ser Leu Leu Arg Pro Leu Thr Pro Asp Val His Glu Gly Cys
            180                 185                 190

Ala Glu Glu Phe Ser Ala Ser Asp Asp Val Ala Leu Gly Phe Ser Gly
        195                 200                 205

Pro His Ser Leu Ala Ala Phe Pro Ala Trp Gly Thr Gln Asp Glu Gly
    210                 215                 220

Thr Leu Glu Phe Thr Leu Thr Thr Gln Ser Arg Gln Ala Pro Leu Ala
225                 230                 235                 240

Phe Gln Ala Gly Gly Arg Arg Gly Asp Phe Ile Tyr Val Asp Ile Phe
                245                 250                 255

Glu Gly His Leu Arg Ala Val Val Glu Lys Gly Gln Gly Thr Val Leu
            260                 265                 270

Leu His Asn Ser Val Pro Val Ala Asp Gly Gln Pro His Glu Val Ser
        275                 280                 285

Val His Ile Asn Ala His Arg Leu Glu Ile Ser Val Asp Gln Tyr Pro
    290                 295                 300

Thr His Thr Ser Asn Arg Gly Val Leu Ser Tyr Leu Glu Pro Arg Gly
305                 310                 315                 320

Ser Leu Leu Leu Gly Gly Leu Asp Ala Glu Ala Ser Arg His Leu Gln
                325                 330                 335

Glu His Arg Leu Gly Leu Thr Pro Glu Ala Thr Asn Ala Ser Leu Leu
            340                 345                 350

Gly Cys Met Glu Asp Leu Ser Val Asn Gly Gln Arg Arg Gly Leu Arg
        355                 360                 365

Glu Ala Leu Leu Thr Arg Asn Met Ala Ala Gly Cys Arg Leu Glu Glu
    370                 375                 380

Glu Glu Tyr Glu Asp Asp Ala Tyr Gly His Tyr Glu Ala Phe Ser Thr
385                 390                 395                 400

Leu Ala Pro Glu Ala Trp Pro Ala Met Glu Leu Pro Glu Pro Cys Val
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               405                 410                 415

Pro Glu Pro Gly Leu Pro Pro Val Phe Ala Asn Phe Thr Gln Leu Leu
           420                 425                 430

Thr Ile Ser Pro Leu Val Val Ala Glu Gly Gly Thr Ala Trp Leu Glu
       435                 440                 445

Trp Arg His Val Gln Pro Thr Leu Asp Leu Met Glu Ala Glu Leu Arg
   450                 455                 460

Lys Ser Gln Val Leu Phe Ser Val Thr Arg Gly Ala Arg His Gly Glu
465                 470                 475                 480

Leu Glu Leu Asp Ile Pro Gly Ala Gln Ala Arg Lys Met Phe Thr Leu
               485                 490                 495

Leu Asp Val Val Asn Arg Lys Ala Arg Phe Ile His Asp Gly Ser Glu
           500                 505                 510

Asp Thr Ser Asp Gln Leu Val Leu Glu Val Ser Val Thr Ala Arg Val
       515                 520                 525

Pro Met Pro Ser Cys Leu Arg Arg Gly Gln Thr Tyr Leu Leu Pro Ile
   530                 535                 540

Gln Val Asn Pro Val Asn Asp Pro Pro His Ile Ile Phe Pro His Gly
545                 550                 555                 560

Ser Leu Met Val Ile Leu Glu His Thr Gln Lys Pro Leu Gly Pro Glu
               565                 570                 575

Val Phe Gln Ala Tyr Asp Pro Asp Ser Ala Cys Glu Gly Leu Thr Phe
           580                 585                 590

Gln Val Leu Gly Thr Ser Ser Gly Leu Pro Val Glu Arg Arg Asp Gln
       595                 600                 605

Pro Gly Glu Pro Ala Thr Glu Phe Ser Cys Arg Glu Leu Glu Ala Gly
   610                 615                 620

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

Arg Val Ser Asp Gly Leu Gln Ala Ser Pro Pro Ala Thr Leu Lys Val
               645                 650                 655

Val Ala Ile Arg Pro Ala Ile Gln Ile His Arg Ser Thr Gly Leu Arg
           660                 665                 670

Leu Ala Gln Gly Ser Ala Met Pro Ile Leu Pro Ala Asn Leu Ser Val
       675                 680                 685

Glu Thr Asn Ala Val Gly Gln Asp Val Ser Val Leu Phe Arg Val Thr
   690                 695                 700

Gly Ala Leu Gln Phe Gly Glu Leu Gln Lys Gln Gly Ala Gly Gly Val
705                 710                 715                 720

Glu Gly Ala Glu Trp Trp Ala Thr Gln Ala Phe His Gln Arg Asp Val
               725                 730                 735

Glu Gln Gly Arg Val Arg Tyr Leu Ser Thr Asp Pro Gln His His Ala
           740                 745                 750

Tyr Asp Thr Val Glu Asn Leu Ala Leu Glu Val Gln Val Gly Gln Glu
       755                 760                 765

Ile Leu Ser Asn Leu Ser Phe Pro Val Thr Ile Gln Arg Ala Thr Val
   770                 775                 780

Trp Met Leu Arg Leu Glu Pro Leu His Thr Gln Asn Thr Gln Gln Glu
785                 790                 795                 800

Thr Leu Thr Thr Ala His Leu Glu Ala Thr Leu Glu Glu Ala Gly Pro
               805                 810                 815
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Ser Pro Pro Thr Phe His Tyr Glu Val Val Gln Ala Pro Arg Lys Gly
            820                 825                 830

Asn Leu Gln Leu Gln Gly Thr Arg Leu Ser Asp Gly Gln Gly Phe Thr
        835                 840                 845

Gln Asp Asp Ile Gln Ala Gly Arg Val Thr Tyr Gly Ala Thr Ala Arg
    850                 855                 860

Ala Ser Glu Ala Val Glu Asp Thr Phe Arg Phe Arg Val Thr Ala Pro
865                 870                 875                 880

Pro Tyr Phe Ser Pro Leu Tyr Thr Phe Pro Ile His Ile Gly Gly Asp
                885                 890                 895

Pro Asp Ala Pro Val Leu Thr Asn Val Leu Leu Val Val Pro Glu Gly
            900                 905                 910

Gly Glu Gly Val Leu Ser Ala Asp His Leu Phe Val Lys Ser Leu Asn
        915                 920                 925

Ser Ala Ser Tyr Leu Tyr Glu Val Met Glu Arg Pro Arg His Gly Arg
    930                 935                 940

Leu Ala Trp Arg Gly Thr Gln Asp Lys Thr Thr Met Val Thr Ser Phe
945                 950                 955                 960

Thr Asn Glu Asp Leu Leu Arg Gly Arg Leu Val Tyr Gln His Asp Asp
                965                 970                 975

Ser Glu Thr Thr Glu Asp Asp Ile Pro Phe Val Ala Thr Arg Gln Gly
            980                 985                 990

Glu Ser Ser Gly Asp Met Ala Trp  Glu Glu Val Arg Gly  Val Phe Arg
        995                 1000                1005

Val Ala  Ile Gln Pro Val Asn  Asp His Ala Pro Val  Gln Thr Ile
    1010                1015                1020

Ser Arg  Ile Phe His Val Ala  Arg Gly Gly Arg Arg  Leu Leu Thr
    1025                1030                1035

Thr Asp  Asp Val Ala Phe Ser  Asp Ala Asp Ser Gly  Phe Ala Asp
    1040                1045                1050

Ala Gln  Leu Val Leu Thr Arg  Lys Asp Leu Leu Phe  Gly Ser Ile
    1055                1060                1065

Val Ala  Val Asp Glu Pro Thr  Arg Pro Ile Tyr Arg  Phe Thr Gln
    1070                1075                1080

Glu Asp  Leu Arg Lys Arg Arg  Val Leu Phe Val His  Ser Gly Ala
    1085                1090                1095

Asp Arg  Gly Trp Ile Gln Leu  Gln Val Ser Asp Gly  Gln His Gln
    1100                1105                1110

Ala Thr  Ala Leu Leu Glu Val  Gln Ala Ser Glu Pro  Tyr Leu Arg
    1115                1120                1125

Val Ala  Asn Gly Ser Ser Leu  Val Val Pro Gln Gly  Gly Gln Gly
    1130                1135                1140

Thr Ile  Asp Thr Ala Val Leu  His Leu Asp Thr Asn  Leu Asp Ile
    1145                1150                1155

Arg Ser  Gly Asp Glu Val His  Tyr His Val Thr Ala  Gly Pro Arg
    1160                1165                1170

Trp Gly  Gln Leu Val Arg Ala  Gly Gln Pro Ala Thr  Ala Phe Ser
    1175                1180                1185

Gln Gln  Asp Leu Leu Asp Gly  Ala Val Leu Tyr Ser  His Asn Gly
    1190                1195                1200
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Ser Leu  Ser Pro Arg Asp Thr  Met Ala Phe Ser Val  Glu Ala Gly
    1205                 1210                 1215

Pro Val  His Thr Asp Ala Thr  Leu Gln Val Thr Ile  Ala Leu Glu
    1220                 1225                 1230

Gly Pro  Leu Ala Pro Leu Lys  Leu Val Arg His Lys  Lys Ile Tyr
    1235                 1240                 1245

Val Phe  Gln Gly Glu Ala Ala  Glu Ile Arg Arg Asp  Gln Leu Glu
    1250                 1255                 1260

Ala Ala  Gln Glu Ala Val Pro  Pro Ala Asp Ile Val  Phe Ser Val
    1265                 1270                 1275

Lys Ser  Pro Pro Ser Ala Gly  Tyr Leu Val Met Val  Ser Arg Gly
    1280                 1285                 1290

Ala Leu  Ala Asp Glu Pro Pro  Ser Leu Asp Pro Val  Gln Ser Phe
    1295                 1300                 1305

Ser Gln  Glu Ala Val Asp Thr  Gly Arg Val Leu Tyr  Leu His Ser
    1310                 1315                 1320

Arg Pro  Glu Ala Trp Ser Asp  Ala Phe Ser Leu Asp  Val Ala Ser
    1325                 1330                 1335

Gly Leu  Gly Ala Pro Leu Glu  Gly Val Leu Val Glu  Leu Glu Val
    1340                 1345                 1350

Leu Pro  Ala Ala Ile Pro Leu  Glu Ala Gln Asn Phe  Ser Val Pro
    1355                 1360                 1365

Glu Gly  Gly Ser Leu Thr Leu  Ala Pro Pro Leu Leu  Arg Val Ser
    1370                 1375                 1380

Gly Pro  Tyr Phe Pro Thr Leu  Leu Gly Leu Ser Leu  Gln Val Leu
    1385                 1390                 1395

Glu Pro  Pro Gln His Gly Ala  Leu Gln Lys Glu Asp  Gly Pro Gln
    1400                 1405                 1410

Ala Arg  Thr Leu Ser Ala Phe  Ser Trp Arg Met Val  Glu Glu Gln
    1415                 1420                 1425

Leu Ile  Arg Tyr Val His Asp  Gly Ser Glu Thr Leu  Thr Asp Ser
    1430                 1435                 1440

Phe Val  Leu Met Ala Asn Ala  Ser Glu Met Asp Arg  Gln Ser His
    1445                 1450                 1455

Pro Val  Ala Phe Thr Val Thr  Val Leu Pro Val Asn  Asp Gln Pro
    1460                 1465                 1470

Pro Ile  Leu Thr Thr Asn Thr  Gly Leu Gln Met Trp  Glu Gly Ala
    1475                 1480                 1485

Thr Ala  Pro Ile Pro Ala Glu  Ala Leu Arg Ser Thr  Asp Gly Asp
    1490                 1495                 1500

Ser Gly  Ser Glu Asp Leu Val  Tyr Thr Ile Glu Gln  Pro Ser Asn
    1505                 1510                 1515

Gly Arg  Val Val Leu Arg Gly  Ala Pro Gly Thr Glu  Val Arg Ser
    1520                 1525                 1530

Phe Thr  Gln Ala Gln Leu Asp  Gly Gly Leu Val Leu  Phe Ser His
    1535                 1540                 1545

Arg Gly  Thr Leu Asp Gly Gly  Phe Arg Phe Arg Leu  Ser Asp Gly
    1550                 1555                 1560

Glu His  Thr Ser Pro Gly His  Phe Phe Arg Val Thr  Ala Gln Lys
    1565                 1570                 1575

Gln Val  Leu Leu Ser Leu Lys  Gly Ser Gln Thr Leu  Thr Val Cys
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    1580                1585                1590

Pro Gly  Ser Val Gln Pro Leu  Ser Ser Gln Thr Leu  Arg Ala Ser
    1595                1600                1605

Ser Ser  Ala Gly Thr Asp Pro  Gln Leu Leu Leu Tyr  Arg Val Val
    1610                1615                1620

Arg Gly  Pro Gln Leu Gly Arg  Leu Phe His Ala Gln  Gln Asp Ser
    1625                1630                1635

Thr Gly  Glu Ala Leu Val Asn  Phe Thr Gln Ala Glu  Val Tyr Ala
    1640                1645                1650

Gly Asn  Ile Leu Tyr Glu His  Glu Met Pro Pro Glu  Pro Phe Trp
    1655                1660                1665

Glu Ala  His Asp Thr Leu Glu  Leu Gln Leu Ser Ser  Pro Pro Ala
    1670                1675                1680

Arg Asp  Val Ala Ala Thr Leu  Ala Val Ala Val Ser  Phe Glu Ala
    1685                1690                1695

Ala Cys  Pro Gln Arg Pro Ser  His Leu Trp Lys Asn  Lys Gly Leu
    1700                1705                1710

Trp Val  Pro Glu Gly Gln Arg  Ala Arg Ile Thr Val  Ala Ala Leu
    1715                1720                1725

Asp Ala  Ser Asn Leu Leu Ala  Ser Val Pro Ser Pro  Gln Arg Ser
    1730                1735                1740

Glu His  Asp Val Leu Phe Gln  Val Thr Gln Phe Pro  Ser Arg Gly
    1745                1750                1755

Gln Leu  Leu Val Ser Glu Glu  Pro Leu His Ala Gly  Gln Pro His
    1760                1765                1770

Phe Leu  Gln Ser Gln Leu Ala  Ala Gly Gln Leu Val  Tyr Ala His
    1775                1780                1785

Gly Gly  Gly Gly Thr Gln Gln  Asp Gly Phe His Phe  Arg Ala His
    1790                1795                1800

Leu Gln  Gly Pro Ala Gly Ala  Ser Val Ala Gly Pro  Gln Thr Ser
    1805                1810                1815

Glu Ala  Phe Ala Ile Thr Val  Arg Asp Val Asn Glu  Arg Pro Pro
    1820                1825                1830

Gln Pro  Gln Ala Ser Val Pro  Leu Arg Leu Thr Arg  Gly Ser Arg
    1835                1840                1845

Ala Pro  Ile Ser Arg Ala Gln  Leu Ser Val Val Asp  Pro Asp Ser
    1850                1855                1860

Ala Pro  Gly Glu Ile Glu Tyr  Glu Val Gln Arg Ala  Pro His Asn
    1865                1870                1875

Gly Phe  Leu Ser Leu Val Gly  Gly Gly Leu Gly Pro  Val Thr Arg
    1880                1885                1890

Phe Thr  Gln Ala Asp Val Asp  Ser Gly Arg Leu Ala  Phe Val Ala
    1895                1900                1905

Asn Gly  Ser Ser Val Ala Gly  Ile Phe Gln Leu Ser  Met Ser Asp
    1910                1915                1920

Gly Ala  Ser Pro Pro Leu Pro  Met Ser Leu Ala Val  Asp Ile Leu
    1925                1930                1935

Pro Ser  Ala Ile Glu Val Gln  Leu Arg Ala Pro Leu  Glu Val Pro
    1940                1945                1950

Gln Ala  Leu Gly Arg Ser Ser  Leu Ser Gln Gln Gln  Leu Arg Val
    1955                1960                1965
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Val Ser  Asp Arg Glu Glu Pro  Glu Ala Ala Tyr Arg  Leu Ile Gln
    1970                 1975                 1980

Gly Pro  Gln Tyr Gly His Leu  Leu Val Gly Gly Arg  Pro Thr Ser
    1985                 1990                 1995

Ala Phe  Ser Gln Phe Gln Ile  Asp Gln Gly Glu Val  Val Phe Ala
    2000                 2005                 2010

Phe Thr  Asn Phe Ser Ser Ser  His Asp His Phe Arg  Val Leu Ala
    2015                 2020                 2025

Leu Ala  Arg Gly Val Asn Ala  Ser Ala Val Val Asn  Val Thr Val
    2030                 2035                 2040

Arg Ala  Leu Leu His Val Trp  Ala Gly Gly Pro Trp  Pro Gln Gly
    2045                 2050                 2055

Ala Thr  Leu Arg Leu Asp Pro  Thr Val Leu Asp Ala  Gly Glu Leu
    2060                 2065                 2070

Ala Asn  Arg Thr Gly Ser Val  Pro Arg Phe Arg Leu  Leu Glu Gly
    2075                 2080                 2085

Pro Arg  His Gly Arg Val Val  Arg Val Pro Arg Ala  Arg Thr Glu
    2090                 2095                 2100

Pro Gly  Gly Ser Gln Leu Val  Glu Gln Phe Thr Gln  Gln Asp Leu
    2105                 2110                 2115

Glu Asp  Gly Arg Leu Gly Leu  Glu Val Gly Arg Pro  Glu Gly Arg
    2120                 2125                 2130

Ala Pro  Gly Pro Ala Gly Asp  Ser Leu Thr Leu Glu  Leu Trp Ala
    2135                 2140                 2145

Gln Gly  Val Pro Pro Ala Val  Ala Ser Leu Asp Phe  Ala Thr Glu
    2150                 2155                 2160

Pro Tyr  Asn Ala Ala Arg Pro  Tyr Ser Val Ala Leu  Leu Ser Val
    2165                 2170                 2175

Pro Glu  Ala Ala Arg Thr Glu  Ala Gly Lys Pro Glu  Ser Ser Thr
    2180                 2185                 2190

Pro Thr  Gly Glu Pro Gly Pro  Met Ala Ser Ser Pro  Glu Pro Ala
    2195                 2200                 2205

Val Ala  Lys Gly Gly Phe Leu  Ser Phe Leu Glu Ala  Asn Met Phe
    2210                 2215                 2220

Ser Val  Ile Ile Pro Met Cys  Leu Val Leu Leu Leu  Leu Ala Leu
    2225                 2230                 2235

Ile Leu  Pro Leu Leu Phe Tyr  Leu Arg Lys Arg Asn  Lys Thr Gly
    2240                 2245                 2250

Lys His  Asp Val Gln Val Leu  Thr Ala Lys Pro Arg  Asn Gly Leu
    2255                 2260                 2265

Ala Gly  Asp Thr Glu Thr Phe  Arg Lys Val Glu Pro  Gly Gln Ala
    2270                 2275                 2280

Ile Pro  Leu Thr Ala Val Pro  Gly Gln Gly Pro Pro  Pro Gly Gly
    2285                 2290                 2295

Gln Pro  Asp Pro Glu Leu Leu  Gln Phe Cys Arg Thr  Pro Asn Pro
    2300                 2305                 2310

Ala Leu  Lys Asn Gly Gln Tyr  Trp Val
    2315                 2320
```

<210> SEQ ID NO 12
<211> LENGTH: 314

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<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 12

Met Arg Ile Ala Val Ile Cys Phe Cys Leu Leu Gly Ile Thr Cys Ala
1 5 10 15

Ile Pro Val Lys Gln Ala Asp Ser Gly Ser Ser Glu Glu Lys Gln Leu
20 25 30

Tyr Asn Lys Tyr Pro Asp Ala Val Ala Thr Trp Leu Asn Pro Asp Pro
35 40 45

Ser Gln Lys Gln Asn Leu Leu Ala Pro Gln Asn Ala Val Ser Ser Glu
50 55 60

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

Ser His Asp His Met Asp Asp Met Asp Asp Glu Asp Asp Asp Asp His
85 90 95

Val Asp Ser Gln Asp Ser Ile Asp Ser Asn Asp Ser Asp Asp Val Asp
100 105 110

Asp Thr Asp Asp Ser His Gln Ser Asp Glu Ser His His Ser Asp Glu
115 120 125

Ser Asp Glu Leu Val Thr Asp Phe Pro Thr Asp Leu Pro Ala Thr Glu
130 135 140

Val Phe Thr Pro Val Val Pro Thr Val Asp Thr Tyr Asp Gly Arg Gly
145 150 155 160

Asp Ser Val Val Tyr Gly Leu Arg Ser Lys Ser Lys Lys Phe Arg Arg
165 170 175

Pro Asp Ile Gln Tyr Pro Asp Ala Thr Asp Glu Asp Ile Thr Ser His
180 185 190

Met Glu Ser Glu Glu Leu Asn Gly Ala Tyr Lys Ala Ile Pro Val Ala
195 200 205

Gln Asp Leu Asn Ala Pro Ser Asp Trp Asp Ser Arg Gly Lys Asp Ser
210 215 220

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

Lys Gln Ser Arg Leu Tyr Lys Arg Lys Ala Asn Asp Glu Ser Asn Glu
245 250 255

His Ser Asp Val Ile Asp Ser Gln Glu Leu Ser Lys Val Ser Arg Glu
260 265 270

Phe His Ser His Glu Phe His Ser His Glu Asp Met Leu Val Val Asp
275 280 285

Pro Lys Ser Lys Glu Glu Asp Lys His Leu Lys Phe Arg Ile Ser His
290 295 300

Glu Leu Asp Ser Ala Ser Ser Glu Val Asn
305 310

<210> SEQ ID NO 13
<211> LENGTH: 201
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 13

Met Thr Glu Lys Ala Pro Glu Pro His Val Glu Glu Asp Asp Asp Asp
1 5 10 15

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```
Glu Leu Asp Ser Lys Leu Asn Tyr Lys Pro Pro Pro Gln Lys Ser Leu
            20                  25                  30

Lys Glu Leu Gln Glu Met Asp Lys Asp Asp Glu Ser Leu Ile Lys Tyr
        35                  40                  45

Lys Lys Thr Leu Leu Gly Asp Gly Pro Val Val Thr Asp Pro Lys Ala
    50                  55                  60

Pro Asn Val Val Val Thr Arg Leu Thr Leu Val Cys Glu Ser Ala Pro
65                  70                  75                  80

Gly Pro Ile Thr Met Asp Leu Thr Gly Asp Leu Glu Ala Leu Lys Lys
                85                  90                  95

Glu Thr Ile Val Leu Lys Glu Gly Ser Glu Tyr Arg Val Lys Ile His
            100                 105                 110

Phe Lys Val Asn Arg Asp Ile Val Ser Gly Leu Lys Tyr Val Gln His
        115                 120                 125

Thr Tyr Arg Thr Gly Val Lys Val Asp Lys Ala Thr Phe Met Val Gly
    130                 135                 140

Ser Tyr Gly Pro Arg Pro Glu Glu Tyr Glu Phe Leu Thr Pro Val Glu
145                 150                 155                 160

Glu Ala Pro Lys Gly Met Leu Ala Arg Gly Thr Tyr His Asn Lys Ser
                165                 170                 175

Phe Phe Thr Asp Asp Asp Lys Gln Asp His Leu Ser Trp Glu Trp Asn
            180                 185                 190

Leu Ser Ile Lys Lys Glu Trp Thr Glu
        195                 200


<210> SEQ ID NO 14
<211> LENGTH: 260
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 14

Met Ser His His Trp Gly Tyr Gly Lys His Asn Gly Pro Glu His Trp
1               5                   10                  15

His Lys Asp Phe Pro Ile Ala Lys Gly Glu Arg Gln Ser Pro Val Asp
            20                  25                  30

Ile Asp Thr His Thr Ala Lys Tyr Asp Pro Ser Leu Lys Pro Leu Ser
        35                  40                  45

Val Ser Tyr Asp Gln Ala Thr Ser Leu Arg Ile Leu Asn Asn Gly His
    50                  55                  60

Ala Phe Asn Val Glu Phe Asp Asp Ser Gln Asp Lys Ala Val Leu Lys
65                  70                  75                  80

Gly Gly Pro Leu Asp Gly Thr Tyr Arg Leu Ile Gln Phe His Phe His
                85                  90                  95

Trp Gly Ser Leu Asp Gly Gln Gly Ser Glu His Thr Val Asp Lys Lys
            100                 105                 110

Lys Tyr Ala Ala Glu Leu His Leu Val His Trp Asn Thr Lys Tyr Gly
        115                 120                 125

Asp Phe Gly Lys Ala Val Gln Gln Pro Asp Gly Leu Ala Val Leu Gly
    130                 135                 140

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

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

Tyr Pro Gly Ser Leu Thr Thr Pro Pro Leu Leu Glu Cys Val Thr Trp
        195                 200                 205

Ile Val Leu Lys Glu Pro Ile Ser Val Ser Ser Glu Gln Val Leu Lys
    210                 215                 220

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

Val Asp Asn Trp Arg Pro Ala Gln Pro Leu Lys Asn Arg Gln Ile Lys
                245                 250                 255

Ala Ser Phe Lys
            260


<210> SEQ ID NO 15
<211> LENGTH: 198
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 15

Met Pro Leu Gly Leu Leu Trp Leu Gly Leu Ala Leu Leu Gly Ala Leu
1               5                   10                  15

His Ala Gln Ala Gln Asp Ser Thr Ser Asp Leu Ile Pro Ala Pro Pro
            20                  25                  30

Leu Ser Lys Val Pro Leu Gln Gln Asn Phe Gln Asp Asn Gln Phe Gln
        35                  40                  45

Gly Lys Trp Tyr Val Val Gly Leu Ala Gly Asn Ala Ile Leu Arg Glu
    50                  55                  60

Asp Lys Asp Pro Gln Lys Met Tyr Ala Thr Ile Tyr Glu Leu Lys Glu
65                  70                  75                  80

Asp Lys Ser Tyr Asn Val Thr Ser Val Leu Phe Arg Lys Lys Lys Cys
                85                  90                  95

Asp Tyr Trp Ile Arg Thr Phe Val Pro Gly Cys Gln Pro Gly Glu Phe
            100                 105                 110

Thr Leu Gly Asn Ile Lys Ser Tyr Pro Gly Leu Thr Ser Tyr Leu Val
        115                 120                 125

Arg Val Val Ser Thr Asn Tyr Asn Gln His Ala Met Val Phe Phe Lys
    130                 135                 140

Lys Val Ser Gln Asn Arg Glu Tyr Phe Lys Ile Thr Leu Tyr Gly Arg
145                 150                 155                 160

Thr Lys Glu Leu Thr Ser Glu Leu Lys Glu Asn Phe Ile Arg Phe Ser
                165                 170                 175

Lys Ser Leu Gly Leu Pro Glu Asn His Ile Val Phe Pro Val Pro Ile
            180                 185                 190

Asp Gln Cys Ile Asp Gly
        195


<210> SEQ ID NO 16
<211> LENGTH: 1685
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 16

Met Lys Leu Arg Gly Val Ser Leu Ala Ala Gly Leu Phe Leu Leu Ala
1               5                   10                  15
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```
Leu Ser Leu Trp Gly Gln Pro Ala Glu Ala Ala Ala Cys Tyr Gly Cys
            20                  25                  30

Ser Pro Gly Ser Lys Cys Asp Cys Ser Gly Ile Lys Gly Glu Lys Gly
        35                  40                  45

Glu Arg Gly Phe Pro Gly Leu Glu Gly His Pro Gly Leu Pro Gly Phe
    50                  55                  60

Pro Gly Pro Glu Gly Pro Pro Gly Pro Arg Gly Gln Lys Gly Asp Asp
65                  70                  75                  80

Gly Ile Pro Gly Pro Pro Gly Pro Lys Gly Ile Arg Gly Pro Pro Gly
                85                  90                  95

Leu Pro Gly Phe Pro Gly Thr Pro Gly Leu Pro Gly Met Pro Gly His
            100                 105                 110

Asp Gly Ala Pro Gly Pro Gln Gly Ile Pro Gly Cys Asn Gly Thr Lys
        115                 120                 125

Gly Glu Arg Gly Phe Pro Gly Ser Pro Gly Phe Pro Gly Leu Gln Gly
    130                 135                 140

Pro Pro Gly Pro Pro Gly Ile Pro Gly Met Lys Gly Glu Pro Gly Ser
145                 150                 155                 160

Ile Ile Met Ser Ser Leu Pro Gly Pro Lys Gly Asn Pro Gly Tyr Pro
                165                 170                 175

Gly Pro Pro Gly Ile Gln Gly Leu Pro Gly Pro Thr Gly Ile Pro Gly
            180                 185                 190

Pro Ile Gly Pro Pro Gly Pro Pro Gly Leu Met Gly Pro Pro Gly Pro
        195                 200                 205

Pro Gly Leu Pro Gly Pro Lys Gly Asn Met Gly Leu Asn Phe Gln Gly
    210                 215                 220

Pro Lys Gly Glu Lys Gly Glu Gln Gly Leu Gln Gly Pro Pro Gly Pro
225                 230                 235                 240

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

Lys Gly Asp Gln Gly Leu Pro Gly Asp Arg Gly Pro Pro Gly Pro Pro
            260                 265                 270

Gly Ile Arg Gly Pro Pro Gly Pro Pro Gly Gly Glu Lys Gly Glu Lys
        275                 280                 285

Gly Glu Gln Gly Glu Pro Gly Lys Arg Gly Lys Pro Gly Lys Asp Gly
    290                 295                 300

Glu Asn Gly Gln Pro Gly Ile Pro Gly Leu Pro Gly Asp Pro Gly Tyr
305                 310                 315                 320

Pro Gly Glu Pro Gly Arg Asp Gly Glu Lys Gly Gln Lys Gly Asp Thr
                325                 330                 335

Gly Pro Pro Gly Pro Pro Gly Leu Val Ile Pro Arg Pro Gly Thr Gly
            340                 345                 350

Ile Thr Ile Gly Glu Lys Gly Asn Ile Gly Leu Pro Gly Leu Pro Gly
        355                 360                 365

Glu Lys Gly Glu Arg Gly Phe Pro Gly Ile Gln Gly Pro Pro Gly Leu
    370                 375                 380

Pro Gly Pro Pro Gly Ala Ala Val Met Gly Pro Pro Gly Pro Pro Gly
385                 390                 395                 400

Phe Pro Gly Glu Arg Gly Gln Lys Gly Asp Glu Gly Pro Pro Gly Ile
                405                 410                 415
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```
Ser Ile Pro Gly Pro Pro Gly Leu Asp Gly Gln Pro Gly Ala Pro Gly
            420                 425                 430

Leu Pro Gly Pro Pro Gly Pro Ala Gly Pro His Ile Pro Pro Ser Asp
        435                 440                 445

Glu Ile Cys Glu Pro Gly Pro Pro Gly Pro Pro Gly Ser Pro Gly Asp
    450                 455                 460

Lys Gly Leu Gln Gly Glu Gln Gly Val Lys Gly Asp Lys Gly Asp Thr
465                 470                 475                 480

Cys Phe Asn Cys Ile Gly Thr Gly Ile Ser Gly Pro Pro Gly Gln Pro
                485                 490                 495

Gly Leu Pro Gly Leu Pro Gly Pro Pro Gly Ser Leu Gly Phe Pro Gly
            500                 505                 510

Gln Lys Gly Glu Lys Gly Gln Ala Gly Ala Thr Gly Pro Lys Gly Leu
        515                 520                 525

Pro Gly Ile Pro Gly Ala Pro Gly Ala Pro Gly Phe Pro Gly Ser Lys
    530                 535                 540

Gly Glu Pro Gly Asp Ile Leu Thr Phe Pro Gly Met Lys Gly Asp Lys
545                 550                 555                 560

Gly Glu Leu Gly Ser Pro Gly Ala Pro Gly Leu Pro Gly Leu Pro Gly
                565                 570                 575

Thr Pro Gly Gln Asp Gly Leu Pro Gly Leu Pro Gly Pro Lys Gly Glu
            580                 585                 590

Pro Gly Gly Ile Thr Phe Lys Gly Glu Arg Gly Pro Pro Gly Asn Pro
        595                 600                 605

Gly Leu Pro Gly Leu Pro Gly Asn Ile Gly Pro Met Gly Pro Pro Gly
    610                 615                 620

Phe Gly Pro Pro Gly Pro Val Gly Glu Lys Gly Ile Gln Gly Val Ala
625                 630                 635                 640

Gly Asn Pro Gly Gln Pro Gly Ile Pro Gly Pro Lys Gly Asp Pro Gly
                645                 650                 655

Gln Thr Ile Thr Gln Pro Gly Lys Pro Gly Leu Pro Gly Asn Pro Gly
            660                 665                 670

Arg Asp Gly Asp Val Gly Leu Pro Gly Asp Pro Gly Leu Pro Gly Gln
        675                 680                 685

Pro Gly Leu Pro Gly Ile Pro Gly Ser Lys Gly Glu Pro Gly Ile Pro
    690                 695                 700

Gly Ile Gly Leu Pro Gly Pro Pro Gly Pro Lys Gly Phe Pro Gly Ile
705                 710                 715                 720

Pro Gly Pro Pro Gly Ala Pro Gly Thr Pro Gly Arg Ile Gly Leu Glu
                725                 730                 735

Gly Pro Pro Gly Pro Pro Gly Phe Pro Gly Pro Lys Gly Glu Pro Gly
            740                 745                 750

Phe Ala Leu Pro Gly Pro Pro Gly Pro Pro Gly Leu Pro Gly Phe Lys
        755                 760                 765

Gly Ala Leu Gly Pro Lys Gly Asp Arg Gly Phe Pro Gly Pro Pro Gly
    770                 775                 780

Pro Pro Gly Arg Thr Gly Leu Asp Gly Leu Pro Gly Pro Lys Gly Asp
785                 790                 795                 800

Val Gly Pro Asn Gly Gln Pro Gly Pro Met Gly Pro Pro Gly Leu Pro
                805                 810                 815

Gly Ile Gly Val Gln Gly Pro Pro Gly Pro Pro Gly Ile Pro Gly Pro
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            820                 825                 830

Ile Gly Gln Pro Gly Leu His Gly Ile Pro Gly Glu Lys Gly Asp Pro
        835                 840                 845

Gly Pro Pro Gly Leu Asp Val Pro Gly Pro Pro Gly Glu Arg Gly Ser
    850                 855                 860

Pro Gly Ile Pro Gly Ala Pro Gly Pro Ile Gly Pro Pro Gly Ser Pro
865                 870                 875                 880

Gly Leu Pro Gly Lys Ala Gly Ala Ser Gly Phe Pro Gly Thr Lys Gly
                885                 890                 895

Glu Met Gly Met Met Gly Pro Pro Gly Pro Pro Gly Pro Leu Gly Ile
            900                 905                 910

Pro Gly Arg Ser Gly Val Pro Gly Leu Lys Gly Asp Asp Gly Leu Gln
        915                 920                 925

Gly Gln Pro Gly Leu Pro Gly Pro Thr Gly Glu Lys Gly Ser Lys Gly
    930                 935                 940

Glu Pro Gly Leu Pro Gly Pro Pro Gly Pro Met Asp Pro Asn Leu Leu
945                 950                 955                 960

Gly Ser Lys Gly Glu Lys Gly Glu Pro Gly Leu Pro Gly Ile Pro Gly
                965                 970                 975

Val Ser Gly Pro Lys Gly Tyr Gln Gly Leu Pro Gly Asp Pro Gly Gln
            980                 985                 990

Pro Gly Leu Ser Gly Gln Pro Gly  Leu Pro Gly Pro Pro  Gly Pro Lys
        995                 1000                1005

Gly Asn  Pro Gly Leu Pro Gly  Gln Pro Gly Leu Ile  Gly Pro Pro
    1010                1015                1020

Gly Leu  Lys Gly Thr Ile Gly  Asp Met Gly Phe Pro  Gly Pro Gln
    1025                1030                1035

Gly Val  Glu Gly Pro Pro Gly  Pro Ser Gly Val Pro  Gly Gln Pro
    1040                1045                1050

Gly Ser  Pro Gly Leu Pro Gly  Gln Lys Gly Asp Lys  Gly Asp Pro
    1055                1060                1065

Gly Ile  Ser Ser Ile Gly Leu  Pro Gly Leu Pro Gly  Pro Lys Gly
    1070                1075                1080

Glu Pro  Gly Leu Pro Gly Tyr  Pro Gly Asn Pro Gly  Ile Lys Gly
    1085                1090                1095

Ser Val  Gly Asp Pro Gly Leu  Pro Gly Leu Pro Gly  Thr Pro Gly
    1100                1105                1110

Ala Lys  Gly Gln Pro Gly Leu  Pro Gly Phe Pro Gly  Thr Pro Gly
    1115                1120                1125

Pro Pro  Gly Pro Lys Gly Ile  Ser Gly Pro Pro Gly  Asn Pro Gly
    1130                1135                1140

Leu Pro  Gly Glu Pro Gly Pro  Val Gly Gly Gly Gly  His Pro Gly
    1145                1150                1155

Gln Pro  Gly Pro Pro Gly Glu  Lys Gly Lys Pro Gly  Gln Asp Gly
    1160                1165                1170

Ile Pro  Gly Pro Ala Gly Gln  Lys Gly Glu Pro Gly  Gln Pro Gly
    1175                1180                1185

Phe Gly  Asn Pro Gly Pro Pro  Gly Leu Pro Gly Leu  Ser Gly Gln
    1190                1195                1200

Lys Gly  Asp Gly Gly Leu Pro  Gly Ile Pro Gly Asn  Pro Gly Leu
    1205                1210                1215
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Pro Gly  Pro Lys Gly Glu Pro  Gly Phe His Gly Phe  Pro Gly Val
    1220                 1225                 1230

Gln Gly  Pro Pro Gly Pro Pro  Gly Ser Pro Gly Pro  Ala Leu Glu
    1235                 1240                 1245

Gly Pro  Lys Gly Asn Pro Gly  Pro Gln Gly Pro Pro  Gly Arg Pro
    1250                 1255                 1260

Gly Leu  Pro Gly Pro Glu Gly  Pro Pro Gly Leu Pro  Gly Asn Gly
    1265                 1270                 1275

Gly Ile  Lys Gly Glu Lys Gly  Asn Pro Gly Gln Pro  Gly Leu Pro
    1280                 1285                 1290

Gly Leu  Pro Gly Leu Lys Gly  Asp Gln Gly Pro Pro  Gly Leu Gln
    1295                 1300                 1305

Gly Asn  Pro Gly Arg Pro Gly  Leu Asn Gly Met Lys  Gly Asp Pro
    1310                 1315                 1320

Gly Leu  Pro Gly Val Pro Gly  Phe Pro Gly Met Lys  Gly Pro Ser
    1325                 1330                 1335

Gly Val  Pro Gly Ser Ala Gly  Pro Glu Gly Glu Pro  Gly Leu Ile
    1340                 1345                 1350

Gly Pro  Pro Gly Pro Pro Gly  Leu Pro Gly Pro Ser  Gly Gln Ser
    1355                 1360                 1365

Ile Ile  Ile Lys Gly Asp Ala  Gly Pro Pro Gly Ile  Pro Gly Gln
    1370                 1375                 1380

Pro Gly  Leu Lys Gly Leu Pro  Gly Pro Gln Gly Pro  Gln Gly Leu
    1385                 1390                 1395

Pro Gly  Pro Thr Gly Pro Pro  Gly Asp Pro Gly Arg  Asn Gly Leu
    1400                 1405                 1410

Pro Gly  Phe Asp Gly Ala Gly  Gly Arg Lys Gly Asp  Pro Gly Leu
    1415                 1420                 1425

Pro Gly  Gln Pro Gly Thr Arg  Gly Leu Asp Gly Pro  Pro Gly Pro
    1430                 1435                 1440

Asp Gly  Leu Gln Gly Pro Pro  Gly Pro Pro Gly Thr  Ser Ser Val
    1445                 1450                 1455

Ala His  Gly Phe Leu Ile Thr  Arg His Ser Gln Thr  Thr Asp Ala
    1460                 1465                 1470

Pro Gln  Cys Pro Gln Gly Thr  Leu Gln Val Tyr Glu  Gly Phe Ser
    1475                 1480                 1485

Leu Leu  Tyr Val Gln Gly Asn  Lys Arg Ala His Gly  Gln Asp Leu
    1490                 1495                 1500

Gly Thr  Ala Gly Ser Cys Leu  Arg Arg Phe Ser Thr  Met Pro Phe
    1505                 1510                 1515

Met Phe  Cys Asn Ile Asn Asn  Val Cys Asn Phe Ala  Ser Arg Asn
    1520                 1525                 1530

Asp Tyr  Ser Tyr Trp Leu Ser  Thr Pro Glu Pro Met  Pro Met Ser
    1535                 1540                 1545

Met Gln  Pro Leu Lys Gly Gln  Ser Ile Gln Pro Phe  Ile Ser Arg
    1550                 1555                 1560

Cys Ala  Val Cys Glu Ala Pro  Ala Val Val Ile Ala  Val His Ser
    1565                 1570                 1575

Gln Thr  Ile Gln Ile Pro His  Cys Pro Gln Gly Trp  Asp Ser Leu
    1580                 1585                 1590
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Trp Ile  Gly Tyr Ser Phe Met  Met His Thr Ser Ala  Gly Ala Glu
    1595                 1600                 1605

Gly Ser  Gly Gln Ala Leu Ala  Ser Pro Gly Ser Cys  Leu Glu Glu
    1610                 1615                 1620

Phe Arg  Ser Ala Pro Phe Ile  Glu Cys His Gly Arg  Gly Thr Cys
    1625                 1630                 1635

Asn Tyr  Tyr Ala Asn Ser Tyr  Ser Phe Trp Leu Ala  Thr Val Asp
    1640                 1645                 1650

Val Ser  Asp Met Phe Ser Lys  Pro Gln Ser Glu Thr  Leu Lys Ala
    1655                 1660                 1665

Gly Asp  Leu Arg Thr Arg Ile  Ser Arg Cys Gln Val  Cys Met Lys
    1670                 1675                 1680

Arg Thr
    1685


<210> SEQ ID NO 17
<211> LENGTH: 349
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 17

Met Thr Ala Ala Ser Met Gly Pro Val Arg Val Ala Phe Val Val Leu
1               5                   10                  15

Leu Ala Leu Cys Ser Arg Pro Ala Val Gly Gln Asn Cys Ser Gly Pro
            20                  25                  30

Cys Arg Cys Pro Asp Glu Pro Ala Pro Arg Cys Pro Ala Gly Val Ser
        35                  40                  45

Leu Val Leu Asp Gly Cys Gly Cys Cys Arg Val Cys Ala Lys Gln Leu
    50                  55                  60

Gly Glu Leu Cys Thr Glu Arg Asp Pro Cys Asp Pro His Lys Gly Leu
65                  70                  75                  80

Phe Cys His Phe Gly Ser Pro Ala Asn Arg Lys Ile Gly Val Cys Thr
                85                  90                  95

Ala Lys Asp Gly Ala Pro Cys Ile Phe Gly Gly Thr Val Tyr Arg Ser
            100                 105                 110

Gly Glu Ser Phe Gln Ser Ser Cys Lys Tyr Gln Cys Thr Cys Leu Asp
        115                 120                 125

Gly Ala Val Gly Cys Met Pro Leu Cys Ser Met Asp Val Arg Leu Pro
    130                 135                 140

Ser Pro Asp Cys Pro Phe Pro Arg Arg Val Lys Leu Pro Gly Lys Cys
145                 150                 155                 160

Cys Glu Glu Trp Val Cys Asp Glu Pro Lys Asp Gln Thr Val Val Gly
                165                 170                 175

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

Thr Met Ile Arg Ala Asn Cys Leu Val Gln Thr Thr Glu Trp Ser Ala
        195                 200                 205

Cys Ser Lys Thr Cys Gly Met Gly Ile Ser Thr Arg Val Thr Asn Asp
    210                 215                 220

Asn Ala Ser Cys Arg Leu Glu Lys Gln Ser Arg Leu Cys Met Val Arg
225                 230                 235                 240

Pro Cys Glu Ala Asp Leu Glu Glu Asn Ile Lys Lys Gly Lys Lys Cys
                245                 250                 255
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Ile Arg Thr Pro Lys Ile Ser Lys Pro Ile Lys Phe Glu Leu Ser Gly
            260                 265                 270

Cys Thr Ser Met Lys Thr Tyr Arg Ala Lys Phe Cys Gly Val Cys Thr
        275                 280                 285

Asp Gly Arg Cys Cys Thr Pro His Arg Thr Thr Thr Leu Pro Val Glu
    290                 295                 300

Phe Lys Cys Pro Asp Gly Glu Val Met Lys Lys Asn Met Met Phe Ile
305                 310                 315                 320

Lys Thr Cys Ala Cys His Tyr Asn Cys Pro Gly Asp Asn Asp Ile Phe
                325                 330                 335

Glu Ser Leu Tyr Tyr Arg Lys Met Tyr Gly Asp Met Ala
            340                 345


<210> SEQ ID NO 18
<211> LENGTH: 554
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 18

Met Thr Ala Pro Gly Ala Ala Gly Arg Cys Pro Pro Thr Thr Trp Leu
1               5                   10                  15

Gly Ser Leu Leu Leu Leu Val Cys Leu Leu Ala Ser Arg Ser Ile Thr
            20                  25                  30

Glu Glu Val Ser Glu Tyr Cys Ser His Met Ile Gly Ser Gly His Leu
        35                  40                  45

Gln Ser Leu Gln Arg Leu Ile Asp Ser Gln Met Glu Thr Ser Cys Gln
    50                  55                  60

Ile Thr Phe Glu Phe Val Asp Gln Glu Gln Leu Lys Asp Pro Val Cys
65                  70                  75                  80

Tyr Leu Lys Lys Ala Phe Leu Leu Val Gln Asp Ile Met Glu Asp Thr
                85                  90                  95

Met Arg Phe Arg Asp Asn Thr Pro Asn Ala Ile Ala Ile Val Gln Leu
            100                 105                 110

Gln Glu Leu Ser Leu Arg Leu Lys Ser Cys Phe Thr Lys Asp Tyr Glu
        115                 120                 125

Glu His Asp Lys Ala Cys Val Arg Thr Phe Tyr Glu Thr Pro Leu Gln
    130                 135                 140

Leu Leu Glu Lys Val Lys Asn Val Phe Asn Glu Thr Lys Asn Leu Leu
145                 150                 155                 160

Asp Lys Asp Trp Asn Ile Phe Ser Lys Asn Cys Asn Asn Ser Phe Ala
                165                 170                 175

Glu Cys Ser Ser Gln Asp Val Val Thr Lys Pro Asp Cys Asn Cys Leu
            180                 185                 190

Tyr Pro Lys Ala Ile Pro Ser Ser Asp Pro Ala Ser Val Ser Pro His
        195                 200                 205

Gln Pro Leu Ala Pro Ser Met Ala Pro Val Ala Gly Leu Thr Trp Glu
    210                 215                 220

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

Leu His Thr Val Asp Pro Gly Ser Ala Lys Gln Arg Pro Pro Arg Ser
                245                 250                 255

Thr Cys Gln Ser Phe Glu Pro Pro Glu Thr Pro Val Val Lys Asp Ser
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            260                 265                 270

Thr Ile Gly Gly Ser Pro Gln Pro Arg Pro Ser Val Gly Ala Phe Asn
        275                 280                 285

Pro Gly Met Glu Asp Ile Leu Asp Ser Ala Met Gly Thr Asn Trp Val
    290                 295                 300

Pro Glu Glu Ala Ser Gly Glu Ala Ser Glu Ile Pro Val Pro Gln Gly
305                 310                 315                 320

Thr Glu Leu Ser Pro Ser Arg Pro Gly Gly Gly Ser Met Gln Thr Glu
                325                 330                 335

Pro Ala Arg Pro Ser Asn Phe Leu Ser Ala Ser Ser Pro Leu Pro Ala
            340                 345                 350

Ser Ala Lys Gly Gln Gln Pro Ala Asp Val Thr Gly Thr Ala Leu Pro
        355                 360                 365

Arg Val Gly Pro Val Arg Pro Thr Gly Gln Asp Trp Asn His Thr Pro
    370                 375                 380

Gln Lys Thr Asp His Pro Ser Ala Leu Leu Arg Asp Pro Pro Glu Pro
385                 390                 395                 400

Gly Ser Pro Arg Ile Ser Ser Leu Arg Pro Gln Gly Leu Ser Asn Pro
                405                 410                 415

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

Ser Val Leu Pro Leu Gly Glu Leu Glu Gly Arg Arg Ser Thr Arg Asp
        435                 440                 445

Arg Arg Ser Pro Ala Glu Pro Glu Gly Gly Pro Ala Ser Glu Gly Ala
    450                 455                 460

Ala Arg Pro Leu Pro Arg Phe Asn Ser Val Pro Leu Thr Asp Thr Gly
465                 470                 475                 480

His Glu Arg Gln Ser Glu Gly Ser Ser Ser Pro Gln Leu Gln Glu Ser
                485                 490                 495

Val Phe His Leu Leu Val Pro Ser Val Ile Leu Val Leu Leu Ala Val
            500                 505                 510

Gly Gly Leu Leu Phe Tyr Arg Trp Arg Arg Arg Ser His Gln Glu Pro
        515                 520                 525

Gln Arg Ala Asp Ser Pro Leu Glu Gln Pro Glu Gly Ser Pro Leu Thr
    530                 535                 540

Gln Asp Asp Arg Gln Val Glu Leu Pro Val
545                 550


<210> SEQ ID NO 19
<211> LENGTH: 816
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 19

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

Gly Ala Val Trp Gly Leu Gly Val Asp Pro Ser Leu Gln Ile Asp Val
            20                  25                  30

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

Pro Gly Leu His Asn Gly Thr Lys Ala Phe Leu Phe Gln Asp Thr Pro
    50                  55                  60
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Arg Ser Ile Lys Ala Ser Thr Ala Thr Ala Glu Gln Phe Phe Gln Lys
65                  70                  75                  80

Leu Arg Asn Lys His Glu Phe Thr Ile Leu Val Thr Leu Lys Gln Thr
                85                  90                  95

His Leu Asn Ser Gly Val Ile Leu Ser Ile His His Leu Asp His Arg
            100                 105                 110

Tyr Leu Glu Leu Glu Ser Ser Gly His Arg Asn Glu Val Arg Leu His
        115                 120                 125

Tyr Arg Ser Gly Ser His Arg Pro His Thr Glu Val Phe Pro Tyr Ile
    130                 135                 140

Leu Ala Asp Asp Lys Trp His Lys Leu Ser Leu Ala Ile Ser Ala Ser
145                 150                 155                 160

His Leu Ile Leu His Ile Asp Cys Asn Lys Ile Tyr Glu Arg Val Val
                165                 170                 175

Glu Lys Pro Ser Thr Asp Leu Pro Leu Gly Thr Thr Phe Trp Leu Gly
            180                 185                 190

Gln Arg Asn Asn Ala His Gly Tyr Phe Lys Gly Ile Met Gln Asp Val
        195                 200                 205

Gln Leu Leu Val Met Pro Gln Gly Phe Ile Ala Gln Cys Pro Asp Leu
    210                 215                 220

Asn Arg Thr Cys Pro Thr Cys Asn Asp Phe His Gly Leu Val Gln Lys
225                 230                 235                 240

Ile Met Glu Leu Gln Asp Ile Leu Ala Lys Thr Ser Ala Lys Leu Ser
                245                 250                 255

Arg Ala Glu Gln Arg Met Asn Arg Leu Asp Gln Cys Tyr Cys Glu Arg
            260                 265                 270

Thr Cys Thr Met Lys Gly Thr Thr Tyr Arg Glu Phe Glu Ser Trp Ile
        275                 280                 285

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

Thr Leu Ile Cys Pro Asn Pro Asp Cys Pro Leu Lys Ser Ala Leu Ala
305                 310                 315                 320

Tyr Val Asp Gly Lys Cys Cys Lys Glu Cys Lys Ser Ile Cys Gln Phe
                325                 330                 335

Gln Gly Arg Thr Tyr Phe Glu Gly Glu Arg Asn Thr Val Tyr Ser Ser
            340                 345                 350

Ser Gly Val Cys Val Leu Tyr Glu Cys Lys Asp Gln Thr Met Lys Leu
        355                 360                 365

Val Glu Ser Ser Gly Cys Pro Ala Leu Asp Cys Pro Glu Ser His Gln
    370                 375                 380

Ile Thr Leu Ser His Ser Cys Cys Lys Val Cys Lys Gly Tyr Asp Phe
385                 390                 395                 400

Cys Ser Glu Arg His Asn Cys Met Glu Asn Ser Ile Cys Arg Asn Leu
                405                 410                 415

Asn Asp Arg Ala Val Cys Ser Cys Arg Asp Gly Phe Arg Ala Leu Arg
            420                 425                 430

Glu Asp Asn Ala Tyr Cys Glu Asp Ile Asp Glu Cys Ala Glu Gly Arg
        435                 440                 445

His Tyr Cys Arg Glu Asn Thr Met Cys Val Asn Thr Pro Gly Ser Phe
    450                 455                 460

Met Cys Ile Cys Lys Thr Gly Tyr Ile Arg Ile Asp Asp Tyr Ser Cys
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465                 470                 475                 480

Thr Glu His Asp Glu Cys Ile Thr Asn Gln His Asn Cys Asp Glu Asn
                485                 490                 495

Ala Leu Cys Phe Asn Thr Val Gly Gly His Asn Cys Val Cys Lys Pro
            500                 505                 510

Gly Tyr Thr Gly Asn Gly Thr Thr Cys Lys Ala Phe Cys Lys Asp Gly
        515                 520                 525

Cys Arg Asn Gly Gly Ala Cys Ile Ala Ala Asn Val Cys Ala Cys Pro
    530                 535                 540

Gln Gly Phe Thr Gly Pro Ser Cys Glu Thr Asp Ile Asp Glu Cys Ser
545                 550                 555                 560

Asp Gly Phe Val Gln Cys Asp Ser Arg Ala Asn Cys Ile Asn Leu Pro
                565                 570                 575

Gly Trp Tyr His Cys Glu Cys Arg Asp Gly Tyr His Asp Asn Gly Met
            580                 585                 590

Phe Ser Pro Ser Gly Glu Ser Cys Glu Asp Ile Asp Glu Cys Gly Thr
        595                 600                 605

Gly Arg His Ser Cys Ala Asn Asp Thr Ile Cys Phe Asn Leu Asp Gly
    610                 615                 620

Gly Tyr Asp Cys Arg Cys Pro His Gly Lys Asn Cys Thr Gly Asp Cys
625                 630                 635                 640

Ile His Asp Gly Lys Val Lys His Asn Gly Gln Ile Trp Val Leu Glu
                645                 650                 655

Asn Asp Arg Cys Ser Val Cys Ser Cys Gln Asn Gly Phe Val Met Cys
            660                 665                 670

Arg Arg Met Val Cys Asp Cys Glu Asn Pro Thr Val Asp Leu Phe Cys
        675                 680                 685

Cys Pro Glu Cys Asp Pro Arg Leu Ser Ser Gln Cys Leu His Gln Asn
    690                 695                 700

Gly Glu Thr Leu Tyr Asn Ser Gly Asp Thr Trp Val Gln Asn Cys Gln
705                 710                 715                 720

Gln Cys Arg Cys Leu Gln Gly Glu Val Asp Cys Trp Pro Leu Pro Cys
                725                 730                 735

Pro Asp Val Glu Cys Glu Phe Ser Ile Leu Pro Glu Asn Glu Cys Cys
            740                 745                 750

Pro Arg Cys Val Thr Asp Pro Cys Gln Ala Asp Thr Ile Arg Asn Asp
        755                 760                 765

Ile Thr Lys Thr Cys Leu Asp Glu Met Asn Val Val Arg Phe Thr Gly
    770                 775                 780

Ser Ser Trp Ile Lys His Gly Thr Glu Cys Thr Leu Cys Gln Cys Lys
785                 790                 795                 800

Asn Gly His Ile Cys Cys Ser Val Asp Pro Gln Cys Leu Gln Glu Leu
                805                 810                 815


<210> SEQ ID NO 20
<211> LENGTH: 172
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 20

Met Val Gly Pro Ala Pro Arg Arg Arg Leu Arg Pro Leu Ala Ala Leu
1               5                   10                  15
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Ala Leu Val Leu Ala Leu Ala Pro Gly Leu Pro Thr Ala Arg Ala Gly
            20                  25                  30

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

Glu Glu Glu Leu Ala Arg Tyr Gly Gly Glu Glu Glu Asp Gln Pro Ile
    50                  55                  60

Tyr Leu Ala Val Lys Gly Val Val Phe Asp Val Thr Ser Gly Lys Glu
65                  70                  75                  80

Phe Tyr Gly Arg Gly Ala Pro Tyr Asn Ala Leu Thr Gly Lys Asp Ser
                85                  90                  95

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

Asp Thr Thr Gly Leu Thr Ala Lys Glu Leu Glu Ala Leu Asp Glu Val
        115                 120                 125

Phe Thr Lys Val Tyr Lys Ala Lys Tyr Pro Ile Val Gly Tyr Thr Ala
    130                 135                 140

Arg Arg Ile Leu Asn Glu Asp Gly Ser Pro Asn Leu Asp Phe Lys Pro
145                 150                 155                 160

Glu Asp Gln Pro His Phe Asp Ile Lys Asp Glu Phe
                165                 170


<210> SEQ ID NO 21
<211> LENGTH: 508
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 21

Met Leu Arg Arg Ala Leu Leu Cys Leu Ala Val Ala Ala Leu Val Arg
1               5                   10                  15

Ala Asp Ala Pro Glu Glu Glu Asp His Val Leu Val Leu Arg Lys Ser
            20                  25                  30

Asn Phe Ala Glu Ala Leu Ala Ala His Lys Tyr Leu Leu Val Glu Phe
        35                  40                  45

Tyr Ala Pro Trp Cys Gly His Cys Lys Ala Leu Ala Pro Glu Tyr Ala
    50                  55                  60

Lys Ala Ala Gly Lys Leu Lys Ala Glu Gly Ser Glu Ile Arg Leu Ala
65                  70                  75                  80

Lys Val Asp Ala Thr Glu Glu Ser Asp Leu Ala Gln Gln Tyr Gly Val
                85                  90                  95

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

Pro Lys Glu Tyr Thr Ala Gly Arg Glu Ala Asp Asp Ile Val Asn Trp
        115                 120                 125

Leu Lys Lys Arg Thr Gly Pro Ala Ala Thr Thr Leu Pro Asp Gly Ala
    130                 135                 140

Ala Ala Glu Ser Leu Val Glu Ser Ser Glu Val Ala Val Ile Gly Phe
145                 150                 155                 160

Phe Lys Asp Val Glu Ser Asp Ser Ala Lys Gln Phe Leu Gln Ala Ala
                165                 170                 175

Glu Ala Ile Asp Asp Ile Pro Phe Gly Ile Thr Ser Asn Ser Asp Val
            180                 185                 190

Phe Ser Lys Tyr Gln Leu Asp Lys Asp Gly Val Val Leu Phe Lys Lys
        195                 200                 205
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Phe Asp Glu Gly Arg Asn Asn Phe Glu Gly Glu Val Thr Lys Glu Asn
    210                 215                 220

Leu Leu Asp Phe Ile Lys His Asn Gln Leu Pro Leu Val Ile Glu Phe
225                 230                 235                 240

Thr Glu Gln Thr Ala Pro Lys Ile Phe Gly Gly Glu Ile Lys Thr His
                245                 250                 255

Ile Leu Leu Phe Leu Pro Lys Ser Val Ser Asp Tyr Asp Gly Lys Leu
            260                 265                 270

Ser Asn Phe Lys Thr Ala Ala Glu Ser Phe Lys Gly Lys Ile Leu Phe
        275                 280                 285

Ile Phe Ile Asp Ser Asp His Thr Asp Asn Gln Arg Ile Leu Glu Phe
    290                 295                 300

Phe Gly Leu Lys Lys Glu Glu Cys Pro Ala Val Arg Leu Ile Thr Leu
305                 310                 315                 320

Glu Glu Glu Met Thr Lys Tyr Lys Pro Glu Ser Glu Glu Leu Thr Ala
                325                 330                 335

Glu Arg Ile Thr Glu Phe Cys His Arg Phe Leu Glu Gly Lys Ile Lys
            340                 345                 350

Pro His Leu Met Ser Gln Glu Leu Pro Glu Asp Trp Asp Lys Gln Pro
        355                 360                 365

Val Lys Val Leu Val Gly Lys Asn Phe Glu Asp Val Ala Phe Asp Glu
    370                 375                 380

Lys Lys Asn Val Phe Val Glu Phe Tyr Ala Pro Trp Cys Gly His Cys
385                 390                 395                 400

Lys Gln Leu Ala Pro Ile Trp Asp Lys Leu Gly Glu Thr Tyr Lys Asp
                405                 410                 415

His Glu Asn Ile Val Ile Ala Lys Met Asp Ser Thr Ala Asn Glu Val
            420                 425                 430

Glu Ala Val Lys Val His Ser Phe Pro Thr Leu Lys Phe Phe Pro Ala
        435                 440                 445

Ser Ala Asp Arg Thr Val Ile Asp Tyr Asn Gly Glu Arg Thr Leu Asp
    450                 455                 460

Gly Phe Lys Lys Phe Leu Glu Ser Gly Gly Gln Asp Gly Ala Gly Asp
465                 470                 475                 480

Asp Asp Asp Leu Glu Asp Leu Glu Glu Ala Glu Glu Pro Asp Met Glu
                485                 490                 495

Glu Asp Asp Asp Gln Lys Ala Val Lys Asp Glu Leu
            500                 505


<210> SEQ ID NO 22
<211> LENGTH: 156
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 22

Met Ala Leu Glu Lys Ser Leu Val Arg Leu Leu Leu Leu Val Leu Ile
1               5                   10                  15

Leu Leu Val Leu Gly Trp Val Gln Pro Ser Leu Gly Lys Glu Ser Arg
            20                  25                  30

Ala Lys Lys Phe Gln Arg Gln His Met Asp Ser Asp Ser Ser Pro Ser
        35                  40                  45

Ser Ser Ser Thr Tyr Cys Asn Gln Met Met Arg Arg Arg Asn Met Thr
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    50                  55                  60

Gln Gly Arg Cys Lys Pro Val Asn Thr Phe Val His Glu Pro Leu Val
65                  70                  75                  80

Asp Val Gln Asn Val Cys Phe Gln Glu Lys Val Thr Cys Lys Asn Gly
                85                  90                  95

Gln Gly Asn Cys Tyr Lys Ser Asn Ser Ser Met His Ile Thr Asp Cys
            100                 105                 110

Arg Leu Thr Asn Gly Ser Arg Tyr Pro Asn Cys Ala Tyr Arg Thr Ser
        115                 120                 125

Pro Lys Glu Arg His Ile Ile Val Ala Cys Glu Gly Ser Pro Tyr Val
    130                 135                 140

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


<210> SEQ ID NO 23
<211> LENGTH: 383
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 23

Met Thr Ala Thr Glu Ala Leu Leu Arg Val Leu Leu Leu Leu Leu Ala
1               5                   10                  15

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

Gln Asn Gly Phe Cys Glu Asp Asp Asn Val Cys Arg Cys Gln Pro Gly
        35                  40                  45

Trp Gln Gly Pro Leu Cys Asp Gln Cys Val Thr Ser Pro Gly Cys Leu
    50                  55                  60

His Gly Leu Cys Gly Glu Pro Gly Gln Cys Ile Cys Thr Asp Gly Trp
65                  70                  75                  80

Asp Gly Glu Leu Cys Asp Arg Asp Val Arg Ala Cys Ser Ser Ala Pro
                85                  90                  95

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

Cys Ser Cys Ala Pro Gly Tyr Ser Gly Lys Asp Cys Gln Lys Lys Asp
        115                 120                 125

Gly Pro Cys Val Ile Asn Gly Ser Pro Cys Gln His Gly Gly Thr Cys
    130                 135                 140

Val Asp Asp Glu Gly Arg Ala Ser His Ala Ser Cys Leu Cys Pro Pro
145                 150                 155                 160

Gly Phe Ser Gly Asn Phe Cys Glu Ile Val Ala Asn Ser Cys Thr Pro
                165                 170                 175

Asn Pro Cys Glu Asn Asp Gly Val Cys Thr Asp Ile Gly Gly Asp Phe
            180                 185                 190

Arg Cys Arg Cys Pro Ala Gly Phe Ile Asp Lys Thr Cys Ser Arg Pro
        195                 200                 205

Val Thr Asn Cys Ala Ser Ser Pro Cys Gln Asn Gly Gly Thr Cys Leu
    210                 215                 220

Gln His Thr Gln Val Ser Tyr Glu Cys Leu Cys Lys Pro Glu Phe Thr
225                 230                 235                 240

Gly Leu Thr Cys Val Lys Lys Arg Ala Leu Ser Pro Gln Gln Val Thr
                245                 250                 255
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```
Arg Leu Pro Ser Gly Tyr Gly Leu Ala Tyr Arg Leu Thr Pro Gly Val
            260                 265                 270

His Glu Leu Pro Val Gln Gln Pro Glu His Arg Ile Leu Lys Val Ser
        275                 280                 285

Met Lys Glu Leu Asn Lys Lys Thr Pro Leu Leu Thr Glu Gly Gln Ala
    290                 295                 300

Ile Cys Phe Thr Ile Leu Gly Val Leu Thr Ser Leu Val Val Leu Gly
305                 310                 315                 320

Thr Val Gly Ile Val Phe Leu Asn Lys Cys Glu Thr Trp Val Ser Asn
                325                 330                 335

Leu Arg Tyr Asn His Met Leu Arg Lys Lys Lys Asn Leu Leu Leu Gln
            340                 345                 350

Tyr Asn Ser Gly Glu Asp Leu Ala Val Asn Ile Ile Phe Pro Glu Lys
        355                 360                 365

Ile Asp Met Thr Thr Phe Ser Lys Glu Ala Gly Asp Glu Glu Ile
    370                 375                 380


<210> SEQ ID NO 24
<211> LENGTH: 457
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 24

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

Thr Ala Leu Pro Val Asn Ser Pro Met Asn Lys Gly Asp Thr Glu Val
            20                  25                  30

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

Pro Met Pro Val Ser Gln Glu Cys Phe Glu Thr Leu Arg Gly Asp Glu
    50                  55                  60

Arg Ile Leu Ser Ile Leu Arg His Gln Asn Leu Leu Lys Glu Leu Gln
65                  70                  75                  80

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

His Ser Gly Phe Glu Asp Glu Leu Ser Glu Val Leu Glu Asn Gln Ser
            100                 105                 110

Ser Gln Ala Glu Leu Lys Glu Ala Val Glu Glu Pro Ser Ser Lys Asp
        115                 120                 125

Val Met Glu Lys Arg Glu Asp Ser Lys Glu Ala Glu Lys Ser Gly Glu
    130                 135                 140

Ala Thr Asp Gly Ala Arg Pro Gln Ala Leu Pro Glu Pro Met Gln Glu
145                 150                 155                 160

Ser Lys Ala Glu Gly Asn Asn Gln Ala Pro Gly Glu Glu Glu Glu Glu
                165                 170                 175

Glu Glu Glu Ala Thr Asn Thr His Pro Pro Ala Ser Leu Pro Ser Gln
            180                 185                 190

Lys Tyr Pro Gly Pro Gln Ala Glu Gly Asp Ser Glu Gly Leu Ser Gln
        195                 200                 205

Gly Leu Val Asp Arg Glu Lys Gly Leu Ser Ala Glu Pro Gly Trp Gln
    210                 215                 220

Ala Lys Arg Glu Glu Glu Glu Glu Glu Glu Glu Glu Ala Glu Ala Gly
225                 230                 235                 240
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Glu Glu Ala Val Pro Glu Glu Glu Gly Pro Thr Val Val Leu Asn Pro
                245                 250                 255

His Pro Ser Leu Gly Tyr Lys Glu Ile Arg Lys Gly Glu Ser Arg Ser
            260                 265                 270

Glu Ala Leu Ala Val Asp Gly Ala Gly Lys Pro Gly Ala Glu Glu Ala
        275                 280                 285

Gln Asp Pro Glu Gly Lys Gly Glu Gln Glu His Ser Gln Gln Lys Glu
    290                 295                 300

Glu Glu Glu Glu Met Ala Val Val Pro Gln Gly Leu Phe Arg Gly Gly
305                 310                 315                 320

Lys Ser Gly Glu Leu Glu Gln Glu Glu Glu Arg Leu Ser Lys Glu Trp
                325                 330                 335

Glu Asp Ser Lys Arg Trp Ser Lys Met Asp Gln Leu Ala Lys Glu Leu
            340                 345                 350

Thr Ala Glu Lys Arg Leu Glu Gly Gln Glu Glu Glu Glu Asp Asn Arg
        355                 360                 365

Asp Ser Ser Met Lys Leu Ser Phe Arg Ala Arg Ala Tyr Gly Phe Arg
    370                 375                 380

Gly Pro Gly Pro Gln Leu Arg Arg Gly Trp Arg Pro Ser Ser Arg Glu
385                 390                 395                 400

Asp Ser Leu Glu Ala Gly Leu Pro Leu Gln Val Arg Gly Tyr Pro Glu
                405                 410                 415

Glu Lys Lys Glu Glu Glu Gly Ser Ala Asn Arg Arg Pro Glu Asp Gln
            420                 425                 430

Glu Leu Glu Ser Leu Ser Ala Ile Glu Ala Glu Leu Glu Lys Val Ala
        435                 440                 445

His Gln Leu Gln Ala Leu Arg Arg Gly
    450                 455


<210> SEQ ID NO 25
<211> LENGTH: 421
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 25

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

Lys Val His Cys Gln Tyr Glu Thr Tyr Gln Trp Asp Glu Asp Tyr Asp
            20                  25                  30

Gln Glu Pro Asp Asp Asp Tyr Gln Thr Gly Phe Pro Phe Arg Gln Asn
        35                  40                  45

Val Asp Tyr Gly Val Pro Phe His Gln Tyr Thr Leu Gly Cys Val Ser
    50                  55                  60

Glu Cys Phe Cys Pro Thr Asn Phe Pro Ser Ser Met Tyr Cys Asp Asn
65                  70                  75                  80

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

Tyr Leu Gln Phe Asn Glu Ile Glu Ala Val Thr Ala Asn Ser Phe Ile
            100                 105                 110

Asn Ala Thr His Leu Lys Glu Ile Asn Leu Ser His Asn Lys Ile Lys
        115                 120                 125

Ser Gln Lys Ile Asp Tyr Gly Val Phe Ala Lys Leu Pro Asn Leu Leu
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    130                 135                 140

Gln Leu His Leu Glu His Asn Asn Leu Glu Glu Phe Pro Phe Pro Leu
145                 150                 155                 160

Pro Lys Ser Leu Glu Arg Leu Leu Leu Gly Tyr Asn Glu Ile Ser Lys
                165                 170                 175

Leu Gln Thr Asn Ala Met Asp Gly Leu Val Asn Leu Thr Met Leu Asp
            180                 185                 190

Leu Cys Tyr Asn Tyr Leu His Asp Ser Leu Leu Lys Asp Lys Ile Phe
        195                 200                 205

Ala Lys Met Glu Lys Leu Met Gln Leu Asn Leu Cys Ser Asn Arg Leu
    210                 215                 220

Glu Ser Met Pro Pro Gly Leu Pro Ser Ser Leu Met Tyr Leu Ser Leu
225                 230                 235                 240

Glu Asn Asn Ser Ile Ser Ser Ile Pro Glu Lys Tyr Phe Asp Lys Leu
                245                 250                 255

Pro Lys Leu His Thr Leu Arg Met Ser His Asn Lys Leu Gln Asp Ile
            260                 265                 270

Pro Tyr Asn Ile Phe Asn Leu Pro Asn Ile Val Glu Leu Ser Val Gly
        275                 280                 285

His Asn Lys Leu Lys Gln Ala Phe Tyr Ile Pro Arg Asn Leu Glu His
    290                 295                 300

Leu Tyr Leu Gln Asn Asn Glu Ile Glu Lys Met Asn Leu Thr Val Met
305                 310                 315                 320

Cys Pro Ser Ile Asp Pro Leu His Tyr His His Leu Thr Tyr Ile Arg
                325                 330                 335

Val Asp Gln Asn Lys Leu Lys Glu Pro Ile Ser Ser Tyr Ile Phe Phe
            340                 345                 350

Cys Phe Pro His Ile His Thr Ile Tyr Tyr Gly Glu Gln Arg Ser Thr
        355                 360                 365

Asn Gly Gln Thr Ile Gln Leu Lys Thr Gln Val Phe Arg Arg Phe Pro
    370                 375                 380

Asp Asp Asp Asp Glu Ser Glu Asp His Asp Asp Pro Asp Asn Ala His
385                 390                 395                 400

Glu Ser Pro Glu Gln Glu Gly Ala Glu Gly His Phe Asp Leu His Tyr
                405                 410                 415

Tyr Glu Asn Gln Glu
            420


<210> SEQ ID NO 26
<211> LENGTH: 1366
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 26

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

Leu Cys Leu Ala Thr Cys Gln Ser Leu Gln Glu Glu Thr Val Arg Lys
            20                  25                  30

Gly Pro Ala Gly Asp Arg Gly Pro Arg Gly Glu Arg Gly Pro Pro Gly
        35                  40                  45

Pro Pro Gly Arg Asp Gly Glu Asp Gly Pro Thr Gly Pro Pro Gly Pro
    50                  55                  60
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Pro Gly Pro Pro Gly Pro Pro Gly Leu Gly Gly Asn Phe Ala Ala Gln
65                  70                  75                  80

Tyr Asp Gly Lys Gly Val Gly Leu Gly Pro Gly Pro Met Gly Leu Met
                85                  90                  95

Gly Pro Arg Gly Pro Pro Gly Ala Ala Gly Ala Pro Gly Pro Gln Gly
            100                 105                 110

Phe Gln Gly Pro Ala Gly Glu Pro Gly Glu Pro Gly Gln Thr Gly Pro
        115                 120                 125

Ala Gly Ala Arg Gly Pro Ala Gly Pro Pro Gly Lys Ala Gly Glu Asp
    130                 135                 140

Gly His Pro Gly Lys Pro Gly Arg Pro Gly Glu Arg Gly Val Val Gly
145                 150                 155                 160

Pro Gln Gly Ala Arg Gly Phe Pro Gly Thr Pro Gly Leu Pro Gly Phe
                165                 170                 175

Lys Gly Ile Arg Gly His Asn Gly Leu Asp Gly Leu Lys Gly Gln Pro
            180                 185                 190

Gly Ala Pro Gly Val Lys Gly Glu Pro Gly Ala Pro Gly Glu Asn Gly
        195                 200                 205

Thr Pro Gly Gln Thr Gly Ala Arg Gly Leu Pro Gly Glu Arg Gly Arg
    210                 215                 220

Val Gly Ala Pro Gly Pro Ala Gly Ala Arg Gly Ser Asp Gly Ser Val
225                 230                 235                 240

Gly Pro Val Gly Pro Ala Gly Pro Ile Gly Ser Ala Gly Pro Pro Gly
                245                 250                 255

Phe Pro Gly Ala Pro Gly Pro Lys Gly Glu Ile Gly Ala Val Gly Asn
            260                 265                 270

Ala Gly Pro Ala Gly Pro Ala Gly Pro Arg Gly Glu Val Gly Leu Pro
        275                 280                 285

Gly Leu Ser Gly Pro Val Gly Pro Pro Gly Asn Pro Gly Ala Asn Gly
    290                 295                 300

Leu Thr Gly Ala Lys Gly Ala Ala Gly Leu Pro Gly Val Ala Gly Ala
305                 310                 315                 320

Pro Gly Leu Pro Gly Pro Arg Gly Ile Pro Gly Pro Val Gly Ala Ala
                325                 330                 335

Gly Ala Thr Gly Ala Arg Gly Leu Val Gly Glu Pro Gly Pro Ala Gly
            340                 345                 350

Ser Lys Gly Glu Ser Gly Asn Lys Gly Glu Pro Gly Ser Ala Gly Pro
        355                 360                 365

Gln Gly Pro Pro Gly Pro Ser Gly Glu Glu Gly Lys Arg Gly Pro Asn
    370                 375                 380

Gly Glu Ala Gly Ser Ala Gly Pro Pro Gly Pro Pro Gly Leu Arg Gly
385                 390                 395                 400

Ser Pro Gly Ser Arg Gly Leu Pro Gly Ala Asp Gly Arg Ala Gly Val
                405                 410                 415

Met Gly Pro Pro Gly Ser Arg Gly Ala Ser Gly Pro Ala Gly Val Arg
            420                 425                 430

Gly Pro Asn Gly Asp Ala Gly Arg Pro Gly Glu Pro Gly Leu Met Gly
        435                 440                 445

Pro Arg Gly Leu Pro Gly Ser Pro Gly Asn Ile Gly Pro Ala Gly Lys
    450                 455                 460

Glu Gly Pro Val Gly Leu Pro Gly Ile Asp Gly Arg Pro Gly Pro Ile
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465                 470                 475                 480

Gly Pro Ala Gly Ala Arg Gly Glu Pro Gly Asn Ile Gly Phe Pro Gly
                485                 490                 495

Pro Lys Gly Pro Thr Gly Asp Pro Gly Lys Asn Gly Asp Lys Gly His
            500                 505                 510

Ala Gly Leu Ala Gly Ala Arg Gly Ala Pro Gly Pro Asp Gly Asn Asn
        515                 520                 525

Gly Ala Gln Gly Pro Pro Gly Pro Gln Gly Val Gln Gly Gly Lys Gly
    530                 535                 540

Glu Gln Gly Pro Ala Gly Pro Pro Gly Phe Gln Gly Leu Pro Gly Pro
545                 550                 555                 560

Ser Gly Pro Ala Gly Glu Val Gly Lys Pro Gly Glu Arg Gly Leu His
                565                 570                 575

Gly Glu Phe Gly Leu Pro Gly Pro Ala Gly Pro Arg Gly Glu Arg Gly
            580                 585                 590

Pro Pro Gly Glu Ser Gly Ala Ala Gly Pro Thr Gly Pro Ile Gly Ser
        595                 600                 605

Arg Gly Pro Ser Gly Pro Pro Gly Pro Asp Gly Asn Lys Gly Glu Pro
    610                 615                 620

Gly Val Val Gly Ala Val Gly Thr Ala Gly Pro Ser Gly Pro Ser Gly
625                 630                 635                 640

Leu Pro Gly Glu Arg Gly Ala Ala Gly Ile Pro Gly Gly Lys Gly Glu
                645                 650                 655

Lys Gly Glu Pro Gly Leu Arg Gly Glu Ile Gly Asn Pro Gly Arg Asp
            660                 665                 670

Gly Ala Arg Gly Ala Pro Gly Ala Val Gly Ala Pro Gly Pro Ala Gly
        675                 680                 685

Ala Thr Gly Asp Arg Gly Glu Ala Gly Ala Ala Gly Pro Ala Gly Pro
    690                 695                 700

Ala Gly Pro Arg Gly Ser Pro Gly Glu Arg Gly Glu Val Gly Pro Ala
705                 710                 715                 720

Gly Pro Asn Gly Phe Ala Gly Pro Ala Gly Ala Ala Gly Gln Pro Gly
                725                 730                 735

Ala Lys Gly Glu Arg Gly Ala Lys Gly Pro Lys Gly Glu Asn Gly Val
            740                 745                 750

Val Gly Pro Thr Gly Pro Val Gly Ala Ala Gly Pro Ala Gly Pro Asn
        755                 760                 765

Gly Pro Pro Gly Pro Ala Gly Ser Arg Gly Asp Gly Gly Pro Pro Gly
    770                 775                 780

Met Thr Gly Phe Pro Gly Ala Ala Gly Arg Thr Gly Pro Pro Gly Pro
785                 790                 795                 800

Ser Gly Ile Ser Gly Pro Pro Gly Pro Pro Gly Pro Ala Gly Lys Glu
                805                 810                 815

Gly Leu Arg Gly Pro Arg Gly Asp Gln Gly Pro Val Gly Arg Thr Gly
            820                 825                 830

Glu Val Gly Ala Val Gly Pro Pro Gly Phe Ala Gly Glu Lys Gly Pro
        835                 840                 845

Ser Gly Glu Ala Gly Thr Ala Gly Pro Pro Gly Thr Pro Gly Pro Gln
    850                 855                 860

Gly Leu Leu Gly Ala Pro Gly Ile Leu Gly Leu Pro Gly Ser Arg Gly
865                 870                 875                 880
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Glu Arg Gly Leu Pro Gly Val Ala Gly Ala Val Gly Glu Pro Gly Pro
               885                 890                 895

Leu Gly Ile Ala Gly Pro Pro Gly Ala Arg Gly Pro Pro Gly Ala Val
           900                 905                 910

Gly Ser Pro Gly Val Asn Gly Ala Pro Gly Glu Ala Gly Arg Asp Gly
       915                 920                 925

Asn Pro Gly Asn Asp Gly Pro Pro Gly Arg Asp Gly Gln Pro Gly His
   930                 935                 940

Lys Gly Glu Arg Gly Tyr Pro Gly Asn Ile Gly Pro Val Gly Ala Ala
945                 950                 955                 960

Gly Ala Pro Gly Pro His Gly Pro Val Gly Pro Ala Gly Lys His Gly
               965                 970                 975

Asn Arg Gly Glu Thr Gly Pro Ser Gly Pro Val Gly Pro Ala Gly Ala
           980                 985                 990

Val Gly Pro Arg Gly Pro Ser Gly  Pro Gln Gly Ile Arg  Gly Asp Lys
       995                 1000                1005

Gly Glu  Pro Gly Glu Lys Gly  Pro Arg Gly Leu Pro  Gly Leu Lys
   1010                1015                1020

Gly His  Asn Gly Leu Gln Gly  Leu Pro Gly Ile Ala  Gly His His
   1025                1030                1035

Gly Asp  Gln Gly Ala Pro Gly  Ser Val Gly Pro Ala  Gly Pro Arg
   1040                1045                1050

Gly Pro  Ala Gly Pro Ser Gly  Pro Ala Gly Lys Asp  Gly Arg Thr
   1055                1060                1065

Gly His  Pro Gly Thr Val Gly  Pro Ala Gly Ile Arg  Gly Pro Gln
   1070                1075                1080

Gly His  Gln Gly Pro Ala Gly  Pro Pro Gly Pro Pro  Gly Pro Pro
   1085                1090                1095

Gly Pro  Pro Gly Val Ser Gly  Gly Gly Tyr Asp Phe  Gly Tyr Asp
   1100                1105                1110

Gly Asp  Phe Tyr Arg Ala Asp  Gln Pro Arg Ser Ala  Pro Ser Leu
   1115                1120                1125

Arg Pro  Lys Asp Tyr Glu Val  Asp Ala Thr Leu Lys  Ser Leu Asn
   1130                1135                1140

Asn Gln  Ile Glu Thr Leu Leu  Thr Pro Glu Gly Ser  Arg Lys Asn
   1145                1150                1155

Pro Ala  Arg Thr Cys Arg Asp  Leu Arg Leu Ser His  Pro Glu Trp
   1160                1165                1170

Ser Ser  Gly Tyr Tyr Trp Ile  Asp Pro Asn Gln Gly  Cys Thr Met
   1175                1180                1185

Asp Ala  Ile Lys Val Tyr Cys  Asp Phe Ser Thr Gly  Glu Thr Cys
   1190                1195                1200

Ile Arg  Ala Gln Pro Glu Asn  Ile Pro Ala Lys Asn  Trp Tyr Arg
   1205                1210                1215

Ser Ser  Lys Asp Lys Lys His  Val Trp Leu Gly Glu  Thr Ile Asn
   1220                1225                1230

Ala Gly  Ser Gln Phe Glu Tyr  Asn Val Glu Gly Val  Thr Ser Lys
   1235                1240                1245

Glu Met  Ala Thr Gln Leu Ala  Phe Met Arg Leu Leu  Ala Asn Tyr
   1250                1255                1260
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Ala Ser  Gln Asn Ile Thr Tyr  His Cys Lys Asn Ser  Ile Ala Tyr
    1265                1270                1275

Met Asp  Glu Glu Thr Gly Asn  Leu Lys Lys Ala Val  Ile Leu Gln
    1280                1285                1290

Gly Ser  Asn Asp Val Glu Leu  Val Ala Glu Gly Asn  Ser Arg Phe
    1295                1300                1305

Thr Tyr  Thr Val Leu Val Asp  Gly Cys Ser Lys Lys  Thr Asn Glu
    1310                1315                1320

Trp Gly  Lys Thr Ile Ile Glu  Tyr Lys Thr Asn Lys  Pro Ser Arg
    1325                1330                1335

Leu Pro  Phe Leu Asp Ile Ala  Pro Leu Asp Ile Gly  Gly Ala Asp
    1340                1345                1350

Gln Glu  Phe Phe Val Asp Ile  Gly Pro Val Cys Phe  Lys
    1355                1360                1365


<210> SEQ ID NO 27
<211> LENGTH: 4544
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 27

Met Leu Thr Pro Pro Leu Leu Leu Leu Leu Pro Leu Leu Ser Ala Leu
1               5                  10                  15

Val Ala Ala Ala Ile Asp Ala Pro Lys Thr Cys Ser Pro Lys Gln Phe
            20                  25                  30

Ala Cys Arg Asp Gln Ile Thr Cys Ile Ser Lys Gly Trp Arg Cys Asp
        35                  40                  45

Gly Glu Arg Asp Cys Pro Asp Gly Ser Asp Glu Ala Pro Glu Ile Cys
    50                  55                  60

Pro Gln Ser Lys Ala Gln Arg Cys Gln Pro Asn Glu His Asn Cys Leu
65                  70                  75                  80

Gly Thr Glu Leu Cys Val Pro Met Ser Arg Leu Cys Asn Gly Val Gln
                85                  90                  95

Asp Cys Met Asp Gly Ser Asp Glu Gly Pro His Cys Arg Glu Leu Gln
            100                 105                 110

Gly Asn Cys Ser Arg Leu Gly Cys Gln His His Cys Val Pro Thr Leu
        115                 120                 125

Asp Gly Pro Thr Cys Tyr Cys Asn Ser Ser Phe Gln Leu Gln Ala Asp
    130                 135                 140

Gly Lys Thr Cys Lys Asp Phe Asp Glu Cys Ser Val Tyr Gly Thr Cys
145                 150                 155                 160

Ser Gln Leu Cys Thr Asn Thr Asp Gly Ser Phe Ile Cys Gly Cys Val
                165                 170                 175

Glu Gly Tyr Leu Leu Gln Pro Asp Asn Arg Ser Cys Lys Ala Lys Asn
            180                 185                 190

Glu Pro Val Asp Arg Pro Pro Val Leu Leu Ile Ala Asn Ser Gln Asn
        195                 200                 205

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

Thr Ser Thr Arg Gln Thr Thr Ala Met Asp Phe Ser Tyr Ala Asn Glu
225                 230                 235                 240

Thr Val Cys Trp Val His Val Gly Asp Ser Ala Ala Gln Thr Gln Leu
                245                 250                 255
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Lys Cys Ala Arg Met Pro Gly Leu Lys Gly Phe Val Asp Glu His Thr
            260                 265                 270

Ile Asn Ile Ser Leu Ser Leu His His Val Glu Gln Met Ala Ile Asp
        275                 280                 285

Trp Leu Thr Gly Asn Phe Tyr Phe Val Asp Asp Ile Asp Asp Arg Ile
    290                 295                 300

Phe Val Cys Asn Arg Asn Gly Asp Thr Cys Val Thr Leu Leu Asp Leu
305                 310                 315                 320

Glu Leu Tyr Asn Pro Lys Gly Ile Ala Leu Asp Pro Ala Met Gly Lys
                325                 330                 335

Val Phe Phe Thr Asp Tyr Gly Gln Ile Pro Lys Val Glu Arg Cys Asp
            340                 345                 350

Met Asp Gly Gln Asn Arg Thr Lys Leu Val Asp Ser Lys Ile Val Phe
        355                 360                 365

Pro His Gly Ile Thr Leu Asp Leu Val Ser Arg Leu Val Tyr Trp Ala
    370                 375                 380

Asp Ala Tyr Leu Asp Tyr Ile Glu Val Val Asp Tyr Glu Gly Lys Gly
385                 390                 395                 400

Arg Gln Thr Ile Ile Gln Gly Ile Leu Ile Glu His Leu Tyr Gly Leu
                405                 410                 415

Thr Val Phe Glu Asn Tyr Leu Tyr Ala Thr Asn Ser Asp Asn Ala Asn
            420                 425                 430

Ala Gln Gln Lys Thr Ser Val Ile Arg Val Asn Arg Phe Asn Ser Thr
        435                 440                 445

Glu Tyr Gln Val Val Thr Arg Val Asp Lys Gly Gly Ala Leu His Ile
    450                 455                 460

Tyr His Gln Arg Arg Gln Pro Arg Val Arg Ser His Ala Cys Glu Asn
465                 470                 475                 480

Asp Gln Tyr Gly Lys Pro Gly Gly Cys Ser Asp Ile Cys Leu Leu Ala
                485                 490                 495

Asn Ser His Lys Ala Arg Thr Cys Arg Cys Arg Ser Gly Phe Ser Leu
            500                 505                 510

Gly Ser Asp Gly Lys Ser Cys Lys Lys Pro Glu His Glu Leu Phe Leu
        515                 520                 525

Val Tyr Gly Lys Gly Arg Pro Gly Ile Ile Arg Gly Met Asp Met Gly
    530                 535                 540

Ala Lys Val Pro Asp Glu His Met Ile Pro Ile Glu Asn Leu Met Asn
545                 550                 555                 560

Pro Arg Ala Leu Asp Phe His Ala Glu Thr Gly Phe Ile Tyr Phe Ala
                565                 570                 575

Asp Thr Thr Ser Tyr Leu Ile Gly Arg Gln Lys Ile Asp Gly Thr Glu
            580                 585                 590

Arg Glu Thr Ile Leu Lys Asp Gly Ile His Asn Val Glu Gly Val Ala
        595                 600                 605

Val Asp Trp Met Gly Asp Asn Leu Tyr Trp Thr Asp Asp Gly Pro Lys
    610                 615                 620

Lys Thr Ile Ser Val Ala Arg Leu Glu Lys Ala Ala Gln Thr Arg Lys
625                 630                 635                 640

Thr Leu Ile Glu Gly Lys Met Thr His Pro Arg Ala Ile Val Val Asp
                645                 650                 655
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Pro Leu Asn Gly Trp Met Tyr Trp Thr Asp Trp Glu Glu Asp Pro Lys
            660                 665                 670

Asp Ser Arg Arg Gly Arg Leu Glu Arg Ala Trp Met Asp Gly Ser His
        675                 680                 685

Arg Asp Ile Phe Val Thr Ser Lys Thr Val Leu Trp Pro Asn Gly Leu
    690                 695                 700

Ser Leu Asp Ile Pro Ala Gly Arg Leu Tyr Trp Val Asp Ala Phe Tyr
705                 710                 715                 720

Asp Arg Ile Glu Thr Ile Leu Leu Asn Gly Thr Asp Arg Lys Ile Val
                725                 730                 735

Tyr Glu Gly Pro Glu Leu Asn His Ala Phe Gly Leu Cys His His Gly
            740                 745                 750

Asn Tyr Leu Phe Trp Thr Glu Tyr Arg Ser Gly Ser Val Tyr Arg Leu
        755                 760                 765

Glu Arg Gly Val Gly Gly Ala Pro Pro Thr Val Thr Leu Leu Arg Ser
    770                 775                 780

Glu Arg Pro Pro Ile Phe Glu Ile Arg Met Tyr Asp Ala Gln Gln Gln
785                 790                 795                 800

Gln Val Gly Thr Asn Lys Cys Arg Val Asn Asn Gly Gly Cys Ser Ser
                805                 810                 815

Leu Cys Leu Ala Thr Pro Gly Ser Arg Gln Cys Ala Cys Ala Glu Asp
            820                 825                 830

Gln Val Leu Asp Ala Asp Gly Val Thr Cys Leu Ala Asn Pro Ser Tyr
        835                 840                 845

Val Pro Pro Pro Gln Cys Gln Pro Gly Glu Phe Ala Cys Ala Asn Ser
    850                 855                 860

Arg Cys Ile Gln Glu Arg Trp Lys Cys Asp Gly Asp Asn Asp Cys Leu
865                 870                 875                 880

Asp Asn Ser Asp Glu Ala Pro Ala Leu Cys His Gln His Thr Cys Pro
                885                 890                 895

Ser Asp Arg Phe Lys Cys Glu Asn Asn Arg Cys Ile Pro Asn Arg Trp
            900                 905                 910

Leu Cys Asp Gly Asp Asn Asp Cys Gly Asn Ser Glu Asp Glu Ser Asn
        915                 920                 925

Ala Thr Cys Ser Ala Arg Thr Cys Pro Pro Asn Gln Phe Ser Cys Ala
    930                 935                 940

Ser Gly Arg Cys Ile Pro Ile Ser Trp Thr Cys Asp Leu Asp Asp Asp
945                 950                 955                 960

Cys Gly Asp Arg Ser Asp Glu Ser Ala Ser Cys Ala Tyr Pro Thr Cys
                965                 970                 975

Phe Pro Leu Thr Gln Phe Thr Cys Asn Asn Gly Arg Cys Ile Asn Ile
            980                 985                 990

Asn Trp Arg Cys Asp Asn Asp Asn  Asp Cys Gly Asp Asn  Ser Asp Glu
        995                 1000                1005

Ala Gly  Cys Ser His Ser Cys  Ser Ser Thr Gln Phe  Lys Cys Asn
    1010                1015                1020

Ser Gly  Arg Cys Ile Pro Glu  His Trp Thr Cys Asp  Gly Asp Asn
    1025                1030                1035

Asp Cys  Gly Asp Tyr Ser Asp  Glu Thr His Ala Asn  Cys Thr Asn
    1040                1045                1050

Gln Ala  Thr Arg Pro Pro Gly  Gly Cys His Thr Asp  Glu Phe Gln
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    1055                1060                1065

Cys Arg  Leu Asp Gly Leu Cys  Ile Pro Leu Arg Trp  Arg Cys Asp
    1070                1075                1080

Gly Asp  Thr Asp Cys Met Asp  Ser Ser Asp Glu Lys  Ser Cys Glu
    1085                1090                1095

Gly Val  Thr His Val Cys Asp  Pro Ser Val Lys Phe  Gly Cys Lys
    1100                1105                1110

Asp Ser  Ala Arg Cys Ile Ser  Lys Ala Trp Val Cys  Asp Gly Asp
    1115                1120                1125

Asn Asp  Cys Glu Asp Asn Ser  Asp Glu Glu Asn Cys  Glu Ser Leu
    1130                1135                1140

Ala Cys  Arg Pro Pro Ser His  Pro Cys Ala Asn Asn  Thr Ser Val
    1145                1150                1155

Cys Leu  Pro Pro Asp Lys Leu  Cys Asp Gly Asn Asp  Asp Cys Gly
    1160                1165                1170

Asp Gly  Ser Asp Glu Gly Glu  Leu Cys Asp Gln Cys  Ser Leu Asn
    1175                1180                1185

Asn Gly  Gly Cys Ser His Asn  Cys Ser Val Ala Pro  Gly Glu Gly
    1190                1195                1200

Ile Val  Cys Ser Cys Pro Leu  Gly Met Glu Leu Gly  Pro Asp Asn
    1205                1210                1215

His Thr  Cys Gln Ile Gln Ser  Tyr Cys Ala Lys His  Leu Lys Cys
    1220                1225                1230

Ser Gln  Lys Cys Asp Gln Asn  Lys Phe Ser Val Lys  Cys Ser Cys
    1235                1240                1245

Tyr Glu  Gly Trp Val Leu Glu  Pro Asp Gly Glu Ser  Cys Arg Ser
    1250                1255                1260

Leu Asp  Pro Phe Lys Pro Phe  Ile Ile Phe Ser Asn  Arg His Glu
    1265                1270                1275

Ile Arg  Arg Ile Asp Leu His  Lys Gly Asp Tyr Ser  Val Leu Val
    1280                1285                1290

Pro Gly  Leu Arg Asn Thr Ile  Ala Leu Asp Phe His  Leu Ser Gln
    1295                1300                1305

Ser Ala  Leu Tyr Trp Thr Asp  Val Val Glu Asp Lys  Ile Tyr Arg
    1310                1315                1320

Gly Lys  Leu Leu Asp Asn Gly  Ala Leu Thr Ser Phe  Glu Val Val
    1325                1330                1335

Ile Gln  Tyr Gly Leu Ala Thr  Pro Glu Gly Leu Ala  Val Asp Trp
    1340                1345                1350

Ile Ala  Gly Asn Ile Tyr Trp  Val Glu Ser Asn Leu  Asp Gln Ile
    1355                1360                1365

Glu Val  Ala Lys Leu Asp Gly  Thr Leu Arg Thr Thr  Leu Leu Ala
    1370                1375                1380

Gly Asp  Ile Glu His Pro Arg  Ala Ile Ala Leu Asp  Pro Arg Asp
    1385                1390                1395

Gly Ile  Leu Phe Trp Thr Asp  Trp Asp Ala Ser Leu  Pro Arg Ile
    1400                1405                1410

Glu Ala  Ala Ser Met Ser Gly  Ala Gly Arg Arg Thr  Val His Arg
    1415                1420                1425

Glu Thr  Gly Ser Gly Gly Trp  Pro Asn Gly Leu Thr  Val Asp Tyr
    1430                1435                1440
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Leu Glu  Lys Arg Ile Leu Trp  Ile Asp Ala Arg Ser  Asp Ala Ile
    1445                1450                1455

Tyr Ser  Ala Arg Tyr Asp Gly  Ser Gly His Met Glu  Val Leu Arg
    1460                1465                1470

Gly His  Glu Phe Leu Ser His  Pro Phe Ala Val Thr  Leu Tyr Gly
    1475                1480                1485

Gly Glu  Val Tyr Trp Thr Asp  Trp Arg Thr Asn Thr  Leu Ala Lys
    1490                1495                1500

Ala Asn  Lys Trp Thr Gly His  Asn Val Thr Val Val  Gln Arg Thr
    1505                1510                1515

Asn Thr  Gln Pro Phe Asp Leu  Gln Val Tyr His Pro  Ser Arg Gln
    1520                1525                1530

Pro Met  Ala Pro Asn Pro Cys  Glu Ala Asn Gly Gly  Gln Gly Pro
    1535                1540                1545

Cys Ser  His Leu Cys Leu Ile  Asn Tyr Asn Arg Thr  Val Ser Cys
    1550                1555                1560

Ala Cys  Pro His Leu Met Lys  Leu His Lys Asp Asn  Thr Thr Cys
    1565                1570                1575

Tyr Glu  Phe Lys Lys Phe Leu  Leu Tyr Ala Arg Gln  Met Glu Ile
    1580                1585                1590

Arg Gly  Val Asp Leu Asp Ala  Pro Tyr Tyr Asn Tyr  Ile Ile Ser
    1595                1600                1605

Phe Thr  Val Pro Asp Ile Asp  Asn Val Thr Val Leu  Asp Tyr Asp
    1610                1615                1620

Ala Arg  Glu Gln Arg Val Tyr  Trp Ser Asp Val Arg  Thr Gln Ala
    1625                1630                1635

Ile Lys  Arg Ala Phe Ile Asn  Gly Thr Gly Val Glu  Thr Val Val
    1640                1645                1650

Ser Ala  Asp Leu Pro Asn Ala  His Gly Leu Ala Val  Asp Trp Val
    1655                1660                1665

Ser Arg  Asn Leu Phe Trp Thr  Ser Tyr Asp Thr Asn  Lys Lys Gln
    1670                1675                1680

Ile Asn  Val Ala Arg Leu Asp  Gly Ser Phe Lys Asn  Ala Val Val
    1685                1690                1695

Gln Gly  Leu Glu Gln Pro His  Gly Leu Val Val His  Pro Leu Arg
    1700                1705                1710

Gly Lys  Leu Tyr Trp Thr Asp  Gly Asp Asn Ile Ser  Met Ala Asn
    1715                1720                1725

Met Asp  Gly Ser Asn Arg Thr  Leu Leu Phe Ser Gly  Gln Lys Gly
    1730                1735                1740

Pro Val  Gly Leu Ala Ile Asp  Phe Pro Glu Ser Lys  Leu Tyr Trp
    1745                1750                1755

Ile Ser  Ser Gly Asn His Thr  Ile Asn Arg Cys Asn  Leu Asp Gly
    1760                1765                1770

Ser Gly  Leu Glu Val Ile Asp  Ala Met Arg Ser Gln  Leu Gly Lys
    1775                1780                1785

Ala Thr  Ala Leu Ala Ile Met  Gly Asp Lys Leu Trp  Trp Ala Asp
    1790                1795                1800

Gln Val  Ser Glu Lys Met Gly  Thr Cys Ser Lys Ala  Asp Gly Ser
    1805                1810                1815
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Gly Ser  Val Val Leu Arg Asn  Ser Thr Thr Leu Val  Met His Met
    1820                 1825                 1830

Lys Val  Tyr Asp Glu Ser Ile  Gln Leu Asp His Lys  Gly Thr Asn
    1835                 1840                 1845

Pro Cys  Ser Val Asn Asn Gly  Asp Cys Ser Gln Leu  Cys Leu Pro
    1850                 1855                 1860

Thr Ser  Glu Thr Thr Arg Ser  Cys Met Cys Thr Ala  Gly Tyr Ser
    1865                 1870                 1875

Leu Arg  Ser Gly Gln Gln Ala  Cys Glu Gly Val Gly  Ser Phe Leu
    1880                 1885                 1890

Leu Tyr  Ser Val His Glu Gly  Ile Arg Gly Ile Pro  Leu Asp Pro
    1895                 1900                 1905

Asn Asp  Lys Ser Asp Ala Leu  Val Pro Val Ser Gly  Thr Ser Leu
    1910                 1915                 1920

Ala Val  Gly Ile Asp Phe His  Ala Glu Asn Asp Thr  Ile Tyr Trp
    1925                 1930                 1935

Val Asp  Met Gly Leu Ser Thr  Ile Ser Arg Ala Lys  Arg Asp Gln
    1940                 1945                 1950

Thr Trp  Arg Glu Asp Val Val  Thr Asn Gly Ile Gly  Arg Val Glu
    1955                 1960                 1965

Gly Ile  Ala Val Asp Trp Ile  Ala Gly Asn Ile Tyr  Trp Thr Asp
    1970                 1975                 1980

Gln Gly  Phe Asp Val Ile Glu  Val Ala Arg Leu Asn  Gly Ser Phe
    1985                 1990                 1995

Arg Tyr  Val Val Ile Ser Gln  Gly Leu Asp Lys Pro  Arg Ala Ile
    2000                 2005                 2010

Thr Val  His Pro Glu Lys Gly  Tyr Leu Phe Trp Thr  Glu Trp Gly
    2015                 2020                 2025

Gln Tyr  Pro Arg Ile Glu Arg  Ser Arg Leu Asp Gly  Thr Glu Arg
    2030                 2035                 2040

Val Val  Leu Val Asn Val Ser  Ile Ser Trp Pro Asn  Gly Ile Ser
    2045                 2050                 2055

Val Asp  Tyr Gln Asp Gly Lys  Leu Tyr Trp Cys Asp  Ala Arg Thr
    2060                 2065                 2070

Asp Lys  Ile Glu Arg Ile Asp  Leu Glu Thr Gly Glu  Asn Arg Glu
    2075                 2080                 2085

Val Val  Leu Ser Ser Asn Asn  Met Asp Met Phe Ser  Val Ser Val
    2090                 2095                 2100

Phe Glu  Asp Phe Ile Tyr Trp  Ser Asp Arg Thr His  Ala Asn Gly
    2105                 2110                 2115

Ser Ile  Lys Arg Gly Ser Lys  Asp Asn Ala Thr Asp  Ser Val Pro
    2120                 2125                 2130

Leu Arg  Thr Gly Ile Gly Val  Gln Leu Lys Asp Ile  Lys Val Phe
    2135                 2140                 2145

Asn Arg  Asp Arg Gln Lys Gly  Thr Asn Val Cys Ala  Val Ala Asn
    2150                 2155                 2160

Gly Gly  Cys Gln Gln Leu Cys  Leu Tyr Arg Gly Arg  Gly Gln Arg
    2165                 2170                 2175

Ala Cys  Ala Cys Ala His Gly  Met Leu Ala Glu Asp  Gly Ala Ser
    2180                 2185                 2190

Cys Arg  Glu Tyr Ala Gly Tyr  Leu Leu Tyr Ser Glu  Arg Thr Ile
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    2195                2200                2205

Leu Lys  Ser Ile His Leu Ser  Asp Glu Arg Asn Leu  Asn Ala Pro
    2210                2215                2220

Val Gln  Pro Phe Glu Asp Pro  Glu His Met Lys Asn  Val Ile Ala
    2225                2230                2235

Leu Ala  Phe Asp Tyr Arg Ala  Gly Thr Ser Pro Gly  Thr Pro Asn
    2240                2245                2250

Arg Ile  Phe Phe Ser Asp Ile  His Phe Gly Asn Ile  Gln Gln Ile
    2255                2260                2265

Asn Asp  Asp Gly Ser Arg Arg  Ile Thr Ile Val Glu  Asn Val Gly
    2270                2275                2280

Ser Val  Glu Gly Leu Ala Tyr  His Arg Gly Trp Asp  Thr Leu Tyr
    2285                2290                2295

Trp Thr  Ser Tyr Thr Thr Ser  Thr Ile Thr Arg His  Thr Val Asp
    2300                2305                2310

Gln Thr  Arg Pro Gly Ala Phe  Glu Arg Glu Thr Val  Ile Thr Met
    2315                2320                2325

Ser Gly  Asp Asp His Pro Arg  Ala Phe Val Leu Asp  Glu Cys Gln
    2330                2335                2340

Asn Leu  Met Phe Trp Thr Asn  Trp Asn Glu Gln His  Pro Ser Ile
    2345                2350                2355

Met Arg  Ala Ala Leu Ser Gly  Ala Asn Val Leu Thr  Leu Ile Glu
    2360                2365                2370

Lys Asp  Ile Arg Thr Pro Asn  Gly Leu Ala Ile Asp  His Arg Ala
    2375                2380                2385

Glu Lys  Leu Tyr Phe Ser Asp  Ala Thr Leu Asp Lys  Ile Glu Arg
    2390                2395                2400

Cys Glu  Tyr Asp Gly Ser His  Arg Tyr Val Ile Leu  Lys Ser Glu
    2405                2410                2415

Pro Val  His Pro Phe Gly Leu  Ala Val Tyr Gly Glu  His Ile Phe
    2420                2425                2430

Trp Thr  Asp Trp Val Arg Arg  Ala Val Gln Arg Ala  Asn Lys His
    2435                2440                2445

Val Gly  Ser Asn Met Lys Leu  Leu Arg Val Asp Ile  Pro Gln Gln
    2450                2455                2460

Pro Met  Gly Ile Ile Ala Val  Ala Asn Asp Thr Asn  Ser Cys Glu
    2465                2470                2475

Leu Ser  Pro Cys Arg Ile Asn  Asn Gly Gly Cys Gln  Asp Leu Cys
    2480                2485                2490

Leu Leu  Thr His Gln Gly His  Val Asn Cys Ser Cys  Arg Gly Gly
    2495                2500                2505

Arg Ile  Leu Gln Asp Asp Leu  Thr Cys Arg Ala Val  Asn Ser Ser
    2510                2515                2520

Cys Arg  Ala Gln Asp Glu Phe  Glu Cys Ala Asn Gly  Glu Cys Ile
    2525                2530                2535

Asn Phe  Ser Leu Thr Cys Asp  Gly Val Pro His Cys  Lys Asp Lys
    2540                2545                2550

Ser Asp  Glu Lys Pro Ser Tyr  Cys Asn Ser Arg Arg  Cys Lys Lys
    2555                2560                2565

Thr Phe  Arg Gln Cys Ser Asn  Gly Arg Cys Val Ser  Asn Met Leu
    2570                2575                2580
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Trp Cys  Asn Gly Ala Asp Asp  Cys Gly Asp Gly Ser  Asp Glu Ile
    2585                 2590                 2595

Pro Cys  Asn Lys Thr Ala Cys  Gly Val Gly Glu Phe  Arg Cys Arg
    2600                 2605                 2610

Asp Gly  Thr Cys Ile Gly Asn  Ser Ser Arg Cys Asn  Gln Phe Val
    2615                 2620                 2625

Asp Cys  Glu Asp Ala Ser Asp  Glu Met Asn Cys Ser  Ala Thr Asp
    2630                 2635                 2640

Cys Ser  Ser Tyr Phe Arg Leu  Gly Val Lys Gly Val  Leu Phe Gln
    2645                 2650                 2655

Pro Cys  Glu Arg Thr Ser Leu  Cys Tyr Ala Pro Ser  Trp Val Cys
    2660                 2665                 2670

Asp Gly  Ala Asn Asp Cys Gly  Asp Tyr Ser Asp Glu  Arg Asp Cys
    2675                 2680                 2685

Pro Gly  Val Lys Arg Pro Arg  Cys Pro Leu Asn Tyr  Phe Ala Cys
    2690                 2695                 2700

Pro Ser  Gly Arg Cys Ile Pro  Met Ser Trp Thr Cys  Asp Lys Glu
    2705                 2710                 2715

Asp Asp  Cys Glu His Gly Glu  Asp Glu Thr His Cys  Asn Lys Phe
    2720                 2725                 2730

Cys Ser  Glu Ala Gln Phe Glu  Cys Gln Asn His Arg  Cys Ile Ser
    2735                 2740                 2745

Lys Gln  Trp Leu Cys Asp Gly  Ser Asp Asp Cys Gly  Asp Gly Ser
    2750                 2755                 2760

Asp Glu  Ala Ala His Cys Glu  Gly Lys Thr Cys Gly  Pro Ser Ser
    2765                 2770                 2775

Phe Ser  Cys Pro Gly Thr His  Val Cys Val Pro Glu  Arg Trp Leu
    2780                 2785                 2790

Cys Asp  Gly Asp Lys Asp Cys  Ala Asp Gly Ala Asp  Glu Ser Ile
    2795                 2800                 2805

Ala Ala  Gly Cys Leu Tyr Asn  Ser Thr Cys Asp Asp  Arg Glu Phe
    2810                 2815                 2820

Met Cys  Gln Asn Arg Gln Cys  Ile Pro Lys His Phe  Val Cys Asp
    2825                 2830                 2835

His Asp  Arg Asp Cys Ala Asp  Gly Ser Asp Glu Ser  Pro Glu Cys
    2840                 2845                 2850

Glu Tyr  Pro Thr Cys Gly Pro  Ser Glu Phe Arg Cys  Ala Asn Gly
    2855                 2860                 2865

Arg Cys  Leu Ser Ser Arg Gln  Trp Glu Cys Asp Gly  Glu Asn Asp
    2870                 2875                 2880

Cys His  Asp Gln Ser Asp Glu  Ala Pro Lys Asn Pro  His Cys Thr
    2885                 2890                 2895

Ser Pro  Glu His Lys Cys Asn  Ala Ser Ser Gln Phe  Leu Cys Ser
    2900                 2905                 2910

Ser Gly  Arg Cys Val Ala Glu  Ala Leu Leu Cys Asn  Gly Gln Asp
    2915                 2920                 2925

Asp Cys  Gly Asp Ser Ser Asp  Glu Arg Gly Cys His  Ile Asn Glu
    2930                 2935                 2940

Cys Leu  Ser Arg Lys Leu Ser  Gly Cys Ser Gln Asp  Cys Glu Asp
    2945                 2950                 2955
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Leu Lys  Ile Gly Phe Lys Cys  Arg Cys Arg Pro Gly  Phe Arg Leu
    2960                2965                2970

Lys Asp  Asp Gly Arg Thr Cys  Ala Asp Val Asp Glu  Cys Ser Thr
    2975                2980                2985

Thr Phe  Pro Cys Ser Gln Arg  Cys Ile Asn Thr His  Gly Ser Tyr
    2990                2995                3000

Lys Cys  Leu Cys Val Glu Gly  Tyr Ala Pro Arg Gly  Gly Asp Pro
    3005                3010                3015

His Ser  Cys Lys Ala Val Thr  Asp Glu Glu Pro Phe  Leu Ile Phe
    3020                3025                3030

Ala Asn  Arg Tyr Tyr Leu Arg  Lys Leu Asn Leu Asp  Gly Ser Asn
    3035                3040                3045

Tyr Thr  Leu Leu Lys Gln Gly  Leu Asn Asn Ala Val  Ala Leu Asp
    3050                3055                3060

Phe Asp  Tyr Arg Glu Gln Met  Ile Tyr Trp Thr Asp  Val Thr Thr
    3065                3070                3075

Gln Gly  Ser Met Ile Arg Arg  Met His Leu Asn Gly  Ser Asn Val
    3080                3085                3090

Gln Val  Leu His Arg Thr Gly  Leu Ser Asn Pro Asp  Gly Leu Ala
    3095                3100                3105

Val Asp  Trp Val Gly Gly Asn  Leu Tyr Trp Cys Asp  Lys Gly Arg
    3110                3115                3120

Asp Thr  Ile Glu Val Ser Lys  Leu Asn Gly Ala Tyr  Arg Thr Val
    3125                3130                3135

Leu Val  Ser Ser Gly Leu Arg  Glu Pro Arg Ala Leu  Val Val Asp
    3140                3145                3150

Val Gln  Asn Gly Tyr Leu Tyr  Trp Thr Asp Trp Gly  Asp His Ser
    3155                3160                3165

Leu Ile  Gly Arg Ile Gly Met  Asp Gly Ser Ser Arg  Ser Val Ile
    3170                3175                3180

Val Asp  Thr Lys Ile Thr Trp  Pro Asn Gly Leu Thr  Leu Asp Tyr
    3185                3190                3195

Val Thr  Glu Arg Ile Tyr Trp  Ala Asp Ala Arg Glu  Asp Tyr Ile
    3200                3205                3210

Glu Phe  Ala Ser Leu Asp Gly  Ser Asn Arg His Val  Val Leu Ser
    3215                3220                3225

Gln Asp  Ile Pro His Ile Phe  Ala Leu Thr Leu Phe  Glu Asp Tyr
    3230                3235                3240

Val Tyr  Trp Thr Asp Trp Glu  Thr Lys Ser Ile Asn  Arg Ala His
    3245                3250                3255

Lys Thr  Thr Gly Thr Asn Lys  Thr Leu Leu Ile Ser  Thr Leu His
    3260                3265                3270

Arg Pro  Met Asp Leu His Val  Phe His Ala Leu Arg  Gln Pro Asp
    3275                3280                3285

Val Pro  Asn His Pro Cys Lys  Val Asn Asn Gly Gly  Cys Ser Asn
    3290                3295                3300

Leu Cys  Leu Leu Ser Pro Gly  Gly Gly His Lys Cys  Ala Cys Pro
    3305                3310                3315

Thr Asn  Phe Tyr Leu Gly Ser  Asp Gly Arg Thr Cys  Val Ser Asn
    3320                3325                3330

Cys Thr  Ala Ser Gln Phe Val  Cys Lys Asn Asp Lys  Cys Ile Pro
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    3335                3340                3345

Phe Trp  Trp Lys Cys Asp Thr  Glu Asp Asp Cys Gly  Asp His Ser
    3350                3355                3360

Asp Glu  Pro Pro Asp Cys Pro  Glu Phe Lys Cys Arg  Pro Gly Gln
    3365                3370                3375

Phe Gln  Cys Ser Thr Gly Ile  Cys Thr Asn Pro Ala  Phe Ile Cys
    3380                3385                3390

Asp Gly  Asp Asn Asp Cys Gln  Asp Asn Ser Asp Glu  Ala Asn Cys
    3395                3400                3405

Asp Ile  His Val Cys Leu Pro  Ser Gln Phe Lys Cys  Thr Asn Thr
    3410                3415                3420

Asn Arg  Cys Ile Pro Gly Ile  Phe Arg Cys Asn Gly  Gln Asp Asn
    3425                3430                3435

Cys Gly  Asp Gly Glu Asp Glu  Arg Asp Cys Pro Glu  Val Thr Cys
    3440                3445                3450

Ala Pro  Asn Gln Phe Gln Cys  Ser Ile Thr Lys Arg  Cys Ile Pro
    3455                3460                3465

Arg Val  Trp Val Cys Asp Arg  Asp Asn Asp Cys Val  Asp Gly Ser
    3470                3475                3480

Asp Glu  Pro Ala Asn Cys Thr  Gln Met Thr Cys Gly  Val Asp Glu
    3485                3490                3495

Phe Arg  Cys Lys Asp Ser Gly  Arg Cys Ile Pro Ala  Arg Trp Lys
    3500                3505                3510

Cys Asp  Gly Glu Asp Asp Cys  Gly Asp Gly Ser Asp  Glu Pro Lys
    3515                3520                3525

Glu Glu  Cys Asp Glu Arg Thr  Cys Glu Pro Tyr Gln  Phe Arg Cys
    3530                3535                3540

Lys Asn  Asn Arg Cys Val Pro  Gly Arg Trp Gln Cys  Asp Tyr Asp
    3545                3550                3555

Asn Asp  Cys Gly Asp Asn Ser  Asp Glu Glu Ser Cys  Thr Pro Arg
    3560                3565                3570

Pro Cys  Ser Glu Ser Glu Phe  Ser Cys Ala Asn Gly  Arg Cys Ile
    3575                3580                3585

Ala Gly  Arg Trp Lys Cys Asp  Gly Asp His Asp Cys  Ala Asp Gly
    3590                3595                3600

Ser Asp  Glu Lys Asp Cys Thr  Pro Arg Cys Asp Met  Asp Gln Phe
    3605                3610                3615

Gln Cys  Lys Ser Gly His Cys  Ile Pro Leu Arg Trp  Arg Cys Asp
    3620                3625                3630

Ala Asp  Ala Asp Cys Met Asp  Gly Ser Asp Glu Glu  Ala Cys Gly
    3635                3640                3645

Thr Gly  Val Arg Thr Cys Pro  Leu Asp Glu Phe Gln  Cys Asn Asn
    3650                3655                3660

Thr Leu  Cys Lys Pro Leu Ala  Trp Lys Cys Asp Gly  Glu Asp Asp
    3665                3670                3675

Cys Gly  Asp Asn Ser Asp Glu  Asn Pro Glu Glu Cys  Ala Arg Phe
    3680                3685                3690

Val Cys  Pro Pro Asn Arg Pro  Phe Arg Cys Lys Asn  Asp Arg Val
    3695                3700                3705

Cys Leu  Trp Ile Gly Arg Gln  Cys Asp Gly Thr Asp  Asn Cys Gly
    3710                3715                3720
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Asp Gly  Thr Asp Glu Glu Asp  Cys Glu Pro Pro Thr  Ala His Thr
    3725                 3730                 3735

Thr His  Cys Lys Asp Lys Lys  Glu Phe Leu Cys Arg  Asn Gln Arg
    3740                 3745                 3750

Cys Leu  Ser Ser Ser Leu Arg  Cys Asn Met Phe Asp  Asp Cys Gly
    3755                 3760                 3765

Asp Gly  Ser Asp Glu Glu Asp  Cys Ser Ile Asp Pro  Lys Leu Thr
    3770                 3775                 3780

Ser Cys  Ala Thr Asn Ala Ser  Ile Cys Gly Asp Glu  Ala Arg Cys
    3785                 3790                 3795

Val Arg  Thr Glu Lys Ala Ala  Tyr Cys Ala Cys Arg  Ser Gly Phe
    3800                 3805                 3810

His Thr  Val Pro Gly Gln Pro  Gly Cys Gln Asp Ile  Asn Glu Cys
    3815                 3820                 3825

Leu Arg  Phe Gly Thr Cys Ser  Gln Leu Cys Asn Asn  Thr Lys Gly
    3830                 3835                 3840

Gly His  Leu Cys Ser Cys Ala  Arg Asn Phe Met Lys  Thr His Asn
    3845                 3850                 3855

Thr Cys  Lys Ala Glu Gly Ser  Glu Tyr Gln Val Leu  Tyr Ile Ala
    3860                 3865                 3870

Asp Asp  Asn Glu Ile Arg Ser  Leu Phe Pro Gly His  Pro His Ser
    3875                 3880                 3885

Ala Tyr  Glu Gln Ala Phe Gln  Gly Asp Glu Ser Val  Arg Ile Asp
    3890                 3895                 3900

Ala Met  Asp Val His Val Lys  Ala Gly Arg Val Tyr  Trp Thr Asn
    3905                 3910                 3915

Trp His  Thr Gly Thr Ile Ser  Tyr Arg Ser Leu Pro  Pro Ala Ala
    3920                 3925                 3930

Pro Pro  Thr Thr Ser Asn Arg  His Arg Arg Gln Ile  Asp Arg Gly
    3935                 3940                 3945

Val Thr  His Leu Asn Ile Ser  Gly Leu Lys Met Pro  Arg Gly Ile
    3950                 3955                 3960

Ala Ile  Asp Trp Val Ala Gly  Asn Val Tyr Trp Thr  Asp Ser Gly
    3965                 3970                 3975

Arg Asp  Val Ile Glu Val Ala  Gln Met Lys Gly Glu  Asn Arg Lys
    3980                 3985                 3990

Thr Leu  Ile Ser Gly Met Ile  Asp Glu Pro His Ala  Ile Val Val
    3995                 4000                 4005

Asp Pro  Leu Arg Gly Thr Met  Tyr Trp Ser Asp Trp  Gly Asn His
    4010                 4015                 4020

Pro Lys  Ile Glu Thr Ala Ala  Met Asp Gly Thr Leu  Arg Glu Thr
    4025                 4030                 4035

Leu Val  Gln Asp Asn Ile Gln  Trp Pro Thr Gly Leu  Ala Val Asp
    4040                 4045                 4050

Tyr His  Asn Glu Arg Leu Tyr  Trp Ala Asp Ala Lys  Leu Ser Val
    4055                 4060                 4065

Ile Gly  Ser Ile Arg Leu Asn  Gly Thr Asp Pro Ile  Val Ala Ala
    4070                 4075                 4080

Asp Ser  Lys Arg Gly Leu Ser  His Pro Phe Ser Ile  Asp Val Phe
    4085                 4090                 4095
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Glu Asp  Tyr Ile Tyr Gly Val  Thr Tyr Ile Asn Asn  Arg Val Phe
    4100                 4105                 4110

Lys Ile  His Lys Phe Gly His  Ser Pro Leu Val Asn  Leu Thr Gly
    4115                 4120                 4125

Gly Leu  Ser His Ala Ser Asp  Val Val Leu Tyr His  Gln His Lys
    4130                 4135                 4140

Gln Pro  Glu Val Thr Asn Pro  Cys Asp Arg Lys Lys  Cys Glu Trp
    4145                 4150                 4155

Leu Cys  Leu Leu Ser Pro Ser  Gly Pro Val Cys Thr  Cys Pro Asn
    4160                 4165                 4170

Gly Lys  Arg Leu Asp Asn Gly  Thr Cys Val Pro Val  Pro Ser Pro
    4175                 4180                 4185

Thr Pro  Pro Pro Asp Ala Pro  Arg Pro Gly Thr Cys  Asn Leu Gln
    4190                 4195                 4200

Cys Phe  Asn Gly Gly Ser Cys  Phe Leu Asn Ala Arg  Arg Gln Pro
    4205                 4210                 4215

Lys Cys  Arg Cys Gln Pro Arg  Tyr Thr Gly Asp Lys  Cys Glu Leu
    4220                 4225                 4230

Asp Gln  Cys Trp Glu His Cys  Arg Asn Gly Gly Thr  Cys Ala Ala
    4235                 4240                 4245

Ser Pro  Ser Gly Met Pro Thr  Cys Arg Cys Pro Thr  Gly Phe Thr
    4250                 4255                 4260

Gly Pro  Lys Cys Thr Gln Gln  Val Cys Ala Gly Tyr  Cys Ala Asn
    4265                 4270                 4275

Asn Ser  Thr Cys Thr Val Asn  Gln Gly Asn Gln Pro  Gln Cys Arg
    4280                 4285                 4290

Cys Leu  Pro Gly Phe Leu Gly  Asp Arg Cys Gln Tyr  Arg Gln Cys
    4295                 4300                 4305

Ser Gly  Tyr Cys Glu Asn Phe  Gly Thr Cys Gln Met  Ala Ala Asp
    4310                 4315                 4320

Gly Ser  Arg Gln Cys Arg Cys  Thr Ala Tyr Phe Glu  Gly Ser Arg
    4325                 4330                 4335

Cys Glu  Val Asn Lys Cys Ser  Arg Cys Leu Glu Gly  Ala Cys Val
    4340                 4345                 4350

Val Asn  Lys Gln Ser Gly Asp  Val Thr Cys Asn Cys  Thr Asp Gly
    4355                 4360                 4365

Arg Val  Ala Pro Ser Cys Leu  Thr Cys Val Gly His  Cys Ser Asn
    4370                 4375                 4380

Gly Gly  Ser Cys Thr Met Asn  Ser Lys Met Met Pro  Glu Cys Gln
    4385                 4390                 4395

Cys Pro  Pro His Met Thr Gly  Pro Arg Cys Glu Glu  His Val Phe
    4400                 4405                 4410

Ser Gln  Gln Gln Pro Gly His  Ile Ala Ser Ile Leu  Ile Pro Leu
    4415                 4420                 4425

Leu Leu  Leu Leu Leu Leu Val  Leu Val Ala Gly Val  Val Phe Trp
    4430                 4435                 4440

Tyr Lys  Arg Arg Val Gln Gly  Ala Lys Gly Phe Gln  His Gln Arg
    4445                 4450                 4455

Met Thr  Asn Gly Ala Met Asn  Val Glu Ile Gly Asn  Pro Thr Tyr
    4460                 4465                 4470

Lys Met  Tyr Glu Gly Gly Glu  Pro Asp Asp Val Gly  Gly Leu Leu
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    4475                4480                4485

Asp Ala  Asp Phe Ala Leu Asp  Pro Asp Lys Pro Thr  Asn Phe Thr
    4490                4495                4500

Asn Pro  Val Tyr Ala Thr Leu  Tyr Met Gly Gly His  Gly Ser Arg
    4505                4510                4515

His Ser  Leu Ala Ser Thr Asp  Glu Lys Arg Glu Leu  Leu Gly Arg
    4520                4525                4530

Gly Pro  Glu Asp Glu Ile Gly  Asp Pro Leu Ala
    4535                4540


<210> SEQ ID NO 28
<211> LENGTH: 1609
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 28

Met Arg Gly Ser His Arg Ala Ala Pro Ala Leu Arg Pro Arg Gly Arg
1               5                   10                  15

Leu Trp Pro Val Leu Ala Val Leu Ala Ala Ala Ala Ala Ala Gly Cys
            20                  25                  30

Ala Gln Ala Ala Met Asp Glu Cys Thr Asp Glu Gly Gly Arg Pro Gln
        35                  40                  45

Arg Cys Met Pro Glu Phe Val Asn Ala Ala Phe Asn Val Thr Val Val
    50                  55                  60

Ala Thr Asn Thr Cys Gly Thr Pro Pro Glu Glu Tyr Cys Val Gln Thr
65                  70                  75                  80

Gly Val Thr Gly Val Thr Lys Ser Cys His Leu Cys Asp Ala Gly Gln
                85                  90                  95

Pro His Leu Gln His Gly Ala Ala Phe Leu Thr Asp Tyr Asn Asn Gln
            100                 105                 110

Ala Asp Thr Thr Trp Trp Gln Ser Gln Thr Met Leu Ala Gly Val Gln
        115                 120                 125

Tyr Pro Ser Ser Ile Asn Leu Thr Leu His Leu Gly Lys Ala Phe Asp
    130                 135                 140

Ile Thr Tyr Val Arg Leu Lys Phe His Thr Ser Arg Pro Glu Ser Phe
145                 150                 155                 160

Ala Ile Tyr Lys Arg Thr Arg Glu Asp Gly Pro Trp Ile Pro Tyr Gln
                165                 170                 175

Tyr Tyr Ser Gly Ser Cys Glu Asn Thr Tyr Ser Lys Ala Asn Arg Gly
            180                 185                 190

Phe Ile Arg Thr Gly Gly Asp Glu Gln Gln Ala Leu Cys Thr Asp Glu
        195                 200                 205

Phe Ser Asp Phe Ser Pro Leu Thr Gly Gly Asn Val Ala Phe Ser Thr
    210                 215                 220

Leu Glu Gly Arg Pro Ser Ala Tyr Asn Phe Asp Asn Ser Pro Val Leu
225                 230                 235                 240

Gln Glu Trp Val Thr Ala Thr Asp Ile Arg Val Thr Leu Asn Arg Leu
                245                 250                 255

Asn Thr Phe Gly Asp Glu Val Phe Asn Asp Pro Lys Val Leu Lys Ser
            260                 265                 270

Tyr Tyr Tyr Ala Ile Ser Asp Phe Ala Val Gly Gly Arg Cys Lys Cys
        275                 280                 285
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Asn Gly His Ala Ser Glu Cys Met Lys Asn Glu Phe Asp Lys Leu Val
    290                 295                 300

Cys Asn Cys Lys His Asn Thr Tyr Gly Val Asp Cys Glu Lys Cys Leu
305                 310                 315                 320

Pro Phe Phe Asn Asp Arg Pro Trp Arg Arg Ala Thr Ala Glu Ser Ala
                325                 330                 335

Ser Glu Cys Leu Pro Cys Asp Cys Asn Gly Arg Ser Gln Glu Cys Tyr
            340                 345                 350

Phe Asp Pro Glu Leu Tyr Arg Ser Thr Gly His Gly Gly His Cys Thr
        355                 360                 365

Asn Cys Gln Asp Asn Thr Asp Gly Ala His Cys Glu Arg Cys Arg Glu
    370                 375                 380

Asn Phe Phe Arg Leu Gly Asn Asn Glu Ala Cys Ser Ser Cys His Cys
385                 390                 395                 400

Ser Pro Val Gly Ser Leu Ser Thr Gln Cys Asp Ser Tyr Gly Arg Cys
                405                 410                 415

Ser Cys Lys Pro Gly Val Met Gly Asp Lys Cys Asp Arg Cys Gln Pro
            420                 425                 430

Gly Phe His Ser Leu Thr Glu Ala Gly Cys Arg Pro Cys Ser Cys Asp
        435                 440                 445

Pro Ser Gly Ser Ile Asp Glu Cys Asn Val Glu Thr Gly Arg Cys Val
    450                 455                 460

Cys Lys Asp Asn Val Glu Gly Phe Asn Cys Glu Arg Cys Lys Pro Gly
465                 470                 475                 480

Phe Phe Asn Leu Glu Ser Ser Asn Pro Arg Gly Cys Thr Pro Cys Phe
                485                 490                 495

Cys Phe Gly His Ser Ser Val Cys Thr Asn Ala Val Gly Tyr Ser Val
            500                 505                 510

Tyr Ser Ile Ser Ser Thr Phe Gln Ile Asp Glu Asp Gly Trp Arg Ala
        515                 520                 525

Glu Gln Arg Asp Gly Ser Glu Ala Ser Leu Glu Trp Ser Ser Glu Arg
    530                 535                 540

Gln Asp Ile Ala Val Ile Ser Asp Ser Tyr Phe Pro Arg Tyr Phe Ile
545                 550                 555                 560

Ala Pro Ala Lys Phe Leu Gly Lys Gln Val Leu Ser Tyr Gly Gln Asn
                565                 570                 575

Leu Ser Phe Ser Phe Arg Val Asp Arg Arg Asp Thr Arg Leu Ser Ala
            580                 585                 590

Glu Asp Leu Val Leu Glu Gly Ala Gly Leu Arg Val Ser Val Pro Leu
        595                 600                 605

Ile Ala Gln Gly Asn Ser Tyr Pro Ser Glu Thr Thr Val Lys Tyr Val
    610                 615                 620

Phe Arg Leu His Glu Ala Thr Asp Tyr Pro Trp Arg Pro Ala Leu Thr
625                 630                 635                 640

Pro Phe Glu Phe Gln Lys Leu Leu Asn Asn Leu Thr Ser Ile Lys Ile
                645                 650                 655

Arg Gly Thr Tyr Ser Glu Arg Ser Ala Gly Tyr Leu Asp Asp Val Thr
            660                 665                 670

Leu Ala Ser Ala Arg Pro Gly Pro Gly Val Pro Ala Thr Trp Val Glu
        675                 680                 685

Ser Cys Thr Cys Pro Val Gly Tyr Gly Gly Gln Phe Cys Glu Met Cys
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    690                 695                 700

Leu Ser Gly Tyr Arg Arg Glu Thr Pro Asn Leu Gly Pro Tyr Ser Pro
705                 710                 715                 720

Cys Val Leu Cys Ala Cys Asn Gly His Ser Glu Thr Cys Asp Pro Glu
                725                 730                 735

Thr Gly Val Cys Asn Cys Arg Asp Asn Thr Ala Gly Pro His Cys Glu
            740                 745                 750

Lys Cys Ser Asp Gly Tyr Tyr Gly Asp Ser Thr Ala Gly Thr Ser Ser
        755                 760                 765

Asp Cys Gln Pro Cys Pro Cys Pro Gly Gly Ser Ser Cys Ala Val Val
    770                 775                 780

Pro Lys Thr Lys Glu Val Val Cys Thr Asn Cys Pro Thr Gly Thr Thr
785                 790                 795                 800

Gly Lys Arg Cys Glu Leu Cys Asp Asp Gly Tyr Phe Gly Asp Pro Leu
                805                 810                 815

Gly Arg Asn Gly Pro Val Arg Leu Cys Arg Leu Cys Gln Cys Ser Asp
            820                 825                 830

Asn Ile Asp Pro Asn Ala Val Gly Asn Cys Asn Arg Leu Thr Gly Glu
        835                 840                 845

Cys Leu Lys Cys Ile Tyr Asn Thr Ala Gly Phe Tyr Cys Asp Arg Cys
    850                 855                 860

Lys Asp Gly Phe Phe Gly Asn Pro Leu Ala Pro Asn Pro Ala Asp Lys
865                 870                 875                 880

Cys Lys Ala Cys Asn Cys Asn Pro Tyr Gly Thr Met Lys Gln Gln Ser
                885                 890                 895

Ser Cys Asn Pro Val Thr Gly Gln Cys Glu Cys Leu Pro His Val Thr
            900                 905                 910

Gly Gln Asp Cys Gly Ala Cys Asp Pro Gly Phe Tyr Asn Leu Gln Ser
        915                 920                 925

Gly Gln Gly Cys Glu Arg Cys Asp Cys His Ala Leu Gly Ser Thr Asn
    930                 935                 940

Gly Gln Cys Asp Ile Arg Thr Gly Gln Cys Glu Cys Gln Pro Gly Ile
945                 950                 955                 960

Thr Gly Gln His Cys Glu Arg Cys Glu Val Asn His Phe Gly Phe Gly
                965                 970                 975

Pro Glu Gly Cys Lys Pro Cys Asp Cys His Pro Glu Gly Ser Leu Ser
            980                 985                 990

Leu Gln Cys Lys Asp Asp Gly Arg  Cys Glu Cys Arg Glu  Gly Phe Val
        995                 1000                1005

Gly Asn  Arg Cys Asp Gln Cys  Glu Glu Asn Tyr Phe  Tyr Asn Arg
    1010                1015                1020

Ser Trp  Pro Gly Cys Gln Glu  Cys Pro Ala Cys Tyr  Arg Leu Val
    1025                1030                1035

Lys Asp  Lys Val Ala Asp His  Arg Val Lys Leu Gln  Glu Leu Glu
    1040                1045                1050

Ser Leu  Ile Ala Asn Leu Gly  Thr Gly Asp Glu Met  Val Thr Asp
    1055                1060                1065

Gln Ala  Phe Glu Asp Arg Leu  Lys Glu Ala Glu Arg  Glu Val Met
    1070                1075                1080

Asp Leu  Leu Arg Glu Ala Gln  Asp Val Lys Asp Val  Asp Gln Asn
    1085                1090                1095
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```
Leu Met  Asp Arg Leu Gln Arg  Val Asn Asn Thr Leu  Ser Ser Gln
    1100                1105                1110

Ile Ser  Arg Leu Gln Asn Ile  Arg Asn Thr Ile Glu  Glu Thr Gly
    1115                1120                1125

Asn Leu  Ala Glu Gln Ala Arg  Ala His Val Glu Asn  Thr Glu Arg
    1130                1135                1140

Leu Ile  Glu Ile Ala Ser Arg  Glu Leu Glu Lys Ala  Lys Val Ala
    1145                1150                1155

Ala Ala  Asn Val Ser Val Thr  Gln Pro Glu Ser Thr  Gly Asp Pro
    1160                1165                1170

Asn Asn  Met Thr Leu Leu Ala  Glu Glu Ala Arg Lys  Leu Ala Glu
    1175                1180                1185

Arg His  Lys Gln Glu Ala Asp  Asp Ile Val Arg Val  Ala Lys Thr
    1190                1195                1200

Ala Asn  Asp Thr Ser Thr Glu  Ala Tyr Asn Leu Leu  Leu Arg Thr
    1205                1210                1215

Leu Ala  Gly Glu Asn Gln Thr  Ala Phe Glu Ile Glu  Glu Leu Asn
    1220                1225                1230

Arg Lys  Tyr Glu Gln Ala Lys  Asn Ile Ser Gln Asp  Leu Glu Lys
    1235                1240                1245

Gln Ala  Ala Arg Val His Glu  Glu Ala Lys Arg Ala  Gly Asp Lys
    1250                1255                1260

Ala Val  Glu Ile Tyr Ala Ser  Val Ala Gln Leu Ser  Pro Leu Asp
    1265                1270                1275

Ser Glu  Thr Leu Glu Asn Glu  Ala Asn Asn Ile Lys  Met Glu Ala
    1280                1285                1290

Glu Asn  Leu Glu Gln Leu Ile  Asp Gln Lys Leu Lys  Asp Tyr Glu
    1295                1300                1305

Asp Leu  Arg Glu Asp Met Arg  Gly Lys Glu Leu Glu  Val Lys Asn
    1310                1315                1320

Leu Leu  Glu Lys Gly Lys Thr  Glu Gln Gln Thr Ala  Asp Gln Leu
    1325                1330                1335

Leu Ala  Arg Ala Asp Ala Ala  Lys Ala Leu Ala Glu  Glu Ala Ala
    1340                1345                1350

Lys Lys  Gly Arg Asp Thr Leu  Gln Glu Ala Asn Asp  Ile Leu Asn
    1355                1360                1365

Asn Leu  Lys Asp Phe Asp Arg  Arg Val Asn Asp Asn  Lys Thr Ala
    1370                1375                1380

Ala Glu  Glu Ala Leu Arg Lys  Ile Pro Ala Ile Asn  Gln Thr Ile
    1385                1390                1395

Thr Glu  Ala Asn Glu Lys Thr  Arg Glu Ala Gln Gln  Ala Leu Gly
    1400                1405                1410

Ser Ala  Ala Ala Asp Ala Thr  Glu Ala Lys Asn Lys  Ala His Glu
    1415                1420                1425

Ala Glu  Arg Ile Ala Ser Ala  Val Gln Lys Asn Ala  Thr Ser Thr
    1430                1435                1440

Lys Ala  Glu Ala Glu Arg Thr  Phe Ala Glu Val Thr  Asp Leu Asp
    1445                1450                1455

Asn Glu  Val Asn Asn Met Leu  Lys Gln Leu Gln Glu  Ala Glu Lys
    1460                1465                1470
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Glu Leu  Lys Arg Lys Gln Asp  Asp Ala Asp Gln Asp  Met Met Met
    1475                1480                1485

Ala Gly  Met Ala Ser Gln Ala  Ala Gln Glu Ala Glu  Ile Asn Ala
    1490                1495                1500

Arg Lys  Ala Lys Asn Ser Val  Thr Ser Leu Leu Ser  Ile Ile Asn
    1505                1510                1515

Asp Leu  Leu Glu Gln Leu Gly  Gln Leu Asp Thr Val  Asp Leu Asn
    1520                1525                1530

Lys Leu  Asn Glu Ile Glu Gly  Thr Leu Asn Lys Ala  Lys Asp Glu
    1535                1540                1545

Met Lys  Val Ser Asp Leu Asp  Arg Lys Val Ser Asp  Leu Glu Asn
    1550                1555                1560

Glu Ala  Lys Lys Gln Glu Ala  Ala Ile Met Asp Tyr  Asn Arg Asp
    1565                1570                1575

Ile Glu  Glu Ile Met Lys Asp  Ile Arg Asn Leu Glu  Asp Ile Arg
    1580                1585                1590

Lys Thr  Leu Pro Ser Gly Cys  Phe Asn Thr Pro Ser  Ile Glu Lys
    1595                1600                1605

Pro
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<210> SEQ ID NO 29
<211> LENGTH: 1786
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 29

```
Met Gly Leu Leu Gln Leu Leu Ala Phe Ser Phe Leu Ala Leu Cys Arg
1               5                   10                  15

Ala Arg Val Arg Ala Gln Glu Pro Glu Phe Ser Tyr Gly Cys Ala Glu
            20                  25                  30

Gly Ser Cys Tyr Pro Ala Thr Gly Asp Leu Leu Ile Gly Arg Ala Gln
        35                  40                  45

Lys Leu Ser Val Thr Ser Thr Cys Gly Leu His Lys Pro Glu Pro Tyr
    50                  55                  60

Cys Ile Val Ser His Leu Gln Glu Asp Lys Lys Cys Phe Ile Cys Asn
65                  70                  75                  80

Ser Gln Asp Pro Tyr His Glu Thr Leu Asn Pro Asp Ser His Leu Ile
                85                  90                  95

Glu Asn Val Val Thr Thr Phe Ala Pro Asn Arg Leu Lys Ile Trp Trp
            100                 105                 110

Gln Ser Glu Asn Gly Val Glu Asn Val Thr Ile Gln Leu Asp Leu Glu
        115                 120                 125

Ala Glu Phe His Phe Thr His Leu Ile Met Thr Phe Lys Thr Phe Arg
    130                 135                 140

Pro Ala Ala Met Leu Ile Glu Arg Ser Ser Asp Phe Gly Lys Thr Trp
145                 150                 155                 160

Gly Val Tyr Arg Tyr Phe Ala Tyr Asp Cys Glu Ala Ser Phe Pro Gly
                165                 170                 175

Ile Ser Thr Gly Pro Met Lys Lys Val Asp Asp Ile Ile Cys Asp Ser
            180                 185                 190

Arg Tyr Ser Asp Ile Glu Pro Ser Thr Glu Gly Glu Val Ile Phe Arg
        195                 200                 205
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Ala Leu Asp Pro Ala Phe Lys Ile Glu Asp Pro Tyr Ser Pro Arg Ile
    210                 215                 220

Gln Asn Leu Leu Lys Ile Thr Asn Leu Arg Ile Lys Phe Val Lys Leu
225                 230                 235                 240

His Thr Leu Gly Asp Asn Leu Leu Asp Ser Arg Met Glu Ile Arg Glu
                245                 250                 255

Lys Tyr Tyr Tyr Ala Val Tyr Asp Met Val Val Arg Gly Asn Cys Phe
            260                 265                 270

Cys Tyr Gly His Ala Ser Glu Cys Ala Pro Val Asp Gly Phe Asn Glu
        275                 280                 285

Glu Val Glu Gly Met Val His Gly His Cys Met Cys Arg His Asn Thr
    290                 295                 300

Lys Gly Leu Asn Cys Glu Leu Cys Met Asp Phe Tyr His Asp Leu Pro
305                 310                 315                 320

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

Cys Asn Glu His Ser Ile Ser Cys His Phe Asp Met Ala Val Tyr Leu
            340                 345                 350

Ala Thr Gly Asn Val Ser Gly Gly Val Cys Asp Asp Cys Gln His Asn
        355                 360                 365

Thr Met Gly Arg Asn Cys Glu Gln Cys Lys Pro Phe Tyr Tyr Gln His
    370                 375                 380

Pro Glu Arg Asp Ile Arg Asp Pro Asn Phe Cys Glu Arg Cys Thr Cys
385                 390                 395                 400

Asp Pro Ala Gly Ser Gln Asn Glu Gly Ile Cys Asp Ser Tyr Thr Asp
                405                 410                 415

Phe Ser Thr Gly Leu Ile Ala Gly Gln Cys Arg Cys Lys Leu Asn Val
            420                 425                 430

Glu Gly Glu His Cys Asp Val Cys Lys Glu Gly Phe Tyr Asp Leu Ser
        435                 440                 445

Ser Glu Asp Pro Phe Gly Cys Lys Ser Cys Ala Cys Asn Pro Leu Gly
    450                 455                 460

Thr Ile Pro Gly Gly Asn Pro Cys Asp Ser Glu Thr Gly His Cys Tyr
465                 470                 475                 480

Cys Lys Arg Leu Val Thr Gly Gln His Cys Asp Gln Cys Leu Pro Glu
                485                 490                 495

His Trp Gly Leu Ser Asn Asp Leu Asp Gly Cys Arg Pro Cys Asp Cys
            500                 505                 510

Asp Leu Gly Gly Ala Leu Asn Asn Ser Cys Phe Ala Glu Ser Gly Gln
        515                 520                 525

Cys Ser Cys Arg Pro His Met Ile Gly Arg Gln Cys Asn Glu Val Glu
    530                 535                 540

Pro Gly Tyr Tyr Phe Ala Thr Leu Asp His Tyr Leu Tyr Glu Ala Glu
545                 550                 555                 560

Glu Ala Asn Leu Gly Pro Gly Val Ser Ile Val Glu Arg Gln Tyr Ile
                565                 570                 575

Gln Asp Arg Ile Pro Ser Trp Thr Gly Ala Gly Phe Val Arg Val Pro
            580                 585                 590

Glu Gly Ala Tyr Leu Glu Phe Phe Ile Asp Asn Ile Pro Tyr Ser Met
        595                 600                 605

Glu Tyr Asp Ile Leu Ile Arg Tyr Glu Pro Gln Leu Pro Asp His Trp
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    610                 615                 620

Glu Lys Ala Val Ile Thr Val Gln Arg Pro Gly Arg Ile Pro Thr Ser
625                 630                 635                 640

Ser Arg Cys Gly Asn Thr Ile Pro Asp Asp Asp Asn Gln Val Val Ser
                645                 650                 655

Leu Ser Pro Gly Ser Arg Tyr Val Val Leu Pro Arg Pro Val Cys Phe
            660                 665                 670

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

Ser Ser Asp Ser Asp Val Glu Ser Pro Tyr Thr Leu Ile Asp Ser Leu
    690                 695                 700

Val Leu Met Pro Tyr Cys Lys Ser Leu Asp Ile Phe Thr Val Gly Gly
705                 710                 715                 720

Ser Gly Asp Gly Val Val Thr Asn Ser Ala Trp Glu Thr Phe Gln Arg
                725                 730                 735

Tyr Arg Cys Leu Glu Asn Ser Arg Ser Val Val Lys Thr Pro Met Thr
            740                 745                 750

Asp Val Cys Arg Asn Ile Ile Phe Ser Ile Ser Ala Leu Leu His Gln
        755                 760                 765

Thr Gly Leu Ala Cys Glu Cys Asp Pro Gln Gly Ser Leu Ser Ser Val
    770                 775                 780

Cys Asp Pro Asn Gly Gly Gln Cys Gln Cys Arg Pro Asn Val Val Gly
785                 790                 795                 800

Arg Thr Cys Asn Arg Cys Ala Pro Gly Thr Phe Gly Phe Gly Pro Ser
                805                 810                 815

Gly Cys Lys Pro Cys Glu Cys His Leu Gln Gly Ser Val Asn Ala Phe
            820                 825                 830

Cys Asn Pro Val Thr Gly Gln Cys His Cys Phe Gln Gly Val Tyr Ala
        835                 840                 845

Arg Gln Cys Asp Arg Cys Leu Pro Gly His Trp Gly Phe Pro Ser Cys
    850                 855                 860

Gln Pro Cys Gln Cys Asn Gly His Ala Asp Asp Cys Asp Pro Val Thr
865                 870                 875                 880

Gly Glu Cys Leu Asn Cys Gln Asp Tyr Thr Met Gly His Asn Cys Glu
                885                 890                 895

Arg Cys Leu Ala Gly Tyr Tyr Gly Asp Pro Ile Ile Gly Ser Gly Asp
            900                 905                 910

His Cys Arg Pro Cys Pro Cys Pro Asp Gly Pro Asp Ser Gly Arg Gln
        915                 920                 925

Phe Ala Arg Ser Cys Tyr Gln Asp Pro Val Thr Leu Gln Leu Ala Cys
    930                 935                 940

Val Cys Asp Pro Gly Tyr Ile Gly Ser Arg Cys Asp Asp Cys Ala Ser
945                 950                 955                 960

Gly Tyr Phe Gly Asn Pro Ser Glu Val Gly Gly Ser Cys Gln Pro Cys
                965                 970                 975

Gln Cys His Asn Asn Ile Asp Thr Thr Asp Pro Glu Ala Cys Asp Lys
            980                 985                 990

Glu Thr Gly Arg Cys Leu Lys Cys  Leu Tyr His Thr Glu  Gly Glu His
        995                 1000                1005

Cys Gln  Phe Cys Arg Phe Gly  Tyr Tyr Gly Asp Ala  Leu Arg Gln
    1010                1015                1020
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Asp Cys  Arg Lys Cys Val Cys  Asn Tyr Leu Gly Thr  Val Gln Glu
    1025                1030                1035

His Cys  Asn Gly Ser Asp Cys  Gln Cys Asp Lys Ala  Thr Gly Gln
    1040                1045                1050

Cys Leu  Cys Leu Pro Asn Val  Ile Gly Gln Asn Cys  Asp Arg Cys
    1055                1060                1065

Ala Pro  Asn Thr Trp Gln Leu  Ala Ser Gly Thr Gly  Cys Asp Pro
    1070                1075                1080

Cys Asn  Cys Asn Ala Ala His  Ser Phe Gly Pro Ser  Cys Asn Glu
    1085                1090                1095

Phe Thr  Gly Gln Cys Gln Cys  Met Pro Gly Phe Gly  Gly Arg Thr
    1100                1105                1110

Cys Ser  Glu Cys Gln Glu Leu  Phe Trp Gly Asp Pro  Asp Val Glu
    1115                1120                1125

Cys Arg  Ala Cys Asp Cys Asp  Pro Arg Gly Ile Glu  Thr Pro Gln
    1130                1135                1140

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

Gly Pro  Arg Cys Asp Lys Cys  Thr Arg Gly Tyr Ser  Gly Val Phe
    1160                1165                1170

Pro Asp  Cys Thr Pro Cys His  Gln Cys Phe Ala Leu  Trp Asp Val
    1175                1180                1185

Ile Ile  Ala Glu Leu Thr Asn  Arg Thr His Arg Phe  Leu Glu Lys
    1190                1195                1200

Ala Lys  Ala Leu Lys Ile Ser  Gly Val Ile Gly Pro  Tyr Arg Glu
    1205                1210                1215

Thr Val  Asp Ser Val Glu Arg  Lys Val Ser Glu Ile  Lys Asp Ile
    1220                1225                1230

Leu Ala  Gln Ser Pro Ala Ala  Glu Pro Leu Lys Asn  Ile Gly Asn
    1235                1240                1245

Leu Phe  Glu Glu Ala Glu Lys  Leu Ile Lys Asp Val  Thr Glu Met
    1250                1255                1260

Met Ala  Gln Val Glu Val Lys  Leu Ser Asp Thr Thr  Ser Gln Ser
    1265                1270                1275

Asn Ser  Thr Ala Lys Glu Leu  Asp Ser Leu Gln Thr  Glu Ala Glu
    1280                1285                1290

Ser Leu  Asp Asn Thr Val Lys  Glu Leu Ala Glu Gln  Leu Glu Phe
    1295                1300                1305

Ile Lys  Asn Ser Asp Ile Arg  Gly Ala Leu Asp Ser  Ile Thr Lys
    1310                1315                1320

Tyr Phe  Gln Met Ser Leu Glu  Ala Glu Glu Arg Val  Asn Ala Ser
    1325                1330                1335

Thr Thr  Glu Pro Asn Ser Thr  Val Glu Gln Ser Ala  Leu Met Arg
    1340                1345                1350

Asp Arg  Val Glu Asp Val Met  Met Glu Arg Glu Ser  Gln Phe Lys
    1355                1360                1365

Glu Lys  Gln Glu Glu Gln Ala  Arg Leu Leu Asp Glu  Leu Ala Gly
    1370                1375                1380

Lys Leu  Gln Ser Leu Asp Leu  Ser Ala Ala Ala Glu  Met Thr Cys
    1385                1390                1395
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Gly Thr  Pro Pro Gly Ala Ser  Cys Ser Glu Thr Glu  Cys Gly Gly
    1400                1405                1410

Pro Asn  Cys Arg Thr Asp Glu  Gly Glu Arg Lys Cys  Gly Gly Pro
    1415                1420                1425

Gly Cys  Gly Gly Leu Val Thr  Val Ala His Asn Ala  Trp Gln Lys
    1430                1435                1440

Ala Met  Asp Leu Asp Gln Asp  Val Leu Ser Ala Leu  Ala Glu Val
    1445                1450                1455

Glu Gln  Leu Ser Lys Met Val  Ser Glu Ala Lys Leu  Arg Ala Asp
    1460                1465                1470

Glu Ala  Lys Gln Ser Ala Glu  Asp Ile Leu Leu Lys  Thr Asn Ala
    1475                1480                1485

Thr Lys  Glu Lys Met Asp Lys  Ser Asn Glu Glu Leu  Arg Asn Leu
    1490                1495                1500

Ile Lys  Gln Ile Arg Asn Phe  Leu Thr Gln Asp Ser  Ala Asp Leu
    1505                1510                1515

Asp Ser  Ile Glu Ala Val Ala  Asn Glu Val Leu Lys  Met Glu Met
    1520                1525                1530

Pro Ser  Thr Pro Gln Gln Leu  Gln Asn Leu Thr Glu  Asp Ile Arg
    1535                1540                1545

Glu Arg  Val Glu Ser Leu Ser  Gln Val Glu Val Ile  Leu Gln His
    1550                1555                1560

Ser Ala  Ala Asp Ile Ala Arg  Ala Glu Met Leu Leu  Glu Glu Ala
    1565                1570                1575

Lys Arg  Ala Ser Lys Ser Ala  Thr Asp Val Lys Val  Thr Ala Asp
    1580                1585                1590

Met Val  Lys Glu Ala Leu Glu  Glu Ala Glu Lys Ala  Gln Val Ala
    1595                1600                1605

Ala Glu  Lys Ala Ile Lys Gln  Ala Asp Glu Asp Ile  Gln Gly Thr
    1610                1615                1620

Gln Asn  Leu Leu Thr Ser Ile  Glu Ser Glu Thr Ala  Ala Ser Glu
    1625                1630                1635

Glu Thr  Leu Phe Asn Ala Ser  Gln Arg Ile Ser Glu  Leu Glu Arg
    1640                1645                1650

Asn Val  Glu Glu Leu Lys Arg  Lys Ala Ala Gln Asn  Ser Gly Glu
    1655                1660                1665

Ala Glu  Tyr Ile Glu Lys Val  Val Tyr Thr Val Lys  Gln Ser Ala
    1670                1675                1680

Glu Asp  Val Lys Lys Thr Leu  Asp Gly Glu Leu Asp  Glu Lys Tyr
    1685                1690                1695

Lys Lys  Val Glu Asn Leu Ile  Ala Lys Lys Thr Glu  Glu Ser Ala
    1700                1705                1710

Asp Ala  Arg Arg Lys Ala Glu  Met Leu Gln Asn Glu  Ala Lys Thr
    1715                1720                1725

Leu Leu  Ala Gln Ala Asn Ser  Lys Leu Gln Leu Leu  Lys Asp Leu
    1730                1735                1740

Glu Arg  Lys Tyr Glu Asp Asn  Gln Arg Tyr Leu Glu  Asp Lys Ala
    1745                1750                1755

Gln Glu  Leu Ala Arg Leu Glu  Gly Glu Val Arg Ser  Leu Leu Lys
    1760                1765                1770

Asp Ile  Ser Gln Lys Val Ala  Val Tyr Ser Thr Cys  Leu
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1775 1780 1785

<210> SEQ ID NO 30
<211> LENGTH: 1487
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 30

Met Ile Arg Leu Gly Ala Pro Gln Thr Leu Val Leu Leu Thr Leu Leu
1 5 10 15

Val Ala Ala Val Leu Arg Cys Gln Gly Gln Asp Val Gln Glu Ala Gly
20 25 30

Ser Cys Val Gln Asp Gly Gln Arg Tyr Asn Asp Lys Asp Val Trp Lys
35 40 45

Pro Glu Pro Cys Arg Ile Cys Val Cys Asp Thr Gly Thr Val Leu Cys
50 55 60

Asp Asp Ile Ile Cys Glu Asp Val Lys Asp Cys Leu Ser Pro Glu Ile
65 70 75 80

Pro Phe Gly Glu Cys Cys Pro Ile Cys Pro Thr Asp Leu Ala Thr Ala
85 90 95

Ser Gly Gln Pro Gly Pro Lys Gly Gln Lys Gly Glu Pro Gly Asp Ile
100 105 110

Lys Asp Ile Val Gly Pro Lys Gly Pro Pro Gly Pro Gln Gly Pro Ala
115 120 125

Gly Glu Gln Gly Pro Arg Gly Asp Arg Gly Asp Lys Gly Glu Lys Gly
130 135 140

Ala Pro Gly Pro Arg Gly Arg Asp Gly Glu Pro Gly Thr Pro Gly Asn
145 150 155 160

Pro Gly Pro Pro Gly Pro Pro Gly Pro Pro Gly Pro Pro Gly Leu Gly
165 170 175

Gly Asn Phe Ala Ala Gln Met Ala Gly Gly Phe Asp Glu Lys Ala Gly
180 185 190

Gly Ala Gln Leu Gly Val Met Gln Gly Pro Met Gly Pro Met Gly Pro
195 200 205

Arg Gly Pro Pro Gly Pro Ala Gly Ala Pro Gly Pro Gln Gly Phe Gln
210 215 220

Gly Asn Pro Gly Glu Pro Gly Glu Pro Gly Val Ser Gly Pro Met Gly
225 230 235 240

Pro Arg Gly Pro Pro Gly Pro Pro Gly Lys Pro Gly Asp Asp Gly Glu
245 250 255

Ala Gly Lys Pro Gly Lys Ala Gly Glu Arg Gly Pro Pro Gly Pro Gln
260 265 270

Gly Ala Arg Gly Phe Pro Gly Thr Pro Gly Leu Pro Gly Val Lys Gly
275 280 285

His Arg Gly Tyr Pro Gly Leu Asp Gly Ala Lys Gly Glu Ala Gly Ala
290 295 300

Pro Gly Val Lys Gly Glu Ser Gly Ser Pro Gly Glu Asn Gly Ser Pro
305 310 315 320

Gly Pro Met Gly Pro Arg Gly Leu Pro Gly Glu Arg Gly Arg Thr Gly
325 330 335

Pro Ala Gly Ala Ala Gly Ala Arg Gly Asn Asp Gly Gln Pro Gly Pro
340 345 350

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Ala Gly Pro Pro Gly Pro Val Gly Pro Ala Gly Gly Pro Gly Phe Pro
        355                 360                 365

Gly Ala Pro Gly Ala Lys Gly Glu Ala Gly Pro Thr Gly Ala Arg Gly
    370                 375                 380

Pro Glu Gly Ala Gln Gly Pro Arg Gly Glu Pro Gly Thr Pro Gly Ser
385                 390                 395                 400

Pro Gly Pro Ala Gly Ala Ser Gly Asn Pro Gly Thr Asp Gly Ile Pro
                405                 410                 415

Gly Ala Lys Gly Ser Ala Gly Ala Pro Gly Ile Ala Gly Ala Pro Gly
            420                 425                 430

Phe Pro Gly Pro Arg Gly Pro Pro Gly Pro Gln Gly Ala Thr Gly Pro
        435                 440                 445

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

Gly Glu Gln Gly Pro Lys Gly Glu Pro Gly Pro Ala Gly Pro Gln Gly
465                 470                 475                 480

Ala Pro Gly Pro Ala Gly Glu Glu Gly Lys Arg Gly Ala Arg Gly Glu
                485                 490                 495

Pro Gly Gly Val Gly Pro Ile Gly Pro Pro Gly Glu Arg Gly Ala Pro
            500                 505                 510

Gly Asn Arg Gly Phe Pro Gly Gln Asp Gly Leu Ala Gly Pro Lys Gly
        515                 520                 525

Ala Pro Gly Glu Arg Gly Pro Ser Gly Leu Ala Gly Pro Lys Gly Ala
    530                 535                 540

Asn Gly Asp Pro Gly Arg Pro Gly Glu Pro Gly Leu Pro Gly Ala Arg
545                 550                 555                 560

Gly Leu Thr Gly Arg Pro Gly Asp Ala Gly Pro Gln Gly Lys Val Gly
                565                 570                 575

Pro Ser Gly Ala Pro Gly Glu Asp Gly Arg Pro Gly Pro Pro Gly Pro
            580                 585                 590

Gln Gly Ala Arg Gly Gln Pro Gly Val Met Gly Phe Pro Gly Pro Lys
        595                 600                 605

Gly Ala Asn Gly Glu Pro Gly Lys Ala Gly Glu Lys Gly Leu Pro Gly
    610                 615                 620

Ala Pro Gly Leu Arg Gly Leu Pro Gly Lys Asp Gly Glu Thr Gly Ala
625                 630                 635                 640

Ala Gly Pro Pro Gly Pro Ala Gly Pro Ala Gly Glu Arg Gly Glu Gln
                645                 650                 655

Gly Ala Pro Gly Pro Ser Gly Phe Gln Gly Leu Pro Gly Pro Pro Gly
            660                 665                 670

Pro Pro Gly Glu Gly Gly Lys Pro Gly Asp Gln Gly Val Pro Gly Glu
        675                 680                 685

Ala Gly Ala Pro Gly Leu Val Gly Pro Arg Gly Glu Arg Gly Phe Pro
    690                 695                 700

Gly Glu Arg Gly Ser Pro Gly Ala Gln Gly Leu Gln Gly Pro Arg Gly
705                 710                 715                 720

Leu Pro Gly Thr Pro Gly Thr Asp Gly Pro Lys Gly Ala Ser Gly Pro
                725                 730                 735

Ala Gly Pro Pro Gly Ala Gln Gly Pro Pro Gly Leu Gln Gly Met Pro
            740                 745                 750

Gly Glu Arg Gly Ala Ala Gly Ile Ala Gly Pro Lys Gly Asp Arg Gly
```

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        755                 760                 765

Asp Val Gly Glu Lys Gly Pro Glu Gly Ala Pro Gly Lys Asp Gly Gly
    770                 775                 780

Arg Gly Leu Thr Gly Pro Ile Gly Pro Pro Gly Pro Ala Gly Ala Asn
785                 790                 795                 800

Gly Glu Lys Gly Glu Val Gly Pro Pro Gly Pro Ala Gly Ser Ala Gly
                805                 810                 815

Ala Arg Gly Ala Pro Gly Glu Arg Gly Glu Thr Gly Pro Pro Gly Pro
            820                 825                 830

Ala Gly Phe Ala Gly Pro Pro Gly Ala Asp Gly Gln Pro Gly Ala Lys
        835                 840                 845

Gly Glu Gln Gly Glu Ala Gly Gln Lys Gly Asp Ala Gly Ala Pro Gly
    850                 855                 860

Pro Gln Gly Pro Ser Gly Ala Pro Gly Pro Gln Gly Pro Thr Gly Val
865                 870                 875                 880

Thr Gly Pro Lys Gly Ala Arg Gly Ala Gln Gly Pro Pro Gly Ala Thr
                885                 890                 895

Gly Phe Pro Gly Ala Ala Gly Arg Val Gly Pro Pro Gly Ser Asn Gly
            900                 905                 910

Asn Pro Gly Pro Pro Gly Pro Pro Gly Pro Ser Gly Lys Asp Gly Pro
        915                 920                 925

Lys Gly Ala Arg Gly Asp Ser Gly Pro Pro Gly Arg Ala Gly Glu Pro
    930                 935                 940

Gly Leu Gln Gly Pro Ala Gly Pro Pro Gly Glu Lys Gly Glu Pro Gly
945                 950                 955                 960

Asp Asp Gly Pro Ser Gly Ala Glu Gly Pro Pro Gly Pro Gln Gly Leu
                965                 970                 975

Ala Gly Gln Arg Gly Ile Val Gly Leu Pro Gly Gln Arg Gly Glu Arg
            980                 985                 990

Gly Phe Pro Gly Leu Pro Gly Pro  Ser Gly Glu Pro Gly  Lys Gln Gly
        995                 1000                1005

Ala Pro  Gly Ala Ser Gly Asp  Arg Gly Pro Pro Gly  Pro Val Gly
    1010                1015                1020

Pro Pro  Gly Leu Thr Gly Pro  Ala Gly Glu Pro Gly  Arg Glu Gly
    1025                1030                1035

Ser Pro  Gly Ala Asp Gly Pro  Pro Gly Arg Asp Gly  Ala Ala Gly
    1040                1045                1050

Val Lys  Gly Asp Arg Gly Glu  Thr Gly Ala Val Gly  Ala Pro Gly
    1055                1060                1065

Ala Pro  Gly Pro Pro Gly Ser  Pro Gly Pro Ala Gly  Pro Thr Gly
    1070                1075                1080

Lys Gln  Gly Asp Arg Gly Glu  Ala Gly Ala Gln Gly  Pro Met Gly
    1085                1090                1095

Pro Ser  Gly Pro Ala Gly Ala  Arg Gly Ile Gln Gly  Pro Gln Gly
    1100                1105                1110

Pro Arg  Gly Asp Lys Gly Glu  Ala Gly Glu Pro Gly  Glu Arg Gly
    1115                1120                1125

Leu Lys  Gly His Arg Gly Phe  Thr Gly Leu Gln Gly  Leu Pro Gly
    1130                1135                1140

Pro Pro  Gly Pro Ser Gly Asp  Gln Gly Ala Ser Gly  Pro Ala Gly
    1145                1150                1155
```

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```
Pro Ser  Gly Pro Arg Gly Pro  Pro Gly Pro Val Gly  Pro Ser Gly
    1160                 1165                 1170

Lys Asp  Gly Ala Asn Gly Ile  Pro Gly Pro Ile Gly  Pro Pro Gly
    1175                 1180                 1185

Pro Arg  Gly Arg Ser Gly Glu  Thr Gly Pro Ala Gly  Pro Pro Gly
    1190                 1195                 1200

Asn Pro  Gly Pro Pro Gly Pro  Pro Gly Pro Pro Gly  Pro Gly Ile
    1205                 1210                 1215

Asp Met  Ser Ala Phe Ala Gly  Leu Gly Pro Arg Glu  Lys Gly Pro
    1220                 1225                 1230

Asp Pro  Leu Gln Tyr Met Arg  Ala Asp Gln Ala Ala  Gly Gly Leu
    1235                 1240                 1245

Arg Gln  His Asp Ala Glu Val  Asp Ala Thr Leu Lys  Ser Leu Asn
    1250                 1255                 1260

Asn Gln  Ile Glu Ser Ile Arg  Ser Pro Glu Gly Ser  Arg Lys Asn
    1265                 1270                 1275

Pro Ala  Arg Thr Cys Arg Asp  Leu Lys Leu Cys His  Pro Glu Trp
    1280                 1285                 1290

Lys Ser  Gly Asp Tyr Trp Ile  Asp Pro Asn Gln Gly  Cys Thr Leu
    1295                 1300                 1305

Asp Ala  Met Lys Val Phe Cys  Asn Met Glu Thr Gly  Glu Thr Cys
    1310                 1315                 1320

Val Tyr  Pro Asn Pro Ala Asn  Val Pro Lys Lys Asn  Trp Trp Ser
    1325                 1330                 1335

Ser Lys  Ser Lys Glu Lys Lys  His Ile Trp Phe Gly  Glu Thr Ile
    1340                 1345                 1350

Asn Gly  Gly Phe His Phe Ser  Tyr Gly Asp Asp Asn  Leu Ala Pro
    1355                 1360                 1365

Asn Thr  Ala Asn Val Gln Met  Thr Phe Leu Arg Leu  Leu Ser Thr
    1370                 1375                 1380

Glu Gly  Ser Gln Asn Ile Thr  Tyr His Cys Lys Asn  Ser Ile Ala
    1385                 1390                 1395

Tyr Leu  Asp Glu Ala Ala Gly  Asn Leu Lys Lys Ala  Leu Leu Ile
    1400                 1405                 1410

Gln Gly  Ser Asn Asp Val Glu  Ile Arg Ala Glu Gly  Asn Ser Arg
    1415                 1420                 1425

Phe Thr  Tyr Thr Ala Leu Lys  Asp Gly Cys Thr Lys  His Thr Gly
    1430                 1435                 1440

Lys Trp  Gly Lys Thr Val Ile  Glu Tyr Arg Ser Gln  Lys Thr Ser
    1445                 1450                 1455

Arg Leu  Pro Ile Ile Asp Ile  Ala Pro Met Asp Ile  Gly Gly Pro
    1460                 1465                 1470

Glu Gln  Glu Phe Gly Val Asp  Ile Gly Pro Val Cys  Phe Leu
    1475                 1480                 1485
```

<210> SEQ ID NO 31
<211> LENGTH: 207
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 31

```
Met Ala Pro Phe Glu Pro Leu Ala Ser Gly Ile Leu Leu Leu Leu Trp
```

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```
1               5                   10                  15

Leu Ile Ala Pro Ser Arg Ala Cys Thr Cys Val Pro Pro His Pro Gln
            20                  25                  30

Thr Ala Phe Cys Asn Ser Asp Leu Val Ile Arg Ala Lys Phe Val Gly
        35                  40                  45

Thr Pro Glu Val Asn Gln Thr Thr Leu Tyr Gln Arg Tyr Glu Ile Lys
    50                  55                  60

Met Thr Lys Met Tyr Lys Gly Phe Gln Ala Leu Gly Asp Ala Ala Asp
65                  70                  75                  80

Ile Arg Phe Val Tyr Thr Pro Ala Met Glu Ser Val Cys Gly Tyr Phe
                85                  90                  95

His Arg Ser His Asn Arg Ser Glu Glu Phe Leu Ile Ala Gly Lys Leu
            100                 105                 110

Gln Asp Gly Leu Leu His Ile Thr Thr Cys Ser Phe Val Ala Pro Trp
        115                 120                 125

Asn Ser Leu Ser Leu Ala Gln Arg Arg Gly Phe Thr Lys Thr Tyr Thr
    130                 135                 140

Val Gly Cys Glu Glu Cys Thr Val Phe Pro Cys Leu Ser Ile Pro Cys
145                 150                 155                 160

Lys Leu Gln Ser Gly Thr His Cys Leu Trp Thr Asp Gln Leu Leu Gln
                165                 170                 175

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

Glu Pro Gly Leu Cys Thr Trp Gln Ser Leu Arg Ser Gln Ile Ala
        195                 200                 205


<210> SEQ ID NO 32
<211> LENGTH: 227
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 32

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

Leu Leu Thr Phe Tyr Val Ile Ser Gln Val Phe Glu Ile Lys Met Asp
            20                  25                  30

Ala Ser Leu Gly Asn Leu Phe Ala Arg Ser Ala Leu Asp Thr Ala Ala
        35                  40                  45

Arg Ser Thr Lys Pro Pro Arg Tyr Lys Cys Gly Ile Ser Lys Ala Cys
    50                  55                  60

Pro Glu Lys His Phe Ala Phe Lys Met Ala Ser Gly Ala Ala Asn Val
65                  70                  75                  80

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

Lys Asn Asn Val Gly Arg Gly Ile Asn Val Ala Leu Ala Asn Gly Lys
            100                 105                 110

Thr Gly Glu Val Leu Asp Thr Lys Tyr Phe Asp Met Trp Gly Gly Asp
        115                 120                 125

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

Val Leu Met Gly Thr Tyr Asp Asp Gly Ala Thr Lys Leu Asn Asp Glu
145                 150                 155                 160
```

-continued

```
Ala Arg Arg Leu Ile Ala Asp Leu Gly Ser Thr Ser Ile Thr Asn Leu
                165                 170                 175

Gly Phe Arg Asp Asn Trp Val Phe Cys Gly Gly Lys Gly Ile Lys Thr
            180                 185                 190

Lys Ser Pro Phe Glu Gln His Ile Lys Asn Asn Lys Asp Thr Asn Lys
        195                 200                 205

Tyr Glu Gly Trp Pro Glu Val Val Glu Met Glu Gly Cys Ile Pro Gln
    210                 215                 220

Lys Gln Asp
225
```

<210> SEQ ID NO 33
<211> LENGTH: 892
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 33

```
Met Asp His Tyr Asp Ser Gln Gln Thr Asn Asp Tyr Met Gln Pro Glu
1               5                   10                  15

Glu Asp Trp Asp Arg Asp Leu Leu Leu Asp Pro Ala Trp Glu Lys Gln
            20                  25                  30

Gln Arg Lys Thr Phe Thr Ala Trp Cys Asn Ser His Leu Arg Lys Ala
        35                  40                  45

Gly Thr Gln Ile Glu Asn Ile Glu Glu Asp Phe Arg Asp Gly Leu Lys
    50                  55                  60

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

Glu Arg Gly Lys Met Arg Val His Lys Ile Ser Asn Val Asn Lys Ala
                85                  90                  95

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

Glu Glu Ile Val Asp Gly Asn Val Lys Met Thr Leu Gly Met Ile Trp
        115                 120                 125

Thr Ile Ile Leu Arg Phe Ala Ile Gln Asp Ile Ser Val Glu Glu Thr
    130                 135                 140

Ser Ala Lys Glu Gly Leu Leu Leu Trp Cys Gln Arg Lys Thr Ala Pro
145                 150                 155                 160

Tyr Lys Asn Val Asn Ile Gln Asn Phe His Ile Ser Trp Lys Asp Gly
                165                 170                 175

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

Tyr Gly Lys Leu Arg Lys Asp Asp Pro Leu Thr Asn Leu Asn Thr Ala
        195                 200                 205

Phe Asp Val Ala Glu Lys Tyr Leu Asp Ile Pro Lys Met Leu Asp Ala
    210                 215                 220

Glu Asp Ile Val Gly Thr Ala Arg Pro Asp Glu Lys Ala Ile Met Thr
225                 230                 235                 240

Tyr Val Ser Ser Phe Tyr His Ala Phe Ser Gly Ala Gln Lys Ala Glu
                245                 250                 255

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

Glu Gln Leu Met Glu Asp Tyr Glu Lys Leu Ala Ser Asp Leu Leu Glu
        275                 280                 285
```

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```
Trp Ile Arg Arg Thr Ile Pro Trp Leu Glu Asn Arg Val Pro Glu Asn
    290                 295                 300

Thr Met His Ala Met Gln Gln Lys Leu Glu Asp Phe Arg Asp Tyr Arg
305                 310                 315                 320

Arg Leu His Lys Pro Pro Lys Val Gln Glu Lys Cys Gln Leu Glu Ile
                325                 330                 335

Asn Phe Asn Thr Leu Gln Thr Lys Leu Arg Leu Ser Asn Arg Pro Ala
            340                 345                 350

Phe Met Pro Ser Glu Gly Arg Met Val Ser Asp Ile Asn Asn Ala Trp
        355                 360                 365

Gly Cys Leu Glu Gln Val Glu Lys Gly Tyr Glu Glu Trp Leu Leu Asn
    370                 375                 380

Glu Ile Arg Arg Leu Glu Arg Leu Asp His Leu Ala Glu Lys Phe Arg
385                 390                 395                 400

Gln Lys Ala Ser Ile His Glu Ala Trp Thr Asp Gly Lys Glu Ala Met
                405                 410                 415

Leu Arg Gln Lys Asp Tyr Glu Thr Ala Thr Leu Ser Glu Ile Lys Ala
            420                 425                 430

Leu Leu Lys Lys His Glu Ala Phe Glu Ser Asp Leu Ala Ala His Gln
        435                 440                 445

Asp Arg Val Glu Gln Ile Ala Ala Ile Ala Gln Glu Leu Asn Glu Leu
    450                 455                 460

Asp Tyr Tyr Asp Ser Pro Ser Val Asn Ala Arg Cys Gln Lys Ile Cys
465                 470                 475                 480

Asp Gln Trp Asp Asn Leu Gly Ala Leu Thr Gln Lys Arg Arg Glu Ala
                485                 490                 495

Leu Glu Arg Thr Glu Lys Leu Leu Glu Thr Ile Asp Gln Leu Tyr Leu
            500                 505                 510

Glu Tyr Ala Lys Arg Ala Ala Pro Phe Asn Asn Trp Met Glu Gly Ala
        515                 520                 525

Met Glu Asp Leu Gln Asp Thr Phe Ile Val His Thr Ile Glu Glu Ile
    530                 535                 540

Gln Gly Leu Thr Thr Ala His Glu Gln Phe Lys Ala Thr Leu Pro Asp
545                 550                 555                 560

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

Lys Ile Val Gln Thr Tyr His Val Asn Met Ala Gly Thr Asn Pro Tyr
            580                 585                 590

Thr Thr Ile Thr Pro Gln Glu Ile Asn Gly Lys Trp Asp His Val Arg
        595                 600                 605

Gln Leu Val Pro Arg Arg Asp Gln Ala Leu Thr Glu Glu His Ala Arg
    610                 615                 620

Gln Gln His Asn Glu Arg Leu Arg Lys Gln Phe Gly Ala Gln Ala Asn
625                 630                 635                 640

Val Ile Gly Pro Trp Ile Gln Thr Lys Met Glu Glu Ile Gly Arg Ile
                645                 650                 655

Ser Ile Glu Met His Gly Thr Leu Glu Asp Gln Leu Ser His Leu Arg
            660                 665                 670

Gln Tyr Glu Lys Ser Ile Val Asn Tyr Lys Pro Lys Ile Asp Gln Leu
        675                 680                 685
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```
Glu Gly Asp His Gln Leu Ile Gln Glu Ala Leu Ile Phe Asp Asn Lys
    690                 695                 700

His Thr Asn Tyr Thr Met Glu His Ile Arg Val Gly Trp Glu Gln Leu
705                 710                 715                 720

Leu Thr Thr Ile Ala Arg Thr Ile Asn Glu Val Glu Asn Gln Ile Leu
                725                 730                 735

Thr Arg Asp Ala Lys Gly Ile Ser Gln Glu Gln Met Asn Glu Phe Arg
            740                 745                 750

Ala Ser Phe Asn His Phe Asp Arg Asp His Ser Gly Thr Leu Gly Pro
        755                 760                 765

Glu Glu Phe Lys Ala Cys Leu Ile Ser Leu Gly Tyr Asp Ile Gly Asn
    770                 775                 780

Asp Pro Gln Gly Glu Ala Glu Phe Ala Arg Ile Met Ser Ile Val Asp
785                 790                 795                 800

Pro Asn Arg Leu Gly Val Val Thr Phe Gln Ala Phe Ile Asp Phe Met
                805                 810                 815

Ser Arg Glu Thr Ala Asp Thr Asp Thr Ala Asp Gln Val Met Ala Ser
            820                 825                 830

Phe Lys Ile Leu Ala Gly Asp Lys Asn Tyr Ile Thr Met Asp Glu Leu
        835                 840                 845

Arg Arg Glu Leu Pro Pro Asp Gln Ala Glu Tyr Cys Ile Ala Arg Met
    850                 855                 860

Ala Pro Tyr Thr Gly Pro Asp Ser Val Pro Gly Ala Leu Asp Tyr Met
865                 870                 875                 880

Ser Phe Ser Thr Ala Leu Tyr Gly Glu Ser Asp Leu
                885                 890


<210> SEQ ID NO 34
<211> LENGTH: 286
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 34

Met Ala Asp Phe Asp Asp Arg Val Ser Asp Glu Glu Lys Val Arg Ile
1               5                   10                  15

Ala Ala Lys Phe Ile Thr His Ala Pro Pro Gly Glu Phe Asn Glu Val
            20                  25                  30

Phe Asn Asp Val Arg Leu Leu Leu Asn Asn Asp Asn Leu Leu Arg Glu
        35                  40                  45

Gly Ala Ala His Ala Phe Ala Gln Tyr Asn Met Asp Gln Phe Thr Pro
    50                  55                  60

Val Lys Ile Glu Gly Tyr Glu Asp Gln Val Leu Ile Thr Glu His Gly
65                  70                  75                  80

Asp Leu Gly Asn Ser Arg Phe Leu Asp Pro Arg Asn Lys Ile Ser Phe
                85                  90                  95

Lys Phe Asp His Leu Arg Lys Glu Ala Ser Asp Pro Gln Pro Glu Glu
            100                 105                 110

Ala Asp Gly Gly Leu Lys Ser Trp Arg Glu Ser Cys Asp Ser Ala Leu
        115                 120                 125

Arg Ala Tyr Val Lys Asp His Tyr Ser Asn Gly Phe Cys Thr Val Tyr
    130                 135                 140

Ala Lys Thr Ile Asp Gly Gln Gln Thr Ile Ile Ala Cys Ile Glu Ser
145                 150                 155                 160
```

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```
His Gln Phe Gln Pro Lys Asn Phe Trp Asn Gly Arg Trp Arg Ser Glu
                165                 170                 175

Trp Lys Phe Thr Ile Thr Pro Pro Thr Ala Gln Val Val Gly Val Leu
            180                 185                 190

Lys Ile Gln Val His Tyr Tyr Glu Asp Gly Asn Val Gln Leu Val Ser
        195                 200                 205

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

Ala Lys Glu Phe Ile Lys Ile Ile Glu Asn Ala Glu Asn Glu Tyr Gln
225                 230                 235                 240

Thr Ala Ile Ser Glu Asn Tyr Gln Thr Met Ser Asp Thr Thr Phe Lys
                245                 250                 255

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

Lys Ile Leu Ser Tyr Lys Ile Gly Lys Glu Met Gln Asn Ala
        275                 280                 285


<210> SEQ ID NO 35
<211> LENGTH: 967
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 35

Met Ala Lys Gly Phe Tyr Ile Ser Lys Ser Leu Gly Ile Leu Gly Ile
1               5                   10                  15

Leu Leu Gly Val Ala Ala Val Cys Thr Ile Ile Ala Leu Ser Val Val
            20                  25                  30

Tyr Ser Gln Glu Lys Asn Lys Asn Ala Asn Ser Ser Pro Val Ala Ser
        35                  40                  45

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

Leu Asp Gln Ser Lys Ala Trp Asn Arg Tyr Arg Leu Pro Asn Thr Leu
65                  70                  75                  80

Lys Pro Asp Ser Tyr Arg Val Thr Leu Arg Pro Tyr Leu Thr Pro Asn
                85                  90                  95

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

Cys Lys Glu Ala Thr Asp Val Ile Ile Ile His Ser Lys Lys Leu Asn
        115                 120                 125

Tyr Thr Leu Ser Gln Gly His Arg Val Val Leu Arg Gly Val Gly Gly
    130                 135                 140

Ser Gln Pro Pro Asp Ile Asp Lys Thr Glu Leu Val Glu Pro Thr Glu
145                 150                 155                 160

Tyr Leu Val Val His Leu Lys Gly Ser Leu Val Lys Asp Ser Gln Tyr
                165                 170                 175

Glu Met Asp Ser Glu Phe Glu Gly Glu Leu Ala Asp Asp Leu Ala Gly
            180                 185                 190

Phe Tyr Arg Ser Glu Tyr Met Glu Gly Asn Val Arg Lys Val Val Ala
        195                 200                 205

Thr Thr Gln Met Gln Ala Ala Asp Ala Arg Lys Ser Phe Pro Cys Phe
    210                 215                 220

Asp Glu Pro Ala Met Lys Ala Glu Phe Asn Ile Thr Leu Ile His Pro
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225                 230                 235                 240

Lys Asp Leu Thr Ala Leu Ser Asn Met Leu Pro Lys Gly Pro Ser Thr
                245                 250                 255

Pro Leu Pro Glu Asp Pro Asn Trp Asn Val Thr Glu Phe His Thr Thr
            260                 265                 270

Pro Lys Met Ser Thr Tyr Leu Leu Ala Phe Ile Val Ser Glu Phe Asp
        275                 280                 285

Tyr Val Glu Lys Gln Ala Ser Asn Gly Val Leu Ile Arg Ile Trp Ala
    290                 295                 300

Arg Pro Ser Ala Ile Ala Ala Gly His Gly Asp Tyr Ala Leu Asn Val
305                 310                 315                 320

Thr Gly Pro Ile Leu Asn Phe Phe Ala Gly His Tyr Asp Thr Pro Tyr
                325                 330                 335

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

Ala Met Glu Asn Trp Gly Leu Val Thr Tyr Arg Glu Asn Ser Leu Leu
        355                 360                 365

Phe Asp Pro Leu Ser Ser Ser Ser Ser Asn Lys Glu Arg Val Val Thr
    370                 375                 380

Val Ile Ala His Glu Leu Ala His Gln Trp Phe Gly Asn Leu Val Thr
385                 390                 395                 400

Ile Glu Trp Trp Asn Asp Leu Trp Leu Asn Glu Gly Phe Ala Ser Tyr
                405                 410                 415

Val Glu Tyr Leu Gly Ala Asp Tyr Ala Glu Pro Thr Trp Asn Leu Lys
            420                 425                 430

Asp Leu Met Val Leu Asn Asp Val Tyr Arg Val Met Ala Val Asp Ala
        435                 440                 445

Leu Ala Ser Ser His Pro Leu Ser Thr Pro Ala Ser Glu Ile Asn Thr
    450                 455                 460

Pro Ala Gln Ile Ser Glu Leu Phe Asp Ala Ile Ser Tyr Ser Lys Gly
465                 470                 475                 480

Ala Ser Val Leu Arg Met Leu Ser Ser Phe Leu Ser Glu Asp Val Phe
                485                 490                 495

Lys Gln Gly Leu Ala Ser Tyr Leu His Thr Phe Ala Tyr Gln Asn Thr
            500                 505                 510

Ile Tyr Leu Asn Leu Trp Asp His Leu Gln Glu Ala Val Asn Asn Arg
        515                 520                 525

Ser Ile Gln Leu Pro Thr Thr Val Arg Asp Ile Met Asn Arg Trp Thr
    530                 535                 540

Leu Gln Met Gly Phe Pro Val Ile Thr Val Asp Thr Ser Thr Gly Thr
545                 550                 555                 560

Leu Ser Gln Glu His Phe Leu Leu Asp Pro Asp Ser Asn Val Thr Arg
                565                 570                 575

Pro Ser Glu Phe Asn Tyr Val Trp Ile Val Pro Ile Thr Ser Ile Arg
            580                 585                 590

Asp Gly Arg Gln Gln Gln Asp Tyr Trp Leu Ile Asp Val Arg Ala Gln
        595                 600                 605

Asn Asp Leu Phe Ser Thr Ser Gly Asn Glu Trp Val Leu Leu Asn Leu
    610                 615                 620

Asn Val Thr Gly Tyr Tyr Arg Val Asn Tyr Asp Glu Glu Asn Trp Arg
625                 630                 635                 640
```

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```
Lys Ile Gln Thr Gln Leu Gln Arg Asp His Ser Ala Ile Pro Val Ile
                645                 650                 655

Asn Arg Ala Gln Ile Ile Asn Asp Ala Phe Asn Leu Ala Ser Ala His
            660                 665                 670

Lys Val Pro Val Thr Leu Ala Leu Asn Asn Thr Leu Phe Leu Ile Glu
        675                 680                 685

Glu Arg Gln Tyr Met Pro Trp Glu Ala Ala Leu Ser Ser Leu Ser Tyr
    690                 695                 700

Phe Lys Leu Met Phe Asp Arg Ser Glu Val Tyr Gly Pro Met Lys Asn
705                 710                 715                 720

Tyr Leu Lys Lys Gln Val Thr Pro Leu Phe Ile His Phe Arg Asn Asn
                725                 730                 735

Thr Asn Asn Trp Arg Glu Ile Pro Glu Asn Leu Met Asp Gln Tyr Ser
            740                 745                 750

Glu Val Asn Ala Ile Ser Thr Ala Cys Ser Asn Gly Val Pro Glu Cys
        755                 760                 765

Glu Glu Met Val Ser Gly Leu Phe Lys Gln Trp Met Glu Asn Pro Asn
    770                 775                 780

Asn Asn Pro Ile His Pro Asn Leu Arg Ser Thr Val Tyr Cys Asn Ala
785                 790                 795                 800

Ile Ala Gln Gly Gly Glu Glu Glu Trp Asp Phe Ala Trp Glu Gln Phe
                805                 810                 815

Arg Asn Ala Thr Leu Val Asn Glu Ala Asp Lys Leu Arg Ala Ala Leu
            820                 825                 830

Ala Cys Ser Lys Glu Leu Trp Ile Leu Asn Arg Tyr Leu Ser Tyr Thr
        835                 840                 845

Leu Asn Pro Asp Leu Ile Arg Lys Gln Asp Ala Thr Ser Thr Ile Ile
    850                 855                 860

Ser Ile Thr Asn Asn Val Ile Gly Gln Gly Leu Val Trp Asp Phe Val
865                 870                 875                 880

Gln Ser Asn Trp Lys Lys Leu Phe Asn Asp Tyr Gly Gly Gly Ser Phe
                885                 890                 895

Ser Phe Ser Asn Leu Ile Gln Ala Val Thr Arg Arg Phe Ser Thr Glu
            900                 905                 910

Tyr Glu Leu Gln Gln Leu Glu Gln Phe Lys Lys Asp Asn Glu Glu Thr
        915                 920                 925

Gly Phe Gly Ser Gly Thr Arg Ala Leu Glu Gln Ala Leu Glu Lys Thr
    930                 935                 940

Lys Ala Asn Ile Lys Trp Val Lys Glu Asn Lys Glu Val Val Leu Gln
945                 950                 955                 960

Trp Phe Thr Glu Asn Ser Lys
                965


<210> SEQ ID NO 36
<211> LENGTH: 259
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 36

Met Ser Glu Val Pro Val Ala Arg Val Trp Leu Val Leu Leu Leu Leu
1               5                   10                  15

Thr Val Gln Val Gly Val Thr Ala Gly Ala Pro Trp Gln Cys Ala Pro
```

-continued

```
            20                  25                  30

Cys Ser Ala Glu Lys Leu Ala Leu Cys Pro Pro Val Ser Ala Ser Cys
        35                  40                  45

Ser Glu Val Thr Arg Ser Ala Gly Cys Gly Cys Cys Pro Met Cys Ala
    50                  55                  60

Leu Pro Leu Gly Ala Ala Cys Gly Val Ala Thr Ala Arg Cys Ala Arg
65                  70                  75                  80

Gly Leu Ser Cys Arg Ala Leu Pro Gly Glu Gln Gln Pro Leu His Ala
                85                  90                  95

Leu Thr Arg Gly Gln Gly Ala Cys Val Gln Glu Ser Asp Ala Ser Ala
            100                 105                 110

Pro His Ala Ala Glu Ala Gly Ser Pro Glu Ser Pro Glu Ser Thr Glu
        115                 120                 125

Ile Thr Glu Glu Glu Leu Leu Asp Asn Phe His Leu Met Ala Pro Ser
    130                 135                 140

Glu Glu Asp His Ser Ile Leu Trp Asp Ala Ile Ser Thr Tyr Asp Gly
145                 150                 155                 160

Ser Lys Ala Leu His Val Thr Asn Ile Lys Lys Trp Lys Glu Pro Cys
                165                 170                 175

Arg Ile Glu Leu Tyr Arg Val Val Glu Ser Leu Ala Lys Ala Gln Glu
            180                 185                 190

Thr Ser Gly Glu Glu Ile Ser Lys Phe Tyr Leu Pro Asn Cys Asn Lys
        195                 200                 205

Asn Gly Phe Tyr His Ser Arg Gln Cys Glu Thr Ser Met Asp Gly Glu
    210                 215                 220

Ala Gly Leu Cys Trp Cys Val Tyr Pro Trp Asn Gly Lys Arg Ile Pro
225                 230                 235                 240

Gly Ser Pro Glu Ile Arg Gly Asp Pro Asn Cys Gln Ile Tyr Phe Asn
                245                 250                 255

Val Gln Asn


<210> SEQ ID NO 37
<211> LENGTH: 442
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 37

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

Ala Ala Ala Ala Pro Pro Gly Leu Arg Leu Arg Leu Leu Leu Leu Leu
            20                  25                  30

Phe Ser Ala Ala Ala Leu Ile Pro Thr Gly Asp Gly Gln Asn Leu Phe
        35                  40                  45

Thr Lys Asp Val Thr Val Ile Glu Gly Glu Val Ala Thr Ile Ser Cys
    50                  55                  60

Gln Val Asn Lys Ser Asp Asp Ser Val Ile Gln Leu Leu Asn Pro Asn
65                  70                  75                  80

Arg Gln Thr Ile Tyr Phe Arg Asp Phe Arg Pro Leu Lys Asp Ser Arg
                85                  90                  95

Phe Gln Leu Leu Asn Phe Ser Ser Ser Glu Leu Lys Val Ser Leu Thr
            100                 105                 110

Asn Val Ser Ile Ser Asp Glu Gly Arg Tyr Phe Cys Gln Leu Tyr Thr
```

-continued

```
        115                 120                 125

Asp Pro Pro Gln Glu Ser Tyr Thr Thr Ile Thr Val Leu Val Pro Pro
    130                 135                 140

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

Glu Ile Glu Val Asn Cys Thr Ala Met Ala Ser Lys Pro Ala Thr Thr
                165                 170                 175

Ile Arg Trp Phe Lys Gly Asn Thr Glu Leu Lys Gly Lys Ser Glu Val
            180                 185                 190

Glu Glu Trp Ser Asp Met Tyr Thr Val Thr Ser Gln Leu Met Leu Lys
        195                 200                 205

Val His Lys Glu Asp Asp Gly Val Pro Val Ile Cys Gln Val Glu His
    210                 215                 220

Pro Ala Val Thr Gly Asn Leu Gln Thr Gln Arg Tyr Leu Glu Val Gln
225                 230                 235                 240

Tyr Lys Pro Gln Val His Ile Gln Met Thr Tyr Pro Leu Gln Gly Leu
                245                 250                 255

Thr Arg Glu Gly Asp Ala Leu Glu Leu Thr Cys Glu Ala Ile Gly Lys
            260                 265                 270

Pro Gln Pro Val Met Val Thr Trp Val Arg Val Asp Asp Glu Met Pro
        275                 280                 285

Gln His Ala Val Leu Ser Gly Pro Asn Leu Phe Ile Asn Asn Leu Asn
    290                 295                 300

Lys Thr Asp Asn Gly Thr Tyr Arg Cys Glu Ala Ser Asn Ile Val Gly
305                 310                 315                 320

Lys Ala His Ser Asp Tyr Met Leu Tyr Val Tyr Asp Pro Pro Thr Thr
                325                 330                 335

Ile Pro Pro Pro Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr Thr
            340                 345                 350

Thr Ile Leu Thr Ile Ile Thr Asp Ser Arg Ala Gly Glu Glu Gly Ser
        355                 360                 365

Ile Arg Ala Val Asp His Ala Val Ile Gly Gly Val Val Ala Val Val
    370                 375                 380

Val Phe Ala Met Leu Cys Leu Leu Ile Ile Leu Gly Arg Tyr Phe Ala
385                 390                 395                 400

Arg His Lys Gly Thr Tyr Phe Thr His Glu Ala Lys Gly Ala Asp Asp
                405                 410                 415

Ala Ala Asp Ala Asp Thr Ala Ile Ile Asn Ala Glu Gly Gly Gln Asn
            420                 425                 430

Asn Ser Glu Glu Lys Lys Glu Tyr Phe Ile
        435                 440


<210> SEQ ID NO 38
<211> LENGTH: 339
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 38

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

Ala Arg Ser Arg Pro Ser Phe His Pro Leu Ser Asp Glu Leu Val Asn
            20                  25                  30
```

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```
Tyr Val Asn Lys Arg Asn Thr Thr Trp Gln Ala Gly His Asn Phe Tyr
        35                  40                  45

Asn Val Asp Met Ser Tyr Leu Lys Arg Leu Cys Gly Thr Phe Leu Gly
    50                  55                  60

Gly Pro Lys Pro Pro Gln Arg Val Met Phe Thr Glu Asp Leu Lys Leu
65                  70                  75                  80

Pro Ala Ser Phe Asp Ala Arg Glu Gln Trp Pro Gln Cys Pro Thr Ile
                85                  90                  95

Lys Glu Ile Arg Asp Gln Gly Ser Cys Gly Ser Cys Trp Ala Phe Gly
            100                 105                 110

Ala Val Glu Ala Ile Ser Asp Arg Ile Cys Ile His Thr Asn Ala His
        115                 120                 125

Val Ser Val Glu Val Ser Ala Glu Asp Leu Leu Thr Cys Cys Gly Ser
    130                 135                 140

Met Cys Gly Asp Gly Cys Asn Gly Gly Tyr Pro Ala Glu Ala Trp Asn
145                 150                 155                 160

Phe Trp Thr Arg Lys Gly Leu Val Ser Gly Gly Leu Tyr Glu Ser His
                165                 170                 175

Val Gly Cys Arg Pro Tyr Ser Ile Pro Pro Cys Glu His His Val Asn
            180                 185                 190

Gly Ser Arg Pro Pro Cys Thr Gly Glu Gly Asp Thr Pro Lys Cys Ser
        195                 200                 205

Lys Ile Cys Glu Pro Gly Tyr Ser Pro Thr Tyr Lys Gln Asp Lys His
    210                 215                 220

Tyr Gly Tyr Asn Ser Tyr Ser Val Ser Asn Ser Glu Lys Asp Ile Met
225                 230                 235                 240

Ala Glu Ile Tyr Lys Asn Gly Pro Val Glu Gly Ala Phe Ser Val Tyr
                245                 250                 255

Ser Asp Phe Leu Leu Tyr Lys Ser Gly Val Tyr Gln His Val Thr Gly
            260                 265                 270

Glu Met Met Gly Gly His Ala Ile Arg Ile Leu Gly Trp Gly Val Glu
        275                 280                 285

Asn Gly Thr Pro Tyr Trp Leu Val Ala Asn Ser Trp Asn Thr Asp Trp
    290                 295                 300

Gly Asp Asn Gly Phe Phe Lys Ile Leu Arg Gly Gln Asp His Cys Gly
305                 310                 315                 320

Ile Glu Ser Glu Val Val Ala Gly Ile Pro Arg Thr Asp Gln Tyr Trp
                325                 330                 335

Glu Lys Ile


<210> SEQ ID NO 39
<211> LENGTH: 718
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 39

Met Cys Ala Ser Val Lys Tyr Asn Ile Arg Gly Pro Ala Leu Ile Pro
1               5                   10                  15

Arg Met Lys Thr Lys His Arg Ile Tyr Tyr Ile Thr Leu Phe Ser Ile
            20                  25                  30

Val Leu Leu Gly Leu Ile Ala Thr Gly Met Phe Gln Phe Trp Pro His
        35                  40                  45
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Ser Ile Glu Ser Ser Asn Asp Trp Asn Val Glu Lys Arg Ser Ile Arg
    50                  55                  60

Asp Val Pro Val Val Arg Leu Pro Ala Asp Ser Pro Ile Pro Glu Arg
65                  70                  75                  80

Gly Asp Leu Ser Cys Arg Met His Thr Cys Phe Asp Val Tyr Arg Cys
                85                  90                  95

Gly Phe Asn Pro Lys Asn Lys Ile Lys Val Tyr Ile Tyr Ala Leu Lys
            100                 105                 110

Lys Tyr Val Asp Asp Phe Gly Val Ser Val Ser Asn Thr Ile Ser Arg
        115                 120                 125

Glu Tyr Asn Glu Leu Leu Met Ala Ile Ser Asp Ser Asp Tyr Tyr Thr
    130                 135                 140

Asp Asp Ile Asn Arg Ala Cys Leu Phe Val Pro Ser Ile Asp Val Leu
145                 150                 155                 160

Asn Gln Asn Thr Leu Arg Ile Lys Glu Thr Ala Gln Ala Met Ala Gln
                165                 170                 175

Leu Ser Arg Trp Asp Arg Gly Thr Asn His Leu Leu Phe Asn Met Leu
            180                 185                 190

Pro Gly Gly Pro Pro Asp Tyr Asn Thr Ala Leu Asp Val Pro Arg Asp
        195                 200                 205

Arg Ala Leu Leu Ala Gly Gly Gly Phe Ser Thr Trp Thr Tyr Arg Gln
    210                 215                 220

Gly Tyr Asp Val Ser Ile Pro Val Tyr Ser Pro Leu Ser Ala Glu Val
225                 230                 235                 240

Asp Leu Pro Glu Lys Gly Pro Gly Pro Arg Gln Tyr Phe Leu Leu Ser
                245                 250                 255

Ser Gln Val Gly Leu His Pro Glu Tyr Arg Glu Asp Leu Glu Ala Leu
            260                 265                 270

Gln Val Lys His Gly Glu Ser Val Leu Val Leu Asp Lys Cys Thr Asn
        275                 280                 285

Leu Ser Glu Gly Val Leu Ser Val Arg Lys Arg Cys His Lys His Gln
    290                 295                 300

Val Phe Asp Tyr Pro Gln Val Leu Gln Glu Ala Thr Phe Cys Val Val
305                 310                 315                 320

Leu Arg Gly Ala Arg Leu Gly Gln Ala Val Leu Ser Asp Val Leu Gln
                325                 330                 335

Ala Gly Cys Val Pro Val Val Ile Ala Asp Ser Tyr Ile Leu Pro Phe
            340                 345                 350

Ser Glu Val Leu Asp Trp Lys Arg Ala Ser Val Val Val Pro Glu Glu
        355                 360                 365

Lys Met Ser Asp Val Tyr Ser Ile Leu Gln Ser Ile Pro Gln Arg Gln
    370                 375                 380

Ile Glu Glu Met Gln Arg Gln Ala Arg Trp Phe Trp Glu Ala Tyr Phe
385                 390                 395                 400

Gln Ser Ile Lys Ala Ile Ala Leu Ala Thr Leu Gln Ile Ile Asn Asp
                405                 410                 415

Arg Ile Tyr Pro Tyr Ala Ala Ile Ser Tyr Glu Glu Trp Asn Asp Pro
            420                 425                 430

Pro Ala Val Lys Trp Gly Ser Val Ser Asn Pro Leu Phe Leu Pro Leu
        435                 440                 445

Ile Pro Pro Gln Ser Gln Gly Phe Thr Ala Ile Val Leu Thr Tyr Asp
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    450                 455                 460

Arg Val Glu Ser Leu Phe Arg Val Ile Thr Glu Val Ser Lys Val Pro
465                 470                 475                 480

Ser Leu Ser Lys Leu Leu Val Val Trp Asn Asn Gln Asn Lys Asn Pro
                485                 490                 495

Pro Glu Asp Ser Leu Trp Pro Lys Ile Arg Val Pro Leu Lys Val Val
            500                 505                 510

Arg Thr Ala Glu Asn Lys Leu Ser Asn Arg Phe Phe Pro Tyr Asp Glu
        515                 520                 525

Ile Glu Thr Glu Ala Val Leu Ala Ile Asp Asp Asp Ile Ile Met Leu
    530                 535                 540

Thr Ser Asp Glu Leu Gln Phe Gly Tyr Glu Val Trp Arg Glu Phe Pro
545                 550                 555                 560

Asp Arg Leu Val Gly Tyr Pro Gly Arg Leu His Leu Trp Asp His Glu
                565                 570                 575

Met Asn Lys Trp Lys Tyr Glu Ser Glu Trp Thr Asn Glu Val Ser Met
            580                 585                 590

Val Leu Thr Gly Ala Ala Phe Tyr His Lys Tyr Phe Asn Tyr Leu Tyr
        595                 600                 605

Thr Tyr Lys Met Pro Gly Asp Ile Lys Asn Trp Val Asp Ala His Met
    610                 615                 620

Asn Cys Glu Asp Ile Ala Met Asn Phe Leu Val Ala Asn Val Thr Gly
625                 630                 635                 640

Lys Ala Val Ile Lys Val Thr Pro Arg Lys Lys Phe Lys Cys Pro Glu
                645                 650                 655

Cys Thr Ala Ile Asp Gly Leu Ser Leu Asp Gln Thr His Met Val Glu
            660                 665                 670

Arg Ser Glu Cys Ile Asn Lys Phe Ala Ser Val Phe Gly Thr Met Pro
        675                 680                 685

Leu Lys Val Val Glu His Arg Ala Asp Pro Val Leu Tyr Lys Asp Asp
    690                 695                 700

Phe Pro Glu Lys Leu Lys Ser Phe Pro Asn Ile Gly Ser Leu
705                 710                 715


<210> SEQ ID NO 40
<211> LENGTH: 412
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 40

Met Gln Pro Ser Ser Leu Leu Pro Leu Ala Leu Cys Leu Leu Ala Ala
1               5                   10                  15

Pro Ala Ser Ala Leu Val Arg Ile Pro Leu His Lys Phe Thr Ser Ile
            20                  25                  30

Arg Arg Thr Met Ser Glu Val Gly Gly Ser Val Glu Asp Leu Ile Ala
        35                  40                  45

Lys Gly Pro Val Ser Lys Tyr Ser Gln Ala Val Pro Ala Val Thr Glu
    50                  55                  60

Gly Pro Ile Pro Glu Val Leu Lys Asn Tyr Met Asp Ala Gln Tyr Tyr
65                  70                  75                  80

Gly Glu Ile Gly Ile Gly Thr Pro Pro Gln Cys Phe Thr Val Val Phe
                85                  90                  95
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Asp Thr Gly Ser Ser Asn Leu Trp Val Pro Ser Ile His Cys Lys Leu
            100                 105                 110

Leu Asp Ile Ala Cys Trp Ile His His Lys Tyr Asn Ser Asp Lys Ser
        115                 120                 125

Ser Thr Tyr Val Lys Asn Gly Thr Ser Phe Asp Ile His Tyr Gly Ser
    130                 135                 140

Gly Ser Leu Ser Gly Tyr Leu Ser Gln Asp Thr Val Ser Val Pro Cys
145                 150                 155                 160

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

Gln Val Phe Gly Glu Ala Thr Lys Gln Pro Gly Ile Thr Phe Ile Ala
            180                 185                 190

Ala Lys Phe Asp Gly Ile Leu Gly Met Ala Tyr Pro Arg Ile Ser Val
        195                 200                 205

Asn Asn Val Leu Pro Val Phe Asp Asn Leu Met Gln Gln Lys Leu Val
    210                 215                 220

Asp Gln Asn Ile Phe Ser Phe Tyr Leu Ser Arg Asp Pro Asp Ala Gln
225                 230                 235                 240

Pro Gly Gly Glu Leu Met Leu Gly Gly Thr Asp Ser Lys Tyr Tyr Lys
                245                 250                 255

Gly Ser Leu Ser Tyr Leu Asn Val Thr Arg Lys Ala Tyr Trp Gln Val
            260                 265                 270

His Leu Asp Gln Val Glu Val Ala Ser Gly Leu Thr Leu Cys Lys Glu
        275                 280                 285

Gly Cys Glu Ala Ile Val Asp Thr Gly Thr Ser Leu Met Val Gly Pro
    290                 295                 300

Val Asp Glu Val Arg Glu Leu Gln Lys Ala Ile Gly Ala Val Pro Leu
305                 310                 315                 320

Ile Gln Gly Glu Tyr Met Ile Pro Cys Glu Lys Val Ser Thr Leu Pro
                325                 330                 335

Ala Ile Thr Leu Lys Leu Gly Gly Lys Gly Tyr Lys Leu Ser Pro Glu
            340                 345                 350

Asp Tyr Thr Leu Lys Val Ser Gln Ala Gly Lys Thr Leu Cys Leu Ser
        355                 360                 365

Gly Phe Met Gly Met Asp Ile Pro Pro Pro Ser Gly Pro Leu Trp Ile
    370                 375                 380

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

Asn Asn Arg Val Gly Phe Ala Glu Ala Ala Arg Leu
                405                 410


<210> SEQ ID NO 41
<211> LENGTH: 2321
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 41

Met Gly Pro Gly Ala Arg Gly Arg Arg Arg Arg Arg Arg Pro Met Ser
1               5                   10                  15

Pro Pro Pro Pro Pro Pro Pro Val Arg Ala Leu Pro Leu Leu Leu Leu
            20                  25                  30

Leu Ala Gly Pro Gly Ala Ala Ala Pro Pro Cys Leu Asp Gly Ser Pro
        35                  40                  45
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Cys Ala Asn Gly Gly Arg Cys Thr Gln Leu Pro Ser Arg Glu Ala Ala
    50                  55                  60

Cys Leu Cys Pro Pro Gly Trp Val Gly Glu Arg Cys Gln Leu Glu Asp
65                  70                  75                  80

Pro Cys His Ser Gly Pro Cys Ala Gly Arg Gly Val Cys Gln Ser Ser
                85                  90                  95

Val Val Ala Gly Thr Ala Arg Phe Ser Cys Arg Cys Pro Arg Gly Phe
            100                 105                 110

Arg Gly Pro Asp Cys Ser Leu Pro Asp Pro Cys Leu Ser Ser Pro Cys
        115                 120                 125

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

Ser Cys Pro Pro Gly Tyr Gln Gly Arg Ser Cys Arg Ser Asp Val Asp
145                 150                 155                 160

Glu Cys Arg Val Gly Glu Pro Cys Arg His Gly Gly Thr Cys Leu Asn
                165                 170                 175

Thr Pro Gly Ser Phe Arg Cys Gln Cys Pro Ala Gly Tyr Thr Gly Pro
            180                 185                 190

Leu Cys Glu Asn Pro Ala Val Pro Cys Ala Pro Ser Pro Cys Arg Asn
        195                 200                 205

Gly Gly Thr Cys Arg Gln Ser Gly Asp Leu Thr Tyr Asp Cys Ala Cys
    210                 215                 220

Leu Pro Gly Phe Glu Gly Gln Asn Cys Glu Val Asn Val Asp Asp Cys
225                 230                 235                 240

Pro Gly His Arg Cys Leu Asn Gly Gly Thr Cys Val Asp Gly Val Asn
                245                 250                 255

Thr Tyr Asn Cys Gln Cys Pro Pro Glu Trp Thr Gly Gln Phe Cys Thr
            260                 265                 270

Glu Asp Val Asp Glu Cys Gln Leu Gln Pro Asn Ala Cys His Asn Gly
        275                 280                 285

Gly Thr Cys Phe Asn Thr Leu Gly Gly His Ser Cys Val Cys Val Asn
    290                 295                 300

Gly Trp Thr Gly Glu Ser Cys Ser Gln Asn Ile Asp Asp Cys Ala Thr
305                 310                 315                 320

Ala Val Cys Phe His Gly Ala Thr Cys His Asp Arg Val Ala Ser Phe
                325                 330                 335

Tyr Cys Ala Cys Pro Met Gly Lys Thr Gly Leu Leu Cys His Leu Asp
            340                 345                 350

Asp Ala Cys Val Ser Asn Pro Cys His Glu Asp Ala Ile Cys Asp Thr
        355                 360                 365

Asn Pro Val Asn Gly Arg Ala Ile Cys Thr Cys Pro Pro Gly Phe Thr
    370                 375                 380

Gly Gly Ala Cys Asp Gln Asp Val Asp Glu Cys Ser Ile Gly Ala Asn
385                 390                 395                 400

Pro Cys Glu His Leu Gly Arg Cys Val Asn Thr Gln Gly Ser Phe Leu
                405                 410                 415

Cys Gln Cys Gly Arg Gly Tyr Thr Gly Pro Arg Cys Glu Thr Asp Val
            420                 425                 430

Asn Glu Cys Leu Ser Gly Pro Cys Arg Asn Gln Ala Thr Cys Leu Asp
        435                 440                 445
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Arg Ile Gly Gln Phe Thr Cys Ile Cys Met Ala Gly Phe Thr Gly Thr
    450                 455                 460

Tyr Cys Glu Val Asp Ile Asp Glu Cys Gln Ser Ser Pro Cys Val Asn
465                 470                 475                 480

Gly Gly Val Cys Lys Asp Arg Val Asn Gly Phe Ser Cys Thr Cys Pro
                485                 490                 495

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

Ser Thr Pro Cys Arg Asn Gly Ala Lys Cys Val Asp Gln Pro Asp Gly
        515                 520                 525

Tyr Glu Cys Arg Cys Ala Glu Gly Phe Glu Gly Thr Leu Cys Asp Arg
    530                 535                 540

Asn Val Asp Asp Cys Ser Pro Asp Pro Cys His His Gly Arg Cys Val
545                 550                 555                 560

Asp Gly Ile Ala Ser Phe Ser Cys Ala Cys Ala Pro Gly Tyr Thr Gly
                565                 570                 575

Thr Arg Cys Glu Ser Gln Val Asp Glu Cys Arg Ser Gln Pro Cys Arg
            580                 585                 590

His Gly Gly Lys Cys Leu Asp Leu Val Asp Lys Tyr Leu Cys Arg Cys
        595                 600                 605

Pro Ser Gly Thr Thr Gly Val Asn Cys Glu Val Asn Ile Asp Asp Cys
    610                 615                 620

Ala Ser Asn Pro Cys Thr Phe Gly Val Cys Arg Asp Gly Ile Asn Arg
625                 630                 635                 640

Tyr Asp Cys Val Cys Gln Pro Gly Phe Thr Gly Pro Leu Cys Asn Val
                645                 650                 655

Glu Ile Asn Glu Cys Ala Ser Ser Pro Cys Gly Glu Gly Gly Ser Cys
            660                 665                 670

Val Asp Gly Glu Asn Gly Phe Arg Cys Leu Cys Pro Pro Gly Ser Leu
        675                 680                 685

Pro Pro Leu Cys Leu Pro Pro Ser His Pro Cys Ala His Glu Pro Cys
    690                 695                 700

Ser His Gly Ile Cys Tyr Asp Ala Pro Gly Gly Phe Arg Cys Val Cys
705                 710                 715                 720

Glu Pro Gly Trp Ser Gly Pro Arg Cys Ser Gln Ser Leu Ala Arg Asp
                725                 730                 735

Ala Cys Glu Ser Gln Pro Cys Arg Ala Gly Gly Thr Cys Ser Ser Asp
            740                 745                 750

Gly Met Gly Phe His Cys Thr Cys Pro Pro Gly Val Gln Gly Arg Gln
        755                 760                 765

Cys Glu Leu Leu Ser Pro Cys Thr Pro Asn Pro Cys Glu His Gly Gly
    770                 775                 780

Arg Cys Glu Ser Ala Pro Gly Gln Leu Pro Val Cys Ser Cys Pro Gln
785                 790                 795                 800

Gly Trp Gln Gly Pro Arg Cys Gln Gln Asp Val Asp Glu Cys Ala Gly
                805                 810                 815

Pro Ala Pro Cys Gly Pro His Gly Ile Cys Thr Asn Leu Ala Gly Ser
            820                 825                 830

Phe Ser Cys Thr Cys His Gly Gly Tyr Thr Gly Pro Ser Cys Asp Gln
        835                 840                 845

Asp Ile Asn Asp Cys Asp Pro Asn Pro Cys Leu Asn Gly Gly Ser Cys
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    850                 855                 860

Gln Asp Gly Val Gly Ser Phe Ser Cys Ser Cys Leu Pro Gly Phe Ala
865                 870                 875                 880

Gly Pro Arg Cys Ala Arg Asp Val Asp Glu Cys Leu Ser Asn Pro Cys
                885                 890                 895

Gly Pro Gly Thr Cys Thr Asp His Val Ala Ser Phe Thr Cys Thr Cys
            900                 905                 910

Pro Pro Gly Tyr Gly Gly Phe His Cys Glu Gln Asp Leu Pro Asp Cys
        915                 920                 925

Ser Pro Ser Ser Cys Phe Asn Gly Gly Thr Cys Val Asp Gly Val Asn
    930                 935                 940

Ser Phe Ser Cys Leu Cys Arg Pro Gly Tyr Thr Gly Ala His Cys Gln
945                 950                 955                 960

His Glu Ala Asp Pro Cys Leu Ser Arg Pro Cys Leu His Gly Gly Val
                965                 970                 975

Cys Ser Ala Ala His Pro Gly Phe Arg Cys Thr Cys Leu Glu Ser Phe
            980                 985                 990

Thr Gly Pro Gln Cys Gln Thr Leu  Val Asp Trp Cys Ser  Arg Gln Pro
        995                 1000                1005

Cys Gln  Asn Gly Gly Arg Cys  Val Gln Thr Gly Ala  Tyr Cys Leu
    1010                1015                1020

Cys Pro  Pro Gly Trp Ser Gly  Arg Leu Cys Asp Ile  Arg Ser Leu
    1025                1030                1035

Pro Cys  Arg Glu Ala Ala Ala  Gln Ile Gly Val Arg  Leu Glu Gln
    1040                1045                1050

Leu Cys  Gln Ala Gly Gly Gln  Cys Val Asp Glu Asp  Ser Ser His
    1055                1060                1065

Tyr Cys  Val Cys Pro Glu Gly  Arg Thr Gly Ser His  Cys Glu Gln
    1070                1075                1080

Glu Val  Asp Pro Cys Leu Ala  Gln Pro Cys Gln His  Gly Gly Thr
    1085                1090                1095

Cys Arg  Gly Tyr Met Gly Gly  Tyr Met Cys Glu Cys  Leu Pro Gly
    1100                1105                1110

Tyr Asn  Gly Asp Asn Cys Glu  Asp Asp Val Asp Glu  Cys Ala Ser
    1115                1120                1125

Gln Pro  Cys Gln His Gly Gly  Ser Cys Ile Asp Leu  Val Ala Arg
    1130                1135                1140

Tyr Leu  Cys Ser Cys Pro Pro  Gly Thr Leu Gly Val  Leu Cys Glu
    1145                1150                1155

Ile Asn  Glu Asp Asp Cys Gly  Pro Gly Pro Pro Leu  Asp Ser Gly
    1160                1165                1170

Pro Arg  Cys Leu His Asn Gly  Thr Cys Val Asp Leu  Val Gly Gly
    1175                1180                1185

Phe Arg  Cys Thr Cys Pro Pro  Gly Tyr Thr Gly Leu  Arg Cys Glu
    1190                1195                1200

Ala Asp  Ile Asn Glu Cys Arg  Ser Gly Ala Cys His  Ala Ala His
    1205                1210                1215

Thr Arg  Asp Cys Leu Gln Asp  Pro Gly Gly Gly Phe  Arg Cys Leu
    1220                1225                1230

Cys His  Ala Gly Phe Ser Gly  Pro Arg Cys Gln Thr  Val Leu Ser
    1235                1240                1245
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Pro Cys  Glu Ser Gln Pro Cys  Gln His Gly Gly Gln  Cys Arg Pro
    1250                 1255                 1260

Ser Pro  Gly Pro Gly Gly Gly  Leu Thr Phe Thr Cys  His Cys Ala
    1265                 1270                 1275

Gln Pro  Phe Trp Gly Pro Arg  Cys Glu Arg Val Ala  Arg Ser Cys
    1280                 1285                 1290

Arg Glu  Leu Gln Cys Pro Val  Gly Val Pro Cys Gln  Gln Thr Pro
    1295                 1300                 1305

Arg Gly  Pro Arg Cys Ala Cys  Pro Pro Gly Leu Ser  Gly Pro Ser
    1310                 1315                 1320

Cys Arg  Ser Phe Pro Gly Ser  Pro Pro Gly Ala Ser  Asn Ala Ser
    1325                 1330                 1335

Cys Ala  Ala Ala Pro Cys Leu  His Gly Gly Ser Cys  Arg Pro Ala
    1340                 1345                 1350

Pro Leu  Ala Pro Phe Phe Arg  Cys Ala Cys Ala Gln  Gly Trp Thr
    1355                 1360                 1365

Gly Pro  Arg Cys Glu Ala Pro  Ala Ala Ala Pro Glu  Val Ser Glu
    1370                 1375                 1380

Glu Pro  Arg Cys Pro Arg Ala  Ala Cys Gln Ala Lys  Arg Gly Asp
    1385                 1390                 1395

Gln Arg  Cys Asp Arg Glu Cys  Asn Ser Pro Gly Cys  Gly Trp Asp
    1400                 1405                 1410

Gly Gly  Asp Cys Ser Leu Ser  Val Gly Asp Pro Trp  Arg Gln Cys
    1415                 1420                 1425

Glu Ala  Leu Gln Cys Trp Arg  Leu Phe Asn Asn Ser  Arg Cys Asp
    1430                 1435                 1440

Pro Ala  Cys Ser Ser Pro Ala  Cys Leu Tyr Asp Asn  Phe Asp Cys
    1445                 1450                 1455

His Ala  Gly Gly Arg Glu Arg  Thr Cys Asn Pro Val  Tyr Glu Lys
    1460                 1465                 1470

Tyr Cys  Ala Asp His Phe Ala  Asp Gly Arg Cys Asp  Gln Gly Cys
    1475                 1480                 1485

Asn Thr  Glu Glu Cys Gly Trp  Asp Gly Leu Asp Cys  Ala Ser Glu
    1490                 1495                 1500

Val Pro  Ala Leu Leu Ala Arg  Gly Val Leu Val Leu  Thr Val Leu
    1505                 1510                 1515

Leu Pro  Pro Glu Glu Leu Leu  Arg Ser Ser Ala Asp  Phe Leu Gln
    1520                 1525                 1530

Arg Leu  Ser Ala Ile Leu Arg  Thr Ser Leu Arg Phe  Arg Leu Asp
    1535                 1540                 1545

Ala His  Gly Gln Ala Met Val  Phe Pro Tyr His Arg  Pro Ser Pro
    1550                 1555                 1560

Gly Ser  Glu Pro Arg Ala Arg  Arg Glu Leu Ala Pro  Glu Val Ile
    1565                 1570                 1575

Gly Ser  Val Val Met Leu Glu  Ile Asp Asn Arg Leu  Cys Leu Gln
    1580                 1585                 1590

Ser Pro  Glu Asn Asp His Cys  Phe Pro Asp Ala Gln  Ser Ala Ala
    1595                 1600                 1605

Asp Tyr  Leu Gly Ala Leu Ser  Ala Val Glu Arg Leu  Asp Phe Pro
    1610                 1615                 1620
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Tyr Pro  Leu Arg Asp Val Arg  Gly Glu Pro Leu Glu  Pro Pro Glu
    1625                 1630                 1635

Pro Ser  Val Pro Leu Leu Pro  Leu Leu Val Ala Gly  Ala Val Leu
    1640                 1645                 1650

Leu Leu  Val Ile Leu Val Leu  Gly Val Met Val Ala  Arg Arg Lys
    1655                 1660                 1665

Arg Glu  His Ser Thr Leu Trp  Phe Pro Glu Gly Phe  Ser Leu His
    1670                 1675                 1680

Lys Asp  Val Ala Ser Gly His  Lys Gly Arg Arg Glu  Pro Val Gly
    1685                 1690                 1695

Gln Asp  Ala Leu Gly Met Lys  Asn Met Ala Lys Gly  Glu Ser Leu
    1700                 1705                 1710

Met Gly  Glu Val Ala Thr Asp  Trp Met Asp Thr Glu  Cys Pro Glu
    1715                 1720                 1725

Ala Lys  Arg Leu Lys Val Glu  Glu Pro Gly Met Gly  Ala Glu Glu
    1730                 1735                 1740

Ala Val  Asp Cys Arg Gln Trp  Thr Gln His His Leu  Val Ala Ala
    1745                 1750                 1755

Asp Ile  Arg Val Ala Pro Ala  Met Ala Leu Thr Pro  Pro Gln Gly
    1760                 1765                 1770

Asp Ala  Asp Ala Asp Gly Met  Asp Val Asn Val Arg  Gly Pro Asp
    1775                 1780                 1785

Gly Phe  Thr Pro Leu Met Leu  Ala Ser Phe Cys Gly  Gly Ala Leu
    1790                 1795                 1800

Glu Pro  Met Pro Thr Glu Glu  Asp Glu Ala Asp Asp  Thr Ser Ala
    1805                 1810                 1815

Ser Ile  Ile Ser Asp Leu Ile  Cys Gln Gly Ala Gln  Leu Gly Ala
    1820                 1825                 1830

Arg Thr  Asp Arg Thr Gly Glu  Thr Ala Leu His Leu  Ala Ala Arg
    1835                 1840                 1845

Tyr Ala  Arg Ala Asp Ala Ala  Lys Arg Leu Leu Asp  Ala Gly Ala
    1850                 1855                 1860

Asp Thr  Asn Ala Gln Asp His  Ser Gly Arg Thr Pro  Leu His Thr
    1865                 1870                 1875

Ala Val  Thr Ala Asp Ala Gln  Gly Val Phe Gln Ile  Leu Ile Arg
    1880                 1885                 1890

Asn Arg  Ser Thr Asp Leu Asp  Ala Arg Met Ala Asp  Gly Ser Thr
    1895                 1900                 1905

Ala Leu  Ile Leu Ala Ala Arg  Leu Ala Val Glu Gly  Met Val Glu
    1910                 1915                 1920

Glu Leu  Ile Ala Ser His Ala  Asp Val Asn Ala Val  Asp Glu Leu
    1925                 1930                 1935

Gly Lys  Ser Ala Leu His Trp  Ala Ala Ala Val Asn  Asn Val Glu
    1940                 1945                 1950

Ala Thr  Leu Ala Leu Leu Lys  Asn Gly Ala Asn Lys  Asp Met Gln
    1955                 1960                 1965

Asp Ser  Lys Glu Glu Thr Pro  Leu Phe Leu Ala Ala  Arg Glu Gly
    1970                 1975                 1980

Ser Tyr  Glu Ala Ala Lys Leu  Leu Leu Asp His Phe  Ala Asn Arg
    1985                 1990                 1995

Glu Ile  Thr Asp His Leu Asp  Arg Leu Pro Arg Asp  Val Ala Gln
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    2000                2005                2010

Glu Arg  Leu His Gln Asp Ile  Val Arg Leu Leu Asp  Gln Pro Ser
    2015                2020                2025

Gly Pro  Arg Ser Pro Pro Gly  Pro His Gly Leu Gly  Pro Leu Leu
    2030                2035                2040

Cys Pro  Pro Gly Ala Phe Leu  Pro Gly Leu Lys Ala  Ala Gln Ser
    2045                2050                2055

Gly Ser  Lys Lys Ser Arg Arg  Pro Pro Gly Lys Ala  Gly Leu Gly
    2060                2065                2070

Pro Gln  Gly Pro Arg Gly Arg  Gly Lys Lys Leu Thr  Leu Ala Cys
    2075                2080                2085

Pro Gly  Pro Leu Ala Asp Ser  Ser Val Thr Leu Ser  Pro Val Asp
    2090                2095                2100

Ser Leu  Asp Ser Pro Arg Pro  Phe Gly Gly Pro Pro  Ala Ser Pro
    2105                2110                2115

Gly Gly  Phe Pro Leu Glu Gly  Pro Tyr Ala Ala Ala  Thr Ala Thr
    2120                2125                2130

Ala Val  Ser Leu Ala Gln Leu  Gly Gly Pro Gly Arg  Ala Gly Leu
    2135                2140                2145

Gly Arg  Gln Pro Pro Gly Gly  Cys Val Leu Ser Leu  Gly Leu Leu
    2150                2155                2160

Asn Pro  Val Ala Val Pro Leu  Asp Trp Ala Arg Leu  Pro Pro Pro
    2165                2170                2175

Ala Pro  Pro Gly Pro Ser Phe  Leu Leu Pro Leu Ala  Pro Gly Pro
    2180                2185                2190

Gln Leu  Leu Asn Pro Gly Thr  Pro Val Ser Pro Gln  Glu Arg Pro
    2195                2200                2205

Pro Pro  Tyr Leu Ala Val Pro  Gly His Gly Glu Glu  Tyr Pro Val
    2210                2215                2220

Ala Gly  Ala His Ser Ser Pro  Pro Lys Ala Arg Phe  Leu Arg Val
    2225                2230                2235

Pro Ser  Glu His Pro Tyr Leu  Thr Pro Ser Pro Glu  Ser Pro Glu
    2240                2245                2250

His Trp  Ala Ser Pro Ser Pro  Pro Ser Leu Ser Asp  Trp Ser Glu
    2255                2260                2265

Ser Thr  Pro Ser Pro Ala Thr  Ala Thr Gly Ala Met  Ala Thr Thr
    2270                2275                2280

Thr Gly  Ala Leu Pro Ala Gln  Pro Leu Pro Leu Ser  Val Pro Ser
    2285                2290                2295

Ser Leu  Ala Gln Ala Gln Thr  Gln Leu Gly Pro Gln  Pro Glu Val
    2300                2305                2310

Thr Pro  Lys Arg Gln Val Leu  Ala
    2315                2320


<210> SEQ ID NO 42
<211> LENGTH: 149
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 42

Met Ala Arg Ser Asn Leu Pro Leu Ala Leu Gly Leu Ala Leu Val Ala
1               5                  10                  15
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Phe Cys Leu Leu Ala Leu Pro Arg Asp Ala Arg Ala Arg Pro Gln Glu
            20                  25                  30

Arg Met Val Gly Glu Leu Arg Asp Leu Ser Pro Asp Asp Pro Gln Val
        35                  40                  45

Gln Lys Ala Ala Gln Ala Ala Val Ala Ser Tyr Asn Met Gly Ser Asn
    50                  55                  60

Ser Ile Tyr Tyr Phe Arg Asp Thr His Ile Ile Lys Ala Gln Ser Gln
65                  70                  75                  80

Leu Val Ala Gly Ile Lys Tyr Phe Leu Thr Met Glu Met Gly Ser Thr
                85                  90                  95

Asp Cys Arg Lys Thr Arg Val Thr Gly Asp His Val Asp Leu Thr Thr
            100                 105                 110

Cys Pro Leu Ala Ala Gly Ala Gln Gln Glu Lys Leu Arg Cys Asp Phe
        115                 120                 125

Glu Val Leu Val Val Pro Trp Gln Asn Ser Ser Gln Leu Leu Lys His
    130                 135                 140

Asn Cys Val Gln Met
145


<210> SEQ ID NO 43
<211> LENGTH: 485
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 43

Met Ser Val Pro Leu Leu Lys Ile Gly Val Val Leu Ser Thr Met Ala
1               5                   10                  15

Met Ile Thr Asn Trp Met Ser Gln Thr Leu Pro Ser Leu Val Gly Leu
            20                  25                  30

Asn Thr Thr Lys Leu Ser Ala Ala Gly Gly Gly Thr Leu Asp Arg Ser
        35                  40                  45

Thr Gly Val Leu Pro Thr Asn Pro Glu Glu Ser Trp Gln Val Tyr Ser
    50                  55                  60

Ser Ala Gln Asp Ser Glu Gly Arg Cys Ile Cys Thr Val Val Ala Pro
65                  70                  75                  80

Gln Gln Thr Met Cys Ser Arg Asp Ala Arg Thr Lys Gln Leu Arg Gln
                85                  90                  95

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

Arg Arg Thr Gln Arg Asp Leu Gln Tyr Val Glu Lys Met Glu Asn Gln
        115                 120                 125

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

Gln His Leu Ala Arg Gln Phe Lys Ala Ile Lys Ala Lys Met Asp Glu
145                 150                 155                 160

Leu Arg Pro Leu Ile Pro Val Leu Glu Glu Tyr Lys Ala Asp Ala Lys
                165                 170                 175

Leu Val Leu Gln Phe Lys Glu Glu Val Gln Asn Leu Thr Ser Val Leu
            180                 185                 190

Asn Glu Leu Gln Glu Glu Ile Gly Ala Tyr Asp Tyr Asp Glu Leu Gln
        195                 200                 205

Ser Arg Val Ser Asn Leu Glu Glu Arg Leu Arg Ala Cys Met Gln Lys
    210                 215                 220
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Leu Ala Cys Gly Lys Leu Thr Gly Ile Ser Asp Pro Val Thr Val Lys
225                 230                 235                 240

Thr Ser Gly Ser Arg Phe Gly Ser Trp Met Thr Asp Pro Leu Ala Pro
                245                 250                 255

Glu Gly Asp Asn Arg Val Trp Tyr Met Asp Gly Tyr His Asn Asn Arg
            260                 265                 270

Phe Val Arg Glu Tyr Lys Ser Met Val Asp Phe Met Asn Thr Asp Asn
        275                 280                 285

Phe Thr Ser His Arg Leu Pro His Pro Trp Ser Gly Thr Gly Gln Val
    290                 295                 300

Val Tyr Asn Gly Ser Ile Tyr Phe Asn Lys Phe Gln Ser His Ile Ile
305                 310                 315                 320

Ile Arg Phe Asp Leu Lys Thr Glu Thr Ile Leu Lys Thr Arg Ser Leu
                325                 330                 335

Asp Tyr Ala Gly Tyr Asn Asn Met Tyr His Tyr Ala Trp Gly Gly His
            340                 345                 350

Ser Asp Ile Asp Leu Met Val Asp Glu Ser Gly Leu Trp Ala Val Tyr
        355                 360                 365

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

Val Ser Leu Gln Thr Leu Gln Thr Trp Asn Thr Ser Tyr Pro Lys Arg
385                 390                 395                 400

Ser Ala Gly Glu Ala Phe Ile Ile Cys Gly Thr Leu Tyr Val Thr Asn
                405                 410                 415

Gly Tyr Ser Gly Gly Thr Lys Val His Tyr Ala Tyr Gln Thr Asn Ala
            420                 425                 430

Ser Thr Tyr Glu Tyr Ile Asp Ile Pro Phe Gln Asn Lys Tyr Ser His
        435                 440                 445

Ile Ser Met Leu Asp Tyr Asn Pro Lys Asp Arg Ala Leu Tyr Ala Trp
    450                 455                 460

Asn Asn Gly His Gln Ile Leu Tyr Asn Val Thr Leu Phe His Val Ile
465                 470                 475                 480

Arg Ser Asp Glu Leu
                485


<210> SEQ ID NO 44
<211> LENGTH: 328
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 44

Met Leu Pro Arg Val Gly Cys Pro Ala Leu Pro Leu Pro Pro Pro Pro
1               5                   10                  15

Leu Leu Pro Leu Leu Pro Leu Leu Leu Leu Leu Leu Gly Ala Ser Gly
            20                  25                  30

Gly Gly Gly Gly Ala Arg Ala Glu Val Leu Phe Arg Cys Pro Pro Cys
        35                  40                  45

Thr Pro Glu Arg Leu Ala Ala Cys Gly Pro Pro Pro Val Ala Pro Pro
    50                  55                  60

Ala Ala Val Ala Ala Val Ala Gly Gly Ala Arg Met Pro Cys Ala Glu
65                  70                  75                  80

Leu Val Arg Glu Pro Gly Cys Gly Cys Cys Ser Val Cys Ala Arg Leu
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                85                  90                  95

Glu Gly Glu Ala Cys Gly Val Tyr Thr Pro Arg Cys Gly Gln Gly Leu
            100                 105                 110

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

Met Gly Glu Gly Thr Cys Glu Lys Arg Arg Asp Ala Glu Tyr Gly Ala
    130                 135                 140

Ser Pro Glu Gln Val Ala Asp Asn Gly Asp Asp His Ser Glu Gly Gly
145                 150                 155                 160

Leu Val Glu Asn His Val Asp Ser Thr Met Asn Met Leu Gly Gly Gly
                165                 170                 175

Gly Ser Ala Gly Arg Lys Pro Leu Lys Ser Gly Met Lys Glu Leu Ala
            180                 185                 190

Val Phe Arg Glu Lys Val Thr Glu Gln His Arg Gln Met Gly Lys Gly
        195                 200                 205

Gly Lys His His Leu Gly Leu Glu Glu Pro Lys Lys Leu Arg Pro Pro
    210                 215                 220

Pro Ala Arg Thr Pro Cys Gln Gln Glu Leu Asp Gln Val Leu Glu Arg
225                 230                 235                 240

Ile Ser Thr Met Arg Leu Pro Asp Glu Arg Gly Pro Leu Glu His Leu
                245                 250                 255

Tyr Ser Leu His Ile Pro Asn Cys Asp Lys His Gly Leu Tyr Asn Leu
            260                 265                 270

Lys Gln Cys Lys Met Ser Leu Asn Gly Gln Arg Gly Glu Cys Trp Cys
        275                 280                 285

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

Gly Asp Pro Glu Cys His Leu Phe Tyr Asn Glu Gln Gln Glu Ala Arg
305                 310                 315                 320

Gly Val His Thr Gln Arg Met Gln
                325


<210> SEQ ID NO 45
<211> LENGTH: 803
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 45

Met Arg Ala Leu Trp Val Leu Gly Leu Cys Cys Val Leu Leu Thr Phe
1               5                   10                  15

Gly Ser Val Arg Ala Asp Asp Glu Val Asp Val Asp Gly Thr Val Glu
            20                  25                  30

Glu Asp Leu Gly Lys Ser Arg Glu Gly Ser Arg Thr Asp Asp Glu Val
        35                  40                  45

Val Gln Arg Glu Glu Glu Ala Ile Gln Leu Asp Gly Leu Asn Ala Ser
    50                  55                  60

Gln Ile Arg Glu Leu Arg Glu Lys Ser Glu Lys Phe Ala Phe Gln Ala
65                  70                  75                  80

Glu Val Asn Arg Met Met Lys Leu Ile Ile Asn Ser Leu Tyr Lys Asn
                85                  90                  95

Lys Glu Ile Phe Leu Arg Glu Leu Ile Ser Asn Ala Ser Asp Ala Leu
            100                 105                 110
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Asp Lys Ile Arg Leu Ile Ser Leu Thr Asp Glu Asn Ala Leu Ser Gly
        115                 120                 125

Asn Glu Glu Leu Thr Val Lys Ile Lys Cys Asp Lys Glu Lys Asn Leu
    130                 135                 140

Leu His Val Thr Asp Thr Gly Val Gly Met Thr Arg Glu Glu Leu Val
145                 150                 155                 160

Lys Asn Leu Gly Thr Ile Ala Lys Ser Gly Thr Ser Glu Phe Leu Asn
                165                 170                 175

Lys Met Thr Glu Ala Gln Glu Asp Gly Gln Ser Thr Ser Glu Leu Ile
            180                 185                 190

Gly Gln Phe Gly Val Gly Phe Tyr Ser Ala Phe Leu Val Ala Asp Lys
        195                 200                 205

Val Ile Val Thr Ser Lys His Asn Asn Asp Thr Gln His Ile Trp Glu
    210                 215                 220

Ser Asp Ser Asn Glu Phe Ser Val Ile Ala Asp Pro Arg Gly Asn Thr
225                 230                 235                 240

Leu Gly Arg Gly Thr Thr Ile Thr Leu Val Leu Lys Glu Glu Ala Ser
                245                 250                 255

Asp Tyr Leu Glu Leu Asp Thr Ile Lys Asn Leu Val Lys Lys Tyr Ser
            260                 265                 270

Gln Phe Ile Asn Phe Pro Ile Tyr Val Trp Ser Ser Lys Thr Glu Thr
        275                 280                 285

Val Glu Glu Pro Met Glu Glu Glu Glu Ala Ala Lys Glu Glu Lys Glu
    290                 295                 300

Glu Ser Asp Asp Glu Ala Ala Val Glu Glu Glu Glu Glu Glu Lys Lys
305                 310                 315                 320

Pro Lys Thr Lys Lys Val Glu Lys Thr Val Trp Asp Trp Glu Leu Met
                325                 330                 335

Asn Asp Ile Lys Pro Ile Trp Gln Arg Pro Ser Lys Glu Val Glu Glu
            340                 345                 350

Asp Glu Tyr Lys Ala Phe Tyr Lys Ser Phe Ser Lys Glu Ser Asp Asp
        355                 360                 365

Pro Met Ala Tyr Ile His Phe Thr Ala Glu Gly Glu Val Thr Phe Lys
    370                 375                 380

Ser Ile Leu Phe Val Pro Thr Ser Ala Pro Arg Gly Leu Phe Asp Glu
385                 390                 395                 400

Tyr Gly Ser Lys Lys Ser Asp Tyr Ile Lys Leu Tyr Val Arg Arg Val
                405                 410                 415

Phe Ile Thr Asp Asp Phe His Asp Met Met Pro Lys Tyr Leu Asn Phe
            420                 425                 430

Val Lys Gly Val Val Asp Ser Asp Asp Leu Pro Leu Asn Val Ser Arg
        435                 440                 445

Glu Thr Leu Gln Gln His Lys Leu Leu Lys Val Ile Arg Lys Lys Leu
    450                 455                 460

Val Arg Lys Thr Leu Asp Met Ile Lys Lys Ile Ala Asp Asp Lys Tyr
465                 470                 475                 480

Asn Asp Thr Phe Trp Lys Glu Phe Gly Thr Asn Ile Lys Leu Gly Val
                485                 490                 495

Ile Glu Asp His Ser Asn Arg Thr Arg Leu Ala Lys Leu Leu Arg Phe
            500                 505                 510

Gln Ser Ser His His Pro Thr Asp Ile Thr Ser Leu Asp Gln Tyr Val
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        515                 520                 525

Glu Arg Met Lys Glu Lys Gln Asp Lys Ile Tyr Phe Met Ala Gly Ser
    530                 535                 540

Ser Arg Lys Glu Ala Glu Ser Ser Pro Phe Val Glu Arg Leu Leu Lys
545                 550                 555                 560

Lys Gly Tyr Glu Val Ile Tyr Leu Thr Glu Pro Val Asp Glu Tyr Cys
                565                 570                 575

Ile Gln Ala Leu Pro Glu Phe Asp Gly Lys Arg Phe Gln Asn Val Ala
            580                 585                 590

Lys Glu Gly Val Lys Phe Asp Glu Ser Glu Lys Thr Lys Glu Ser Arg
        595                 600                 605

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

Lys Ala Leu Lys Asp Lys Ile Glu Lys Ala Val Val Ser Gln Arg Leu
625                 630                 635                 640

Thr Glu Ser Pro Cys Ala Leu Val Ala Ser Gln Tyr Gly Trp Ser Gly
                645                 650                 655

Asn Met Glu Arg Ile Met Lys Ala Gln Ala Tyr Gln Thr Gly Lys Asp
            660                 665                 670

Ile Ser Thr Asn Tyr Tyr Ala Ser Gln Lys Lys Thr Phe Glu Ile Asn
        675                 680                 685

Pro Arg His Pro Leu Ile Arg Asp Met Leu Arg Arg Ile Lys Glu Asp
    690                 695                 700

Glu Asp Asp Lys Thr Val Leu Asp Leu Ala Val Val Leu Phe Glu Thr
705                 710                 715                 720

Ala Thr Leu Arg Ser Gly Tyr Leu Leu Pro Asp Thr Lys Ala Tyr Gly
                725                 730                 735

Asp Arg Ile Glu Arg Met Leu Arg Leu Ser Leu Asn Ile Asp Pro Asp
            740                 745                 750

Ala Lys Val Glu Glu Glu Pro Glu Glu Glu Pro Glu Glu Thr Ala Glu
        755                 760                 765

Asp Thr Thr Glu Asp Thr Glu Gln Asp Glu Asp Glu Glu Met Asp Val
    770                 775                 780

Gly Thr Asp Glu Glu Glu Glu Thr Ala Lys Glu Ser Thr Ala Glu Lys
785                 790                 795                 800

Asp Glu Leu


<210> SEQ ID NO 46
<211> LENGTH: 692
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 46

Met Gly Thr Val Ser Ser Arg Arg Ser Trp Trp Pro Leu Pro Leu Leu
1               5                   10                  15

Leu Leu Leu Leu Leu Leu Leu Gly Pro Ala Gly Ala Arg Ala Gln Glu
            20                  25                  30

Asp Glu Asp Gly Asp Tyr Glu Glu Leu Val Leu Ala Leu Arg Ser Glu
        35                  40                  45

Glu Asp Gly Leu Ala Glu Ala Pro Glu His Gly Thr Thr Ala Thr Phe
    50                  55                  60

His Arg Cys Ala Lys Asp Pro Trp Arg Leu Pro Gly Thr Tyr Val Val
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65                  70                  75                  80

Val Leu Lys Glu Glu Thr His Leu Ser Gln Ser Glu Arg Thr Ala Arg
                85                  90                  95

Arg Leu Gln Ala Gln Ala Ala Arg Arg Gly Tyr Leu Thr Lys Ile Leu
            100                 105                 110

His Val Phe His Gly Leu Leu Pro Gly Phe Leu Val Lys Met Ser Gly
        115                 120                 125

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

Glu Asp Ser Ser Val Phe Ala Gln Ser Ile Pro Trp Asn Leu Glu Arg
145                 150                 155                 160

Ile Thr Pro Pro Arg Tyr Arg Ala Asp Glu Tyr Gln Pro Pro Asp Gly
                165                 170                 175

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

His Arg Glu Ile Glu Gly Arg Val Met Val Thr Asp Phe Glu Asn Val
        195                 200                 205

Pro Glu Glu Asp Gly Thr Arg Phe His Arg Gln Ala Ser Lys Cys Asp
    210                 215                 220

Ser His Gly Thr His Leu Ala Gly Val Val Ser Gly Arg Asp Ala Gly
225                 230                 235                 240

Val Ala Lys Gly Ala Ser Met Arg Ser Leu Arg Val Leu Asn Cys Gln
                245                 250                 255

Gly Lys Gly Thr Val Ser Gly Thr Leu Ile Gly Leu Glu Phe Ile Arg
            260                 265                 270

Lys Ser Gln Leu Val Gln Pro Val Gly Pro Leu Val Val Leu Leu Pro
        275                 280                 285

Leu Ala Gly Gly Tyr Ser Arg Val Leu Asn Ala Ala Cys Gln Arg Leu
    290                 295                 300

Ala Arg Ala Gly Val Val Leu Val Thr Ala Ala Gly Asn Phe Arg Asp
305                 310                 315                 320

Asp Ala Cys Leu Tyr Ser Pro Ala Ser Ala Pro Glu Val Ile Thr Val
                325                 330                 335

Gly Ala Thr Asn Ala Gln Asp Gln Pro Val Thr Leu Gly Thr Leu Gly
            340                 345                 350

Thr Asn Phe Gly Arg Cys Val Asp Leu Phe Ala Pro Gly Glu Asp Ile
        355                 360                 365

Ile Gly Ala Ser Ser Asp Cys Ser Thr Cys Phe Val Ser Gln Ser Gly
    370                 375                 380

Thr Ser Gln Ala Ala Ala His Val Ala Gly Ile Ala Ala Met Met Leu
385                 390                 395                 400

Ser Ala Glu Pro Glu Leu Thr Leu Ala Glu Leu Arg Gln Arg Leu Ile
                405                 410                 415

His Phe Ser Ala Lys Asp Val Ile Asn Glu Ala Trp Phe Pro Glu Asp
            420                 425                 430

Gln Arg Val Leu Thr Pro Asn Leu Val Ala Ala Leu Pro Pro Ser Thr
        435                 440                 445

His Gly Ala Gly Trp Gln Leu Phe Cys Arg Thr Val Trp Ser Ala His
    450                 455                 460

Ser Gly Pro Thr Arg Met Ala Thr Ala Ile Ala Arg Cys Ala Pro Asp
465                 470                 475                 480
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Glu Glu Leu Leu Ser Cys Ser Ser Phe Ser Arg Ser Gly Lys Arg Arg
                485                 490                 495

Gly Glu Arg Met Glu Ala Gln Gly Gly Lys Leu Val Cys Arg Ala His
            500                 505                 510

Asn Ala Phe Gly Gly Glu Gly Val Tyr Ala Ile Ala Arg Cys Cys Leu
        515                 520                 525

Leu Pro Gln Ala Asn Cys Ser Val His Thr Ala Pro Pro Ala Glu Ala
    530                 535                 540

Ser Met Gly Thr Arg Val His Cys His Gln Gln Gly His Val Leu Thr
545                 550                 555                 560

Gly Cys Ser Ser His Trp Glu Val Glu Asp Leu Gly Thr His Lys Pro
                565                 570                 575

Pro Val Leu Arg Pro Arg Gly Gln Pro Asn Gln Cys Val Gly His Arg
            580                 585                 590

Glu Ala Ser Ile His Ala Ser Cys Cys His Ala Pro Gly Leu Glu Cys
        595                 600                 605

Lys Val Lys Glu His Gly Ile Pro Ala Pro Gln Glu Gln Val Thr Val
    610                 615                 620

Ala Cys Glu Glu Gly Trp Thr Leu Thr Gly Cys Ser Ala Leu Pro Gly
625                 630                 635                 640

Thr Ser His Val Leu Gly Ala Tyr Ala Val Asp Asn Thr Cys Val Val
                645                 650                 655

Arg Ser Arg Asp Val Ser Thr Thr Gly Ser Thr Ser Glu Glu Ala Val
            660                 665                 670

Thr Ala Val Ala Ile Cys Cys Arg Ser Arg His Leu Ala Gln Ala Ser
        675                 680                 685

Gln Glu Leu Gln
    690


<210> SEQ ID NO 47
<211> LENGTH: 605
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 47

Met Ala Leu Arg Lys Gly Gly Leu Ala Leu Ala Leu Leu Leu Leu Ser
1               5                   10                  15

Trp Val Ala Leu Gly Pro Arg Ser Leu Glu Gly Ala Asp Pro Gly Thr
            20                  25                  30

Pro Gly Glu Ala Glu Gly Pro Ala Cys Pro Ala Ala Cys Val Cys Ser
        35                  40                  45

Tyr Asp Asp Asp Ala Asp Glu Leu Ser Val Phe Cys Ser Ser Arg Asn
    50                  55                  60

Leu Thr Arg Leu Pro Asp Gly Val Pro Gly Gly Thr Gln Ala Leu Trp
65                  70                  75                  80

Leu Asp Gly Asn Asn Leu Ser Ser Val Pro Pro Ala Ala Phe Gln Asn
                85                  90                  95

Leu Ser Ser Leu Gly Phe Leu Asn Leu Gln Gly Gly Gln Leu Gly Ser
            100                 105                 110

Leu Glu Pro Gln Ala Leu Leu Gly Leu Glu Asn Leu Cys His Leu His
        115                 120                 125

Leu Glu Arg Asn Gln Leu Arg Ser Leu Ala Leu Gly Thr Phe Ala His
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    130                 135                 140

Thr Pro Ala Leu Ala Ser Leu Gly Leu Ser Asn Asn Arg Leu Ser Arg
145                 150                 155                 160

Leu Glu Asp Gly Leu Phe Glu Gly Leu Gly Ser Leu Trp Asp Leu Asn
                165                 170                 175

Leu Gly Trp Asn Ser Leu Ala Val Leu Pro Asp Ala Ala Phe Arg Gly
            180                 185                 190

Leu Gly Ser Leu Arg Glu Leu Val Leu Ala Gly Asn Arg Leu Ala Tyr
        195                 200                 205

Leu Gln Pro Ala Leu Phe Ser Gly Leu Ala Glu Leu Arg Glu Leu Asp
    210                 215                 220

Leu Ser Arg Asn Ala Leu Arg Ala Ile Lys Ala Asn Val Phe Val Gln
225                 230                 235                 240

Leu Pro Arg Leu Gln Lys Leu Tyr Leu Asp Arg Asn Leu Ile Ala Ala
                245                 250                 255

Val Ala Pro Gly Ala Phe Leu Gly Leu Lys Ala Leu Arg Trp Leu Asp
            260                 265                 270

Leu Ser His Asn Arg Val Ala Gly Leu Leu Glu Asp Thr Phe Pro Gly
        275                 280                 285

Leu Leu Gly Leu Arg Val Leu Arg Leu Ser His Asn Ala Ile Ala Ser
    290                 295                 300

Leu Arg Pro Arg Thr Phe Lys Asp Leu His Phe Leu Glu Glu Leu Gln
305                 310                 315                 320

Leu Gly His Asn Arg Ile Arg Gln Leu Ala Glu Arg Ser Phe Glu Gly
                325                 330                 335

Leu Gly Gln Leu Glu Val Leu Thr Leu Asp His Asn Gln Leu Gln Glu
            340                 345                 350

Val Lys Ala Gly Ala Phe Leu Gly Leu Thr Asn Val Ala Val Met Asn
        355                 360                 365

Leu Ser Gly Asn Cys Leu Arg Asn Leu Pro Glu Gln Val Phe Arg Gly
    370                 375                 380

Leu Gly Lys Leu His Ser Leu His Leu Glu Gly Ser Cys Leu Gly Arg
385                 390                 395                 400

Ile Arg Pro His Thr Phe Thr Gly Leu Ser Gly Leu Arg Arg Leu Phe
                405                 410                 415

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

Leu Ala Glu Leu Leu Glu Leu Asp Leu Thr Ser Asn Gln Leu Thr His
        435                 440                 445

Leu Pro His Arg Leu Phe Gln Gly Leu Gly Lys Leu Glu Tyr Leu Leu
    450                 455                 460

Leu Ser Arg Asn Arg Leu Ala Glu Leu Pro Ala Asp Ala Leu Gly Pro
465                 470                 475                 480

Leu Gln Arg Ala Phe Trp Leu Asp Val Ser His Asn Arg Leu Glu Ala
                485                 490                 495

Leu Pro Asn Ser Leu Leu Ala Pro Leu Gly Arg Leu Arg Tyr Leu Ser
            500                 505                 510

Leu Arg Asn Asn Ser Leu Arg Thr Phe Thr Pro Gln Pro Pro Gly Leu
        515                 520                 525

Glu Arg Leu Trp Leu Glu Gly Asn Pro Trp Asp Cys Gly Cys Pro Leu
    530                 535                 540
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Lys Ala Leu Arg Asp Phe Ala Leu Gln Asn Pro Ser Ala Val Pro Arg
545                 550                 555                 560

Phe Val Gln Ala Ile Cys Glu Gly Asp Asp Cys Gln Pro Pro Ala Tyr
                565                 570                 575

Thr Tyr Asn Asn Ile Thr Cys Ala Ser Pro Pro Glu Val Val Gly Leu
            580                 585                 590

Asp Leu Arg Asp Leu Ser Glu Ala His Phe Ala Pro Cys
        595                 600                 605


<210> SEQ ID NO 48
<211> LENGTH: 586
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 48

Met Pro Lys Pro Ile Asn Val Arg Val Thr Thr Met Asp Ala Glu Leu
1               5                   10                  15

Glu Phe Ala Ile Gln Pro Asn Thr Thr Gly Lys Gln Leu Phe Asp Gln
            20                  25                  30

Val Val Lys Thr Ile Gly Leu Arg Glu Val Trp Tyr Phe Gly Leu His
        35                  40                  45

Tyr Val Asp Asn Lys Gly Phe Pro Thr Trp Leu Lys Leu Asp Lys Lys
    50                  55                  60

Val Ser Ala Gln Glu Val Arg Lys Glu Asn Pro Leu Gln Phe Lys Phe
65                  70                  75                  80

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

Ile Thr Gln Lys Leu Phe Phe Leu Gln Val Lys Glu Gly Ile Leu Ser
            100                 105                 110

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

Ala Val Gln Ala Lys Phe Gly Asp Tyr Asn Lys Glu Val His Lys Ser
    130                 135                 140

Gly Tyr Leu Ser Ser Glu Arg Leu Ile Pro Gln Arg Val Met Asp Gln
145                 150                 155                 160

His Lys Leu Thr Arg Asp Gln Trp Glu Asp Arg Ile Gln Val Trp His
                165                 170                 175

Ala Glu His Arg Gly Met Leu Lys Asp Asn Ala Met Leu Glu Tyr Leu
            180                 185                 190

Lys Ile Ala Gln Asp Leu Glu Met Tyr Gly Ile Asn Tyr Phe Glu Ile
        195                 200                 205

Lys Asn Lys Lys Gly Thr Asp Leu Trp Leu Gly Val Asp Ala Leu Gly
    210                 215                 220

Leu Asn Ile Tyr Glu Lys Asp Asp Lys Leu Thr Pro Lys Ile Gly Phe
225                 230                 235                 240

Pro Trp Ser Glu Ile Arg Asn Ile Ser Phe Asn Asp Lys Lys Phe Val
                245                 250                 255

Ile Lys Pro Ile Asp Lys Lys Ala Pro Asp Phe Val Phe Tyr Ala Pro
            260                 265                 270

Arg Leu Arg Ile Asn Lys Arg Ile Leu Gln Leu Cys Met Gly Asn His
        275                 280                 285

Glu Leu Tyr Met Arg Arg Arg Lys Pro Asp Thr Ile Glu Val Gln Gln
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    290                 295                 300

Met Lys Ala Gln Ala Arg Glu Glu Lys His Gln Lys Gln Leu Glu Arg
305                 310                 315                 320

Gln Gln Leu Glu Thr Glu Lys Lys Arg Arg Glu Thr Val Glu Arg Glu
                325                 330                 335

Lys Glu Gln Met Met Arg Glu Lys Glu Glu Leu Met Leu Arg Leu Gln
            340                 345                 350

Asp Tyr Glu Glu Lys Thr Lys Lys Ala Glu Arg Glu Leu Ser Glu Gln
        355                 360                 365

Ile Gln Arg Ala Leu Gln Leu Glu Glu Glu Arg Lys Arg Ala Gln Glu
    370                 375                 380

Glu Ala Glu Arg Leu Glu Ala Asp Arg Met Ala Ala Leu Arg Ala Lys
385                 390                 395                 400

Glu Glu Leu Glu Arg Gln Ala Val Asp Gln Ile Lys Ser Gln Glu Gln
                405                 410                 415

Leu Ala Ala Glu Leu Ala Glu Tyr Thr Ala Lys Ile Ala Leu Leu Glu
            420                 425                 430

Glu Ala Arg Arg Arg Lys Glu Asp Glu Val Glu Glu Trp Gln His Arg
        435                 440                 445

Ala Lys Glu Ala Gln Asp Asp Leu Val Lys Thr Lys Glu Glu Leu His
    450                 455                 460

Leu Val Met Thr Ala Pro Pro Pro Pro Pro Pro Pro Val Tyr Glu Pro
465                 470                 475                 480

Val Ser Tyr His Val Gln Glu Ser Leu Gln Asp Glu Gly Ala Glu Pro
                485                 490                 495

Thr Gly Tyr Ser Ala Glu Leu Ser Ser Glu Gly Ile Arg Asp Asp Arg
            500                 505                 510

Asn Glu Glu Lys Arg Ile Thr Glu Ala Glu Lys Asn Glu Arg Val Gln
        515                 520                 525

Arg Gln Leu Leu Thr Leu Ser Ser Glu Leu Ser Gln Ala Arg Asp Glu
    530                 535                 540

Asn Lys Arg Thr His Asn Asp Ile Ile His Asn Glu Asn Met Arg Gln
545                 550                 555                 560

Gly Arg Asp Lys Tyr Lys Thr Leu Arg Gln Ile Arg Gln Gly Asn Thr
                565                 570                 575

Lys Gln Arg Ile Asp Glu Phe Glu Ala Leu
            580                 585


<210> SEQ ID NO 49
<211> LENGTH: 127
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 49

Met Ser Phe Ser Gly Lys Tyr Gln Leu Gln Ser Gln Glu Asn Phe Glu
1               5                   10                  15

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

Lys Asp Ile Lys Gly Val Ser Glu Ile Val Gln Asn Gly Lys His Phe
        35                  40                  45

Lys Phe Thr Ile Thr Ala Gly Ser Lys Val Ile Gln Asn Glu Phe Thr
    50                  55                  60
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Val Gly Glu Glu Cys Glu Leu Glu Thr Met Thr Gly Glu Lys Val Lys
65                  70                  75                  80

Thr Val Val Gln Leu Glu Gly Asp Asn Lys Leu Val Thr Thr Phe Lys
                85                  90                  95

Asn Ile Lys Ser Val Thr Glu Leu Asn Gly Asp Ile Ile Thr Asn Thr
            100                 105                 110

Met Thr Leu Gly Asp Ile Val Phe Lys Arg Ile Ser Lys Arg Ile
        115                 120                 125


<210> SEQ ID NO 50
<211> LENGTH: 1346
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 50

Met Lys Ser Pro Arg Arg Thr Thr Leu Cys Leu Met Phe Ile Val Ile
1               5                   10                  15

Tyr Ser Ser Lys Ala Ala Leu Asn Trp Asn Tyr Glu Ser Thr Ile His
            20                  25                  30

Pro Leu Ser Leu His Glu His Glu Pro Ala Gly Glu Glu Ala Leu Arg
        35                  40                  45

Gln Lys Arg Ala Val Ala Thr Lys Ser Pro Thr Ala Glu Glu Tyr Thr
    50                  55                  60

Val Asn Ile Glu Ile Ser Phe Glu Asn Ala Ser Phe Leu Asp Pro Ile
65                  70                  75                  80

Lys Ala Tyr Leu Asn Ser Leu Ser Phe Pro Ile His Gly Asn Asn Thr
                85                  90                  95

Asp Gln Ile Thr Asp Ile Leu Ser Ile Asn Val Thr Thr Val Cys Arg
            100                 105                 110

Pro Ala Gly Asn Glu Ile Trp Cys Ser Cys Glu Thr Gly Tyr Gly Trp
        115                 120                 125

Pro Arg Glu Arg Cys Leu His Asn Leu Ile Cys Gln Glu Arg Asp Val
    130                 135                 140

Phe Leu Pro Gly His His Cys Ser Cys Leu Lys Glu Leu Pro Pro Asn
145                 150                 155                 160

Gly Pro Phe Cys Leu Leu Gln Glu Asp Val Thr Leu Asn Met Arg Val
                165                 170                 175

Arg Leu Asn Val Gly Phe Gln Glu Asp Leu Met Asn Thr Ser Ser Ala
            180                 185                 190

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

Tyr Gly Ile Leu Pro Gly Phe Lys Gly Val Thr Val Thr Gly Phe Lys
    210                 215                 220

Ser Gly Ser Val Val Val Thr Tyr Glu Val Lys Thr Thr Pro Pro Ser
225                 230                 235                 240

Leu Glu Leu Ile His Lys Ala Asn Glu Gln Val Val Gln Ser Leu Asn
                245                 250                 255

Gln Thr Tyr Lys Met Asp Tyr Asn Ser Phe Gln Ala Val Thr Ile Asn
            260                 265                 270

Glu Ser Asn Phe Phe Val Thr Pro Glu Ile Ile Phe Glu Gly Asp Thr
        275                 280                 285

Val Ser Leu Val Cys Glu Lys Glu Val Leu Ser Ser Asn Val Ser Trp
    290                 295                 300
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Arg Tyr Glu Glu Gln Gln Leu Glu Ile Gln Asn Ser Ser Arg Phe Ser
305                 310                 315                 320

Ile Tyr Thr Ala Leu Phe Asn Asn Met Thr Ser Val Ser Lys Leu Thr
                325                 330                 335

Ile His Asn Ile Thr Pro Gly Asp Ala Gly Glu Tyr Val Cys Lys Leu
            340                 345                 350

Ile Leu Asp Ile Phe Glu Tyr Glu Cys Lys Lys Lys Ile Asp Val Met
        355                 360                 365

Pro Ile Gln Ile Leu Ala Asn Glu Glu Met Lys Val Met Cys Asp Asn
    370                 375                 380

Asn Pro Val Ser Leu Asn Cys Cys Ser Gln Gly Asn Val Asn Trp Ser
385                 390                 395                 400

Lys Val Glu Trp Lys Gln Glu Gly Lys Ile Asn Ile Pro Gly Thr Pro
                405                 410                 415

Glu Thr Asp Ile Asp Ser Ser Cys Ser Arg Tyr Thr Leu Lys Ala Asp
            420                 425                 430

Gly Thr Gln Cys Pro Ser Gly Ser Ser Gly Thr Thr Val Ile Tyr Thr
        435                 440                 445

Cys Glu Phe Ile Ser Ala Tyr Gly Ala Arg Gly Ser Ala Asn Ile Lys
    450                 455                 460

Val Thr Phe Ile Ser Val Ala Asn Leu Thr Ile Thr Pro Asp Pro Ile
465                 470                 475                 480

Ser Val Ser Glu Gly Gln Asn Phe Ser Ile Lys Cys Ile Ser Asp Val
                485                 490                 495

Ser Asn Tyr Asp Glu Val Tyr Trp Asn Thr Ser Ala Gly Ile Lys Ile
            500                 505                 510

Tyr Gln Arg Phe Tyr Thr Thr Arg Arg Tyr Leu Asp Gly Ala Glu Ser
        515                 520                 525

Val Leu Thr Val Lys Thr Ser Thr Arg Glu Trp Asn Gly Thr Tyr His
    530                 535                 540

Cys Ile Phe Arg Tyr Lys Asn Ser Tyr Ser Ile Ala Thr Lys Asp Val
545                 550                 555                 560

Ile Val His Pro Leu Pro Leu Lys Leu Asn Ile Met Val Asp Pro Leu
                565                 570                 575

Glu Ala Thr Val Ser Cys Ser Gly Ser His His Ile Lys Cys Cys Ile
            580                 585                 590

Glu Glu Asp Gly Asp Tyr Lys Val Thr Phe His Met Gly Ser Ser Ser
        595                 600                 605

Leu Pro Ala Ala Lys Glu Val Asn Lys Lys Gln Val Cys Tyr Lys His
    610                 615                 620

Asn Phe Asn Ala Ser Ser Val Ser Trp Cys Ser Lys Thr Val Asp Val
625                 630                 635                 640

Cys Cys His Phe Thr Asn Ala Ala Asn Asn Ser Val Trp Ser Pro Ser
                645                 650                 655

Met Lys Leu Asn Leu Val Pro Gly Glu Asn Ile Thr Cys Gln Asp Pro
            660                 665                 670

Val Ile Gly Val Gly Glu Pro Gly Lys Val Ile Gln Lys Leu Cys Arg
        675                 680                 685

Phe Ser Asn Val Pro Ser Ser Pro Glu Ser Pro Ile Gly Gly Thr Ile
    690                 695                 700
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Thr Tyr Lys Cys Val Gly Ser Gln Trp Glu Glu Lys Arg Asn Asp Cys
705                 710                 715                 720

Ile Ser Ala Pro Ile Asn Ser Leu Leu Gln Met Ala Lys Ala Leu Ile
                725                 730                 735

Lys Ser Pro Ser Gln Asp Glu Met Leu Pro Thr Tyr Leu Lys Asp Leu
            740                 745                 750

Ser Ile Ser Ile Asp Lys Ala Glu His Glu Ile Ser Ser Ser Pro Gly
        755                 760                 765

Ser Leu Gly Ala Ile Ile Asn Ile Leu Asp Leu Leu Ser Thr Val Pro
    770                 775                 780

Thr Gln Val Asn Ser Glu Met Met Thr His Val Leu Ser Thr Val Asn
785                 790                 795                 800

Val Ile Leu Gly Lys Pro Val Leu Asn Thr Trp Lys Val Leu Gln Gln
                805                 810                 815

Gln Trp Thr Asn Gln Ser Ser Gln Leu Leu His Ser Val Glu Arg Phe
            820                 825                 830

Ser Gln Ala Leu Gln Ser Gly Asp Ser Pro Pro Leu Ser Phe Ser Gln
        835                 840                 845

Thr Asn Val Gln Met Ser Ser Thr Val Ile Lys Ser Ser His Pro Glu
    850                 855                 860

Thr Tyr Gln Gln Arg Phe Val Phe Pro Tyr Phe Asp Leu Trp Gly Asn
865                 870                 875                 880

Val Val Ile Asp Lys Ser Tyr Leu Glu Asn Leu Gln Ser Asp Ser Ser
                885                 890                 895

Ile Val Thr Met Ala Phe Pro Thr Leu Gln Ala Ile Leu Ala Gln Asp
            900                 905                 910

Ile Gln Glu Asn Asn Phe Ala Glu Ser Leu Val Met Thr Thr Thr Val
        915                 920                 925

Ser His Asn Thr Thr Met Pro Phe Arg Ile Ser Met Thr Phe Lys Asn
    930                 935                 940

Asn Ser Pro Ser Gly Gly Glu Thr Lys Cys Val Phe Trp Asn Phe Arg
945                 950                 955                 960

Leu Ala Asn Asn Thr Gly Gly Trp Asp Ser Ser Gly Cys Tyr Val Glu
                965                 970                 975

Glu Gly Asp Gly Asp Asn Val Thr Cys Ile Cys Asp His Leu Thr Ser
            980                 985                 990

Phe Ser Ile Leu Met Ser Pro Asp  Ser Pro Asp Pro Ser  Ser Leu Leu
        995                 1000                1005

Gly Ile  Leu Leu Asp Ile Ile  Ser Tyr Val Gly Val  Gly Phe Ser
    1010                1015                1020

Ile Leu  Ser Leu Ala Ala Cys  Leu Val Val Glu Ala  Val Val Trp
    1025                1030                1035

Lys Ser  Val Thr Lys Asn Arg  Thr Ser Tyr Met Arg  His Thr Cys
    1040                1045                1050

Ile Val  Asn Ile Ala Ala Ser  Leu Leu Val Ala Asn  Thr Trp Phe
    1055                1060                1065

Ile Val  Val Ala Ala Ile Gln  Asp Asn Arg Tyr Ile  Leu Cys Lys
    1070                1075                1080

Thr Ala  Cys Val Ala Ala Thr  Phe Phe Ile His Phe  Phe Tyr Leu
    1085                1090                1095

Ser Val  Phe Phe Trp Met Leu  Thr Leu Gly Leu Met  Leu Phe Tyr
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    1100                1105                1110

Arg Leu  Val Phe Ile Leu His  Glu Thr Ser Arg Ser  Thr Gln Lys
    1115                1120                1125

Ala Ile  Ala Phe Cys Leu Gly  Tyr Gly Cys Pro Leu  Ala Ile Ser
    1130                1135                1140

Val Ile  Thr Leu Gly Ala Thr  Gln Pro Arg Glu Val  Tyr Thr Arg
    1145                1150                1155

Lys Asn  Val Cys Trp Leu Asn  Trp Glu Asp Thr Lys  Ala Leu Leu
    1160                1165                1170

Ala Phe  Ala Ile Pro Ala Leu  Ile Ile Val Val Val  Asn Ile Thr
    1175                1180                1185

Ile Thr  Ile Val Val Ile Thr  Lys Ile Leu Arg Pro  Ser Ile Gly
    1190                1195                1200

Asp Lys  Pro Cys Lys Gln Glu  Lys Ser Ser Leu Phe  Gln Ile Ser
    1205                1210                1215

Lys Ser  Ile Gly Val Leu Thr  Pro Leu Leu Gly Leu  Thr Trp Gly
    1220                1225                1230

Phe Gly  Leu Thr Thr Val Phe  Pro Gly Thr Asn Leu  Val Phe His
    1235                1240                1245

Ile Ile  Phe Ala Ile Leu Asn  Val Phe Gln Gly Leu  Phe Ile Leu
    1250                1255                1260

Leu Phe  Gly Cys Leu Trp Asp  Leu Lys Val Gln Glu  Ala Leu Leu
    1265                1270                1275

Asn Lys  Phe Ser Leu Ser Arg  Trp Ser Ser Gln His  Ser Lys Ser
    1280                1285                1290

Thr Ser  Leu Gly Ser Ser Thr  Pro Val Phe Ser Met  Ser Ser Pro
    1295                1300                1305

Ile Ser  Arg Arg Phe Asn Asn  Leu Phe Gly Lys Thr  Gly Thr Tyr
    1310                1315                1320

Asn Val  Ser Thr Pro Glu Ala  Thr Ser Ser Ser Leu  Glu Asn Ser
    1325                1330                1335

Ser Ser  Ala Ser Ser Leu Leu  Asn
    1340                1345


<210> SEQ ID NO 51
<211> LENGTH: 760
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 51

Met Lys Thr Trp Val Lys Ile Val Phe Gly Val Ala Thr Ser Ala Val
1               5                   10                  15

Leu Ala Leu Leu Val Met Cys Ile Val Leu Arg Pro Ser Arg Val His
            20                  25                  30

Asn Ser Glu Glu Asn Thr Met Arg Ala Leu Thr Leu Lys Asp Ile Leu
        35                  40                  45

Asn Gly Thr Phe Ser Tyr Lys Thr Phe Phe Pro Asn Trp Ile Ser Gly
    50                  55                  60

Gln Glu Tyr Leu His Gln Ser Ala Asp Asn Asn Ile Val Leu Tyr Asn
65                  70                  75                  80

Ile Glu Thr Gly Gln Ser Tyr Thr Ile Leu Ser Asn Arg Thr Met Lys
                85                  90                  95
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Ser Val Asn Ala Ser Asn Tyr Gly Leu Ser Pro Asp Arg Gln Phe Val
            100                 105                 110

Tyr Leu Glu Ser Asp Tyr Ser Lys Leu Trp Arg Tyr Ser Tyr Thr Ala
        115                 120                 125

Thr Tyr Tyr Ile Tyr Asp Leu Ser Asn Gly Glu Phe Val Arg Gly Asn
    130                 135                 140

Glu Leu Pro Arg Pro Ile Gln Tyr Leu Cys Trp Ser Pro Val Gly Ser
145                 150                 155                 160

Lys Leu Ala Tyr Val Tyr Gln Asn Asn Ile Tyr Leu Lys Gln Arg Pro
                165                 170                 175

Gly Asp Pro Pro Phe Gln Ile Thr Phe Asn Gly Arg Glu Asn Lys Ile
            180                 185                 190

Phe Asn Gly Ile Pro Asp Trp Val Tyr Glu Glu Glu Met Leu Pro Thr
        195                 200                 205

Lys Tyr Ala Leu Trp Trp Ser Pro Asn Gly Lys Phe Leu Ala Tyr Ala
    210                 215                 220

Glu Phe Asn Asp Thr Asp Ile Pro Val Ile Ala Tyr Ser Tyr Tyr Gly
225                 230                 235                 240

Asp Glu Gln Tyr Pro Arg Thr Ile Asn Ile Pro Tyr Pro Lys Ala Gly
                245                 250                 255

Ala Lys Asn Pro Val Val Arg Ile Phe Ile Ile Asp Thr Thr Tyr Pro
            260                 265                 270

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

Ser Asp Tyr Tyr Phe Ser Trp Leu Thr Trp Val Thr Asp Glu Arg Val
    290                 295                 300

Cys Leu Gln Trp Leu Lys Arg Val Gln Asn Val Ser Val Leu Ser Ile
305                 310                 315                 320

Cys Asp Phe Arg Glu Asp Trp Gln Thr Trp Asp Cys Pro Lys Thr Gln
                325                 330                 335

Glu His Ile Glu Glu Ser Arg Thr Gly Trp Ala Gly Gly Phe Phe Val
            340                 345                 350

Ser Thr Pro Val Phe Ser Tyr Asp Ala Ile Ser Tyr Tyr Lys Ile Phe
        355                 360                 365

Ser Asp Lys Asp Gly Tyr Lys His Ile His Tyr Ile Lys Asp Thr Val
    370                 375                 380

Glu Asn Ala Ile Gln Ile Thr Ser Gly Lys Trp Glu Ala Ile Asn Ile
385                 390                 395                 400

Phe Arg Val Thr Gln Asp Ser Leu Phe Tyr Ser Ser Asn Glu Phe Glu
                405                 410                 415

Glu Tyr Pro Gly Arg Arg Asn Ile Tyr Arg Ile Ser Ile Gly Ser Tyr
            420                 425                 430

Pro Pro Ser Lys Lys Cys Val Thr Cys His Leu Arg Lys Glu Arg Cys
        435                 440                 445

Gln Tyr Tyr Thr Ala Ser Phe Ser Asp Tyr Ala Lys Tyr Tyr Ala Leu
    450                 455                 460

Val Cys Tyr Gly Pro Gly Ile Pro Ile Ser Thr Leu His Asp Gly Arg
465                 470                 475                 480

Thr Asp Gln Glu Ile Lys Ile Leu Glu Glu Asn Lys Glu Leu Glu Asn
                485                 490                 495

Ala Leu Lys Asn Ile Gln Leu Pro Lys Glu Glu Ile Lys Lys Leu Glu
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            500                 505                 510

Val Asp Glu Ile Thr Leu Trp Tyr Lys Met Ile Leu Pro Pro Gln Phe
        515                 520                 525

Asp Arg Ser Lys Lys Tyr Pro Leu Leu Ile Gln Val Tyr Gly Gly Pro
    530                 535                 540

Cys Ser Gln Ser Val Arg Ser Val Phe Ala Val Asn Trp Ile Ser Tyr
545                 550                 555                 560

Leu Ala Ser Lys Glu Gly Met Val Ile Ala Leu Val Asp Gly Arg Gly
                565                 570                 575

Thr Ala Phe Gln Gly Asp Lys Leu Leu Tyr Ala Val Tyr Arg Lys Leu
            580                 585                 590

Gly Val Tyr Glu Val Glu Asp Gln Ile Thr Ala Val Arg Lys Phe Ile
        595                 600                 605

Glu Met Gly Phe Ile Asp Glu Lys Arg Ile Ala Ile Trp Gly Trp Ser
    610                 615                 620

Tyr Gly Gly Tyr Val Ser Ser Leu Ala Leu Ala Ser Gly Thr Gly Leu
625                 630                 635                 640

Phe Lys Cys Gly Ile Ala Val Ala Pro Val Ser Ser Trp Glu Tyr Tyr
                645                 650                 655

Ala Ser Val Tyr Thr Glu Arg Phe Met Gly Leu Pro Thr Lys Asp Asp
            660                 665                 670

Asn Leu Glu His Tyr Lys Asn Ser Thr Val Met Ala Arg Ala Glu Tyr
        675                 680                 685

Phe Arg Asn Val Asp Tyr Leu Leu Ile His Gly Thr Ala Asp Asp Asn
    690                 695                 700

Val His Phe Gln Asn Ser Ala Gln Ile Ala Lys Ala Leu Val Asn Ala
705                 710                 715                 720

Gln Val Asp Phe Gln Ala Met Trp Tyr Ser Asp Gln Asn His Gly Leu
                725                 730                 735

Ser Gly Leu Ser Thr Asn His Leu Tyr Thr His Met Thr His Phe Leu
            740                 745                 750

Lys Gln Cys Phe Ser Leu Ser Asp
        755                 760


<210> SEQ ID NO 52
<211> LENGTH: 545
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 52

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

Val Ser Pro Val Ala Leu Asp Pro Cys Ser Ala Tyr Ile Ser Leu Asn
            20                  25                  30

Glu Pro Trp Arg Asn Thr Asp His Gln Leu Asp Glu Ser Gln Gly Pro
        35                  40                  45

Pro Leu Cys Asp Asn His Val Asn Gly Glu Trp Tyr His Phe Thr Gly
    50                  55                  60

Met Ala Gly Asp Ala Met Pro Thr Phe Cys Ile Pro Glu Asn His Cys
65                  70                  75                  80

Gly Thr His Ala Pro Val Trp Leu Asn Gly Ser His Pro Leu Glu Gly
                85                  90                  95
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Asp Gly Ile Val Gln Arg Gln Ala Cys Ala Ser Phe Asn Gly Asn Cys
            100                 105                 110

Cys Leu Trp Asn Thr Thr Val Glu Val Lys Ala Cys Pro Gly Gly Tyr
        115                 120                 125

Tyr Val Tyr Arg Leu Thr Lys Pro Ser Val Cys Phe His Val Tyr Cys
    130                 135                 140

Gly His Phe Tyr Asp Ile Cys Asp Glu Asp Cys His Gly Ser Cys Ser
145                 150                 155                 160

Asp Thr Ser Glu Cys Thr Cys Ala Pro Gly Thr Val Leu Gly Pro Asp
                165                 170                 175

Arg Gln Thr Cys Phe Asp Glu Asn Glu Cys Glu Gln Asn Asn Gly Gly
            180                 185                 190

Cys Ser Glu Ile Cys Val Asn Leu Lys Asn Ser Tyr Arg Cys Glu Cys
        195                 200                 205

Gly Val Gly Arg Val Leu Arg Ser Asp Gly Lys Thr Cys Glu Asp Val
    210                 215                 220

Glu Gly Cys His Asn Asn Asn Gly Gly Cys Ser His Ser Cys Leu Gly
225                 230                 235                 240

Ser Glu Lys Gly Tyr Gln Cys Glu Cys Pro Arg Gly Leu Val Leu Ser
                245                 250                 255

Glu Asp Asn His Thr Cys Gln Val Pro Val Leu Cys Lys Ser Asn Ala
            260                 265                 270

Ile Glu Val Asn Ile Pro Arg Glu Leu Val Gly Gly Leu Glu Leu Phe
        275                 280                 285

Leu Thr Asn Thr Ser Cys Arg Gly Val Ser Asn Gly Thr His Val Asn
    290                 295                 300

Ile Leu Phe Ser Leu Lys Thr Cys Gly Thr Val Val Asp Val Val Asn
305                 310                 315                 320

Asp Lys Ile Val Ala Ser Asn Leu Val Thr Gly Leu Pro Lys Gln Thr
                325                 330                 335

Pro Gly Ser Ser Gly Asp Phe Ile Ile Arg Thr Ser Lys Leu Leu Ile
            340                 345                 350

Pro Val Thr Cys Glu Phe Pro Arg Leu Tyr Thr Ile Ser Glu Gly Tyr
        355                 360                 365

Val Pro Asn Leu Arg Asn Ser Pro Leu Glu Ile Met Ser Arg Asn His
    370                 375                 380

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

Glu Pro Tyr Arg Glu Ala Leu Pro Thr Leu Lys Leu Arg Asp Ser Leu
                405                 410                 415

Tyr Phe Gly Ile Glu Pro Val Val His Val Ser Gly Leu Glu Ser Leu
            420                 425                 430

Val Glu Ser Cys Phe Ala Thr Pro Thr Ser Lys Ile Asp Glu Val Leu
        435                 440                 445

Lys Tyr Tyr Leu Ile Arg Asp Gly Cys Val Ser Asp Asp Ser Val Lys
    450                 455                 460

Gln Tyr Thr Ser Arg Asp His Leu Ala Lys His Phe Gln Val Pro Val
465                 470                 475                 480

Phe Lys Phe Val Gly Lys Asp His Lys Glu Val Phe Leu His Cys Arg
                485                 490                 495

Val Leu Val Cys Gly Val Leu Asp Glu Arg Ser Arg Cys Ala Gln Gly
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            500                 505                 510

Cys His Arg Arg Met Arg Arg Gly Ala Gly Gly Glu Asp Ser Ala Gly
        515                 520                 525

Leu Gln Gly Gln Thr Leu Thr Gly Gly Pro Ile Arg Ile Asp Trp Glu
    530                 535                 540

Asp
545


<210> SEQ ID NO 53
<211> LENGTH: 999
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 53

Met Ala Asp Lys Val Arg Arg Gln Arg Pro Arg Arg Arg Val Cys Trp
1               5                   10                  15

Ala Leu Val Ala Val Leu Leu Ala Asp Leu Leu Ala Leu Ser Asp Thr
            20                  25                  30

Leu Ala Val Met Ser Val Asp Leu Gly Ser Glu Ser Met Lys Val Ala
        35                  40                  45

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

Arg Arg Lys Thr Pro Val Ile Val Thr Leu Lys Glu Asn Glu Arg Phe
65                  70                  75                  80

Phe Gly Asp Ser Ala Ala Ser Met Ala Ile Lys Asn Pro Lys Ala Thr
                85                  90                  95

Leu Arg Tyr Phe Gln His Leu Leu Gly Lys Gln Ala Asp Asn Pro His
            100                 105                 110

Val Ala Leu Tyr Gln Ala Arg Phe Pro Glu His Glu Leu Thr Phe Asp
        115                 120                 125

Pro Gln Arg Gln Thr Val His Phe Gln Ile Ser Ser Gln Leu Gln Phe
    130                 135                 140

Ser Pro Glu Glu Val Leu Gly Met Val Leu Asn Tyr Ser Arg Ser Leu
145                 150                 155                 160

Ala Glu Asp Phe Ala Glu Gln Pro Ile Lys Asp Ala Val Ile Thr Val
                165                 170                 175

Pro Val Phe Phe Asn Gln Ala Glu Arg Arg Ala Val Leu Gln Ala Ala
            180                 185                 190

Arg Met Ala Gly Leu Lys Val Leu Gln Leu Ile Asn Asp Asn Thr Ala
        195                 200                 205

Thr Ala Leu Ser Tyr Gly Val Phe Arg Arg Lys Asp Ile Asn Thr Thr
    210                 215                 220

Ala Gln Asn Ile Met Phe Tyr Asp Met Gly Ser Gly Ser Thr Val Cys
225                 230                 235                 240

Thr Ile Val Thr Tyr Gln Met Val Lys Thr Lys Glu Ala Gly Met Gln
                245                 250                 255

Pro Gln Leu Gln Ile Arg Gly Val Gly Phe Asp Arg Thr Leu Gly Gly
            260                 265                 270

Leu Glu Met Glu Leu Arg Leu Arg Glu Arg Leu Ala Gly Leu Phe Asn
        275                 280                 285

Glu Gln Arg Lys Gly Gln Arg Ala Lys Asp Val Arg Glu Asn Pro Arg
    290                 295                 300
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Ala Met Ala Lys Leu Leu Arg Glu Ala Asn Arg Leu Lys Thr Val Leu
305                 310                 315                 320

Ser Ala Asn Ala Asp His Met Ala Gln Ile Glu Gly Leu Met Asp Asp
                325                 330                 335

Val Asp Phe Lys Ala Lys Val Thr Arg Val Glu Phe Glu Glu Leu Cys
            340                 345                 350

Ala Asp Leu Phe Glu Arg Val Pro Gly Pro Val Gln Gln Ala Leu Gln
        355                 360                 365

Ser Ala Glu Met Ser Leu Asp Glu Ile Glu Gln Val Ile Leu Val Gly
    370                 375                 380

Gly Ala Thr Arg Val Pro Arg Val Gln Glu Val Leu Leu Lys Ala Val
385                 390                 395                 400

Gly Lys Glu Glu Leu Gly Lys Asn Ile Asn Ala Asp Glu Ala Ala Ala
                405                 410                 415

Met Gly Ala Val Tyr Gln Ala Ala Ala Leu Ser Lys Ala Phe Lys Val
            420                 425                 430

Lys Pro Phe Val Val Arg Asp Ala Val Val Tyr Pro Ile Leu Val Glu
        435                 440                 445

Phe Thr Arg Glu Val Glu Glu Glu Pro Gly Ile His Ser Leu Lys His
    450                 455                 460

Asn Lys Arg Val Leu Phe Ser Arg Met Gly Pro Tyr Pro Gln Arg Lys
465                 470                 475                 480

Val Ile Thr Phe Asn Arg Tyr Ser His Asp Phe Asn Phe His Ile Asn
                485                 490                 495

Tyr Gly Asp Leu Gly Phe Leu Gly Pro Glu Asp Leu Arg Val Phe Gly
            500                 505                 510

Ser Gln Asn Leu Thr Thr Val Lys Leu Lys Gly Val Gly Asp Ser Phe
        515                 520                 525

Lys Lys Tyr Pro Asp Tyr Glu Ser Lys Gly Ile Lys Ala His Phe Asn
    530                 535                 540

Leu Asp Glu Ser Gly Val Leu Ser Leu Asp Arg Val Glu Ser Val Phe
545                 550                 555                 560

Glu Thr Leu Val Glu Asp Ser Ala Glu Glu Glu Ser Thr Leu Thr Lys
                565                 570                 575

Leu Gly Asn Thr Ile Ser Ser Leu Phe Gly Gly Gly Thr Thr Pro Asp
            580                 585                 590

Ala Lys Glu Asn Gly Thr Asp Thr Val Gln Glu Glu Glu Glu Ser Pro
        595                 600                 605

Ala Glu Gly Ser Lys Asp Glu Pro Gly Glu Gln Val Glu Leu Lys Glu
    610                 615                 620

Glu Ala Glu Ala Pro Val Glu Asp Gly Ser Gln Pro Pro Pro Pro Glu
625                 630                 635                 640

Pro Lys Gly Asp Ala Thr Pro Glu Gly Glu Lys Ala Thr Glu Lys Glu
                645                 650                 655

Asn Gly Asp Lys Ser Glu Ala Gln Lys Pro Ser Glu Lys Ala Glu Ala
            660                 665                 670

Gly Pro Glu Gly Val Ala Pro Ala Pro Glu Gly Glu Lys Lys Gln Lys
        675                 680                 685

Pro Ala Arg Lys Arg Arg Met Val Glu Glu Ile Gly Val Glu Leu Val
    690                 695                 700

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

Gln Lys Leu Gln Asp Leu Thr Leu Arg Asp Leu Glu Lys Gln Glu Arg
                725                 730                 735

Glu Lys Ala Ala Asn Ser Leu Glu Ala Phe Ile Phe Glu Thr Gln Asp
            740                 745                 750

Lys Leu Tyr Gln Pro Glu Tyr Gln Glu Val Ser Thr Glu Glu Gln Arg
        755                 760                 765

Glu Glu Ile Ser Gly Lys Leu Ser Ala Ala Ser Thr Trp Leu Glu Asp
    770                 775                 780

Glu Gly Val Gly Ala Thr Thr Val Met Leu Lys Glu Lys Leu Ala Glu
785                 790                 795                 800

Leu Arg Lys Leu Cys Gln Gly Leu Phe Phe Arg Val Glu Glu Arg Lys
                805                 810                 815

Lys Trp Pro Glu Arg Leu Ser Ala Leu Asp Asn Leu Leu Asn His Ser
            820                 825                 830

Ser Met Phe Leu Lys Gly Ala Arg Leu Ile Pro Glu Met Asp Gln Ile
        835                 840                 845

Phe Thr Glu Val Glu Met Thr Thr Leu Glu Lys Val Ile Asn Glu Thr
    850                 855                 860

Trp Ala Trp Lys Asn Ala Thr Leu Ala Glu Gln Ala Lys Leu Pro Ala
865                 870                 875                 880

Thr Glu Lys Pro Val Leu Leu Ser Lys Asp Ile Glu Ala Lys Met Met
                885                 890                 895

Ala Leu Asp Arg Glu Val Gln Tyr Leu Leu Asn Lys Ala Lys Phe Thr
            900                 905                 910

Lys Pro Arg Pro Arg Pro Lys Asp Lys Asn Gly Thr Arg Ala Glu Pro
        915                 920                 925

Pro Leu Asn Ala Ser Ala Ser Asp Gln Gly Glu Lys Val Ile Pro Pro
    930                 935                 940

Ala Gly Gln Thr Glu Asp Ala Glu Pro Ile Ser Glu Pro Glu Lys Val
945                 950                 955                 960

Glu Thr Gly Ser Glu Pro Gly Asp Thr Glu Pro Leu Glu Leu Gly Gly
                965                 970                 975

Pro Gly Ala Glu Pro Glu Gln Lys Glu Gln Ser Thr Gly Gln Lys Arg
            980                 985                 990

Pro Leu Lys Asn Asp Glu Leu
        995


<210> SEQ ID NO 54
<211> LENGTH: 480
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 54

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

Ala Val Pro Leu Leu Ala Thr Glu Ser Val Lys Gln Glu Glu Ala Gly
            20                  25                  30

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

Arg Pro Gly Gly Ser Thr Lys Ser His Pro Glu Pro Gln Thr Pro Lys
    50                  55                  60
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Asp Ser Pro Ser Lys Ser Ser Ala Glu Ala Gln Thr Pro Glu Asp Thr
65                  70                  75                  80

Pro Asn Lys Ser Gly Ala Glu Ala Lys Thr Gln Lys Asp Ser Ser Asn
                85                  90                  95

Lys Ser Gly Ala Glu Ala Lys Thr Gln Lys Gly Ser Thr Ser Lys Ser
            100                 105                 110

Gly Ser Glu Ala Gln Thr Thr Lys Asp Ser Thr Ser Lys Ser His Pro
        115                 120                 125

Glu Leu Gln Thr Pro Lys Asp Ser Thr Gly Lys Ser Gly Ala Glu Ala
    130                 135                 140

Gln Thr Pro Glu Asp Ser Pro Asn Arg Ser Gly Ala Glu Ala Lys Thr
145                 150                 155                 160

Gln Lys Asp Ser Pro Ser Lys Ser Gly Ser Glu Ala Gln Thr Thr Lys
                165                 170                 175

Asp Val Pro Asn Lys Ser Gly Ala Asp Gly Gln Thr Pro Lys Asp Gly
            180                 185                 190

Ser Ser Lys Ser Gly Ala Glu Asp Gln Thr Pro Lys Asp Val Pro Asn
        195                 200                 205

Lys Ser Gly Ala Glu Lys Gln Thr Pro Lys Asp Gly Ser Asn Lys Ser
    210                 215                 220

Gly Ala Glu Glu Gln Gly Pro Ile Asp Gly Pro Ser Lys Ser Gly Ala
225                 230                 235                 240

Glu Glu Gln Thr Ser Lys Asp Ser Pro Asn Lys Val Val Pro Glu Gln
                245                 250                 255

Pro Ser Arg Lys Asp His Ser Lys Pro Ile Ser Asn Pro Ser Asp Asn
            260                 265                 270

Lys Glu Leu Pro Lys Ala Asp Thr Asn Gln Leu Ala Asp Lys Gly Lys
        275                 280                 285

Leu Ser Pro His Ala Phe Lys Thr Glu Ser Gly Glu Glu Thr Asp Leu
    290                 295                 300

Ile Ser Pro Pro Gln Glu Glu Val Lys Ser Ser Glu Pro Thr Glu Asp
305                 310                 315                 320

Val Glu Pro Lys Glu Ala Glu Asp Asp Asp Thr Gly Pro Glu Glu Gly
                325                 330                 335

Ser Pro Pro Lys Glu Glu Lys Glu Lys Met Ser Gly Ser Ala Ser Ser
            340                 345                 350

Glu Asn Arg Glu Gly Thr Leu Ser Asp Ser Thr Gly Ser Glu Lys Asp
        355                 360                 365

Asp Leu Tyr Pro Asn Gly Ser Gly Asn Gly Ser Ala Glu Ser Ser His
    370                 375                 380

Phe Phe Ala Tyr Leu Val Thr Ala Ala Ile Leu Val Ala Val Leu Tyr
385                 390                 395                 400

Ile Ala His His Asn Lys Arg Lys Ile Ile Ala Phe Val Leu Glu Gly
                405                 410                 415

Lys Arg Ser Lys Val Thr Arg Arg Pro Lys Ala Ser Asp Tyr Gln Arg
            420                 425                 430

Leu Asp Gln Lys Tyr Val Leu Ile Leu Asn Val Phe Pro Ala Pro Pro
        435                 440                 445

Lys Arg Ser Phe Leu Pro Gln Val Leu Thr Glu Trp Tyr Ile Pro Leu
    450                 455                 460

Glu Lys Asp Glu Arg His Gln Trp Ile Val Leu Leu Ser Phe Gln Leu
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465                 470                 475                 480


<210> SEQ ID NO 55
<211> LENGTH: 623
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 55

Met Glu Ser Tyr His Lys Pro Asp Gln Gln Lys Leu Gln Ala Leu Lys
1               5                   10                  15

Asp Thr Ala Asn Arg Leu Arg Ile Ser Ser Ile Gln Ala Thr Thr Ala
            20                  25                  30

Ala Gly Ser Gly His Pro Thr Ser Cys Cys Ser Ala Ala Glu Ile Met
        35                  40                  45

Ala Val Leu Phe Phe His Thr Met Arg Tyr Lys Ser Gln Asp Pro Arg
    50                  55                  60

Asn Pro His Asn Asp Arg Phe Val Leu Ser Lys Gly His Ala Ala Pro
65                  70                  75                  80

Ile Leu Tyr Ala Val Trp Ala Glu Ala Gly Phe Leu Ala Glu Ala Glu
                85                  90                  95

Leu Leu Asn Leu Arg Lys Ile Ser Ser Asp Leu Asp Gly His Pro Val
            100                 105                 110

Pro Lys Gln Ala Phe Thr Asp Val Ala Thr Gly Ser Leu Gly Gln Gly
        115                 120                 125

Leu Gly Ala Ala Cys Gly Met Ala Tyr Thr Gly Lys Tyr Phe Asp Lys
    130                 135                 140

Ala Ser Tyr Arg Val Tyr Cys Leu Leu Gly Asp Gly Glu Leu Ser Glu
145                 150                 155                 160

Gly Ser Val Trp Glu Ala Met Ala Phe Ala Ser Ile Tyr Lys Leu Asp
                165                 170                 175

Asn Leu Val Ala Ile Leu Asp Ile Asn Arg Leu Gly Gln Ser Asp Pro
            180                 185                 190

Ala Pro Leu Gln His Gln Met Asp Ile Tyr Gln Lys Arg Cys Glu Ala
        195                 200                 205

Phe Gly Trp His Ala Ile Ile Val Asp Gly His Ser Val Glu Glu Leu
    210                 215                 220

Cys Lys Ala Phe Gly Gln Ala Lys His Gln Pro Thr Ala Ile Ile Ala
225                 230                 235                 240

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

Trp His Gly Lys Pro Leu Pro Lys Asn Met Ala Glu Gln Ile Ile Gln
            260                 265                 270

Glu Ile Tyr Ser Gln Ile Gln Ser Lys Lys Lys Ile Leu Ala Thr Pro
        275                 280                 285

Pro Gln Glu Asp Ala Pro Ser Val Asp Ile Ala Asn Ile Arg Met Pro
    290                 295                 300

Ser Leu Pro Ser Tyr Lys Val Gly Asp Lys Ile Ala Thr Arg Lys Ala
305                 310                 315                 320

Tyr Gly Gln Ala Leu Ala Lys Leu Gly His Ala Ser Asp Arg Ile Ile
                325                 330                 335

Ala Leu Asp Gly Asp Thr Lys Asn Ser Thr Phe Ser Glu Ile Phe Lys
            340                 345                 350
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Lys Glu His Pro Asp Arg Phe Ile Glu Cys Tyr Ile Ala Glu Gln Asn
        355                 360                 365

Met Val Ser Ile Ala Val Gly Cys Ala Thr Arg Asn Arg Thr Val Pro
    370                 375                 380

Phe Cys Ser Thr Phe Ala Ala Phe Phe Thr Arg Ala Phe Asp Gln Ile
385                 390                 395                 400

Arg Met Ala Ala Ile Ser Glu Ser Asn Ile Asn Leu Cys Gly Ser His
                405                 410                 415

Cys Gly Val Ser Ile Gly Glu Asp Gly Pro Ser Gln Met Ala Leu Glu
            420                 425                 430

Asp Leu Ala Met Phe Arg Ser Val Pro Thr Ser Thr Val Phe Tyr Pro
        435                 440                 445

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

Lys Gly Ile Cys Phe Ile Arg Thr Ser Arg Pro Glu Asn Ala Ile Ile
465                 470                 475                 480

Tyr Asn Asn Asn Glu Asp Phe Gln Val Gly Gln Ala Lys Val Val Leu
                485                 490                 495

Lys Ser Lys Asp Asp Gln Val Thr Val Ile Gly Ala Gly Val Thr Leu
            500                 505                 510

His Glu Ala Leu Ala Ala Ala Glu Leu Leu Lys Lys Glu Lys Ile Asn
        515                 520                 525

Ile Arg Val Leu Asp Pro Phe Thr Ile Lys Pro Leu Asp Arg Lys Leu
    530                 535                 540

Ile Leu Asp Ser Ala Arg Ala Thr Lys Gly Arg Ile Leu Thr Val Glu
545                 550                 555                 560

Asp His Tyr Tyr Glu Gly Gly Ile Gly Glu Ala Val Ser Ser Ala Val
                565                 570                 575

Val Gly Glu Pro Gly Ile Thr Val Thr His Leu Ala Val Asn Arg Val
            580                 585                 590

Pro Arg Ser Gly Lys Pro Ala Glu Leu Leu Lys Met Phe Gly Ile Asp
        595                 600                 605

Arg Asp Ala Ile Ala Gln Ala Val Arg Gly Leu Ile Thr Lys Ala
    610                 615                 620


<210> SEQ ID NO 56
<211> LENGTH: 1897
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 56

Met Val Pro Leu Val Pro Ala Leu Val Met Leu Gly Leu Val Ala Gly
1               5                   10                  15

Ala His Gly Asp Ser Lys Pro Val Phe Ile Lys Val Pro Glu Asp Gln
            20                  25                  30

Thr Gly Leu Ser Gly Gly Val Ala Ser Phe Val Cys Gln Ala Thr Gly
        35                  40                  45

Glu Pro Lys Pro Arg Ile Thr Trp Met Lys Lys Gly Lys Lys Val Ser
    50                  55                  60

Ser Gln Arg Phe Glu Val Ile Glu Phe Asp Asp Gly Ala Gly Ser Val
65                  70                  75                  80

Leu Arg Ile Gln Pro Leu Arg Val Gln Arg Asp Glu Ala Ile Tyr Glu
                85                  90                  95
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Cys Thr Ala Thr Asn Ser Leu Gly Glu Ile Asn Thr Ser Ala Lys Leu
            100                 105                 110

Ser Val Leu Glu Glu Glu Gln Leu Pro Pro Gly Phe Pro Ser Ile Asp
        115                 120                 125

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

Leu Cys Ala Ala Gly Gly Asn Pro Asp Pro Glu Ile Ser Trp Phe Lys
145                 150                 155                 160

Asp Phe Leu Pro Val Asp Pro Ala Thr Ser Asn Gly Arg Ile Lys Gln
                165                 170                 175

Leu Arg Ser Gly Ala Leu Gln Ile Glu Ser Ser Glu Glu Ser Asp Gln
            180                 185                 190

Gly Lys Tyr Glu Cys Val Ala Thr Asn Ser Ala Gly Thr Arg Tyr Ser
        195                 200                 205

Ala Pro Ala Asn Leu Tyr Val Arg Val Arg Arg Val Ala Pro Arg Phe
    210                 215                 220

Ser Ile Pro Pro Ser Ser Gln Glu Val Met Pro Gly Gly Ser Val Asn
225                 230                 235                 240

Leu Thr Cys Val Ala Val Gly Ala Pro Met Pro Tyr Val Lys Trp Met
                245                 250                 255

Met Gly Ala Glu Glu Leu Thr Lys Glu Asp Glu Met Pro Val Gly Arg
            260                 265                 270

Asn Val Leu Glu Leu Ser Asn Val Val Arg Ser Ala Asn Tyr Thr Cys
        275                 280                 285

Val Ala Ile Ser Ser Leu Gly Met Ile Glu Ala Thr Ala Gln Val Thr
    290                 295                 300

Val Lys Ala Leu Pro Lys Pro Pro Ile Asp Leu Val Val Thr Glu Thr
305                 310                 315                 320

Thr Ala Thr Ser Val Thr Leu Thr Trp Asp Ser Gly Asn Ser Glu Pro
                325                 330                 335

Val Thr Tyr Tyr Gly Ile Gln Tyr Arg Ala Ala Gly Thr Glu Gly Pro
            340                 345                 350

Phe Gln Glu Val Asp Gly Val Ala Thr Thr Arg Tyr Ser Ile Gly Gly
        355                 360                 365

Leu Ser Pro Phe Ser Glu Tyr Ala Phe Arg Val Leu Ala Val Asn Ser
    370                 375                 380

Ile Gly Arg Gly Pro Pro Ser Glu Ala Val Arg Ala Arg Thr Gly Glu
385                 390                 395                 400

Gln Ala Pro Ser Ser Pro Pro Arg Arg Val Gln Ala Arg Met Leu Ser
                405                 410                 415

Ala Ser Thr Met Leu Val Gln Trp Glu Pro Pro Glu Glu Pro Asn Gly
            420                 425                 430

Leu Val Arg Gly Tyr Arg Val Tyr Tyr Thr Pro Asp Ser Arg Arg Pro
        435                 440                 445

Pro Asn Ala Trp His Lys His Asn Thr Asp Ala Gly Leu Leu Thr Thr
    450                 455                 460

Val Gly Ser Leu Leu Pro Gly Ile Thr Tyr Ser Leu Arg Val Leu Ala
465                 470                 475                 480

Phe Thr Ala Val Gly Asp Gly Pro Pro Ser Pro Thr Ile Gln Val Lys
                485                 490                 495
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Thr Gln Gln Gly Val Pro Ala Gln Pro Ala Asp Phe Gln Ala Glu Val
            500                 505                 510

Glu Ser Asp Thr Arg Ile Gln Leu Ser Trp Leu Leu Pro Pro Gln Glu
        515                 520                 525

Arg Ile Ile Met Tyr Glu Leu Val Tyr Trp Ala Ala Glu Asp Glu Asp
    530                 535                 540

Gln Gln His Lys Val Thr Phe Asp Pro Thr Ser Ser Tyr Thr Leu Glu
545                 550                 555                 560

Asp Leu Lys Pro Asp Thr Leu Tyr Arg Phe Gln Leu Ala Ala Arg Ser
                565                 570                 575

Asp Met Gly Val Gly Val Phe Thr Pro Thr Ile Glu Ala Arg Thr Ala
            580                 585                 590

Gln Ser Thr Pro Ser Ala Pro Pro Gln Lys Val Met Cys Val Ser Met
        595                 600                 605

Gly Ser Thr Thr Val Arg Val Ser Trp Val Pro Pro Pro Ala Asp Ser
    610                 615                 620

Arg Asn Gly Val Ile Thr Gln Tyr Ser Val Ala His Glu Ala Val Asp
625                 630                 635                 640

Gly Glu Asp Arg Gly Arg His Val Val Asp Gly Ile Ser Arg Glu His
                645                 650                 655

Ser Ser Trp Asp Leu Val Gly Leu Glu Lys Trp Thr Glu Tyr Arg Val
            660                 665                 670

Trp Val Arg Ala His Thr Asp Val Gly Pro Gly Pro Glu Ser Ser Pro
        675                 680                 685

Val Leu Val Arg Thr Asp Glu Asp Val Pro Ser Gly Pro Pro Arg Lys
    690                 695                 700

Val Glu Val Glu Pro Leu Asn Ser Thr Ala Val His Val Tyr Trp Lys
705                 710                 715                 720

Leu Pro Val Pro Ser Lys Gln His Gly Gln Ile Arg Gly Tyr Gln Val
                725                 730                 735

Thr Tyr Val Arg Leu Glu Asn Gly Glu Pro Arg Gly Leu Pro Ile Ile
            740                 745                 750

Gln Asp Val Met Leu Ala Glu Ala Gln Trp Arg Pro Glu Glu Ser Glu
        755                 760                 765

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

Val Thr Val Ala Ala Tyr Thr Thr Lys Gly Asp Gly Ala Arg Ser Lys
785                 790                 795                 800

Pro Lys Ile Val Thr Thr Thr Gly Ala Val Pro Gly Arg Pro Thr Met
                805                 810                 815

Met Ile Ser Thr Thr Ala Met Asn Thr Ala Leu Leu Gln Trp His Pro
            820                 825                 830

Pro Lys Glu Leu Pro Gly Glu Leu Leu Gly Tyr Arg Leu Gln Tyr Cys
        835                 840                 845

Arg Ala Asp Glu Ala Arg Pro Asn Thr Ile Asp Phe Gly Lys Asp Asp
    850                 855                 860

Gln His Phe Thr Val Thr Gly Leu His Lys Gly Thr Thr Tyr Ile Phe
865                 870                 875                 880

Arg Leu Ala Ala Lys Asn Arg Ala Gly Leu Gly Glu Glu Phe Glu Lys
                885                 890                 895

Glu Ile Arg Thr Pro Glu Asp Leu Pro Ser Gly Phe Pro Gln Asn Leu
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           900                 905                 910

His Val Thr Gly Leu Thr Thr Ser Thr Thr Glu Leu Ala Trp Asp Pro
       915                 920                 925

Pro Val Leu Ala Glu Arg Asn Gly Arg Ile Ile Ser Tyr Thr Val Val
    930                 935                 940

Phe Arg Asp Ile Asn Ser Gln Gln Glu Leu Gln Asn Ile Thr Thr Asp
945                 950                 955                 960

Thr Arg Phe Thr Leu Thr Gly Leu Lys Pro Asp Thr Thr Tyr Asp Ile
               965                 970                 975

Lys Val Arg Ala Trp Thr Ser Lys Gly Ser Gly Pro Leu Ser Pro Ser
           980                 985                 990

Ile Gln Ser Arg Thr Met Pro Val  Glu Gln Val Phe Ala  Lys Asn Phe
       995                 1000                1005

Arg Val  Ala Ala Ala Met Lys  Thr Ser Val Leu Leu  Ser Trp Glu
    1010                1015                1020

Val Pro  Asp Ser Tyr Lys Ser  Ala Val Pro Phe Lys  Ile Leu Tyr
    1025                1030                1035

Asn Gly  Gln Ser Val Glu Val  Asp Gly His Ser Met  Arg Lys Leu
    1040                1045                1050

Ile Ala  Asp Leu Gln Pro Asn  Thr Glu Tyr Ser Phe  Val Leu Met
    1055                1060                1065

Asn Arg  Gly Ser Ser Ala Gly  Gly Leu Gln His Leu  Val Ser Ile
    1070                1075                1080

Arg Thr  Ala Pro Asp Leu Leu  Pro His Lys Pro Leu  Pro Ala Ser
    1085                1090                1095

Ala Tyr  Ile Glu Asp Gly Arg  Phe Asp Leu Ser Met  Pro His Val
    1100                1105                1110

Gln Asp  Pro Ser Leu Val Arg  Trp Phe Tyr Ile Val  Val Val Pro
    1115                1120                1125

Ile Asp  Arg Val Gly Gly Ser  Met Leu Thr Pro Arg  Trp Ser Thr
    1130                1135                1140

Pro Glu  Glu Leu Glu Leu Asp  Glu Leu Leu Glu Ala  Ile Glu Gln
    1145                1150                1155

Gly Gly  Glu Glu Gln Arg Arg  Arg Arg Arg Gln Ala  Glu Arg Leu
    1160                1165                1170

Lys Pro  Tyr Val Ala Ala Gln  Leu Asp Val Leu Pro  Glu Thr Phe
    1175                1180                1185

Thr Leu  Gly Asp Lys Lys Asn  Tyr Arg Gly Phe Tyr  Asn Arg Pro
    1190                1195                1200

Leu Ser  Pro Asp Leu Ser Tyr  Gln Cys Phe Val Leu  Ala Ser Leu
    1205                1210                1215

Lys Glu  Pro Met Asp Gln Lys  Arg Tyr Ala Ser Ser  Pro Tyr Ser
    1220                1225                1230

Asp Glu  Ile Val Val Gln Val  Thr Pro Ala Gln Gln  Gln Glu Glu
    1235                1240                1245

Pro Glu  Met Leu Trp Val Thr  Gly Pro Val Leu Ala  Val Ile Leu
    1250                1255                1260

Ile Ile  Leu Ile Val Ile Ala  Ile Leu Leu Phe Lys  Arg Lys Arg
    1265                1270                1275

Thr His  Ser Pro Ser Ser Lys  Asp Glu Gln Ser Ile  Gly Leu Lys
    1280                1285                1290
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Asp Ser  Leu Leu Ala His Ser  Ser Asp Pro Val Glu  Met Arg Arg
    1295                 1300                 1305

Leu Asn  Tyr Gln Thr Pro Gly  Met Arg Asp His Pro  Pro Ile Pro
    1310                 1315                 1320

Ile Thr  Asp Leu Ala Asp Asn  Ile Glu Arg Leu Lys  Ala Asn Asp
    1325                 1330                 1335

Gly Leu  Lys Phe Ser Gln Glu  Tyr Glu Ser Ile Asp  Pro Gly Gln
    1340                 1345                 1350

Gln Phe  Thr Trp Glu Asn Ser  Asn Leu Glu Val Asn  Lys Pro Lys
    1355                 1360                 1365

Asn Arg  Tyr Ala Asn Val Ile  Ala Tyr Asp His Ser  Arg Val Ile
    1370                 1375                 1380

Leu Thr  Ser Ile Asp Gly Val  Pro Gly Ser Asp Tyr  Ile Asn Ala
    1385                 1390                 1395

Asn Tyr  Ile Asp Gly Tyr Arg  Lys Gln Asn Ala Tyr  Ile Ala Thr
    1400                 1405                 1410

Gln Gly  Pro Leu Pro Glu Thr  Met Gly Asp Phe Trp  Arg Met Val
    1415                 1420                 1425

Trp Glu  Gln Arg Thr Ala Thr  Val Val Met Met Thr  Arg Leu Glu
    1430                 1435                 1440

Glu Lys  Ser Arg Val Lys Cys  Asp Gln Tyr Trp Pro  Ala Arg Gly
    1445                 1450                 1455

Thr Glu  Thr Cys Gly Leu Ile  Gln Val Thr Leu Leu  Asp Thr Val
    1460                 1465                 1470

Glu Leu  Ala Thr Tyr Thr Val  Arg Thr Phe Ala Leu  His Lys Ser
    1475                 1480                 1485

Gly Ser  Ser Glu Lys Arg Glu  Leu Arg Gln Phe Gln  Phe Met Ala
    1490                 1495                 1500

Trp Pro  Asp His Gly Val Pro  Glu Tyr Pro Thr Pro  Ile Leu Ala
    1505                 1510                 1515

Phe Leu  Arg Arg Val Lys Ala  Cys Asn Pro Leu Asp  Ala Gly Pro
    1520                 1525                 1530

Met Val  Val His Cys Ser Ala  Gly Val Gly Arg Thr  Gly Cys Phe
    1535                 1540                 1545

Ile Val  Ile Asp Ala Met Leu  Glu Arg Met Lys His  Glu Lys Thr
    1550                 1555                 1560

Val Asp  Ile Tyr Gly His Val  Thr Cys Met Arg Ser  Gln Arg Asn
    1565                 1570                 1575

Tyr Met  Val Gln Thr Glu Asp  Gln Tyr Val Phe Ile  His Glu Ala
    1580                 1585                 1590

Leu Leu  Glu Ala Ala Thr Cys  Gly His Thr Glu Val  Pro Ala Arg
    1595                 1600                 1605

Asn Leu  Tyr Ala His Ile Gln  Lys Leu Gly Gln Val  Pro Pro Gly
    1610                 1615                 1620

Glu Ser  Val Thr Ala Met Glu  Leu Glu Phe Lys Leu  Leu Ala Ser
    1625                 1630                 1635

Ser Lys  Ala His Thr Ser Arg  Phe Ile Ser Ala Asn  Leu Pro Cys
    1640                 1645                 1650

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

Tyr Ile  Asn Ala Ser Phe Leu  Asp Gly Tyr Arg Gln  Gln Lys Ala
    1685                 1690                 1695

Tyr Ile  Ala Thr Gln Gly Pro  Leu Ala Glu Ser Thr  Glu Asp Phe
    1700                 1705                 1710

Trp Arg  Met Leu Trp Glu His  Asn Ser Thr Ile Ile  Val Met Leu
    1715                 1720                 1725

Thr Lys  Leu Arg Glu Met Gly  Arg Glu Lys Cys His  Gln Tyr Trp
    1730                 1735                 1740

Pro Ala  Glu Arg Ser Ala Arg  Tyr Gln Tyr Phe Val  Val Asp Pro
    1745                 1750                 1755

Met Ala  Glu Tyr Asn Met Pro  Gln Tyr Ile Leu Arg  Glu Phe Lys
    1760                 1765                 1770

Val Thr  Asp Ala Arg Asp Gly  Gln Ser Arg Thr Ile  Arg Gln Phe
    1775                 1780                 1785

Gln Phe  Thr Asp Trp Pro Glu  Gln Gly Val Pro Lys  Thr Gly Glu
    1790                 1795                 1800

Gly Phe  Ile Asp Phe Ile Gly  Gln Val His Lys Thr  Lys Glu Gln
    1805                 1810                 1815

Phe Gly  Gln Asp Gly Pro Ile  Thr Val His Cys Ser  Ala Gly Val
    1820                 1825                 1830

Gly Arg  Thr Gly Val Phe Ile  Thr Leu Ser Ile Val  Leu Glu Arg
    1835                 1840                 1845

Met Arg  Tyr Glu Gly Val Val  Asp Met Phe Gln Thr  Val Lys Thr
    1850                 1855                 1860

Leu Arg  Thr Gln Arg Pro Ala  Met Val Gln Thr Glu  Asp Gln Tyr
    1865                 1870                 1875

Gln Leu  Cys Tyr Arg Ala Ala  Leu Glu Tyr Leu Gly  Ser Phe Asp
    1880                 1885                 1890

His Tyr  Ala Thr
    1895


<210> SEQ ID NO 57
<211> LENGTH: 532
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 57

Met Ala Pro Ser Ser Pro Arg Pro Ala Leu Pro Ala Leu Leu Val Leu
1               5                  10                  15

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

Pro Ser Lys Val Ile Leu Pro Arg Gly Gly Ser Val Leu Val Thr Cys
        35                  40                  45

Ser Thr Ser Cys Asp Gln Pro Lys Leu Leu Gly Ile Glu Thr Pro Leu
    50                  55                  60

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

Leu Ser Asn Val Gln Glu Asp Ser Gln Pro Met Cys Tyr Ser Asn Cys
                85                  90                  95

Pro Asp Gly Gln Ser Thr Ala Lys Thr Phe Leu Thr Val Tyr Trp Thr
            100                 105                 110
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Pro Glu Arg Val Glu Leu Ala Pro Leu Pro Ser Trp Gln Pro Val Gly
        115                 120                 125

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

Asn Leu Thr Val Val Leu Leu Arg Gly Glu Lys Glu Leu Lys Arg Glu
145                 150                 155                 160

Pro Ala Val Gly Glu Pro Ala Glu Val Thr Thr Thr Val Leu Val Arg
                165                 170                 175

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

Arg Pro Gln Gly Leu Glu Leu Phe Glu Asn Thr Ser Ala Pro Tyr Gln
        195                 200                 205

Leu Gln Thr Phe Val Leu Pro Ala Thr Pro Pro Gln Leu Val Ser Pro
    210                 215                 220

Arg Val Leu Glu Val Asp Thr Gln Gly Thr Val Val Cys Ser Leu Asp
225                 230                 235                 240

Gly Leu Phe Pro Val Ser Glu Ala Gln Val His Leu Ala Leu Gly Asp
                245                 250                 255

Gln Arg Leu Asn Pro Thr Val Thr Tyr Gly Asn Asp Ser Phe Ser Ala
            260                 265                 270

Lys Ala Ser Val Ser Val Thr Ala Glu Asp Glu Gly Thr Gln Arg Leu
        275                 280                 285

Thr Cys Ala Val Ile Leu Gly Asn Gln Ser Gln Glu Thr Leu Gln Thr
    290                 295                 300

Val Thr Ile Tyr Ser Phe Pro Ala Pro Asn Val Ile Leu Thr Lys Pro
305                 310                 315                 320

Glu Val Ser Glu Gly Thr Glu Val Thr Val Lys Cys Glu Ala His Pro
                325                 330                 335

Arg Ala Lys Val Thr Leu Asn Gly Val Pro Ala Gln Pro Leu Gly Pro
            340                 345                 350

Arg Ala Gln Leu Leu Leu Lys Ala Thr Pro Glu Asp Asn Gly Arg Ser
        355                 360                 365

Phe Ser Cys Ser Ala Thr Leu Glu Val Ala Gly Gln Leu Ile His Lys
    370                 375                 380

Asn Gln Thr Arg Glu Leu Arg Val Leu Tyr Gly Pro Arg Leu Asp Glu
385                 390                 395                 400

Arg Asp Cys Pro Gly Asn Trp Thr Trp Pro Glu Asn Ser Gln Gln Thr
                405                 410                 415

Pro Met Cys Gln Ala Trp Gly Asn Pro Leu Pro Glu Leu Lys Cys Leu
            420                 425                 430

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

Arg Asp Leu Glu Gly Thr Tyr Leu Cys Arg Ala Arg Ser Thr Gln Gly
    450                 455                 460

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

Ile Val Ile Ile Thr Val Val Ala Ala Ala Val Ile Met Gly Thr Ala
                485                 490                 495

Gly Leu Ser Thr Tyr Leu Tyr Asn Arg Gln Arg Lys Ile Lys Lys Tyr
            500                 505                 510
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Arg Leu Gln Gln Ala Gln Lys Gly Thr Pro Met Lys Pro Asn Thr Gln
        515                 520                 525

Ala Thr Pro Pro
    530


<210> SEQ ID NO 58
<211> LENGTH: 860
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 58

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

Ala Ala Ala Gly Thr Ala Val Gly Asp Arg Cys Glu Arg Asn Glu Phe
            20                  25                  30

Gln Cys Gln Asp Gly Lys Cys Ile Ser Tyr Lys Trp Val Cys Asp Gly
        35                  40                  45

Ser Ala Glu Cys Gln Asp Gly Ser Asp Glu Ser Gln Glu Thr Cys Leu
    50                  55                  60

Ser Val Thr Cys Lys Ser Gly Asp Phe Ser Cys Gly Gly Arg Val Asn
65                  70                  75                  80

Arg Cys Ile Pro Gln Phe Trp Arg Cys Asp Gly Gln Val Asp Cys Asp
                85                  90                  95

Asn Gly Ser Asp Glu Gln Gly Cys Pro Pro Lys Thr Cys Ser Gln Asp
            100                 105                 110

Glu Phe Arg Cys His Asp Gly Lys Cys Ile Ser Arg Gln Phe Val Cys
        115                 120                 125

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

Val Leu Thr Cys Gly Pro Ala Ser Phe Gln Cys Asn Ser Ser Thr Cys
145                 150                 155                 160

Ile Pro Gln Leu Trp Ala Cys Asp Asn Asp Pro Asp Cys Glu Asp Gly
                165                 170                 175

Ser Asp Glu Trp Pro Gln Arg Cys Arg Gly Leu Tyr Val Phe Gln Gly
            180                 185                 190

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

Cys Ile His Ser Ser Trp Arg Cys Asp Gly Gly Pro Asp Cys Lys Asp
    210                 215                 220

Lys Ser Asp Glu Glu Asn Cys Ala Val Ala Thr Cys Arg Pro Asp Glu
225                 230                 235                 240

Phe Gln Cys Ser Asp Gly Asn Cys Ile His Gly Ser Arg Gln Cys Asp
                245                 250                 255

Arg Glu Tyr Asp Cys Lys Asp Met Ser Asp Glu Val Gly Cys Val Asn
            260                 265                 270

Val Thr Leu Cys Glu Gly Pro Asn Lys Phe Lys Cys His Ser Gly Glu
        275                 280                 285

Cys Ile Thr Leu Asp Lys Val Cys Asn Met Ala Arg Asp Cys Arg Asp
    290                 295                 300

Trp Ser Asp Glu Pro Ile Lys Glu Cys Gly Thr Asn Glu Cys Leu Asp
305                 310                 315                 320

Asn Asn Gly Gly Cys Ser His Val Cys Asn Asp Leu Lys Ile Gly Tyr
                325                 330                 335
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```
Glu Cys Leu Cys Pro Asp Gly Phe Gln Leu Val Ala Gln Arg Arg Cys
            340                 345                 350

Glu Asp Ile Asp Glu Cys Gln Asp Pro Asp Thr Cys Ser Gln Leu Cys
        355                 360                 365

Val Asn Leu Glu Gly Gly Tyr Lys Cys Gln Cys Glu Glu Gly Phe Gln
    370                 375                 380

Leu Asp Pro His Thr Lys Ala Cys Lys Ala Val Gly Ser Ile Ala Tyr
385                 390                 395                 400

Leu Phe Phe Thr Asn Arg His Glu Val Arg Lys Met Thr Leu Asp Arg
                405                 410                 415

Ser Glu Tyr Thr Ser Leu Ile Pro Asn Leu Arg Asn Val Val Ala Leu
            420                 425                 430

Asp Thr Glu Val Ala Ser Asn Arg Ile Tyr Trp Ser Asp Leu Ser Gln
        435                 440                 445

Arg Met Ile Cys Ser Thr Gln Leu Asp Arg Ala His Gly Val Ser Ser
    450                 455                 460

Tyr Asp Thr Val Ile Ser Arg Asp Ile Gln Ala Pro Asp Gly Leu Ala
465                 470                 475                 480

Val Asp Trp Ile His Ser Asn Ile Tyr Trp Thr Asp Ser Val Leu Gly
                485                 490                 495

Thr Val Ser Val Ala Asp Thr Lys Gly Val Lys Arg Lys Thr Leu Phe
            500                 505                 510

Arg Glu Asn Gly Ser Lys Pro Arg Ala Ile Val Val Asp Pro Val His
        515                 520                 525

Gly Phe Met Tyr Trp Thr Asp Trp Gly Thr Pro Ala Lys Ile Lys Lys
    530                 535                 540

Gly Gly Leu Asn Gly Val Asp Ile Tyr Ser Leu Val Thr Glu Asn Ile
545                 550                 555                 560

Gln Trp Pro Asn Gly Ile Thr Leu Asp Leu Leu Ser Gly Arg Leu Tyr
                565                 570                 575

Trp Val Asp Ser Lys Leu His Ser Ile Ser Ser Ile Asp Val Asn Gly
            580                 585                 590

Gly Asn Arg Lys Thr Ile Leu Glu Asp Glu Lys Arg Leu Ala His Pro
        595                 600                 605

Phe Ser Leu Ala Val Phe Glu Asp Lys Val Phe Trp Thr Asp Ile Ile
    610                 615                 620

Asn Glu Ala Ile Phe Ser Ala Asn Arg Leu Thr Gly Ser Asp Val Asn
625                 630                 635                 640

Leu Leu Ala Glu Asn Leu Leu Ser Pro Glu Asp Met Val Leu Phe His
                645                 650                 655

Asn Leu Thr Gln Pro Arg Gly Val Asn Trp Cys Glu Arg Thr Thr Leu
            660                 665                 670

Ser Asn Gly Gly Cys Gln Tyr Leu Cys Leu Pro Ala Pro Gln Ile Asn
        675                 680                 685

Pro His Ser Pro Lys Phe Thr Cys Ala Cys Pro Asp Gly Met Leu Leu
    690                 695                 700

Ala Arg Asp Met Arg Ser Cys Leu Thr Glu Ala Glu Ala Ala Val Ala
705                 710                 715                 720

Thr Gln Glu Thr Ser Thr Val Arg Leu Lys Val Ser Ser Thr Ala Val
                725                 730                 735
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Arg Thr Gln His Thr Thr Thr Arg Pro Val Pro Asp Thr Ser Arg Leu
            740                 745                 750

Pro Gly Ala Thr Pro Gly Leu Thr Thr Val Glu Ile Val Thr Met Ser
        755                 760                 765

His Gln Ala Leu Gly Asp Val Ala Gly Arg Gly Asn Glu Lys Lys Pro
    770                 775                 780

Ser Ser Val Arg Ala Leu Ser Ile Val Leu Pro Ile Val Leu Leu Val
785                 790                 795                 800

Phe Leu Cys Leu Gly Val Phe Leu Leu Trp Lys Asn Trp Arg Leu Lys
                805                 810                 815

Asn Ile Asn Ser Ile Asn Phe Asp Asn Pro Val Tyr Gln Lys Thr Thr
            820                 825                 830

Glu Asp Glu Val His Ile Cys His Asn Gln Asp Gly Tyr Ser Tyr Pro
        835                 840                 845

Ser Arg Gln Met Val Ser Leu Glu Asp Asp Val Ala
    850                 855                 860


<210> SEQ ID NO 59
<211> LENGTH: 654
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 59

Met Lys Leu Ser Leu Val Ala Ala Met Leu Leu Leu Leu Ser Ala Ala
1               5                   10                  15

Arg Ala Glu Glu Glu Asp Lys Lys Glu Asp Val Gly Thr Val Val Gly
            20                  25                  30

Ile Asp Leu Gly Thr Thr Tyr Ser Cys Val Gly Val Phe Lys Asn Gly
        35                  40                  45

Arg Val Glu Ile Ile Ala Asn Asp Gln Gly Asn Arg Ile Thr Pro Ser
    50                  55                  60

Tyr Val Ala Phe Thr Pro Glu Gly Glu Arg Leu Ile Gly Asp Ala Ala
65                  70                  75                  80

Lys Asn Gln Leu Thr Ser Asn Pro Glu Asn Thr Val Phe Asp Ala Lys
                85                  90                  95

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

Lys Phe Leu Pro Phe Lys Val Val Glu Lys Lys Thr Lys Pro Tyr Ile
        115                 120                 125

Gln Val Asp Ile Gly Gly Gly Gln Thr Lys Thr Phe Ala Pro Glu Glu
    130                 135                 140

Ile Ser Ala Met Val Leu Thr Lys Met Lys Glu Thr Ala Glu Ala Tyr
145                 150                 155                 160

Leu Gly Lys Lys Val Thr His Ala Val Val Thr Val Pro Ala Tyr Phe
                165                 170                 175

Asn Asp Ala Gln Arg Gln Ala Thr Lys Asp Ala Gly Thr Ile Ala Gly
            180                 185                 190

Leu Asn Val Met Arg Ile Ile Asn Glu Pro Thr Ala Ala Ala Ile Ala
        195                 200                 205

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

Leu Gly Gly Gly Thr Phe Asp Val Ser Leu Leu Thr Ile Asp Asn Gly
225                 230                 235                 240
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Val Phe Glu Val Val Ala Thr Asn Gly Asp Thr His Leu Gly Gly Glu
                245                 250                 255

Asp Phe Asp Gln Arg Val Met Glu His Phe Ile Lys Leu Tyr Lys Lys
            260                 265                 270

Lys Thr Gly Lys Asp Val Arg Lys Asp Asn Arg Ala Val Gln Lys Leu
        275                 280                 285

Arg Arg Glu Val Glu Lys Ala Lys Arg Ala Leu Ser Ser Gln His Gln
    290                 295                 300

Ala Arg Ile Glu Ile Glu Ser Phe Tyr Glu Gly Glu Asp Phe Ser Glu
305                 310                 315                 320

Thr Leu Thr Arg Ala Lys Phe Glu Glu Leu Asn Met Asp Leu Phe Arg
                325                 330                 335

Ser Thr Met Lys Pro Val Gln Lys Val Leu Glu Asp Ser Asp Leu Lys
            340                 345                 350

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

Pro Lys Ile Gln Gln Leu Val Lys Glu Phe Phe Asn Gly Lys Glu Pro
    370                 375                 380

Ser Arg Gly Ile Asn Pro Asp Glu Ala Val Ala Tyr Gly Ala Ala Val
385                 390                 395                 400

Gln Ala Gly Val Leu Ser Gly Asp Gln Asp Thr Gly Asp Leu Val Leu
                405                 410                 415

Leu Asp Val Cys Pro Leu Thr Leu Gly Ile Glu Thr Val Gly Gly Val
            420                 425                 430

Met Thr Lys Leu Ile Pro Arg Asn Thr Val Val Pro Thr Lys Lys Ser
        435                 440                 445

Gln Ile Phe Ser Thr Ala Ser Asp Asn Gln Pro Thr Val Thr Ile Lys
    450                 455                 460

Val Tyr Glu Gly Glu Arg Pro Leu Thr Lys Asp Asn His Leu Leu Gly
465                 470                 475                 480

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

Ile Glu Val Thr Phe Glu Ile Asp Val Asn Gly Ile Leu Arg Val Thr
            500                 505                 510

Ala Glu Asp Lys Gly Thr Gly Asn Lys Asn Lys Ile Thr Ile Thr Asn
        515                 520                 525

Asp Gln Asn Arg Leu Thr Pro Glu Glu Ile Glu Arg Met Val Asn Asp
    530                 535                 540

Ala Glu Lys Phe Ala Glu Glu Asp Lys Lys Leu Lys Glu Arg Ile Asp
545                 550                 555                 560

Thr Arg Asn Glu Leu Glu Ser Tyr Ala Tyr Ser Leu Lys Asn Gln Ile
                565                 570                 575

Gly Asp Lys Glu Lys Leu Gly Gly Lys Leu Ser Ser Glu Asp Lys Glu
            580                 585                 590

Thr Met Glu Lys Ala Val Glu Glu Lys Ile Glu Trp Leu Glu Ser His
        595                 600                 605

Gln Asp Ala Asp Ile Glu Asp Phe Lys Ala Lys Lys Lys Glu Leu Glu
    610                 615                 620

Glu Ile Val Gln Pro Ile Ile Ser Lys Leu Tyr Gly Ser Ala Gly Pro
625                 630                 635                 640
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Pro Pro Thr Gly Glu Glu Asp Thr Ala Glu Lys Asp Glu Leu
                645                 650


<210> SEQ ID NO 60
<211> LENGTH: 1250
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 60

Met Ala Arg Gly Asp Ala Gly Arg Gly Arg Gly Leu Leu Ala Leu Thr
1               5                   10                  15

Phe Cys Leu Leu Ala Ala Arg Gly Glu Leu Leu Leu Pro Gln Glu Thr
            20                  25                  30

Thr Val Glu Leu Ser Cys Gly Val Gly Pro Leu Gln Val Ile Leu Gly
        35                  40                  45

Pro Glu Gln Ala Ala Val Leu Asn Cys Ser Leu Gly Ala Ala Ala Ala
    50                  55                  60

Gly Pro Pro Thr Arg Val Thr Trp Ser Lys Asp Gly Asp Thr Leu Leu
65                  70                  75                  80

Glu His Asp His Leu His Leu Leu Pro Asn Gly Ser Leu Trp Leu Ser
                85                  90                  95

Gln Pro Leu Ala Pro Asn Gly Ser Asp Glu Ser Val Pro Glu Ala Val
            100                 105                 110

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

Val Leu Ala Ser Gln Thr Ala Val Val Lys Leu Ala Thr Leu Ala Asp
    130                 135                 140

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

Arg Phe Glu Cys His Ile Glu Gly Leu Pro Ala Pro Ile Ile Thr Trp
                165                 170                 175

Glu Lys Asp Gln Val Thr Leu Pro Glu Glu Pro Arg Leu Ile Val Leu
            180                 185                 190

Pro Asn Gly Val Leu Gln Ile Leu Asp Val Gln Glu Ser Asp Ala Gly
        195                 200                 205

Pro Tyr Arg Cys Val Ala Thr Asn Ser Ala Arg Gln His Phe Ser Gln
    210                 215                 220

Glu Ala Leu Leu Ser Val Ala His Arg Gly Ser Leu Ala Ser Thr Arg
225                 230                 235                 240

Gly Gln Asp Val Val Ile Val Ala Ala Pro Glu Asn Thr Thr Val Val
                245                 250                 255

Ser Gly Gln Ser Val Val Met Glu Cys Val Ala Ser Ala Asp Pro Thr
            260                 265                 270

Pro Phe Val Ser Trp Val Arg Gln Asp Gly Lys Pro Ile Ser Thr Asp
        275                 280                 285

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

Trp His Ser Gly Val Tyr Val Cys Arg Ala Asn Lys Pro Arg Thr Arg
305                 310                 315                 320

Asp Phe Ala Thr Ala Ala Ala Glu Leu Arg Val Leu Ala Ala Pro Ala
                325                 330                 335

Ile Thr Gln Ala Pro Glu Ala Leu Ser Arg Thr Arg Ala Ser Thr Ala
            340                 345                 350
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Arg Phe Val Cys Arg Ala Ser Gly Glu Pro Arg Pro Ala Leu Arg Trp
        355                 360                 365

Leu His Asn Gly Ala Pro Leu Arg Pro Asn Gly Arg Val Lys Val Gln
    370                 375                 380

Gly Gly Gly Gly Ser Leu Val Ile Thr Gln Ile Gly Leu Gln Asp Ala
385                 390                 395                 400

Gly Tyr Tyr Gln Cys Val Ala Glu Asn Ser Ala Gly Met Ala Cys Ala
                405                 410                 415

Ala Ala Ser Leu Ala Val Val Val Arg Glu Gly Leu Pro Ser Ala Pro
            420                 425                 430

Thr Arg Val Thr Ala Thr Pro Leu Ser Ser Ser Ala Val Leu Val Ala
        435                 440                 445

Trp Glu Arg Pro Glu Met His Ser Glu Gln Ile Ile Gly Phe Ser Leu
    450                 455                 460

His Tyr Gln Lys Ala Arg Gly Met Asp Asn Val Glu Tyr Gln Phe Ala
465                 470                 475                 480

Val Asn Asn Asp Thr Thr Glu Leu Gln Val Arg Asp Leu Glu Pro Asn
                485                 490                 495

Thr Asp Tyr Glu Phe Tyr Val Val Ala Tyr Ser Gln Leu Gly Ala Ser
            500                 505                 510

Arg Thr Ser Thr Pro Ala Leu Val His Thr Leu Asp Asp Val Pro Ser
        515                 520                 525

Ala Ala Pro Gln Leu Ser Leu Ser Ser Pro Asn Pro Ser Asp Ile Arg
    530                 535                 540

Val Ala Trp Leu Pro Leu Pro Pro Ser Leu Ser Asn Gly Gln Val Val
545                 550                 555                 560

Lys Tyr Lys Ile Glu Tyr Gly Leu Gly Lys Glu Asp Gln Ile Phe Ser
                565                 570                 575

Thr Glu Val Arg Gly Asn Glu Thr Gln Leu Met Leu Asn Ser Leu Gln
            580                 585                 590

Pro Asn Lys Val Tyr Arg Val Arg Ile Ser Ala Gly Thr Ala Ala Gly
        595                 600                 605

Phe Gly Ala Pro Ser Gln Trp Met His His Arg Thr Pro Ser Met His
    610                 615                 620

Asn Gln Ser His Val Pro Phe Ala Pro Ala Glu Leu Lys Val Gln Ala
625                 630                 635                 640

Lys Met Glu Ser Leu Val Val Ser Trp Gln Pro Pro Pro His Pro Thr
                645                 650                 655

Gln Ile Ser Gly Tyr Lys Leu Tyr Trp Arg Glu Val Gly Ala Glu Glu
            660                 665                 670

Glu Ala Asn Gly Asp Arg Leu Pro Gly Gly Arg Gly Asp Gln Ala Trp
        675                 680                 685

Asp Val Gly Pro Val Arg Leu Lys Lys Lys Val Lys Gln Tyr Glu Leu
    690                 695                 700

Thr Gln Leu Val Pro Gly Arg Leu Tyr Glu Val Lys Leu Val Ala Phe
705                 710                 715                 720

Asn Lys His Glu Asp Gly Tyr Ala Ala Val Trp Lys Gly Lys Thr Glu
                725                 730                 735

Lys Ala Pro Ala Pro Asp Met Pro Ile Gln Arg Gly Pro Pro Leu Pro
            740                 745                 750
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Pro Ala His Val His Ala Glu Ser Asn Ser Ser Thr Ser Ile Trp Leu
        755                 760                 765

Arg Trp Lys Lys Pro Asp Phe Thr Thr Val Lys Ile Val Asn Tyr Thr
    770                 775                 780

Val Arg Phe Ser Pro Trp Gly Leu Arg Asn Ala Ser Leu Val Thr Tyr
785                 790                 795                 800

Tyr Thr Ser Ser Gly Glu Asp Ile Leu Ile Gly Gly Leu Lys Pro Phe
                805                 810                 815

Thr Lys Tyr Glu Phe Ala Val Gln Ser His Gly Val Asp Met Asp Gly
            820                 825                 830

Pro Phe Gly Ser Val Val Glu Arg Ser Thr Leu Pro Asp Arg Pro Ser
        835                 840                 845

Thr Pro Pro Ser Asp Leu Arg Leu Ser Pro Leu Thr Pro Ser Thr Val
    850                 855                 860

Arg Leu His Trp Cys Pro Pro Thr Glu Pro Asn Gly Glu Ile Val Glu
865                 870                 875                 880

Tyr Leu Ile Leu Tyr Ser Ser Asn His Thr Gln Pro Glu His Gln Trp
                885                 890                 895

Thr Leu Leu Thr Thr Gln Gly Asn Ile Phe Ser Ala Glu Val His Gly
            900                 905                 910

Leu Glu Ser Asp Thr Arg Tyr Phe Phe Lys Met Gly Ala Arg Thr Glu
        915                 920                 925

Val Gly Pro Gly Pro Phe Ser Arg Leu Gln Asp Val Ile Thr Leu Gln
    930                 935                 940

Glu Lys Leu Ser Asp Ser Leu Asp Met His Ser Val Thr Gly Ile Ile
945                 950                 955                 960

Val Gly Val Cys Leu Gly Leu Leu Cys Leu Leu Ala Cys Met Cys Ala
                965                 970                 975

Gly Leu Arg Arg Ser Pro His Arg Glu Ser Leu Pro Gly Leu Ser Ser
            980                 985                 990

Thr Ala Thr Pro Gly Asn Pro Ala  Leu Tyr Ser Arg Ala  Arg Leu Gly
        995                 1000                 1005

Pro Pro  Ser Pro Pro Ala Ala  His Glu Leu Glu Ser  Leu Val His
    1010                1015                1020

Pro His  Pro Gln Asp Trp Ser  Pro Pro Pro Ser Asp  Val Glu Asp
    1025                1030                1035

Arg Ala  Glu Val His Ser Leu  Met Gly Gly Gly Val  Ser Glu Gly
    1040                1045                1050

Arg Ser  His Ser Lys Arg Lys  Ile Ser Trp Ala Gln  Pro Ser Gly
    1055                1060                1065

Leu Ser  Trp Ala Gly Ser Trp  Ala Gly Cys Glu Leu  Pro Gln Ala
    1070                1075                1080

Gly Pro  Arg Pro Ala Leu Thr  Arg Ala Leu Leu Pro  Pro Ala Gly
    1085                1090                1095

Thr Gly  Gln Thr Leu Leu Leu  Gln Ala Leu Val Tyr  Asp Ala Ile
    1100                1105                1110

Lys Gly  Asn Gly Arg Lys Lys  Ser Pro Pro Ala Cys  Arg Asn Gln
    1115                1120                1125

Val Glu  Ala Glu Val Ile Val  His Ser Asp Phe Ser  Ala Ser Asn
    1130                1135                1140

Gly Asn  Pro Asp Leu His Leu  Gln Asp Leu Glu Pro  Glu Asp Pro
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    1145                1150                1155

Leu Pro  Pro Glu Ala Pro Asp  Leu Ile Ser Gly Val  Gly Asp Pro
    1160                1165                1170

Gly Gln  Gly Ala Ala Trp Leu  Asp Arg Glu Leu Gly  Gly Cys Glu
    1175                1180                1185

Leu Ala  Ala Pro Gly Pro Asp  Arg Leu Thr Cys Leu  Pro Glu Ala
    1190                1195                1200

Ala Ser  Ala Ser Cys Ser Tyr  Pro Asp Leu Gln Pro  Gly Glu Val
    1205                1210                1215

Leu Glu  Glu Thr Pro Gly Asp  Ser Cys Gln Leu Lys  Ser Pro Cys
    1220                1225                1230

Pro Leu  Gly Ala Ser Pro Gly  Leu Pro Arg Ser Pro  Val Ser Ser
    1235                1240                1245

Ser Ala
    1250


<210> SEQ ID NO 61
<211> LENGTH: 653
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 61

Met Pro Val Gly Gly Leu Leu Pro Leu Phe Ser Ser Pro Ala Gly Gly
1               5                   10                  15

Val Leu Gly Gly Gly Leu Gly Gly Gly Gly Gly Arg Lys Gly Ser Gly
            20                  25                  30

Pro Ala Ala Leu Arg Leu Thr Glu Lys Phe Val Leu Leu Leu Val Phe
        35                  40                  45

Ser Ala Phe Ile Thr Leu Cys Phe Gly Ala Ile Phe Phe Leu Pro Asp
    50                  55                  60

Ser Ser Lys Leu Leu Ser Gly Val Leu Phe His Ser Ser Pro Ala Leu
65                  70                  75                  80

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

Ala Ala Glu Gly Arg Ala Arg Arg Arg Glu Glu Gly Ala Pro Gly Asp
            100                 105                 110

Pro Glu Ala Ala Leu Glu Asp Asn Leu Ala Arg Ile Arg Glu Asn His
        115                 120                 125

Glu Arg Ala Leu Arg Glu Ala Lys Glu Thr Leu Gln Lys Leu Pro Glu
    130                 135                 140

Glu Ile Gln Arg Asp Ile Leu Leu Glu Lys Lys Lys Val Ala Gln Asp
145                 150                 155                 160

Gln Leu Arg Asp Lys Ala Pro Phe Arg Gly Leu Pro Pro Val Asp Phe
                165                 170                 175

Val Pro Pro Ile Gly Val Glu Ser Arg Glu Pro Ala Asp Ala Ala Ile
            180                 185                 190

Arg Glu Lys Arg Ala Lys Ile Lys Glu Met Met Lys His Ala Trp Asn
        195                 200                 205

Asn Tyr Lys Gly Tyr Ala Trp Gly Leu Asn Glu Leu Lys Pro Ile Ser
    210                 215                 220

Lys Gly Gly His Ser Ser Ser Leu Phe Gly Asn Ile Lys Gly Ala Thr
225                 230                 235                 240
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Ile Val Asp Ala Leu Asp Thr Leu Phe Ile Met Glu Met Lys His Glu
                245                 250                 255

Phe Glu Glu Ala Lys Ser Trp Val Glu Glu Asn Leu Asp Phe Asn Val
            260                 265                 270

Asn Ala Glu Ile Ser Val Phe Glu Val Asn Ile Arg Phe Val Gly Gly
        275                 280                 285

Leu Leu Ser Ala Tyr Tyr Leu Ser Gly Glu Glu Ile Phe Arg Lys Lys
    290                 295                 300

Ala Val Glu Leu Gly Val Lys Leu Leu Pro Ala Phe His Thr Pro Ser
305                 310                 315                 320

Gly Ile Pro Trp Ala Leu Leu Asn Met Lys Ser Gly Ile Gly Arg Asn
                325                 330                 335

Trp Pro Trp Ala Ser Gly Gly Ser Ser Ile Leu Ala Glu Phe Gly Thr
            340                 345                 350

Leu His Leu Glu Phe Met His Leu Ser His Leu Ser Gly Asn Pro Ile
        355                 360                 365

Phe Ala Glu Lys Val Met Asn Ile Arg Thr Val Leu Asn Lys Leu Glu
    370                 375                 380

Lys Pro Gln Gly Leu Tyr Pro Asn Tyr Leu Asn Pro Ser Ser Gly Gln
385                 390                 395                 400

Trp Gly Gln His His Val Ser Val Gly Gly Leu Gly Asp Ser Phe Tyr
                405                 410                 415

Glu Tyr Leu Leu Lys Ala Trp Leu Met Ser Asp Lys Thr Asp Leu Glu
            420                 425                 430

Ala Lys Lys Met Tyr Phe Asp Ala Val Gln Ala Ile Glu Thr His Leu
        435                 440                 445

Ile Arg Lys Ser Ser Ser Gly Leu Thr Tyr Ile Ala Glu Trp Lys Gly
    450                 455                 460

Gly Leu Leu Glu His Lys Met Gly His Leu Thr Cys Phe Ala Gly Gly
465                 470                 475                 480

Met Phe Ala Leu Gly Ala Asp Ala Ala Pro Glu Gly Met Ala Gln His
                485                 490                 495

Tyr Leu Glu Leu Gly Ala Glu Ile Ala Arg Thr Cys His Glu Ser Tyr
            500                 505                 510

Asn Arg Thr Phe Met Lys Leu Gly Pro Glu Ala Phe Arg Phe Asp Gly
        515                 520                 525

Gly Val Glu Ala Ile Ala Thr Arg Gln Asn Glu Lys Tyr Tyr Ile Leu
    530                 535                 540

Arg Pro Glu Val Met Glu Thr Tyr Met Tyr Met Trp Arg Leu Thr His
545                 550                 555                 560

Asp Pro Lys Tyr Arg Lys Trp Ala Trp Glu Ala Val Glu Ala Leu Glu
                565                 570                 575

Asn His Cys Arg Val Asn Gly Gly Tyr Ser Gly Leu Arg Asp Val Tyr
            580                 585                 590

Leu Leu His Glu Ser Tyr Asp Asp Val Gln Gln Ser Phe Phe Leu Ala
        595                 600                 605

Glu Thr Leu Lys Tyr Leu Tyr Leu Ile Phe Ser Asp Asp Asp Leu Leu
    610                 615                 620

Pro Leu Glu His Trp Ile Phe Asn Ser Glu Ala His Leu Leu Pro Ile
625                 630                 635                 640

Leu Pro Lys Asp Lys Lys Glu Val Glu Ile Arg Glu Glu
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645 650

<210> SEQ ID NO 62
<211> LENGTH: 531
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 62

Met Ser Lys Pro His Ser Glu Ala Gly Thr Ala Phe Ile Gln Thr Gln
1 5 10 15

Gln Leu His Ala Ala Met Ala Asp Thr Phe Leu Glu His Met Cys Arg
20 25 30

Leu Asp Ile Asp Ser Pro Pro Ile Thr Ala Arg Asn Thr Gly Ile Ile
35 40 45

Cys Thr Ile Gly Pro Ala Ser Arg Ser Val Glu Thr Leu Lys Glu Met
50 55 60

Ile Lys Ser Gly Met Asn Val Ala Arg Leu Asn Phe Ser His Gly Thr
65 70 75 80

His Glu Tyr His Ala Glu Thr Ile Lys Asn Val Arg Thr Ala Thr Glu
85 90 95

Ser Phe Ala Ser Asp Pro Ile Leu Tyr Arg Pro Val Ala Val Ala Leu
100 105 110

Asp Thr Lys Gly Pro Glu Ile Arg Thr Gly Leu Ile Lys Gly Ser Gly
115 120 125

Thr Ala Glu Val Glu Leu Lys Lys Gly Ala Thr Leu Lys Ile Thr Leu
130 135 140

Asp Asn Ala Tyr Met Glu Lys Cys Asp Glu Asn Ile Leu Trp Leu Asp
145 150 155 160

Tyr Lys Asn Ile Cys Lys Val Val Glu Val Gly Ser Lys Ile Tyr Val
165 170 175

Asp Asp Gly Leu Ile Ser Leu Gln Val Lys Gln Lys Gly Ala Asp Phe
180 185 190

Leu Val Thr Glu Val Glu Asn Gly Gly Ser Leu Gly Ser Lys Lys Gly
195 200 205

Val Asn Leu Pro Gly Ala Ala Val Asp Leu Pro Ala Val Ser Glu Lys
210 215 220

Asp Ile Gln Asp Leu Lys Phe Gly Val Glu Gln Asp Val Asp Met Val
225 230 235 240

Phe Ala Ser Phe Ile Arg Lys Ala Ser Asp Val His Glu Val Arg Lys
245 250 255

Val Leu Gly Glu Lys Gly Lys Asn Ile Lys Ile Ile Ser Lys Ile Glu
260 265 270

Asn His Glu Gly Val Arg Arg Phe Asp Glu Ile Leu Glu Ala Ser Asp
275 280 285

Gly Ile Met Val Ala Arg Gly Asp Leu Gly Ile Glu Ile Pro Ala Glu
290 295 300

Lys Val Phe Leu Ala Gln Lys Met Met Ile Gly Arg Cys Asn Arg Ala
305 310 315 320

Gly Lys Pro Val Ile Cys Ala Thr Gln Met Leu Glu Ser Met Ile Lys
325 330 335

Lys Pro Arg Pro Thr Arg Ala Glu Gly Ser Asp Val Ala Asn Ala Val
340 345 350

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Leu Asp Gly Ala Asp Cys Ile Met Leu Ser Gly Glu Thr Ala Lys Gly
        355                 360                 365

Asp Tyr Pro Leu Glu Ala Val Arg Met Gln His Leu Ile Ala Arg Glu
    370                 375                 380

Ala Glu Ala Ala Ile Tyr His Leu Gln Leu Phe Glu Glu Leu Arg Arg
385                 390                 395                 400

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

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

Lys Ser Gly Arg Ser Ala His Gln Val Ala Arg Tyr Arg Pro Arg Ala
        435                 440                 445

Pro Ile Ile Ala Val Thr Arg Asn Pro Gln Thr Ala Arg Gln Ala His
    450                 455                 460

Leu Tyr Arg Gly Ile Phe Pro Val Leu Cys Lys Asp Pro Val Gln Glu
465                 470                 475                 480

Ala Trp Ala Glu Asp Val Asp Leu Arg Val Asn Phe Ala Met Asn Val
                485                 490                 495

Gly Lys Ala Arg Gly Phe Phe Lys Lys Gly Asp Val Val Ile Val Leu
            500                 505                 510

Thr Gly Trp Arg Pro Gly Ser Gly Phe Thr Asn Thr Met Arg Val Val
        515                 520                 525

Pro Val Pro
    530


<210> SEQ ID NO 63
<211> LENGTH: 543
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 63

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

Val Gly Asn Ile Asp Asp Ala Leu Gln Cys Tyr Ser Glu Ala Ile Lys
            20                  25                  30

Leu Asp Pro His Asn His Val Leu Tyr Ser Asn Arg Ser Ala Ala Tyr
        35                  40                  45

Ala Lys Lys Gly Asp Tyr Gln Lys Ala Tyr Glu Asp Gly Cys Lys Thr
    50                  55                  60

Val Asp Leu Lys Pro Asp Trp Gly Lys Gly Tyr Ser Arg Lys Ala Ala
65                  70                  75                  80

Ala Leu Glu Phe Leu Asn Arg Phe Glu Glu Ala Lys Arg Thr Tyr Glu
                85                  90                  95

Glu Gly Leu Lys His Glu Ala Asn Asn Pro Gln Leu Lys Glu Gly Leu
            100                 105                 110

Gln Asn Met Glu Ala Arg Leu Ala Glu Arg Lys Phe Met Asn Pro Phe
        115                 120                 125

Asn Met Pro Asn Leu Tyr Gln Lys Leu Glu Ser Asp Pro Arg Thr Arg
    130                 135                 140

Thr Leu Leu Ser Asp Pro Thr Tyr Arg Glu Leu Ile Glu Gln Leu Arg
145                 150                 155                 160

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

Glu Glu Glu Ile Ala Thr Pro Pro Pro Pro Pro Pro Pro Lys Lys Glu
        195                 200                 205

Thr Lys Pro Glu Pro Met Glu Glu Asp Leu Pro Glu Asn Lys Lys Gln
    210                 215                 220

Ala Leu Lys Glu Lys Glu Leu Gly Asn Asp Ala Tyr Lys Lys Lys Asp
225                 230                 235                 240

Phe Asp Thr Ala Leu Lys His Tyr Asp Lys Ala Lys Glu Leu Asp Pro
                245                 250                 255

Thr Asn Met Thr Tyr Ile Thr Asn Gln Ala Ala Val Tyr Phe Glu Lys
            260                 265                 270

Gly Asp Tyr Asn Lys Cys Arg Glu Leu Cys Glu Lys Ala Ile Glu Val
        275                 280                 285

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

Arg Ile Gly Asn Ser Tyr Phe Lys Glu Glu Lys Tyr Lys Asp Ala Ile
305                 310                 315                 320

His Phe Tyr Asn Lys Ser Leu Ala Glu His Arg Thr Pro Asp Val Leu
                325                 330                 335

Lys Lys Cys Gln Gln Ala Glu Lys Ile Leu Lys Glu Gln Glu Arg Leu
            340                 345                 350

Ala Tyr Ile Asn Pro Asp Leu Ala Leu Glu Glu Lys Asn Lys Gly Asn
        355                 360                 365

Glu Cys Phe Gln Lys Gly Asp Tyr Pro Gln Ala Met Lys His Tyr Thr
    370                 375                 380

Glu Ala Ile Lys Arg Asn Pro Lys Asp Ala Lys Leu Tyr Ser Asn Arg
385                 390                 395                 400

Ala Ala Cys Tyr Thr Lys Leu Leu Glu Phe Gln Leu Ala Leu Lys Asp
                405                 410                 415

Cys Glu Glu Cys Ile Gln Leu Glu Pro Thr Phe Ile Lys Gly Tyr Thr
            420                 425                 430

Arg Lys Ala Ala Ala Leu Glu Ala Met Lys Asp Tyr Thr Lys Ala Met
        435                 440                 445

Asp Val Tyr Gln Lys Ala Leu Asp Leu Asp Ser Ser Cys Lys Glu Ala
    450                 455                 460

Ala Asp Gly Tyr Gln Arg Cys Met Met Ala Gln Tyr Asn Arg His Asp
465                 470                 475                 480

Ser Pro Glu Asp Val Lys Arg Arg Ala Met Ala Asp Pro Glu Val Gln
                485                 490                 495

Gln Ile Met Ser Asp Pro Ala Met Arg Leu Ile Leu Glu Gln Met Gln
            500                 505                 510

Lys Asp Pro Gln Ala Leu Ser Glu His Leu Lys Asn Pro Val Ile Ala
        515                 520                 525

Gln Lys Ile Gln Lys Leu Met Asp Val Gly Leu Ile Ala Ile Arg
    530                 535                 540
```

<210> SEQ ID NO 64
<211> LENGTH: 707
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 64

Met Ser Leu Trp Gln Pro Leu Val Leu Val Leu Leu Val Leu Gly Cys
1 5 10 15

Cys Phe Ala Ala Pro Arg Gln Arg Gln Ser Thr Leu Val Leu Phe Pro
20 25 30

Gly Asp Leu Arg Thr Asn Leu Thr Asp Arg Gln Leu Ala Glu Glu Tyr
35 40 45

Leu Tyr Arg Tyr Gly Tyr Thr Arg Val Ala Glu Met Arg Gly Glu Ser
50 55 60

Lys Ser Leu Gly Pro Ala Leu Leu Leu Leu Gln Lys Gln Leu Ser Leu
65 70 75 80

Pro Glu Thr Gly Glu Leu Asp Ser Ala Thr Leu Lys Ala Met Arg Thr
85 90 95

Pro Arg Cys Gly Val Pro Asp Leu Gly Arg Phe Gln Thr Phe Glu Gly
100 105 110

Asp Leu Lys Trp His His His Asn Ile Thr Tyr Trp Ile Gln Asn Tyr
115 120 125

Ser Glu Asp Leu Pro Arg Ala Val Ile Asp Asp Ala Phe Ala Arg Ala
130 135 140

Phe Ala Leu Trp Ser Ala Val Thr Pro Leu Thr Phe Thr Arg Val Tyr
145 150 155 160

Ser Arg Asp Ala Asp Ile Val Ile Gln Phe Gly Val Ala Glu His Gly
165 170 175

Asp Gly Tyr Pro Phe Asp Gly Lys Asp Gly Leu Leu Ala His Ala Phe
180 185 190

Pro Pro Gly Pro Gly Ile Gln Gly Asp Ala His Phe Asp Asp Asp Glu
195 200 205

Leu Trp Ser Leu Gly Lys Gly Val Val Val Pro Thr Arg Phe Gly Asn
210 215 220

Ala Asp Gly Ala Ala Cys His Phe Pro Phe Ile Phe Glu Gly Arg Ser
225 230 235 240

Tyr Ser Ala Cys Thr Thr Asp Gly Arg Ser Asp Gly Leu Pro Trp Cys
245 250 255

Ser Thr Thr Ala Asn Tyr Asp Thr Asp Asp Arg Phe Gly Phe Cys Pro
260 265 270

Ser Glu Arg Leu Tyr Thr Arg Asp Gly Asn Ala Asp Gly Lys Pro Cys
275 280 285

Gln Phe Pro Phe Ile Phe Gln Gly Gln Ser Tyr Ser Ala Cys Thr Thr
290 295 300

Asp Gly Arg Ser Asp Gly Tyr Arg Trp Cys Ala Thr Thr Ala Asn Tyr
305 310 315 320

Asp Arg Asp Lys Leu Phe Gly Phe Cys Pro Thr Arg Ala Asp Ser Thr
325 330 335

Val Met Gly Gly Asn Ser Ala Gly Glu Leu Cys Val Phe Pro Phe Thr
340 345 350

Phe Leu Gly Lys Glu Tyr Ser Thr Cys Thr Ser Glu Gly Arg Gly Asp
355 360 365

Gly Arg Leu Trp Cys Ala Thr Thr Ser Asn Phe Asp Ser Asp Lys Lys
370 375 380

Trp Gly Phe Cys Pro Asp Gln Gly Tyr Ser Leu Phe Leu Val Ala Ala
385 390 395 400

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His Glu Phe Gly His Ala Leu Gly Leu Asp His Ser Ser Val Pro Glu
                405                 410                 415

Ala Leu Met Tyr Pro Met Tyr Arg Phe Thr Glu Gly Pro Pro Leu His
            420                 425                 430

Lys Asp Asp Val Asn Gly Ile Arg His Leu Tyr Gly Pro Arg Pro Glu
        435                 440                 445

Pro Glu Pro Arg Pro Pro Thr Thr Thr Thr Pro Gln Pro Thr Ala Pro
    450                 455                 460

Pro Thr Val Cys Pro Thr Gly Pro Pro Thr Val His Pro Ser Glu Arg
465                 470                 475                 480

Pro Thr Ala Gly Pro Thr Gly Pro Pro Ser Ala Gly Pro Thr Gly Pro
                485                 490                 495

Pro Thr Ala Gly Pro Ser Thr Ala Thr Thr Val Pro Leu Ser Pro Val
            500                 505                 510

Asp Asp Ala Cys Asn Val Asn Ile Phe Asp Ala Ile Ala Glu Ile Gly
        515                 520                 525

Asn Gln Leu Tyr Leu Phe Lys Asp Gly Lys Tyr Trp Arg Phe Ser Glu
    530                 535                 540

Gly Arg Gly Ser Arg Pro Gln Gly Pro Phe Leu Ile Ala Asp Lys Trp
545                 550                 555                 560

Pro Ala Leu Pro Arg Lys Leu Asp Ser Val Phe Glu Glu Pro Leu Ser
                565                 570                 575

Lys Lys Leu Phe Phe Phe Ser Gly Arg Gln Val Trp Val Tyr Thr Gly
            580                 585                 590

Ala Ser Val Leu Gly Pro Arg Arg Leu Asp Lys Leu Gly Leu Gly Ala
        595                 600                 605

Asp Val Ala Gln Val Thr Gly Ala Leu Arg Ser Gly Arg Gly Lys Met
    610                 615                 620

Leu Leu Phe Ser Gly Arg Arg Leu Trp Arg Phe Asp Val Lys Ala Gln
625                 630                 635                 640

Met Val Asp Pro Arg Ser Ala Ser Glu Val Asp Arg Met Phe Pro Gly
                645                 650                 655

Val Pro Leu Asp Thr His Asp Val Phe Gln Tyr Arg Glu Lys Ala Tyr
            660                 665                 670

Phe Cys Gln Asp Arg Phe Tyr Trp Arg Val Ser Ser Arg Ser Glu Leu
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Asn Gln Val Asp Gln Val Gly Tyr Val Thr Tyr Asp Ile Leu Gln Cys
    690                 695                 700

Pro Glu Asp
705


<210> SEQ ID NO 65
<211> LENGTH: 1231
<212> TYPE: PRT
<213> ORGANISM: Homo Sapiens

<400> SEQUENCE: 65

Met Arg Leu Leu Ala Lys Ile Ile Cys Leu Met Leu Trp Ala Ile Cys
1               5                   10                  15

Val Ala Glu Asp Cys Asn Glu Leu Pro Pro Arg Arg Asn Thr Glu Ile
            20                  25                  30

Leu Thr Gly Ser Trp Ser Asp Gln Thr Tyr Pro Glu Gly Gly Thr Gln
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        35                  40                  45

Ala Ile Tyr Lys Cys Arg Pro Gly Tyr Arg Ser Leu Gly Asn Val Ile
    50                  55                  60

Met Val Cys Arg Lys Gly Glu Trp Val Ala Leu Asn Pro Leu Arg Lys
65                  70                  75                  80

Cys Gln Lys Arg Pro Cys Gly His Pro Gly Asp Thr Pro Phe Gly Thr
                85                  90                  95

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

Tyr Thr Cys Asn Glu Gly Tyr Gln Leu Leu Gly Glu Ile Asn Tyr Arg
        115                 120                 125

Glu Cys Asp Thr Asp Gly Trp Thr Asn Asp Ile Pro Ile Cys Glu Val
    130                 135                 140

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

Ser Ala Met Glu Pro Asp Arg Glu Tyr His Phe Gly Gln Ala Val Arg
                165                 170                 175

Phe Val Cys Asn Ser Gly Tyr Lys Ile Glu Gly Asp Glu Glu Met His
            180                 185                 190

Cys Ser Asp Asp Gly Phe Trp Ser Lys Glu Lys Pro Lys Cys Val Glu
        195                 200                 205

Ile Ser Cys Lys Ser Pro Asp Val Ile Asn Gly Ser Pro Ile Ser Gln
    210                 215                 220

Lys Ile Ile Tyr Lys Glu Asn Glu Arg Phe Gln Tyr Lys Cys Asn Met
225                 230                 235                 240

Gly Tyr Glu Tyr Ser Glu Arg Gly Asp Ala Val Cys Thr Glu Ser Gly
                245                 250                 255

Trp Arg Pro Leu Pro Ser Cys Glu Glu Lys Ser Cys Asp Asn Pro Tyr
            260                 265                 270

Ile Pro Asn Gly Asp Tyr Ser Pro Leu Arg Leu Lys His Arg Thr Gly
        275                 280                 285

Asp Glu Leu Thr Tyr Gln Cys Arg Asn Gly Phe Tyr Pro Ala Thr Arg
    290                 295                 300

Gly Asn Thr Ala Lys Cys Thr Ser Thr Gly Trp Ile Pro Ala Pro Arg
305                 310                 315                 320

Cys Thr Leu Lys Pro Cys Asp Tyr Pro Asp Ile Lys His Gly Gly Leu
                325                 330                 335

Tyr His Glu Asn Met Arg Arg Pro Tyr Phe Pro Val Ala Val Gly Lys
            340                 345                 350

Tyr Tyr Ser Tyr Tyr Cys Asp Glu His Phe Glu Thr Pro Ser Gly Ser
        355                 360                 365

Tyr Trp Asp His Ile His Cys Thr Gln Asp Gly Trp Ser Pro Ala Val
    370                 375                 380

Pro Cys Leu Arg Lys Cys Tyr Phe Pro Tyr Leu Glu Asn Gly Tyr Asn
385                 390                 395                 400

Gln Asn His Gly Arg Lys Phe Val Gln Gly Lys Ser Ile Asp Val Ala
                405                 410                 415

Cys His Pro Gly Tyr Ala Leu Pro Lys Ala Gln Thr Thr Val Thr Cys
            420                 425                 430

Met Glu Asn Gly Trp Ser Pro Thr Pro Arg Cys Ile Arg Val Lys Thr
        435                 440                 445
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Cys Ser Lys Ser Ser Ile Asp Ile Glu Asn Gly Phe Ile Ser Glu Ser
    450                 455                 460

Gln Tyr Thr Tyr Ala Leu Lys Glu Lys Ala Lys Tyr Gln Cys Lys Leu
465                 470                 475                 480

Gly Tyr Val Thr Ala Asp Gly Glu Thr Ser Gly Ser Ile Arg Cys Gly
                485                 490                 495

Lys Asp Gly Trp Ser Ala Gln Pro Thr Cys Ile Lys Ser Cys Asp Ile
            500                 505                 510

Pro Val Phe Met Asn Ala Arg Thr Lys Asn Asp Phe Thr Trp Phe Lys
        515                 520                 525

Leu Asn Asp Thr Leu Asp Tyr Glu Cys His Asp Gly Tyr Glu Ser Asn
    530                 535                 540

Thr Gly Ser Thr Thr Gly Ser Ile Val Cys Gly Tyr Asn Gly Trp Ser
545                 550                 555                 560

Asp Leu Pro Ile Cys Tyr Glu Arg Glu Cys Glu Leu Pro Lys Ile Asp
                565                 570                 575

Val His Leu Val Pro Asp Arg Lys Lys Asp Gln Tyr Lys Val Gly Glu
            580                 585                 590

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

Val Gln Cys Tyr His Phe Gly Leu Ser Pro Asp Leu Pro Ile Cys Lys
    610                 615                 620

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

Val Lys Glu Lys Thr Lys Glu Glu Tyr Gly His Ser Glu Val Val Glu
                645                 650                 655

Tyr Tyr Cys Asn Pro Arg Phe Leu Met Lys Gly Pro Asn Lys Ile Gln
            660                 665                 670

Cys Val Asp Gly Glu Trp Thr Thr Leu Pro Val Cys Ile Val Glu Glu
        675                 680                 685

Ser Thr Cys Gly Asp Ile Pro Glu Leu Glu His Gly Trp Ala Gln Leu
    690                 695                 700

Ser Ser Pro Pro Tyr Tyr Tyr Gly Asp Ser Val Glu Phe Asn Cys Ser
705                 710                 715                 720

Glu Ser Phe Thr Met Ile Gly His Arg Ser Ile Thr Cys Ile His Gly
                725                 730                 735

Val Trp Thr Gln Leu Pro Gln Cys Val Ala Ile Asp Lys Leu Lys Lys
            740                 745                 750

Cys Lys Ser Ser Asn Leu Ile Ile Leu Glu Glu His Leu Lys Asn Lys
        755                 760                 765

Lys Glu Phe Asp His Asn Ser Asn Ile Arg Tyr Arg Cys Arg Gly Lys
    770                 775                 780

Glu Gly Trp Ile His Thr Val Cys Ile Asn Gly Arg Trp Asp Pro Glu
785                 790                 795                 800

Val Asn Cys Ser Met Ala Gln Ile Gln Leu Cys Pro Pro Pro Pro Gln
                805                 810                 815

Ile Pro Asn Ser His Asn Met Thr Thr Thr Leu Asn Tyr Arg Asp Gly
            820                 825                 830

Glu Lys Val Ser Val Leu Cys Gln Glu Asn Tyr Leu Ile Gln Glu Gly
        835                 840                 845
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Glu Glu Ile Thr Cys Lys Asp Gly Arg Trp Gln Ser Ile Pro Leu Cys
    850                 855                 860

Val Glu Lys Ile Pro Cys Ser Gln Pro Pro Gln Ile Glu His Gly Thr
865                 870                 875                 880

Ile Asn Ser Ser Arg Ser Ser Gln Glu Ser Tyr Ala His Gly Thr Lys
                885                 890                 895

Leu Ser Tyr Thr Cys Glu Gly Gly Phe Arg Ile Ser Glu Glu Asn Glu
            900                 905                 910

Thr Thr Cys Tyr Met Gly Lys Trp Ser Ser Pro Pro Gln Cys Glu Gly
        915                 920                 925

Leu Pro Cys Lys Ser Pro Pro Glu Ile Ser His Gly Val Val Ala His
    930                 935                 940

Met Ser Asp Ser Tyr Gln Tyr Gly Glu Glu Val Thr Tyr Lys Cys Phe
945                 950                 955                 960

Glu Gly Phe Gly Ile Asp Gly Pro Ala Ile Ala Lys Cys Leu Gly Glu
                965                 970                 975

Lys Trp Ser His Pro Pro Ser Cys Ile Lys Thr Asp Cys Leu Ser Leu
            980                 985                 990

Pro Ser Phe Glu Asn Ala Ile Pro  Met Gly Glu Lys Lys  Asp Val Tyr
        995                 1000                1005

Lys Ala  Gly Glu Gln Val Thr  Tyr Thr Cys Ala Thr  Tyr Tyr Lys
    1010                1015                1020

Met Asp  Gly Ala Ser Asn Val  Thr Cys Ile Asn Ser  Arg Trp Thr
    1025                1030                1035

Gly Arg  Pro Thr Cys Arg Asp  Thr Ser Cys Val Asn  Pro Pro Thr
    1040                1045                1050

Val Gln  Asn Ala Tyr Ile Val  Ser Arg Gln Met Ser  Lys Tyr Pro
    1055                1060                1065

Ser Gly  Glu Arg Val Arg Tyr  Gln Cys Arg Ser Pro  Tyr Glu Met
    1070                1075                1080

Phe Gly  Asp Glu Glu Val Met  Cys Leu Asn Gly Asn  Trp Thr Glu
    1085                1090                1095

Pro Pro  Gln Cys Lys Asp Ser  Thr Gly Lys Gly Gly  Pro Pro Pro
    1100                1105                1110

Pro Ile  Asp Asn Gly Asp Ile  Thr Ser Phe Pro Leu  Ser Val Tyr
    1115                1120                1125

Ala Pro  Ala Ser Ser Val Glu  Tyr Gln Cys Gln Asn  Leu Tyr Gln
    1130                1135                1140

Leu Glu  Gly Asn Lys Arg Ile  Thr Cys Arg Asn Gly  Gln Trp Ser
    1145                1150                1155

Glu Pro  Pro Lys Cys Leu His  Pro Cys Val Ile Ser  Arg Glu Ile
    1160                1165                1170

Met Glu  Asn Tyr Asn Ile Ala  Leu Arg Trp Thr Ala  Lys Gln Lys
    1175                1180                1185

Leu Tyr  Ser Arg Thr Gly Glu  Ser Val Glu Phe Val  Cys Lys Arg
    1190                1195                1200

Gly Tyr  Arg Leu Ser Ser Arg  Ser His Thr Leu Arg  Thr Thr Cys
    1205                1210                1215

Trp Asp  Gly Lys Leu Glu Tyr  Pro Thr Cys Ala Lys  Arg
    1220                1225                1230
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1. A method for diagnosis of neonatal sepsis in a mammalian subject comprising:

(a) testing in a sample of biological fluid obtained from said subject the level of one or more proteins selected from the group consisting of C-reactive protein precursor (SEQ ID NO:1), Interleukin-1 receptor accessory protein precursor (SEQ ID NO:2), Interleukin-6 precursor (SEQ ID NO:3), Interleukin-1 receptor-like 1 precursor (SEQ ID NO:4), Serum amyloid A protein precursor (SEQ ID NO:5), CD5 antigen-like precursor (SEQ ID NO:6), Beta-2-microglobulin precursor (SEQ ID NO:7), Bone-marrow proteoglycan precursor (SEQ ID NO:8), Selenium-binding protein 1 (SEQ ID NO:9), Lipopolysaccharide-binding protein precursor (SEQ ID NO:10), Chondroitin sulfate proteoglycan 4 precursor (SEQ ID NO:11), Osteopontin precursor (SEQ ID NO:12), Rho GDP-dissociation inhibitor 2 (SEQ ID NO:13), Carbonic anhydrase 2 (SEQ ID NO:14), Neutrophil gelatinase-associated lipocalin precursor (SEQ ID NO:15), Collagen alpha-5(IV) chain precursor (SEQ ID NO:16), Connective tissue growth factor precursor (SEQ ID NO:17), Macrophage colony-stimulating factor 1 precursor (SEQ ID NO:18), Protein kinase C-binding protein NELL2 precursor (SEQ ID NO:19), Neudesin precursor (SEQ ID NO:20), Protein disulfide-isomerase precursor (SEQ ID NO:21), Ribonuclease pancreatic precursor (SEQ ID NO:22), Delta-like protein precursor (SEQ ID NO:23), Chromogranin-A precursor (SEQ ID NO:24), Osteomodulin precursor (SEQ ID NO:25), Collagen alpha-2(I) chain precursor (SEQ ID NO:26), Prolow-density lipoprotein receptor-related protein 1 precursor (SEQ ID NO:27), Laminin subunit gamma-1 precursor (SEQ ID NO:28), Laminin subunit beta-1 precursor (SEQ ID NO:29), Collagen alpha-1(II) chain precursor (SEQ ID NO:30), Metalloproteinase inhibitor 1 precursor (SEQ ID NO:31), Protein FAM3C precursor (SEQ ID NO:32), Alpha-actinin-1 (SEQ ID NO:33), F-actin-capping protein subunit alpha-1 (SEQ ID NO:34), Aminopeptidase N (SEQ ID NO:35), Insulin-like growth factor-binding protein 1 precursor (SEQ ID NO:36), Cell adhesion molecule 1 precursor (SEQ ID NO:37), Cathepsin B precursor (SEQ ID NO:38), Exostosin-2 (SEQ ID NO:39), Cathepsin D precursor (SEQ ID NO:40), Neurogenic locus notch homolog protein 3 precursor (SEQ ID NO:41), Cystatin-M precursor (SEQ ID NO:42), Noelin precursor (SEQ ID NO:43), Insulin-like growth factor-binding protein 2 precursor (SEQ ID NO:44), Endoplasmin precursor (SEQ ID NO:45), Proprotein convertase subtilisin/kexin type 9 precursor (SEQ ID NO:46), Insulin-like growth factor-binding protein complex acid labile chain precursor (SEQ ID NO:47), Ezrin (SEQ ID NO:48), Fatty acid-binding protein, liver (SEQ ID NO:49), Probable G-protein coupled receptor 116 precursor (SEQ ID NO:50), Seprase (SEQ ID NO:51), Oncoprotein-induced transcript 3 protein precursor (SEQ ID NO:52), Hypoxia up-regulated protein 1 precursor (SEQ ID NO:53), Trans-Golgi network integral membrane protein 2 precursor (SEQ ID NO:54), Transketolase (SEQ ID NO:55), Receptor-type tyrosine-protein phosphatase F precursor (SEQ ID NO:56), Intercellular adhesion molecule 1 precursor (SEQ ID NO:57), Low-density lipoprotein receptor precursor (SEQ ID NO:58), 78 kDa glucose-regulated protein precursor (SEQ ID NO:59), Neighbor of punc e11 precursor (SEQ ID NO:60), Mannosyl-oligosaccharide 1,2-alpha-mannosidase IA (SEQ ID NO:61), Pyruvate kinase isozymes M1/M2 (SEQ ID NO:62), Matrix metalloproteinase-9 (SEQ ID NO:64), Alpha-1-acid glycoprotein 1 (SEQ ID NO:65), and Stress-induced-phosphoprotein 1 (SEQ ID NO:63), relative to the level in normal biological fluid or biological fluid known to be indicative of neonatal sepsis; and

(b) diagnosing said subject with neonatal sepsis if said level shows a statistically significant difference relative to the level in said normal biological fluid, or does not show a statistically significant difference relative to the level in said biological fluid known to be indicative of neonatal sepsis.

2. The method of claim 1, wherein the subject is a human patient.

3. The method of claim 2, wherein said testing is implemented using an apparatus adapted to determine the level of said proteins.

4. The method of claim 2, wherein said testing is performed by using a software program executed by a suitable processor.

5. The method of claim 4, wherein the program is embodied in software stored on a tangible medium.

6. The method of claim 5, wherein the tangible medium is selected from the group consisting of a CD-ROM, a floppy disk, a hard drive, a DVD, and a memory associated with the processor.

7. The method of any one of claims 2 to 6, further comprising the step of preparing a report recording the results of said testing or the diagnosis.

8. The method of claim 7, wherein said report is recorded or stored on a tangible medium.

9. The method of claim 8, wherein the tangible medium is paper.

10. The method of claim 8, wherein the tangible medium is selected from the group consisting of a CD-ROM, a floppy disk, a hard drive, a DVD, and a memory associated with the processor.

11. The method of any one of claims 2 to 6, further comprising the step of communicating the results of said diagnosis to an interested party.

12. The method of claim 11, wherein the interested party is the patient or the attending physician.

13. The method of claim 11, wherein the communication is in writing, by email, or by telephone.

14. The method of claim 1, wherein said biological fluid is selected from the group consisting of cord blood, cerebrospinal fluid, and neonatal serum.

15. The method of claim 14, wherein said biological fluid is cord blood.

16. The method of claim 2, wherein said diagnosis is determined within 24 hours of birth.

17. The method of claim 2 comprising testing the level of at least two of said proteins.

18. The method of claim 2 comprising testing the level of at least three of said proteins.

19. The method of claim 2 comprising testing the level of at least four of said proteins.

20. The method of claim 2 comprising testing the level of proteins Insulin-like growth factor-binding protein 1 precursor (SEQ ID NO:36), Interleukin-6 precursor (SEQ ID NO:3), C-reactive protein precursor (SEQ ID NO:1), Beta-2-microglobulin precursor (SEQ ID NO:7), Cathepsin B pre-

cursor (SEQ ID NO:38), Cystatin-M precursor (SEQ ID NO:42), Insulin-like growth factor-binding protein 2 precursor (SEQ ID NO:44), Matrix metalloproteinase-9 (SEQ ID NO:64), Metalloproteinase inhibitor 1 precursor (SEQ ID NO:31), and Alpha-1-acid glycoprotein 1 (SEQ ID NO:65), and diagnosing said subject with neonatal sepsis, if one or more of said tested proteins shows a significant difference in the cord blood sample relative to normal cord blood.

21. The method of claim **20** comprising diagnosing said subject with neonatal sepsis, if all of said tested proteins show a significant difference in the cord blood sample relative to normal cord blood.

22. The method of claim **2** wherein said level is determined by an immunoassay.

23. The method of claim **2** wherein level is determined by mass spectrometry.

24. The method of claim **2** wherein level is determined using a protein array.

25. Use of any one or more proteins selected from the group consisting of C-reactive protein precursor (SEQ ID NO:1), Interleukin-1 receptor accessory protein precursor (SEQ ID NO:2), Interleukin-6 precursor (SEQ ID NO:3), Interleukin-1 receptor-like 1 precursor (SEQ ID NO:4), Serum amyloid A protein precursor (SEQ ID NO:5), CD5 antigen-like precursor (SEQ ID NO:6), Beta-2-microglobulin precursor (SEQ ID NO:7), Bone-marrow proteoglycan precursor (SEQ ID NO:8), Selenium-binding protein 1 (SEQ ID NO:9), Lipopolysaccharide-binding protein precursor (SEQ ID NO:10), Chondroitin sulfate proteoglycan 4 precursor (SEQ ID NO:11), Osteopontin precursor (SEQ ID NO:12), Rho GDP-dissociation inhibitor 2 (SEQ ID NO:13), Carbonic anhydrase 2 (SEQ ID NO:14), Neutrophil gelatinase-associated lipocalin precursor (SEQ ID NO:15), Collagen alpha-5 (IV) chain precursor (SEQ ID NO:16), Connective tissue growth factor precursor (SEQ ID NO:17), Macrophage colony-stimulating factor 1 precursor (SEQ ID NO:18), Protein kinase C-binding protein NELL2 precursor (SEQ ID NO:19), Neudesin precursor (SEQ ID NO:20), Protein disulfide-isomerase precursor (SEQ ID NO:21), Ribonuclease pancreatic precursor (SEQ ID NO:22), Delta-like protein precursor (SEQ ID NO:23), Chromogranin-A precursor (SEQ ID NO:24), Osteomodulin precursor (SEQ ID NO:25), Collagen alpha-2(I) chain precursor (SEQ ID NO:26), Prolow-density lipoprotein receptor-related protein 1 precursor (SEQ ID NO:27), Laminin subunit gamma-1 precursor (SEQ ID NO:28), Laminin subunit beta-1 precursor (SEQ ID NO:29), Collagen alpha-1(II) chain precursor (SEQ ID NO:30), Metalloproteinase inhibitor 1 precursor (SEQ ID NO:31), Protein FAM3C precursor (SEQ ID NO:32), Alpha-actinin-1 (SEQ ID NO:33), F-actin-capping protein subunit alpha-1 (SEQ ID NO:34), Aminopeptidase N (SEQ ID NO:35), Insulin-like growth factor-binding protein 1 precursor (SEQ ID NO:36), Cell adhesion molecule 1 precursor (SEQ ID NO:37), Cathepsin B precursor (SEQ ID NO:38), Exostosin-2 (SEQ ID NO:39), Cathepsin D precursor (SEQ ID NO:40), Neurogenic locus notch homolog protein 3 precursor (SEQ ID NO:41), Cystatin-M precursor (SEQ ID NO:42), Noelin precursor (SEQ ID NO:43), Insulin-like growth factor-binding protein 2 precursor (SEQ ID NO:44), Endoplasmin precursor (SEQ ID NO:45), Proprotein convertase subtilisin/kexin type 9 precursor (SEQ ID NO:46), Insulin-like growth factor-binding protein complex acid labile chain precursor (SEQ ID NO:47), Ezrin (SEQ ID NO:48), Fatty acid-binding protein, liver (SEQ ID NO:49), Probable G-protein coupled receptor 116 precursor (SEQ ID NO:50), Seprase (SEQ ID NO:51), Oncoprotein-induced transcript 3 protein precursor (SEQ ID NO:52), Hypoxia up-regulated protein 1 precursor (SEQ ID NO:53), Trans-Golgi network integral membrane protein 2 precursor (SEQ ID NO:54), Transketolase (SEQ ID NO:55), Receptor-type tyrosine-protein phosphatase F precursor (SEQ ID NO:56), Intercellular adhesion molecule 1 precursor (SEQ ID NO:57), Low-density lipoprotein receptor precursor (SEQ ID NO:58), 78 kDa glucose-regulated protein precursor (SEQ ID NO:59), Neighbor of punc e11 precursor (SEQ ID NO:60), Mannosyl-oligosaccharide 1,2-alpha-mannosidase IA (SEQ ID NO:61), Pyruvate kinase isozymes M1/M2 (SEQ ID NO:62), Matrix metalloproteinase-9 (SEQ ID NO:64), Alpha-1-acid glycoprotein 1 (SEQ ID NO:65), and Stress-induced-phosphoprotein 1 (SEQ ID NO:63), in the manufacture of a proteomic profile of a biological fluid for the early diagnosis of neonatal sepsis in a subject.

26. The use of claim **25** wherein the subject is a human patient.

27. The use of claim **25** wherein the biological fluid is selected from the group consisting of cord blood, neonatal serum and cerebrospinal fluid.

28. The use of claim **26** wherein the proteomic profile comprises information of the level of said proteins and wherein the diagnosis of said subject with neonatal sepsis is made if one or more of said tested proteins shows a significant difference in the biological fluid sample relative to normal biological fluid.

29. The use of claim **26**, wherein said diagnosis is determined within 24 hours of birth.

30. The use of claim **26** wherein the proteomic profile comprises information of the level of at least two of said proteins.

31. The use of claim **26** wherein the proteomic profile comprises information of the level of at least three of said proteins.

32. The use of claim **26** wherein the proteomic profile comprises information of the level of at least four of said proteins.

33. The use of claim **2** wherein the proteomic profile comprises information of the level of proteins Insulin-like growth factor-binding protein 1 precursor (SEQ ID NO:36), Interleukin-6 precursor (SEQ ID NO:3), C-reactive protein precursor (SEQ ID NO:1), Beta-2-microglobulin precursor (SEQ ID NO:7), Cathepsin B precursor (SEQ ID NO:38), Cystatin-M precursor (SEQ ID NO:42), Insulin-like growth factor-binding protein 2 precursor (SEQ ID NO:44), Matrix metalloproteinase-9 (SEQ ID NO:64), Metalloproteinase inhibitor 1 precursor (SEQ ID NO:31), and Alpha-1-acid glycoprotein 1 (SEQ ID NO:65), and wherein the diagnosis of said subject with neonatal sepsis is made if one or more of said tested proteins shows a significant difference in the biological fluid sample relative to normal biological fluid.

34. The use of claim **33** wherein the diagnosis of said subject with neonatal sepsis is made if all of said tested proteins show a significant difference in the biological fluid sample relative to normal biological fluid.

35. The use of claim **26** wherein said level is determined by an immunoassay.

36. The use of claim **26** wherein said level is determined by mass spectrometry.

37. The use of claim **26** wherein said level is determined using a protein array.

38. An immunoassay kit comprising antibodies and reagents for the detection of one or more proteins selected from the group consisting of C-reactive protein precursor (SEQ ID NO:1), Interleukin-1 receptor accessory protein precursor (SEQ ID NO:2), Interleukin-6 precursor (SEQ ID NO:3), Interleukin-1 receptor-like 1 precursor (SEQ ID NO:4), Serum amyloid A protein precursor (SEQ ID NO:5), CD5 antigen-like precursor (SEQ ID NO:6), Beta-2-microglobulin precursor (SEQ ID NO:7), Bone-marrow proteoglycan precursor (SEQ ID NO:8), Selenium-binding protein 1 (SEQ ID NO:9), Lipopolysaccharide-binding protein precursor (SEQ ID NO:10), Chondroitin sulfate proteoglycan 4 precursor (SEQ ID NO:11), Osteopontin precursor (SEQ ID NO:12), Rho GDP-dissociation inhibitor 2 (SEQ ID NO:13), Carbonic anhydrase 2 (SEQ ID NO:14), Neutrophil gelatinase-associated lipocalin precursor (SEQ ID NO:15), Collagen alpha-5(IV) chain precursor (SEQ ID NO:16), Connective tissue growth factor precursor (SEQ ID NO:17), Macrophage colony-stimulating factor 1 precursor (SEQ ID NO:18), Protein kinase C-binding protein NELL2 precursor (SEQ ID NO:19), Neudesin precursor (SEQ ID NO:20), Protein disulfide-isomerase precursor (SEQ ID NO:21), Ribonuclease pancreatic precursor (SEQ ID NO:22), Delta-like protein precursor (SEQ ID NO:23), Chromogranin-A precursor (SEQ ID NO:24), Osteomodulin precursor (SEQ ID NO:25), Collagen alpha-2(I) chain precursor (SEQ ID NO:26), Prolow-density lipoprotein receptor-related protein 1 precursor (SEQ ID NO:27), Laminin subunit gamma-1 precursor (SEQ ID NO:28), Laminin subunit beta-1 precursor (SEQ ID NO:29), Collagen alpha-1(II) chain precursor (SEQ ID NO:30), Metalloproteinase inhibitor 1 precursor (SEQ ID NO:31), Protein FAM3C precursor (SEQ ID NO:32), Alpha-actinin-1 (SEQ ID NO:33), F-actin-capping protein subunit alpha-1 (SEQ ID NO:34), Aminopeptidase N (SEQ ID NO:35), Insulin-like growth factor-binding protein 1 precursor (SEQ ID NO:36), Cell adhesion molecule 1 precursor (SEQ ID NO:37), Cathepsin B precursor (SEQ ID NO:38), Exostosin-2 (SEQ ID NO:39), Cathepsin D precursor (SEQ ID NO:40), Neurogenic locus notch homolog protein 3 precursor (SEQ ID NO:41), Cystatin-M precursor (SEQ ID NO:42), Noelin precursor (SEQ ID NO:43), Insulin-like growth factor-binding protein 2 precursor (SEQ ID NO:44), Endoplasmin precursor (SEQ ID NO:45), Proprotein convertase subtilisin/kexin type 9 precursor (SEQ ID NO:46), Insulin-like growth factor-binding protein complex acid labile chain precursor (SEQ ID NO:47), Ezrin (SEQ ID NO:48), Fatty acid-binding protein, liver (SEQ ID NO:49), Probable G-protein coupled receptor 116 precursor (SEQ ID NO:50), Seprase (SEQ ID NO:51), Oncoprotein-induced transcript 3 protein precursor (SEQ ID NO:52), Hypoxia up-regulated protein 1 precursor (SEQ ID NO:53), Trans-Golgi network integral membrane protein 2 precursor (SEQ ID NO:54), Transketolase (SEQ ID NO:55), Receptor-type tyrosine-protein phosphatase F precursor (SEQ ID NO:56), Intercellular adhesion molecule 1 precursor (SEQ ID NO:57), Low-density lipoprotein receptor precursor (SEQ ID NO:58), 78 kDa glucose-regulated protein precursor (SEQ ID NO:59), Neighbor of punc e11 precursor (SEQ ID NO:60), Mannosyl-oligosaccharide 1,2-alpha-mannosidase IA (SEQ ID NO:61), Pyruvate kinase isozymes M1/M2 (SEQ ID NO:62), Matrix metalloproteinase-9 (SEQ ID NO:64), Alpha-1-acid glycoprotein 1 (SEQ ID NO:65), and Stress-induced-phosphoprotein 1 (SEQ ID NO:63).

39. An immunoassay kit comprising antibodies and reagents for the detection of one or more proteins selected from the group consisting of Insulin-like growth factor-binding protein 1 precursor (SEQ ID NO:36), Interleukin-6 precursor (SEQ ID NO:3), C-reactive protein precursor (SEQ ID NO:1), Beta-2-microglobulin precursor (SEQ ID NO:7), Cathepsin B precursor (SEQ ID NO:38), Cystatin-M precursor (SEQ ID NO:42), Insulin-like growth factor-binding protein 2 precursor (SEQ ID NO:44), Matrix metalloproteinase-9 (SEQ ID NO:64), Metalloproteinase inhibitor 1 precursor (SEQ ID NO:31), and Alpha-1-acid glycoprotein 1 (SEQ ID NO:65).

40. The immunoassay kit of claim **38** comprising antibodies and reagents for the detection of all of said proteins.

41. A report comprising the results of and/or diagnosis based on a test comprising

(a) testing in a sample of biological fluid obtained from said subject the level of one or more proteins selected from the group consisting of C-reactive protein precursor (SEQ ID NO:1), Interleukin-1 receptor accessory protein precursor (SEQ ID NO:2), Interleukin-6 precursor (SEQ ID NO:3), Interleukin-1 receptor-like 1 precursor (SEQ ID NO:4), Serum amyloid A protein precursor (SEQ ID NO:5), CD5 antigen-like precursor (SEQ ID NO:6), Beta-2-microglobulin precursor (SEQ ID NO:7), Bone-marrow proteoglycan precursor (SEQ ID NO:8), Selenium-binding protein 1 (SEQ ID NO:9), Lipopolysaccharide-binding protein precursor (SEQ ID NO:10), Chondroitin sulfate proteoglycan 4 precursor (SEQ ID NO:11), Osteopontin precursor (SEQ ID NO:12), Rho GDP-dissociation inhibitor 2 (SEQ ID NO:13), Carbonic anhydrase 2 (SEQ ID NO:14), Neutrophil gelatinase-associated lipocalin precursor (SEQ ID NO:15), Collagen alpha-5(IV) chain precursor (SEQ ID NO:16), Connective tissue growth factor precursor (SEQ ID NO:17), Macrophage colony-stimulating factor 1 precursor (SEQ ID NO:18), Protein kinase C-binding protein NELL2 precursor (SEQ ID NO:19), Neudesin precursor (SEQ ID NO:20), Protein disulfide-isomerase precursor (SEQ ID NO:21), Ribonuclease pancreatic precursor (SEQ ID NO:22), Delta-like protein precursor (SEQ ID NO:23), Chromogranin-A precursor (SEQ ID NO:24), Osteomodulin precursor (SEQ ID NO:25), Collagen alpha-2(I) chain precursor (SEQ ID NO:26), Prolow-density lipoprotein receptor-related protein 1 precursor (SEQ ID NO:27), Laminin subunit gamma-1 precursor (SEQ ID NO:28), Laminin subunit beta-1 precursor (SEQ ID NO:29), Collagen alpha-1(II) chain precursor (SEQ ID NO:30), Metalloproteinase inhibitor 1 precursor (SEQ ID NO:31), Protein FAM3C precursor (SEQ ID NO:32), Alpha-actinin-1 (SEQ ID NO:33), F-actin-capping protein subunit alpha-1 (SEQ ID NO:34), Aminopeptidase N (SEQ ID NO:35), Insulin-like growth factor-binding protein 1 precursor (SEQ ID NO:36), Cell adhesion molecule 1 precursor (SEQ ID NO:37), Cathepsin B precursor (SEQ ID NO:38), Exostosin-2 (SEQ ID NO:39), Cathepsin D precursor (SEQ ID NO:40), Neurogenic locus notch homolog protein 3 precursor (SEQ ID NO:41), Cystatin-M precursor (SEQ ID NO:42), Noelin precursor (SEQ ID NO:43), Insulin-like growth factor-binding protein 2 precursor (SEQ ID NO:44), Endoplasmin precursor (SEQ ID NO:45), Proprotein convertase subtilisin/kexin type 9 precursor (SEQ ID NO:46), Insulin-like growth factor-binding

protein complex acid labile chain precursor (SEQ ID NO:47), Ezrin (SEQ ID NO:48), Fatty acid-binding protein, liver (SEQ ID NO:49), Probable G-protein coupled receptor 116 precursor (SEQ ID NO:50), Seprase (SEQ ID NO:51), Oncoprotein-induced transcript 3 protein precursor (SEQ ID NO:52), Hypoxia up-regulated protein 1 precursor (SEQ ID NO:53), Trans-Golgi network integral membrane protein 2 precursor (SEQ ID NO:54), Transketolase (SEQ ID NO:55), Receptor-type tyrosine-protein phosphatase F precursor (SEQ ID NO:56), Intercellular adhesion molecule 1 precursor (SEQ ID NO:57), Low-density lipoprotein receptor precursor (SEQ ID NO:58), 78 kDa glucose-regulated protein precursor (SEQ ID NO:59), Neighbor of punc e11 precursor (SEQ ID NO:60), Mannosyl-oligosaccharide 1,2-alpha-mannosidase IA (SEQ ID NO:61), Pyruvate kinase isozymes M1/M2 (SEQ ID NO:62), Matrix metalloproteinase-9 (SEQ ID NO:64), Alpha-1-acid glycoprotein 1 (SEQ ID NO:65), and Stress-induced-phosphoprotein 1 (SEQ ID NO:63), relative to the level in normal biological fluid or biological fluid known to be indicative of neonatal sepsis; and

(b) diagnosing said subject with neonatal sepsis if said level shows a statistically significant difference relative to the level in said normal biological fluid, or does not show a statistically significant difference relative to the level in said biological fluid known to be indicative of neonatal sepsis.

42. A tangible medium storing the results of and/or diagnosis based on a test comprising

(a) testing in a sample of biological fluid obtained from said subject the level of one or more proteins selected from the group consisting of C-reactive protein precursor (SEQ ID NO:1), Interleukin-1 receptor accessory protein precursor (SEQ ID NO:2), Interleukin-6 precursor (SEQ ID NO:3), Interleukin-1 receptor-like 1 precursor (SEQ ID NO:4), Serum amyloid A protein precursor (SEQ ID NO:5), CD5 antigen-like precursor (SEQ ID NO:6), Beta-2-microglobulin precursor (SEQ ID NO:7), Bone-marrow proteoglycan precursor (SEQ ID NO:8), Selenium-binding protein 1 (SEQ ID NO:9), Lipopolysaccharide-binding protein precursor (SEQ ID NO:10), Chondroitin sulfate proteoglycan 4 precursor (SEQ ID NO:11), Osteopontin precursor (SEQ ID NO:12), Rho GDP-dissociation inhibitor 2 (SEQ ID NO:13), Carbonic anhydrase 2 (SEQ ID NO:14), Neutrophil gelatinase-associated lipocalin precursor (SEQ ID NO:15), Collagen alpha-5(IV) chain precursor (SEQ ID NO:16), Connective tissue growth factor precursor (SEQ ID NO:17), Macrophage colony-stimulating factor 1 precursor (SEQ ID NO:18), Protein kinase C-binding protein NELL2 precursor (SEQ ID NO:19), Neudesin precursor (SEQ ID NO:20), Protein disulfide-isomerase precursor (SEQ ID NO:21), Ribonuclease pancreatic precursor (SEQ ID NO:22), Delta-like protein precursor (SEQ ID NO:23), Chromogranin-A precursor (SEQ ID NO:24), Osteomodulin precursor (SEQ ID NO:25), Collagen alpha-2(I) chain precursor (SEQ ID NO:26), Prolow-density lipoprotein receptor-related protein 1 precursor (SEQ ID NO:27), Laminin subunit gamma-1 precursor (SEQ ID NO:28), Laminin subunit beta-1 precursor (SEQ ID NO:29), Collagen alpha-1(II) chain precursor (SEQ ID NO:30), Metalloproteinase inhibitor 1 precursor (SEQ ID NO:31), Protein FAM3C precursor (SEQ ID NO:32), Alpha-actinin-1 (SEQ ID NO:33), F-actin-capping protein subunit alpha-1 (SEQ ID NO:34), Aminopeptidase N (SEQ ID NO:35), Insulin-like growth factor-binding protein 1 precursor (SEQ ID NO:36), Cell adhesion molecule 1 precursor (SEQ ID NO:37), Cathepsin B precursor (SEQ ID NO:38), Exostosin-2 (SEQ ID NO:39), Cathepsin D precursor (SEQ ID NO:40), Neurogenic locus notch homolog protein 3 precursor (SEQ ID NO:41), Cystatin-M precursor (SEQ ID NO:42), Noelin precursor (SEQ ID NO:43), Insulin-like growth factor-binding protein 2 precursor (SEQ ID NO:44), Endoplasmin precursor (SEQ ID NO:45), Proprotein convertase subtilisin/kexin type 9 precursor (SEQ ID NO:46), Insulin-like growth factor-binding protein complex acid labile chain precursor (SEQ ID NO:47), Ezrin (SEQ ID NO:48), Fatty acid-binding protein, liver (SEQ ID NO:49), Probable G-protein coupled receptor 116 precursor (SEQ ID NO:50), Seprase (SEQ ID NO:51), Oncoprotein-induced transcript 3 protein precursor (SEQ ID NO:52), Hypoxia up-regulated protein 1 precursor (SEQ ID NO:53), Trans-Golgi network integral membrane protein 2 precursor (SEQ ID NO:54), Transketolase (SEQ ID NO:55), Receptor-type tyrosine-protein phosphatase F precursor (SEQ ID NO:56), Intercellular adhesion molecule 1 precursor (SEQ ID NO:57), Low-density lipoprotein receptor precursor (SEQ ID NO:58), 78 kDa glucose-regulated protein precursor (SEQ ID NO:59), Neighbor of punc e11 precursor (SEQ ID NO:60), Mannosyl-oligosaccharide 1,2-alpha-mannosidase IA (SEQ ID NO:61), Pyruvate kinase isozymes M1/M2 (SEQ ID NO:62), Matrix metalloproteinase-9 (SEQ ID NO:64), Alpha-1-acid glycoprotein 1 (SEQ ID NO:65), and Stress-induced-phosphoprotein 1 (SEQ ID NO:63), relative to the level in normal biological fluid or biological fluid known to be indicative of neonatal sepsis; and

(b) diagnosing said subject with neonatal sepsis if said level shows a statistically significant difference relative to the level in said normal biological fluid, or does not show a statistically significant difference relative to the level in said biological fluid known to be indicative of neonatal sepsis.

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专利名称(译)	用于检测生物液中新生儿败血症的生物标志物		
公开(公告)号	US20100190652A1	公开(公告)日	2010-07-29
申请号	US12/693387	申请日	2010-01-25
[标]申请(专利权)人(译)	NAGALLA斯里尼瓦沙 格拉维特米迦勒		
申请(专利权)人(译)	NAGALLA斯里尼瓦沙 格拉维特米迦勒		
当前申请(专利权)人(译)	NAGALLA斯里尼瓦沙 格拉维特米迦勒		
[标]发明人	NAGALLA SRINIVASA GRAVETT MICHAEL		
发明人	NAGALLA, SRINIVASA GRAVETT, MICHAEL		
IPC分类号	C40B30/00 G01N33/53 G01N33/573		
CPC分类号	G01N33/6893 G01N2800/60 G01N2800/26 G01N2550/00		
优先权	61/147635 2009-01-27 US		
外部链接	Espacenet USPTO		

摘要(译)

本发明涉及使用全局蛋白质组学方法鉴定和检测新生儿败血症的生物流体生物标志物。