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(54) **BIOMARKERS FOR MYOCARDIAL ISCHEMIA**

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16/18; **B01L 3/502**; **B01L 9/54**

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See application file for complete search history.

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Transfer

This patent is subject to a terminal dis-
claimer.

(57) **ABSTRACT**

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Related U.S. Application Data

(63) Continuation of application No. 12/994,034, filed as
application No. PCT/US2009/045168 on May 26,
2009, now Pat. No. 8,497,078.

(60) Provisional application No. 61/128,688, filed on May
23, 2008.

(51) **Int. Cl.**

G01N 31/00 (2006.01)

G01N 33/53 (2006.01)

This invention relates, e.g., to a method for determining if a
subject has myocardial ischemia, comprising (a) providing a
blood sample obtained from a subject suspected of having
myocardial ischemia; (b) determining in the sample the
amount of one or more of the following proteins: (i) Lumican
and/or (ii) Extracellular matrix protein 1 and/or (iii) Carbox-
ypeptidase N; and (c) comparing the amount(s) of the
protein(s) to a baseline value that is indicative of the amount
of the protein in a subject that does not have myocardial
ischemia, wherein a statistically significantly increased
amount of the protein(s) compared to the baseline value is
indicative of myocardial ischemia. Other proteins indicative
of myocardial ischemia are also described, as are methods for
treating a subject based on a diagnostic procedure of the
invention, and kits for carrying out a method of the invention.

2 Claims, 6 Drawing Sheets

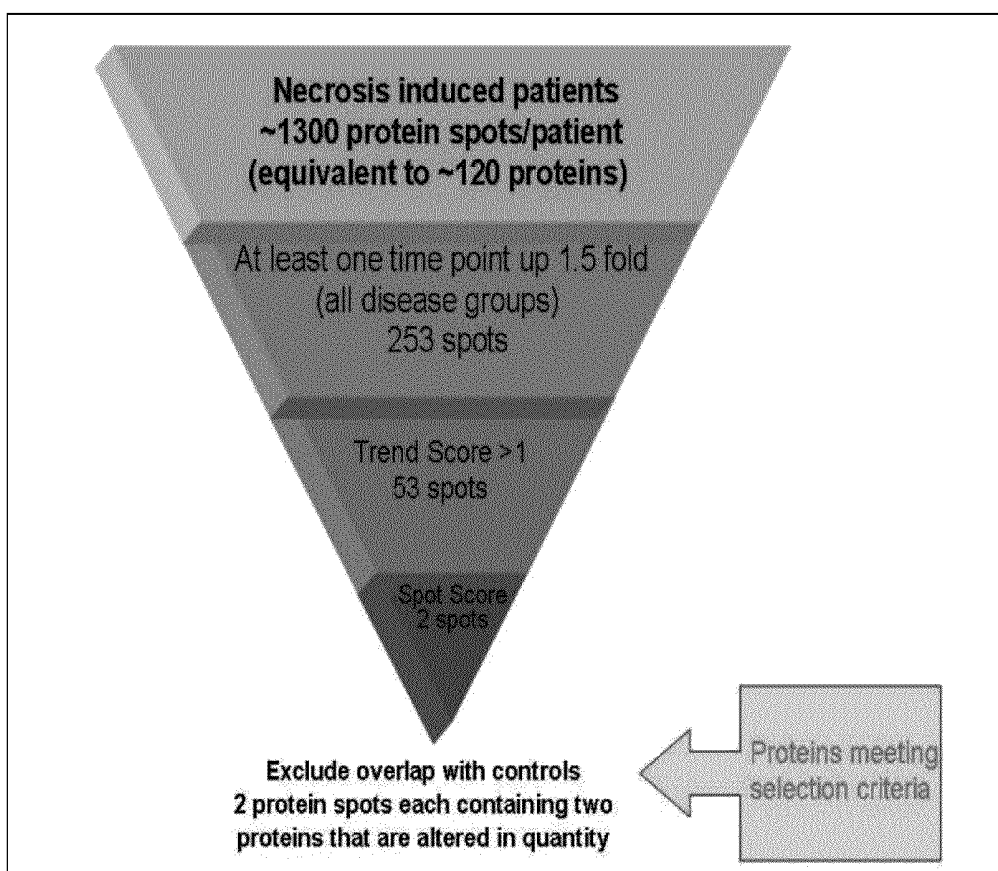


FIG. 1

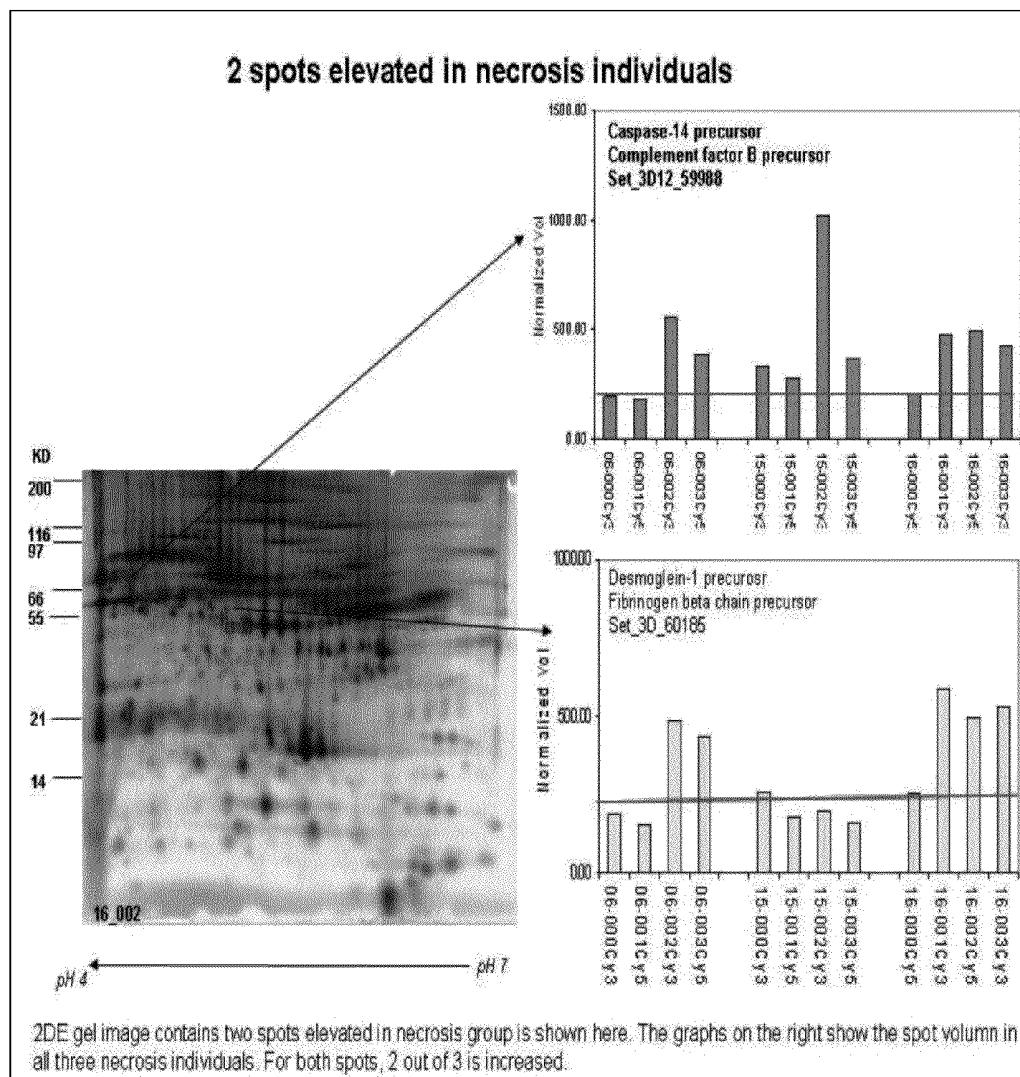


FIG. 2

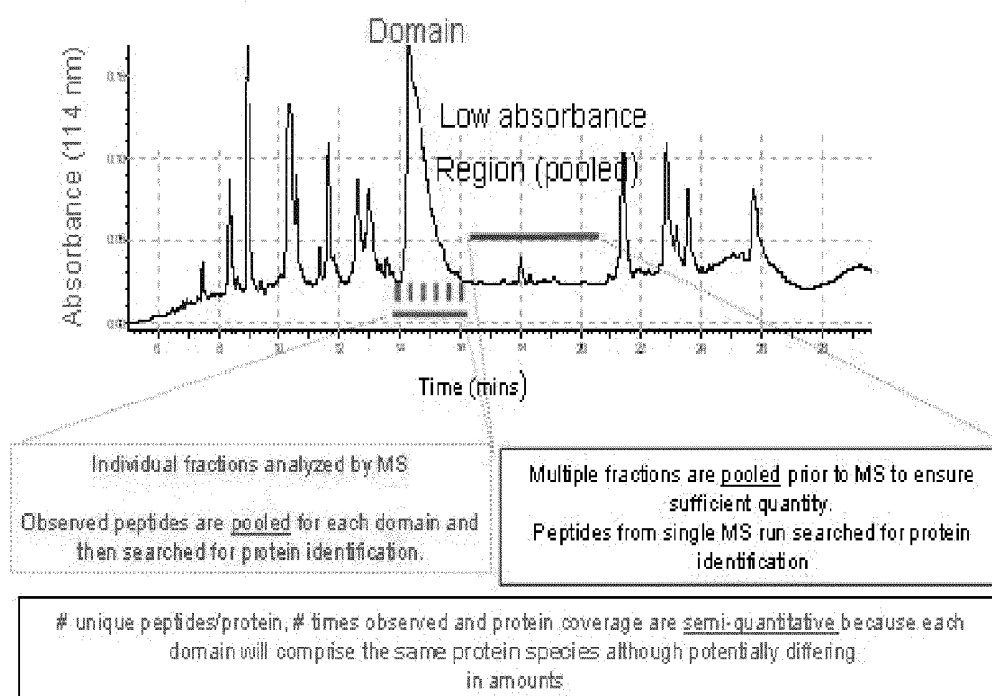


FIG. 3

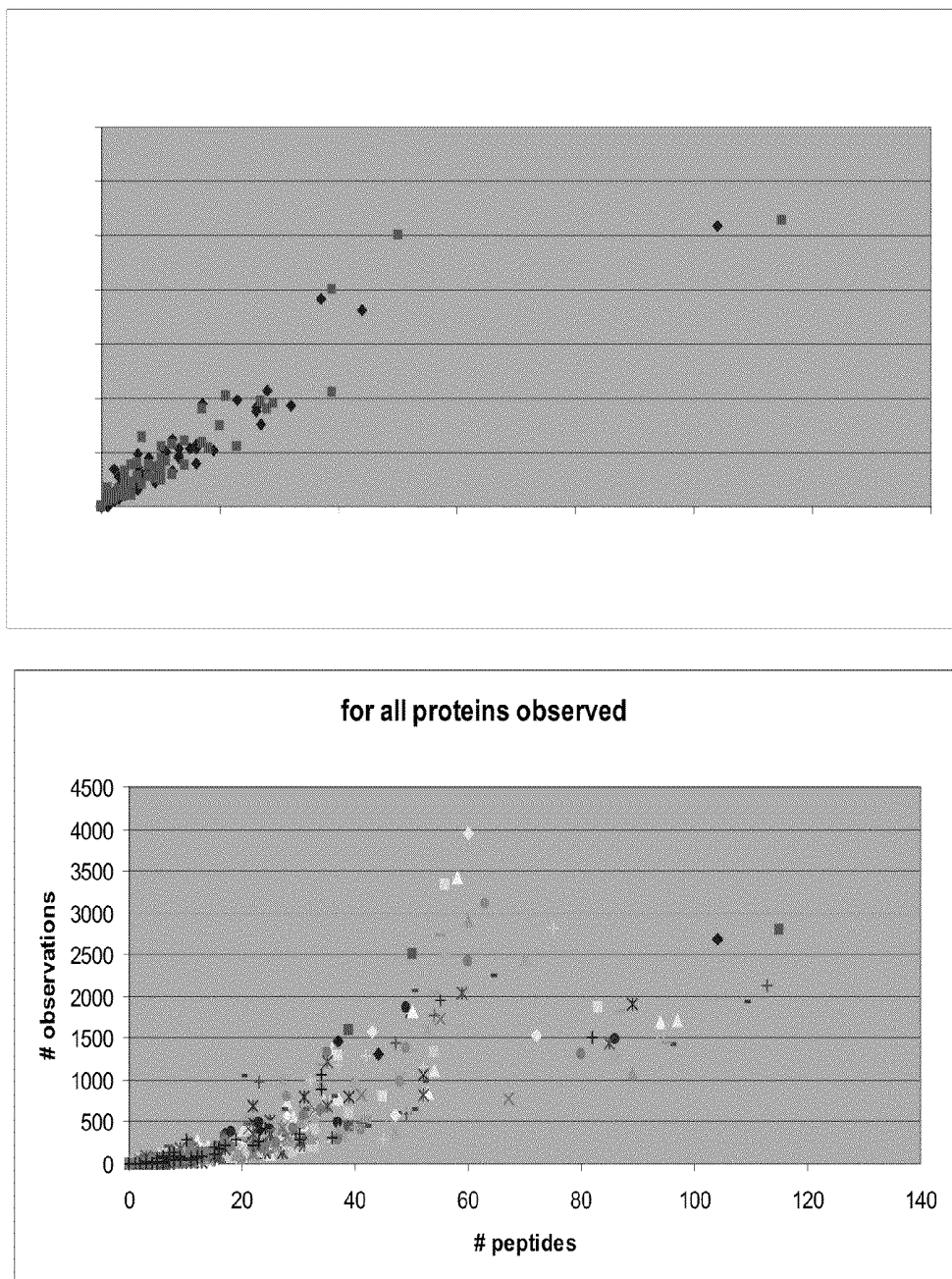


FIG. 4

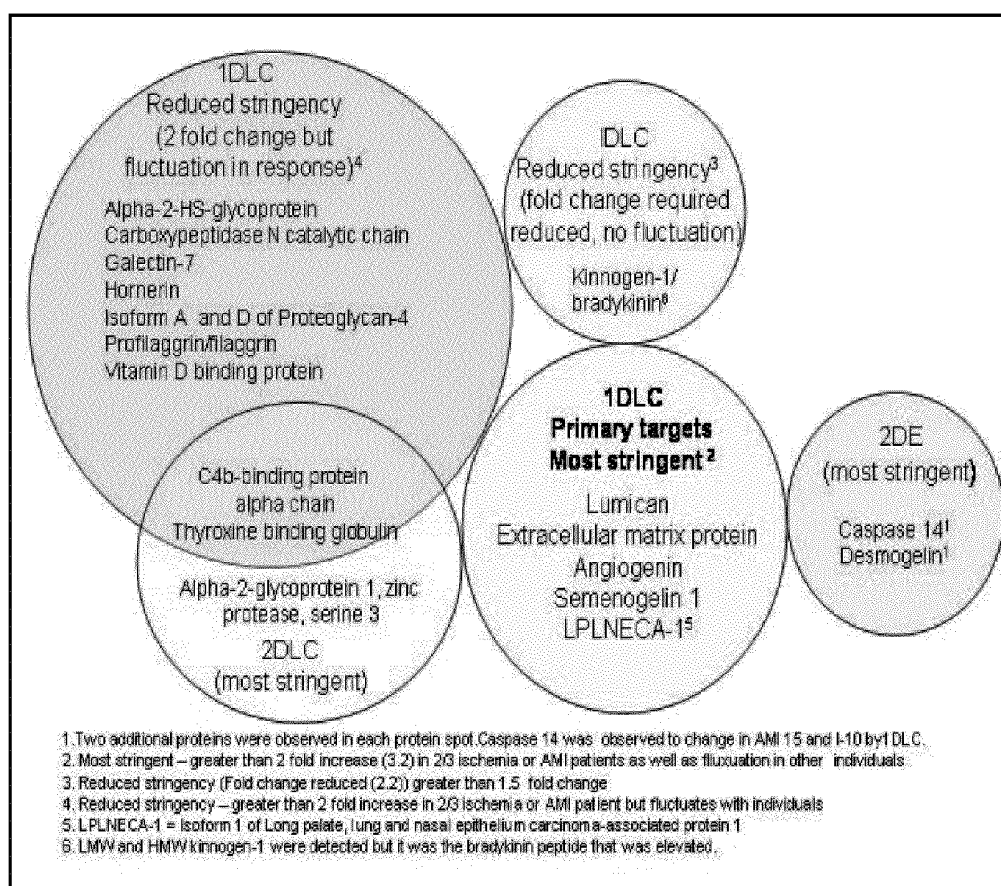


FIG. 5

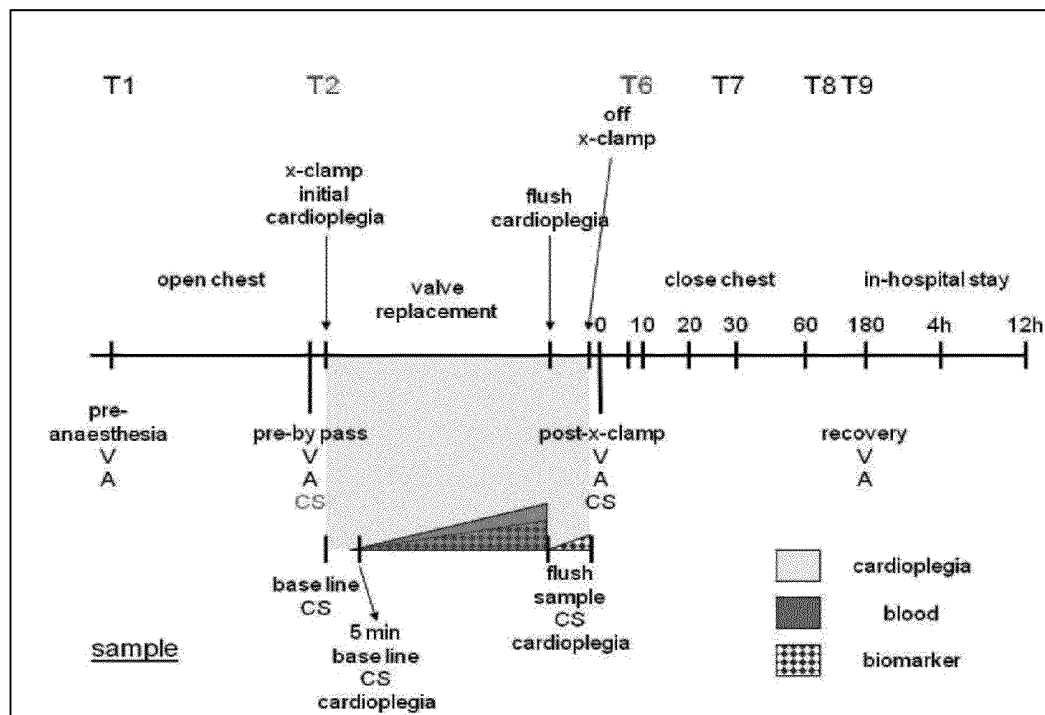


FIG. 6

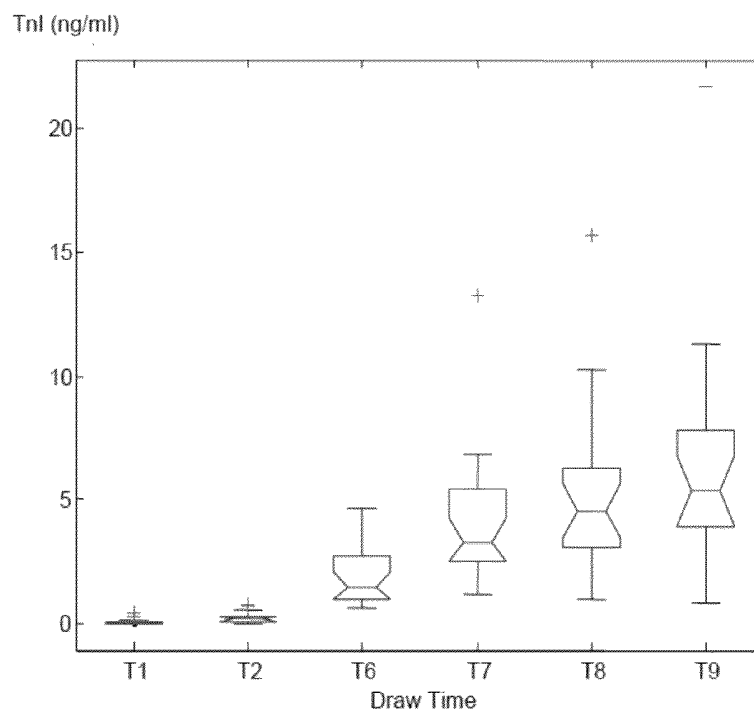


FIG. 7

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BIOMARKERS FOR MYOCARDIAL ISCHEMIA

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation of U.S. patent application 12/994,034, filed Sep. 15, 2001, now U.S. Pat. No. 8,497,078, issued Jul. 30, 2013, which is a 35U.S.C. §371 U.S. national entry of International Application PCT/US2009/045168, having an international filing date of May 26, 2009, which claims the benefit of U.S. Provisional Application No. 61/128,688, filed May 23, 2008, the content of each of the aforementioned applications is herein incorporated by reference in their entirety.

BACKGROUND INFORMATION

Coronary heart disease is the most common single cause of death in the western world, representing about 20% of all deaths. This is equivalent to about 2 million deaths in Europe per year or four people per minute. In the US, over 8 million people exhibit acute (chest pain) symptoms in the Emergency Department (ED) of hospitals, with 1.5 million individuals having confirmed acute coronary symptom (ACS) events, accounting for 500,000 short term deaths. In patients presenting to the emergency room with chest pain, fewer than 15% are ultimately diagnosed as having ischemia or acute myocardial infarction (MI). Currently, blood tests for the cardiac specific isoform of troponin I or troponin T (TnI or TnT, respectively) are generally used for the diagnosis of acute myocardial infarction (due to cardiac muscle (cell) death). Creatine kinase (CK) MB and myoglobin can also be used, but are considered to be less specific for cardiac injury. However, although these cardiac biomarkers can identify patients with even small amounts of myocardial necrosis, there is an earlier time point in which the heart is in ischemia but is not yet in necrosis, and the diagnosis of cardiac ischemia in the absence of necrosis cannot currently be made with accuracy.

It would be useful to be able to identify subjects in this diagnostic window (having non-necrotic ischemia). Such a diagnostic tool would be of great value for triage in the emergency department. For example, it would allow earlier intervention, including earlier perfusion, to allow increased salvage of the injured myocardium; and it would prevent unnecessary admittance to the hospital of patients with non-cardiac chest pain. Furthermore, such an assay could delay therapy in subjects who do not exhibit diagnostic electrocardiographic (ECG) changes, and could help to improve the accuracy of current provocative tests for ischemia, such as exercise stress testing. The sooner intervention can be carried out, the less cardiac damage will occur. Reduced damage is correlated with an increase in long term survival.

DESCRIPTION OF THE DRAWINGS

FIG. 1 shows a schematic representation of protein spot attrition due to stringent criteria, based on a cohort that underwent atrial pacing to induce demand on the heart such that the blood flow was inadequate, thereby potentially causing myocardial ischemia. Blood samples were drawn from the coronary sinuses of individuals subjected to atrial pacing. The change in lactate acid level was an indication of induced ischemia, while the detection of cTnI or cTnT was indicative of cardiac necrosis. Those subjects that did not exhibit any change in lactate acid level or cTnI/cTnT were considered controls.

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FIG. 2 shows a 2DE gel image showing two spots that are elevated in necrosis individuals. Serum samples were initially depleted of immunoglobins (IgG) and albumin, then separated based on pI and MW using gel electrophoresis. The majority of the spots did not change in all of the individuals subjected to atrial pacing. The graphs on the right show the spot volume in all three necrosis individuals. For both spots, 2 out of 3 were increased for those individuals which had cTnI detected after atrial pacing in their coronary sinus blood samples.

FIG. 3 shows 1DLC fractions strategy used in MS analysis. Samples were depleted of immunoglobins (IgG, IgM and IgA) and albumin, then separated based on hydrophobicity (Reversed phase high performance liquid chromatography, RPLC, 1DLC). The number of unique peptides/protein observed, and the number of times observed and protein coverage are semi-quantitative, because each domain will comprise the same protein species, although potentially differing in amounts.

FIG. 4 shows the number of peptides observed vs. the number of spectra count for all individuals and all time points obtained by 1DLC (hydrophobicity, RPLC-MS run 1).

FIG. 5 schematically illustrates the overlap between the three different proteomic methods used: 2DE, 1DLC and 2DLC. For 2DLC, the serum samples were depleted of immunoglobins (IgG, IgM and IgA) and albumin, then separated based on chromatographic focusing (pH from 8.5 to 4.0) and reversed phase HPLC (1DLC). Fractions from areas found to be different in the 2DLC were analyzed by MS. Differences in spectral counting and or number of peptides observed were included as changed. Superscripts 1-6 refer to the following:

1. Two additional proteins were observed in each protein spot. Caspase 14 was observed to change in AMI (individual) 15 and by 1 DLC for individuals (1-10) that underwent atrial pacing
2. Most stringent—greater than 2 fold increase (3.2) in $\frac{2}{3}$ ischemia or AMI patients as well as fluctuation in other individuals
3. Reduced stringency (fold change reduced (2.2)) greater than 1.5 fold change
4. Reduced stringency—greater than 2 fold increase in $\frac{2}{3}$ ischemia or AMI patients but fluctuates with individuals
5. LPLNECA-1=isoform 1 of Long palate, lung and nasal epithelium carcinoma-associated protein 1
6. LMW and HMW kinnogen-1 were detected but it was the bradykinin peptide that was elevated

FIG. 6 shows schematically the collection during valve replacement. In this cohort, coronary sinus samples were obtained from individuals who underwent induced ischemia due to stopping of the heart (with cardioplegia) during valve replacement. Coronary sinus samples were obtained and depleted prior to being separated by 1DLC (as outlined above). Proteins found to be increased with ischemia in the majority of individuals were considered first tier. However, it must be recognized that lower abundant proteins may only be observed in a few patients due to inherent detection limits of this type of MS analysis. These proteins might be actually elevated in many patients and just not observed with this approach.

FIG. 7 shows a box plot of cTnI at all time points for the individuals that underwent valve replacement. Note that all individuals eventually had detectable cTnI/cTnT in their serum, indicating necrosis. However, at the time points at which de novo discovery was undertaken, none of the individuals had detectable cTnT or cTnI. This shows that all were ischemic at the time of study.

The present inventors have identified a number of protein markers for cardiac (myocardial) ischemia, including non-necrotic cardiac (myocardial) ischemia.

Three different types of protein analysis were performed to identify these markers, in order to cover as broad a base as possible of proteome coverage, e.g. to allow the enhanced detection of isoforms and of post-translational modifications (PTM). These types of analysis were two-dimensional electrophoresis (2DE, separating proteins based on pI and molecular weight), two-dimensional liquid chromatography (2DLC, separating proteins based on pI and hydrophobicity) and one-dimensional liquid chromatography (1DLC, separating proteins based on hydrophobicity). Note that the starting pH differs between 2DLC and 1DLC: pH 8.5 and 2.3, respectively. Two different cohorts were analyzed—increased metabolic demand (cohort 1) and reduced supply (cohort 2).

In a first study, ischemia was induced in a first cohort of subjects by metabolic demand: subjects were stimulated by atrial pacing, which makes the heart beat faster and induces ischemia, as indicated by an increase in lactate, and potentially myocardial necrosis (based on detection of cTnI or cTnT in blood). In some cases, individuals did not exhibit any increase in lactate or detectable cTnI/cTnT. These latter individuals were considered controls. Multiple serum samples were obtained for each individual. Differences between baseline (prior to pacing) and those at peaking pacing and up to 60 minutes after were analyzed. Those proteins that were elevated compared to the baseline in the majority of ischemic or necrotic individuals (and not elevated in controls) were considered to be of interest.

This procedure mimics naturally occurring metabolic cardiac events, such as ministrokes, that might precede a full MI. Ischemia is a heterogeneous group of conditions, resulting from different underlying mechanisms, such as demand and supply limitation. We have “mimicked” these two conditions in the different cohorts used in the analysis. Thus, these cohorts are expected to reflect markers that are overexpressed in subjects suffering from ischemia resulting from a variety of such underlying mechanisms. Samples from demand (atrial pacing) were evaluated by 2DE, 2DLC and 1DLC.

In a second study, ischemia was induced in a second cohort by coronary blockage: subjects undergoing valve replacement surgery exhibited ischemia because of blood loss during the procedure. This procedure mimics naturally occurring events in which ischemia is induced by coronary blood vessel blockage. This cohort was evaluated only by 1DLC, the procedure which provided a comparison to the most useful results with the first cohort. Those proteins found to be altered in both cohorts are considered to be “tier one” markers, although strong hits in either cohort may also be considered to be prime candidate markers.

The results of the studies with these two cohorts are summarized in Table 13. Taken together, these studies show that three proteins are implicated as the most highly correlated markers (sometimes referred to herein as “first tier” markers, as they are observed to be elevated in both cohorts) for ischemia, regardless of the cause of the ischemia: Lumican; Extracellular matrix protein 1 (ECM-1); and Carboxypeptidase N (e.g., the catalytic chain).

Three markers in addition to Lumican, ECM-1 and Carboxypeptidase N are implicated as first tier markers for at least subjects similar to those in the first cohort: Angiogenin; Semenogelin (e.g., isoforms 1 and 2); and Long palate, lung and nasal epithelium carcinoma-associated protein 1 (LPL-NECA-1) (e.g., isoform 1; isoforms 2-4 are also present, but

the method of analysis employed in this study, although it supports isoform 1, cannot distinguish among the four isoforms, which are splice variants, so isoforms 2-4 cannot be ruled out due to sequence homology).

Ten markers in addition to Lumican, ECM-1 and Carboxypeptidase N are implicated as first tier markers for at least subjects similar to those in the second cohort: Peroxiredoxin isoform 2; S100 isoforms A7, A8 and A9 (other S100 isoforms were detected and not observed to be altered); Sortilin-related receptor; Catalase; Low density lipoprotein receptor related proteins 1 and 2; and Syntaxin 3.

In addition to these first tier markers, Table 13 lists some “second tier” markers which can also be used for identifying subjects similar to those in both cohorts I and II; in cohort I; or in cohort II. These include, e.g., Alpha-2-HS-glycoprotein; Galectin-7; Hornerin; Proteoglycan-4; Profilaggrin (also called Filaggrin); Vitamin D binding protein; C4b-binding protein alpha chain; Thyroxine binding globulin; Alpha-2-glycoprotein 1, zinc; protease, serine 3; Caspase 14; Desmogelin; Kininogen-1 (we observed the peptide for the intact protein, but our data cannot distinguish between changes to the LMW or HMW, which could also be present); Hepatocyte growth factor like protein; Hepatocyte growth factor activator; and Insulin like growth factor protein 6.

In some embodiments of the invention, it is desirable to distinguish between subjects whose ischemia is induced by metabolic causes (similar to the subjects of cohort I), and subjects whose ischemia is induced by coronary blood vessel blockage (similar to the subjects of cohort II), because different treatment methods can be used for the two classes of subjects. The markers of the invention can be used to make such distinctions.

This invention relates, e.g., to a method for determining if a subject has myocardial ischemia, comprising measuring in a sample from the subject the amount of at least one of the following proteins, compared to a baseline value:

- a) Lumican and/or
- b) Extracellular matrix protein 1 and/or
- c) Carboxypeptidase N,

wherein a significant amount (e.g., at least a statistically significant amount) of over-expression of the protein(s) compared to the baseline value is indicative of myocardial ischemia (e.g., indicates that the subject has, or is likely to have, myocardial ischemia). The amount of expression may be determined for any combination of 1, 2, or all 3, of these proteins, and the determinations can be conducted simultaneously, or in any order.

Another aspect of the invention is a method for identifying subjects that have myocardial ischemia that is induced by a metabolic-induced ischemic event [due to a metabolic limitation, in which the heart is unable to meet metabolic need; (excessive) metabolic demand], comprising determining in the sample from the subject the amount, compared to a baseline value, of at least one of proteins a), b), c) above,

- d) Angiogenin,
- e) Semenogelin, and/or
- f) Long palate, lung and nasal epithelium carcinoma-associated protein 1. The amount of expression may be determined for any combination of 1, 2, 3, 4, 5, or 6 of these proteins, and the determinations can be conducted simultaneously, or in any order.

Another aspect of the invention is a method for identifying subjects that have myocardial ischemia that is induced by coronary blood vessel blockage, which limits the supply of blood, comprising determining in the sample from the subject the amount, compared to a baseline value, of at least one of proteins a), b), c) above,

g) Syntaxin,
 h) Peroxiredoxin isoform 2,
 i) S100 isoform A7,
 j) S100 isoform A8,
 k) S100 isoform A9,
 l) Sortilin-related receptor
 m) Catalase
 n) Low density lipoprotein receptor related protein 1, and/
 or
 o) Low density lipoprotein receptor related protein 2. The amount of expression may be determined for any combination of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12 of these proteins, and the determinations can be conducted simultaneously, or in any order.

In addition to the proteins noted above, one of more of the “second tier” proteins indicated in Table 13 can also be measured. A skilled worker will recognize which of these markers are indicative of a cohort I-type of condition, and which are indicative of a cohort II-type of condition.

Another aspect of the invention is a method for determining if a subject has myocardial ischemia, comprising determining in a sample from the subject the amount, compared to a baseline value, of at least one (e.g., at least four) of at least proteins a)-p) as noted above. The amount of expression may be determined for any combination of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 of these proteins; and the determinations can be conducted simultaneously, or in any order.

In a method of the invention, a determination that increasing numbers of protein markers of the invention are overexpressed in a subject can further indicate that the subject has (or is likely to have) myocardial ischemia.

A method as above may further comprise measuring in the sample the amount of one or more other markers that have been reported to be diagnostic of cardiac necrosis, including cardiac specific isoforms of troponin I (TnI) and/or troponin T (TnT) (although CK-MB, myoglobin, have been used in the past, cTnI and cTnT are the current gold standards), wherein a significant increase (e.g., at least a statistically significant increase) of the one or more markers further is further indicative that the subject has myocardial ischemia.

As noted above, ischemia is a heterogeneous condition caused by a variety of underlying mechanisms. Even if a single marker of the invention is capable of detecting a subject having ischemia resulting from a particular mechanism, it is possible for some markers that the marker is also upregulated in a disease other than myocardial ischemia. In such a case, it would be desirable to screen for upregulation of at least one additional marker that is associated with ischemia caused by a different underlying mechanism. The column labeled “Function” in Table 13 shows that some of the markers of the invention can be divided into particular groups on the basis of their functions. A skilled worker, studying this table, could readily identify markers associated with different mechanisms. In one embodiment of the invention, markers associated with 2, 3, 4 or more underlying mechanisms can be tested together in an assay of the invention.

Another aspect of the method is a method for deciding how to treat a subject suspected of having myocardial ischemia, or a subject that is at high risk for having myocardial ischemia, comprising determining by a method as above if the subject has (or is likely to have) myocardial ischemia and, (1) if the subject is determined to have (or to be likely to have) myocardial ischemia, deciding to treat the subject aggressively [such as with angioplasty (mechanical widening in opening blood vessels), treating with an anti-thrombolysis agent or, if possible, with percutaneous coronary intervention (PCI, or TPA), or undergoing coronary bypass surgery to replace the

injured/blocked coronary artery], or (2) if the subject is determined not to have (or not to be likely to have) myocardial ischemia, deciding to treat the subject non-aggressively [such as with aspirin and/or thrombolysis (e.g., TPA), with periodic monitoring to ensure no future MI events, or by recommending changes in life style. This method can be used to confirm that a subject does not have ischemia (especially if myocardial ischemia is not detectable by cTnI or cTnT elevation), and thus to allow the subject to be released from hospital care.]

Another aspect of the invention is a method for treating a subject suspected of having myocardial ischemia, or a subject that is at high risk for having myocardial ischemia, comprising determining by a method as above if the subject has (or is likely to have) myocardial ischemia and, (1) if the subject is determined to have (or to be likely to have) myocardial ischemia, treating the subject aggressively, as indicated above, or (2) if the subject is determined not to have (or not to be likely to have) myocardial ischemia, treating the subject non-aggressively, as indicated above.

Another aspect of the invention is a kit for detecting the presence of ischemia in a subject, comprising reagents for detecting the amounts of at least one (e.g., any combination of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 of at least proteins a)-o) as noted above.

This invention relates, e.g., to a method for determining if a subject has myocardial ischemia, comprising

(a) providing a sample obtained from a subject suspected of having myocardial ischemia;

(b) determining in the sample the amount of at least one of at least proteins a)-p) as noted above (e.g., any combination of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15) of the proteins); and

(c) comparing the amount(s) of the protein(s) to a baseline value that is indicative of the amount of the protein in a subject that does not have myocardial ischemia, wherein an increased amount (e.g., a statistically significantly increased amount) of the protein(s) compared to the baseline value is indicative of myocardial ischemia.

In one embodiment of the invention, the amount(s) of the protein(s) is compared over time to the baseline value and/or to levels known to be associated with necrosis. The kinetic rise and fall of combinations of proteins is indicative of impending myocardial ischemia (or other cardio and vascular events, such as stroke. A method of the invention can also be used to determine risk in subjects (patients) with stable or unstable angina.

A sample which is “provided” can be obtained by the person (or machine) conducting the assay, or it can have been obtained by another, and transferred to the person (or machine) carrying out the assay.

By a “sample” (e.g. a test sample) from a subject meant a sample that might be expected to contain elevated levels of the protein markers of the invention in a subject having myocardial ischemia. Many suitable sample types will be evident to a skilled worker. In one embodiment of the invention, the sample is a blood sample, such as whole blood, plasma, or serum (plasma from which clotting factors have been removed). For example, peripheral, arterial or venous plasma or serum can be used. In another embodiment, the sample is urine, sweat, or another body fluid into which proteins are sometimes removed from the blood stream. In the case of urine, for example, the protein is likely to be broken down, so diagnostic fragments of the proteins of the invention can be screened for. In another embodiment, the sample is cardiac tissue, which is harvested, e.g., after a heart transplant or the insertion of a pacemaker or defibrillator. Methods for obtain-

ing samples and preparing them for analysis (e.g., for detection of the amount of protein) are conventional and well-known in the art. Some suitable methods are described in the Examples herein or in the references cited therein.

A "subject," as used herein, includes any animal that has, or is suspected of having, myocardial ischemia. Suitable subjects (patients) include laboratory animals (such as mouse, rat, rabbit, guinea pig or pig), farm animals, sporting animals (e.g. dogs or horses) and domestic animals or pets (such as a horse, dog or cat). Non-human primates and human patients are included. For example, human subjects who present with chest pain or other symptoms of cardiac distress, including, e.g. shortness of breath, nausea, vomiting, sweating, weakness, fatigue, or palpitations, can be evaluated by a method of the invention. About 1/4 of MI are silent and without chest pain. Furthermore, patients who have been evaluated in an emergency room or in an ambulance or physician's office and then dismissed as not being ill according to current tests for infarction have an increased risk of having a heart attack in the next 24-48 hours; such patients can be monitored by a method of the invention to determine if and when they begin express markers of the invention, which indicates that, e.g., they are beginning to exhibit ischemia. Subjects can also be monitored by a method of the invention to improve the accuracy of current provocative tests for ischemia, such as exercise stress testing. An individual can be monitored by a method of the invention during exercise stress tests of Dobutamine stress tests to determine if the individual is at risk for ischemia; such monitoring can supplement or replace the test that is currently carried out. Athletes (e.g., humans, racing dogs or race horses) can be monitored during training to ascertain if they are exerting themselves too vigorously and are in danger of undergoing an MI.

In another embodiment of the invention, the method is used as a screen in order to identify a drug (or to improve a cardioplegic solution) that protects the heart from ischemia and necrosis. The detection of one or more of the proteins of the invention in blood (or media if cell culture is used) is indicative of ischemia, and the quantity of the protein(s) is indicative of the severity of the ischemia.

The properties and amino acid sequences of the proteins of the invention are well-known and can be determined routinely, as well as downloaded from various known databases. See, e.g., the database, International Protein Index (IPI) at the world wide web site, ebi.ac.uk/IPI/xrefs.html. A summary of some properties of some of the proteins discussed herein, including their IPI ID number and amino acid sequences, is provided in Examples II and IV. This information is accurate as of the date of filing of this application. However, some of this information, including the sequences, is routinely updated (e.g. to correct mistakes in the previous entries), so updated (corrected) information about the proteins is included in this application. Information provided in the IPI database is incorporated by reference in the present application.

Although much of the data presented in the Examples herein are directed to particular forms of proteins of interest (or peptides thereof), it will be evident to a skilled worker that a variety of forms of these proteins may be indicative of the presence of myocardial ischemia in a subject. For example, the protein may be an intact, full-length protein. If a protein undergoes processing naturally (e.g., is converted from a pre-pro-hormone to a pro-hormone to a fully processed hormone; the N-terminal methionine is cleaved off; the signal sequence is removed, often accompanied by a post-translational modification, such as acetylation; etc.), any of these forms of the protein are included in the invention. Further-

more, in some instances, a protein of the invention may be broken down or degraded (e.g., proteins that are found in the urine). In such a case, an investigator can determine the level of one or more of the fragments or degradation products. A "diagnostic protein fragment," as used herein, is a fragment that is unique to the protein being identified, as detected by the assay. For example, a diagnostic fragment is recognized specifically by an antibody used to detect the full-length protein. Certain isoforms or post translational modifications (PTM) may also be encompassed by the invention. For example, the inventors have obtained data indicating PTM for C4b binding proteins; protease, serine; 3 alpha-2-glycoprotein 1; and zinc caspase 14.

The proteins and combinations of proteins discussed herein are sometimes referred to herein as "proteins (or protein markers) of the invention."

A variety of tests that have been used to detect myocardial events (particularly late occurring events, such as necrotic myocardial ischemia). These include, e.g., determining the levels of cardiac specific isoform(s) of troponin I (TnI) and/or troponin T (TnT), CK-MB (Creatine Kinase-MB), or myoglobin, although only the former two are the current gold standard. CK MB and myoglobin are not cardiac-specific. However, none of these markers is completely satisfactory for the detection of myocardial ischemia. For example, they fail to detect early stages of heart disease, such as non-necrotic myocardial ischemia. The new markers described herein can be used in conjunction with these types of assays.

When the values of more than one protein are being analyzed, a statistical method such as multi-variant analysis or principal component analysis (PCA) is used which takes into account the levels of the various proteins (e.g., using a linear regression score). For verification, we will use either immunoassay or multiple reaction monitoring (MRM, a MS-based targeted method that quantifies peptides that are unique to the protein of interest) on individuals (control, ischemia and MI).

In some embodiments, it is desirable to express the results of an assay in terms of an increase (e.g., a statistically significant increase) in a value (or combination of values) compared to a baseline value.

A "significant" increase in a value, as used herein, can refer to a difference which is reproducible or statistically significant, as determined using statistical methods that are appropriate and well-known in the art, generally with a probability value of less than five percent chance of the change being due to random variation. In general, a statistically significant value is at least two standard deviations from the value in a "normal" healthy control subject. Suitable statistical tests will be evident to a skilled worker. For example, a significant increase in the amount of a protein compared to a baseline value can be about 50%, 2-fold, or more higher. A significantly elevated amount of a protein of the invention compared to a suitable baseline value, then, is indicative that a test subject has myocardial ischemia (indicates that the subject is likely to have myocardial ischemia). A subject is "likely" to have myocardial ischemia if the subject has levels of the marker protein(s) significantly above those of a healthy control or his own baseline (taken at an earlier time point). The extent of the increased levels correlates to the % chance. For example, the subject can have greater than about a 50% chance, e.g., greater than about 70%, 80% 90%, 95% or higher chance, of having the ischemia. In general, the presence of an elevated amount of a marker of the invention is a strong indication that the subject has ischemia.

As used herein, a "baseline value" generally refers to the level (amount) of a protein in a comparable sample (e.g., from the same type of tissue as the tested tissue, such as blood or

serum), from a "normal" healthy subject that does not exhibit myocardial ischemia. If desired, a pool or population of the same tissues from normal subjects can be used, and the baseline value can be an average or mean of the measurements. Suitable baseline values can be determined by those of skill in the art without undue experimentation. Suitable baseline values may be available in a database compiled from the values and/or may be determined based on published data or on retrospective studies of patients' tissues, and other information as would be apparent to a person of ordinary skill implementing a method of the invention. Suitable baseline values may be selected using statistical tools that provide an appropriate confidence interval so that measured levels that fall outside the standard value can be accepted as being aberrant from a diagnostic perspective, and predictive of ischemia.

It is generally not practical in a clinical or research setting to use patient samples as sources for baseline controls. Therefore, one can use any of variety of reference values in which the same or a similar level of expression is found as in a subject that does not have myocardial ischemia.

It will be appreciated by those of skill in the art that a baseline or normal level need not be established for each assay as the assay is performed but rather, baseline or normal levels can be established by referring to a form of stored information regarding a previously determined baseline levels for a given protein or panel of proteins, such as a baseline level established by any of the above-described methods. Such a form of stored information can include, for example, a reference chart, listing or electronic file of population or individual data regarding "normal levels" (negative control) or positive controls; a medical chart for the patient recording data from previous evaluations; a receiver-operator characteristic (ROC) curve; or any other source of data regarding baseline levels that is useful for the patient to be diagnosed. In one embodiment of the invention, the amount of the proteins in a combination of proteins, compared to a baseline value, is expressed as a linear regression score, as described, e.g., in Irwin, in Neter, Kutner, Nachtstein, Wasserman (1996) *Applied Linear Statistical Models*, 4th edition, page 295.

In an embodiment in which the progress of a treatment is being monitored, a baseline value can be based on earlier measurements taken from the same subject, before the treatment was administered.

The amount of a protein can be measured using any suitable method. Some methods involve the use of antibodies, binding ligands, or mass spectrometry tagged peptides specific for a protein of interest. Antibodies suitable for use in assays of the invention are commercially available, or can be prepared routinely. Methods for preparing and using antibodies in assays for proteins of interest are conventional, and are described, e.g., in Green et al., *Production of Polyclonal Antisera*, in *Immunochemical Protocols* (Manson, ed.), (Humana Press 1992); Coligan et al., in *Current Protocols in Immunology*, Sec. 2.4.1 (1992); Kohler & Milstein (1975), *Nature* 256, 495; Coligan et al., sections 2.5.1-2.6.7; and Harlow et al., *Antibodies: A Laboratory Manual*, page 726 (Cold Spring Harbor Laboratory Pub. 1988).

Any of a variety of antibodies can be used in methods of the invention. Such antibodies include, e.g., polyclonal, monoclonal (mAbs), recombinant, humanized or partially humanized, single chain, Fab, and fragments thereof. The antibodies can be of any isotype, e.g., IgM, various IgG isotypes such as IgG₁, IgG_{2a}, etc., and they can be from any animal species that produces antibodies, including goat, rabbit, mouse, chicken or the like. The term, an antibody "specific for" a protein, means that the antibody recognizes a defined sequence of amino acids, or epitope in the protein. An antibody that is

"specific for" a polypeptide refers to an antibody that binds selectively to the polypeptide and not generally to other polypeptides unintended for binding to the antibody. The parameters required to achieve such specificity can be determined routinely, using conventional methods in the art. Conditions that are effective for binding a protein to an antibody which is specific for it are well-known and conventional.

In one embodiment of the invention, antibodies specific for a (one or more) protein of the invention are immobilized on a surface (e.g., are reactive elements on an array, such as a microarray, or are on another surface, such as used for surface plasmon resonance (SPR)-based technology, such as Biacore), and proteins in the sample are detected by virtue of their ability to bind specifically to the antibodies. Alternatively, proteins in the sample can be immobilized on a surface, and detected by virtue of their ability to bind specifically to the antibodies. Methods of preparing the surfaces and performing the analyses, including conditions effective for specific binding, are conventional and well-known in the art.

Among the many types of suitable immunoassays are immunohistochemical staining, ELISA, Western blot (immunoblot), immunoprecipitation, radioimmuno assay (RIA), fluorescence-activated cell sorting (FACS), etc. Assays used in a method of the invention can be based on colorimetric readouts, fluorescent readouts, mass spectrometry, visual inspection, etc. Assays can be carried out, e.g., with suspension beads, or with arrays, in which antibodies or cell or blood samples are attached to a surface such as a glass slide or a chip.

In one embodiment, a tissue sample (e.g. a cardiac tissue sample) is stained with a suitable antibody in a conventional immunohistochemical assay for those proteins which are present in the myocardium. Note that it can be difficult to obtain human tissue unless an individual is undergoing surgery or a routine biopsy (e.g. following heart transplantation), and such subjects are likely to be ischemic to some degree.

Mass spectrometry (MS) can also be used to determine the amount of a protein, using conventional methods. Some typical such methods are described in the Examples herein. Relative ratio between multiple samples can be determined using label free methods (as done in the present Examples), based on spectral count (and the number of unique peptides and the number of observation of each peptide). In the Examples herein, we used a LTQ-Orbitrap LC/MS/MS instrument to obtain the data. Alternatively, quantitative data can be obtained using multiple reaction monitoring (MRM), most often carried out using a triple quadrupole mass spectrometer. In this case, peptides that are unique to a given protein are selected in the MS instrument and quantified. Absolute quantification can be obtained if a known labeled synthetic peptide is used. For detailed methods see, e.g., Qin Fu and J E Van Eyk, in *Clinical Proteomics: from diagnostics to therapy* (Van Eyk J E and Dunn M, eds), Wiley and Son Press; *Current Protocols in Molecular Biology, Preparation of Proteins and Peptides for Mass Spectrometry Analysis in a Bottom-Up Proteomics Workflow*, Gundry et al., chapter 10, 2009, in press).

In general, molecular biology methods referred to herein are well-known in the art and are described, e.g., in Sambrook et al., *Molecular Cloning: A Laboratory Manual*, current edition, Cold Spring Harbor Laboratory, Cold Spring Harbor, N.Y., and Ausubel et al., *Current Protocols in Molecular Biology*, John Wiley & sons, New York, N.Y.

A detection (diagnostic) method of the invention can be adapted for many uses. For example, it can be used to follow the progression of cardiac ischemia. In one embodiment of the invention, the detection is carried out both before (or at

approximately the same time as), and after, the administration of a treatment, and the method is used to monitor the effectiveness of the treatment. A subject can be monitored in this way to determine the effectiveness for that subject of a particular drug regimen, or a drug or other treatment modality can be evaluated in a pre-clinical or clinical trial. If a treatment method is successful, the levels of the protein markers of the invention are expected to decrease.

A method of the invention can be used to suggest a suitable method of treatment for a subject. For example, if a subject is determined by a method of the invention to be likely to have myocardial ischemia, a decision can be made to treat the subject with an aggressive form of treatment; and, in one embodiment, the treatment is then administered. Suitable aggressive treatment modalities include, for example, angioplasty (mechanical widening to open blood vessels); treating with an anti-thrombolysis agent or, if possible, with percutaneous coronary intervention (PCI, or TPA); or undergoing coronary bypass surgery to replace the injured/blocked coronary artery. Methods for carrying out such treatments are conventional and well-known. By contrast, if a subject is determined not to be likely to have myocardial ischemia, a decision can be made to adopt a less aggressive treatment regimen; and, in one embodiment, the subject is then treated with this less aggressive forms of treatment. Suitable less aggressive forms of treatment include, for example, treatment with aspirin and/or agents that bring about thrombolysis (e.g., TPA); periodic monitoring to ensure no future MI events; or recommending changes in life style. A subject that does not have myocardial ischemia is thus spared the unpleasant side-effects associated with the unnecessary, more aggressive forms of treatment. By "treated" is meant that an effective amount of a drug or other anti-heart disease procedure is administered to the subject. An "effective" amount of an agent refers to an amount that elicits a detectable response (e.g. of a therapeutic response) in the subject.

One aspect of the invention is a kit for detecting whether a subject is likely to have myocardial ischemia, comprising one or more agents for detecting the amount of a protein of the invention. As used herein, the singular forms "a," "an" and "the" include plural referents unless the context clearly dictates otherwise. For example, "a" protein of the invention, as used above, includes 2, 3, 4, 5 or more of the proteins. In addition, other markers for ischemia (e.g., as discussed elsewhere herein) can also be present in a kit. If mass spectrometry is to be used to measure protein levels, the following reagents can be included in the kit: known amounts of a labeled (e.g. stable isotope) peptide (synthetic or recombinant) standard for each peptide to be assessed, separately or combined into a single mixture containing all peptides; optionally, a different peptide standard for assessing reproducibility of the assay; and/or, optionally, diluent and trypsin for preparation of the sample. If an antibody-based method is to be used to measure protein levels, the agents in the kit can encompass antibodies specific for the proteins. The kit may also include additional agents suitable for detecting, measuring and/or quantitating the amount of protein, including conventional analytes for creation of standard curves. Among other uses, kits of the invention can be used in experimental applications. A skilled worker will recognize components of kits suitable for carrying out a method of the invention.

Optionally, a kit of the invention may comprise instructions for performing the method. Optional elements of a kit of the invention include suitable buffers, containers, or packaging materials. The reagents of the kit may be in containers in which the reagents are stable, e.g., in lyophilized form or stabilized liquids. The reagents may also be in single use

form, e.g., for the performance of an assay for a single subject. In one embodiment of the invention, the kit is a "home chest pain test kit," that can be used to test blood, urine, or other body fluids for the presence (and/or level) of protein markers of the invention. Thus, a patient who has been released from an Emergency Department (ED) or a cardiac ward, but who is at risk over the next about 48 hours, can take the test over time at home and, if the test produces positive results, return to the ED.

In the foregoing and in the following examples, all temperatures are set forth in uncorrected degrees Celsius; and, unless otherwise indicated, all parts and percentages are by weight.

EXAMPLES

Example I

Identification of Novel Cardiac Biomarkers that are Rapidly Released into the Coronary Sinus in Response to Cardiac Ischemia, Even in the Absence of Detectable Myocyte Necrosis

A. Overview of the Studies

Rapid atrial pacing has been reported to produce reversible and controlled myocardial ischemia, as measured by a coronary sinus lactate concentration that rises above arterial lactate concentration, in approximately 2/3 of patients with fixed epicardial coronary artery disease (>70% diameter stenosis in at least one coronary artery). (Dehmer et al. (1983) *Am Heart J* 106, 114-24; Markham et al. (1983) *Am J Cardiol* 51, 1589-94). Therefore, in the experiments shown in this Example, atrial pacing was used as the human demand ischemia model.

In the studies shown in this Example, three types of protein analysis were conducted to identify protein markers of the invention. There is normally less than 40% overlap (e.g., 3-5) in the proteins observed between the different types of analysis platforms. This is because every protein is intrinsically different with respect to its pI, hydrophobicity and mass. Furthermore, post translational modifications (PTM) alter the intrinsic nature of the protein and thus may display quite different separation or enrichment characteristics. As such, the choice of technology or group of technologies should be dictated by the characteristics of the proteins targeted by the experimental question. In the case of biomarker discovery (and based on the lessons learnt from the biomarker, cTnI), multiple protein separation strategies should (and do) increase proteome coverage.

The present inventors and collaborators have found that the combination of intact protein separation technologies of 2DE (two-dimensional electrophoresis), 2DLC (two-dimensional liquid chromatography) and 1DLC (one-dimensional liquid chromatography) increases the proteome coverage while allowing enhanced detection of isoforms and PTM. 2DE of serum (and plasma) was optimized for separation by using pH 4-7 and 10% Bis-Tris gel (Graham et al. (2005) *Proteomics* 5 2309-14; Fu et al. (2005) *Proteomics* 5, 2656-64), as were the liquid chromatography methods. The combination of chemical depletion and optimized 2DE conditions can achieve good reproducibility (~20% CV) (Fu et al. (supra)). Liquid chromatography (LC) separates proteins based on one or more of their intrinsic properties: mass (size exclusion), isoelectric point (pI, chromatographic focusing or ion exchange), hydrophobicity (reversed phase) or affinity chromatography (bio-specificity). Our laboratory has optimized 2DLC combining chromatographic focusing and reversed

phase HPLC with the commercial Beckman Coulter instrument, the Two-Dimensional Protein Fractionation (PF2D) system (McDonald et al. (2006) *Mol Cell Proteomics* 5, 2392-411; Sheng et al. (2006) *Mol Cell Proteomics* 5, 26-34; Stasna et al. Protein separation: Liquid chromatography, In "Proteomic and Genomic Analysis of Cardiovascular Disease" (eds. Van Eyk J E and Dunn M) 2008 Wiley and Son Press, page 241). Briefly, samples are loaded onto the first dimension column (ion exchange column) at pH 8.5 in presence of urea and detergent and separated based on pI by decreasing the pH to 4.0 (Graham et al. (2006) (supra). Proteins that are bound tightly to the column or have a pI below 4.0 are eluted using 1M salt. We found that including 20% isopropanol in the buffers can eliminate "artificial" binding of a subset of proteins to the first dimension. Fractions are collected throughout the chromatographic separation and each fraction is subsequently separated by reversed phase chromatography using a linear gradient composed of aqueous trifluoroacetic acid (TFA), pH 2.3 and TFA/acetonitrile, pH 2.3. The second dimension elution profile is monitored at 214 nm (peptide bonds) and is semi-quantitative. On average, fractions contain 1-100 proteins in each peak (McDonald et al. (2006); Graham et al. (2006) (both supra)). These samples can be further analyzed by electrophoresis (ME or 2DE) or analyzed directly by mass spectrometry (MS). If so, due to the complexity of the reversed phase fractions they must undergo further online LC separation prior to MS. An overview outlining the process is summarized in Fu et al. (2008) (supra). B. Cohort Information for Atria Pacing Human Model—Cohort I

1. Research Design

Patients >20 years old with stable exertional angina referred for cardiac catheterization were recruited. Exclusion criteria were atrial fibrillation, valvular heart disease, prior coronary artery bypass surgery, depressed left ventricular systolic function, acute coronary syndrome, and/or left bundle branch block. As well, patients were excluded if they reported angina within 48 hours of the catheterization. 19 individuals were recruited. The study was approved by the Institutional Review Boards of UT Southwestern and Parkland Hospital. All patients have signed written informed consent.

A 7 or 8 Fr Gorlin catheter was advanced to the coronary sinus from the right brachial vein. Coronary sinus, peripheral arterial, and peripheral venous serum samples were obtained prior to start of the atrial pacing. The left atrium was paced at 20 beats/minute above the resting heart rate and this was increased every 3 minutes by 20 beats/minute until one of the following occurs: chest pain, AV block, or a heart rate of 160 beats/minutes is achieved. The patient was maximally paced at this rate for 3 minutes. At the end of the three-minute period, repeat blood samples were collected from the coronary sinus and peripheral artery. Repeat sampling from the coronary sinus was performed at 30 and 60 minutes after pacing termination.

TABLE 1

Timing line for serum sample collection				
Location	Baseline	Immediate post-pacing	30 minutes post-pacing	60 minutes post-pacing
Coronary Sinus	X	X	X	X

Blood was immediately placed on ice and was transported to the processing center within 30 minutes of collection. Samples were centrifuged, serum (and plasma) separated, and specimens aliquoted into 100 μ L tubes using an automated micropipette system. No samples were at room temperature for longer than 10 minutes. The longest duration between sample collection and freezing was less than one hour. Lactate and cardiac troponin T (TnT) was measured in heparinized plasma a (see table 2)

2. Cohort and Experimental Group Designation

The cohort was designated based on the following criteria:

- 1) Cases (n=19) Significant coronary artery disease (at least one vessel with a diameter stenosis $\geq 70\%$) and coronary sinus lactate > arterial lactate after pacing (data not shown).
- 2) Controls are individuals with no or little change in lactate pre vs. post.
- 3) Moderate or severe ischemia: individuals with increase in lactate and are cTnT negative.
- 4) Necrosis designation was for individuals with increase in lactate and are cTnT positive.
- 5)

TABLE 2

coronary sinus values								
PA-TIENT	age	csLpre	csLpost	TnT-cs0	TnT-cs1	TnT-cs2	TnT-cs3	Definition
1	50	0.4	0.7	<0.01	<0.01	<0.01	<0.01	ml
2	40	0.8	0.6	<0.01	<0.01	<0.01	<0.01	C
3	60	0.7	0.7	<0.01	<0.01	<0.01	<0.01	C
4	56	0.8	1	<0.01	<0.01	<0.01	<0.01	ml
5	63	0.8	0.9	<0.01	<0.01	<0.01	<0.01	C
6	51	0.7	0.7	<0.01	<0.01	0.016	0.029	N
7	51	0.4	1.2	<0.01	<0.01	<0.01	<0.01	sl
8	52	0.3	0.4	<0.01	<0.01	<0.01	<0.01	C
9	45	0.6	0.6	<0.01	<0.01	NA	NA	C
10	56	0.7	1.3	<0.01	<0.01	<0.01	<0.01	sl
11	50	0.5	0.9	<0.01	<0.01	<0.01	<0.01	sl
12	47	0.3	0.5	<0.01	<0.01	<0.01	<0.01	ml
13	57	1.1	0.9	<0.01	<0.01	NA	NA	excluded
14	62	0.9	1	<0.01	<0.01	<0.01	<0.01	excluded
15	43	0.3	0.8	<0.01	<0.01	0.026	0.109	N
16	52	1.22	1.48	<0.01	<0.01	<0.01	0.041	N
17	47	COAG	0.28	<0.01	<0.01	<0.01	<0.01	excluded
18	47	0.23	0.46	<0.01	<0.01	<0.01	<0.01	ml
19	53	0.17	0.16					C

Pre and post define samples taken at baseline and after maximum pacing

Definition defines, control (c) as no change in lactate and TnT negative, ischemia (I) as increase in lactate and TnT negative and differentiated in to moderate (mI) or severe (sI); necrosis (n) TnT positive and excluded for LC analysis (but included for 2DE).

C. 2-dimensional Gel Electrophoresis Analysis

1. 2DE Cohort

All patients and all time points were analyzed.

2. 2DE Methods

Serum was depleted of IgG using protein G affinity chromatography and depleted of albumin using our in-house affinity/chemical depletion method (Fu et al. (2005) (supra). Protein concentration was determined using BCA assay (Pierce) for each depleted sample. 50 μ g of each time point (baseline time point 1, 2 and 3) per individual was labeled with one of the three Cy dyes (Applied Biosystems Inc.). As well, a pool sample was created from equal amounts of each

time point of a single patient sample. For each individual, equal amount of two labeled sample (two time points) were mixed with the pool sample and then separated simultaneously using optimized pH 4-7 gel, followed by 10% Bis-Tris SDS PAGE. The gels were then imaged on a fluorescent gel imager at the Cy3, Cy5 and Cy2 wavelengths. Subsequently, the gels were stained with silver to allow visualization for spot picking. Gel images were analyzed by Ludesi Inc (<http://www.ludesi.com/>). Gels were aligned, spots matched and quantified. For example, gel images were prepared for an individual that became ischemic or underwent necrosis with pacing. Comparisons were made between baseline and the other subsequent time points for each individual. To avoid a nondetected (zero) value 0.1 was added to all values.

3. Selection Criteria.

Selection criteria for 2DE was based on analysis of all individual in each group (induced ischemia and induced necrosis) and are as follows:

- i) Equal or greater than 1.5 fold increase compared to time point 0 (baseline).
- ii) The spot volume was above (100 units) to allow protein identification by mass spectrometry.
- iii) The spot was resolved.
- iv) The change in the profile remains above baseline once elevated.
- v) A changed in 3 out of the 3 or 2 out of the 3 individuals in a designated group (induced ischemia or induced necrosis) at any time point.

4. Results for 2DE

Approximately 1200 protein spots were resolved on each 2DE gel. Due to stringent criteria for cut offs, most protein spots were deemed not to change or biological variability was too great to be significant (FIG. 1, see breakdown). Caspase 14 and complement factor B (isoform 1) increased specifically in patients with necrosis while fibrinogen beta chain and desmoglein-1 increased in patients with severe ischemia and necrosis (table 3).

TABLE 3

summary of changes detected by 2DE					
Protein name	observed at baseline	control	large ischemia	moderate ischemia	necrosis
Caspase-14	yes	1 out of 5	1 out of 3	0 out of 4	2 out of 3
Isoform 1 of Complement factor B	yes	1 out of 5	1 out of 3	0 out of 4	2 out of 3
Fibrinogen beta chain	yes	2 out of 5	1 out of 3	2 out of 4	2 out of 3
Desmoglein-1	yes	2 out of 5	1 out of 3	2 out of 4	2 out of 3

The majority of proteins observed by 2DE, high abundant soluble proteins, do not change with induced ischemia or necrosis. Without wishing to be bound by any particular mechanism, Caspase 14 (IPI00013885) is proposed to be involved in the death receptor and granzyme B apoptotic pathways. It may act as a downstream signal transducer of cell death. Desmoglein-1 (IPI00025753) is a component of the cell desmosome junctions which are distinct plasma membrane domains. It has a single transmembrane domain. Desmosomes are the most common type of intercellular junction in vertebrate epithelial cells but found in other cell types. This protein is part of a complex comprising plakophilin 1, plakophilin 2, desmoplakin, desmoglein 1, desmoglein 4, plakophilin

globin and corneodesmosin. Other proteins of the desmosome complex as well as caspase 14 are found by 1DLC and 2DLC in a few individuals.

Information sheets summarizing some of the properties of these and other proteins discussed herein are provided as Example II.

D. 1DLC Work Flow

1. 1DLC Cohort

Each individual time sample outlined below (table 4) was analyzed using reversed phase HPLC. The control group samples were selected based on having similar prelatecate concentrations compared to the two disease groups.

TABLE 4

1DLC		
Group designation	Patient numbers	Time points
control	3, 5	0 and 1
ischemia	7, 10, 11	0, 1, 2, 3
necrosis	6, 15, 16	0, 1, 3

2. 1DLC Method

Serum was depleted using an affinity chromatography comprised of IgY antibodies specific for all forms of immunoglobins (IgG, IgA and IgM) and then depleted of albumin using our in-house affinity/chemical depletion method. This was done in order to reduce background of the chromatogram. Protein concentration was determined using BCA assay (Pierce) for each depleted sample. Samples were analyzed on the same 1DLC columns. 50 ug of each sample was run (in duplicate) using our optimized gradient. One set was used for mass spectrometric analysis; the other set was stored at -80°C . Fractions were collected into 96-well plates, stored at -80°C . until analyzed. Protein standard was run every morning to ensure good, consistent and reproducible performance of HPLC system. Extensive washing was carried out between runs to eliminate possible cross-over contamination. Chromatographic images were compared and regions/domains with acceptable intensities from each experimental sample were selected or combined (FIG. 5). Total 650 fractions (26 fractions per sample) were dried down, neutralized, and digested with trypsin. 50% of the digested sample was applied to the LC LTQ-Orbitrap MS.

For LC-MS/MS experiments on the LTQ-Orbitrap (ThermoFinnigan, San Jose, Calif.), peptides were dissolved in 6 μl resuspension buffer (4% acetonitrile in water with 0.1% formic acid). Samples (3 μl) were loaded onto a 75 $\mu\text{m} \times 10\text{ cm}$ BioBasic C18 column (New Objective, Woburn, Mass.). Peptides were eluted into an LTQ-Orbitrap (ThermoFinnigan, San Jose, Calif.) using an Agilent 1200 nano-LC system (Agilent, Santa Clara, Calif.). The HPLC gradient was 5% to 60% B (90% acetonitrile/water in 0.1% Formic acid) over 30 or 60 min depended on sample complexity. The mass spectrometer was operated in data-dependent mode in which every FT-MS scan (survey 350-2000 Da) was followed by MS/MS scans of the 5 most abundant ions.

All mass spectrometry data was analyzed according to a pipeline established and already used in our laboratory, designed to meet stringent criteria from the proteomics community. Data from the LTQ-Orbitrap was searched against the IPI databases where possible, using Sorcerer Sequest (Sagen, San Jose, Calif.). Search results were validated and analyzed using Scaffold (Proteome Systems, Portland, Oreg.). Protein identifications based upon a single peptide observation were handled carefully through manual inspection of the tandem MS (MS/MS) spectra, BLAST searching of the sequence to

ensure it matches only the reported protein, requiring a minimum of 8 amino acids and a peptide probability score of >0.9.

Data analysis was based on the following: peptide redundancy removed, protein name redundancy removed, the number of unique peptides and number of observation for each peptide regardless of charge state (2+, 3+ or 4+) were determined for each protein. The protein was proposed to have a potential PTM if it was identified in multiple non-sequential domain/fractions. This was noted and all data regardless of the fraction was included for quantitation of the protein.

Data reanalysis was carried out using a version of the published algorithm for spectral counting (Old et al. (2005) *Molecular and Cellular Proteomics* 4.10, 1487-502) that added a 1.25 correction factor value to all numbers, in order to eliminate any zero values (non detectable values). The algorithm $R_p = \text{Log}_{10} (P_x + 1.25) / (P_0 + 1.25) + \text{Log}_{10} (TP_0 - P_0 + 1.25) / (TP_x - P_x + 1.25)$ and $R_{sc} = \text{Log}_{10} (SC_x + 1.25) / (SC_0 + SC_x + 1.25) + \text{Log}_{10} (TSC_0 - SC_0 + 1.25) / (TSC_x - SC_x + 1.25)$, where R_p is the Log_{10} ratio of number of unique peptides between time points 0 and x, R_{sc} is the Log_{10} ratio of spectral counts between time points 0 and x, P_0 or P_x is the number of unique peptides at baseline (0) or another time point (x) for the specific protein of interest. TP_0 or TP_x is the number of all

unique peptides for the complete data set for that individual at that specific time point (0 or x). SC_0 and SC_x are the spectral counts at time points 0 and x for the protein. TSC_0 and TSC_x are the total number of spectral counts in the experiment at time points 0 and x. There is a linear correlation between number of peptides observed and the spectra count (under 70 peptides/protein). However, for very abundant protein with 100's of peptides and observations the relationship is more non-linear. A cut off of 0.3 (2 fold) was used to indicate a change.

3. Duplicate MS Analysis

Two independent MS analyses were done on each LC fraction. In both cases, LC fractions were stored (-80°C .) following an independent LC separation of the intact proteins. Image analysis was carried out between the various LC runs to match the fractions as closely as possible. However, the fractions analyzed were not completely identical due to variation in the LC run and exact timing of the fraction collection. The stored fractions were dried down, neutralized and digested with trypsin. The digested sample was applied to the LC LTQ-Orbitrap MS and number of peptides and spectra count were determined (table 5). The total number of peptide and counts for each time points is shown in table 6. This is taken into account when calculating change.

TABLE 5

MS replicate on frozen intact protein sample cohort I, two protein LC runs, separated digestion and MS run						
sample: AMI-15-003 (F = fraction number)						
# peptides	# peptides	# peptides	# peptides	# peptides	# peptides	# peptides
Protein name						
F1 + 2 + 3 + 4-duplicate	F1 + 2 + 3 + 4-original	F15 + 16-duplicate	F15 + 16-original	F25-original	F25-duplicate	
alpha-1 antiproteinase	1	2	20	25	16	16
alpha1-antichymotrypsin	0	0	1	8	7	6
alpha-1-microglobulin/bikunin	0	0	2	0	0	0
Alpha-2-macroglobulin	0	0	7	2	32	31
alpha-2-plasmin inhibitor	0	0	0	0	0	2
Angiotensinogen	0	0	0	0	2	13
Apolipoprotein A-I	2	0	9	7	13	15
apolipoprotein A-IV	0	0	5	4	2	10
Apolipoprotein C-I	0	0	2	3	0	0
apolipoprotein E	0	0	0	0	2	8
Beta2- Glycoprotein	0	2	0	0	0	0
B-factor, properdin	0	0	15	19	2	8
C9 complement protein	0	0	8	2	0	1
carboxypeptidase N	0	0	6	0	0	0
caspase 14	2	0	0	0	0	0
cathelicidin antimicrobial peptide	0	0	2	0	0	0
coagulation factor II (thrombin)	0	0	4	3	0	0
coagulation factor XIII B subunit	2	3	0	0	0	0
complement component 1, s	0	0	0	2	0	0
complement component 2	0	0	0	0	3	2
complement component 3	2	2	33	14	71	81
complement component 4 binding protein, alpha chain	0	0	3	0	0	0
complement component 5	0	0	0	0	0	5
complement component 7	0	0	3	5	0	0
complement component 8, alpha	0	0	3	3	0	0
complement component 8, gamma	0	0	3	6	0	0
complement component C4A	0	0	32	19	16	29
complement component C6	0	0	3	2	0	0
complement component C8 beta chain	0	0	1	9	0	0
complement factor H	17	20	9	7	1	3
complement factor I	0	0	4	0	0	0
dermcidin	2	2	0	0	0	0
filaggrin 2	1	0	0	0	0	0
gelsolin	0	0	13	3	0	5
hemopexin	0	0	5	2	0	0
histidine-rich glycoprotein	0	0	3	0	0	0
hornerin	2	0	0	0	0	0

TABLE 5-continued

MS replicate on frozen intact protein sample cohort I, two protein LC runs, separated digestion and MS run						
sample: AMI-15-003 (F = fraction number)						
	# peptides	# peptides	# peptides	# peptides	# peptides	# peptides
Protein name						
	F1 + 2 + 3 + 4-duplicate	F1 + 2 + 3 + 4-original	F15 + 16-duplicate	F15 + 16-original	F25-original	F25-duplicate
hyaluronan binding protein 2	0	0	0	3	0	0
Insulin-like growth factor-binding protein 3	4	4	0	0	0	0
Inter-alpha-trypsin inhibitor heavy chain H1	0	0	9	6	6	9
Inter-alpha-trypsin inhibitor heavy chain H2	0	0	8	3	6	15
Inter-alpha-trypsin inhibitor heavy chain H3	0	0	6	0	0	0
Inter-alpha-trypsin inhibitor heavy chain H4	0	0	10	2	0	4
kallikrein B, plasma (Fletcher factor) 1	0	0	0	4	0	0
kininogen-1	0	0	1	2	0	0
leucine-rich alpha-2-glycoprotein 1	0	0	5	0	0	0
lumican	0	0	4	5	0	0
pigment epithelium-derived factor precursor (PEDF)	0	0	0	0	10	0
plasma protease (C1) inhibitor	0	0	0	0	0	3
amyloid P	0	0	6	2	0	0
profilaggrin	0	1	0	0	0	0
S100 calcium-binding protein A7	3	4	0	0	0	0
S100 calcium-binding protein A8	1	2	0	0	0	1
S100 calcium-binding protein A9	1	2	0	0	0	1
transferrin	0	0	13	18	7	10
transthyretin	0	0	6	6	0	0
vitronectin	0	0	2	2	0	0

TABLE 6

total number of peptide and spectra count in MS run 1 and 2									
	run 1	run 1	run 1	run 1	run 1	run 1	run 2	run 2	run 2
sample	peptides	counts	peptides	counts	peptides	counts	peptides	counts	peptides
A-15	976	10694	820	10527	767	9761	530	3005	770
A-16	715	9250	737	8615	682	7908	728	4724	709
	run 1	run 1	run 1	run 1	run 1	run 1	run 1	run 1	run 2
time point 0	TP 0	TP 1	TP 1	TP 2	TP 2	TP 3	TP 3	TP 0	
1-7	794	10673	788	10661	806	10806	828	10529	652
1-10	763	12629	810	11952	873	12868	894	12353	693
1-11	997	10783	830	11027	645	15836	830	10666	661
	run 2	run 2	run 2						
sample	counts	peptides	counts						
A-15	TP 1	TP 2	TP 2						
A-16	4702	802	4621						
	4962	695	4683						
	run 2	run 2	run 2	run 2	run 2	run 2	run 2	run 2	run 2
	TP 0	TP 1	TP 1	TP 2	TP 2	TP 3	TP 3		
1-7	3880	654	3338	621	4338	715	3370		
1-10	3398	589	3486	489	2904	746	3493		
1-11	4501	604	4012	603	3865	595	3791		

4. Criteria Selection for 1DLC

Selection criteria for 1DLC was based on analysis of all individuals in each group (induced necrosis or induced ischemia) and are as follows:

i) Changes in the number of unique peptides or the number of time each peptide was observed regardless of charge state (2+, 3+ or 4+) were compared to the equivalent protein (if observed) at time point 0. Changes are based on R_p or R_{sc} values of 0.30 or greater. The fold changes associated with

these R values depend on the number of observations and range from 1:4 ratio ($R=0.36$ before total observation correction, 4 fold change) to a 300:600 ($R=0.3001$ before total observation correction, 2 fold change). The total observation correction will shift the R value depending on the different in size of the 2 sample groups and the proportion of observations for a the protein of interest relative to the entire sample. A 10% difference in sample size between the compared samples could increase or decrease the R value by 0.045ii)

ii) Changes in 2 out of the 3 or 3 out of the 3 individuals in a designated group (induced ischemia or induced necrosis) at any time point.

5. Results

Although the number of unique peptides observed between MS run 1 and 2 were similar, the number of peptide observations was reduced in the second run (Table 6). This did not overly affect the number of proteins observed except for the lower abundant proteins. There were 25 different serum samples analyzed, giving rise to 650 fractions being analyzed per MS analysis (1300 total MS runs). This resulted in, for both MS runs, over 41,000 unique peptides being identified, with these peptides observed over 410,600 times. Table 7 outlines the proteins that met the criteria above and whether they were observed to change by 2DLC.

An additional level of stringency was added in which the variation within an individual was taken into account. The first tier proteins are found consistently to remain elevated. These are highlighted in bold type. Those proteins with variation between patients or time points were ranked as second tier. Bradykinin peptide was also included (rather than kininogen, the parent protein which had a weaker correlation) based on reducing the fold change required to 1.5 fold. It was the only additional protein that met this weaker criterion. For details regarding the proteins see Example II.

TABLE 7

summary of protein changes observed by 1DLC				
protein name	accession	up in ischemia 2 or 3 of 3	up in necrosis 2 or 3 of 3	Protein change detected by 2DLC
Alpha-2-HS-glycoprotein precursor	IPI00022431	yes		
Angiogenin	IPI00008554	yes		
Carboxypeptidase N catalytic chain	IPI00010295	yes		
Extracellular matrix protein 1	IPI00645849	yes		
Galectin-7	IPI00219221	yes		
Homerin	IPI00398625	yes		
Isoform 1 of Long palate, lung and nasal epithelium carcinoma-associated protein 1	IPI00291410	yes		
Isoform 2 of Semenogelin-1	IPI00414684	yes		
Lumican	IPI00020986		yes	
Profilaggrin	IPI00654788	yes		
Thyroxine-binding globulin	IPI00292946	yes		yes
Vitamin D-binding protein	IPI00555812	yes		
Isoform LMW of Kininogen-1 (specifically bradykinin)	IPI00215894		yes	
C4b-binding protein alpha chain	IPI00021727	yes		yes
Proteoglycan-4 (isoforms A and D)	IPI00655676/	yes		

E. 2-dimensional Liquid Chromatography

1. 2DLC Cohort

Since 2DLC requires 2 mg of protein or greater for each analysis and the quantity of sample for the atria pacing cohort was limited so pooling was required for each group as outlined in table 8.

TABLE 8

2DLC pool		
Group designation	Patient numbers pooled	Time points analyzed
control	3, 19, 9	0 (2 mg protein)
	3, 19	3 (2 mg protein)
ischemia	7, 10, 11	0 (2 mg protein)
	7, 10, 11	1 (2 mg protein)
	7, 10, 11	2 and 3 (equal amounts) (2 mg protein)

TABLE 8-continued

2DLC pool		
Group designation	Patient numbers pooled	Time points analyzed
necrosis	15, 16	0 and 1 (equal amounts) (1.9 mg protein)
	15, 16	2 and 3 (equal amounts) (1.9 mg protein)

2. 2DLC Method

Serum was depleted using an affinity chromatography comprised of IgY antibodies specific for 3 major forms of immunoglobins (IgG, IgA and IgM) and then depleted of albumin using our in-house affinity/chemical depletion method. This was done in order to reduce background of the chromatogram. Protein concentration was determined using BCA assay (Pierce). Samples were analyzed on the same set of first and second dimension columns. 2 mg of sample from each time point were sequentially injected on the HPCF first dimension column, followed by HPRF second dimension separation. Fractions were collected into 96-well plates and stored at -80 C until analyzed. Extensive washing was carried out between runs to eliminate possible cross-over contamination.

Chromatographic images were compared and the same regions/domains from multiple-pH fractions were combined based on profile and previous identification. Fractions from high salt wash were analyzed individually without pooling. Total 315 fractions from 7 time points were dried down, neutralized, and digested with trypsin. 50% of the digested sample was applied to the LC LTQ-Orbitrap MS.

For LC-MS/MS experiments on the LTQ-Orbitrap (ThermoFinnigan, San Jose, Calif.), peptides from the digestion of LC fraction were resuspended in 6 μ A resuspension buffer (4% acetonitrile in water with 0.1% formic acid). Samples (3 μ l) were loaded onto a 75 μ m $\times$ 10 cm BioBasic C18 column (New Objective, Woburn, Mass.). Peptides were eluted into an LTQ-Orbitrap (ThermoFinnigan, San Jose, Calif.) using an Agilent 1200 nano-LC system (Agilent, Santa Clara, Calif.). The HPLC gradient was 5% to 60% B (90% acetonitrile/water in 0.1% Formic acid) over 30 or 60 min dependent on sample complexity. The mass spectrometer was operated

in data-dependent mode in which every FT-MS scan (survey 350-2000 Da) was followed by MS/MS scans of the 5 most abundant ions.

All mass spectrometry data was analyzed according to the pipeline established and already used in the Van Eyk laboratory, designed to meet stringent criteria from the proteomics community. Data from the LTQ-Orbitrap was searched against the IPI databases where possible, using Sorcerer Sequest (Sagen, San Jose, Calif.). Search results were validated and analyzed using Scaffold (Proteome Systems, Portland, Oreg.). Protein identifications based upon a single peptide observation were handled carefully through manual inspection of the tandem MS (MS/MS) spectra, BLAST searching of the sequence to ensure it matches only the reported protein, requiring a minimum of 8 amino acids and a peptide probability score of >0.9.

Data analysis flow was based on the following: peptide redundancy removed, protein name redundancy removed, the number of unique peptides and number of observation for each peptide regardless of charge state were determined for each protein and, in the cases where the protein was observed in multiple domains as an indicator of potential PTM this was noted and all data for the protein was included for quantitation.

factor of 1.25 was used in all R value calculations with a R>0.3 as indicative of change. See 1DLC for more detail.

3. Criteria Selection for 2DLC

A) Individual in Each Group (Induced Necrosis or Induced Ischemia)

- i) Changes in the number of unique peptides or the number of times each peptide was observed regardless of charge state (+2, +3 or +4) were compared to the equivalent protein (if observed) at time point 0. All proteins only seen in time points after baseline were included.
- ii) Changes in 3 out of the 3 or 2 out of the 3 individuals in a designated group (induced ischemia or induced necrosis) at any time point.

B) Group

- i) proteins that met the above criteria for either induced ischemia or induced necrosis that did not change in all of the control (non ischemic) samples at any time point.

4. 2DLC Results

Over 7500 spectra were analyzed per pooled sample and thus, over 52,5000 spectra in total. Spectra were removed based on poor quality and each mass was assigned to a single peptide sequence resulting in ~5500 spectra remaining. The number of the proteins that met the criteria are listed below in table 9. See Example II for detailed protein information.

TABLE 9

protein observed changed by 2DLC											
Protein name	IPI accession number	increased in Ischemia	increased in necrosis	potential PTM in any sample	present at baseline	Ische- mia T1/T0	Ische- mia T2/T0	present at baseline	necrosis T1/T0	Control present at baseline	Control_ T1/T0
Protease, serine, 3	IPI00748381	yes	yes	no	0	0	>	0	>	0	0
C4b-binding protein alpha chain	IPI00021727	yes	yes	yes	yes	0	>	yes	>	yes	=
Alpha-2-glycoprotein 1, zinc (no)	IPI00166729	yes	yes	yes	0	>	>	0	>	0	0
Thyroxine-binding globulin precursor	IPI00292946	no	yes	no	yes	0	0	0	>	0	0

Criteria was that both number of peptide and number of count must increased

increased in ischemia = if protein is increases over baseline in the POOLED sample comprising severe ischemia patients. Ischemia was based on increase in lactate over time and no detectable cTnT

increased in necrosis = if protein is increases over baseline in the POOLED sample comprising necrosis patients analyzed. Necrosis was based on detectable cTnT (at time point 2 and or 3)

PTM = protein found in multiple fractions in any of the pooled sample.

Note,

if sequential maybe reflect not PTM but rather large quantity of protein eluting over multiple fractions

yes = present at baseline

0 not detected,

> greater than baseline

< less than baseline

= equal to baseline

yes - detected at baseline

control pool: all T0 = baseline from 13, 19, 9; T1 = time point 1 for 13, 19 and 9

ischemia pool: T0 = baseline from 7, 10, 11; T1 = time point 1 from 7, 10, 11; T2 = time point 2 and 3 from 7, 10, 11

necrosis pool: T0 = baseline and time point 1 for 16, 15; T2 = time points 2 and 3 of patient 16 and 15

The number of unique peptides and total number of counts (number of times each peptide is observed) were dependently used to semi-quantify each protein that was observed. To deal with proteins which peptides were only observed at some but not all time points (resulting in no information) a correction

Interestingly, two proteins, junction plakoglobin, desmoplakin, that are part of the desmosomal protein complex were detected in a few patients but not enough to make it meet the criteria. Desmoglein-1, the other protein of the same complex was found elevated in necrosis individual with 2DE.

name	IPI #	Increase in ischemia	Increase in necrosis	Potential PTM	Ischemia TP1	Ischemia TP2	Ischemia TP3
Junction plakoglobin (catenin gamma isoform 1)	IPI00554711	yes	no	no	0	>	0
DPII isoform (most likely also DPI) Desmoplakin	IPI00217182 (IPI0013933)	yes	no	no	0	>	0

F. Final Summary of all Protein Changes with Three Methods of Proteomic Analysis

Coronary sinus serum samples were analyzed from patients undergoing atrial pacing. Patients were designated into control, ischemia or necrosis groups based on the presence of cTnT at any time point (necrosis group) and an increase in lactate during the pacing protocol (ischemia and necrosis groups). Depleted samples were analyzed for all patients and all time points by 2DE. Depleted samples for 3 patients that were control, ischemia or necrosis were analyzed at multiple time points by 1DLC. Pooling of these individuals (2 or 3) from control, necrosis and ischemia were required for analyzed by 2DLC due to the amount of protein required for this technology. Proteins selection criteria for each method and MS-based quantitation for each method are described above.

The following proteins have been selected as primary or secondary targets based on the robustness of their changes with ischemia and or necrosis and known biological functions. The overlap is schematically shown in FIG. 5. Detailed information about each target is located in Example II.

Primary Targets

Lumican

Extracellular matrix protein 1

Angiogenin

Semenogelin (all isoforms 1 and 2)

Long palate, lung and nasal epithelium carcinoma-associated protein 1 (all isoforms, 1 and 2)

Secondary Targets

Alpha-2-HS-glycoprotein

Carboxypeptidase N (all subunits including catalytic chain)

Galectin-7

Hornerin

Proteoglycan-4 (Isoform A and D)

Profilaggrin (Filaggrin)

Vitamin D binding protein

C4b-binding protein alpha chain

Thyroxine binding globulin

Alpha-2-glycoprotein 1, zinc

protease, serine 3

Caspase 14

Desmogelin

Kininogen-1 (LMW and HMW and bradykinin)

Example II

Summary of Some of the Properties of Proteins Discussed with Regard to Cohort I

A. Vitamin D-Binding Protein

Name: Vitamin D-binding protein

IPI ID: IPI00555812

UniProtKB/Swiss-Prot entry ID: P02774, Q16309, Q16310

Length: 474 aa, molecular weight: 52964 Da (of precursor)

1. Basic Information from UniProtKB/Swiss-Prot Entry

FUNCTION: Multifunctional protein found in plasma, ascitic fluid, cerebrospinal fluid, and urine and on the surface of many cell types. In plasma, it carries the vitamin D sterols and prevents polymerization of actin by binding its monomers. DBP associates with membrane-bound immunoglobulin on the surface of B-lymphocytes and with IgG Fc receptor on the membranes of T-lymphocytes.

SUBCELLULAR LOCATION: Secreted.

POLYMORPHISM: Over 80 variants of human DBP have been identified. The three most common alleles are called GC*1F, GC*1S, and GC*2. The sequence shown is that of the GC*2 allele

2. Sequence

(SEQ ID NO: 1)

```

10 MKRVLVLLLAFAFGHALERGRDYEKNKVCKEFSLGKEDFTSLSLVLY
SRKFPSTGTFEQVSQLVKEVVSLTEACCAEGADPDYDTRTSALSAKSC
SNSPFPVHPGTAECCCKEGLERKLCMAALKHQPEFTTYVEPTNDEICE
15 AFRKDPKEYANQPMWEYSTNYGQAPLSLLVSYTKSYLSVMVSGCCTASAP
TVCFKLERLQLKHLSTLTLNVRVCSQYAAEGEKKSRSLNLIKLAQKVP
TADLEDVLPDAEDITNLSKCCESASEDCMAKELPEHTVKLCDNLSTKN
20 SKFEDCCQEKMTAMDVFCVTFMPAAQLPELPDVELPTNKDVCDPGNTKV
MDKYTFELSRRTHLPEVFLSKVLEPTLKSLEGCCDVEDSTTCFNAKGPL
25 LKKESSSFIDKGQELCADYSENTFTTEYKKKLAERLKAQLPDATPKELAK
LVNKRSDFASNCCSINSPLYCDSEIDAELEKNIL
30

```

1-16 Leader Sequence.

Peptides used in the MS analysis described in this application are indicated by highlighting (shading) in the protein sequences shown herein. A skilled worker can use peptides for some of the proteins which have been described previously by others who have performed MS on those proteins. The sequences of peptides is dependent on the particular type of MS used. For example, the peptides for MALDI can be different from those in ESI. The studies performed herein were ESI.

3. Alternative Names: DBP, Group-specific Component, Gc-globulin, VDB

4. Additional Information on Function

Serum vitamin D3-binding protein (Gc protein) is the precursor for the principal macrophage activating factor (MAF).

Gc protein was deglycosylated by serum alpha-N-acetyl-galactosaminidase (Nagalase)

The level of Gc globulin is reduced in patients with fulminant hepatic failure, septic shock and trauma. Furthermore, low levels of Gc globulin in patients with fulminant hepatic failure and multiple trauma have been found to correlate with the morbidity and mortality of patients. It has not been studied in heart disease.

5. Summary

Assays are available for total Vitamin D binding protein and for the amount of protein which is either free or bound to actin. This protein is known to be diagnostic for several diseases. It seems to be change with cellular injury and decrease with long term chronic disease. Clinical studies and animal models have shown that Gc-globulin has an important role in the clearance of procoagulant actin from the circulation after its release during cell necrosis and tissue injury but it is not known if it is in the heart.

B. Thyroxine-binding Globulin
Name: Thyroxine-binding globulin precursor
IPI ID: IPI00292946
UniProtKB/Swiss-Prot entry ID: P05543
Length: 415 aa, molecular weight: 46325 Da (precursor)
1. Basic Information from UniProtKB/Swiss-Prot Entry
FUNCTION: Major thyroid hormone transport protein in serum.
SUBCELLULAR LOCATION: Secreted.
TISSUE SPECIFICITY: Expressed by the liver and secreted in plasma.
DISEASE: Defects in SERPINA7 are a cause of TBG deficiency [MIM:314200]. Mutations in the SERPINA7 gene can result as a whole spectrum of deficiencies, characterized by either reduced or increased TBG levels in the serum. Patients show, respectively, reduced or elevated protein-bound iodine but are euthyroid.
2. Sequence

5

10

15

was no change compared to control. It has not been studied in myocardial ischemia or events leading up to MI.
C. Lumican
Name: Lumican
IPI ID: IPI00020986
UniProtKB/Swiss-Prot entry ID:
Length: 338 aa, molecular weight: 38429 Da, (of precursor)
1. Basic Information from UniProtKB/Swiss-Prot Entry
SUBUNIT Binds to laminin (By similarity).
SUBCELLULAR LOCATION Secreted, extracellular space, extracellular matrix (By similarity).

(SEQ ID NO: 2)

MSPFLYLVLVLGLHATIHCASPEGKVTACHSSQPNATLYKMSSINADFAFNLYRRFTVE

TPDKNIFFSPVSISAALVMSFGACCSTQTEIVETLGFNLTDTPMVEIQHGEFQHLICSLN

FPKKELELQIGNALFIGKHLKPLAKFLNDVKTLYETEVFSTGDFSNIAAKQEIINSHVEMQ

TKGKVVGLIQDLKPNTIMVLVNYIHFKAQWANPFDPSKTEDSSSFLIDKTTTVQVPMHQ

MEQYYHLVDMELNCTVLQMDYSKNALALFVLPKEGQMESVEAAMSSKTLKKWNRLQKGW

VDLFVPKFSISATYDLGATLLKMGIOHAYSENADFSGLTEDNGLKLSNAAHKAVLHIGEK

GTEAAAVPEVELSDQFENTFLHPITIQIDRSFMLLILERSTRSILFLGKVVNPTEA

2. Sequence

(SEQ ID NO: 3)

MSLSAFTFLALIGGTSQYYDYDFPLSIYGQSSPNCAPECPNCPESYPSAMYCDELKLS

VPMVPPGIKYLYLRNNQIDHIDEKAFENVTDLQWLIIDHNLLENSKIKGRVFSKLGKQKK

LHINHNLTESVGPLPKSLEDLQLTNNKIKLGSFEGLVNLTFIHLQHNRLKEDAVSAAF

KGLKSLEYLDLSFNQIARLPSGLPVSLTLTYLDNNKISNIPDEYFKRENALQYLRSHNE

LADSGIPGNSFNVSSLVELDLSYNKLKNIPTVNENLENYLEVNQLEKFDIKSFCKILGP

LSYSKIKHLRLDGNRISETSLPPDMYECLRVANEVTLN

55

1-20 Signal Sequence
3. Alternative Names: T4-binding Globulin, Serpin A7
4. Summary
Thyroxine-binding globulin binds with high-affinity to the thyroid hormone. It is proposed to be a biomarker for senescence and aging. Chronic treatment with perindopril, an angiotensin I-converting enzyme inhibitor used in cardiac and renal disease, enhanced thyroxine-binding capacity and possibility the protein level itself. In a study on ACS, thyroxine binding globulin was measured in those with acute myocardial infarction after 14 days and there

60

65

1-18 Signal Sequence
3. Alternative Names:
(Keratan Sulfate Proteoglycan Lumican) (KSPG Lumican).
4. Summary
Protein involved in injury response in a number of tissues and is a secreted protein. In a study on the lumican in fibrosis with chronic ischemic and reperfused rat heart (which is not the acute myocardial infarction model, but rather would induce heart failure), the level of lumican mRNA increased, peaking at the fourth week. The protein level was not investigated. This protein is also known to inhibits cell adhesion

and neurite outgrowth and be involved in wound healing of the cornea. It plays an important role in cell migration and proliferation during embryonic development, tissue repair, and tumor growth. It has not been studied in the context of myocardial ischemia or events leading up to MI.

D. Galectin-7

Name: Galectin-7

IPI ID: IPI00219221

UniProtKB/Swiss-Prot entry ID:

Length: 136 aa, molecular weight: 15075 Da

1. Basic Information from UniProtKB/Swiss-Prot Entry

FUNCTION Could be involved in cell-cell and/or cell-matrix interactions necessary for normal growth control. Pro-apoptotic protein that functions intracellularly upstream of JNK activation and cytochrome c release.

SUBCELLULAR LOCATION Cytoplasm. Nucleus. Secreted (Potential). Note=May be secreted by a non-classical secretory pathway.

TISSUE SPECIFICITY Mainly in stratified squamous epithelium.

2. Sequence

(SEQ ID NO: 4)

MSNVPHKSSLP EGI R PGT V L R I R G L V P P N A S R F H V N L L C G E E Q G S D A A L H F N P R L D T S E V

V F N S K E Q G S W G R E E R G P G V P F Q R G Q P F E V L I I A S D D G F K A V V G D A Q Y H H F R H R L P L A R V R

L V E V G G D V Q L D S V R I F

Initial Met is Removed

3. Alternative Names:

Galectin-7 (Gal-7) (HKL-14) (PI7) (p53-induced gene 1 protein).

Homologous 100% to Q6IB87_HUMAN LGALS7 protein (HCG1776519) (HCG42850) [LGALS7]

Note on Sequence:

Note only 36% homology with galectin 3 which is known to be involved in cancer.

4. Additional Information on Function

The literature suggests that galectin 7 is involved in apoptosis. It is most likely is secreted and forms dimers. Galectin

7 is an emerging marker involved in the epidermal development of pluristratified epithelia and in epidermal cell migration. It is elevated in wound healing. It has not been studied in the context of myocardial ischemia or events leading up to MI.

E. Extracellular Matrix Protein 1

Name: Extracellular matrix protein 1

IPI ID: IPI00645849

UniProtKB/Swiss-Prot entry ID: Q5T5G4

Length: 567 AA (includes signal sequence)

Molecular weight: 63563 Da (includes signal sequence)

1. Basic Information from UniProtKB/Swiss-Prot Entry

FUNCTION: Not known

SUBCELLULAR LOCATION: Secreted, extracellular space.

DISEASE: Defects in ECM1 are the cause of lipid proteinosis (LiP); also known as lipid proteinosis of

Urbach and Wiethe or hyalinosis cutis et mucosae. LiP is a rare autosomal recessive disorder characterized by generalized thickening of skin, mucosae and certain viscera. Classical features include beaded eyelid papules and laryngeal infiltration leading to hoarseness. Histologically, there is widespread deposition of hyaline material and disruption/reduplication of basement membrane.

2. Sequence Information from 1DLC

(SEQ ID NO: 5)

M G T T A R A A L V L T Y L A V A S A A S E G G F T A T G Q R Q L R P E H F Q E V G Y A A P S P P L S R S L P M D H P D

S S Q H G P P F E G Q S G K E G R G P R P H S Q P W L G E R V G C S H I P P S I V Q P P P S Q E A T P L Q Q E K L L P A Q

L P A E K E V G P P L P Q E A V P L Q K E L P S L Q H P N E Q K E G T P A P F G D Q S H P E P E S W N A A Q H C Q Q D R S

Q G G W G H R L D G F P P G R P S P D N L N Q I C L P N R Q H V V Y G P W N L P Q S S Y S H L T R Q E T L N F L E I G Y

S R C C H R S H T N R L E C A K L V W E E A M S R F C E A E F S V K T R P H W C C T R Q G E A R F S C F Q E E A F Q P H

Y Q L R A C P S H Q P D I S S G L E L P F P P G V P T L D N I K N I C H L R R F R S V P R N L P A T D P L Q R E L L A L I

Q L E R E F Q R C C R Q G N N H T C T W K A W E D T L D K Y C D R E Y A V K T H H H L C C R H P P S P T R D E C F A R R A

P Y P N Y D R D I L T I D I G R V T P N L M G H L C G N Q R V L T K H K H I P G L I H N M T A R C C D L P P E Q A C C A

E E E K L T F I N D L C G P R R N I W R D P A L C C Y L S P G D E Q V N C F N I N Y L R N V A L V S G D T E N A K G Q G E

Q G S T G G T N I S S T S E P K E E

3. Alternative Names: Secretory Component p85; Q5T5G5, Q8IZ60, Q5T5G6, Q16610

Note on Sequence:

Signal sequence 1-19 is removed in the mature protein.

4. Summary

Mutations of this protein result in lipoid proteinosis, a rare recessive disorder of the skin and mucosae. It binds perlecan, MMP9 and fibulin in the skin. It can inhibit MMP9. Auto antibodies to this protein occur with lichen sclerosus. Neither disease is common and so specificity to ischemia is likely. It has not been studied in the context of myocardial ischemia or events leading up to MI.

F. Semenogelin 1

Name: Semenogelin 1

IPI ID: IPI00414684 (Semenogelin-2 precursor IPI00025415)

UniProtKB/Swiss-Prot entry ID: P04279, Q6X4I9, Q6Y809, Q6Y822, Q6Y823, Q86U64, Q96QM3

Length: 402 aa, molecular weight: 45322 Da

1. Basic Information from UniProtKB/Swiss-Prot Entry

FUNCTION Predominant protein in semen. It participates in the formation of a gel matrix entrapping the accessory gland secretions and ejaculated spermatozoa. Fragments of semenogelin and/or fragments of the related proteins may contribute to the activation of progressive sperm movements as the gel-forming proteins are fragmented by KLK3/PSA.

FUNCTION Alpha-inhibin-92 and alpha-inhibin-31, derived from the proteolytic degradation of semenogelin, inhibit the secretion of pituitary follicle-stimulating hormone.

SUBUNIT Occurs in disulfide-linked complexes which may also contain two less abundant 71- and 76-kDa semenogelin-related polypeptides.

SUBCELLULAR LOCATION Secreted.

ALTERNATIVE PRODUCTS

Event=Alternative splicing; Named isoforms=2;

Name=1;

IsId=P04279-1; Sequence=Displayed;

Name=2;

IsId=P04279-2; Sequence=VSP_004385;

Note=No experimental confirmation available;

TISSUE SPECIFICITY Seminal vesicle. However references show it is also present in other tissues including skeletal muscle

2. Sequence

1-23 Signal Sequence

3. Alternative Names:

SEMG

4. Summary

SGI isoform is found in skeletal muscle as well as epithelial cells. Isoform expression is tissue specific and SGI isoform is found in skeletal muscle as well as epithelial cells. The peptides produced by cleavage of semenogelin I, the predominant human semen coagulum protein, had high levels of antibacterial activity. It has not been studied in the context of myocardial ischemia or events leading up to MI.

G. Isoform 1 of Long Palate, Lung and Nasal Epithelium Carcinoma-associated Protein 1

Name: Isoform 1 of Long palate, lung and nasal epithelium carcinoma-associated protein 1

IPI ID: IPI00291410,

UniProtKB/Swiss-Prot entry ID: Q8TDL5-1

Length: 484 aa, molecular weight: 52442 Da

1. Basic Information from UniProtKB/Swiss-Prot Entry

FUNCTION May play a role in innate immunity in mouth, nose and lungs.

SUBCELLULAR LOCATION Secreted (By similarity).

ALTERNATIVE PRODUCTS

Event=Alternative splicing; Named isoforms=2;

Name=1;

IsId=Q8TDL5-1; Sequence=Displayed;

Name=2;

IsId=Q8TDL5-2; Sequence=VSP_015285, VSP_015286,

VSP 015287,

VSP 015288;

Note=No experimental confirmation available;

TISSUE SPECIFICITY Detected in trachea, nasal septal epithelium and lung. 0 hits

(SEQ ID NO: 6)

MKPNII FVLSLL LILEKQA AVMGQK GSKGR LPS EFSQ FPHGQK GQHYS GQK GKQQTESK

GSFSIQYTYHVDANDHDQSRKSCQYDLNALHKTTSQRHLGSSQQLLHNKQEGRDHDKSK

GHFHRVVIIHKGKKAHRGTQNPSSQDQGNPSGKGISSQYSNTEERLWVHGLSKEQTSVSG

AQGRKQGGSSQSSVYLQTEELVANKQORETKNSHQNKGHYQNVVEVREEHSSKVTSLCP

AHQDKLQHGSKDI FSTGDELLVYNKNQHQTKNLNQDQOHGRKANKISYQSSSTEERLHY

GENGVQKDVSRISIYSQTEKLVAGKSQIQAPNPKQEPWHGENAKGESGQSTNREQDLLSH

EQKGRHQHGHGGGLDIVIIEQEDDSDRHLAQHLNDRNPLFT

2. Sequence

(SEQ ID NO: 7)

MAGPWTFTLLCGLLAATLIQATLSPTAVLILGPKVIKEKLTQELKDHNATSILQQPLLS

AMREKPAGGIPVLGSLVNTVLKHIIWLKVITANILQLQVKPSANDQELLVKIPLDMVAGF

NTPLVKTIVEFHMTTEAWATIRMDTSASGPTRLVLSDCATSHGSLRIQLLHKLSEFLVNAL

AKQVMNLLVPSLPNLVKNQLCPVIEASFNGMYADLLQLVKVPISLSIDRLEFDLLYPAIK

GDTIQLYLGAKLSDSQGVTKWFNNSAASLTMPDLDNIPFSLIVSQDVVKAAVAVALSPE

EFMVLLDSVLPESAHLKSSIGLINEKAADKLGSTQIVKILTQDTPEFFIDQGHAKVAQL

IVLEVFPSSSEALRPLFTLGLIEASSEAQFYTKGDQLILNLNLISSDRIQLMNSGIGWFPQD

VLKNIITETIHSILPNONGKLRSGVPVSLSVKALGFEEAESSLTkdALVLTpaswkpss

PVSQ

1-21 potential signal sequence. Isoform 2 is truncated at N-terminus. Also have insert (underlined) which has no peptides. Therefore, cannot distinguish between isoform one and two

SIMILARITY: Belongs to the pancreatic ribonuclease family.
It is uncertain whether Met-1 or Met-3 is the initiator.
2. Sequence Information from 1DLC

(SEQ ID NO: 8)

MVMGLGVLLL VFVLGLGLTP PTLAQDNSRY THFLTOHYDA KPOGRDDRYC ESIMRRRGLT

SPCKDINTEI HGNKRSIKAI CENKNGNPHR ENLRISKSSF QVTTCKLHGG SPWPPCQYRA

TAGFRNVVVA CENGLPVHLD QSIFRRP

3. Alternative Names: C20orf114

4. Summary

Little is known about this protein or its shorter isoform (2). It has not been studied in the context of myocardial ischemia or events leading up to MI.

H. Angiogenin

Name: Angiogenin, precursor

IPI ID: IPI00008554

UniProtKB/Swiss-Prot entry ID: P03950

Length: 147 AA [This is the length of the unprocessed precursor]

Molecular weight: 42051 Da [This is the MW of the unprocessed precursor]

1. Basic Information from UniProtKB/Swiss-Prot Entry

FUNCTION: May function as a tRNA-specific ribonuclease that binds to actin on the surface of endothelial cells; once bound, angiogenin is endocytosed and translocated to the nucleus, thereby promoting the endothelial invasiveness necessary for blood vessel formation. Angiogenin induces vascularization of normal and malignant tissues. Abolishes protein synthesis by specifically hydrolyzing cellular tRNAs.

INTERACTIONS: May bind alpha-actinin P35609

SUBCELLULAR LOCATION: Secreted

TISSUE SPECIFICITY: Expressed predominantly in the liver.

DEVELOPMENTAL STAGE: Low level expression in the developing fetus, increased in the neonate, and maximal in the adult

Multiple Peptides

3. Alternative Names: RNASE5, Ribonuclease A Family, 5, RNASE4 Protein, ANG Protein Q53x86, Q6P5T2

Note on Sequence:

Most likely have either intact molecule or the mature processed form.

Signal peptide residues 1-24

Additional information on function Angiogenin is a normal constituent of the circulation and contained in a vasculature that rarely undergoes proliferation, but in some physiological and pathological conditions its levels increase in blood, promoting neovascularization. This is a potentially important physiological protein involved in angiogenesis.

4. Summary

Interestingly, this protein may play a role in angiogenesis. Recently it has been potentially linked to poor outcome in ACS patients, which is a chronic condition that can result from many different etiologies. Plasma angiogenin levels was increased in ACS also with ischemic brain damage. However, it has not been studied in the context of myocardial ischemia or events leading up to MI.

I. C4b-binding Protein

Name: C4b-binding protein (alpha chain)r

IPI ID: IPI00021727

UniProtKB/Swiss-Prot entry ID: P04003

Length: 597 AA [This is the length of the unprocessed precursor]

Molecular weight: 67033 Da [This is the MW of the unprocessed precursor]

1. Basic Information from UniProtKB/Swiss-Prot Entry

FUNCTION: Controls the classical pathway of complement activation. It binds as a cofactor to C3b/C4b inactivator (C3bINA), which then hydrolyzes the complement fragment C4b. It also accelerates the degradation of the C4bC2a complex (C3 convertase) by dissociating the complement fragment C2a. Alpha chain binds C4b. It interacts also with anticoagulant protein S and with serum amyloid P component.

SUBUNIT: Disulfide-linked complex of alpha and beta chains of 3 possible sorts: a 570 kDa complex of 7 alpha chains and 1 beta chain, a 530 kDa homoheptamer of alpha chains or a 500 kDa complex of 6 alpha chains and 1 beta chain. The central body of the alpha chain homopolymer supports tentacles, each with the binding site for C4b at the end.

SUBCELLULAR LOCATION: Secreted

TISSUE SPECIFICITY: Chylomicrons in the plasma.

It is uncertain whether Met-1 or Met-17 is the initiator

Additional Information

CRP binds C4b binding proteins and regulations it inhibition of complement system (Regulation of Complement Activation by C-Reactive Protein: Targeting of the Inhibitory Activity of C4b-Binding Protein¹ AP Sjöberg et al., J. Immuno. 2006, 176: 7612-7620).

C4b-binding protein (C4BP), binds strongly to necrotic cells, irrespective of the cell type used or the method of induction. (C4b-binding protein binds to necrotic cells and DNA, limiting DNA release and inhibiting complement activation L. A. Trouw et al., JEM, 2005, 201, 1937-1948)

2. Sequence

3. Alternative Names: IC4b binding protein, C4b binding protein alpha chain, C4b receptor, C4bP, C4bPA, C4bPAL1, Complement component 4 binding protein, alpha like 1, PRP, Proline rich protein Complement component 4 binding protein, alpha. Q5VVQ8

Note on Sequence:

Most likely intact protein. Several patients had protein present in multiple fractions and although sequential appears to be due to PTM rather than bleed over between two fractions. E do not know what the PTM is at this time. This protein has not been studied in the context of myocardial ischemia or events leading up to MI.

J. Carboxypeptidase N Catalytic Chain

Name: Carboxypeptidase N catalytic chain precursor

IPI ID: IPI00021439

UniProtKB/Swiss-Prot entry ID: P15169

20 Length: 458 AA [This is the length of the unprocessed precursor]

Molecular weight: 52286 Da [This is the MW of the unprocessed precursor]

1. Basic Information from UniProtKB/Swiss-Prot Entry

FUNCTION: Protects the body from potent vasoactive and inflammatory peptides containing C-terminal Arg or Lys (such as kinins or anaphylatoxins) which are released into the circulation. Note cleaves bradykinin!

CATALYTIC ACTIVITY: Release of a C-terminal basic amino acid, preferentially lysine.

SUBUNIT: Tetramer of two catalytic chains and two glycosylated inactive chains.

SUBCELLULAR LOCATION: Secreted/extracellular space

SIMILARITY: Belongs to the peptidase M14 family

(SEQ ID NO: 9)

MHPPKTPSGA LHRKRKMAAW PFSRLWKVSD PILFQMTLIA ALLPAVLGNC GPPPTLSFAA

PMDITLTETR FKTGTTLYKT CLPGYVRSHS TQTLTNSDGEWVYNTFCIY KRCRHPGELR

NGQVEIKTDL SFGSQIEFSC SEGFFLIGST TSRCEVQDRG VGWSHPLPQC EIVKCKPPPD

IRNGRHSCEE NFYAYGFSVT YSCDPRFSLP PHASISCTVE NETIGVWRPS PPTCEKITCR

KPDVSHGEMV SGFGPIIYNYK DTIVFKCQKG FVLRGSSVIH CDADSKWNPS PPACEPNSCI

NLPDIPHASW ETYPRPTKED VYVYGTVLRY RCHPGYKPTT DEPTTVICQK NLRWTPYQGC

EALCCPEPKL NNGEITQHRK SRPANHCYVF YGDEISFSCH ETSRFSIAICQ GDGTWSPRTP

SCGDICNFPP KIAHGHYQS SSYSFFKEEI IYECDKGILL VGOAKLSCSY SHWSAPAPQC

KALCRKPELV NGRLSVDKDQ YVEPENVTIQ CDSGYGVVGP QSITCSGNRT WYPEVPKCEW

ETPEGCEQVL TGKRLMQCLP NPEDVKMALE VYKLSLEIEQ LELORDSARQ STLDKEL

Green both 1DLC and 2DLC

Glue only 2DLC

2. Sequence

(SEQ ID NO: 10)

MSDLLSVFLH LLLFLKLVAP VTFRRHRYDD LVRTLKYVQN ECPGITRVYS IGRSVEGRHL

YVLEFSDHPG IHEPPEPEVK YVGNMHGNEA LGRELMLQLS EFLCEEFRNR NQRIVQLIQD

TRIHLPSMN PDGYEVAAC GPNKPGYLVG RNNANGVDLN RNFPLNTYI YYNEKYGGPN

HHLPLPDNWK SQVEPETRAV IRWMHSFNFV LSAHLHGAV VANYPYDKSF EHRVRGVRT

ASTPTPDDKL FQKLAKVYSY AHGWMFQGWV CGDYFPDGIT NGASWYSLSK GMQDFNYLHY

NCFEITLELS CDKFPPEEEL QREWLGNREA LIQFLEQVHQ GIKGMVLNEN YNNLANAVIS

VSGINHDTVTS GDHGDYFRLL LPGIYTVSAT APGYDPETVT VTVGPAEPTL VNFHLKRSIP

QVSPVRRAPS RRHGVRAKVQ PQARKKEMEM RQLQRGPA

3. Alternative Names: CPN, Carboxypeptidase N polypeptide 1, Carboxypeptidase N small subunit; Lysine carboxypeptidase, Arginine carboxypeptidase, Kininase-1, Serum carboxypeptidase NSCPN, Anaphylatoxin inactivator, Plasma carboxypeptidase B Q5T287

Note on Sequence: Signal Sequence 1-20

4. Summary

Interesting protein, which may alter bradykinin levels and creatine kinase levels. Involved in early inflammatory response. Has been shown to be elevated after AMI based on activity assays. Although it has been shown that there is a high degree of variability in carboxypeptidase N in healthy subjects and does not change with acute myocardial infarction patients but may reach maximum at 48 h after onset of chest pain. It has not been studied in the context of myocardial ischemia or events leading up to MI.

K. Profilaggrin/Filaggrin

Name: Profilaggrin (Filaggrin)

IPI ID: IPI00746718

UniProtKB/Swiss-Prot entry ID: P20930 (note only 70% homology)

Length: 4061AA

Molecular weight: 435170 Da

1. Basic Information from UniProtKB/Swiss-Prot Entry
FUNCTION: Aggregates keratin intermediate filaments and promotes disulfide-bond formation among the intermediate filaments during terminal differentiation of mammalian epidermis

PTM: Filaggrin is initially synthesized as a large, insoluble, highly phosphorylated precursor containing many tandem copies of 324 AA, which are not separated by "large linker". The precursor is deposited as keratohyalin granules. During terminal differentiation it is dephosphorylated and proteolytically cleaved.

PTM: Undergoes deimination of some arginine residues (citrullination).

DISEASE: Defects in FLG are the cause of ichthyosis vulgaris [MIM:146700]; also known as ichthyosis simplex. The phenotypic characteristics of ichthyosis vulgaris include palmar hyperlinearity, keratosis pilaris and a fine scale that is most prominent over the lower abdomen, arms, and legs. Ichthyosis vulgaris is characterized histologically by absent or reduced keratohyalin granules in the epidermis and mild hyperkeratosis. The disease can be associated with frequent asthma, eczema or hay fever. Inheritance is autosomal dominant.

2. Sequence (IPI Sequence)

(SEQ ID NO: 11)

MSTLLENIPAIINLKFQYSSKDKNTDTLSKKELKELLEKEFRQILKNPDDPDMVDVPMDH

LDIDHNKKIDFTEFLLMVFKLAQAYYESTRKENLPISGHKRKHSHDKHEDNKQENKE

NRKRPSLERRNNRKNKGRSKSPRETGGKRHESSEKKEKKGYSPTTHREYVGNHNS

SKKEKNKTENTRLGDNKRKLSERLEEKEDNEEGVYDYENTGRMTQKWIQSGHIATYYTIQ

DEAYDTTDSLLEENKIYERSRSSDGKSSQVNRSRHENTSQVPLQESRTRKRRGRSVSQD

RDSEGHSEDSERHSGSASRNHHGSAWEQSRDGSRHPRSHDEDRASHGHSADSSRQSGTRH

AETSSRGQTASSHEQARSSPGERHSGHQQSADSSRHSATGRGQASSAVSDRGHRGSSGS

QASDSEGHSENSDTQSVSGHGKAGLRQQSHQESTRGRSGERSGRSGSFIYQVSTHEQSES

AHGRTRTSTGRRQSGGEGQARDSRHSASQEGQDTIRAHPGSRGRGRQSGSHQESVDRSG

HSGSHSHSTTSQGRSDVSRGQSGSRVSRQTRNEKQSGDGRHSGSRHHEASSRADSSRH

SQVGQGSQSGPRTSRNQSSVSQSDSQGHSEDSERRSGSASRNHHGSAQEQRDGRSRHP

RSHHEDRAHGHGSAESSRQSGTHHAENSSGGQAASSHEQARSAGERHGHSHHQQSADSSR

HSIGIGHGQASSAVRDSGHRGSSGSQASDSEGHSESDTQSVSAHGQAGPHQQSHQESTRG
RSAGRSGRSGSFLYQVSTHEQSESAHGRTRTSTGRRQGSHEQARDSSRHSASQEGQDTI
RGHPGSSRRGRQGSHYEQSVDRSGHSGSGSGTTSQGTSDASRGQSGSRASRQTRNDEQ
SGDGRHSWSHHHEASTQADSSRHSQSGGQSGAGPRTSRNQSSVSQDSDSQGHSEDSER
WSGSASRNHRGSAQEQRDGSRHPTSHHEDRAGHGHSAESSRQSGTHHAENSSGGQAASS
HEQARSSAGERHGHSHHQQSADSSRHSGIGHGQASSAVRDSGHRGSSGSQASDSEGHSEDS
DTQSVSAHGQAGPHQQSHQESTRGRSAGRSGRSGSFLYQVSTHEQSESAHGRAGPSTGGR
QGSRHEQARDSSRHSASQEGQDTIRGHPGSSRRGRQGSYHEQSVDRSGNSGSHSHTTSQ
GRSDASHGQSGS

3. Summary

Peptides observed are unique to Filaggrin (and not to Ifap-
soriasis or Hornerin). This protein has not been studied in the
context of myocardial ischemia or events leading up to MI.
L. Proteoglycan-4
Name: Isoform A and D of Proteoglycan-4 (we cannot dis-
tinguish isoforms due to high degree of sequence homol-
ogy)

IPI ID: IPI00024825 and IPI00655676

UniProtKB/Swiss-Prot entry ID: Q92954, Q6DNC4,
Q6DNC5, Q6ZMZ5, Q9BX49

Length: 1404 aa, molecular weight: 151077 Da

1. Sequence

(SEQ ID NO: 12)
MAWKTLPTYL LLLSVFVIQQVSSQDLSSCAGRCGEGYSRDATCNCNDYNCQHYMECCPDF
KRVCTAELSCKGRCFESFERGRECDCAQCKKYDKCCPDYESFCAEVHNPTSPSSKKAP
PPSGASQTIKSTTKRSPKPPNKKTKKVI ESEEITEHVSSENQESSSSSSSSSSSTIR
KIKSSKNSAANRELQKKLVKDNKKNRTKKKPTPKPPVVDEAGSLDNGDFKVTTPDTST
TQHNKVSTSPKITTAKPINPRPSLPNSDTSKETSLTVNKETTETTKQTSTDG
KEKTTSAKETQSI EKTSKDLAPTSKVLAKPTPKAETTTKGPALTTPKEPTPTTPKEPAS
TTPKEPTPTTIKSAPTTPKEPAPTTTKSAPTTPKEPAPTTTKEPAPTTTPKEPAPTTTKEP
APTTTTSAPTTPKEPAPTTPKKPAPTTPKEPAPTTTPKEPTPTTPKEPAPTTKEPAPTTPK
EPAPTAPKKPAPTTPKEPAPTTPEPAPTTTKEPSPTTPKEPAPTTTKSAPTTPKEPAP
TTKSAPTTPKEPSPTTTKEPAPTTTPKEPAPTTPKKPAPTTPKEPAPTTTPKEPAPTTTKK
APTTPKEPAPTTPKETAPTTPKKTPTTPEKLAPTTPKEPAPTTPEELAPTTPPEPTPTT
PEEPAPTTPKAAAPNTPKEPAPTTTPKEPAPTTTPKEPAPTTPKETAPTTPKGTAPTTLKEP
APTTPKKPAPKELAPTTTKEPTSTTCDKPAPTTPKGTAPTTPKEPAPTTTPKEPAPTTPK
TAPTTLKEPAPTTPKKPAPKELAPTTTKGPTSTTSKDPAPTTPKETAPTTPKEPAPTTPK
KPAPTTPETPPPTTSEVSTPTTKEPTTIHKSPESTPELSAEPKALENSPKPGVPT
TKTPAATKPEMTTTAKDKTTERDLRTPETTTAAPKMTKETATTEKTTESKITATTTQV
TSTTTQDTPFKITTLKTTTLAPKVTTTKKTI TTTEIMNKPEETAKPKDRATNSKATTPK
PQKPTKAPKKPTSTKKPKTMPRVKPKTTPPRKMTSTMPELNPTSRIAEAMLQTTTRPN
QTPNSKLVEVNPKSEDAGGAEGETPHMLLRPHVFMPEVTPDMDYLPVPRVNQGI IINPMLS
DETNICNGKPV DGLTTLRNGTLVAFRGHYFWMLSPFSPSPARRITEVWGIPSPIDTVFT
RCNCEGKTFFFKDSQYWRFTNDIKDAGYKPIFKGFGGLTGQIIVAALSTAKYKNWPESVY
FFKRGGSIQQYIYKQEPVQKCPGRRPALNYPVYGETTQVRRRRFERAIGPSQHTTIRIQY

- continued

SPARLAYQDKGVLHNEVKVSILWRGLPNVVTSAISLPNIRKPDGYDYAFSKDQYVNIIDV

PSRTARAITTTRSGQTLISKVWYNCP

1 24 24 Potential. signal
25 1404 1380 Proteoglycan-4.
1307 1404 98 Proteoglycan-4 C-terminal part.
26 66 41 Missing (in isoform B, isoform D and isoform E).
107 199 93 Missing (in isoform C and isoform D).
157 199 43 Missing (in isoform F).
412 841 430 Missing (in isoform E).

2. Alternative Names: Proteoglycan-4 precursor (Lubricin) (Megakaryocyte-stimulating factor) (Superficial zone proteoglycan) [Contains: Proteoglycan-4 C-terminal part].
3. Summary

PRG4 (proteoglycan 4) is a megakaryocyte stimulating factor and articular superficial zone protein which is expressed in cartilage, liver, heart, lung, and bone. It is known to be involved in the lubrication of mammalian joints. This protein has not been studied in the context of myocardial ischemia or events leading up to MI.

M. Alpha-2-HS-Glycoprotein

Name: Alpha-2-HS-glycoprotein

IPI ID: IPI00022431

UniProtKB/Swiss-Prot entry ID: P02765

Length: 367 aa, molecular weight: 39325 Da

1. Basic Information from UniProtKB/Swiss-Prot Entry

FUNCTION Promotes endocytosis, possesses opsonic properties and influences the mineral phase of bone. Shows affinity for calcium and barium ions.

SUBUNIT Alpha-2-HS glycoprotein derives from this precursor, when the connecting peptide is cleaved off. The two chains A and B are held together by a single disulfide bond. SUBCELLULAR LOCATION Secreted.

TISSUE SPECIFICITY Synthesized in liver and selectively concentrated in bone matrix. Secreted in plasma. It is also found in dentin in much higher quantities than other plasma proteins.

2. Sequence

(SEQ ID NO: 13)
MKSLVLLCLLAQLWGCHSAPHGPGLIYRQPNCDDEPETEEALVAIDYINQ
NLPWGYKHTLNQIDEVKVWPQQPSGELFEIEDTLETTCHVLDPTFVARC
SVRQLKEHAVEGDCDFQLKLDGKFSVVYAKCDSSPDS AEDVRKVCQDC
PLLAPLNDTRVVHAAKAAALAFNAQNNGSNFQLEEISRAQLVPLPPSTY
VEFTVSGTDCVAKEATEAAKCNLLAEKQYGFCKATLSEKLGGAEVATC

- continued

TVFQTQPVTSQPQPEGANEA VPTPVVDPDAPPSPPLGAPGLPPAGSPP
DSHVLLAAPPQHQLHRAHYDLRHTFMGVVSLGSPSGEVSHPRKTRTVVQ
PSVGAAGPVVPPCPGRIRHFKV

1-18 Signal Sequence

3. Alternative Names:

Alpha-2-HS-glycoprotein precursor (Fetuin-A) (Alpha-2-Z-globulin) (Ba-alpha-2-glycoprotein) [Contains: Alpha-2-HS-glycoprotein chain A; Alpha-2-HS-glycoprotein chain B].

4. Summary Very high abundant protein and found to change in many diseases and acts as a calcification inhibitor. It inhibits inflammation. It is elevated late after acute myocardial infarction but did not correlate with peak cardiac troponin values. This protein has not been studied in the context of myocardial ischemia or events leading up to MI.

N. Protease, Serine, 3 (Mesotrypsinogen) IPI00748381

Name: Protease, serine, 3

IPI ID: IPI00748381

UniProtKB/Swiss-Prot entry ID: Q5JT15

Length: 249AA [This is the length of the unprocessed precursor]

Molecular weight: 26914 Da [This is the MW of the unprocessed precursor]

1. Basic Information from UniProtKB/Swiss-Prot Entry

FUNCTION (mesotrypsinogen data): Preferential cleavage: Arg-I-Xaa, Lys-I-Xaa. Cofactor Binds 1 calcium ion per subunit.

INTERACTIONS: This protein binds to Amyloid beta A4 (which we observe but do not see changed) and tissue factor pathway inhibitor (see HPRD)

SUBCELLULAR LOCATION: Secreted.

TISSUE SPECIFICITY: Pancreas and brain.

2. Sequence Information from 2DLC

Note: this protein was identified in different fractions for ischemia vs AMI. This suggests that this protein has undergone a PTM with AMI and thus is physically distinct from the form present during ischemia. We do not know what this PTM(s) is at this time.

Sequence

(SEQ ID NO: 14)
MSPFLILAFVGAAGEVAVPFDDDDKIVGGYTCEENSLPYQVSLNSGSHFCGGLISEQWV
VSAAHCYKTRIQRVLGEHNKIVLEGNEQFINAAKIIIRHPKYNRDTLNDIMLIKLSPPAV

INARVSTISLPTTPPAAGTECLISGWGNTLSFGADYPDELKCLDAPVLTQAECKASYPGK
ITNSMFCVGFLEGGKDSQORDSGGPVVCNGQLQGVVSWGHGCAWKNEPQVYTKVINYVDW

IKDTIAANS

bold amino acids are trypsin-like domain

3. Alternative Names:

Uncharacterized protein PRSS3 A6NN76, Mesotrypsin C Q6ISJ4, Mesotrypsinogen C P35030-3 (98% homologous and not in region of the observed peptides), Isoform C of P35030 P35030-3, Isoform B of P35030 P35030-2. Based on HPRD this is the same protein as trypsinogen IV (has same sequence), protease serine, 4, TRY3, TRY4, trypsin 3, trypsin 4 (Brain), trypsinogen III (pancreatic).

Note: In swiss prot, mesotrypsinogen has three isoforms—two of which are longer proteins at the N-terminus. We can not distinguish between the three isoforms.

Note on Sequence:

We cannot distinguish between the three highly conserved isoforms of mesotrypsinogen based on MS data.

4. Summary

Mesotrypsin is an inhibitor-resistant protease and is secreted from pancreatic juice. Whether it is present in the heart is not known. This protein has not been studied in the context of myocardial ischemia or events leading up to MI.

O. Alpha-2-Glycoprotein 1, zinc IPI00166729

Name: alpha-2-glycoprotein 1, zinc

IPI ID: IPI00166729

UniProtKB/Swiss-Prot entry ID: Q8N4N0 Q5XKQ4

Length: 298 AA [This is the length of the unprocessed precursor]

Molecular weight: 34259 Da [This is the MW of the unprocessed precursor]

1. Basic Information from UniProtKB/Swiss-Prot Entry

FUNCTION: Stimulates lipid degradation in adipocytes and causes the extensive fat losses associated with some advanced cancers. May bind polyunsaturated fatty acids.

SUBCELLULAR LOCATION: Secreted.

TISSUE SPECIFICITY: Blood plasma, seminal plasma, urine, saliva, sweat, epithelial cells of various human glands, liver.

2. Sequence

(SEQ ID NO: 15)

MVRMVPVLLSLLLLLGPAPVQENQDGRYSLTYYTGLSKHVEDVPAFOALGSLNDLQFFR

YNSKDRKSQPMGLWRQVEGMEDWKQDSQLQKAREDFMETLKDIVEYYNDSNGSHVLQGR

FGCEIENNRSSGAFWKYYDGDYIEFNKEIPAWVPFDPAAQITKQKWEAEFPVYVQRAKA

YLEEECPATLRKYLKYSKNI LDRQPPSVVVTSHQAPGEKKKLKCLAYDFYPGKIDVHWT

RAGEVQEPRLRGDVLHNGNGTYQSWVVAVPPQDTAPYSCHVQHSSLAQPLVVPWEAS

Note on sequence: note initiating Met is cleaved. There maybe a PTM with ischemia as the peptides elute at different fractions at T-1 and T-2. We do not know what the PTM is.

3. Alternative Names: Alpha-2-glycoprotein 1 Q5XKQ4, zinc binding; zinc-alpha-2-glycoprotein P25311 (295 AA and 33872 Da, over 95% homology)

4. Summary Zinc-alpha2-glycoprotein (ZAG) is a a lipid mobilizing factor found in adipose tissue. It is increased in a number of cancers. Nothing is known about with respect to the heart and myocardial ischemia. It has not been studied in the context of myocardial ischemia or events leading up to MI.

P. Desmoglein-1

Name: Desmoglein-1

IPI ID: IPI00025753

UniProtKB/Swiss-Prot: Q02413

Length: 1049 AA [This is the length of the unprocessed precursor]

Molecular Weight: 113716 Da

1. Basic Information from UniProtKB/Swiss-Prot Entry Q02413

FUNCTION: Component of intercellular desmosome junctions. Involved in the interaction of plaque proteins and intermediate filaments mediating cell-cell adhesion.

SUBCELLULAR LOCATION: Cell membrane; Single-pass type I membrane protein (By similarity).

SIMILARITY: Contains 4 cadherin domains

TISSUE SPECIFICITY: Epidermis, tongue, tonsil and esophagus.

DISEASE: Defects in DSG1 are the cause of keratosis palmoplantaris striata I (PPKS1) [MIM:148700]; also known as striate palmoplantar keratoderma I (SPPK1). PPKS1 is an autosomal dominant disease characterized by thickening of the skin on the palms and soles, and longitudinal hyperkeratotic lesions on the palms, running the length of each finger.

Protein ID data

SEPARATION METHOD: 2DE

EXPECTED MOLECULAR WEIGHT/PI: 113716 Da/4.90

OBSERVED MOLECULAR WEIGHT/PI: 59 KD/5.8

NOTE: It could be processed the product.

2. Sequence

(SEQ ID NO: 16)

MDWSFFRVVAVLFIFLVVVEVNSEFRIQVRDYNKNGTIKWHISIRQKREWIKFPAACRE

GEDNSKRNP IAKIHSDCAANQVYTRISGVGIDQPPYGIFVINQKTGEINITSIDREVTV

PFFIIYCRALNSMGQDLERPLELRVRVLDINDNPPVFSMATFAGQIEENSANTLVMILN

ATDADEPNLNSKIAFKIIRQEPSDSPMFLINRNTGEIRTMNPLDREQYQYALAVRGS

DRDGGADGMSAECECNIKILDVNDNIPYMEQSSYTIIEIQENTLNSNLLERIVIDLDEEFS

ANWMAVIFFFISGNEGNWFEIEMNERTNVGILKVVKPLDYEAMQSLQLSIGVRNKAEFHHS
IMSQYKCLKASAI~~SVIVLNVIEGPVFRPGSKTYVVTGNMG~~SNDKVGD~~FVATD~~LDLTGRPSTT
VRYVMGNNPADLLAVDSRTGKLT~~LNK~~VTKEQYNMLGGKYQGTILSIDDNLQRTCTGTIN
INIQSFGNDDRTNTEPNTKITTTNTGRQESTSS~~TNYDTSTTSTDSSQVYS~~SEPGNGAKDLL
SDNVHFGPAGIGLLIMGFLVLGLVPFLMICDCGGAPRSAAGFEPVPECS~~DAI~~HSWAVE
GPQPEPRDITTVIPQIPPDNANIIECIDNSGVY~~TNEYGGRE~~MQDLGGGERMTGFELTEGV
KTSGMPEICQEYSGTLRRNSMRECREGGLMNFMESYFCQKAYAYADEDEGRPSNDCLLI
YDIEGVGSPAGSVGCCSFIGEDLDD~~SFLDTL~~GPKFKKLADISLGKESYPDLDP~~SWPPQ~~ST
EPVCLPQETEPVVS~~GHPPI~~SPHFGTTT~~VI~~SESTYPSGPGVLHHPK~~PILDPL~~GYGNVT~~VTES~~
YTTSDTLKPSVHVHDNR~~PASNV~~VTERVVGPI~~S~~GADLHGMLEMPDLRDGSNVIVTERVIA
PSSSLPTSLTIHHPRESSNVV~~TERVI~~QPTSGMIGSLSMHPELANAHNVIVTERV~~VSGAG~~
VTGISGTTGISGGIGSSGLVGTSMGAGSGALSGAGISGGGIGLSSLG~~TASIGHMRSSSD~~
HHFNQTIGSASPSTARSRI~~TKYSTVQYSK~~

3. Summary This protein is part of the desmosome cell junctions in many cell types including the heart. The protein is the antigen for Pemphigus foliaceus is an autoimmune skin disease. It binds to plakophilin 1, plakophilin 2, desmoplakin, desmoglein 1, desmoglein 4, plakoglobin and corneodesmosin, all of which maybe potential biomarkers in myocardial ischemia. It has not been studied in the context of myocardial ischemia or events leading up to MI.

Protein ID data
Separation method: 2DE
Expected molecular weight/pI: 27680 Da/5.44 (pro-caspase-14=242 AA)
Observed molecular weight/pI: 68000 Da/6.8,
Note: There is difference in observed and expected MW, multiple proteins complex?
2. Sequence

(SEQ ID NO: 17)
MSNPRSLEEE KYDMSGARLA LILCVTKARE GSEEDLDALE HMFRLRFES TMKRDPTAEQ
FQEELEKFPQQ AIDSREDPVS CAFVVLMAHG REGFLKGEDG EMVKLENLFE ALNNKNCQAL
RAKPKVYIIQ ACRGEQRDPG ETVGGDEIVM VIKDSPQTIP TYTDALHVS TVEGYIAYRH
DQKGSCFIQT LVDFTKRKG HIDELEL~~TEVT~~ RRMAEAEVLQ EGKARK~~INPE~~ IQSTLRKRLY
LQ

Q. Caspase-14
Name: Caspase-14
IPI ID: IPI00013885
UniProtKB/Swiss-Prot: P31944
Length: 242 AA [this is the length of the unprocessed precursor]
propeptide=1-? AA
sub-unit 1=?-146 AA,
sub-unit 2=147-242 AA
Molecular Weight: 27680 Da [this is the MW of the unprocessed precursor]
1. Basic information from UniProtKB/Swiss-Prot Entry P31944
FUNCTION: May be involved in the death receptor and granzyme B apoptotic pathways. May function as a downstream signal transducer of cell death.
SUBUNIT: May dimerize with large prodomain caspases.
SUBCELLULAR LOCATION: Cytoplasm (By similarity).

3. Summary
Casp14 may play a role in ontogenesis and skin physiology. CASP14 cDNA and determined that CASP14 contains 7 exons encoding a 242-amino acid protein, 2 CASP14 transcripts (CASP14a and CASP14b) differ in the C terminus while an alternative splice acceptor site within intron 5 results in a 74-nucleotide insertion in CASP14b. CASP14b lacks homology with the caspase consensus sequence. CASP14 has been found in epidermis, hair follicles, the sebaceous gland. NO treatment of neonatal mouse cardiomyocytes in culture causes increase in caspase 14. There is also increase in this protein in canine brain during cardiac arrest and resuscitation. This protein has not been studied in the context of myocardial ischemia or events leading up to MI.
R. Hornerin
Name: HORNERIN
IPI ID: IPI00398625
UniProtKB/Swiss-Prot ID: Q86YZ3
Length: 2850 aa, molecular weight: 282390 Da

1. Basic Information from UniProtKB/Swiss-Prot Entry:

FUNCTION	May play a role in cornification.
SUBCELLULAR LOCATION	Cytoplasmic granule (By similarity). Note = Found in keratohyalin granules in the granular cells of the epidermis (By similarity).

2. Sequence:

(SEQ ID NO: 18)

MPKLLQGVITVIDVFYQYATQHGEYDTLNKAELENEFHQILKNPND

PDTVDIILQSLDRDHNKVDFTFTEYLLMIFKLVQARNKIIGKDYCVVSGSK

LRDDTHQHQBEEETEKEENKRQESSFSHSSWSAGENDSYSRNVRGSLKP

GTESISRRLSFQRDFSGQHNSYSGQSSSYGEQNSDSHQSSGRQCQSGSG

QSPNYQHSGSGSQSSNDTHSGSGSQSSGFSQHKSSSQSSGYSQHSGSG

SGHSSGYQHSGSRSGQSSRGERHRSSSGSSSYQHSGSGSRQSLGHGRQG

SGSRQSPSHVRHSGSGHSSSHGQHSGSGSSYSYRGHYESGSGQTSGFGQ

HESGSGQSSGYSKHSGSGHSSSQQHGSTSGQASSSGQHSGSSRQSSSY

GQHESASRHS SGRQHS SSGSQSPGHGQRGSGSGQSPSSGQHTGFGRSS

SSGPYVSGSGYS SFGHHESSEHSSGYTQHSGSGHSSGHGQHGRSGSQ

SSRGERQSSAGSSSYQHSGSGSRQSLGHSRHSGSGSQSPSPSRGRHES

GSRQSSSYGPHGYGSRSSSRGPYESGSGHSSGLHQESRSGQSSGYGQH

GSSSGHSS THGQHGSTSGQSSSCGQHATSGQSSSHGQHSGSGSSRYG

QQSGSGSQSPSRGRHSGDFGHSSSYQHSGSGSGWSSSNGPHGSVSGQSSG

FGHKSGSGQSSGYSQHSGSGSHSSGYRKHGSRSGQSSRSEQHSGSSGLSS

SYGQHSGSGSHQSSGHGRQSGSGHSPSRVRHSGSSGHSSSHGQHSGTSC

SSSCGHYESGSGQASGFGQHESGSGQGYSQHGSASGHFSSQGRHGSTSGQ

SSSSGQHDSSSGQSSSYQHESASHHASGRGRHSGSGSQSPGHGQRGSGS

GQSPSYGRHSGSGGRSSSRGRHSGSGSQSGFGHKS SSGQSSGYTQHSGSG

SGHSSSYEQHGRSGQSSRSEQHSGSSSGSSSYQHSGSGSRQSLGHGQH

SGSQSPSPSRGRHSGSGQSSSYGPYRSGSGWSSSRGPYESGSGHSSGL

GHRESRSGQSSGYQHSGSSGHSS THGQHGSTSGQSSSCGQHASSGQSS

SHGQHSGSGSSQSSGYGRQSGSGSQSPGHGQRGSGSRQSPSYGRHSGSGR

SSSSGQHSGSLGESSGFGHHESSSGQSSSYQHSGSGHSSGYQHGRS

GQSSRGERHSGSSSGSSHYQHSGSGSRQSSGHGRQSGSGHSPSRGRHGS

GLGHSSSHGQHSGSGSRSSSRGPYESRSGHSSVFGQHESGSGHSSAYSQH

GSGSGHFCSQQHGSTSGQSSSTFDQEGSSTGQSSSYGHRGSGSGSSGYG

RHAGSGQSPSRGRHSGSGHSSSYQHSGSGSGWSSSGRSGSGSGQSSG

FGHHESSSWQSSGCTQHSGSGHSSSYEQHGRSGQSSRGERHSGSSGSS

SSYQHSGSGSRQSLGHGQHSGSGSQSPSPSRGRHSGSGQSSSYSPYSG

SGWSSSRGPYESGSSHSSGLGHRESRSGQSSGYQHSGSSGHSS THGQH

STSGQSSSCGQHAGASSGQSSSHGQHSGSGSQSSGYGRQSGSGSQSPGHG

RGSGSRQSPSYGRHSGSGSRSSSGQHSGSLGESSGFGHHESSSGQSSSY

SQHSGSGHSSGYQHGRSGQSSRGERHSGSSSRSSRYQHSGSGSRQSS

-continued

GHGRQSGSGSQSPSRGRHSGSLGHSSSHGQHSGSGSRSSSRGPYESRSGH

5 SSVFGQHESGSGHSSAYSQHSGSGGHFCSQGQHGSTSGQSSSTFDQEGSST

GQSSSHGQHSGSGSQSSSYGQSGSGSQSPSRGRHSGSGHSSSYQHGS

GSWSSSGRSGSGSQSSGFGHHESSSWQSSGYTQHSGSGHSSSYEQH

10 GSRSGQSSRGEQHSGSSGSSSYQHSGSGSRQSLGHGQHSGSGSQSPSPS

RGRHSGSGSQSSSYGPYSGSGWSSSRGPYESGSGHSSGLGHRESRSGQ

15 SGYQHSGSSGHSS THGQHGSASGQSSSCGQHAGASSGQSSSHGQHSGSGS

QSSGYGRQSGSGSQSPGHGQRGSGSRQSPSYGRHSGSGSRSSSGQHGP

20 LGESSGFGHHESSSGQSSSYQHSGSGHSSGYQHGRSGQSSRGERHG

SSSGSSRYQHSGSGSRQSSGHGRQSGSGHSPSRGRHSGSGHSSSHGQ

25 HGSGSGSRSSSRGPYESRSGHSSVFGQHESGSGHSSAYSQHSGSGGHFCSQ

GQHGSTSGQSSSTFDQEGSSTGQSSSHGQHSGSGSSQSSSYGQSGSGQSP

30 SRGRHSGSGHSSSYQHSGSGSGWSSSGRSGSGSGSQSSGFGHHESSSWQ

SSGYTQHSGSGHSSSYEQHGRSGQSSRGERHSGSSSGSSSYQHSGSGS

35 RQSLGHGQHSGSGSQSPSPSRGRHSGSGSQSSSYSPYSGSGWSSSRGPY

ESGSGHSSGLGHRESRSGQSSGYQHSGSSGHSS THGQHGSTSGQSSSCG

40 QHAGASSGQSSSHGQHSGSGSQSSGYGRQSGSGSQSPGHGQRGSGSRQSPS

YGRHSGSGSRSSSGQHSGSLGESSGFGHHESSSGQSSSYQHSGSGHSS

45 SGYQHGRSGRSGQSSRGERHSGSSSGSSHYQHSGSGSRQSSGHGRQSGSGS

QSPSRGRHSGSLGHSSSHGQHSGSGSRSSSRGPYESRLGHSSVFGQHESG

50 SGHSSAYSQHSGSGGHFCSQGQHGSTSGQSSSTFDQEGSSTGQSSSYGHRG

SGSSQSSGYGRHAGSGQSSLHGRHSGSGSQSSSYQHSGSGSQSSGYSQ

55 HGSGSGQDGYSYCKGGSNDGGSSGYFLSFPSTSPYEVQEQRCYFYQ

Little is known about this protein. It has not been studied in the context of myocardial ischemia or events leading up to MI.

S. Kininogen

Name: ISOFORM LMW OF KININOGEN-1

IPI ID: IPI00215894

65 UniProtKB/Swiss-Prot ID: P01042

Length: 427 aa, molecular weight: 47883 Da (of Precursor)

1. Basic Information from UniProtKB/Swiss-Prot Entry:

FUNCTION	(1) Kininogens are inhibitors of thiol proteases; (2) HMW-kininogen plays an important role in blood coagulation by helping to position optimally prekallikrein and factor XI next to factor XII; (3) HMW-kininogen inhibits the thrombin- and plasmin- induced aggregation of thrombocytes; (4) the active peptide bradykinin that is released from HMW-kininogen shows a variety of physiological effects: (4A) influence in smooth muscle contraction, (4B) induction of hypotension, (4C) natriuresis and diuresis, (4D) decrease in blood glucose level, (4E) it is a mediator of inflammation and causes (4E1) increase in vascular permeability, (4E2) stimulation of nociceptors (4E3) release of other mediators of inflammation (e.g. prostaglandins), (4F) it has a cardioprotective effect (directly via bradykinin action, indirectly via endothelium-derived relaxing factor action); (5) LMW-kininogen inhibits the aggregation of thrombocytes; (6) LMW-kininogen is in contrast to HMW-kininogen not involved in blood clotting.
SUBCELLULAR LOCATION	Secreted, extracellular space.

2. Sequence:

(SEQ ID NO: 19)
MKLITITLFLCSRLLLSLTQESQSEEDCNKDLPKAVDAALKKYNQSN
QSNQFVLYRITEATKTGSDTFYSFKYEIKEGDCPVQSGKTWQDCE
YKDAKAATGECTATVGKRSSSTKFSVATQTCQITPAEGPVVTAQYD
CLGCVHPISQSPDLEPILRHGIQYFNNNTQHSSLFMLNEVKRAQRQ
VVAGLNFRITYSIVQTNCSKENFLFLTPDCKSLWNGDTGECTDNAYI
DIQLRIASFQNCDIYPGKDFVQPPTKICVGCPRDIPTNSPELEETLTH
TITKLNAENNATFYFKIDNVKKARVQVAGKKYFIDFVARETTCSKES
NEELTESCETKKLGQSLDCNAEVYVVPWEKKIYPTVNCQPLGMISL
MKRPPGFSPPRSSRIGIEKEETTSHLRSCEYKGRPPKAGAEPASER
EVS

3. Alternative Name(s): High molecular weight kininogen, Short name=HMWK; Williams-Fitzgerald-Flaujeac factor; Fitzgerald factor; Alpha-2-thiol proteinase inhibitor
This protein has not been studied in the context of myocardial ischemia or events leading up to MI.

Example III

Further Studies to Identify Cardiac Biomarkers,
Using as a Cohort of Patients, a Valve Replacement
Cardioplegia Human Model (Cohort II)

A. Overview of the Studies

The 21 patients in this cohort all underwent aortic valve replacement surgery (See FIGS. 6 and 7). Table 10 provides cohort information of this model.

TABLE 10

patient sampling

T1	pre-op sample (before incision).
T2	immediately before the heart gets stopped (prior to CPB).
T6	5 min after the heart went off CPB and was beating on its own again.
T7	30 min after bypass
T8	60 min after bypass
T9	120 min after bypass

There were 6 plasma samples taken. Note that only 19 (out of 21) patients have samples at T9. The sample were normalized to total protein concentration for both targeted and de novo discovery. In the targeted analysis, 15 biomarkers were deter-

mined for each sample, specifically, CRP, GM-CSF, IFN γ , IL10, IL12p70, IL1 β , IL-2, IL-6, IL-8, NT proBNP, SAA, TNF α , cTnI, sICAM, sVCAM. All time points were analyzed. These analyses were done using the MESOSCALE multiplex assay in triplicate. FIG. 7 shows the box blot for cTnI measurement for all patients. For de novo discovery, only T2 and T6 were analyzed.

B. Methods

1. High Abundant Protein Depletion

IgY depletion of the top 12 abundant proteins of samples from each individual sample.

2. Intact Protein Separation by Hydrophobicity

1DLC analysis was carried out for cohort II (20 patients with two time points). All 1DLC analyses were done in duplicate using the optimized gradient developed to eliminate the interference of the unknown contaminants that eluted at the beginning and end of the run. Optimization was required as the contaminants were not MS compatible and co-eluted with proteins found to be interesting in cohort I. The duplicate run for each patient time point were collected into a single plate and stored at -80° C. until analyzed. A total of 80 @ 1DLC runs were carried out (20x2x2=80 (2 time points, 20 patients, in duplicate)). The fractions obtained for each 1DLC run were pooled into 16 fractions, neutralized and dried down, prior to resolubilization in buffer compatible for tryptic digestion.

3. MS Analysis

MS analysis for each digested fraction was carried using the LTQ Orbitrap LC MSMS instrument. Each fraction was run in duplicate. A total 1216 MS runs were carried out (19x2x16x2=1216 (19 patients, 16 fractions per time point, two time points, in duplicate). For LC-MS/MS experiments on the LTQ-Orbitrap (ThermoFinnigan, San Jose, Calif.), peptides were dissolved in 6 μ l resuspension buffer (4% acetonitrile in water with 0.1% formic acid). Samples (3 μ l) were loaded onto a 75 μ m x 10 cm BioBasic C18 column (New Objective, Woburn, Mass.). Peptides were eluted into an LTQ-Orbitrap (ThermoFinnigan, San Jose, Calif.) using an Agilent 1200 nano-LC system (Agilent, Santa Clara, Calif.). The HPLC gradient was 5% to 60% B (90% acetonitrile/water in 0.1% Formic acid) over 30 or 60 min depended on sample complexity. The mass spectrometer was operated in data-dependent mode in which every FT-MS scan (survey 350-2000 Da) was followed by MS/MS scans of the 5 most abundant ions.

Mass spectrometry data were analyzed, and data reanalysis was carried out, as described in Example 1D2 above.

C. Results

1. Optimization of 1DLC

In order for cohort II to be analyzed, optimization of the 1DLC gradient was required to resolve a contaminating peak eluting early on the chromatogram. The contaminating peak overlaid a region in which we found several potential biomarkers and resulted in suppression of the peptides of interest.

2. Optimization and Testing of Reproducibility of MS Analysis

In table 11, the MS reproducibility of several fractions is shown.

TABLE 11

MS reproducibility cohort II sequential. MS run 1 vs. run 2 Same LC fraction, digested, split and MS analyzed				
Method for cohort II	run 1	run 2	run 1	run 2
Fraction 1	# peptides	# peptides	# total spectra	# total spectra
Protein name	Fraction 1	Fraction 1	Fraction 1	Fraction 1
histidine-rich glycoprotein	14	13	35	32
factor H	12	11	27	24
Kininogen 1	10	11	15	18
complement component 4 binding protein	8	10	14	19
Lactoferrin	7	8	16	14
apolipoprotein H	5	4	12	13
Transferrin	5	5	20	18
alpha-1-acid glycoprotein 1	4	4	13	11
haptoglobin	3	4	6	7
fibrinogen, alpha p	3	3	5	5
plasminogen	3	3	6	6
Alpha-1B-glycoprotein	2	0	2	0
alpha2-HS glycoprotein	2	2	3	3
collagen 1 pro-alpha-2 chain	2	1	3	2
selenoprotein P	2	2	5	6
Extracellular matrix protein 1	2	2	3	4
Fraction 2	# peptides	# peptides	# total spectra	# total spectra
Protein name	Fraction 2	Fraction 2	Fraction 2	Fraction 2
complement component C4	27	26	49	47
Antithrombin	22	20	52	78
complement component 3	22	24	42	50
Fibronectin 1	21	24	38	55
Ceruloplasmin	19	21	49	52
Inter-alpha-trypsin inhibitor heavy chain H4	14	12	29	25
Inter-alpha-trypsin inhibitor heavy chain H2	13	15	29	30
Alpha-1B-glycoprotein	11	10	28	24
Alphal Antichymotrypsin	10	11	46	50
Complement factor B	9	11	23	28
gelsolin isoform b	9	9	19	16
leucine-rich alpha-2-glycoprotein 1	9	7	28	16
Inter-alpha-trypsin inhibitor heavy chain H1	9	8	28	37
Kininogen	8	10	18	20
histidine-rich glycoprotein	7	7	15	13
apolipoprotein A-IV	6	9	12	16
alpha2-HS glycoprotein	5	5	8	9
peroxiredoxin 2 isoform	5	4	10	19
Transthyretin	4	4	9	10
complement component C6	4	2	13	4
lumican	3	3	14	5
carboxypeptidase B2 isoform a preproprotein	3	2	5	6
apolipoprotein H precursor	2	4	6	21
Transferrin	2	2	3	3
amyloid P	2	0	2	0
alpha-I-microglobulin	2	2	4	4
Retinol binding protein 4	2	2	3	4
complement component 8, alpha	2	1	3	1
serine or cysteine proteinase inhibitor	2	2	2	2
complement component 4 binding protein	1	1	2	1
hemoglobin	1	0	3	0
C9 complement protein	1	0	2	0
alpha-I-acid glycoprotein 1	0	0	0	0
complement factor H-related 1	0	1	0	2
alpha-I-antichymotrypsin	0	2	0	8

3. Cohort II Analysis

343 non-redundant proteins were compared. Table 12 shows those proteins which were most significantly increased in T6 compared to T0 for cohort II.

TABLE 12

Target proteins in cohort II	
Top hits from cohort II clustered based on related protein family. Below listed the number of individuals the protein was elevated in T6 compared to T2 (increased due to induced ischemia). 20 individuals were analyzed.	
1.	PRDX2 Peroxiredoxin 2 - increased in 17 patients
2.	S100A9 Protein S100-A9 - increased in 17 patients S100 A8 - increased in 11 patients S100 A7- increased in 4 patients
3.	Lactotransferrin increased in 14 patients
4.	CA1 Carbonic anhydrase 1 - increased in 17 patients CA2 Carbonic anhydrase 2 - increased in 3 patients
5.	Conserved hypothetical protein - increased in 12 patients
6.	NCOR2 CTG26 alternate open reading frame (Fragment) - increased in 11 patients
7.	LOC729968 Conserved hypothetical protein - increased in 11 patients
8.	Conserved hypothetical protein - increased in 9 patients
9.	SORL1 Sortilin-related receptor - increased in 11 patients
10.	COL1A1 Collagen alpha-1(I) chain precursor - increased in 11 patients COL1A2 130 kDa protein - increased in 10 patients
11.	CPB2 Isoform 1 of Carboxypeptidase B2 precursor - increased in 10 patients Carboxypeptidase subunit 2 - increased in 8 patients
12.	HBB Hemoglobin subunit beta - increased in 12 patients HBA Hemoglobin subunit alpha - increased in 4 patients
13.	Lactotransferrin - increased in 12 patients
14.	LRP1 Prolow-density lipoprotein receptor-related protein 1 precursor - increased in 9 patients LRP2 Low-density lipoprotein receptor-related protein 2 precursor - increased in 9 patients Together a total of 13 unique patients
15.	CAT Catalase - increased in 11 patients
16.	STX3 Isoform A of Syntaxin-3 - increased in 9 patients
17.	ECM1 Extracellular matrix protein 1 - increased in 10 patients
18.	SERPINA10 Protein Z-dependent protease inhibitor precursor - increased in 8 patients
19.	PTPRK Isoform 1 of Receptor-type tyrosine-protein phosphatase kappa precursor increased in 8 patients
20.	ATRN Isoform 2 of Attractin precursor - increased in 8 patients
21.	PTPRK Protein tyrosine phosphatase, receptor type, K increased in 6 patients
Others of interest due to biology (there are low abundant proteins and may not be observed in higher number of patients due to detection issues)	
22.	MST1 Hepatocyte growth factor-like protein precursor - increased in 7 patients HGFAC Hepatocyte growth factor activator precursor - increased in 4 patients
23.	IGFBP6 Insulin-like growth factor-binding protein 6 precursor - increased in 5 patients IGFBP5 Insulin-like growth factor-binding protein 5 precursor - increased in 1 patients IGFBP2 Insulin-like growth factor-binding protein 2 precursor - increased in 7 patients (same ones as 7) IGFBP7 Insulin-like growth factor-binding protein 7 precursor - increased in 7 patients (same ones as 2) IGFALS Insulin-like growth factor-binding protein complex acid labile chain precursor - increased in 3 patients Total for group 8 patients
24.	SERPINF1 Pigment epithelium-derived factor precursor - increased in 4 patients
25.	GPX3 Glutathione peroxidase 3 precursor - increased in 4 patients
26.	CD14 Monocyte differentiation antigen CD14 precursor - increased in 4 patients
27.	Note there are interesting proteins seen in 2-3 patients which may still be important alternations which are not seen in more patients due to their low abundance. These should be discussed. A summary of some of the properties of these proteins is presented in Example IV.

4. Cohort II and I Comparison

Comparison of the top candidate proteins between cohort I and II are shown in Table 13.

TABLE 13

Protein	IPI number	Cohort I	Cohort II	FUNCTION	Is protein secreted?
Tier One					
Lumican	IPI00020986	Top	Found	May be involved in cell response to injury	Yes
Extracellular matrix protein	IPI00645849	Top	Found	Involved in extracellular matrix composition	Yes
Carboxypeptidase N catalytic chain	IPI00010295	Mid	Found	Protease involved in regulation of vasoactive and inflammatory peptides	Yes
angiogenin	IPI00008554	Top	no	May be involved in angiogenesis	Yes
semenogelin	IPI00414684	Top	no	Forms gel matrix around sperm, unknown role in other cells	Yes
Lung PLNECA-1	IPI00291410	Top	no	May play a role in innate immunity	Yes
Perioxiredoxin 2	IPI00027350	No	Elevated in 17, Top	Involved in redox regulation of the cell.	No
S100 A9	IPI00027462	No	Elevated in 17, Top	Expressed by macrophages in acutely inflamed tissues and in chronic inflammations.	No
S100 A8	IPI00007047	No	Elevated in 11, Top	Expressed by macrophages in chronic inflammations. Also expressed in epithelial cells constitutively or induced during dermatoses.	unknown
S100 A7	IPI00219806	No	Elevated in 4, Lower	unknown	Secreted
Sortilin-related receptor	IPI00022608	No	Elevated in 11, Mid	Likely to be a multifunctional endocytic receptor, which implicates it in the uptake of lipoproteins and of proteases.	No, is a plasma membrane protein
Catalase	IPI00465436	No	Elevated in 11, Mid	Serves to protect cells from the toxic effects of hydrogen peroxide.	No
Low density lipoprotein receptor related protein 1	IPI00020557	No	Elevated in 9, Mid	Endocytic receptor involved in endocytosis and in phagocytosis of apoptotic cells.	No
Low density lipoprotein receptor related protein 2	IPI00024292	No	Elevated in 9, Top	Acts together with cubilin to mediate HDL endocytosis (By similarity).	No
Syntaxin-3	IPI00395768	No	Elevated in 9, Mid	Potentially involved in docking of synaptic vesicles at presynaptic active zones.	No
Tier two					
Hepatocyte growth factor like protein	IPI00292218		+	Unknown	Unknown
Hepatocyte growth factor activator	IPI00029193		+	Activates hepatocyte growth factor (HGF).	Secreted.
Insulin like growth factor protein 6	IPI00029235		+	GF-binding proteins prolong the half-life of the IGFs.	Secreted.
Pigment epithelium-derived factor	IPI00006114		+	Neurotrophic protein; induces extensive neuronal differentiation in retinoblastoma cells. Potent inhibitor of angiogenesis.	Secreted.
Glutathione peroxidase 3	IPI00026199		+	Protects cells and enzymes from oxidative damage.	Secreted.
Monocyte differentiation antigen CD14	IPI00029260		+	Involved in the innate immune response to bacterial lipopolysaccharide (LPS).	No
Lactotransferrin, cDNA FLJ58679, highly similar to Lactotransferrin	IPI00789477		+	unknown	unknown
Attractin	IPI00162735			Involved in the initial immune cell clustering during inflammatory response.	Secreted
Conserved hypothetical protein	IPI00883661		+	Unknown	Unknown
NCOR2 CTG26	IPI00006659		+	unknown	unknown

TABLE 13-continued

Protein	IPI number	Cohort I	Cohort II	FUNCTION	Is protein secreted?
alternate open reading frame					
LOC729968	IPI00884334		+	unknown	unknown
Conserved hypothetical protein					
Protein Z-dependent protease inhibitor	IPI00007199		+	Inhibits factor Xa activity.	Secreted.
Conserved hypothetical protein	IPI00847894			unknown	unknown
Isoform 1 of Receptor-type tyrosine-protein phosphatase kappa	IPI00015756		+	Regulation of processes involving cell contact and adhesion such as growth control, tumor invasion, and metastasis.	No, but present on plasma membrane
Protein tyrosine phosphatase, receptor type, K	IPI00552690		+	Receptor	Unknown, but present on plasma membrane
Sodium channel subunit beta-4	IPI00217376		Elevated in 7 people	Part of sodium channel	No, but present on plasma membrane
Alpha2-HS-glycoprotein	IPI00022431	+	Elevated in 4 people	See previous write up for cohort I	See previous write up for cohort I
Galectin 7	IPI00219221	+	–	See previous write up for cohort I	See previous write up for cohort I
Homerin	IPI00398625	+	Elevated and seen only in one person	See previous write up for cohort I	See previous write up for cohort I
Proteoglycan 4 (isoforms A and D)	IPI00655676	+	Elevated in 4 people	See previous write up for cohort I	See previous write up for cohort I
Proflaggrin (Filaggrin)	IPI00654788	+	–	See previous write up for cohort I	See previous write up for cohort I
Vitamin D binding protein	IPI00555812	+	–	See previous write up for cohort I	See previous write up for cohort I
C4b binding proteins	IPI00021727	+	–	See previous write up for cohort I	See previous write up for cohort I
Thyroxine binding globulin	IPI00292946	+	–	See previous write up for cohort I	See previous write up for cohort I
Alpha 2 glycoprotein 1, zinc	IPI00166729	+	Elevated in 3 people	See previous write up for cohort I	See previous write up for cohort I
Caspase 14		+		See previous write up for cohort I	See previous write up for cohort I
Desmogelin		+		See previous write up for cohort I	See previous write up for cohort I
Kininogen -1	IPI00215894	+		See previous write up for cohort I	See previous write up for cohort I

Some additional proteins were found to be elevated in a subset of the patients in cohort II that exhibit ischemia. See Table 14 below for details.

TABLE 14

Protein name	Protein accession numbers	# individual with ischemic induced increase (max. 20)
PRDX2 Peroxiredoxin-2	IPI00027350	17
S100A9 Protein S100-A9	IPI00027462	17

TABLE 14-continued

Protein name	Protein accession numbers	# individual with ischemic induced increase (max. 20)
LTF Similar to Lactotransferrin	IPI00789477	14
Conserved hypothetical protein	IPI00883661	12
HBB Hemoglobin subunit beta	IPI00654755	12
NCOR2 CTG26 alternate open reading frame	IPI00006659	11
S100A8 Protein S100-A8	IPI00007047	11
SORL1 Sortilin-related receptor	IPI00022608	11
CA1 Carbonic anhydrase 1	IPI00215983	11
COL1A1 Collagen alpha-1(I) chain	IPI00297646	11
CAT Catalase	IPI00465436	11
ALB Isoform 1 of Serum albumin	IPI00745872	11
LOC729968 Conserved hypothetical protein	IPI00884334	11
CFI Complement factor I	IPI00291867	10
CPB2 Isoform 1 of Carboxypeptidase B2	IPI00329775	10
Ig heavy chain V-II region OU	IPI00382534	10
Ig kappa chain V-I region Ka	IPI00387095	10
COL1A2 130 kDa protein	IPI00873137	10
ECM1 Extracellular matrix protein 1	IPI00645849	10
LRP1 Prolow-density lipoprotein receptor-related protein 1	IPI0020557	9
LRP2 Low-density lipoprotein receptor-related protein 2	IPI00024292	9
C7 Complement component C7	IPI00296608	9
STX3 Isoform A of Syntaxin-3	IPI00395768	9
SERPINA1 Isoform 1 of Alpha-1-antitrypsin	IPI00553177	9
LOC440786 Ig kappa chain V-II region		
TEW	IPI00736885	9
Conserved hypothetical protein	IPI00847894	9
SERPINA10 Protein Z-dependent protease inhibitor	IPI00007199	8
PTPRK Isoform 1 of Receptor-type tyrosine-protein phosphatase kappa	IPI00015756	8
AMBP AMBP protein	IPI00022426	8
TF Serotransferrin	IPI00022463	8
C5 Complement C5	IPI00032291	8
ATRN Isoform 2 of Attractin	IPI00162735	8
C1QB complement component 1, q subcomponent, B chain	IPI00477992	8
CPN2 Carboxypeptidase N subunit 2	IPI00479116	8
SERPINA5 Plasma serine protease inhibitor	IPI00007221	7
LUM Lumican	IPI00020986	7
APOB Apolipoprotein B-100	IPI00022229	7
C1QC Complement C1q subcomponent subunit C	IPI00022394	7
SHBG Isoform 1 of Sex hormone-binding globulin	IPI00023019	7
SCN4B Isoform 1 of Sodium channel subunit beta-4	IPI00217376	7
MST1 Hepatocyte growth factor-like protein	IPI00292218	7
MDFI 19 kDa protein	IPI00385435	7
QSOX1 Isoform 2 of Sulfhydryl oxidase 1	IPI00465016	7
FETUB GUGU beta form	IPI00552199	7
SEPP1 selenoprotein P isoform 2	IPI00847381	7
HBA2; HBA1 Alpha 2 globin variant (Fragment)	IPI00853068	7
CPN1 Carboxypeptidase N catalytic chain	IPI00010295	6
AFM Afamin	IPI00019943	6
SOD1 Superoxide dismutase	IPI00218733	6
VTN Vitronectin	IPI00298971	6
SERPINA4 Kallistatin	IPI00328609	6
SERPINA4 Kallistatin	IPI00328609	6
PTPRK Protein tyrosine phosphatase, receptor type, K	IPI00552690	6
SERPINA3 Isoform 1 of Alpha-1-antichymotrypsin	IPI00847635	6
OU domain class 5 transcription factor 1 (Fragment)	IPI00868800	6
ORM1 orosomucoid 1	IPI00884926	6
F12 Coagulation factor XII	IPI00019581	5
APOA1 Apolipoprotein A-I	IPI00021841	5
IGFBP6 Insulin-like growth factor-binding protein 6	IPI00029235	5
FN1 Isoform 3 of Fibronectin	IPI00339223	5
g heavy chain V-III region CAM	IPI00382482	5
LOC388720 similar to ubiquitin and ribosomal protein S27a	IPI00397808	5
CLU clusterin isoform 1	IPI00400826	5
BTD Uncharacterized protein BTD (Fragment)	IPI00744685	5
PROS1 80 kDa protein	IPI00873445	5
SERPINF1 Pigment epithelium-derived factor	IPI00006114	4
C8G Complement component C8 gamma chain	IPI00011261	4
ORM1 Alpha-1-acid glycoprotein 1	IPI00022429	4
AHSG Alpha-2-HS-glycoprotein	IPI00022431	4
GGH Gamma-glutamyl hydrolase	IPI00023728	4
EFNB1 Ephrin-B1	IPI00024307	4
GPX3 Glutathione peroxidase 3	IPI00026199	4
HGFAC Hepatocyte growth factor activator	IPI00029193	4
CD14 Monocyte differentiation antigen CD14	IPI00029260	4

TABLE 14-continued

Protein name	Protein accession numbers	# individual with ischemic induced increase (max. 20)
FGA Isoform 2 of Fibrinogen alpha chain	IPI00029717	4
LRP1B Similar to Candidate tumor suppressor protein	IPI00032063	4
S100A7 Protein S100-A7	IPI00219806	4
C8B Complement component C8 beta chain	IPI00294395	4
DMXL1 DmX-like protein 1	IPI00294728	4
ARSB Arylsulfatase B	IPI00306576	4
LRP8 Isoform 3 of Low-density lipoprotein receptor-related protein 8	IPI00384247	4
HBA2; HBA1 Hemoglobin subunit alpha	IPI00410714	4
ASPN ASPN protein	IPI00418431	4
A2M Alpha-2-macroglobulin	IPI00478003	4
CDH3 Isoform 2 of Cadherin-3	IPI00645614	4
KLKB1 Plasma kallikrein	IPI00654888	4
SERPINA1 Isoform 2 of Alpha-1-antitrypsin	IPI00790784	4
ICAM2 28 kDa protein	IPI00793958	4
C1RL cDNA FLJ14022 fis, clone HEMBA1003538, weakly similar to COMPLEMENT C1R COMPONENT	IPI00795055	4
B2M B2M protein	IPI00796379	4
APOA1 Apolipoprotein A1	IPI00853525	4
Transthyretin	IPI00855916	4
ITIH3 Uncharacterized protein ITIH3	IPI00873416	4
MB 16 kDa protein	IPI00878623	4
SERPINF2 Alpha-2-antiplasmin	IPI00879231	4
COL5A2 Collagen alpha-2(V) chain	IPI00844306	4
JUP Junction plakoglobin	IPI00554711	4
PRG4 Isoform D of Proteoglycan-4	IPI00655676	4
GPR37 Probable G-protein coupled receptor 37	IPI00006166	3
F13B Coagulation factor XIII B chain	IPI00007240	3
CLEC3B Tetranectin	IPI00009028	3
C6 Complement component 6	IPI00009920	3
C8A Complement component C8 alpha chain	IPI00011252	3
DSP Isoform DPI of Desmoplakin	IPI00013933	3
COPS2 Isoform 2 of COP9 signalosome complex subunit 2	IPI00018813	3
F2 Prothrombin (Fragment)	IPI00019568	3
IGFALS Insulin-like growth factor-binding protein complex acid labile chain	IPI00020996	3
ACTG1 Actin, cytoplasmic 2	IPI00021440	3
FGA Isoform 1 of Fibrinogen alpha chain	IPI00021885	3
RBP4 Plasma retinol-binding protein	IPI00022420	3
RBP4 Retinol binding protein 4, plasma	IPI00022420	3
HPX Hemopexin	IPI00022488	3
NPR1 Atrial natriuretic peptide receptor A	IPI00027200	3
SEPP1 Selenoprotein P	IPI00029061	3
ZAK Isoform 2 of Mitogen-activated protein kinase kinase MLT	IPI00029643	3
CST3 Cystatin-C	IPI00032293	3
AZGP1 alpha-2-glycoprotein 1, zinc	IPI00166729	3
CA2 Carbonic anhydrase 2	IPI00218414	3
SELL L-selectin	IPI00218795	3
FGG Isoform Gamma-A of Fibrinogen gamma chain	IPI00219713	3
IGSF5 Immunoglobulin superfamily member 5	IPI00245940	3
LYVE1 Lymphatic vessel endothelial hyaluronin acid receptor 1	IPI00290856	3
SERPING1 Plasma protease C1 inhibitor	IPI00291866	3
C17orf13; ACYP1; C1R Complement C1r subcomponent	IPI00296165	3
F9 Coagulation factor IX	IPI00296176	3
FGB Fibrinogen beta chain	IPI00298497	3
LILRB2 leukocyte immunoglobulin-like receptor, subfamily B, member 2 isoform 1	IPI00303952	3
IGHG1 Putative uncharacterized protein DKFZp686N02209	IPI00384938	3
cDNA FLJ43303 fis, clone NOVAR2000136, moderately similar to Calsequestrin, skeletal muscle isoform	IPI00445889	3
IGHM IGHM protein	IPI00472610	3
PTGDS Prostaglandin D2 synthase 21 kDa	IPI00513767	3
GC Vitamin D-binding protein	IPI00555812	3
HP Haptoglobin	IPI00641737	3
LCN2 Lipocalin 2, Neutrophil gelatinase-associated lipocalin	IPI00643623	3
ITIH2 Inter-alpha (Globulin) inhibitor H2	IPI00645038	3
FETUB GUGU beta form, Fetuin-B	IPI00743766	3
HABP2 Hyaluronan-binding protein 2	IPI00746623	3
C1S Uncharacterized protein C1S	IPI00749179	3
LRP1B Low-density lipoprotein receptor-related protein 1B	IPI00877809	3
SERPIND1 Heparin cofactor 2	IPI00879573	3
APOA4 Apolipoprotein A-IV	IPI00304273	3
CDH22 Cadherin-22	IPI00000436	2

TABLE 14-continued

Protein name	Protein accession numbers	# individual with ischemic induced increase (max. 20)
TAF9 Transcription initiation factor TFIID subunit 9	IPI00002993	2
MBL2 Mannose-binding protein C	IPI00004373	2
CRISP3 cDNA FLJ75207	IPI00004798	2
EFNA4 Isoform 1 of Ephrin-A4	IPI00005125	2
COMT Isoform Membrane-bound of Catechol O-methyltransferase	IPI00011284	2
LRR4C Netrin-G1 ligand	IPI00014223	2
IGFBP7 Insulin-like growth factor-binding protein 7	IPI00016915	2
C1S Complement C1s subcomponent	IPI00017696	2
GGT1 Isoform 1 of Gamma-glutamyltranspeptidase 1	IPI00018901	2
PLG Plasminogen	IPI00019580	2
ORM2 Alpha-1-acid glycoprotein 2	IPI00020091	2
PLXNA3 Plexin-A3	IPI00020884	2
C4BPA C4b-binding protein alpha chain	IPI00021727	2
SERPINF3 Serpin B3	IPI00022204	2
BAI1 Brain-specific angiogenesis inhibitor 1	IPI00022333	2
HRG Histidine-rich glycoprotein	IPI00022371	2
APCS Serum amyloid P-component	IPI00022391	2
C1QA Complement C1q subcomponent subunit A	IPI00022392	2
C9 Complement component C9	IPI00022395	2
NRGN Neurogranin	IPI00022640	2
CDH1 Epithelial cadherin	IPI00025861	2
SOD3 Extracellular superoxide dismutase [Cu—Zn]	IPI00027827	2
KNG1 Isoform HMW of Kininogen-1	IPI00032328	2
PTH2 Tuberoinsulin peptide of 39 residues	IPI00059307	2
PTPRU protein tyrosine phosphatase, receptor type, U isoform 3	IPI00107472	2
PTPRF Receptor-type tyrosine-protein phosphatase F	IPI00107831	2
UBA52 ubiquitin and ribosomal protein L40 , UBB; RPS27A; UBC ubiquitin and ribosomal protein S27a	IPI00179330	2
UBB; RPS27A; UBC ubiquitin and ribosomal protein S27a	IPI00179330	2
TTN Isoform 7 of Titin	IPI00179357	2
CLCN6 Isoform A of Chloride channel protein 6	IPI00180121	2
HIST1H1C Histone H1.2	IPI00217465	2
MB Myoglobin	IPI00217493	2
HRC Sarcoplasmic reticulum histidine-rich calcium-binding protein	IPI00219226	2
SP140 Isoform LYSp100-A of Nuclear body protein SP140	IPI00219535	2
PTPRO Receptor-type tyrosine-protein phosphatase O	IPI00241041	2
CLU Clusterin	IPI00291262	2
SLC44A2 Isoform 2 of Choline transporter-like protein 2	IPI00293074	2
ITIH4 Isoform 1 of Inter-alpha-trypsin inhibitor heavy chain H4	IPI00294193	2
IGFBP2 Insulin-like growth factor-binding protein 2	IPI00297284	2
LTF Growth-inhibiting protein 12	IPI00298860	2
LCN2 Neutrophil gelatinase-associated lipocalin	IPI00299547	2
THBS4 Thrombospondin-4	IPI00328550	2
Ig heavy chain V-III region TEI	IPI00382494	2
VASN Vasorin	IPI00395488	2
FLG2 Ifapsoriasis	IPI00397801	2
SEMG1 Isoform 2 of Semenogelin-1	IPI00414684	2
IGHG1 Putative uncharacterized protein DKFZp686N02209	IPI00423466	2
HUWE1 Isoform 2 of E3 ubiquitin-protein ligase HUWE1	IPI00445401	2
PTPRK Protein tyrosine phosphatase, receptor type, K	IPI00470937	2
HP HP protein	IPI00478493	2
FCGR3A Fc fragment of IgG, low affinity IIIa, receptor for	IPI00640044	2
C2 Complement component 2	IPI00643506	2
CPN2 similar to Carboxypeptidase N subunit 2	IPI00738433	2
A1BG alpha 1 B-glycoprotein	IPI00745089	2
LOC732428 Uncharacterized protein ENSP00000375150	IPI00787862	2
SOD1 Uncharacterized protein SOD1	IPI00789078	2
CLEC3B Putative uncharacterized protein DKFZp686H17246	IPI00792115	2
8 kDa protein	IPI00792845	2
FCGR3B Protein	IPI00795501	2
C5 Complement component 5 variant (Fragment)	IPI00816741	2
PRAP1 Isoform 4 of Proline-rich acidic protein 1	IPI00855875	2
SH3BGR1 13 kDa protein	IPI00872670	2

Summary of Some of the Properties of Proteins
Discussed with Regard to Cohort II

A. Pigment Epithelium-Derived Factor
Name: PIGMENT EPITHELIUM-DERIVED FACTOR
IPI ID: IPI00006114
UniProtKB/Swiss-Prot ID: P36955
Length: 418 aa, molecular weight: 46342 Da
1. Basic Information from UniProtKB/Swiss-Prot Entry:

FUNCTION	Neurotrophic protein; induces extensive neuronal differentiation in retinoblastoma cells. Potent inhibitor of angiogenesis. As it does not undergo the S (stressed) to R (relaxed) conformational transition characteristic of active serpins, it exhibits no serine protease inhibitory activity.
SUBCELLULAR LOCATION	Secreted. Melanosome. Note = Enriched in stage I melanosomes.
PTM	The N-terminus is blocked. Extracellular phosphorylation enhances antiangiogenic activity.

2. Sequence:

(SEQ ID NO: 20)
MQALVLLLCIGALLGHSSCQNPASPPEEGSPDPDSTGALVEEDPFFKV
PVNKLAAAVSNFGYDLRYRSSMSPTTNVLLSPLSVATLSALSGLAEQR
TESIIHRLAYDLISSPDIHGTYKELLDVTAPQKNLKSASRIVFEKKL
RIKSSFVAPELKSQYGRPRVLGTGNPRDLQEIINWVQAQMGKLARSTKE
IPDEISILLGLVAHFKGQWVKFDSRKTSLEDIFYLDEERTVRVPMMSDP
KAVLRYGLSDSLCKIAQLPLTGSMSIIFFLPLKVTQNLTLIEESLTSE
FIHDIDRELKTVQAVLTVPKLSYEGEVTKSLQEMKLQSLFSDPDS
KITGKPIKLTQVEHRAGFEWNEDGAGTTPSPGLQPAHLTFPLDYHLNQ
PFIFVLRDSTDGALLFIGKILDRGP

3. Alternative Name(s): Serpin-F1, EPC-1

Has been used in treatment of retinal ischemic injury. As well, increased levels are observed with retinal diseases and diabetes but none have been related to heart disease including myocardial ischemia.

B. Protein S100-A7
Name: Protein S100-A7
IPI ID: IPI00219806
UniProtKB/Swiss-Prot ID: P31151

Length: 101 aa, molecular weight: 11471 Da
1. Basic Information from UniProtKB/Swiss-Prot Entry:

Subcellular location	Cytoplasm. Secreted.
Subunit structure	Interacts with RANBP9.

2. Sequence:

(SEQ ID NO: 21)
MSNTQAERSIIIGMIDMFHKYTRDDKIEKPSLLTMMKENFPNPLSACDK
KGTNYLADVFEKKDKNEKKIDFSEFLSLLGDIATDYHKQSHGAAPCS
GGSQ

3. Alternative Name(s): S100 Calcium-binding Protein A7; Psoriasin

This protein has not been linked to myocardial ischemia or events leading up to MI.

5 C. Protein S100-A8
Name: Protein S100 A8
IPI ID: IPI00007047
UniProtKB/Swiss-Prot ID: P05109
Length: 93 aa, molecular weight: 10835 Da

10 1. Basic Information from UniProtKB/Swiss-Prot Entry:
Function: Expressed by macrophages in chronic inflammations. Also expressed in epithelial cells constitutively or induced during dermatoses. May interact with components of the intermediate filaments in monocytes and epithelial cells.

2. Sequence:

(SEQ ID NO: 22)
20 MLTELEKALNSIIDVYHKYSLIKGNFHAVYRDDLLKLETECPQYIRKK
GADVWFKELDINTDGA VNFQEFLLILVIKMGVAHKKSHKE

3. Alternative Name(s):
S100 calcium-binding protein A8
25 Calgranulin-A
Migration inhibitory factor-related protein 8
Short name=MRP-8
Short name=P8

30 Cystic fibrosis antigen
Short name=CFAG
Leukocyte L1 complex light chain
Calprotectin L1L subunit
Urinary stone protein band A

35 This protein has not been linked to myocardial ischemia or events leading up to MI.

D. Protein S100-A9
Name: PROTEIN S100-A9
IPI ID: IPI00027462
UniProtKB/Swiss-Prot ID: P06702
Length: 114 aa, molecular weight: 13242 Da

1. Basic Information from UniProtKB/Swiss-Prot Entry:
Function: Expressed by macrophages in acutely inflamed tissues and in chronic inflammations. Seem to be an inhibitor of protein kinases. Also expressed in epithelial cells constitutively or induced during dermatoses. May interact with components of the intermediate filaments in monocytes and epithelial cells.
Subcellular location: cytoplasm and nucleus.

2. Sequence:

(SEQ ID NO: 23)
50 MTKMSQLERNIETIINTFHQYSVKLGHPDTLNQGEFKELVRKDLQNFL
KKENKNEKVI EHI MEDLDTNADKQLSFEEFIMLMARLTWASHEKMHE
GDEGPGHHHKPGLGEGTP

3. Alternative Name(s):
Full=S 100 calcium-binding protein A9;
60 Full=Calgranulin-B;
Full=Migration inhibitory factor-related protein 14;
Short=MRP-14;
Short=P14;
Full=Leukocyte L1 complex heavy chain;
Full=Calprotectin L1H subunit;

65 The mRNA levels of S100 A9 have been shown to increase after ischemic brain injury and after stroke. The protein level

was not determined. This protein has not been linked to myocardial ischemia or events leading up to MI.
E. Protein Tyrosine Phosphatase, Receptor Type, K
Name: PROTEIN TYROSINE PHOSPHATASE, RECEPTOR TYPE, K
IPI ID: IPI00552690
UniProtKB/TrEMBL ID: Q5JY45
Length: 202 aa, molecular weight: 22792 Da
Sequence:

(SEQ ID NO: 24)
MSSVEKETKTQCVRIATKAAATEEPEVDPKQTDREVVKIAGISAGI
LVFILLLLVVLIVKKRRSYYSYLLKAKKRKRDAMGNTRQEMTHMVN
AMDRSYADQSTLHAEDPLSITFMDQHNFSPRLPNDFLPTAVLDEN
HSATAESSRLLDVPRYLCEGTESPYQTGQLHPAIRVADLLQHINLMK
TSDSYGFKEEYE

This protein has not been linked to myocardial ischemia or events leading up to MI.
F. Protein Z-dependent Protease Inhibitor
Name: Protein Z-dependent protease inhibitor
IPI ID: IPI00007199
UniProtKB/Swiss-Prot ID: Q9UK55
Length: 484 aa, molecular weight: 55114 Da (of Precursor)
1. Basic Information from UniProtKB/Swiss-Prot Entry:

FUNCTION	Inhibits factor Xa activity in the presence of protein Z, calcium and phospholipid.
SUBCELLULAR LOCATION	Secreted.

2. Sequence:

(SEQ ID NO: 25)
MSRSTQELLGYHCRLQDKLQEQEGLAAEGRHSLASADHMKVVP SLLL
SVLLAQVWLVPGLAPSPQSPETAPQNTSRVVQAPKEEEEDEQEASEE
KASEEEKAWLMASRQQLAKETS NFGFSLLRKISMRHDGNMVFSPFGMSL
AMTGLMLGATGPETQIKRGLHLQALKPTKGLLPSLFKGLRETL SRNLE
LGLTQGSFAFIHKDFDKETFFNL SKRYFDTECVPMNFRNASQAKRLMN
HYINKETRGIKPKLFDEINPETKLI LVDYILFKGKWLTPFDVPFTEVDTF
HLDKYKTIKVPMMYGAGKFASTFDKNFRCHVLKLPYQGNATMLVVLMEK
MGDHLALEDYLT TDLVETWLRNMKTRNMEVFFPKFKLDQKYEMHELL
RQMGIRRIFSPFADLSELSATGRNLQVSRVLQRTVIEVDERGE TEAVAGIL
SEITAYSMPPVIKVD RPFHFIYEETSGMLLFLGRVVNPTLL

3. Alternative Name(s): Serpin A10

Protein Z was recently shown to act as an essential cofactor for protein Z-dependent protease inhibitor, a potent down-regulator of coagulation Factor Xa. Low levels of protein Z have been correlated with increased risk of stroke. However, protein Z dependent protease inhibitor was not studied. This protein has not been linked to myocardial ischemia or events leading up to MI.
G. Sodium Channel Subunit Beta-4
Name: ISOFORM 10F SODIUM CHANNEL SUBUNIT BETA-4
IPI ID: IPI00217376

UniProtKB/Swiss-Prot ID: Q81WT1-1
Length: 228 aa, molecular weight: 24969 Da (of Precursor)
1. Basic Information from UniProtKB/Swiss-Prot Entry:

5	FUNCTION	Modulates channel gating kinetics. Causes negative shifts in the voltage dependence of activation of certain alpha sodium channels, but does not affect the voltage dependence of inactivation (By similarity).
10	SUBCELLULAR LOCATION	Membrane; Single-pass type I membrane protein (Probable).

2. Sequence:

(SEQ ID NO: 26)
MPGAGDGGKAPARWLGTGLLGLFLLPVTL SLEVSVGKATDIYAVNGT
EILLPCTFSSCFGFEDLHFRWNTYSSDAFKILIEGTVKNEKSDPKVTLK
DDDRITLVGSTKEKMNNISIVLRDLEFSDTGKYTCHVKNPKENNLQHH
20 ATIFLQVVDRL EVDNTVTLLIILAVVGGVIGLLILILLIKKLIIFILKKT
REKKKECLVSSSGNDNTENGLPGSKAEKPPSKV

This protein has not been linked to myocardial ischemia or events leading up to MI.
H. Sortilin-Related Receptor
Name: SORTILIN-RELATED RECEPTOR
IPI ID: IPI00022608
UniProtKB/Swiss-Prot ID: Q92673
Length: 2214 aa, molecular weight: 248441 Da (of Precursor)
1. Basic Information from UniProtKB/Swiss-Prot Entry:

35	FUNTION	Likely to be a multifunctional endocytic receptor, that may be implicated in the uptake of lipoproteins and of proteases. Binds LDL, the major cholesterol-carrying lipoprotein of plasma, and transports it into cells by endocytosis. Binds the receptor-associated protein (RAP). Could play a role in cell-cell interaction.
40	SUBCELLULAR LOCATION	Membrane; Single-pass type I membrane protein (Potential).

2. Sequence:

(SEQ ID NO: 27)
45 MATRSSRRESRLPFLFTLVALLPPGALCEVWTLRHLGGSA PLPQDRGFLV
VQGDPRELRLWARGDARGASRADEKPLRRKRSALQPEPIKVYQVSLND
SHNQMVVHWAGEKSNVIVALARDSLALARPKSSDVVSYDYGKSFKKISD
50 KLNFG LGNRSEAVIAQFYHSPADNKRYIFADAYAQYLWITFDFCNTLQGF
SIPFRAADLLLHASKASNLLLGFD RSHPNKQLWKSDDFGQTWIMI QEHVKS
FSWGIDPYDKPNTIYIERHEPSGYSTVFRSTDFPQSRNQEVILEEVRDF
55 QLRDKYMFATKVVHLLGSEQQSSVQLWVSFGRKPMRAAQFVTRHPINEYY
IADASEDQVFCVSHSNRNTNLYISEA EGLKFSLSLENVLYYSPGGAGSD
TLVRYFANEFPADFHRVEGLQGVYIATLINGSMNEENMRSVITFDKGGTW
60 EFLQAPFTGYGEKINCELSQGC SLHLAQRSLQLNLQLRMRPILSKESA
PGLIIATGSGVGNLASKTNVYISSAGARWREALPGPHYTTWGDHGGIIT
AIAQGMETNELKYSTNEGETWTKTFIFSEKPVFVYGLLTPEGEKSTVFTIF
GSNKENVHSLILQVNATDALGV PCTENDYKLWSPSDERGNECLLGHKTV
FKRRTPHATCFNGEDFDRPVVVSNC SCTR EYECDFGFKMSEDLSLEV CV

69

-continued

PDPEFSKSYSPVPVPCVSGTYRRTGRYRKISGDTCSGGDVPEARLEGELV
 PCPLAEENEFILYAVRKSIYRYDLASGATEQLPLTGLRAAVALDFDYEHN
 CLYWSDLALDVIQRLCLNGSTGQEVIIINSGLTVEALAFEPLSQLLYWVD
 AGFKKIEVANPDGDFRLTIIVNSSVLDRPRALVLPQEGVMFWDWGD LKP
 GIYRSNMDGSAAYHLVSESVKWPNGISVDDQWIYWTDAYLECIERITFSG
 QQRSVILDNLPHPYAIAVFKNEIYWDWSQLSIFRASKYSGSQMEILANQ
 LTGLMDMKIFYKGKNTGSGNACVPRPCSLCLPKANNRSRSCRCPEDVSSSV
 LPSGDLMDCDPQGYQLKNNTCVKEENTCLRNQYRCSNGNCINSIWCDFD
 NDCGDMDSERNCPPTICDLDTQFRQCESGTCIPLSYKCDLEDDCGDNSDE
 SHCEMHQCRSDEYNCSGMCIRSSWVCDGDNDCRDWSDEANCTAIYHTCE
 ASNFQCRNGHCIPQRWACDGDTCQDGSDEDPVNCEKKCNGFRCPNGTCI
 PSSKHCDGLRDCSDGSDEQHCPELCTHFMDFVCKNRQQCLFHSMVCDGII
 QCRDGSDEDAFAGCSQDPEFHKVCDEFQGCQNGVCISLIWKCDGMDDC
 GDYSDEANCENPTEAPNCSRYFQRCENGHCIPNRWKCDRENDGCDWSDE
 KDCGDSHILPFPSTPGPSTCLPNYYRCSGTCVMDTWVCDGYRDCADGSDE
 EACPLLANVTAASPTQLGRCDRFEFECHQPKTCIPNWKRCDGHQDCQDG
 RDEANCPHTSTLTMSREFQCEDGEACIVLSERCDGFLDCSDESDEKACS
 DELTVYKVQNLQWTADPSGDVTLTWMRPMKMPASCVYVYRVVGESIW
 KTLETHSNKNTNTVLKVLKPDTTYQVKVQVQCLSKAHTNDNFVTLRTPGL
 PDAPRNLQLSLPREAEGVIVGHWAPPIHTHGLIREYIVEYSRSGSKMWAS
 QRAASNFTIKNLLVNTLYTVRVAAVTSRGIGNWSDSKSITTIKGVIPP
 PDIHIDSYGENYLSFTLTMSEDIKVNGYVNLFWAFDTHKQERRTLNFRG
 SILSHKVGNLTAHTSYEISAWAKTDLGDSPLAFEHVMTRGVRPPAPSLKA
 KAINQTAVECTWTGPRNVVYGYFATSFLLDLYRNPKSLTSLHNKTVIVS
 KDEQYLFVLRVVVYQGPSSDYVVMKIPDSRLPPRHLHVHTGKTSVVI
 KWESPYDSPDQDLLEYAIAVKDLIRKTDTSYKVKSRNSTVEYTLNKLEPGG
 KYHIIVQLGNMSKSSIKITTVSLSAPDALKIITENDHVLLFWKSLALKE
 KHFNESRGYIEHMFDSAMNITAYLGNTTDNFFKISNLKMGHNYTFTVQAR
 CLFGNQICGEPAILLYDELGSADASATQAARSTDAVAVVVPILFLILLS
 LGVGFAILYTKHRLQSSFTAFANSHYSSRLGSAIFSSGDDLGEDDEDAP
 MITGFSDDVPMVIA

3. Alternative Name(s):

Sorting protein-related receptor containing LDLR class A repeats

Short name= SorLA

SorLA-1

Low-density lipoprotein receptor relative with 11 ligand-binding repeats

Short name= LDLR relative with 11 ligand-binding repeats

Short name= LR11

This protein has not been linked to myocardial ischemia or events leading up to MI.

70

I. Conserved Hypothetical Protein

Name Conserved hypothetical protein

IPI ID: IPI00884334

Length: 168 aa, molecular weight: 18798 Da

5 Sequence:

(SEQ ID NO: 28)
 MRSFLLVWKLFRKDKMKHQRKTATEFKTTEEGETRQDGKDGSLTYRADT
 10 CSPCEAGGPPSSSIASGSSISVGNPSHSHSHTSRRCGSSRSRECCS
 SLHSSRSGSRGSSWSSPPGSTCRWCSCSHHHHSHRSHRSHHCSHH
 HSHHSHGHSHHNFHNHNSNPWCQ

15 This protein has not been linked to myocardial ischemia or events leading up to MI.

J. Catalase

Name: Catalase

IPI ID: IPI00465436

UniProtKB/Swiss-Prot ID: P04040

20 Length: 527 aa, molecular weight: 59756 Da

1. Basic Information from UniProtKB/Swiss-Prot Entry:

Function	Occurs in almost all aerobically respiring organisms and serves to protect cells from the toxic effects of hydrogen peroxide. Promotes growth of cells including T-cells, B-cells, myeloid leukemia cells, melanoma cells, mastocytoma cells and normal and transformed fibroblast cells.
Subcellular location	Peroxisome.

2. Sequence:

(SEQ ID NO: 29)
 35 MADSRDPASDQMQHWEQRAAQKADVLTGAGNPVGDKLNVITVGPRG
 PLLVQDVVFTDEMAHFDRERI PERVVHAKGAGAFGYFEVTHDITKYSKAK
 VFEHIGKKTPIAVRFSTVAGESGSADTVRDPGRFAVKFYTEDGNWDLVGN
 40 NTPIFFIRDPIILFPSFIHSQKRNPQTHLKDPMVWDFWSLRPESLHQVSF
 LFSDRGIPDGHHRMNGYGSHTFKLVNANGEAVYCKPHYKTDQGIKNLSVE
 DAARLSQEDPDYGI RDLFNIAIATGKYPSWTFYIQVMTFNQAEFTFPFNPF
 45 LTKVWPHKDYPLIPVGKLVLRNPNVNYFAVEVEQIAFDPSNMPPGIEASPD
 KMLQGRLEFAYPDTHRHRLGPNYLHIPVNCYPYRVRVANYQRDGPMPQDN
 QGGAPNYPNPSFGAPEQQPSALEHSIQYSGEVRRFNTANDNVTQVRAF
 50 YVNVLNEEQRKRLCENIAGHLKDAQIFIQKKA VKNFTEVHPDYGSHIQA
 LLDKYNAEKPKNAIHTFVQSGSHLAAREKANL

Catalase is an important enzyme in the heart's regulation of oxidative stress. It has been linked to preconditioning in the heart tissue. As a serum marker, it has not been linked to myocardial ischemia or events leading up to MI.

K. Conserved Hypothetical Protein

Name: Conserved hypothetical protein

IPI ID: IPI00883661

UniProt/TrEMBL ID: A6NFT5

Length: 175 aa, molecular weight: 20933 Da

2. Sequence:

(SEQ ID NO: 30)
 MNIIHTCMHIYTHAHTHAHIHTCIHTHTMHHTLTLYTHIHMHTHTQTH
 65 IYTAHIHSCTQINIYTYATLTCTQTHTHICTHAHTLTLYTHIHTCTYKR

-continued

TYIQGHIHMHMTYTCTCTHTHKHHAHIIHHTHTHTDAYTHMDTY
THTYPTHICIHSHTHAHTYTHIRT

This protein has not been linked to myocardial ischemia or events leading up to MI.

L. Glutathione peroxidase 3

Name: Glutathione peroxidase 3

IPI ID: IPI00026199

UniProtKB/Swiss-Prot ID: P22352

Length: 226 aa, molecular weight: 25505 Da

1. Basic Information from UniProtKB/Swiss-Prot Entry:

FUNCTION	Protects cells and enzymes from oxidative damage, by catalyzing the reduction of hydrogen peroxide, lipid peroxides and organic hydroperoxide, by glutathione.
SUBCELLULAR LOCATION	Secreted.
TISSUE SPECIFICITY	Secreted in plasma.

2. Sequence:

(SEQ ID NO: 31)
MARLLQASCLLSLLLAGFVSQSRGQEKSKMDCHGGISGTIYEYGALTIDG
EEYIPFKQYAGKYVLFVNVASYCGLTGQYIELNALQEELAPFGLVILGFP
CNQFGKQEPGENSEILPTLKYVRPGGGFVPNFQLFEKGDVNGEKEQKFYT
FLKNSCPPTSELLGTSDRLEFWPEMPKVHDIRWNFEKFLVGPDGIPIMRWHH
RTTVSNVKMDILSYMRQAALGVKRK

3. Alternative Name(s):

GSHPx-3

Short name=GPx-3

Extracellular glutathione peroxidase

Plasma glutathione peroxidase

GSHPx-P

Short name=GPx-P

GPx 3 is an important enzyme involved in many cells regulation of oxidative stress. As a serum marker it has not been linked to myocardial ischemia or events leading up to MI.

M. Hepatocyte Growth Factor Activator

Name: HEPATOCYTE GROWTH FACTOR ACTIVATOR

IPI ID: IPI00029193

UniProtKB/Swiss-Prot ID: Q04756

Length: 655 aa, molecular weight: 70682 Da (of Precursor)

1. Basic Information from UniProtKB/Swiss-Prot Entry:

FUNCTION	Activates hepatocyte growth factor (HGF) by converting it from a single chain to a heterodimeric form.
SUBCELLULAR LOCATION	Secreted. Note = Secreted as an inactive single-chain precursor and is then activated to a heterodimeric form.

2. Sequence:

(SEQ ID NO: 32)
MGRWAWVSPWPPPGGLGPFLLLLLLLLLLPRGFQPGGNRTESPEPNAT
ATPAIPTILVTSVTSPTATSAPEAGPQSGGLPPPPRAVPSSSSPQAQA
LTEDGRPCRFPFRYGGRLHACTSEGSahrKWCATTHNYDRDRAWGYCVC

-continued

ATPPPGGPAALDPCASGPCNLNGGSCSNTQDPQSYHCSCPRAFTGKDCGTE
KCFDETRYEYLEGGDRWARVRQGHVEQCECFGGRTWCEGTRHTACLSSPC
LNGGTCHLIVATGTTVCACPPGFAGRLCNIEPDERCFLNGTGYRGVAST
SASGLSCLAWNSDLLYQELHVDVSGAAALLGLGPHAYCRPNPDERPWCY
VVKDSALSWEYCRLEACESLTRVQLSPDLLATLPEPASPGRQACGRRHKK
RTFLRPRIIGGSSSLPGSHPLAAIYIGDSFCAGSLVHTCWVVSAAHCFS
HSPPRDSVSVVLGQHFFNRRTDVTQTFTGIEKYIPYTLVSFNPSDHDLVL
IRLKKKGDRCATRSQFVQPICLPEPGSTFPAGHKCQIAGWGHLDENVSGY
SSSLREALVPLVADHKCSSPEVYGADISPNMLCAGYFDCKSDACQGDSSG
PLACEKNGVAYLYGIISWGDGCGRLHKPGVYTRVANYVDWINDRIRPPRR
LVAPS

This protein has not been linked to myocardial ischemia or events leading up to MI.

N. Hepatocyte Growth Factor-Like Protein Homolog

Name: HEPATOCYTE GROWTH FACTOR-LIKE PROTEIN HOMOLOG

IPI ID: IPI00292218

UniProtKB/TrEMBL ID: B7Z557

Length: 697 aa, molecular weight: 78787 Da

Sequence:

(SEQ ID NO: 33)
MLRGPCSPLNDFQVLRGTQLHLLHAVVPGPWQEDVADAEACAGRCGLPM
DCRAFHYNVSSHGCQLLPWTQHSPTHRLRRSGRCDLFQKKDYVRTCIMNN
GVGYRGTMATTVGGLPCQAWSHKFPNDHKYTPTRLNGLEENFCRNPDGDP
GGPWCYTTDPAVRFQSCGIIKSCREAAVCWCNGEEYRGAVDRTESGRECQR
WDLQHPHQHPFEPGKFLDQGLDDNYCRNPDGSERPWCYTTDQPIERFCD
LPRCGSEAQPRQEATTVSCFRKGEGYRGANTTTAGVPCQRWDAQIPHQ
HRFTPEKYACKDLRENFCRNPDGSEAPWCFTLRPGMRAAPCYQIRRCTDD
VRPQDCYHGAGEQYRGTVSKTRKGVQCQRWSAETPHKPQFTFTSEPHAQL
EENFCRNPDGDSHGPPWCYTMDPRTPFDYCALRRCADDQPPSILDPDPQVQ
FEKCGKRVDRLDQRRSKLRVVGHPGNSPWTSLRNRQGHQFCGGSVLKE
QWILTARQCFSSCHMPLTGFEVWLGLTFQNPQHGEPSLQRPVPAKMCVCGP
SGSQLVLLKLEERSVTLNQRVALICLPPWYVVPVPGTKCEIAGWGETKGTG
NDTVLNVALLNVI SNQECNIKHRGRVRESEMCTEGLLAPVGACEGDYGGP
LACFTHNCWVLEGIIPNRVCARSRWPAVFTRVSVFVDWIHKVMRLG

This protein has not been linked to myocardial ischemia or events leading up to MI

O. Insulin-Like Growth Factor-Binding Protein 6

Name: INSULIN-LIKE GROWTH FACTOR-BINDING PROTEIN 6

IPI ID: IPI00029235

UniProtKB/Swiss-Prot ID: P24592

Length: 240 aa, molecular weight: 25322 Da (of Precursor)

1. Basic Information from UniProtKB/Swiss-Prot Entry:

FUNCTION	IGF-binding proteins prolong the half-life of the IGFs and have been shown to either inhibit or stimulate the growth promoting effects of the IGFs on cell culture.
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SUBCELLULAR LOCATION	They alter the interaction of IGFs with their
	cell surface receptors.
Secreted.	

2. Sequence:

(SEQ ID NO: 34)
MTPHRLLPPLLLLLALLLAASPGGALARCPGCGQGVQAGCPGGCVEEDG
GSPAEGCAEAGCLRREGQECGVYTPNCAPGLQCHPPKDDEAPLRALLG
RGRCLPARAPAVAEENPKESKPGAGTARPDVNRRDQQRNPGTSTTPSQP
NSAGVQDTEMGPCCRHLDSVLQQLQTEVYRGAQTLVVPNCDSHRGFRKQ
CRSSQGGRRGPCWCVDRMGKSLPGSPDGNSSSCPTGSSG

3. Synonym: IBP-6

In a swine model of myocardial injury, studied at 3-24, 72, or 168 hrs, it was shown that there was an increased level of mRNA of IGFBP-6 at all time points. In situ hybridisation identified myocytes as the main producers of IGFBP-6 mRNA. However, the protein itself was not investigated. As well, this protein was found to be elevated in a young multiple myeloma patient with high-output cardiac failure. To date, there has been no study indicating the association of this protein with myocardial ischemia or events leading up to MI.
P. Conserved Hypothetical Protein
Name: Conserved hypothetical protein
IPI ID: IPI00847894
Length: 88 aa, molecular weight: 9931 Da
Sequence:

(SEQ ID NO: 35)
MFTLRLFAGKACWFLVLYTMLKEVTCDDVCVVRARCTCMCMVCECMDVC
VRLYTMLKEVTCDDVCARTCVHVCVSAWMCVCTCTQC

This protein has not been linked to myocardial ischemia or events leading up to MI.
Q. Isoform 1 of Receptor-Type Tyrosine-Protein Phosphatase Kappa
Name: ISOFORM 10F RECEPTOR-TYPE TYROSINE-PROTEIN PHOSPHATASE KAPPA
IPI ID: IPI00015756
UniProtKB/Swiss-Prot ID: Q15262-1
Length: 1439 aa, molecular weight: 162102 Da (of Precursor)
1. Basic Information from UniProtKB/Swiss-Prot Entry:

FUNCTION	Regulation of processes involving cell contact and adhesion such as growth control, tumor invasion, and metastasis. Forms complexes with beta-catenin and gamma-catenin/plakoglobin. Beta-catenin may be a substrate for the catalytic activity of PTP-kappa.
SUBCELLULAR LOCATION	Cell junction, adherens junction. Cell membrane; Single-pass type I membrane protein.

2. Sequence:

(SEQ ID NO: 36)
MDTTAAALPAFVALLLLSPWLLGSAQGQFSAGGCTFDDGPGACDYHQD
LYDDFEWVHVSAQEPHYLPPEMPQGSYIMVDS SDHDPGEKARLQLPTMKE
NDTHCIDFSYLLYSQKGLNPGTLNII LVRVNGPLANPIWNVTGFTGRDWL

-continued

RAELAVSTFWPNEYQVIFAEVSGGRSGYIAIDDIQVLSYPCDKSPHFLR
LGDVEVNAGQNFATFQCIATGRDAVHNKLWLQRRNGEDIPVAQTKNINHRR
5 FAASFRLQEVTKTDQDLRYCVTQSERGSGVSNFAQLIVREPPRIAPPQL
LGVGPTYLLIQLNANSIIGDGPIILKEVEYRMTSGSWTETHAVNAPTYKL
WHLDPDTEYEIRVLLTRPGEGGTGLPGPPLITRTKCAEPMRTPKTLKIAE
10 IQARRIAVDWESLGYNITRCHTFNVTICYHYFRGHNSKADCLMDMPKAP
QHVVNHLPPYTNVSLKMLTNPEGRKESEETIIQTDEDVPGVPVKSQSG
TSFENKIFLNWKEPLDPNGIITQYEISYSSIRSFDPAPVPAGPPQTVSNL
15 WNSTHHVFMHLHPGTTYQFFIRASTVKGFGPATAINVTNISAPTLPDYE
GVDASLNETATTITVLLRPAQAKGAPISAYQIVVEELHPHRTKREAGAME
CYQVPVITYQNAMSGGAPYFAAELPPGNLPEPAPFTVGNRTYQGFWNPP
20 LAPRKGYNIFYQAMSSVEKETKTQCVRIATKAATEEPEVIDPAKQTDTRV
VKIAGISAGILVFIILLVILVKKSKLAKKRKADAMGNTRQEMTHMVNA
MDRSYADQSTLHAEDPLSITFMDQHNFSPRYENHSATAESSRLLDVPRYL
25 CEGTESPYQTGQLHPAIRVADLLQHINLMKTSDSYGFKEEYESFFEGQSA
SWDVAKKDQNRKNRYGNIIAYDHSRVI LQPVEDDPSSDIYINANYIDGYQ
RPSHYIATQGPVHETVYDFWRMIWQEQSACIVMVTNLVEVGRVKCYKYWP
30 DDTEVYGDVKVTCVEMEPLAEYVVRTFTLERRGYNEIREVKQFHFTGWD
HGVPHYATGLLSFIRRVKLSNPPSAGPIVHVSAGAGRTGCYIVIDIMLD
MAEREGVVDIYNCVKALRSRRINMVQTEEQYIFIHDAILEACLGETAIP
35 VCEFKAAFYDMIRIDSQTNSSHLKDEFQTLNSVTPRLQAEDCSIACLPRN
HDKNRFMDMLPPDRCLPFLITIDGESSNYINAAALMDSYRQPAAFIVTQYP
LPNTVKDFWRLVYDYGCTSI VMLNEVDLSQGCQPYWPEEGMLRYGPIQVE
40 CMSCSMDCDVINRIFRICNLTRPQEGYLMVQQFQYLGWASHREVPGSKRS
FLKLILQVEKWQEECEEGEGRTIIHCLNGGGRSGMFCAIGIVVEMVKRQN
VVDVFHAVKTLRNSKPNMVEAPEQYRFCYDVALEYLESS
45

This protein has not been linked to myocardial ischemia or events leading up to MI.

R. Isoform 2 of Attractin
Name: ISOFORM 20F ATTRACTIN
IPI ID: IPI00162735
UniProtKB/Swiss-Prot ID: O75882-2

Length: 1272 aa, molecular weight: 141429 Da (of Precursor)
1. Basic Information from UniProtKB/Swiss-Prot Entry:

FUNCTION	Involved in the initial immune cell clustering during inflammatory response and may regulate chemotactic activity of chemokines. May play a role in melanocortin signaling pathways that regulate energy homeostasis and hair color. Low-affinity receptor for agouti (By similarity). Has a critical role in normal myelination in the central nervous system (By similarity).
SUBCELLULAR LOCATION	Secreted.

2. Sequence:

(SEQ ID NO: 37)

MVAAAAATEARLRRRTAATAALAGRSGGPHWDVTRAGRPLGAGLRPL
RLLSPPLRPLRLLLLLLLLLSPPLLLLLLPCAEAAAAAAVSGSAAAEAKE
CDRPCVNGGRCPNPGTGQVCVCPAGWVGEQCQHCGRFRLTGSSGFVTDGPG
NYKYKTKCTWLI EGQPNRIMRLRFNFHATECSWDHLYVVDGDSIYAPLVA
AFSGLIVPERDGNETVPEVATSGYALLHFFSDAAYNLTFGNI TYSFDMC
PNNCSGRGECKI SNSSDTVECECSENWKGACDI PHCTDNCGFPHRGICN
SSDVRGCSCFSDWQPGCSPVPANQSFWTREYSNLKLPRASHKAVVNG
NIMVVGGYMFNHSDDYMNVLAYDLASREWLPLNRSVMNVVRYGHSLALY
KDKIYMYGGKIDSTGNVTNELRVFHIHNSWVLLTPKAKEQYAVVGHSAH
IVTLKNGRVVMLVIFGHCPYGYISNVQYEDLDKNTWSILHTQGALVQGG
YGHSSVDHRTRALYVHGGYKAFSANKYRLADDLYRYDVTQMWTILKDS
RFFRYLHTAVIVSGTMLVFGGNTHTDTSMSHGAKCFSSDFMAYDIACDRW
SVLPRPDLHHDVNRFGHSAVLHNSTMYVFGGFNSLLSDILVFTSEQCDA
HRSEAACLAAGPGIRCWNTGSSQCISWALATDEQEELKSECFKRTLD
HDCDQHTDCYCTANTNDCHWCNDHCVPRNHSCSEGQISIFRYENC PKD
NPMYYCNKKTSCRSALDQNCQWEPNQEIALPENICGIGWHLVGNLCL
KIT TAKENYD NAKLFCRNHNALLASLTQKKVEFVLKQLRIMQSSQSMK
LTLTPWVGLRKINVS YCWEDMSPTNSLLQWMPSEPSDAGFCGILSEPS
TRGLKAATCINPLNGSV CERPANHSAKQCRTPCALRTACGDC TSGSSECM
WCSNMKQCVDSNAYVASFPFGQCMEWYTMSTCPPENC SGYCTCSHCLQP
GCGWCTDPSNTGKGKCI EGSYKGPVKMPSQAPTGNFY PQLLNSMCLED
SRYNWSFIHC PACQCNHGSKCINQSI CEKCNLTGKHCE TCSIGFYGDP
TNGGKCQPCCKNGHASLCNTNTGKCFCTTKGVKGDECQLCEVENRYQGNP
LRGTCCYTTLLIDYQFTFSLSQEDDRYTTAINFVATPDEQNRDLDMFINAS
KNFNLNITWAASFSAGTQAGEEMPVVS KTN IKEYKDSFSNEKDFRNHPN
ITFFVYVSNFTWPIKIQVQTEQ

3. Alternative Name(s): Mahogany homolog; DPPT-L
This protein has not been linked to myocardial ischemia and events leading up to MI.
S. Isoform a of Syntaxin-3
Name: Syntaxin-3 (STX3A)
IPI ID: IPI00395768
UniProtKB/Swiss-Prot ID: Q13277-1 and Q13277-2
Length: 289 aa, molecular weight: 33155 Da-----
Q13277-1
1. Basic Information from UniProtKB/Swiss-Prot Entry:

FUNCTION	Potentially involved in docking of synaptic vesicles at presynaptic active zones.
SUBCELLULAR LOCATION	Membrane; Single-pass type IV membrane protein (Potential).

2. Sequence:

(SEQ ID NO: 38)

5 MKDRLEQLKAKQLTQDDDDTDAVEIAIDNTAFMDEFFSEIETRLNIDKIS
EHVEEAKKLYSIIISAPIPEPKTKDDLEQLTTEIKKRANVRNKLKSMK
HIEEDEVRSSADLRIRKSQHSVLSRKFVEVMKYNEAQVDFRERSKGRIQ
RQLEITGKKTDEELEEMLESGNPAIFTSGIIDSQISKQALSEIEGRHKD
10 IVRLESSIKELHDMFMDIAMLVENQGEMLDNIELNMHTVDHVEKARDET
KKAVKYQSQARKKLI I IIVLVVLLGILALIIGLSVGLN
This protein has not been linked to myocardial ischemia and events leading up to MI.
T. Lactotransferrin
Name: Lactotransferrin
IPI ID: IPI00789477
UniProtKB/TrEMBL ID: B2MV14, B7Z4X2
Length: 666 aa, molecular weight: 73161 Da
Sequence:

(SEQ ID NO: 39)

25 MRKVRGPPVSCIKRDSPIQCIQAIENRADAVTLDDGGFIYEAGLAPYKLR
PVAAEVYGTERRPRTHYYAVAVVKGGSFQNLQGLKSCHTGLRRRTAGW
NVPIGTLRPFNLNWTGPPEPIEA AVARFFSASCVP GADKGQFPNLCRLCAG
30 TGENKCAFSSQEPYFSYSGAFKCLRDGAGDVA FIRESTVPEDLSDEAERD
EYELLCPDNTRKPVDFKFDCHLARVP SHAVVARSVNGKEDAIWNLLRQAQ
EKFGKDKSPKFQLFGPSGQKDLLFKDSAIGFSRVPPRIDSGLYLGSYGF
35 TAIQNLRKSEEEVAARRARVVWCAVGEQELRKCNQWSGLSEGSVTCSSAS
TTEDCIALLVLKGEADAMSLDGGYVYTAGKCLVPVLAENYKSQQSSDPDP
NCVDRPVEGYLAVAVVRRSDTSLTWN SVKGKKSCHTAVDRTAGWNIPMGL
LFNQTGSCCKFDEYFSQSCAPGSDPRSNLCALCIGDEQGENKCVPSNERY
40 YGYTGAPRCLAENAGDVA FVKDVTVLQNTDGNNEAWAKDLKLADFALLC
LDGKRKPVTEARSCHLAMAPNHAVVSRMDKVERLKQVLLHQQAKFGRNGS
DCPDKFCLFQSETKNLLFNDNTECLARLHGKTTYEKLGPQYVAGITNLK
45 KCSTSPLLEACEFLRK

Levels have been shown to increase with leukocyte activation. Therefore, there are increases found during ischemic stroke, following by-pass surgery and after direct stenting in patients with angina. However, no studies that have linked this protein to myocardial ischemia or events leading up to MI.
U. Low-Density Lipoprotein Receptor-Related Protein 2
Name: LOW-DENSITY LIPOPROTEIN RECEPTOR-RELATED PROTEIN 2
55 IPI ID: IPI00024292
UniProtKB/Swiss-Prot ID: P98164
Length: 4655 aa, molecular weight: 521958 Da (of Precursor)
1. Basic Information from UniProtKB/Swiss-Prot Entry:

FUNCTION	Acts together with cubilin to mediate HDL endocytosis (By similarity). May participate in regulation of parathyroid-hormone and para-thyroid-hormone-related protein release.
SUBCELLULAR LOCATION	Membrane; Single-pass type I membrane protein. Membrane, coated pit.

2. Sequence:

(SEQ ID NO: 40)

MDRGPAAVACTLLALLVACLAPASGQECDSAHFRCGSGHCIPADWRCGT

KDCSDDADEIGCAVVTCQQGYFKCQSEGQCIPNSWVCDQDQDCDDGSDER

QDCSQSTCSSHQITCSNGQCIPSEYRCDHVRDCPDGADENDCQYPTCEQL

TCDNAGACYNTSQKCDWKVDCRDSDEINCTEICLHNEFSCGNGECIPRAY

VCDHDNDCQDGSDEHACNYPTCGGYQFTCPSGRCIYQNWVCDGEDDCKDN

GDEDGCEGPHDVHKCSPREWSCPESGRCSIIYKVC D GILD CPGREDENN

TSTGKYCSMTLCSALNCQYCHETPYGGACFCPPGYIINHNSRTEVEFD

DCQIWIGICDQKCESRPGRLCHCEEYILERGQYCKANDSFGEASIIFSN

GRDLLIGDIHGRSFRILVESQNRGVAVGVAPHYHLQRVFWTDTVQNKVFS

VDINGLNIQEVLNVS VETPENLAVDWVNNKIYLVETKVNRI DMVNLDGSY

RVTLITENLGHPRGIAVDPTVGYLFFSDWESLSGEPKLERAFMDGSNRKD

LVKTKLGWPAGVTLDMI SKRVYVWDSRFDIETVTYDGIQRKTVVHGGS

IPHPFGVSLFEGQVFFTDWTKMAVLKANKFTETNPQVYYQASLRPYGTV

YHSLRQPYATNPCKDNNNGCEQCVLSHRTDNDGLGFRCKCTFGQLD

ERHCIAVQNFLIFSSQVAIRGIPFTLSTQEDVMVPVSGNPSFFVGIDFDA

QDSTIFFSDMSKHMIFKQKIDGTGREILANRVENVESLAFDWISKNLW

TDSHYKISIVMLADKTRRTVVQYLNPNRSVVVHPFAGYLFPTDWFRAK

IMRAWSDGSHLLPVINTTLGWPNGLAIDWAASRLYWDAYFDKIEHSTFD

GLDRRLIGHIEQMTHPFLAIFGEHLFFTDWRLGAIIRVRKADGGEMTVI

RSGIAYILHLKSYDVNIQTGSNACNQPTHNGDCSHFCFPVPNFQRVCGC

PYGMRLASNHLTCEGPTNEPPEEQCGLFSFPCKNGRCVPNYLDCGVDD

CHDNSDEQLCGTLNNTCSSAFTCGHGECIPAHWRCDKRND CVDGSD EHN

CPHAPASCLDTQYTCDNHQCISKWVCDTDNDCGDGSDEKNCNSTETCQ

PSQNPCPNHRCIDLSFVCDGDKCVDGSDDEVGCVLNCTASQFKCASGDKC

IGVTNRCDGVFDCSDNSDEAGCPTRPPGMCHSDEFQCCQEDGICIPNFWEC

DGHPDCLYGSDEHNACVPKTCPSYFHCNDNGNCIHRWLCDRDND CGDMS

DEKDCPTQPPRCPSWQWQCLGHNICVNL SVVCDGIFDCPNGTDESPLCNG

NSCSDFNNGGCTHECVQEPFGAKCLCPLGFLLANDSKTCEDIDECDILGSC

SQHCYNMRGSFRSCDTGYMLES DGRCTKV TASESLLL LVASQNKIIADS

VTSQVHNIYSLVENGSYIVAVDPDSISGRIFWSDATQGKTWSAFQNGTDR

RVVFDSSIILTETIAIDWGRNLYWTDYALETIEVSKIDGSHRTVLISKN

LTNPRGLALDPRMNEHLLFWSDWGHPRIERASMDGSMRTVIVQDKIFWP

CGLTIDYPNRLLYFMDSYLDYMDFCYNGHHRRQVIASDLIIRHPYALTL

FEDSVYWTDRATRVRMRANKWHGGNQSVVMYNIQWPLGIVAVHPSKQPN

VNPCAFCRSHLCLLSSQGPHFYSCVCPSGWSLSPDLLNCLRDDQPFLLIT

VRQHIIFGISLNPEVKSNDAMVPIAGIQNGLDVEFDDAEQYIYWVENPGE

IHRVKTDTGTRNTVFASISMVGPMMNLALDWISRNLYSTNPRQTQSIEVLT

HGDIRYKTLIANDGTALGVGFPIGITVDPARGKLYWSDQGTDSGVPAKI

ASANMDGTSVKTLFTGNLEHLECVTLDIEEQKLYWAVTGRGVIERNVDG

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TDRMILVHQLSHPWGI AVHDSFLYYTDEQYEVIERVDKATGANKIVLRDN

VPNLRGLQVYHRRNAAESSNGCSNNMNACQQICLPVPGGLFSCACATGFK

LNPDNRS CSPYNSFI VVSMLS AIRGFSLELSDHSETMVPVAGQGRNALHV

DVDVSSGFIYWCD FSSSVASDN AIRRIKPDGSSLMNIVTHGIGENGVRGI

AVDWVAGNLYFTNAFVSETLIEVLRINTTYRRVLLKVTVDMPRHIVVDPK

NRYLFWADYGRPKIERSFLDCTNRTVLVSEGIVTPRGLAVDRSDGYVYW

VDDSLDIIARIRINGENSEVIRYGSRYPTPYGITVFENSIIWVDRNLKKI

FQASKEPENTEPTTVIRDNINWLRDVTIFDKQVQPRSPAENVNNPCLENN

GGCSHLCFALPGLHTPKCDCAFGLTQSDGKNCAISTENFLIFALSNSLRS

LHLDPENHSPFPQTINVERTVMSLDYDSVSDRIYFTQNLASGVGQISYAT

LSSGIHTPTV IASGIGTADGIAFDWITRRIYYSDYLNQMINMAEDGSNR

TVIARVPKPRAIVLDP CQGYLWADWDTHAKIERATLGGNFRVPIVNSSL

VMPGSLTLDYEEDLLYWVDASLQRIERSTLTGVDRREVIVNAVHAFGLTL

YGQYIYWTDLTYTQRIYRANKYDGSQIAMTNNLSQPRGINTVVKNQKQQ

TCNNPCEQFNNGGCSHICAPGPNGAECQCPHEGNWYLANNRKHCIVDNGER

CGASSFCSNGRCISEWKCDNDND CGDGSDEMESVCLHTCSPTAFTCAN

GRCVQYSYRCDYYND CGDGSDEAGCLFRDCNATTEFCMNNRRCIPREFIC

NGVDNCHDNNSTDEKNC PDRTCQSGYTKCHNSNICIPRVLYCDGDND CGD

NSDENPTYCTTHTCSSEFQCASGRICIPQHWYCDQETDCFDASDEPASC

HSERTCLADEFKCDGGRICIPSEWICDGDND CGDMSDEDKRHQCNQNCSD

SEFLCVNDRPPDRRCIPQSWVCDGDVDC TDGYDENQNTTRTCSENEFTC

GYGLCIPKIFRCDRHND CGDYSDERGCLYQTCQQNQFTCQNGRCISKTFV

CDEDND CGDGSDELMHLCHTPEPTCP PHEFKCDNGRCIEMMKLCNLHDDC

LDNSDEKGC GINECHDPSISGCDHNC TDLT SFYCS CRPGYKLMSDKRTC

VDIDECTEMP FVCSQKCE NVIGSYICKAPGYLREP DGKTCRQNSNIEPY

LIFSNRYLRNLITIDGYFYSLILEGLDNVVALDFRVEKRLYWDITQRQV

IERMFLNKTNKETIINHRLPAESLAVDWVSRKLYWLDARLDGLFVSDLN

GGHRRMLAQHCVDANNTFCFDNPRGLALHPQGYLYWADWGHAYIGRVG

MDGTNKS VIIISTKLEWPNGITIDYTDNLLYWADAHLGYIEYSDLEGHHRH

TVYD GALPHPFAITIFEDTIYWTDWNTRTVEKGNKYDGSNRQTLVNTTHR

PFDIHVYHPYRQPIVSNPCGTNNGGCSHLCLIKPGGKGFTCECPDDFRTL

QLSGSTYCMPCSSSTQFLCANNEKCIPIWKKCDGQKDCSDGSDELALCPQ

RFCRLGQFQCS DGNCTSPQTL CNAHQNPCDGSDEDRLLCENHHCSNEWQ

CANKRCIPESWQCDTFND CEDNSDESSHCASRTC R PGQFR CANGRCIPQ

AWKCDVDND CGDHSDEPIEECMSAHLCDNFTEFSCKTNYRCIPKWAVCN

GVDDCRDNDSEQGCERTCHPVGDFRCKNHHCIPLRWQCDGQND CGDND

EENCAPRECTESEFRVCVNQQCIPSRWICDHYND CGDNSDERDC EMRTCHP

EYFQCTSGHCVHSELKCDGSADCLDASDEADCPTRFPD GAYCQATMFECK

NHVCIPPYWKCDGDDDCGDGSDEELHLC LDVPCNSPNRFRCDNNRCIYSH

EVCNGVDDCGDGTDETEHCRKPTPKPCTEY EYKCGNGHCIPHNDVCDDA

-continued

DDCGDWSDELGCNKGKERTCAENICEQNCITQLNEGFFICSCTAGFETNVF
 DRTSCLDINECEQFGTCPPQHCNRNKGSEYECVACADGFTSMSPDRPGKRCAAE
 GSSPLLLLDPNVIRKYNLSSERFSEYLQDEEYIQAVDYDWDPKDIGLSV
 VYYTVRGEGRFGAIKRAYIPNPFESGRNNLVQEVDLKLKYVMQPDGIAVD
 WVGRHIYWSVKNKRIEVAKLDGRYRKWLISTDLQPAIAVNPGLGLMF
 WTDWGKEPKIESAWMNGEDRNILVFEDLWPTGLSIDYLNNDRIYWSDFK
 EDVIETIKYDGTDRRIVIAKEAMPNPSLDIFEDQLYWISKEKGEVWKQNKF
 GQGKKEKTLVNVNPLTQVRIFHQRLYNKSVNLCQICSHLCLLRPGGYS
 CACPQSSFIEGSTTECDAAIELPINLPPPCRMHGGNCFDETDLPKCK
 CPSGYTKGYCEMAFSKGISPGTTAVAVLLTILLIVVIGALAIAGFFHYRR
 TGSLLPALPKPLSSLVKPSENGNGVTFRSGADLNMDIGVSGFGPETAI
 DRMSAMSEDFVMEMGKQPIIFENPMYSARDSAVKVVQPIQVTVSENVNPK
 NYGSPINPSEIVPETNPTSPAADGTQVTKWNLFKRKSQTTFENPIYAO
 MENEKQESVAATPPSPSLPAKPKPPSRDPTPTYSATEDTFKDTANLVK
 EDSEV

3. Alternative Name(s): Megalin; Glycoprotein 330; Short name=gp330

This protein has not been directly linked to myocardial ischemia or events leading up to MI.

V. Prolow Density Lipoprotein Receptor Related Protein 1
 Name: Prolow density lipoprotein receptor related protein 1
 IPI ID: IPI00020557

UniProtKB/Swiss-Prot ID: Q07954

Length: 4544 aa, molecular weight: 504575 Da (of Precursor)

1. Basic Information from UniProtKB/Swiss-Prot Entry:

Function: Endocytic receptor involved in endocytosis and in phagocytosis of apoptotic cells. Required for early embryonic development. Involved in cellular lipid homeostasis. Involved in the plasma clearance of chylomicron remnants and activated LRPAP1 (alpha 2-macroglobulin), as well as the local metabolism of complexes between plasminogen activators and their endogenous inhibitors. May modulate cellular events, such as APP metabolism, kinase-dependent intracellular signaling, neuronal calcium signaling as well as neurotransmission.

Subcellular location: Low-density lipoprotein receptor-related protein 1 85 kDa subunit: Cell membrane; Single-pass type I membrane protein. Membrane>coated pit. Low-density lipoprotein receptor-related protein 1 515 kDa subunit: Cell membrane; Peripheral membrane protein; Extracellular side. Membrane>coated pit. Low-density lipoprotein receptor-related protein 1 intracellular domain: Cytoplasm. Nucleus. Note=After cleavage, the intracellular domain (LRP1CD) is detected both in the cytoplasm and in the nucleus.

2. Sequence:

(SEQ ID NO: 41)
 MLTPPLLLLLPLLSALVAAIDAPKTCSPKQFACRDQITCISKWRCDE
 RDCPDGSDEAPEICPQSKAQRCPNEHNCLGTCLVPMRSLCNGVQDCMD
 GSDEGPHCRELGQNC SRLGQHHCVP TLDGPTCYCNSSFQLQADGKTCKD
 FDECSVYGTCSQLCTNTDGSFICGCVGYLLQPDNRSCAKNEPVRPPV

-continued

LLIANSONILATYLSGAQVSTITPTSTRQTTAMDPSYANETVCWVHVGD
 AAQTQLKCARMPGLKGFVDEHTINISLSLHHVQMAIDWLTGNFYFVDDI
 5 DDRIFVCNRNGDTCVTLLDLELYNPKGIALDPAMGKVFPTDYGQIPKVER
 CDMGQNRKTLVDSKIVFPHGITLDLVSRLVYWADAYLDYIEVVDYEGKG
 RQTTIQGILIEHLYGLTVFENLYATNSDNANAQKQTSVIRVNRNFSLEY
 10 QVVTRVDKGGALHIYHQRRQPRVRSHACENDQYKPGGCSDICLLANSHK
 ARTCRCSRGSFSLGSDGKSKKPEHELFLVYVGKRPPIIRGMDMGAKVPDE
 HMPIENLMNPRALDFHAETGFIYFADTTSYLIGRQKIDGTERETILKDG
 15 IHNVEGVAVDWMGDNLVWTDGPKKTIISVARLEKAAQTRKTLIEGKMTHP
 RAIVVDPLNGWMYWTDWEEDPKDSRRGRLERAWMDGSHRDI FVTSKTVLW
 PNGLSLDIPAGRLYWVDAFYDRIETILLNGTDRKIVYEGPELNHAFGLCH
 20 HGNYLFWTEYRSGSVYRLERGVGGAPTPTVTLRSERPPIFEIRMYDAQQ
 QVGTNKRNVNNGGCSLCLATPGSRQCACAEDQVLDADGVTCLANPSYVP
 PPQCQPGEFACANSRCIQERWKCDGDNDCLDNDSEAPALCHQHTCPSDRF
 KCENNRCPINRWLDCGDNDCGNSEDESNAATCSARTCPPNQFSCASGRCP
 25 ISWTCDLDDDCGDRSDESASCAYPCTFPLTQFTCNNGRCININWRCDNDN
 DCGDNSDEAGCSHSCSSTQFKCNSGRCPPEHWTCGDNDCCGDSYDETHAN
 CTNQATRPFGGCHTDEFQCRDLGLCIPLRWRCDGTDCCMDSSDEKSCGEV
 30 THVCDPSVKFGCKDSARCISKAWVCDGDNDCEDNSDEENCESLACRPPSH
 PCANNTSVCLPPDKLDCGNDCCGDSDEGELCDQCSLNNGGCSHNCVAP
 GEGIVCSCPLGMELGPDNHTCQIQSYCAHLKCSQKCDQNKFSVKSCSYE
 35 GWVLEPDGESCRSLDPFKPFIIFSNRHEIRRIDLHKGDYSVLVPLGRNTI
 ALDFHLSQSALYWTVDVEDKIIYRKLKLDNGALTSFEVVIQYGLATPEGLA
 VDWIAGNIYWVESNLDQIEVAKLDGTLRTLLLAGDIEHPRAIALDPRDGI
 40 LFWTDWDASLPRIEASMSGAGRRTVHRETSGGGWPNGLTVDYLEKRIW
 IDARSDAIYSARYDGS GHMEVLRGHEFLSHFPAVTLYGGEVYWDWRTNT
 LAKANKWTGHNVTVVQRTNTQPFDLQVYHPSRQPMAPNPCEANGGQGPCS
 45 HLCLINYNRTVSCACPHMLKHKDNTTCYEFKFLLYARQMEIRGVDLDA
 PYYNYIISFTVPDIDNVTVLDYDAREQRVYWSVDRVTAIKRAFINGTGVE
 TVVSADLPNAHGLAVDWVSRNLFWTSYDNTKKQINVARLDGSPKNAVVG
 50 LEQPHGLVVHPLRGKLYWTDGDNISMANMDGSRNLTLLFSGQKGPVGLAID
 FPESKLYWISSGNHTINRCNLDGSGLEVIDAMRSQLGKATALAIMGDKLW
 WADQVSEKMGTC SKADGSGSVVLFNSTTLMHMKVYDESIQLDHKGTNCP
 55 SVNNGDCSQLCLPTSETTRSCMCTAGYSLRSGQQACEGVGSFLLYSVHEG
 IRGIPLDPNDKSDALVPVSGTSLAVGIDFHAENDTIYVWDMGLSTISRAK
 RDQTWREDVVTNGIGRVEGIAVDWIAGNIYWTDQGFVIEVARLNGSFRY
 VVISQGLDKPRAITVHPEKGYLFWTEWQYPRRIERSRLDGTERTVLNVNS
 60 ISWPNGISVDYQDGKLYWCDARTDKIERIDLETGENREVVLSSNNMDMFS
 VSVFEDFIYWSDRTHANGSIKRGSKDNATDSVPLRTGIGVQLKDIKVFNR
 DRQKGTNCAVANGGCQQLCLYRGRGQRACACAHGMLAEDGASCREYAGY
 65 LLYSERTILKSIHLSDERNLNAPVQPFEDPEHMKNVIALAFDYRAGTSPG

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TPNRIFFSDIHFGNIQQINDGSRRTITIVENVGSVEGLAYHRGWDLTLYWT
 SYTTSTITRHTVDQTRPGAFAFERETVITMSGDDHPRAFVLDECQNLMFWTN
 WNEQHPSIMRAALSGANVLTLEKDIRTPNGLAIDHRAEKLYFSDATLDK
 IERCEYDGSRYVILKSEPVHPFGLAVYGEHIFWTDWVRAVQRANKHVG
 SNMKLLRVDIPQQPMGIIAVANDTNSCELSPCRINNGGCQDLCLLTHQGH
 VNCSGRGRILQDDLTCAVNSSCRAQDEFECANGECINFSLTCDGVPHC
 KDKSDEKPSYCNSRRCKTFRQCSNGRCVSNMLWCNGADDCGDSDEIPC
 NKTACGVGEFRCDGTICIGNSSRCNFQVDCEDASDEMNC SATDCSSYFRL
 GVGKVLFPQCERTSLCYAPSWVCDGANDCGDYSDERDCPGVKRPRCPLNY
 FACPSGRICPMSWTCDEDDCEHGEDETHCNKFCSEAQFECQNHRCISKQ
 WLCGSDDCGDSDEAAHCEGKTCGPSSFCPGTHVCVPERWLCGDKDC
 ADGADESIAAGCLYNSTCDDREFMCQNRQCIKHFVCDHDRDCADGSDSE
 PECEYPTCGPSEFRCANGRCLSSRQWECDEGENDCHDQSEAPKNPHCTSP
 EHKCNASSQLCSSGRCAEALLCNGQDDCGDSSDERGCHINECLSRKLS
 GCSQDCEDLKGFKCRCPGRFLKDDGRTCADVDECSTTFPCSQRICINTH
 GSYKLCVEGYAPRGDPHSCKAVTDEEPFLIFANRYLRKLNLDGSNYT
 LLKQGLNNAVALDFDYREQMIYWTDTTQGSIMRRMHLNGSNVQVLHRTG
 KLSNPDLGLAVDWVGGNLYWCDGRDTEIEVSKLNGAYRTVLVSSGLREPRAL
 VVDVQNGYLYWTDWGDHSLIGRIGMDGSSRSVIVDTKI TWPNGLTLDYVT
 ERIYWADAREDYIEFASLDGNSRHVLSQDIPHI FALTLEFDYVYWTDE
 TKSINRAHKTGTGNTLLISTLHRPMDLHVPHALRQPDVPNHPCKVNNGG
 CSNLCLLSPGGGHKACPTNFYLGSDGRTCVSNCTASQFVCKNDKCI PFW
 WKCDTEDDCGDHSDPEPDCPEFKCRPGQFQCSTGICTNPAFICDGDNDQC
 DNSDEANCDIHVCLPSQFKCTNTNRCIPGIFRCNGQDNCGDGEDERDCPE
 VTCAPNQFQCSITKRCIPRVVWCDRNDNCDVGSDEPANCTQMT CGVDEFR
 CKDSGRCI PARWKCDGEDDCGDSDEPKEECDERTCEPYQFRCKNNRCVP
 GRWQCDYDNDCGDNDSEESCTPRPCSESEFSCANGRCIAGRWKCDGDHDC
 ADGSDEKDCPTRCDMDQFQCKSGHCIPLRWRCADADCMDGSDSEACGTG
 VRTCPLDEFQCNNTLCKPLAWKCDGEDDCGDSNDENPEECARFVCPNRP
 FRCKNDRVCLWIGRQCDGTDCGDTDEEDCEPPTAHTTHCKDKKEFLCR
 NQRCLSSSLRCNMFDCCGDSDEEDCSIDPKLTSCATNASICGDEARCVR
 TEKAAACACRSGFHTVPGQPGCQDINECLRFGTCSQLCNNTKGGHLCSCA
 RRNFMKTHNTCKAEGSEYQVLYIADDNEIRSLFPGHPHSAYEQAQGDSE
 VIDAMDVHVKAGRVYWTNWHTGTISYRSLPPAAPPTTSNRHRRQIDRGVT
 RHLNISGLKMPGIAIDWAGNVYWTDSGRDVEI EAVQMKGENRKTLSIGMI
 DEPHAIVVDPLRGTMYSWSDGNHPKIETAAMDGTLRET LVQDNIQWPTGL
 AVDYHNERLYWADAKLSVIGSIRLNGTDPIVAADSKRGLSHSPFSIDVFED
 YIYGVTYINNRVFKIHKFGHSPVLNLTGGLSHASDVVLYHQHKQPEVTNP
 CDRKKCEWLCLLSPSGPVCTCPNGKRLDNGTCVPVPSPTPPDAPRPGTC
 NLQCFNGGSCFLNARRQPKCRCQPRYTGDKCELDQCWEHCRNGGTCAASP

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SGMPTCRCPTGFTGPKCTQQVCAGYCANNSTCTVNQGNQPCRCCLPGFLG
 DRCQYRQCSGYCENFGTCQMAADGSRQCRCTAYFEGRCEVKNKCSRCLG
 5 ACVVNKQSGDVTNCNTDGRVAPSCLT CVGHCSNGGSC TMNSKMMPECQCP
 PHMTGPRCEEHVFSQQQPGHIASILIPLLLLLLLLLVAGVVFYKRRVQG
 AKGFQHQRTMNGAMNVEIGNPTYKMYEGGEPDDVGGLLDADFALDPDKPT

10 NFTNPFVYATLYMGHGSRRHSLASTDEKRELLGRGPEDEIGDPLA

3. Alternative Name(s):

Alpha-2-macroglobulin receptor

Short name=A2MR

15 Apolipoprotein E receptor

Short name=APOER

CD_antigen=CD91

This protien has not been directly linked to myocardial ischemia or events leading up to MI.

20 W. Monocyte Differentiation Antigen CD14

Name: MONOCYTE DIFFERENTIATION ANTIGEN CD14

IPI ID: IPI00029260

UniProtKB/Swiss-Prot ID: P08571

25 Length: 375 aa, molecular weight: 40076 Da (of Precursor)

1. Basic Information from UniProtKB/Swiss-Prot Entry:

FUNCTION	Cooperates with MD-2 and TLR4 to mediate the innate immune response to bacterial lipopolysaccharide (LPS). Acts via MyD88, TIRAP and TRAF6, leading to NF-kappa-B activation, cytokine secretion and the inflammatory response. Up-regulates cell surface molecules, including adhesion molecules.
SUBCELLULAR LOCATION	Cell membrane; Lipid-anchor, GPI-anchor.

35

2. Sequence:

(SEQ ID NO: 42)

40 MERASCLLLLLLPLVHVSATTPEPCELDDDEDFRCVCFNSEPQPDWSEAFQ

CVSAVEVEIHAGGLNLEPFLKRVADADPRQYADTVKALRVRLTVGAAG

VPAQLLVGALRVLAYSRKELTLEDLKITGTMPPLPLEATGLALSRLLR

45 NVSWATGRSWLAELQQWLKPLKVLISIAQAHS PAFSCEQVRAPPALTS LD

LSDNPGLGERGLMAALCPHKFPAIQNLALRNTGMETPTGVCAALAAAGVQ

PHSLDSLHNSLRATVNPSPAPRCMWSALNSLNSFAGLEQVPKGLPAKLR

50 VLDLSCNRLNRPQDELPEVDNLTLDGNPFLVPGTALPHEGSMNSGVVP

ACARSTLSVGVSGLVLVLQGGARGFA

3. Alternative Name(s): Myeloid cell-specific leucine-rich glycoprotein; CD_antigen=CD14 Monocytes and T-cells play an important role in the development of atherosclerotic coronary artery disease. C14 is located on the monocytes and, therefore, changes to this protein can and have been linked to alterations to monocytes (including with coronary artery disease). However, this protein has not been measured in serum in context to myocardial ischemia or events leading up to a MI.

X. Peroxiredoxin-2

Name: Peroxiredoxin-2

IPI ID: IPI00027350

65 UniProtKB/Swiss-Prot ID: P32119; PRDX2_HUMAN; M. Length: 198 aa, molecular weight: 21892 Da, CRC64 checksum: 1AC781D908B32B46

1. Basic Information from UniProtKB/Swiss-Prot Entry:

Function	Involved in redox regulation of the cell. Reduces peroxides with reducing equivalents provided through the thioredoxin system. It is not able to receive electrons from glutaredoxin. May play an important role in eliminating peroxides generated during metabolism. Might participate in the signaling cascades of growth factors and tumor necrosis factor-alpha by regulating the intracellular concentrations of H ₂ O ₂ .
Catalytic activity	2 R'-SH + ROOH = R'-S-S-R' + H ₂ O + ROH.
Subunit structure	Homodimer; disulfide-linked, upon oxidation. May be found as a toroid-shaped decamer composed of 5 dimers, depending on pH and calcium concentration. Interacts with TIPIN.
Subcellular location	Cytoplasm.
Miscellaneous	The active site is the redox-active Cys-51 oxidized to Cys-SOH. Cys-SOH rapidly reacts with Cys-172-SH of the other subunit to form an intermolecular disulfide with a concomitant homodimer formation. The enzyme may be subsequently regenerated by reduction of the disulfide by thioredoxin. Inactivated upon oxidative stress by overoxidation of Cys-51 to Cys-SO ₂ H and Cys-SO ₃ H. Cys-SO ₂ H is retroreduced to Cys-SOH after removal of H ₂ O ₂ , while Cys-SO ₃ H may be irreversibly oxidized.
Sequence similarities	Belongs to the ahpC/TSA family. Contains 1 thioredoxin domain.

2. Sequence:

(SEQ ID NO: 43)

MASGNARIGKPAIDFKATAVVDGAFKEVKLSYKGYVLFYPLDFTFV

CPTEIIAFSNAEDFRKLGCEVLGVSVDSQFTHLAWINTPRKEGGLGPLN

IPLLADVTRRLSEYDGLTKDEGIAYRGLFIIDGKGVLRQITVNDLPVGR

SVDEALRLVQAFQYTDEHGEVCPAGWKPGSDTIKPNVDDSKKEYFSKHN

3. Alternative Name(s): Thioredoxin peroxidase 1

Thioredoxin-dependent peroxide reductase 1

Thiol-specific antioxidant protein

Short name=TSA

PRP

Natural killer cell-enhancing factor B

Short name=NKEF-B

This protein has been found to increase in the serum of a number diseases but none are cardiac related. This protein, to date, has not been shown to be increased in myocardial ischemia or events leading to MI.

Y. NCOR2 CTG26 Alternate Open Reading Frame

Name: CTG26 alternate open reading frame (Fragment)

IPI ID: IPI00006659.3

Basic information: Fragment

1. Sequence:

(SEQ ID NO: 44)

5 SFSSMEASSALCWGMASLLASLAIERVMRPLRLPWLAVLRPLEATAS

FSSLSSEPVSSVFSRLRRSSLSFSTSGFSSSFSASFSSFSFSSWLLRGM

10 GCCCCCCCCCCCCCWLLPRRR

10 This protein has not been linked to myocardial ischemia or events leading up to MI.

Example V

Validation Studies

Antibodies to two or more epitopes on each protein will be generated and used to develop a sandwich ELISA assay (as single or multiplex) that is specific and sensitive for the analyte. The analyte will either be peptide, protein fragment or protein and will be used to generate standard curve. Analysis will be carried out using conventional ELISA or on a Luminex or Mesoscale platform. Assays will be carried out at least in duplicate. For MRM assays, peptides (generated most likely by trypsin, chymotrypsin or Lys C) that are unique to the protein of interest and showing high MS signal response (prototypic peptides) which will help maximize the sensitivity of the assay. 2. Selection of predominant peptide fragments specific (MS/MS) for the parent peptide (useful MRM transition). 3. For each peptide-fragment pair, optimization of specific MS parameters (e.g. the collision energy) to maximize the signal response/sensitivity. 4. Validation of the MRM assay to confirm peptide identity, e.g. by acquiring a full MS2 spectrum of the peptide in the triple quadrupole MS instrument used for MRM. 5. Extraction of the final "coordinates" of the MRM assay, including the selected peptide and peptide fragments, the corresponding mass-to-charge ratios, the fragment intensity ratios, the associated collision energy, and the chromatographic elution time to be optionally used in time-constrained MRM analyses. We will add isotopically labeled internal peptide standards (with known concentrations determined by amino acid analysis) to facilitate absolute quantitation of selected peptides. Assays will be performed on a triple quadrupole mass spectrometer at least in duplicate.

From the foregoing description, one skilled in the art can easily ascertain the essential characteristics of this invention, and without departing from the spirit and scope thereof, can make changes and modifications of the invention to adapt it to various usage and conditions and to utilize the present invention to its fullest extent. The preceding preferred specific embodiments are to be construed as merely illustrative, and not limiting of the scope of the invention in any way whatsoever. The entire disclosure of all applications, patents, and publications (including provisional patent application 61/128,688, filed May 23, 2008) cited above and in the figures are hereby incorporated in their entirety by reference.

SEQUENCE LISTING

<160> NUMBER OF SEQ ID NOS: 44

<210> SEQ ID NO 1

<211> LENGTH: 474

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 1

Met Lys Arg Val Leu Val Leu Leu Leu Ala Val Ala Phe Gly His Ala

1 5 10 15

-continued

Leu Glu Arg Gly Arg Asp Tyr Glu Lys Asn Lys Val Cys Lys Glu Phe
 20 25 30
 Ser His Leu Gly Lys Glu Asp Phe Thr Ser Leu Ser Leu Val Leu Tyr
 35 40 45
 Ser Arg Lys Phe Pro Ser Gly Thr Phe Glu Gln Val Ser Gln Leu Val
 50 55 60
 Lys Glu Val Val Ser Leu Thr Glu Ala Cys Cys Ala Glu Gly Ala Asp
 65 70 75 80
 Pro Asp Cys Tyr Asp Thr Arg Thr Ser Ala Leu Ser Ala Lys Ser Cys
 85 90 95
 Glu Ser Asn Ser Pro Phe Pro Val His Pro Gly Thr Ala Glu Cys Cys
 100 105 110
 Thr Lys Glu Gly Leu Glu Arg Lys Leu Cys Met Ala Ala Leu Lys His
 115 120 125
 Gln Pro Gln Glu Phe Pro Thr Tyr Val Glu Pro Thr Asn Asp Glu Ile
 130 135 140
 Cys Glu Ala Phe Arg Lys Asp Pro Lys Glu Tyr Ala Asn Gln Phe Met
 145 150 155 160
 Trp Glu Tyr Ser Thr Asn Tyr Gly Gln Ala Pro Leu Ser Leu Leu Val
 165 170 175
 Ser Tyr Thr Lys Ser Tyr Leu Ser Met Val Gly Ser Cys Cys Thr Ser
 180 185 190
 Ala Ser Pro Thr Val Cys Phe Leu Lys Glu Arg Leu Gln Leu Lys His
 195 200 205
 Leu Ser Leu Leu Thr Thr Leu Ser Asn Arg Val Cys Ser Gln Tyr Ala
 210 215 220
 Ala Tyr Gly Glu Lys Lys Ser Arg Leu Ser Asn Leu Ile Lys Leu Ala
 225 230 235 240
 Gln Lys Val Pro Thr Ala Asp Leu Glu Asp Val Leu Pro Leu Ala Glu
 245 250 255
 Asp Ile Thr Asn Ile Leu Ser Lys Cys Cys Glu Ser Ala Ser Glu Asp
 260 265 270
 Cys Met Ala Lys Glu Leu Pro Glu His Thr Val Lys Leu Cys Asp Asn
 275 280 285
 Leu Ser Thr Lys Asn Ser Lys Phe Glu Asp Cys Cys Gln Glu Lys Thr
 290 295 300
 Ala Met Asp Val Phe Val Cys Thr Tyr Phe Met Pro Ala Ala Gln Leu
 305 310 315 320
 Pro Glu Leu Pro Asp Val Glu Leu Pro Thr Asn Lys Asp Val Cys Asp
 325 330 335
 Pro Gly Asn Thr Lys Val Met Asp Lys Tyr Thr Phe Glu Leu Ser Arg
 340 345 350
 Arg Thr His Leu Pro Glu Val Phe Leu Ser Lys Val Leu Glu Pro Thr
 355 360 365
 Leu Lys Ser Leu Gly Glu Cys Cys Asp Val Glu Asp Ser Thr Thr Cys
 370 375 380
 Phe Asn Ala Lys Gly Pro Leu Leu Lys Lys Glu Leu Ser Ser Phe Ile
 385 390 395 400
 Asp Lys Gly Gln Glu Leu Cys Ala Asp Tyr Ser Glu Asn Thr Phe Thr
 405 410 415
 Glu Tyr Lys Lys Lys Leu Ala Glu Arg Leu Lys Ala Lys Leu Pro Asp
 420 425 430

-continued

Ala Thr Pro Lys Glu Leu Ala Lys Leu Val Asn Lys Arg Ser Asp Phe
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Ala Ser Asn Cys Cys Ser Ile Asn Ser Pro Pro Leu Tyr Cys Asp Ser
450 455 460

Glu Ile Asp Ala Glu Leu Lys Asn Ile Leu
465 470

<210> SEQ ID NO 2
 <211> LENGTH: 415
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 2

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Thr Ile His Cys Ala Ser Pro Glu Gly Lys Val Thr Ala Cys His Ser
20 25 30

Ser Gln Pro Asn Ala Thr Leu Tyr Lys Met Ser Ser Ile Asn Ala Asp
35 40 45

Phe Ala Phe Asn Leu Tyr Arg Arg Phe Thr Val Glu Thr Pro Asp Lys
50 55 60

Asn Ile Phe Phe Ser Pro Val Ser Ile Ser Ala Ala Leu Val Met Leu
65 70 75 80

Ser Phe Gly Ala Cys Cys Ser Thr Gln Thr Glu Ile Val Glu Thr Leu
85 90 95

Gly Phe Asn Leu Thr Asp Thr Pro Met Val Glu Ile Gln His Gly Phe
100 105 110

Gln His Leu Ile Cys Ser Leu Asn Phe Pro Lys Lys Glu Leu Glu Leu
115 120 125

Gln Ile Gly Asn Ala Leu Phe Ile Gly Lys His Leu Lys Pro Leu Ala
130 135 140

Lys Phe Leu Asn Asp Val Lys Thr Leu Tyr Glu Thr Glu Val Phe Ser
145 150 155 160

Thr Asp Phe Ser Asn Ile Ser Ala Ala Lys Gln Glu Ile Asn Ser His
165 170 175

Val Glu Met Gln Thr Lys Gly Lys Val Val Gly Leu Ile Gln Asp Leu
180 185 190

Lys Pro Asn Thr Ile Met Val Leu Val Asn Tyr Ile His Phe Lys Ala
195 200 205

Gln Trp Ala Asn Pro Phe Asp Pro Ser Lys Thr Glu Asp Ser Ser Ser
210 215 220

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

Met Glu Gln Tyr Tyr His Leu Val Asp Met Glu Leu Asn Cys Thr Val
245 250 255

Leu Gln Met Asp Tyr Ser Lys Asn Ala Leu Ala Leu Phe Val Leu Pro
260 265 270

Lys Glu Gly Gln Met Glu Ser Val Glu Ala Ala Met Ser Ser Lys Thr
275 280 285

Leu Lys Lys Trp Asn Arg Leu Leu Gln Lys Gly Trp Val Asp Leu Phe
290 295 300

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

Leu Lys Met Gly Ile Gln His Ala Tyr Ser Glu Asn Ala Asp Phe Ser
325 330 335

-continued

Gly Leu Thr Glu Asp Asn Gly Leu Lys Leu Ser Asn Ala Ala His Lys
 340 345 350

Ala Val Leu His Ile Gly Glu Lys Gly Thr Glu Ala Ala Ala Val Pro
 355 360 365

Glu Val Glu Leu Ser Asp Gln Pro Glu Asn Thr Phe Leu His Pro Ile
 370 375 380

Ile Gln Ile Asp Arg Ser Phe Met Leu Leu Ile Leu Glu Arg Ser Thr
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Arg Ser Ile Leu Phe Leu Gly Lys Val Val Asn Pro Thr Glu Ala
 405 410 415

<210> SEQ ID NO 3
 <211> LENGTH: 338
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 3

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

Ser Gly Gln Tyr Tyr Asp Tyr Asp Phe Pro Leu Ser Ile Tyr Gly Gln
 20 25 30

Ser Ser Pro Asn Cys Ala Pro Glu Cys Asn Cys Pro Glu Ser Tyr Pro
 35 40 45

Ser Ala Met Tyr Cys Asp Glu Leu Lys Leu Lys Ser Val Pro Met Val
 50 55 60

Pro Pro Gly Ile Lys Tyr Leu Tyr Leu Arg Asn Asn Gln Ile Asp His
 65 70 75 80

Ile Asp Glu Lys Ala Phe Glu Asn Val Thr Asp Leu Gln Trp Leu Ile
 85 90 95

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

Ser Lys Leu Lys Gln Leu Lys Lys Leu His Ile Asn His Asn Asn Leu
 115 120 125

Thr Glu Ser Val Gly Pro Leu Pro Lys Ser Leu Glu Asp Leu Gln Leu
 130 135 140

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

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

Ser Ala Ala Phe Lys Gly Leu Lys Ser Leu Glu Tyr Leu Asp Leu Ser
 180 185 190

Phe Asn Gln Ile Ala Arg Leu Pro Ser Gly Leu Pro Val Ser Leu Leu
 195 200 205

Thr Leu Tyr Leu Asp Asn Asn Lys Ile Ser Asn Ile Pro Asp Glu Tyr
 210 215 220

Phe Lys Arg Phe Asn Ala Leu Gln Tyr Leu Arg Leu Ser His Asn Glu
 225 230 235 240

Leu Ala Asp Ser Gly Ile Pro Gly Asn Ser Phe Asn Val Ser Ser Leu
 245 250 255

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

Asn Glu Asn Leu Glu Asn Tyr Tyr Leu Glu Val Asn Gln Leu Glu Lys
 275 280 285

Phe Asp Ile Lys Ser Phe Cys Lys Ile Leu Gly Pro Leu Ser Tyr Ser

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290	295	300
Lys Ile Lys His Leu Arg Leu Asp Gly Asn Arg Ile Ser Glu Thr Ser		
305	310	315 320
Leu Pro Pro Asp Met Tyr Glu Cys Leu Arg Val Ala Asn Glu Val Thr		
	325	330 335
Leu Asn		

<210> SEQ ID NO 4
 <211> LENGTH: 136
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 4

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

<210> SEQ ID NO 5
 <211> LENGTH: 567
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 5

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

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Pro	Ser	Leu	Gln	His	Pro	Asn	Glu	Gln	Lys	Glu	Gly	Thr	Pro	Ala	Pro	145	150	155	160
Phe	Gly	Asp	Gln	Ser	His	Pro	Glu	Pro	Glu	Ser	Trp	Asn	Ala	Ala	Gln	165	170	175	
His	Cys	Gln	Gln	Asp	Arg	Ser	Gln	Gly	Gly	Trp	Gly	His	Arg	Leu	Asp	180	185	190	
Gly	Phe	Pro	Pro	Gly	Arg	Pro	Ser	Pro	Asp	Asn	Leu	Asn	Gln	Ile	Cys	195	200	205	
Leu	Pro	Asn	Arg	Gln	His	Val	Val	Tyr	Gly	Pro	Trp	Asn	Leu	Pro	Gln	210	215	220	
Ser	Ser	Tyr	Ser	His	Leu	Thr	Arg	Gln	Gly	Glu	Thr	Leu	Asn	Phe	Leu	225	230	235	240
Glu	Ile	Gly	Tyr	Ser	Arg	Cys	Cys	His	Cys	Arg	Ser	His	Thr	Asn	Arg	245	250	255	
Leu	Glu	Cys	Ala	Lys	Leu	Val	Trp	Glu	Glu	Ala	Met	Ser	Arg	Phe	Cys	260	265	270	
Glu	Ala	Glu	Phe	Ser	Val	Lys	Thr	Arg	Pro	His	Trp	Cys	Cys	Thr	Arg	275	280	285	
Gln	Gly	Glu	Ala	Arg	Phe	Ser	Cys	Phe	Gln	Glu	Glu	Ala	Pro	Gln	Pro	290	295	300	
His	Tyr	Gln	Leu	Arg	Ala	Cys	Pro	Ser	His	Gln	Pro	Asp	Ile	Ser	Ser	305	310	315	320
Gly	Leu	Glu	Leu	Pro	Phe	Pro	Pro	Gly	Val	Pro	Thr	Leu	Asp	Asn	Ile	325	330	335	
Lys	Asn	Ile	Cys	His	Leu	Arg	Arg	Phe	Arg	Ser	Val	Pro	Arg	Asn	Leu	340	345	350	
Pro	Ala	Thr	Asp	Pro	Leu	Gln	Arg	Glu	Leu	Leu	Ala	Leu	Ile	Gln	Leu	355	360	365	
Glu	Arg	Glu	Phe	Gln	Arg	Cys	Cys	Arg	Gln	Gly	Asn	Asn	His	Thr	Cys	370	375	380	
Thr	Trp	Lys	Ala	Trp	Glu	Asp	Thr	Leu	Asp	Lys	Tyr	Cys	Asp	Arg	Glu	385	390	395	400
Tyr	Ala	Val	Lys	Thr	His	His	His	Leu	Cys	Arg	His	Pro	Pro	Ser		405	410	415	
Pro	Thr	Arg	Asp	Glu	Cys	Phe	Ala	Arg	Arg	Ala	Pro	Tyr	Pro	Asn	Tyr	420	425	430	
Asp	Arg	Asp	Ile	Leu	Thr	Ile	Asp	Ile	Gly	Arg	Val	Thr	Pro	Asn	Leu	435	440	445	
Met	Gly	His	Leu	Cys	Gly	Asn	Gln	Arg	Val	Leu	Thr	Lys	His	Lys	His	450	455	460	
Ile	Pro	Gly	Leu	Ile	His	Asn	Met	Thr	Ala	Arg	Cys	Cys	Asp	Leu	Pro	465	470	475	480
Phe	Pro	Glu	Gln	Ala	Cys	Cys	Ala	Glu	Glu	Glu	Lys	Leu	Thr	Phe	Ile	485	490	495	
Asn	Asp	Leu	Cys	Gly	Pro	Arg	Arg	Asn	Ile	Trp	Arg	Asp	Pro	Ala	Leu	500	505	510	
Cys	Cys	Tyr	Leu	Ser	Pro	Gly	Asp	Glu	Gln	Val	Asn	Cys	Phe	Asn	Ile	515	520	525	
Asn	Tyr	Leu	Arg	Asn	Val	Ala	Leu	Val	Ser	Gly	Asp	Thr	Glu	Asn	Ala	530	535	540	
Lys	Gly	Gln	Gly	Glu	Gln	Gly	Ser	Thr	Gly	Gly	Thr	Asn	Ile	Ser	Ser	545	550	555	560

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Thr Ser Glu Pro Lys Glu Glu
565

<210> SEQ ID NO 6
 <211> LENGTH: 402
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 6

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

Lys Gln Ala Ala Val Met Gly Gln Lys Gly Gly Ser Lys Gly Arg Leu
 20 25 30

Pro Ser Glu Phe Ser Gln Phe Pro His Gly Gln Lys Gly Gln His Tyr
 35 40 45

Ser Gly Gln Lys Gly Lys Gln Gln Thr Glu Ser Lys Gly Ser Phe Ser
 50 55 60

Ile Gln Tyr Thr Tyr His Val Asp Ala Asn Asp His Asp Gln Ser Arg
 65 70 75 80

Lys Ser Gln Gln Tyr Asp Leu Asn Ala Leu His Lys Thr Thr Lys Ser
 85 90 95

Gln Arg His Leu Gly Gly Ser Gln Gln Leu Leu His Asn Lys Gln Glu
 100 105 110

Gly Arg Asp His Asp Lys Ser Lys Gly His Phe His Arg Val Val Ile
 115 120 125

His His Lys Gly Gly Lys Ala His Arg Gly Thr Gln Asn Pro Ser Gln
 130 135 140

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

Asn Thr Glu Glu Arg Leu Trp Val His Gly Leu Ser Lys Glu Gln Thr
 165 170 175

Ser Val Ser Gly Ala Gln Lys Gly Arg Lys Gln Gly Gly Ser Gln Ser
 180 185 190

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

Glu Thr Lys Asn Ser His Gln Asn Lys Gly His Tyr Gln Asn Val Val
 210 215 220

Glu Val Arg Glu Glu His Ser Ser Lys Val Gln Thr Ser Leu Cys Pro
 225 230 235 240

Ala His Gln Asp Lys Leu Gln His Gly Ser Lys Asp Ile Phe Ser Thr
 245 250 255

Gln Asp Glu Leu Leu Val Tyr Asn Lys Asn Gln His Gln Thr Lys Asn
 260 265 270

Leu Asn Gln Asp Gln Gln His Gly Arg Lys Ala Asn Lys Ile Ser Tyr
 275 280 285

Gln Ser Ser Ser Thr Glu Glu Arg Arg Leu His Tyr Gly Glu Asn Gly
 290 295 300

Val Gln Lys Asp Val Ser Gln Arg Ser Ile Tyr Ser Gln Thr Glu Lys
 305 310 315 320

Leu Val Ala Gly Lys Ser Gln Ile Gln Ala Pro Asn Pro Lys Gln Glu
 325 330 335

Pro Trp His Gly Glu Asn Ala Lys Gly Glu Ser Gly Gln Ser Thr Asn
 340 345 350

Arg Glu Gln Asp Leu Leu Ser His Glu Gln Lys Gly Arg His Gln His
 355 360 365

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Gly Ser His Gly Gly Leu Asp Ile Val Ile Ile Glu Gln Glu Asp Asp
 370 375 380
 Ser Asp Arg His Leu Ala Gln His Leu Asn Asn Asp Arg Asn Pro Leu
 385 390 395 400
 Phe Thr
 <210> SEQ ID NO 7
 <211> LENGTH: 484
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens
 <400> SEQUENCE: 7
 Met Ala Gly Pro Trp Thr Phe Thr Leu Leu Cys Gly Leu Leu Ala Ala
 1 5 10 15
 Thr Leu Ile Gln Ala Thr Leu Ser Pro Thr Ala Val Leu Ile Leu Gly
 20 25 30
 Pro Lys Val Ile Lys Glu Lys Leu Thr Gln Glu Leu Lys Asp His Asn
 35 40 45
 Ala Thr Ser Ile Leu Gln Gln Leu Pro Leu Leu Ser Ala Met Arg Glu
 50 55 60
 Lys Pro Ala Gly Gly Ile Pro Val Leu Gly Ser Leu Val Asn Thr Val
 65 70 75 80
 Leu Lys His Ile Ile Trp Leu Lys Val Ile Thr Ala Asn Ile Leu Gln
 85 90 95
 Leu Gln Val Lys Pro Ser Ala Asn Asp Gln Glu Leu Leu Val Lys Ile
 100 105 110
 Pro Leu Asp Met Val Ala Gly Phe Asn Thr Pro Leu Val Lys Thr Ile
 115 120 125
 Val Glu Phe His Met Thr Thr Glu Ala Gln Ala Thr Ile Arg Met Asp
 130 135 140
 Thr Ser Ala Ser Gly Pro Thr Arg Leu Val Leu Ser Asp Cys Ala Thr
 145 150 155 160
 Ser His Gly Ser Leu Arg Ile Gln Leu Leu His Lys Leu Ser Phe Leu
 165 170 175
 Val Asn Ala Leu Ala Lys Gln Val Met Asn Leu Leu Val Pro Ser Leu
 180 185 190
 Pro Asn Leu Val Lys Asn Gln Leu Cys Pro Val Ile Glu Ala Ser Phe
 195 200 205
 Asn Gly Met Tyr Ala Asp Leu Leu Gln Leu Val Lys Val Pro Ile Ser
 210 215 220
 Leu Ser Ile Asp Arg Leu Glu Phe Asp Leu Leu Tyr Pro Ala Ile Lys
 225 230 235 240
 Gly Asp Thr Ile Gln Leu Tyr Leu Gly Ala Lys Leu Leu Asp Ser Gln
 245 250 255
 Gly Lys Val Thr Lys Trp Phe Asn Asn Ser Ala Ala Ser Leu Thr Met
 260 265 270
 Pro Thr Leu Asp Asn Ile Pro Phe Ser Leu Ile Val Ser Gln Asp Val
 275 280 285
 Val Lys Ala Ala Val Ala Ala Val Leu Ser Pro Glu Glu Phe Met Val
 290 295 300
 Leu Leu Asp Ser Val Leu Pro Glu Ser Ala His Arg Leu Lys Ser Ser
 305 310 315 320
 Ile Gly Leu Ile Asn Glu Lys Ala Ala Asp Lys Leu Gly Ser Thr Gln
 325 330 335

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Ile Val Lys Ile Leu Thr Gln Asp Thr Pro Glu Phe Phe Ile Asp Gln
 340 345 350

Gly His Ala Lys Val Ala Gln Leu Ile Val Leu Glu Val Phe Pro Ser
 355 360 365

Ser Glu Ala Leu Arg Pro Leu Phe Thr Leu Gly Ile Glu Ala Ser Ser
 370 375 380

Glu Ala Gln Phe Tyr Thr Lys Gly Asp Gln Leu Ile Leu Asn Leu Asn
 385 390 395 400

Asn Ile Ser Ser Asp Arg Ile Gln Leu Met Asn Ser Gly Ile Gly Trp
 405 410 415

Phe Gln Pro Asp Val Leu Lys Asn Ile Ile Thr Glu Ile Ile His Ser
 420 425 430

Ile Leu Leu Pro Asn Gln Asn Gly Lys Leu Arg Ser Gly Val Pro Val
 435 440 445

Ser Leu Val Lys Ala Leu Gly Phe Glu Ala Ala Glu Ser Ser Leu Thr
 450 455 460

Lys Asp Ala Leu Val Leu Thr Pro Ala Ser Leu Trp Lys Pro Ser Ser
 465 470 475 480

Pro Val Ser Gln

<210> SEQ ID NO 8
 <211> LENGTH: 147
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 8

Met Val Met Gly Leu Gly Val Leu Leu Leu Val Phe Val Leu Gly Leu
 1 5 10 15

Gly Leu Thr Pro Pro Thr Leu Ala Gln Asp Asn Ser Arg Tyr Thr His
 20 25 30

Phe Leu Thr Gln His Tyr Asp Ala Lys Pro Gln Gly Arg Asp Asp Arg
 35 40 45

Tyr Cys Glu Ser Ile Met Arg Arg Arg Gly Leu Thr Ser Pro Cys Lys
 50 55 60

Asp Ile Asn Thr Phe Ile His Gly Asn Lys Arg Ser Ile Lys Ala Ile
 65 70 75 80

Cys Glu Asn Lys Asn Gly Asn Pro His Arg Glu Asn Leu Arg Ile Ser
 85 90 95

Lys Ser Ser Phe Gln Val Thr Thr Cys Lys Leu His Gly Gly Ser Pro
 100 105 110

Trp Pro Pro Cys Gln Tyr Arg Ala Thr Ala Gly Phe Arg Asn Val Val
 115 120 125

Val Ala Cys Glu Asn Gly Leu Pro Val His Leu Asp Gln Ser Ile Phe
 130 135 140

Arg Arg Pro
 145

<210> SEQ ID NO 9
 <211> LENGTH: 597
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 9

Met His Pro Pro Lys Thr Pro Ser Gly Ala Leu His Arg Lys Arg Lys
 1 5 10 15

Met	Ala	Ala	Trp	Pro	Phe	Ser	Arg	Leu	Trp	Lys	Val	Ser	Asp	Pro	Ile
			20				25						30		
Leu	Phe	Gln	Met	Thr	Leu	Ile	Ala	Ala	Leu	Leu	Pro	Ala	Val	Leu	Gly
			35				40						45		
Asn	Cys	Gly	Pro	Pro	Pro	Thr	Leu	Ser	Phe	Ala	Ala	Pro	Met	Asp	Ile
			50				55						60		
Thr	Leu	Thr	Glu	Thr	Arg	Phe	Lys	Thr	Gly	Thr	Thr	Leu	Lys	Tyr	Thr
			65				70						75		
Cys	Leu	Pro	Gly	Tyr	Val	Arg	Ser	His	Ser	Thr	Gln	Thr	Leu	Thr	Cys
			85				90						95		
Asn	Ser	Asp	Gly	Glu	Trp	Val	Tyr	Asn	Thr	Phe	Cys	Ile	Tyr	Lys	Arg
			100				105						110		
Cys	Arg	His	Pro	Gly	Glu	Leu	Arg	Asn	Gly	Gln	Val	Glu	Ile	Lys	Thr
			115				120						125		
Asp	Leu	Ser	Phe	Gly	Ser	Gln	Ile	Glu	Phe	Ser	Cys	Ser	Glu	Gly	Phe
			130				135						140		
Phe	Leu	Ile	Gly	Ser	Thr	Thr	Ser	Arg	Cys	Glu	Val	Gln	Asp	Arg	Gly
			145				150						155		
Val	Gly	Trp	Ser	His	Pro	Leu	Pro	Gln	Cys	Glu	Ile	Val	Lys	Cys	Lys
			165				170						175		
Pro	Pro	Pro	Asp	Ile	Arg	Asn	Gly	Arg	His	Ser	Gly	Glu	Glu	Asn	Phe
			180				185						190		
Tyr	Ala	Tyr	Gly	Phe	Ser	Val	Thr	Tyr	Ser	Cys	Asp	Pro	Arg	Phe	Ser
			195				200						205		
Leu	Leu	Gly	His	Ala	Ser	Ile	Ser	Cys	Thr	Val	Glu	Asn	Glu	Thr	Ile
			210				215						220		
Gly	Val	Trp	Arg	Pro	Ser	Pro	Pro	Thr	Cys	Glu	Lys	Ile	Thr	Cys	Arg
			225				230						235		
Lys	Pro	Asp	Val	Ser	His	Gly	Glu	Met	Val	Ser	Gly	Phe	Gly	Pro	Ile
			245				250						255		
Tyr	Asn	Tyr	Lys	Asp	Thr	Ile	Val	Phe	Lys	Cys	Gln	Lys	Gly	Phe	Val
			260				265						270		
Leu	Arg	Gly	Ser	Ser	Val	Ile	His	Cys	Asp	Ala	Asp	Ser	Lys	Trp	Asn
			275				280						285		
Pro	Ser	Pro	Pro	Ala	Cys	Glu	Pro	Asn	Ser	Cys	Ile	Asn	Leu	Pro	Asp
			290				295						300		
Ile	Pro	His	Ala	Ser	Trp	Glu	Thr	Tyr	Pro	Arg	Pro	Thr	Lys	Glu	Asp
			305				310						315		
Val	Tyr	Val	Val	Gly	Thr	Val	Leu	Arg	Tyr	Arg	Cys	His	Pro	Gly	Tyr
			325				330						335		
Lys	Pro	Thr	Thr	Asp	Glu	Pro	Thr	Thr	Val	Ile	Cys	Gln	Lys	Asn	Leu
			340				345						350		
Arg	Trp	Thr	Pro	Tyr	Gln	Gly	Cys	Glu	Ala	Leu	Cys	Cys	Pro	Glu	Pro
			355				360						365		
Lys	Leu	Asn	Asn	Gly	Glu	Ile	Thr	Gln	His	Arg	Lys	Ser	Arg	Pro	Ala
			370				375						380		
Asn	His	Cys	Val	Tyr	Phe	Tyr	Gly	Asp	Glu	Ile	Ser	Phe	Ser	Cys	His
			385				390						395		
Glu	Thr	Ser	Arg	Phe	Ser	Ala	Ile	Cys	Gln	Gly	Asp	Gly	Thr	Trp	Ser
			405				410						415		
Pro	Arg	Thr	Pro	Ser	Cys	Gly	Asp	Ile	Cys	Asn	Phe	Pro	Pro	Lys	Ile
			420				425						430		

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435	440	445
Glu Ile Ile Tyr Glu Cys Asp Lys Gly Tyr Ile Leu Val Gly Gln Ala		
450	455	460
Lys Leu Ser Cys Ser Tyr Ser His Trp Ser Ala Pro Ala Pro Gln Cys		
465	470	475
Lys Ala Leu Cys Arg Lys Pro Glu Leu Val Asn Gly Arg Leu Ser Val		
485	490	495
Asp Lys Asp Gln Tyr Val Glu Pro Glu Asn Val Thr Ile Gln Cys Asp		
500	505	510
Ser Gly Tyr Gly Val Val Gly Pro Gln Ser Ile Thr Cys Ser Gly Asn		
515	520	525
Arg Thr Trp Tyr Pro Glu Val Pro Lys Cys Glu Trp Glu Thr Pro Glu		
530	535	540
Gly Cys Glu Gln Val Leu Thr Gly Lys Arg Leu Met Gln Cys Leu Pro		
545	550	555
Asn Pro Glu Asp Val Lys Met Ala Leu Glu Val Tyr Lys Leu Ser Leu		
565	570	575
Glu Ile Glu Gln Leu Glu Leu Gln Arg Asp Ser Ala Arg Gln Ser Thr		
580	585	590
Leu Asp Lys Glu Leu		
595		
<210> SEQ ID NO 10		
<211> LENGTH: 458		
<212> TYPE: PRT		
<213> ORGANISM: Homo sapiens		
<400> SEQUENCE: 10		
Met Ser Asp Leu Leu Ser Val Phe Leu His Leu Leu Leu Leu Phe Lys		
1	5	10
Leu Val Ala Pro Val Thr Phe Arg His His Arg Tyr Asp Asp Leu Val		
20	25	30
Arg Thr Leu Tyr Lys Val Gln Asn Glu Cys Pro Gly Ile Thr Arg Val		
35	40	45
Tyr Ser Ile Gly Arg Ser Val Glu Gly Arg His Leu Tyr Val Leu Glu		
50	55	60
Phe Ser Asp His Pro Gly Ile His Glu Pro Leu Glu Pro Glu Val Lys		
65	70	75
Tyr Val Gly Asn Met His Gly Asn Glu Ala Leu Gly Arg Glu Leu Met		
85	90	95
Leu Gln Leu Ser Glu Phe Leu Cys Glu Glu Phe Arg Asn Arg Asn Gln		
100	105	110
Arg Ile Val Gln Leu Ile Gln Asp Thr Arg Ile His Ile Leu Pro Ser		
115	120	125
Met Asn Pro Asp Gly Tyr Glu Val Ala Ala Ala Gln Gly Pro Asn Lys		
130	135	140
Pro Gly Tyr Leu Val Gly Arg Asn Asn Ala Asn Gly Val Asp Leu Asn		
145	150	155
Arg Asn Phe Pro Asp Leu Asn Thr Tyr Ile Tyr Tyr Asn Glu Lys Tyr		
165	170	175
Gly Gly Pro Asn His His Leu Pro Leu Pro Asp Asn Trp Lys Ser Gln		
180	185	190
Val Glu Pro Glu Thr Arg Ala Val Ile Arg Trp Met His Ser Phe Asn		
195	200	205

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Phe Val Leu Ser Ala Asn Leu His Gly Gly Ala Val Val Ala Asn Tyr
 210                215                220

Pro Tyr Asp Lys Ser Phe Glu His Arg Val Arg Gly Val Arg Arg Thr
225                230                235                240

Ala Ser Thr Pro Thr Pro Asp Asp Lys Leu Phe Gln Lys Leu Ala Lys
                245                250                255

Val Tyr Ser Tyr Ala His Gly Trp Met Phe Gln Gly Trp Asn Cys Gly
                260                265                270

Asp Tyr Phe Pro Asp Gly Ile Thr Asn Gly Ala Ser Trp Tyr Ser Leu
                275                280                285

Ser Lys Gly Met Gln Asp Phe Asn Tyr Leu His Thr Asn Cys Phe Glu
                290                295                300

Ile Thr Leu Glu Leu Ser Cys Asp Lys Phe Pro Pro Glu Glu Glu Leu
305                310                315                320

Gln Arg Glu Trp Leu Gly Asn Arg Glu Ala Leu Ile Gln Phe Leu Glu
                325                330                335

Gln Val His Gln Gly Ile Lys Gly Met Val Leu Asp Glu Asn Tyr Asn
                340                345                350

Asn Leu Ala Asn Ala Val Ile Ser Val Ser Gly Ile Asn His Asp Val
                355                360                365

Thr Ser Gly Asp His Gly Asp Tyr Phe Arg Leu Leu Leu Pro Gly Ile
                370                375                380

Tyr Thr Val Ser Ala Thr Ala Pro Gly Tyr Asp Pro Glu Thr Val Thr
385                390                395                400

Val Thr Val Gly Pro Ala Glu Pro Thr Leu Val Asn Phe His Leu Lys
                405                410                415

Arg Ser Ile Pro Gln Val Ser Pro Val Arg Arg Ala Pro Ser Arg Arg
                420                425                430

His Gly Val Arg Ala Lys Val Gln Pro Gln Ala Arg Lys Lys Glu Met
                435                440                445

Glu Met Arg Gln Leu Gln Arg Gly Pro Ala
                450                455

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<210> SEQ ID NO 11
<211> LENGTH: 1212
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 11

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

Gln Tyr Ser Lys Lys Asp Lys Asn Thr Asp Thr Leu Ser Lys Lys Glu
                20                25                30

Leu Lys Glu Leu Leu Glu Lys Glu Phe Arg Gln Ile Leu Lys Asn Pro
                35                40                45

Asp Asp Pro Asp Met Val Asp Val Phe Met Asp His Leu Asp Ile Asp
                50                55                60

His Asn Lys Lys Ile Asp Phe Thr Glu Phe Leu Leu Met Val Phe Lys
                65                70                75                80

Leu Ala Gln Ala Tyr Tyr Glu Ser Thr Arg Lys Glu Asn Leu Pro Ile
                85                90                95

Ser Gly His Lys His Arg Lys His Ser His His Asp Lys His Glu Asp
                100                105                110

Asn Lys Gln Glu Glu Asn Lys Glu Asn Arg Lys Arg Pro Ser Ser Leu
                115                120                125

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Glu Arg Arg Asn Asn Arg Lys Gly Asn Lys Gly Arg Ser Lys Ser Pro
 130 135 140
 Arg Glu Thr Gly Gly Lys Arg His Glu Ser Ser Ser Glu Lys Lys Glu
 145 150 155 160
 Arg Lys Gly Tyr Ser Pro Thr His Arg Glu Glu Glu Tyr Gly Lys Asn
 165 170 175
 His His Asn Ser Ser Lys Lys Glu Lys Asn Lys Thr Glu Asn Thr Arg
 180 185 190
 Leu Gly Asp Asn Arg Lys Arg Leu Ser Glu Arg Leu Glu Glu Lys Glu
 195 200 205
 Asp Asn Glu Glu Gly Val Tyr Asp Tyr Glu Asn Thr Gly Arg Met Thr
 210 215 220
 Gln Lys Trp Ile Gln Ser Gly His Ile Ala Thr Tyr Tyr Thr Ile Gln
 225 230 235 240
 Asp Glu Ala Tyr Asp Thr Thr Asp Ser Leu Leu Glu Glu Asn Lys Ile
 245 250 255
 Tyr Glu Arg Ser Arg Ser Ser Asp Gly Lys Ser Ser Ser Gln Val Asn
 260 265 270
 Arg Ser Arg His Glu Asn Thr Ser Gln Val Pro Leu Gln Glu Ser Arg
 275 280 285
 Thr Arg Lys Arg Arg Gly Ser Arg Val Ser Gln Asp Arg Asp Ser Glu
 290 295 300
 Gly His Ser Glu Asp Ser Glu Arg His Ser Gly Ser Ala Ser Arg Asn
 305 310 315 320
 His His Gly Ser Ala Trp Glu Gln Ser Arg Asp Gly Ser Arg His Pro
 325 330 335
 Arg Ser His Asp Glu Asp Arg Ala Ser His Gly His Ser Ala Asp Ser
 340 345 350
 Ser Arg Gln Ser Gly Thr Arg His Ala Glu Thr Ser Ser Arg Gly Gln
 355 360 365
 Thr Ala Ser Ser His Glu Gln Ala Arg Ser Ser Pro Gly Glu Arg His
 370 375 380
 Gly Ser Gly His Gln Gln Ser Ala Asp Ser Ser Arg His Ser Ala Thr
 385 390 395 400
 Gly Arg Gly Gln Ala Ser Ser Ala Val Ser Asp Arg Gly His Arg Gly
 405 410 415
 Ser Ser Gly Ser Gln Ala Ser Asp Ser Glu Gly His Ser Glu Asn Ser
 420 425 430
 Asp Thr Gln Ser Val Ser Gly His Gly Lys Ala Gly Leu Arg Gln Gln
 435 440 445
 Ser His Gln Glu Ser Thr Arg Gly Arg Ser Gly Glu Arg Ser Gly Arg
 450 455 460
 Ser Gly Ser Phe Ile Tyr Gln Val Ser Thr His Glu Gln Ser Glu Ser
 465 470 475 480
 Ala His Gly Arg Thr Arg Thr Ser Thr Gly Arg Arg Gln Gly Ser His
 485 490 495
 His Glu Gln Ala Arg Asp Ser Ser Arg His Ser Ala Ser Gln Glu Gly
 500 505 510
 Gln Asp Thr Ile Arg Ala His Pro Gly Ser Arg Arg Gly Gly Arg Gln
 515 520 525
 Gly Ser His His Glu Gln Ser Val Asp Arg Ser Gly His Ser Gly Ser
 530 535 540

His 545	His	Ser	His	Thr	Thr 550	Ser	Gln	Gly	Arg 555	Ser	Asp	Val	Ser	Arg	Gly 560
Gln	Ser	Gly	Ser	Arg 565	Ser	Val	Ser	Arg	Gln 570	Thr	Arg	Asn	Glu	Lys	Gln
Ser	Gly	Asp	Gly 580	Ser	Arg	His	Ser	Gly 585	Ser	Arg	His	His	Glu	Ala	Ser
Ser	Arg	Ala 595	Asp	Ser	Ser	Arg	His 600	Ser	Gln	Val	Gly	Gln	Gly	Gln	Ser
Ser	Gly 610	Pro	Arg	Thr	Ser	Arg 615	Asn	Gln	Gly	Ser	Ser	Val	Ser	Gln	Asp
Ser	Asp	Ser	Gln	Gly 630	His	Ser	Glu	Asp	Ser	Glu 635	Arg	Arg	Ser	Gly	Ser
Ala	Ser	Arg	Asn	His 645	His	Gly	Ser	Ala	Gln 650	Glu	Gln	Ser	Arg	Asp	Gly
Ser	Arg	His	Pro 660	Arg	Ser	His	His	Glu	Asp 665	Arg	Ala	Gly	His	Gly	His
Ser	Ala 675	Glu	Ser	Ser	Arg	Gln	Ser	Gly 680	Thr	His	His	Ala	Glu	Asn	Ser
Ser	Gly 690	Gly	Gln	Ala	Ala 695	Ser	Ser	His	Glu	Gln	Ala	Arg	Ser	Ser	Ala
Gly 705	Glu	Arg	His	Gly 710	Ser	His	His	Gln	Gln 715	Ser	Ala	Asp	Ser	Ser	Arg
His	Ser	Gly	Ile 725	Gly	His	Gly	Gln	Ala	Ser 730	Ser	Ala	Val	Arg	Asp	Ser
Gly	His	Arg	Gly 740	Ser	Ser	Gly	Ser	Gln	Ala 745	Ser	Asp	Ser	Glu	Gly	His
Ser	Glu 755	Asp	Ser	Asp	Thr	Gln	Ser	Val	Ser 760	Ala	His	Gly	Gln	Ala	Gly
Pro 770	His	Gln	Gln	Ser	His	Gln 775	Glu	Ser	Thr	Arg	Gly	Arg	Ser	Ala	Gly
Arg 785	Ser	Gly	Arg	Ser	Gly 790	Ser	Phe	Leu	Tyr	Gln	Val	Ser	Thr	His	Glu
Gln	Ser	Glu	Ser	Ala 805	His	Gly	Arg	Thr	Arg 810	Thr	Ser	Thr	Gly	Arg	Arg
Gln	Gly	Ser	His 820	His	Glu	Gln	Ala	Arg	Asp 825	Ser	Ser	Arg	His	Ser	Ala
Ser	Gln 835	Glu	Gly	Gln	Asp	Thr	Ile 840	Arg	Gly	His	Pro	Gly	Ser	Ser	Arg
Arg 850	Gly	Arg	Gln	Gly	Ser	His 855	Tyr	Glu	Gln	Ser	Val	Asp	Arg	Ser	Gly
His 865	Ser	Gly	Ser	His	His 870	Ser	His	Thr	Thr	Ser	Gln	Gly	Arg	Ser	Asp
Ala	Ser	Arg	Gly 885	Gln	Ser	Gly	Ser	Arg	Ser 890	Ala	Ser	Arg	Gln	Thr	Arg
Asn	Asp	Glu	Gln 900	Ser	Gly	Asp	Gly	Ser	Arg 905	His	Ser	Trp	Ser	His	His
His	Glu 915	Ala	Ser	Thr	Gln	Ala	Asp	Ser	Ser 920	Arg	His	Ser	Gln	Ser	Gly
Gln 930	Gly	Gln	Ser	Ala	Gly	Pro 935	Arg	Thr	Ser	Arg	Asn	Gln	Gly	Ser	Ser
Val 945	Ser	Gln	Asp	Ser	Asp 950	Ser	Gln	Gly	His	Ser 955	Glu	Asp	Ser	Glu	Arg
Trp	Ser	Gly	Ser	Ala	Ser	Arg	Asn	His	Arg	Gly	Ser	Ala	Gln	Glu	Gly

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965				970				975							
Ser	Arg	Asp	Gly	Ser	Arg	His	Pro	Thr	Ser	His	His	Glu	Asp	Arg	Ala
			980												990
Gly	His	Gly	His	Ser	Ala	Glu	Ser	Ser	Arg	Gln	Ser	Gly	Thr	His	His
			995				1000								1005
Ala	Glu	Asn	Ser	Ser	Gly	Gly	Gln	Ala	Ala	Ser	Ser	His	Glu	Gln	
			1010				1015								1020
Ala	Arg	Ser	Ser	Ala	Gly	Glu	Arg	His	Gly	Ser	His	His	Gln	Gln	
			1025				1030								1035
Ser	Ala	Asp	Ser	Ser	Arg	His	Ser	Gly	Ile	Gly	His	Gly	Gln	Ala	
			1040				1045								1050
Ser	Ser	Ala	Val	Arg	Asp	Ser	Gly	His	Arg	Gly	Ser	Ser	Gly	Ser	
			1055				1060								1065
Gln	Ala	Ser	Asp	Ser	Glu	Gly	His	Ser	Glu	Asp	Ser	Asp	Thr	Gln	
			1070				1075								1080
Ser	Val	Ser	Ala	His	Gly	Gln	Ala	Gly	Pro	His	Gln	Gln	Ser	His	
			1085				1090								1095
Gln	Glu	Ser	Thr	Arg	Gly	Arg	Ser	Ala	Gly	Arg	Ser	Gly	Arg	Ser	
			1100				1105								1110
Gly	Ser	Phe	Leu	Tyr	Gln	Val	Ser	Thr	His	Glu	Gln	Ser	Glu	Ser	
			1115				1120								1125
Ala	His	Gly	Arg	Ala	Gly	Pro	Ser	Thr	Gly	Gly	Arg	Gln	Gly	Ser	
			1130				1135								1140
Arg	His	Glu	Gln	Ala	Arg	Asp	Ser	Ser	Arg	His	Ser	Ala	Ser	Gln	
			1145				1150								1155
Glu	Gly	Gln	Asp	Thr	Ile	Arg	Gly	His	Pro	Gly	Ser	Arg	Arg	Gly	
			1160				1165								1170
Gly	Arg	Gln	Gly	Ser	Tyr	His	Glu	Gln	Ser	Val	Asp	Arg	Ser	Gly	
			1175				1180								1185
His	Ser	Gly	Ser	His	His	Ser	His	Thr	Thr	Ser	Gln	Gly	Arg	Ser	
			1190				1195								1200
Asp	Ala	Ser	His	Gly	Gln	Ser	Gly	Ser							
			1205				1210								

<210> SEQ ID NO 12

<211> LENGTH: 1404

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 12

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

Pro	Pro	Ser	Ser	Lys	Lys	Ala	Pro	Pro	Pro	Ser	Gly	Ala	Ser	Gln	Thr
115						120				125					
Ile	Lys	Ser	Thr	Thr	Lys	Arg	Ser	Pro	Lys	Pro	Pro	Asn	Lys	Lys	Lys
130						135				140					
Thr	Lys	Lys	Val	Ile	Glu	Ser	Glu	Glu	Ile	Thr	Glu	Glu	His	Ser	Val
145				150						155		160			
Ser	Glu	Asn	Gln	Glu	Ser	Ser	Ser	Ser	Ser	Ser	Ser	Ser	Ser	Ser	Ser
				165				170				175			
Ser	Thr	Ile	Arg	Lys	Ile	Lys	Ser	Ser	Lys	Asn	Ser	Ala	Ala	Asn	Arg
		180						185				190			
Glu	Leu	Gln	Lys	Lys	Leu	Lys	Val	Lys	Asp	Asn	Lys	Lys	Asn	Arg	Thr
195						200						205			
Lys	Lys	Lys	Pro	Thr	Pro	Lys	Pro	Pro	Val	Val	Asp	Glu	Ala	Gly	Ser
210						215				220					
Gly	Leu	Asp	Asn	Gly	Asp	Phe	Lys	Val	Thr	Thr	Pro	Asp	Thr	Ser	Thr
225				230						235		240			
Thr	Gln	His	Asn	Lys	Val	Ser	Thr	Ser	Pro	Lys	Ile	Thr	Thr	Ala	Lys
				245				250				255			
Pro	Ile	Asn	Pro	Arg	Pro	Ser	Leu	Pro	Pro	Asn	Ser	Asp	Thr	Ser	Lys
		260						265				270			
Glu	Thr	Ser	Leu	Thr	Val	Asn	Lys	Glu	Thr	Thr	Val	Glu	Thr	Lys	Glu
275						280						285			
Thr	Thr	Thr	Thr	Asn	Lys	Gln	Thr	Ser	Thr	Asp	Gly	Lys	Glu	Lys	Thr
290						295				300					
Thr	Ser	Ala	Lys	Glu	Thr	Gln	Ser	Ile	Glu	Lys	Thr	Ser	Ala	Lys	Asp
305				310				315				320			
Leu	Ala	Pro	Thr	Ser	Lys	Val	Leu	Ala	Lys	Pro	Thr	Pro	Lys	Ala	Glu
				325				330				335			
Thr	Thr	Thr	Lys	Gly	Pro	Ala	Leu	Thr	Thr	Pro	Lys	Glu	Pro	Thr	Pro
		340				345						350			
Thr	Thr	Pro	Lys	Glu	Pro	Ala	Ser	Thr	Thr	Pro	Lys	Glu	Pro	Thr	Pro
355						360						365			
Thr	Thr	Ile	Lys	Ser	Ala	Pro	Thr	Thr	Pro	Lys	Glu	Pro	Ala	Pro	Thr
370						375				380					
Thr	Thr	Lys	Ser	Ala	Pro	Thr	Thr	Pro	Lys	Glu	Pro	Ala	Pro	Thr	Thr
385				390				395				400			
Thr	Lys	Glu	Pro	Ala	Pro	Thr	Thr	Pro	Lys	Glu	Pro	Ala	Pro	Thr	Thr
		405						410				415			
Thr	Lys	Glu	Pro	Ala	Pro	Thr	Thr	Thr	Lys	Ser	Ala	Pro	Thr	Thr	Pro
		420				425						430			
Lys	Glu	Pro	Ala	Pro	Thr	Thr	Pro	Lys	Lys	Pro	Ala	Pro	Thr	Thr	Pro
435						440						445			
Lys	Glu	Pro	Ala	Pro	Thr	Thr	Pro	Lys	Glu	Pro	Thr	Pro	Thr	Thr	Pro
450						455				460					
Lys	Glu	Pro	Ala	Pro	Thr	Thr	Lys	Glu	Pro	Ala	Pro	Thr	Thr	Pro	Lys
465				470				475				480			
Glu	Pro	Ala	Pro	Thr	Ala	Pro	Lys	Lys	Pro	Ala	Pro	Thr	Thr	Pro	Lys
		485						490				495			
Glu	Pro														

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530	535	540
Ala Pro Thr Thr Pro Lys Glu Pro Ser Pro Thr Thr Thr Lys Glu Pro 545 550 555 560		
Ala Pro Thr Thr Pro Lys Glu Pro Ala Pro Thr Thr Pro Lys Lys Pro 565 570 575		
Ala Pro Thr Thr Pro Lys Glu Pro Ala Pro Thr Thr Pro Lys Glu Pro 580 585 590		
Ala Pro Thr Thr Thr Lys Lys Pro Ala Pro Thr Thr Pro Lys Glu Pro 595 600 605		
Ala Pro Thr Thr Pro Lys Glu Thr Ala Pro Thr Thr Pro Lys Lys Leu 610 615 620		
Thr Pro Thr Thr Pro Glu Lys Leu Ala Pro Thr Thr Pro Glu Lys Pro 625 630 635 640		
Ala Pro Thr Thr Pro Glu Glu Leu Ala Pro Thr Thr Pro Glu Glu Pro 645 650 655		
Thr Pro Thr Thr Pro Glu Glu Pro Ala Pro Thr Thr Pro Lys Ala Ala 660 665 670		
Ala Pro Asn Thr Pro Lys Glu Pro Ala Pro Thr Thr Pro Lys Glu Pro 675 680 685		
Ala Pro Thr Thr Pro Lys Glu Pro Ala Pro Thr Thr Pro Lys Glu Thr 690 695 700		
Ala Pro Thr Thr Pro Lys Gly Thr Ala Pro Thr Thr Leu Lys Glu Pro 705 710 715 720		
Ala Pro Thr Thr Pro Lys Lys Pro Ala Pro Lys Glu Leu Ala Pro Thr 725 730 735		
Thr Thr Lys Glu Pro Thr Ser Thr Thr Cys Asp Lys Pro Ala Pro Thr 740 745 750		
Thr Pro Lys Gly Thr Ala Pro Thr Thr Pro Lys Glu Pro Ala Pro Thr 755 760 765		
Thr Pro Lys Glu Pro Ala Pro Thr Thr Pro Lys Gly Thr Ala Pro Thr 770 775 780		
Thr Leu Lys Glu Pro Ala Pro Thr Thr Pro Lys Lys Pro Ala Pro Lys 785 790 795 800		
Glu Leu Ala Pro Thr Thr Thr Lys Gly Pro Thr Ser Thr Thr Ser Asp 805 810 815		
Lys Pro Ala Pro Thr Thr Pro Lys Glu Thr Ala Pro Thr Thr Pro Lys 820 825 830		
Glu Pro Ala Pro Thr Thr Pro Lys Lys Pro Ala Pro Thr Thr Pro Glu 835 840 845		
Thr Pro Pro Pro Thr Thr Ser Glu Val Ser Thr Pro Thr Thr Thr Lys 850 855 860		
Glu Pro Thr Thr Ile His Lys Ser Pro Asp Glu Ser Thr Pro Glu Leu 865 870 875 880		
Ser Ala Glu Pro Thr Pro Lys Ala Leu Glu Asn Ser Pro Lys Glu Pro 885 890 895		
Gly Val Pro Thr Thr Lys Thr Pro Ala Ala Thr Lys Pro Glu Met Thr 900 905 910		
Thr Thr Ala Lys Asp Lys Thr Thr Glu Arg Asp Leu Arg Thr Thr Pro 915 920 925		
Glu Thr Thr Thr Ala Ala Pro Lys Met Thr Lys Glu Thr Ala Thr Thr 930 935 940		
Thr Glu Lys Thr Thr Glu Ser Lys Ile Thr Ala Thr Thr Thr Gln Val 945 950 955 960		

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Thr	Ser	Thr	Thr	Thr	Gln	Asp	Thr	Thr	Pro	Phe	Lys	Ile	Thr	Thr	Leu
				965					970						975
Lys	Thr	Thr	Thr	Leu	Ala	Pro	Lys	Val	Thr	Thr	Thr	Lys	Lys	Thr	Ile
				980				985					990		
Thr	Thr	Thr	Glu	Ile	Met	Asn	Lys	Pro	Glu	Glu	Thr	Ala	Lys	Pro	Lys
			995				1000					1005			
Asp	Arg	Ala	Thr	Asn	Ser	Lys	Ala	Thr	Thr	Pro	Lys	Pro	Gln	Lys	
	1010					1015					1020				
Pro	Thr	Lys	Ala	Pro	Lys	Lys	Pro	Thr	Ser	Thr	Lys	Lys	Pro	Lys	
	1025					1030					1035				
Thr	Met	Pro	Arg	Val	Arg	Lys	Pro	Lys	Thr	Thr	Pro	Thr	Pro	Arg	
	1040					1045					1050				
Lys	Met	Thr	Ser	Thr	Met	Pro	Glu	Leu	Asn	Pro	Thr	Ser	Arg	Ile	
	1055					1060					1065				
Ala	Glu	Ala	Met	Leu	Gln	Thr	Thr	Thr	Arg	Pro	Asn	Gln	Thr	Pro	
	1070					1075					1080				
Asn	Ser	Lys	Leu	Val	Glu	Val	Asn	Pro	Lys	Ser	Glu	Asp	Ala	Gly	
	1085					1090					1095				
Gly	Ala	Glu	Gly	Glu	Thr	Pro	His	Met	Leu	Leu	Arg	Pro	His	Val	
	1100					1105					1110				
Phe	Met	Pro	Glu	Val	Thr	Pro	Asp	Met	Asp	Tyr	Leu	Pro	Arg	Val	
	1115					1120					1125				
Pro	Asn	Gln	Gly	Ile	Ile	Ile	Asn	Pro	Met	Leu	Ser	Asp	Glu	Thr	
	1130					1135					1140				
Asn	Ile	Cys	Asn	Gly	Lys	Pro	Val	Asp	Gly	Leu	Thr	Thr	Leu	Arg	
	1145					1150					1155				
Asn	Gly	Thr	Leu	Val	Ala	Phe	Arg	Gly	His	Tyr	Phe	Trp	Met	Leu	
	1160					1165					1170				
Ser	Pro	Phe	Ser	Pro	Pro	Ser	Pro	Ala	Arg	Arg	Ile	Thr	Glu	Val	
	1175					1180					1185				
Trp	Gly	Ile	Pro	Ser	Pro	Ile	Asp	Thr	Val	Phe	Thr	Arg	Cys	Asn	
	1190					1195					1200				
Cys	Glu	Gly	Lys	Thr	Phe	Phe	Phe	Lys	Asp	Ser	Gln	Tyr	Trp	Arg	
	1205					1210					1215				
Phe	Thr	Asn	Asp	Ile	Lys	Asp	Ala	Gly	Tyr	Pro	Lys	Pro	Ile	Phe	
	1220					1225					1230				
Lys	Gly	Phe	Gly	Gly	Leu	Thr	Gly	Gln	Ile	Val	Ala	Ala	Leu	Ser	
	1235					1240					1245				
Thr	Ala	Lys	Tyr	Lys	Asn	Trp	Pro	Glu	Ser	Val	Tyr	Phe	Phe	Lys	
	1250					1255					1260				
Arg	Gly	Gly	Ser	Ile	Gln	Gln	Tyr	Ile	Tyr	Lys	Gln	Glu	Pro	Val	
	1265					1270					1275				
Gln	Lys	Cys	Pro	Gly	Arg	Arg	Pro	Ala	Leu	Asn	Tyr	Pro	Val	Tyr	
	1280					1285					1290				
Gly	Glu	Thr	Thr	Gln	Val	Arg	Arg	Arg	Arg	Phe	Glu	Arg	Ala	Ile	
	1295					1300					1305				
Gly	Pro	Ser	Gln	Thr	His	Thr	Ile	Arg	Ile	Gln	Tyr	Ser	Pro	Ala	
	1310					1315					1320				
Arg	Leu	Ala	Tyr	Gln	Asp	Lys	Gly	Val	Leu	His	Asn	Glu	Val	Lys	
	1325					1330					1335				
Val	Ser	Ile	Leu	Trp	Arg	Gly	Leu	Pro	Asn	Val	Val	Thr	Ser	Ala	
	1340					1345					1350				

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Ile Ser  Leu Pro Asn Ile Arg  Lys Pro Asp Gly Tyr  Asp Tyr Tyr
1355                                1360                    1365

Ala Phe  Ser Lys Asp Gln Tyr  Tyr Asn Ile Asp Val  Pro Ser Arg
1370                                1375                    1380

Thr Ala  Arg Ala Ile Thr  Thr  Arg Ser Gly Gln Thr  Leu Ser Lys
1385                                1390                    1395

Val Trp  Tyr Asn Cys Pro
1400

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<210> SEQ ID NO 13
<211> LENGTH: 367
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 13

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Met Lys Ser Leu Val Leu Leu Leu Cys Leu Ala Gln Leu Trp Gly Cys
1          5          10          15

His Ser Ala Pro His Gly Pro Gly Leu Ile Tyr Arg Gln Pro Asn Cys
          20          25          30

Asp Asp Pro Glu Thr Glu Glu Ala Ala Leu Val Ala Ile Asp Tyr Ile
          35          40          45

Asn Gln Asn Leu Pro Trp Gly Tyr Lys His Thr Leu Asn Gln Ile Asp
          50          55          60

Glu Val Lys Val Trp Pro Gln Gln Pro Ser Gly Glu Leu Phe Glu Ile
65          70          75          80

Glu Ile Asp Thr Leu Glu Thr Thr Cys His Val Leu Asp Pro Thr Pro
          85          90          95

Val Ala Arg Cys Ser Val Arg Gln Leu Lys Glu His Ala Val Glu Gly
          100          105          110

Asp Cys Asp Phe Gln Leu Leu Lys Leu Asp Gly Lys Phe Ser Val Val
          115          120          125

Tyr Ala Lys Cys Asp Ser Ser Pro Asp Ser Ala Glu Asp Val Arg Lys
          130          135          140

Val Cys Gln Asp Cys Pro Leu Leu Ala Pro Leu Asn Asp Thr Arg Val
145          150          155          160

Val His Ala Ala Lys Ala Ala Leu Ala Ala Phe Asn Ala Gln Asn Asn
          165          170          175

Gly Ser Asn Phe Gln Leu Glu Glu Ile Ser Arg Ala Gln Leu Val Pro
          180          185          190

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

Val Ala Lys Glu Ala Thr Glu Ala Ala Lys Cys Asn Leu Leu Ala Glu
          210          215          220

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

Ala Glu Val Ala Val Thr Cys Thr Val Phe Gln Thr Gln Pro Val Thr
          245          250          255

Ser Gln Pro Gln Pro Glu Gly Ala Asn Glu Ala Val Pro Thr Pro Val
          260          265          270

Val Asp Pro Asp Ala Pro Pro Ser Pro Pro Leu Gly Ala Pro Gly Leu
          275          280          285

Pro Pro Ala Gly Ser Pro Pro Asp Ser His Val Leu Leu Ala Ala Pro
          290          295          300

Pro Gly His Gln Leu His Arg Ala His Tyr Asp Leu Arg His Thr Phe
305          310          315          320

```

Met	Gly	Val	Val	Ser	Leu	Gly	Ser	Pro	Ser	Gly	Glu	Val	Ser	His	Pro
				325					330					335	
Arg	Lys	Thr	Arg	Thr	Val	Val	Gln	Pro	Ser	Val	Gly	Ala	Ala	Ala	Gly
				340				345					350		
Pro	Val	Val	Pro	Pro	Cys	Pro	Gly	Arg	Ile	Arg	His	Phe	Lys	Val	
				355			360					365			

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<210> SEQ ID NO 14
<211> LENGTH: 249
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens
```

<400> SEQUENCE: 14

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

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<210> SEQ ID NO 15
<211> LENGTH: 298
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens
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<400> SEQUENCE: 15

Met Val Arg Met Val Pro Val Leu Leu Ser Leu Leu Leu Leu Leu Gly
1 5 10 15

Pro Ala Val Pro Gln Glu Asn Gln Asp Gly Arg Tyr Ser Leu Thr Tyr
20 25 30

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Ile Tyr Thr Gly Leu Ser Lys His Val Glu Asp Val Pro Ala Phe Gln
   35                               40                               45

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

Asp Arg Lys Ser Gln Pro Met Gly Leu Trp Arg Gln Val Glu Gly Met
   65                               70                               75                               80

Glu Asp Trp Lys Gln Asp Ser Gln Leu Gln Lys Ala Arg Glu Asp Ile
   85                               90                               95

Phe Met Glu Thr Leu Lys Asp Ile Val Glu Tyr Tyr Asn Asp Ser Asn
   100                              105                              110

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

Arg Ser Ser Gly Ala Phe Trp Lys Tyr Tyr Tyr Asp Gly Lys Asp Tyr
   130                              135                              140

Ile Glu Phe Asn Lys Glu Ile Pro Ala Trp Val Pro Phe Asp Pro Ala
   145                              150                              155                              160

Ala Gln Ile Thr Lys Gln Lys Trp Glu Ala Glu Pro Val Tyr Val Gln
   165                              170                              175

Arg Ala Lys Ala Tyr Leu Glu Glu Glu Cys Pro Ala Thr Leu Arg Lys
   180                              185                              190

Tyr Leu Lys Tyr Ser Lys Asn Ile Leu Asp Arg Gln Asp Pro Pro Ser
   195                              200                              205

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

Cys Leu Ala Tyr Asp Phe Tyr Pro Gly Lys Ile Asp Val His Trp Thr
   225                              230                              235                              240

Arg Ala Gly Glu Val Gln Glu Pro Glu Leu Arg Gly Asp Val Leu His
   245                              250                              255

Asn Gly Asn Gly Thr Tyr Gln Ser Trp Val Val Val Ala Val Pro Pro
   260                              265                              270

Gln Asp Thr Ala Pro Tyr Ser Cys His Val Gln His Ser Ser Leu Ala
   275                              280                              285

Gln Pro Leu Val Val Pro Trp Glu Ala Ser
   290                              295

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<210> SEQ ID NO 16

<211> LENGTH: 1049

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 16

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Met Asp Trp Ser Phe Phe Arg Val Val Ala Val Leu Phe Ile Phe Leu
   1                               5                               10                               15

Val Val Val Glu Val Asn Ser Glu Phe Arg Ile Gln Val Arg Asp Tyr
   20                               25                               30

Asn Thr Lys Asn Gly Thr Ile Lys Trp His Ser Ile Arg Arg Gln Lys
   35                               40                               45

Arg Glu Trp Ile Lys Phe Ala Ala Ala Cys Arg Glu Gly Glu Asp Asn
   50                               55                               60

Ser Lys Arg Asn Pro Ile Ala Lys Ile His Ser Asp Cys Ala Ala Asn
   65                               70                               75                               80

Gln Gln Val Thr Tyr Arg Ile Ser Gly Val Gly Ile Asp Gln Pro Pro
   85                               90                               95

Tyr Gly Ile Phe Val Ile Asn Gln Lys Thr Gly Glu Ile Asn Ile Thr

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100					105					110						
Ser	Ile	Val	Asp	Arg	Glu	Val	Thr	Pro	Phe	Phe	Ile	Ile	Tyr	Cys	Arg	
115					120					125						
Ala	Leu	Asn	Ser	Met	Gly	Gln	Asp	Leu	Glu	Arg	Pro	Leu	Glu	Leu	Arg	
130					135					140						
Val	Arg	Val	Leu	Asp	Ile	Asn	Asp	Asn	Pro	Pro	Val	Phe	Ser	Met	Ala	
145					150					155					160	
Thr	Phe	Ala	Gly	Gln	Ile	Glu	Glu	Asn	Ser	Asn	Ala	Asn	Thr	Leu	Val	
165					170					175						
Met	Ile	Leu	Asn	Ala	Thr	Asp	Ala	Asp	Glu	Pro	Asn	Asn	Leu	Asn	Ser	
180					185					190						
Lys	Ile	Ala	Phe	Lys	Ile	Ile	Arg	Gln	Glu	Pro	Ser	Asp	Ser	Pro	Met	
195					200					205						
Phe	Ile	Ile	Asn	Arg	Asn	Thr	Gly	Glu	Ile	Arg	Thr	Met	Asn	Asn	Phe	
210					215					220						
Leu	Asp	Arg	Glu	Gln	Tyr	Gly	Gln	Tyr	Ala	Leu	Ala	Val	Arg	Gly	Ser	
225					230					235					240	
Asp	Arg	Asp	Gly	Gly	Ala	Asp	Gly	Met	Ser	Ala	Glu	Cys	Glu	Cys	Asn	
245					250					255						
Ile	Lys	Ile	Leu	Asp	Val	Asn	Asp	Asn	Ile	Pro	Tyr	Met	Glu	Gln	Ser	
260					265					270						
Ser	Tyr	Thr	Ile	Glu	Ile	Gln	Glu	Asn	Thr	Leu	Asn	Ser	Asn	Leu	Leu	
275					280					285						
Glu	Ile	Arg	Val	Ile	Asp	Leu	Asp	Glu	Glu	Phe	Ser	Ala	Asn	Trp	Met	
290					295					300						
Ala	Val	Ile	Phe	Phe	Ile	Ser	Gly	Asn	Glu	Gly	Asn	Trp	Phe	Glu	Ile	
305					310					315					320	
Glu	Met	Asn	Glu	Arg	Thr	Asn	Val	Gly	Ile	Leu	Lys	Val	Val	Lys	Pro	
325					330					335						
Leu	Asp	Tyr	Glu	Ala	Met	Gln	Ser	Leu	Gln	Leu	Ser	Ile	Gly	Val	Arg	
340					345					350						
Asn	Lys	Ala	Glu	Phe	His	His	Ser	Ile	Met	Ser	Gln	Tyr	Lys	Leu	Lys	
355					360					365						
Ala	Ser	Ala	Ile	Ser	Val	Thr	Val	Leu	Asn	Val	Ile	Glu	Gly	Pro	Val	
370					375					380						
Phe	Arg	Pro	Gly	Ser	Lys	Thr	Tyr	Val	Val	Thr	Gly	Asn	Met	Gly	Ser	
385					390					395					400	
Asn	Asp	Lys	Val	Gly	Asp	Phe	Val	Ala	Thr	Asp	Leu	Asp	Thr	Gly	Arg	
405					410					415						
Pro	Ser	Thr	Thr	Val	Arg	Tyr	Val	Met	Gly	Asn	Asn	Pro	Ala	Asp	Leu	
420					425					430						
Leu	Ala	Val	Asp	Ser	Arg	Thr	Gly	Lys	Leu	Thr	Leu	Lys	Asn	Lys	Val	
435					440					445						
Thr	Lys	Glu	Gln	Tyr	Asn	Met	Leu	Gly	Gly	Lys	Tyr	Gln	Gly	Thr	Ile	
450					455					460						
Leu	Ser	Ile	Asp	Asp	Asn	Leu	Gln	Arg	Thr	Cys	Thr	Gly	Thr	Ile	Asn	
465					470					475					480	
Ile	Asn	Ile	Gln	Ser	Phe	Gly	Asn	Asp	Asp	Arg	Thr	Asn	Thr	Glu	Pro	
485					490					495						
Asn	Thr	Lys	Ile	Thr	Thr	Asn	Thr	Gly	Arg	Gln	Glu	Ser	Thr	Ser	Ser	
500					505					510						
Thr	Asn	Tyr	Asp	Thr	Ser	Thr	Thr	Ser	Thr	Asp	Ser	Ser	Gln	Val	Tyr	
515					520					525						

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Ser Ser Glu Pro Gly Asn Gly Ala Lys Asp Leu Leu Ser Asp Asn Val
 530 535 540
 His Phe Gly Pro Ala Gly Ile Gly Leu Leu Ile Met Gly Phe Leu Val
 545 550 555 560
 Leu Gly Leu Val Pro Phe Leu Met Ile Cys Cys Asp Cys Gly Gly Ala
 565 570 575
 Pro Arg Ser Ala Ala Gly Phe Glu Pro Val Pro Glu Cys Ser Asp Gly
 580 585 590
 Ala Ile His Ser Trp Ala Val Glu Gly Pro Gln Pro Glu Pro Arg Asp
 595 600 605
 Ile Thr Thr Val Ile Pro Gln Ile Pro Pro Asp Asn Ala Asn Ile Ile
 610 615 620
 Glu Cys Ile Asp Asn Ser Gly Val Tyr Thr Asn Glu Tyr Gly Gly Arg
 625 630 635 640
 Glu Met Gln Asp Leu Gly Gly Gly Glu Arg Met Thr Gly Phe Glu Leu
 645 650 655
 Thr Glu Gly Val Lys Thr Ser Gly Met Pro Glu Ile Cys Gln Glu Tyr
 660 665 670
 Ser Gly Thr Leu Arg Arg Asn Ser Met Arg Glu Cys Arg Glu Gly Gly
 675 680 685
 Leu Asn Met Asn Phe Met Glu Ser Tyr Phe Cys Gln Lys Ala Tyr Ala
 690 695 700
 Tyr Ala Asp Glu Asp Glu Gly Arg Pro Ser Asn Asp Cys Leu Leu Ile
 705 710 715 720
 Tyr Asp Ile Glu Gly Val Gly Ser Pro Ala Gly Ser Val Gly Cys Cys
 725 730 735
 Ser Phe Ile Gly Glu Asp Leu Asp Asp Ser Phe Leu Asp Thr Leu Gly
 740 745 750
 Pro Lys Phe Lys Lys Leu Ala Asp Ile Ser Leu Gly Lys Glu Ser Tyr
 755 760 765
 Pro Asp Leu Asp Pro Ser Trp Pro Pro Gln Ser Thr Glu Pro Val Cys
 770 775 780
 Leu Pro Gln Glu Thr Glu Pro Val Val Ser Gly His Pro Pro Ile Ser
 785 790 795 800
 Pro His Phe Gly Thr Thr Thr Val Ile Ser Glu Ser Thr Tyr Pro Ser
 805 810 815
 Gly Pro Gly Val Leu His Pro Lys Pro Ile Leu Asp Pro Leu Gly Tyr
 820 825 830
 Gly Asn Val Thr Val Thr Glu Ser Tyr Thr Thr Ser Asp Thr Leu Lys
 835 840 845
 Pro Ser Val His Val His Asp Asn Arg Pro Ala Ser Asn Val Val Val
 850 855 860
 Thr Glu Arg Val Val Gly Pro Ile Ser Gly Ala Asp Leu His Gly Met
 865 870 875 880
 Leu Glu Met Pro Asp Leu Arg Asp Gly Ser Asn Val Ile Val Thr Glu
 885 890 895
 Arg Val Ile Ala Pro Ser Ser Ser Leu Pro Thr Ser Leu Thr Ile His
 900 905 910
 His Pro Arg Glu Ser Ser Asn Val Val Val Thr Glu Arg Val Ile Gln
 915 920 925
 Pro Thr Ser Gly Met Ile Gly Ser Leu Ser Met His Pro Glu Leu Ala
 930 935 940

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Asn Ala His Asn Val Ile Val Thr Glu Arg Val Val Ser Gly Ala Gly
 945 950 955 960
 Val Thr Gly Ile Ser Gly Thr Thr Gly Ile Ser Gly Gly Ile Gly Ser
 965 970 975
 Ser Gly Leu Val Gly Thr Ser Met Gly Ala Gly Ser Gly Ala Leu Ser
 980 985 990
 Gly Ala Gly Ile Ser Gly Gly Gly Ile Gly Leu Ser Ser Leu Gly Gly
 995 1000 1005
 Thr Ala Ser Ile Gly His Met Arg Ser Ser Ser Asp His His Phe
 1010 1015 1020
 Asn Gln Thr Ile Gly Ser Ala Ser Pro Ser Thr Ala Arg Ser Arg
 1025 1030 1035
 Ile Thr Lys Tyr Ser Thr Val Gln Tyr Ser Lys
 1040 1045

<210> SEQ ID NO 17
 <211> LENGTH: 242
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 17

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

<210> SEQ ID NO 18
 <211> LENGTH: 2850

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<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 18

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

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Gly Gln His Glu Ser Ala Ser Arg His Ser Ser Gly Arg Gly Gln His
 405 410 415
 Ser Ser Gly Ser Gly Gln Ser Pro Gly His Gly Gln Arg Gly Ser Gly
 420 425 430
 Ser Gly Gln Ser Pro Ser Ser Gly Gln His Gly Thr Gly Phe Gly Arg
 435 440 445
 Ser Ser Ser Ser Gly Pro Tyr Val Ser Gly Ser Gly Tyr Ser Ser Gly
 450 455 460
 Phe Gly His His Glu Ser Ser Ser Glu His Ser Ser Gly Tyr Thr Gln
 465 470 475 480
 His Gly Ser Gly Ser Gly His Ser Ser Gly His Gly Gln His Gly Ser
 485 490 495
 Arg Ser Gly Gln Ser Ser Arg Gly Glu Arg Gln Gly Ser Ser Ala Gly
 500 505 510
 Ser Ser Ser Ser Tyr Gly Gln His Gly Ser Gly Ser Arg Gln Ser Leu
 515 520 525
 Gly His Ser Arg His Gly Ser Gly Ser Gly Gln Ser Pro Ser Pro Ser
 530 535 540
 Arg Gly Arg His Glu Ser Gly Ser Arg Gln Ser Ser Ser Tyr Gly Pro
 545 550 555 560
 His Gly Tyr Gly Ser Gly Arg Ser Ser Ser Arg Gly Pro Tyr Glu Ser
 565 570 575
 Gly Ser Gly His Ser Ser Gly Leu Gly His Gln Glu Ser Arg Ser Gly
 580 585 590
 Gln Ser Ser Gly Tyr Gly Gln His Gly Ser Ser Ser Gly His Ser Ser
 595 600 605
 Thr His Gly Gln His Gly Ser Thr Ser Gly Gln Ser Ser Ser Cys Gly
 610 615 620
 Gln His Gly Ala Thr Ser Gly Gln Ser Ser Ser His Gly Gln His Gly
 625 630 635 640
 Ser Gly Ser Ser Gln Ser Ser Arg Tyr Gly Gln Gln Gly Ser Gly Ser
 645 650 655
 Gly Gln Ser Pro Ser Arg Gly Arg His Gly Ser Asp Phe Gly His Ser
 660 665 670
 Ser Ser Tyr Gly Gln His Gly Ser Gly Ser Gly Trp Ser Ser Ser Asn
 675 680 685
 Gly Pro His Gly Ser Val Ser Gly Gln Ser Ser Gly Phe Gly His Lys
 690 695 700
 Ser Gly Ser Gly Gln Ser Ser Gly Tyr Ser Gln His Gly Ser Gly Ser
 705 710 715 720
 Ser His Ser Ser Gly Tyr Arg Lys His Gly Ser Arg Ser Gly Gln Ser
 725 730 735
 Ser Arg Ser Glu Gln His Gly Ser Ser Ser Gly Leu Ser Ser Ser Tyr
 740 745 750
 Gly Gln His Gly Ser Gly Ser His Gln Ser Ser Gly His Gly Arg Gln
 755 760 765
 Gly Ser Gly Ser Gly His Ser Pro Ser Arg Val Arg His Gly Ser Ser
 770 775 780
 Ser Gly His Ser Ser Ser His Gly Gln His Gly Ser Gly Thr Ser Cys
 785 790 795 800
 Ser Ser Ser Cys Gly His Tyr Glu Ser Gly Ser Gly Gln Ala Ser Gly
 805 810 815

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Phe Gly Gln His Glu Ser Gly Ser Gly Gln Gly Tyr Ser Gln His Gly
 820 825 830

Ser Ala Ser Gly His Phe Ser Ser Gln Gly Arg His Gly Ser Thr Ser
 835 840 845

Gly Gln Ser Ser Ser Ser Gly Gln His Asp Ser Ser Ser Gly Gln Ser
 850 855 860

Ser Ser Tyr Gly Gln His Glu Ser Ala Ser His His Ala Ser Gly Arg
 865 870 875 880

Gly Arg His Gly Ser Gly Ser Gly Gln Ser Pro Gly His Gly Gln Arg
 885 890 895

Gly Ser Gly Ser Gly Gln Ser Pro Ser Tyr Gly Arg His Gly Ser Gly
 900 905 910

Ser Gly Arg Ser Ser Ser Ser Gly Arg His Gly Ser Gly Ser Gly Gln
 915 920 925

Ser Ser Gly Phe Gly His Lys Ser Ser Ser Gly Gln Ser Ser Gly Tyr
 930 935 940

Thr Gln His Gly Ser Gly Ser Gly His Ser Ser Ser Tyr Glu Gln His
 945 950 955 960

Gly Ser Arg Ser Gly Gln Ser Ser Arg Ser Glu Gln His Gly Ser Ser
 965 970 975

Ser Gly Ser Ser Ser Ser Tyr Gly Gln His Gly Ser Gly Ser Arg Gln
 980 985 990

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

Pro Ser Arg Gly Arg His Gly Ser Gly Ser Gly Gln Ser Ser Ser
 1010 1015 1020

Tyr Gly Pro Tyr Arg Ser Gly Ser Gly Trp Ser Ser Ser Arg Gly
 1025 1030 1035

Pro Tyr Glu Ser Gly Ser Gly His Ser Ser Gly Leu Gly His Arg
 1040 1045 1050

Glu Ser Arg Ser Gly Gln Ser Ser Gly Tyr Gly Gln His Gly Ser
 1055 1060 1065

Ser Ser Gly His Ser Ser Thr His Gly Gln His Gly Ser Thr Ser
 1070 1075 1080

Gly Gln Ser Ser Ser Cys Gly Gln His Gly Ala Ser Ser Gly Gln
 1085 1090 1095

Ser Ser Ser His Gly Gln His Gly Ser Gly Ser Ser Gln Ser Ser
 1100 1105 1110

Gly Tyr Gly Arg Gln Gly Ser Gly Ser Gly Gln Ser Pro Gly His
 1115 1120 1125

Gly Gln Arg Gly Ser Gly Ser Arg Gln Ser Pro Ser Tyr Gly Arg
 1130 1135 1140

His Gly Ser Gly Ser Gly Arg Ser Ser Ser Ser Gly Gln His Gly
 1145 1150 1155

Ser Gly Leu Gly Glu Ser Ser Gly Phe Gly His His Glu Ser Ser
 1160 1165 1170

Ser Gly Gln Ser Ser Ser Tyr Ser Gln His Gly Ser Gly Ser Gly
 1175 1180 1185

His Ser Ser Gly Tyr Gly Gln His Gly Ser Arg Ser Gly Gln Ser
 1190 1195 1200

Ser Arg Gly Glu Arg His Gly Ser Ser Ser Gly Ser Ser Ser His
 1205 1210 1215

Tyr Gly Gln His Gly Ser Gly Ser Arg Gln Ser Ser Gly His Gly

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1220	1225	1230
Arg Gln Gly Ser Gly Ser	Gly His Ser Pro Ser	Arg Gly Arg His
1235	1240	1245
Gly Ser Gly Leu Gly His	Ser Ser Ser His Gly	Gln His Gly Ser
1250	1255	1260
Gly Ser Gly Arg Ser Ser	Ser Arg Gly Pro Tyr	Glu Ser Arg Ser
1265	1270	1275
Gly His Ser Ser Val Phe	Gly Gln His Glu Ser	Gly Ser Gly His
1280	1285	1290
Ser Ser Ala Tyr Ser Gln	His Gly Ser Gly Ser	Gly His Phe Cys
1295	1300	1305
Ser Gln Gly Gln His Gly	Ser Thr Ser Gly Gln	Ser Ser Thr Phe
1310	1315	1320
Asp Gln Glu Gly Ser Ser	Thr Gly Gln Ser Ser	Ser Tyr Gly His
1325	1330	1335
Arg Gly Ser Gly Ser Ser	Gln Ser Ser Gly Tyr	Gly Arg His Gly
1340	1345	1350
Ala Gly Ser Gly Gln Ser	Pro Ser Arg Gly Arg	His Gly Ser Gly
1355	1360	1365
Ser Gly His Ser Ser Ser	Tyr Gly Gln His Gly	Ser Gly Ser Gly
1370	1375	1380
Trp Ser Ser Ser Ser Gly	Arg His Gly Ser Gly	Ser Gly Gln Ser
1385	1390	1395
Ser Gly Phe Gly His His	Glu Ser Ser Ser Trp	Gln Ser Ser Gly
1400	1405	1410
Cys Thr Gln His Gly Ser	Gly Ser Gly His Ser	Ser Ser Tyr Glu
1415	1420	1425
Gln His Gly Ser Arg Ser	Gly Gln Ser Ser Arg	Gly Glu Arg His
1430	1435	1440
Gly Ser Ser Ser Gly Ser	Ser Ser Tyr Gly Gln	His Gly Ser
1445	1450	1455
Gly Ser Arg Gln Ser Leu	Gly His Gly Gln His	Gly Ser Gly Ser
1460	1465	1470
Gly Gln Ser Pro Ser Pro	Ser Arg Gly Arg His	Gly Ser Gly Ser
1475	1480	1485
Gly Gln Ser Ser Ser Tyr	Ser Pro Tyr Gly Ser	Gly Ser Gly Trp
1490	1495	1500
Ser Ser Ser Arg Gly Pro	Tyr Glu Ser Gly Ser	Ser His Ser Ser
1505	1510	1515
Gly Leu Gly His Arg Glu	Ser Arg Ser Gly Gln	Ser Ser Gly Tyr
1520	1525	1530
Gly Gln His Gly Ser Ser	Ser Gly His Ser Ser	Thr His Gly Gln
1535	1540	1545
His Gly Ser Thr Ser Gly	Gln Ser Ser Ser Cys	Gly Gln His Gly
1550	1555	1560
Ala Ser Ser Gly Gln Ser	Ser Ser His Gly Gln	His Gly Ser Gly
1565	1570	1575
Ser Ser Gln Ser Ser Gly	Tyr Gly Arg Gln Gly	Ser Gly Ser Gly
1580	1585	1590
Gln Ser Pro Gly His Gly	Gln Arg Gly Ser Gly	Ser Arg Gln Ser
1595	1600	1605
Pro Ser Tyr Gly Arg His	Gly Ser Gly Ser Gly	Arg Ser Ser Ser
1610	1615	1620

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Ser Gly 1625	Gln His Gly Ser 1630	Leu Gly Glu Ser Ser 1635	Gly Phe Gly
His His 1640	Glu Ser Ser Ser 1645	Gln Ser Ser Ser Tyr 1650	Ser Gln His
Gly Ser 1655	Gly Ser Gly His 1660	Ser Gly Tyr Gly Gln 1665	His Gly Ser
Arg Ser 1670	Gly Gln Ser Ser 1675	Gly Glu Arg His Gly 1680	Ser Ser Ser
Arg Ser 1685	Ser Ser Arg Tyr 1690	Gln His Gly Ser Gly 1695	Ser Arg Gln
Ser Ser 1700	Gly His Gly Arg 1705	Gln Gly Ser Gly Ser Gly 1710	Gln Ser Pro
Ser Arg 1715	Gly Arg His Gly 1720	Gly Leu Gly His Ser 1725	Ser Ser His
Gly Gln 1730	His Gly Ser Gly 1735	Gly Arg Ser Ser Ser 1740	Arg Gly Pro
Tyr Glu 1745	Ser Arg Ser Gly 1750	Ser Ser Val Phe Gly 1755	Gln His Glu
Ser Gly 1760	Ser Gly His Ser 1765	Ala Tyr Ser Gln His 1770	Gly Ser Gly
Ser Gly 1775	His Phe Cys Ser 1780	Gln Gly Gln His Gly Ser 1785	Thr Ser Gly
Gln Ser 1790	Ser Thr Phe Asp 1795	Gln Glu Gly Ser Ser Thr 1800	Gly Gln Ser
Ser Ser 1805	His Gly Gln His 1810	Ser Gly Ser Ser Gln 1815	Ser Ser Ser
Tyr Gly 1820	Gln Gln Gly Ser 1825	Ser Gly Gln Ser Pro 1830	Ser Arg Gly
Arg His 1835	Gly Ser Gly Ser 1840	His Ser Ser Ser Tyr 1845	Gly Gln His
Gly Ser 1850	Gly Ser Gly Trp 1855	Ser Ser Ser Gly Arg 1860	His Gly Ser
Gly Ser 1865	Gly Gln Ser Ser 1870	Phe Gly His His Glu 1875	Ser Ser Ser
Trp Gln 1880	Ser Ser Gly Tyr 1885	Gln His Gly Ser Gly 1890	Ser Gly His
Ser Ser 1895	Ser Tyr Glu Gln 1900	Gly Ser Arg Ser Gly 1905	Gln Ser Ser
Arg Gly 1910	Glu Gln His Gly 1915	Ser Ser Gly Ser Ser 1920	Ser Ser Tyr
Gly Gln 1925	His Gly Ser Gly 1930	Arg Gln Ser Leu Gly 1935	His Gly Gln
His Gly 1940	Ser Gly Ser Gly 1945	Ser Pro Ser Pro Ser 1950	Arg Gly Arg
His Gly 1955	Ser Gly Ser Gly 1960	Ser Ser Ser Tyr Gly 1965	Pro Tyr Gly
Ser Gly 1970	Ser Gly Trp Ser 1975	Ser Arg Gly Pro Tyr 1980	Glu Ser Gly
Ser Gly 1985	His Ser Ser Gly 1990	Leu Gly His Arg Glu 1995	Arg Ser Gly
Gln Ser 2000	Ser Gly Tyr Gly 2005	His Gly Ser Ser Ser 2010	Gly His Ser

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Ser Thr 2015	His Gly Gln His 2020	Gly Ser Ala Ser Gly Gln 2025	Ser Ser Ser
Cys Gly 2030	Gln His Gly Ala Ser 2035	Ser Gly Gln Ser Ser 2040	Ser His Gly
Gln His 2045	Gly Ser Gly Ser Ser 2050	Gln Ser Ser Gly Tyr 2055	Gly Arg Gln
Gly Ser 2060	Gly Ser Gly Gln Ser 2065	Pro Gly His Gly Gln 2070	Arg Gly Ser
Gly Ser 2075	Arg Gln Ser Pro Ser 2080	Tyr Gly Arg His Gly 2085	Ser Gly Ser
Gly Arg 2090	Ser Ser Ser Ser Gly 2095	Gln His Gly Pro Gly 2100	Leu Gly Glu
Ser Ser 2105	Gly Phe Gly His His 2110	Glu Ser Ser Ser Gly 2115	Gln Ser Ser
Ser Tyr 2120	Ser Gln His Gly Ser 2125	Gly Ser Gly His Ser 2130	Ser Gly Tyr
Gly Gln 2135	His Gly Ser Arg Ser 2140	Gly Gln Ser Ser Arg 2145	Gly Glu Arg
His Gly 2150	Ser Ser Ser Gly Ser 2155	Ser Ser Arg Tyr Gly 2160	Gln His Gly
Ser Gly 2165	Ser Arg Gln Ser Ser 2170	Gly His Gly Arg Gln 2175	Gly Ser Gly
Ser Gly 2180	His Ser Pro Ser Arg 2185	Gly Arg His Gly Ser 2190	Gly Ser Gly
His Ser 2195	Ser Ser His Gly Gln 2200	His Gly Ser Gly Ser 2205	Gly Arg Ser
Ser Ser 2210	Arg Gly Pro Tyr Glu 2215	Ser Arg Ser Gly His 2220	Ser Ser Val
Phe Gly 2225	Gln His Glu Ser Gly 2230	Ser Gly His Ser Ser 2235	Ala Tyr Ser
Gln His 2240	Gly Ser Gly Ser Gly 2245	His Phe Cys Ser Gln 2250	Gly Gln His
Gly Ser 2255	Thr Ser Gly Gln Ser 2260	Ser Thr Phe Asp Gln 2265	Glu Gly Ser
Ser Thr 2270	Gly Gln Ser Ser Ser 2275	His Gly Gln His Gly 2280	Ser Gly Ser
Ser Gln 2285	Ser Ser Ser Tyr Gly 2290	Gln Gln Gly Ser Gly 2295	Ser Gly Gln
Ser Pro 2300	Ser Arg Gly Arg His 2305	Gly Ser Gly Ser Gly 2310	His Ser Ser
Ser Tyr 2315	Gly Gln His Gly Ser 2320	Gly Ser Gly Trp Ser 2325	Ser Ser Ser
Gly Arg 2330	His Gly Ser Gly Ser 2335	Gly Gln Ser Ser Gly 2340	Phe Gly His
His Glu 2345	Ser Ser Ser Trp Gln 2350	Ser Ser Gly Tyr Thr 2355	Gln His Gly
Ser Gly 2360	Ser Gly His Ser Ser 2365	Ser Tyr Glu Gln His 2370	Gly Ser Arg
Ser Gly 2375	Gln Ser Ser Arg Gly 2380	Glu Arg His Gly Ser 2385	Ser Ser Gly
Ser Ser 2390	Ser Ser Tyr Gly Gln 2395	His Gly Ser Gly Ser 2400	Arg Gln Ser
Leu Gly	His Gly Gln His Gly	Ser Gly Ser Gly Gln	Ser Pro Ser

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2405	2410	2415
Pro Ser Arg Gly Arg His Gly Ser Gly Ser Gly Gln Ser Ser Ser		
2420	2425	2430
Tyr Ser Pro Tyr Gly Ser Gly Ser Gly Trp Ser Ser Ser Arg Gly		
2435	2440	2445
Pro Tyr Glu Ser Gly Ser Gly His Ser Ser Gly Leu Gly His Arg		
2450	2455	2460
Glu Ser Arg Ser Gly Gln Ser Ser Gly Tyr Gly Gln His Gly Ser		
2465	2470	2475
Ser Ser Gly His Ser Ser Thr His Gly Gln His Gly Ser Thr Ser		
2480	2485	2490
Gly Gln Ser Ser Ser Cys Gly Gln His Gly Ala Ser Ser Gly Gln		
2495	2500	2505
Ser Ser Ser His Gly Gln His Gly Ser Gly Ser Ser Gln Ser Ser		
2510	2515	2520
Gly Tyr Gly Arg Gln Gly Ser Gly Ser Gly Gln Ser Pro Gly His		
2525	2530	2535
Gly Gln Arg Gly Ser Gly Ser Arg Gln Ser Pro Ser Tyr Gly Arg		
2540	2545	2550
His Gly Ser Gly Ser Gly Arg Ser Ser Ser Ser Gly Gln His Gly		
2555	2560	2565
Ser Gly Leu Gly Glu Ser Ser Gly Phe Gly His His Glu Ser Ser		
2570	2575	2580
Ser Gly Gln Ser Ser Ser Tyr Ser Gln His Gly Ser Gly Ser Gly		
2585	2590	2595
His Ser Ser Gly Tyr Gly Gln His Gly Ser Arg Ser Gly Gln Ser		
2600	2605	2610
Ser Arg Gly Glu Arg His Gly Ser Ser Ser Gly Ser Ser Ser His		
2615	2620	2625
Tyr Gly Gln His Gly Ser Gly Ser Arg Gln Ser Ser Gly His Gly		
2630	2635	2640
Arg Gln Gly Ser Gly Ser Gly Gln Ser Pro Ser Arg Gly Arg His		
2645	2650	2655
Gly Ser Gly Leu Gly His Ser Ser Ser His Gly Gln His Gly Ser		
2660	2665	2670
Gly Ser Gly Arg Ser Ser Ser Arg Gly Pro Tyr Glu Ser Arg Leu		
2675	2680	2685
Gly His Ser Ser Val Phe Gly Gln His Glu Ser Gly Ser Gly His		
2690	2695	2700
Ser Ser Ala Tyr Ser Gln His Gly Ser Gly Ser Gly His Phe Cys		
2705	2710	2715
Ser Gln Gly Gln His Gly Ser Thr Ser Gly Gln Ser Ser Thr Phe		
2720	2725	2730
Asp Gln Glu Gly Ser Ser Thr Gly Gln Ser Ser Ser Tyr Gly His		
2735	2740	2745
Arg Gly Ser Gly Ser Ser Gln Ser Ser Gly Tyr Gly Arg His Gly		
2750	2755	2760
Ala Gly Ser Gly Gln Ser Leu Ser His Gly Arg His Gly Ser Gly		
2765	2770	2775
Ser Gly Gln Ser Ser Ser Tyr Gly Gln His Gly Ser Gly Ser Gly		
2780	2785	2790
Gln Ser Ser Gly Tyr Ser Gln His Gly Ser Gly Ser Gly Gln Asp		
2795	2800	2805

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Gly Tyr Ser Tyr Cys Lys Gly Gly Ser Asn His Asp Gly Gly Ser
 2810 2815 2820

Ser Gly Ser Tyr Phe Leu Ser Phe Pro Ser Ser Thr Ser Pro Tyr
 2825 2830 2835

Glu Tyr Val Gln Glu Gln Arg Cys Tyr Phe Tyr Gln
 2840 2845 2850

<210> SEQ ID NO 19
 <211> LENGTH: 427
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 19

Met Lys Leu Ile Thr Ile Leu Phe Leu Cys Ser Arg Leu Leu Leu Ser
 1 5 10 15

Leu Thr Gln Glu Ser Gln Ser Glu Glu Ile Asp Cys Asn Asp Lys Asp
 20 25 30

Leu Phe Lys Ala Val Asp Ala Ala Leu Lys Lys Tyr Asn Ser Gln Asn
 35 40 45

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

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

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

Lys Asp Ala Ala Lys Ala Ala Thr Gly Glu Cys Thr Ala Thr Val Gly
 100 105 110

Lys Arg Ser Ser Thr Lys Phe Ser Val Ala Thr Gln Thr Cys Gln Ile
 115 120 125

Thr Pro Ala Glu Gly Pro Val Val Thr Ala Gln Tyr Asp Cys Leu Gly
 130 135 140

Cys Val His Pro Ile Ser Thr Gln Ser Pro Asp Leu Glu Pro Ile Leu
 145 150 155 160

Arg His Gly Ile Gln Tyr Phe Asn Asn Asn Thr Gln His Ser Ser Leu
 165 170 175

Phe Met Leu Asn Glu Val Lys Arg Ala Gln Arg Gln Val Val Ala Gly
 180 185 190

Leu Asn Phe Arg Ile Thr Tyr Ser Ile Val Gln Thr Asn Cys Ser Lys
 195 200 205

Glu Asn Phe Leu Phe Leu Thr Pro Asp Cys Lys Ser Leu Trp Asn Gly
 210 215 220

Asp Thr Gly Glu Cys Thr Asp Asn Ala Tyr Ile Asp Ile Gln Leu Arg
 225 230 235 240

Ile Ala Ser Phe Ser Gln Asn Cys Asp Ile Tyr Pro Gly Lys Asp Phe
 245 250 255

Val Gln Pro Pro Thr Lys Ile Cys Val Gly Cys Pro Arg Asp Ile Pro
 260 265 270

Thr Asn Ser Pro Glu Leu Glu Glu Thr Leu Thr His Thr Ile Thr Lys
 275 280 285

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

Lys Lys Ala Arg Val Gln Val Val Ala Gly Lys Lys Tyr Phe Ile Asp
 305 310 315 320

Phe Val Ala Arg Glu Thr Thr Cys Ser Lys Glu Ser Asn Glu Glu Leu

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Thr	Glu	Ser	Cys	Glu	Thr	Lys	Lys	Leu	Gly	Gln	Ser	Leu	Asp	Cys	Asn
			340					345					350		
Ala	Glu	Val	Tyr	Val	Val	Pro	Trp	Glu	Lys	Lys	Ile	Tyr	Pro	Thr	Val
		355					360					365			
Asn	Cys	Gln	Pro	Leu	Gly	Met	Ile	Ser	Leu	Met	Lys	Arg	Pro	Pro	Gly
	370					375					380				
Phe	Ser	Pro	Phe	Arg	Ser	Ser	Arg	Ile	Gly	Glu	Ile	Lys	Glu	Glu	Thr
385					390					395					400
Thr	Ser	His	Leu	Arg	Ser	Cys	Glu	Tyr	Lys	Gly	Arg	Pro	Pro	Lys	Ala
			405						410					415	
Gly	Ala	Glu	Pro	Ala	Ser	Glu	Arg	Glu	Val	Ser					
			420					425							

<210> SEQ ID NO 20
 <211> LENGTH: 418
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens
 <400> SEQUENCE: 20

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

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Ser Ile Ile Phe Phe Leu Pro Leu Lys Val Thr Gln Asn Leu Thr Leu
 275 280 285

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

Leu Lys Thr Val Gln Ala Val Leu Thr Val Pro Lys Leu Lys Leu Ser
 305 310 315 320

Tyr Glu Gly Glu Val Thr Lys Ser Leu Gln Glu Met Lys Leu Gln Ser
 325 330 335

Leu Phe Asp Ser Pro Asp Phe Ser Lys Ile Thr Gly Lys Pro Ile Lys
 340 345 350

Leu Thr Gln Val Glu His Arg Ala Gly Phe Glu Trp Asn Glu Asp Gly
 355 360 365

Ala Gly Thr Thr Pro Ser Pro Gly Leu Gln Pro Ala His Leu Thr Phe
 370 375 380

Pro Leu Asp Tyr His Leu Asn Gln Pro Phe Ile Phe Val Leu Arg Asp
 385 390 395 400

Thr Asp Thr Gly Ala Leu Leu Phe Ile Gly Lys Ile Leu Asp Pro Arg
 405 410 415

Gly Pro

<210> SEQ ID NO 21
 <211> LENGTH: 101
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 21

Met Ser Asn Thr Gln Ala Glu Arg Ser Ile Ile Gly Met Ile Asp Met
 1 5 10 15

Phe His Lys Tyr Thr Arg Arg Asp Asp Lys Ile Glu Lys Pro Ser Leu
 20 25 30

Leu Thr Met Met Lys Glu Asn Phe Pro Asn Phe Leu Ser Ala Cys Asp
 35 40 45

Lys Lys Gly Thr Asn Tyr Leu Ala Asp Val Phe Glu Lys Lys Asp Lys
 50 55 60

Asn Glu Asp Lys Lys Ile Asp Phe Ser Glu Phe Leu Ser Leu Leu Gly
 65 70 75 80

Asp Ile Ala Thr Asp Tyr His Lys Gln Ser His Gly Ala Ala Pro Cys
 85 90 95

Ser Gly Gly Ser Gln
 100

<210> SEQ ID NO 22
 <211> LENGTH: 93
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 22

Met Leu Thr Glu Leu Glu Lys Ala Leu Asn Ser Ile Ile Asp Val Tyr
 1 5 10 15

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

Asp Leu Lys Lys Leu Leu Glu Thr Glu Cys Pro Gln Tyr Ile Arg Lys
 35 40 45

Lys Gly Ala Asp Val Trp Phe Lys Glu Leu Asp Ile Asn Thr Asp Gly
 50 55 60

Ala Val Asn Phe Gln Glu Phe Leu Ile Leu Val Ile Lys Met Gly Val

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65              70              75              80
Ala Ala His Lys Lys Ser His Glu Glu Ser His Lys Glu
              85              90

<210> SEQ ID NO 23
<211> LENGTH: 114
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 23

Met Thr Cys Lys Met Ser Gln Leu Glu Arg Asn Ile Glu Thr Ile Ile
1              5              10              15

Asn Thr Phe His Gln Tyr Ser Val Lys Leu Gly His Pro Asp Thr Leu
              20              25              30

Asn Gln Gly Glu Phe Lys Glu Leu Val Arg Lys Asp Leu Gln Asn Phe
              35              40              45

Leu Lys Lys Glu Asn Lys Asn Glu Lys Val Ile Glu His Ile Met Glu
              50              55              60

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

Met Leu Met Ala Arg Leu Thr Trp Ala Ser His Glu Lys Met His Glu
              85              90              95

Gly Asp Glu Gly Pro Gly His His His Lys Pro Gly Leu Gly Glu Gly
              100              105              110

Thr Pro

<210> SEQ ID NO 24
<211> LENGTH: 202
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 24

Met Ser Ser Val Glu Lys Glu Thr Lys Thr Gln Cys Val Arg Ile Ala
1              5              10              15

Thr Lys Ala Ala Ala Thr Glu Glu Pro Glu Val Ile Pro Asp Pro Ala
              20              25              30

Lys Gln Thr Asp Arg Val Val Lys Ile Ala Gly Ile Ser Ala Gly Ile
              35              40              45

Leu Val Phe Ile Leu Leu Leu Leu Val Val Ile Leu Ile Val Lys Lys
              50              55              60

Arg Arg Ser Tyr Tyr Ser Tyr Ser Tyr Tyr Leu Lys Leu Ala Lys Lys
65              70              75              80

Arg Lys Asp Ala Met Gly Asn Thr Arg Gln Glu Met Thr His Met Val
              85              90              95

Asn Ala Met Asp Arg Ser Tyr Ala Asp Gln Ser Thr Leu His Ala Glu
              100              105              110

Asp Pro Leu Ser Ile Thr Phe Met Asp Gln His Asn Phe Ser Pro Arg
              115              120              125

Leu Pro Asn Asp Pro Leu Val Pro Thr Ala Val Leu Asp Glu Asn His
              130              135              140

Ser Ala Thr Ala Glu Ser Ser Arg Leu Leu Asp Val Pro Arg Tyr Leu
145              150              155              160

Cys Glu Gly Thr Glu Ser Pro Tyr Gln Thr Gly Gln Leu His Pro Ala
              165              170              175

Ile Arg Val Ala Asp Leu Leu Gln His Ile Asn Leu Met Lys Thr Ser
              180              185              190

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Asp Ser Tyr Gly Phe Lys Glu Glu Tyr Glu
195 200

<210> SEQ ID NO 25

<211> LENGTH: 484

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 25

Met Ser Arg Ser Thr Gln Glu Leu Leu Gly Tyr His Cys Arg Leu Gln
1 5 10 15

Asp Lys Leu Gln Glu Gln Glu Gly Ser Leu Ala Ala Glu Gly Arg His
20 25 30

Ser Leu Ala Ser Ala Ala Asp His Met Lys Val Val Pro Ser Leu Leu
35 40 45

Leu Ser Val Leu Leu Ala Gln Val Trp Leu Val Pro Gly Leu Ala Pro
50 55 60

Ser Pro Gln Ser Pro Glu Thr Pro Ala Pro Gln Asn Gln Thr Ser Arg
65 70 75 80

Val Val Gln Ala Pro Lys Glu Glu Glu Glu Asp Glu Gln Glu Ala Ser
85 90 95

Glu Glu Lys Ala Ser Glu Glu Glu Lys Ala Trp Leu Met Ala Ser Arg
100 105 110

Gln Gln Leu Ala Lys Glu Thr Ser Asn Phe Gly Phe Ser Leu Leu Arg
115 120 125

Lys Ile Ser Met Arg His Asp Gly Asn Met Val Phe Ser Pro Phe Gly
130 135 140

Met Ser Leu Ala Met Thr Gly Leu Met Leu Gly Ala Thr Gly Pro Thr
145 150 155 160

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

Lys Pro Gly Leu Leu Pro Ser Leu Phe Lys Gly Leu Arg Glu Thr Leu
180 185 190

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

His Lys Asp Phe Asp Val Lys Glu Thr Phe Phe Asn Leu Ser Lys Arg
210 215 220

Tyr Phe Asp Thr Glu Cys Val Pro Met Asn Phe Arg Asn Ala Ser Gln
225 230 235 240

Ala Lys Arg Leu Met Asn His Tyr Ile Asn Lys Glu Thr Arg Gly Lys
245 250 255

Ile Pro Lys Leu Phe Asp Glu Ile Asn Pro Glu Thr Lys Leu Ile Leu
260 265 270

Val Asp Tyr Ile Leu Phe Lys Gly Lys Trp Leu Thr Pro Phe Asp Pro
275 280 285

Val Phe Thr Glu Val Asp Thr Phe His Leu Asp Lys Tyr Lys Thr Ile
290 295 300

Lys Val Pro Met Met Tyr Gly Ala Gly Lys Phe Ala Ser Thr Phe Asp
305 310 315 320

Lys Asn Phe Arg Cys His Val Leu Lys Leu Pro Tyr Gln Gly Asn Ala
325 330 335

Thr Met Leu Val Val Leu Met Glu Lys Met Gly Asp His Leu Ala Leu
340 345 350

Glu Asp Tyr Leu Thr Thr Asp Leu Val Glu Thr Trp Leu Arg Asn Met

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Lys Thr Arg Asn Met Glu Val Phe Phe Pro Lys Phe Lys Leu Asp Gln	355	360	365
370	375	380	
Lys Tyr Glu Met His Glu Leu Leu Arg Gln Met Gly Ile Arg Arg Ile			
385	390	395	400
Phe Ser Pro Phe Ala Asp Leu Ser Glu Leu Ser Ala Thr Gly Arg Asn			
	405	410	415
Leu Gln Val Ser Arg Val Leu Gln Arg Thr Val Ile Glu Val Asp Glu			
	420	425	430
Arg Gly Thr Glu Ala Val Ala Gly Ile Leu Ser Glu Ile Thr Ala Tyr			
	435	440	445
Ser Met Pro Pro Val Ile Lys Val Asp Arg Pro Phe His Phe Met Ile			
450	455	460	
Tyr Glu Glu Thr Ser Gly Met Leu Leu Phe Leu Gly Arg Val Val Asn			
465	470	475	480
Pro Thr Leu Leu			

<210> SEQ ID NO 26

<211> LENGTH: 228

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 26

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

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<210> SEQ ID NO 27
<211> LENGTH: 2214
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 27

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

Thr Leu Val Ala Leu Leu Pro Pro Gly Ala Leu Cys Glu Val Trp Thr
          20          25          30

Gln Arg Leu His Gly Gly Ser Ala Pro Leu Pro Gln Asp Arg Gly Phe
          35          40          45

Leu Val Val Gln Gly Asp Pro Arg Glu Leu Arg Leu Trp Ala Arg Gly
50          55          60

Asp Ala Arg Gly Ala Ser Arg Ala Asp Glu Lys Pro Leu Arg Arg Lys
65          70          75          80

Arg Ser Ala Ala Leu Gln Pro Glu Pro Ile Lys Val Tyr Gly Gln Val
          85          90          95

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

Lys Ser Asn Val Ile Val Ala Leu Ala Arg Asp Ser Leu Ala Leu Ala
115          120          125

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

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

Glu Ala Val Ile Ala Gln Phe Tyr His Ser Pro Ala Asp Asn Lys Arg
165          170          175

Tyr Ile Phe Ala Asp Ala Tyr Ala Gln Tyr Leu Trp Ile Thr Phe Asp
180          185          190

Phe Cys Asn Thr Leu Gln Gly Phe Ser Ile Pro Phe Arg Ala Ala Asp
195          200          205

Leu Leu Leu His Ser Lys Ala Ser Asn Leu Leu Leu Gly Phe Asp Arg
210          215          220

Ser His Pro Asn Lys Gln Leu Trp Lys Ser Asp Asp Phe Gly Gln Thr
225          230          235          240

Trp Ile Met Ile Gln Glu His Val Lys Ser Phe Ser Trp Gly Ile Asp
245          250          255

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

Gly Tyr Ser Thr Val Phe Arg Ser Thr Asp Phe Phe Gln Ser Arg Glu
275          280          285

Asn Gln Glu Val Ile Leu Glu Glu Val Arg Asp Phe Gln Leu Arg Asp
290          295          300

Lys Tyr Met Phe Ala Thr Lys Val Val His Leu Leu Gly Ser Glu Gln
305          310          315          320

Gln Ser Ser Val Gln Leu Trp Val Ser Phe Gly Arg Lys Pro Met Arg
325          330          335

Ala Ala Gln Phe Val Thr Arg His Pro Ile Asn Glu Tyr Tyr Ile Ala
340          345          350

Asp Ala Ser Glu Asp Gln Val Phe Val Cys Val Ser His Ser Asn Asn
355          360          365

Arg Thr Asn Leu Tyr Ile Ser Glu Ala Glu Gly Leu Lys Phe Ser Leu
370          375          380

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Ser	Leu	Glu	Asn	Val	Leu	Tyr	Tyr	Ser	Pro	Gly	Gly	Ala	Gly	Ser	Asp
385					390					395					400
Thr	Leu	Val	Arg	Tyr	Phe	Ala	Asn	Glu	Pro	Phe	Ala	Asp	Phe	His	Arg
				405					410					415	
Val	Glu	Gly	Leu	Gln	Gly	Val	Tyr	Ile	Ala	Thr	Leu	Ile	Asn	Gly	Ser
				420				425					430		
Met	Asn	Glu	Glu	Asn	Met	Arg	Ser	Val	Ile	Thr	Phe	Asp	Lys	Gly	Gly
				435			440					445			
Thr	Trp	Glu	Phe	Leu	Gln	Ala	Pro	Ala	Phe	Thr	Gly	Tyr	Gly	Glu	Lys
	450					455					460				
Ile	Asn	Cys	Glu	Leu	Ser	Gln	Gly	Cys	Ser	Leu	His	Leu	Ala	Gln	Arg
465					470					475					480
Leu	Ser	Gln	Leu	Leu	Asn	Leu	Gln	Leu	Arg	Arg	Met	Pro	Ile	Leu	Ser
				485					490					495	
Lys	Glu	Ser	Ala	Pro	Gly	Leu	Ile	Ile	Ala	Thr	Gly	Ser	Val	Gly	Lys
			500					505					510		
Asn	Leu	Ala	Ser	Lys	Thr	Asn	Val	Tyr	Ile	Ser	Ser	Ser	Ala	Gly	Ala
		515					520					525			
Arg	Trp	Arg	Glu	Ala	Leu	Pro	Gly	Pro	His	Tyr	Tyr	Thr	Trp	Gly	Asp
	530					535					540				
His	Gly	Gly	Ile	Ile	Thr	Ala	Ile	Ala	Gln	Gly	Met	Glu	Thr	Asn	Glu
545				550						555					560
Leu	Lys	Tyr	Ser	Thr	Asn	Glu	Gly	Glu	Thr	Trp	Lys	Thr	Phe	Ile	Phe
				565					570					575	
Ser	Glu	Lys	Pro	Val	Phe	Val	Tyr	Gly	Leu	Leu	Thr	Glu	Pro	Gly	Glu
			580					585					590		
Lys	Ser	Thr	Val	Phe	Thr	Ile	Phe	Gly	Ser	Asn	Lys	Glu	Asn	Val	His
		595					600					605			
Ser	Trp	Leu	Ile	Leu	Gln	Val	Asn	Ala	Thr	Asp	Ala	Leu	Gly	Val	Pro
	610					615					620				
Cys	Thr	Glu	Asn	Asp	Tyr	Lys	Leu	Trp	Ser	Pro	Ser	Asp	Glu	Arg	Gly
625					630					635					640
Asn	Glu	Cys	Leu	Leu	Gly	His	Lys	Thr	Val	Phe	Lys	Arg	Arg	Thr	Pro
				645					650					655	
His	Ala	Thr	Cys	Phe	Asn	Gly	Glu	Asp	Phe	Asp	Arg	Pro	Val	Val	Val
			660					665					670		
Ser	Asn	Cys	Ser	Cys	Thr	Arg	Glu	Asp	Tyr	Glu	Cys	Asp	Phe	Gly	Phe
		675					680					685			
Lys	Met	Ser	Glu	Asp	Leu	Ser	Leu	Glu	Val	Cys	Val	Pro	Asp	Pro	Glu
	690					695					700				
Phe	Ser	Gly	Lys	Ser	Tyr	Ser	Pro	Pro	Val	Pro	Cys	Pro	Val	Gly	Ser
705					710					715					720
Thr	Tyr	Arg	Arg	Thr	Arg	Gly	Tyr	Arg	Lys	Ile	Ser	Gly	Asp	Thr	Cys
				725					730					735	
Ser	Gly	Gly	Asp												

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805						810						815					
Leu	Asn	Gly	Ser	Thr	Gly	Gln	Glu	Val	Ile	Ile	Asn	Ser	Gly	Leu	Glu		
820						825						830					
Thr	Val	Glu	Ala	Leu	Ala	Phe	Glu	Pro	Leu	Ser	Gln	Leu	Leu	Tyr	Trp		
835						840						845					
Val	Asp	Ala	Gly	Phe	Lys	Lys	Ile	Glu	Val	Ala	Asn	Pro	Asp	Gly	Asp		
850						855						860					
Phe	Arg	Leu	Thr	Ile	Val	Asn	Ser	Ser	Val	Leu	Asp	Arg	Pro	Arg	Ala		
865						870						875					
Leu	Val	Leu	Val	Pro	Gln	Glu	Gly	Val	Met	Phe	Trp	Thr	Asp	Trp	Gly		
885						890						895					
Asp	Leu	Lys	Pro	Gly	Ile	Tyr	Arg	Ser	Asn	Met	Asp	Gly	Ser	Ala	Ala		
900						905						910					
Tyr	His	Leu	Val	Ser	Glu	Asp	Val	Lys	Trp	Pro	Asn	Gly	Ile	Ser	Val		
915						920						925					
Asp	Asp	Gln	Trp	Ile	Tyr	Trp	Thr	Asp	Ala	Tyr	Leu	Glu	Cys	Ile	Glu		
930						935						940					
Arg	Ile	Thr	Phe	Ser	Gly	Gln	Gln	Arg	Ser	Val	Ile	Leu	Asp	Asn	Leu		
945						950						955					
Pro	His	Pro	Tyr	Ala	Ile	Ala	Val	Phe	Lys	Asn	Glu	Ile	Tyr	Trp	Asp		
965						970						975					
Asp	Trp	Ser	Gln	Leu	Ser	Ile	Phe	Arg	Ala	Ser	Lys	Tyr	Ser	Gly	Ser		
980						985						990					
Gln	Met	Glu	Ile	Leu	Ala	Asn	Gln	Leu	Thr	Gly	Leu	Met	Asp	Met	Lys		
995						1000						1005					
Ile	Phe	Tyr	Lys	Gly	Lys	Asn	Thr	Gly	Ser	Asn	Ala	Cys	Val	Pro			
1010						1015						1020					
Arg	Pro	Cys	Ser	Leu	Leu	Cys	Leu	Pro	Lys	Ala	Asn	Asn	Ser	Arg			
1025						1030						1035					
Ser	Cys	Arg	Cys	Pro	Glu	Asp	Val	Ser	Ser	Ser	Val	Leu	Pro	Ser			
1040						1045						1050					
Gly	Asp	Leu	Met	Cys	Asp	Cys	Pro	Gln	Gly	Tyr	Gln	Leu	Lys	Asn			
1055						1060						1065					
Asn	Thr	Cys	Val	Lys	Glu	Glu	Asn	Thr	Cys	Leu	Arg	Asn	Gln	Tyr			
1070						1075						1080					
Arg	Cys	Ser	Asn	Gly	Asn	Cys	Ile	Asn	Ser	Ile	Trp	Trp	Cys	Asp			
1085						1090						1095					
Phe	Asp	Asn	Asp	Cys	Gly	Asp	Met	Ser	Asp	Glu	Arg	Asn	Cys	Pro			
1100						1105						1110					
Thr	Thr	Ile	Cys	Asp	Leu	Asp	Thr	Gln	Phe	Arg	Cys	Gln	Glu	Ser			
1115						1120						1125					
Gly	Thr	Cys	Ile	Pro	Leu	Ser	Tyr	Lys	Cys	Asp	Leu	Glu	Asp	Asp			
1130						1135						1140					
Cys	Gly	Asp	Asn	Ser	Asp	Glu	Ser	His	Cys	Glu	Met	His	Gln	Cys			
1145						1150						1155					
Arg	Ser	Asp	Glu	Tyr	Asn	Cys	Ser	Ser	Gly	Met	Cys	Ile	Arg	Ser			
1160						1165						1170					
Ser	Trp	Val	Cys	Asp	Gly	Asp	Asn	Asp	Cys	Arg	Asp	Trp	Ser	Asp			
1175						1180						1185					
Glu	Ala	Asn	Cys	Thr	Ala	Ile	Tyr	His	Thr	Cys	Glu	Ala	Ser	Asn			
1190						1195						1200					
Phe	Gln	Cys	Arg	Asn	Gly	His	Cys	Ile	Pro	Gln	Arg	Trp	Ala	Cys			
1205						1210						1215					

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Asp Gly 1220	Asp Thr Asp Cys Gln 1225	Asp Gly Ser Asp Glu 1230	Asp Pro Val
Asn Cys 1235	Glu Lys Lys Cys Asn 1240	Gly Phe Arg Cys Pro 1245	Asn Gly Thr
Cys Ile 1250	Pro Ser Ser Lys His 1255	Cys Asp Gly Leu Arg 1260	Asp Cys Ser
Asp Gly 1265	Ser Asp Glu Gln His 1270	Cys Glu Pro Leu Cys 1275	Thr His Phe
Met Asp 1280	Phe Val Cys Lys Asn 1285	Arg Gln Gln Cys Leu 1290	Phe His Ser
Met Val 1295	Cys Asp Gly Ile Ile 1300	Gln Cys Arg Asp Gly 1305	Ser Asp Glu
Asp Ala 1310	Ala Phe Ala Gly Cys 1315	Ser Gln Asp Pro Glu 1320	Phe His Lys
Val Cys 1325	Asp Glu Phe Gly Phe 1330	Gln Cys Gln Asn Gly 1335	Val Cys Ile
Ser Leu 1340	Ile Trp Lys Cys Asp 1345	Gly Met Asp Asp Cys 1350	Gly Asp Tyr
Ser Asp 1355	Glu Ala Asn Cys Glu 1360	Asn Pro Thr Glu Ala 1365	Pro Asn Cys
Ser Arg 1370	Tyr Phe Gln Phe Arg 1375	Cys Glu Asn Gly His 1380	Cys Ile Pro
Asn Arg 1385	Trp Lys Cys Asp Arg 1390	Glu Asn Asp Cys Gly 1395	Asp Trp Ser
Asp Glu 1400	Lys Asp Cys Gly Asp 1405	Ser His Ile Leu Pro 1410	Phe Ser Thr
Pro Gly 1415	Pro Ser Thr Cys Leu 1420	Pro Asn Tyr Tyr Arg 1425	Cys Ser Ser
Gly Thr 1430	Cys Val Met Asp Thr 1435	Trp Val Cys Asp Gly 1440	Tyr Arg Asp
Cys Ala 1445	Asp Gly Ser Asp Glu 1450	Glu Ala Cys Pro Leu 1455	Leu Ala Asn
Val Thr 1460	Ala Ala Ser Thr Pro 1465	Thr Gln Leu Gly Arg 1470	Cys Asp Arg
Phe Glu 1475	Phe Glu Cys His Gln 1480	Pro Lys Thr Cys Ile 1485	Pro Asn Trp
Lys Arg 1490	Cys Asp Gly His Gln 1495	Asp Cys Gln Asp Gly 1500	Arg Asp Glu
Ala Asn 1505	Cys Pro Thr His Ser 1510	Thr Leu Thr Cys Met 1515	Ser Arg Glu
Phe Gln 1520	Cys Glu Asp Gly Glu 1525	Ala Cys Ile Val Leu 1530	Ser Glu Arg
Cys Asp 1535	Gly Phe Leu Asp Cys 1540	Ser Asp Glu Ser Asp 1545	Glu Lys Ala
Cys Ser 1550	Asp Glu Leu Thr Val 1555	Tyr Lys Val Gln Asn 1560	Leu Gln Trp
Thr Ala 1565	Asp Phe Ser Gly Asp 1570	Val Thr Leu Thr Trp 1575	Met Arg Pro
Lys Lys 1580	Met Pro Ser Ala Ser 1585	Cys Val Tyr Asn Val 1590	Tyr Tyr Arg
Val Val 1595	Gly Glu Ser Ile Trp 1600	Lys Thr Leu Glu Thr 1605	His Ser Asn

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Lys Thr 1610	Asn Thr Val Leu 1615	Lys Val Leu Lys Pro 1620	Asp Thr Thr Tyr
Gln Val 1625	Lys Val Gln Val 1630	Gln Cys Leu Ser Lys Ala 1635	His Asn Thr
Asn Asp 1640	Phe Val Thr Leu 1645	Arg Thr Pro Glu Gly Leu 1650	Pro Asp Ala
Pro Arg 1655	Asn Leu Gln Leu 1660	Ser Leu Pro Arg Glu Ala 1665	Glu Gly Val
Ile Val 1670	Gly His Trp Ala 1675	Pro Pro Ile His Thr His 1680	Gly Leu Ile
Arg Glu 1685	Tyr Ile Val Glu 1690	Tyr Ser Arg Ser Gly Ser 1695	Lys Met Trp
Ala Ser 1700	Gln Arg Ala Ala 1705	Ser Asn Phe Thr Glu Ile 1710	Lys Asn Leu
Leu Val 1715	Asn Thr Leu Tyr 1720	Thr Val Arg Val Ala Ala 1725	Val Thr Ser
Arg Gly 1730	Ile Gly Asn Trp 1735	Ser Asp Ser Lys Ser Ile 1740	Thr Thr Ile
Lys Gly 1745	Lys Val Ile Pro 1750	Pro Pro Asp Ile His Ile 1755	Asp Ser Tyr
Gly Glu 1760	Asn Tyr Leu Ser 1765	Phe Thr Leu Thr Met Glu 1770	Ser Asp Ile
Lys Val 1775	Asn Gly Tyr Val 1780	Val Asn Leu Phe Trp Ala 1785	Phe Asp Thr
His Lys 1790	Gln Glu Arg Arg 1795	Thr Leu Asn Phe Arg Gly 1800	Ser Ile Leu
Ser His 1805	Lys Val Gly Asn 1810	Leu Thr Ala His Thr Ser 1815	Tyr Glu Ile
Ser Ala 1820	Trp Ala Lys Thr 1825	Asp Leu Gly Asp Ser Pro 1830	Leu Ala Phe
Glu His 1835	Val Met Thr Arg 1840	Gly Val Arg Pro Pro Ala 1845	Pro Ser Leu
Lys Ala 1850	Lys Ala Ile Asn 1855	Gln Thr Ala Val Glu Cys 1860	Thr Trp Thr
Gly Pro 1865	Arg Asn Val Val 1870	Tyr Gly Ile Phe Tyr Ala 1875	Thr Ser Phe
Leu Asp 1880	Leu Tyr Arg Asn 1885	Pro Lys Ser Leu Thr Thr 1890	Ser Leu His
Asn Lys 1895	Thr Val Ile Val 1900	Ser Lys Asp Glu Gln Tyr 1905	Leu Phe Leu
Val Arg 1910	Val Val Val Pro 1915	Tyr Gln Gly Pro Ser Ser 1920	Asp Tyr Val
Val Val 1925	Lys Met Ile Pro 1930	Asp Ser Arg Leu Pro Pro 1935	Arg His Leu
His Val 1940	Val His Thr Gly 1945	Lys Thr Ser Val Val Ile 1950	Lys Trp Glu
Ser Pro 1955	Tyr Asp Ser Pro 1960	Asp Gln Asp Leu Leu Tyr 1965	Ala Ile Ala
Val Lys 1970	Asp Leu Ile Arg 1975	Lys Thr Asp Arg Ser Tyr 1980	Lys Val Lys
Ser Arg 1985	Asn Ser Thr Val 1990	Glu Tyr Thr Leu Asn Lys 1995	Leu Glu Pro
Gly Gly	Lys Tyr His Ile Ile	Val Gln Leu Gly Asn	Met Ser Lys

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2000	2005	2010
Asp Ser Ser Ile Lys Ile	Thr Thr Val Ser Leu Ser	Ala Pro Asp
2015	2020	2025
Ala Leu Lys Ile Ile Thr	Glu Asn Asp His Val Leu	Leu Phe Trp
2030	2035	2040
Lys Ser Leu Ala Leu Lys	Glu Lys His Phe Asn Glu	Ser Arg Gly
2045	2050	2055
Tyr Glu Ile His Met Phe	Asp Ser Ala Met Asn Ile	Thr Ala Tyr
2060	2065	2070
Leu Gly Asn Thr Thr Asp	Asn Phe Phe Lys Ile Ser	Asn Leu Lys
2075	2080	2085
Met Gly His Asn Tyr Thr	Phe Thr Val Gln Ala Arg	Cys Leu Phe
2090	2095	2100
Gly Asn Gln Ile Cys Gly	Glu Pro Ala Ile Leu Leu	Tyr Asp Glu
2105	2110	2115
Leu Gly Ser Gly Ala Asp	Ala Ser Ala Thr Gln Ala	Ala Arg Ser
2120	2125	2130
Thr Asp Val Ala Ala Val	Val Val Pro Ile Leu Phe	Leu Ile Leu
2135	2140	2145
Leu Ser Leu Gly Val Gly	Phe Ala Ile Leu Tyr Thr	Lys His Arg
2150	2155	2160
Arg Leu Gln Ser Ser Phe	Thr Ala Phe Ala Asn Ser	His Tyr Ser
2165	2170	2175
Ser Arg Leu Gly Ser Ala	Ile Phe Ser Ser Gly Asp	Asp Leu Gly
2180	2185	2190
Glu Asp Asp Glu Asp Ala	Pro Met Ile Thr Gly Phe	Ser Asp Asp
2195	2200	2205
Val Pro Met Val Ile Ala		
2210		

<210> SEQ ID NO 28

<211> LENGTH: 168

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 28

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

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His	His	Ser	His	His	His	Ser	Gly	His	His	Ser	His	His	Asn	Phe	His
145					150					155					160

Asn	His	Ser	Asn	Pro	Trp	Cys	Gln
			165				

<210> SEQ ID NO 29

<211> LENGTH: 527

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 29

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

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Gly Arg Leu Phe Ala Tyr Pro Asp Thr His Arg His Arg Leu Gly Pro
 355 360 365
 Asn Tyr Leu His Ile Pro Val Asn Cys Pro Tyr Arg Ala Arg Val Ala
 370 375 380
 Asn Tyr Gln Arg Asp Gly Pro Met Cys Met Gln Asp Asn Gln Gly Gly
 385 390 395 400
 Ala Pro Asn Tyr Tyr Pro Asn Ser Phe Gly Ala Pro Glu Gln Gln Pro
 405 410 415
 Ser Ala Leu Glu His Ser Ile Gln Tyr Ser Gly Glu Val Arg Arg Phe
 420 425 430
 Asn Thr Ala Asn Asp Asp Asn Val Thr Gln Val Arg Ala Phe Tyr Val
 435 440 445
 Asn Val Leu Asn Glu Glu Gln Arg Lys Arg Leu Cys Glu Asn Ile Ala
 450 455 460
 Gly His Leu Lys Asp Ala Gln Ile Phe Ile Gln Lys Lys Ala Val Lys
 465 470 475 480
 Asn Phe Thr Glu Val His Pro Asp Tyr Gly Ser His Ile Gln Ala Leu
 485 490 495
 Leu Asp Lys Tyr Asn Ala Glu Lys Pro Lys Asn Ala Ile His Thr Phe
 500 505 510
 Val Gln Ser Gly Ser His Leu Ala Ala Arg Glu Lys Ala Asn Leu
 515 520 525

<210> SEQ ID NO 30
 <211> LENGTH: 175
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 30

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

<210> SEQ ID NO 31
 <211> LENGTH: 226
 <212> TYPE: PRT

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<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 31

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

<210> SEQ ID NO 32

<211> LENGTH: 655

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 32

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

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115						120						125					
His	Arg	Lys	Trp	Cys	Ala	Thr	Thr	His	Asn	Tyr	Asp	Arg	Asp	Arg	Ala		
130						135					140						
Trp	Gly	Tyr	Cys	Val	Glu	Ala	Thr	Pro	Pro	Pro	Gly	Gly	Pro	Ala	Ala		
145					150					155					160		
Leu	Asp	Pro	Cys	Ala	Ser	Gly	Pro	Cys	Leu	Asn	Gly	Gly	Ser	Cys	Ser		
				165					170					175			
Asn	Thr	Gln	Asp	Pro	Gln	Ser	Tyr	His	Cys	Ser	Cys	Pro	Arg	Ala	Phe		
			180					185					190				
Thr	Gly	Lys	Asp	Cys	Gly	Thr	Glu	Lys	Cys	Phe	Asp	Glu	Thr	Arg	Tyr		
		195					200					205					
Glu	Tyr	Leu	Glu	Gly	Gly	Asp	Arg	Trp	Ala	Arg	Val	Arg	Gln	Gly	His		
210						215					220						
Val	Glu	Gln	Cys	Glu	Cys	Phe	Gly	Gly	Arg	Thr	Trp	Cys	Glu	Gly	Thr		
225					230					235					240		
Arg	His	Thr	Ala	Cys	Leu	Ser	Ser	Pro	Cys	Leu	Asn	Gly	Gly	Thr	Cys		
				245					250					255			
His	Leu	Ile	Val	Ala	Thr	Gly	Thr	Thr	Val	Cys	Ala	Cys	Pro	Pro	Gly		
			260					265					270				
Phe	Ala	Gly	Arg	Leu	Cys	Asn	Ile	Glu	Pro	Asp	Glu	Arg	Cys	Phe	Leu		
		275					280				285						
Gly	Asn	Gly	Thr	Gly	Tyr	Arg	Gly	Val	Ala	Ser	Thr	Ser	Ala	Ser	Gly		
290						295					300						
Leu	Ser	Cys	Leu	Ala	Trp	Asn	Ser	Asp	Leu	Leu	Tyr	Gln	Glu	Leu	His		
305					310					315					320		
Val	Asp	Ser	Val	Gly	Ala	Ala	Ala	Leu	Leu	Gly	Leu	Gly	Pro	His	Ala		
				325				330						335			
Tyr	Cys	Arg	Asn	Pro	Asp	Asn	Asp	Glu	Arg	Pro	Trp	Cys	Tyr	Val	Val		
			340					345					350				
Lys	Asp	Ser	Ala	Leu	Ser	Trp	Glu	Tyr	Cys	Arg	Leu	Glu	Ala	Cys	Glu		
	355						360					365					
Ser	Leu	Thr	Arg	Val	Gln	Leu	Ser	Pro	Asp	Leu	Leu	Ala	Thr	Leu	Pro		
	370					375						380					
Glu	Pro	Ala	Ser	Pro	Gly	Arg	Gln	Ala	Cys	Gly	Arg	Arg	His	Lys	Lys		
385					390					395					400		
Arg	Thr	Phe	Leu	Arg	Pro	Arg	Ile	Ile	Gly	Gly	Ser	Ser	Ser	Leu	Pro		
			405						410					415			
Gly	Ser	His	Pro	Trp	Leu	Ala	Ala	Ile	Tyr	Ile	Gly	Asp	Ser	Phe	Cys		
			420					425					430				
Ala	Gly	Ser	Leu	Val	His	Thr	Cys	Trp	Val	Val	Ser	Ala	Ala	His	Cys		
		435					440					445					
Phe	Ser	His	Ser	Pro	Pro	Arg	Asp	Ser	Val	Ser	Val	Val	Leu	Gly	Gln		
	450					455					460						
His	Phe	Phe	Asn	Arg	Thr	Thr	Asp	Val	Thr	Gln	Thr	Phe	Gly	Ile	Glu		
465					470					475					480		
Lys	Tyr	Ile	Pro	Tyr	Thr	Leu	Tyr	Ser	Val	Phe	Asn	Pro	Ser	Asp	His		
			485						490					495			
Asp	Leu	Val	Leu	Ile	Arg	Leu	Lys	Lys	Lys	Gly	Asp	Arg	Cys	Ala	Thr		
			500					505					510				
Arg	Ser	Gln	Phe	Val	Gln	Pro	Ile	Cys	Leu	Pro	Glu	Pro	Gly	Ser	Thr		
		515					520					525					
Phe	Pro	Ala	Gly	His	Lys	Cys	Gln	Ile	Ala	Gly	Trp	Gly	His	Leu	Asp		
	530					535					540						

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Glu Asn Val Ser Gly Tyr Ser Ser Ser Leu Arg Glu Ala Leu Val Pro
 545 550 555 560
 Leu Val Ala Asp His Lys Cys Ser Ser Pro Glu Val Tyr Gly Ala Asp
 565 570 575
 Ile Ser Pro Asn Met Leu Cys Ala Gly Tyr Phe Asp Cys Lys Ser Asp
 580 585 590
 Ala Cys Gln Gly Asp Ser Gly Gly Pro Leu Ala Cys Glu Lys Asn Gly
 595 600 605
 Val Ala Tyr Leu Tyr Gly Ile Ile Ser Trp Gly Asp Gly Cys Gly Arg
 610 615 620
 Leu His Lys Pro Gly Val Tyr Thr Arg Val Ala Asn Tyr Val Asp Trp
 625 630 635 640
 Ile Asn Asp Arg Ile Arg Pro Pro Arg Arg Leu Val Ala Pro Ser
 645 650 655

<210> SEQ ID NO 33
 <211> LENGTH: 697
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 33

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

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260						265						270					
Lys	Gly	Glu	Gly	Tyr	Arg	Gly	Thr	Ala	Asn	Thr	Thr	Thr	Ala	Gly	Val		
275						280						285					
Pro	Cys	Gln	Arg	Trp	Asp	Ala	Gln	Ile	Pro	His	Gln	His	Arg	Phe	Thr		
290						295						300					
Pro	Glu	Lys	Tyr	Ala	Cys	Lys	Asp	Leu	Arg	Glu	Asn	Phe	Cys	Arg	Asn		
305						310						315					
Pro	Asp	Gly	Ser	Glu	Ala	Pro	Trp	Cys	Phe	Thr	Leu	Arg	Pro	Gly	Met		
325						330						335					
Arg	Ala	Ala	Phe	Cys	Tyr	Gln	Ile	Arg	Arg	Cys	Thr	Asp	Asp	Val	Arg		
340						345						350					
Pro	Gln	Asp	Cys	Tyr	His	Gly	Ala	Gly	Glu	Gln	Tyr	Arg	Gly	Thr	Val		
355						360						365					
Ser	Lys	Thr	Arg	Lys	Gly	Val	Gln	Cys	Gln	Arg	Trp	Ser	Ala	Glu	Thr		
370						375						380					
Pro	His	Lys	Pro	Gln	Phe	Thr	Phe	Thr	Ser	Glu	Pro	His	Ala	Gln	Leu		
385						390						395					
Glu	Glu	Asn	Phe	Cys	Arg	Asn	Pro	Asp	Gly	Asp	Ser	His	Gly	Pro	Trp		
405						410						415					
Cys	Tyr	Thr	Met	Asp	Pro	Arg	Thr	Pro	Phe	Asp	Tyr	Cys	Ala	Leu	Arg		
420						425						430					
Arg	Cys	Ala	Asp	Asp	Gln	Pro	Pro	Ser	Ile	Leu	Asp	Pro	Pro	Asp	Gln		
435						440						445					
Val	Gln	Phe	Glu	Lys	Cys	Gly	Lys	Arg	Val	Asp	Arg	Leu	Asp	Gln	Arg		
450						455						460					
Arg	Ser	Lys	Leu	Arg	Val	Val	Gly	Gly	His	Pro	Gly	Asn	Ser	Pro	Trp		
465						470						475					
Thr	Val	Ser	Leu	Arg	Asn	Arg	Gln	Gly	Gln	His	Phe	Cys	Gly	Gly	Ser		
485						490						495					
Leu	Val	Lys	Glu	Gln	Trp	Ile	Leu	Thr	Ala	Arg	Gln	Cys	Phe	Ser	Ser		
500						505						510					
Cys	His	Met	Pro	Leu	Thr	Gly	Tyr	Glu	Val	Trp	Leu	Gly	Thr	Leu	Phe		
515						520						525					
Gln	Asn	Pro	Gln	His	Gly	Glu	Pro	Ser	Leu	Gln	Arg	Val	Pro	Val	Ala		
530						535						540					
Lys	Met	Val	Cys	Gly	Pro	Ser	Gly	Ser	Gln	Leu	Val	Leu	Leu	Lys	Leu		
545						550						555					
Glu	Arg	Ser	Val	Thr	Leu	Asn	Gln	Arg	Val	Ala	Leu	Ile	Cys	Leu	Pro		
565						570						575					
Pro	Glu	Trp	Tyr	Val	Val	Pro	Pro	Gly	Thr	Lys	Cys	Glu	Ile	Ala	Gly		
580						585						590					
Trp	Gly	Glu	Thr	Lys	Gly	Thr	Gly	Asn	Asp	Thr	Val	Leu	Asn	Val	Ala		
595						600						605					
Leu	Leu	Asn	Val	Ile	Ser	Asn	Gln	Glu	Cys	Asn	Ile	Lys	His	Arg	Gly		
610						615						620					
Arg	Val	Arg	Glu	Ser	Glu	Met	Cys	Thr	Glu	Gly	Leu	Leu	Ala	Pro	Val		
625						630						635					
Gly	Ala	Cys	Glu	Gly	Asp	Tyr	Gly	Gly	Pro	Leu	Ala	Cys	Phe	Thr	His		
645						650						655					
Asn	Cys	Trp	Val	Leu	Glu	Gly	Ile	Ile	Ile	Pro	Asn	Arg	Val	Cys	Ala		
660						665						670					
Arg	Ser	Arg	Trp	Pro	Ala	Val	Phe	Thr	Arg	Val	Ser	Val	Phe	Val	Asp		
675						680						685					

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Trp Ile His Lys Val Met Arg Leu Gly
690 695

<210> SEQ ID NO 34

<211> LENGTH: 240

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 34

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

<210> SEQ ID NO 35

<211> LENGTH: 88

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 35

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

-continued

Cys Val Cys Thr Cys Thr Gln Cys
85

<210> SEQ ID NO 36

<211> LENGTH: 1439

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 36

Met Asp Thr Thr Ala Ala Ala Leu Pro Ala Phe Val Ala Leu Leu
1 5 10 15

Leu Leu Ser Pro Trp Pro Leu Leu Gly Ser Ala Gln Gly Gln Phe Ser
20 25 30

Ala Gly Gly Cys Thr Phe Asp Asp Gly Pro Gly Ala Cys Asp Tyr His
35 40 45

Gln Asp Leu Tyr Asp Asp Phe Glu Trp Val His Val Ser Ala Gln Glu
50 55 60

Pro His Tyr Leu Pro Pro Glu Met Pro Gln Gly Ser Tyr Met Ile Val
65 70 75 80

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

Thr Met Lys Glu Asn Asp Thr His Cys Ile Asp Phe Ser Tyr Leu Leu
100 105 110

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

Val Asn Lys Gly Pro Leu Ala Asn Pro Ile Trp Asn Val Thr Gly Phe
130 135 140

Thr Gly Arg Asp Trp Leu Arg Ala Glu Leu Ala Val Ser Thr Phe Trp
145 150 155 160

Pro Asn Glu Tyr Gln Val Ile Phe Glu Ala Glu Val Ser Gly Gly Arg
165 170 175

Ser Gly Tyr Ile Ala Ile Asp Asp Ile Gln Val Leu Ser Tyr Pro Cys
180 185 190

Asp Lys Ser Pro His Phe Leu Arg Leu Gly Asp Val Glu Val Asn Ala
195 200 205

Gly Gln Asn Ala Thr Phe Gln Cys Ile Ala Thr Gly Arg Asp Ala Val
210 215 220

His Asn Lys Leu Trp Leu Gln Arg Arg Asn Gly Glu Asp Ile Pro Val
225 230 235 240

Ala Gln Thr Lys Asn Ile Asn His Arg Arg Phe Ala Ala Ser Phe Arg
245 250 255

Leu Gln Glu Val Thr Lys Thr Asp Gln Asp Leu Tyr Arg Cys Val Thr
260 265 270

Gln Ser Glu Arg Gly Ser Gly Val Ser Asn Phe Ala Gln Leu Ile Val
275 280 285

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

Pro Thr Tyr Leu Leu Ile Gln Leu Asn Ala Asn Ser Ile Ile Gly Asp
305 310 315 320

Gly Pro Ile Ile Leu Lys Glu Val Glu Tyr Arg Met Thr Ser Gly Ser
325 330 335

Trp Thr Glu Thr His Ala Val Asn Ala Pro Thr Tyr Lys Leu Trp His
340 345 350

Leu Asp Pro Asp Thr Glu Tyr Glu Ile Arg Val Leu Leu Thr Arg Pro

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355					360					365					
Gly 370	Glu	Gly	Gly	Thr	Gly 375	Leu	Pro	Gly	Pro	Pro	Leu 380	Ile	Thr	Arg	Thr
Lys 385	Cys	Ala	Glu	Pro	Met 390	Arg	Thr	Pro	Lys	Thr 395	Leu	Lys	Ile	Ala	Glu 400
Ile	Gln	Ala	Arg	Arg 405	Ile	Ala	Val	Asp	Trp 410	Glu	Ser	Leu	Gly	Tyr 415	Asn
Ile	Thr	Arg	Cys	His 420	Thr	Phe	Asn	Val	Thr 425	Ile	Cys	Tyr	His	Tyr 430	Phe
Arg	Gly	His	Asn	Glu	Ser	Lys 440	Ala	Asp	Cys	Leu	Asp 445	Met	Asp	Pro	Lys
Ala 450	Pro	Gln	His	Val	Val 455	Asn	His	Leu	Pro	Pro	Tyr 460	Thr	Asn	Val	Ser
Leu 465	Lys	Met	Ile	Leu	Thr 470	Asn	Pro	Glu	Gly	Arg 475	Lys	Glu	Ser	Glu	Glu 480
Thr	Ile	Ile	Gln	Thr 485	Asp	Glu	Asp	Val	Pro 490	Gly	Pro	Val	Pro	Val 495	Lys
Ser	Leu	Gln	Gly	Thr 500	Ser	Phe	Glu	Asn	Lys 505	Ile	Phe	Leu	Asn	Trp	Lys
Glu	Pro	Leu	Asp	Pro	Asn	Gly 520	Ile	Ile	Thr	Gln	Tyr 525	Glu	Ile	Ser	Tyr
Ser 530	Ser	Ile	Arg	Ser	Phe 535	Asp	Pro	Ala	Val	Pro	Val 540	Ala	Gly	Pro	Pro
Gln 545	Thr	Val	Ser	Asn	Leu 550	Trp	Asn	Ser	Thr	His 555	His	Val	Phe	Met	His 560
Leu	His	Pro	Gly	Thr 565	Thr	Tyr	Gln	Phe	Phe 570	Ile	Arg	Ala	Ser	Thr 575	Val
Lys	Gly	Phe	Gly	Pro 580	Ala	Thr	Ala	Ile	Asn 585	Val	Thr	Thr	Asn	Ile	Ser
Ala	Pro	Thr	Leu	Pro 595	Asp	Tyr	Glu	Gly	Val 600	Asp	Ala	Ser	Leu	Asn	Glu
Thr 610	Ala	Thr	Thr	Ile	Thr 615	Val	Leu	Leu	Arg	Pro	Ala 620	Gln	Ala	Lys	Gly
Ala 625	Pro	Ile	Ser	Ala	Tyr 630	Gln	Ile	Val	Val	Glu 635	Glu	Leu	His	Pro	His 640
Arg	Thr	Lys	Arg	Glu 645	Ala	Gly	Ala	Met	Glu 650	Cys	Tyr	Gln	Val	Pro 655	Val
Thr	Tyr	Gln	Asn	Ala 660	Met	Ser	Gly	Gly	Ala 665	Pro	Tyr	Tyr	Phe	Ala 670	Ala
Glu	Leu	Pro	Pro	Gly 675	Asn	Leu	Pro	Glu	Pro 680	Ala	Pro	Phe	Thr	Val 685	Gly
Asp 690	Asn	Arg	Thr	Tyr	Gln 695	Gly	Phe	Trp	Asn	Pro	Pro 700	Leu	Ala	Pro	Arg
Lys 705	Gly	Tyr	Asn	Ile 710	Tyr	Phe	Gln	Ala	Met	Ser 715	Ser	Val	Glu	Lys	Glu 720
Thr	Lys	Thr	Gln	Cys 725	Val	Arg	Ile	Ala	Thr 730	Lys	Ala	Ala	Thr	Glu 735	Glu
Pro	Glu	Val	Ile	Pro 740	Asp	Pro	Ala	Lys	Gln 745	Thr	Asp	Arg	Val	Val 750	Lys
Ile	Ala	Gly	Ile	Ser	Ala	Gly 760	Ile	Leu	Val	Phe	Ile	Leu	Leu	Leu	Leu
Val 770	Val	Ile	Leu	Ile	Val	Lys 775	Lys	Ser	Lys	Leu	Ala	Lys	Lys	Arg	Lys

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Asp	Ala	Met	Gly	Asn	Thr	Arg	Gln	Glu	Met	Thr	His	Met	Val	Asn	Ala	785	790	795	800
Met	Asp	Arg	Ser	Tyr	Ala	Asp	Gln	Ser	Thr	Leu	His	Ala	Glu	Asp	Pro	805	810	815	
Leu	Ser	Ile	Thr	Phe	Met	Asp	Gln	His	Asn	Phe	Ser	Pro	Arg	Tyr	Glu	820	825	830	
Asn	His	Ser	Ala	Thr	Ala	Glu	Ser	Ser	Arg	Leu	Leu	Asp	Val	Pro	Arg	835	840	845	
Tyr	Leu	Cys	Glu	Gly	Thr	Glu	Ser	Pro	Tyr	Gln	Thr	Gly	Gln	Leu	His	850	855	860	
Pro	Ala	Ile	Arg	Val	Ala	Asp	Leu	Leu	Gln	His	Ile	Asn	Leu	Met	Lys	865	870	875	880
Thr	Ser	Asp	Ser	Tyr	Gly	Phe	Lys	Glu	Glu	Tyr	Glu	Ser	Phe	Phe	Glu	885	890	895	
Gly	Gln	Ser	Ala	Ser	Trp	Asp	Val	Ala	Lys	Lys	Asp	Gln	Asn	Arg	Ala	900	905	910	
Lys	Asn	Arg	Tyr	Gly	Asn	Ile	Ile	Ala	Tyr	Asp	His	Ser	Arg	Val	Ile	915	920	925	
Leu	Gln	Pro	Val	Glu	Asp	Asp	Pro	Ser	Ser	Asp	Tyr	Ile	Asn	Ala	Asn	930	935	940	
Tyr	Ile	Asp	Gly	Tyr	Gln	Arg	Pro	Ser	His	Tyr	Ile	Ala	Thr	Gln	Gly	945	950	955	960
Pro	Val	His	Glu	Thr	Val	Tyr	Asp	Phe	Trp	Arg	Met	Ile	Trp	Gln	Glu	965	970	975	
Gln	Ser	Ala	Cys	Ile	Val	Met	Val	Thr	Asn	Leu	Val	Glu	Val	Gly	Arg	980	985	990	
Val	Lys	Cys	Tyr	Lys	Tyr	Trp	Pro	Asp	Asp	Thr	Glu	Val	Tyr	Gly	Asp	995	1000	1005	
Phe	Lys	Val	Thr	Cys	Val	Glu	Met	Glu	Pro	Leu	Ala	Glu	Tyr	Val		1010	1015	1020	
Val	Arg	Thr	Phe	Thr	Leu	Glu	Arg	Arg	Gly	Tyr	Asn	Glu	Ile	Arg		1025	1030	1035	
Glu	Val	Lys	Gln	Phe	His	Phe	Thr	Gly	Trp	Pro	Asp	His	Gly	Val		1040	1045	1050	
Pro	Tyr	His	Ala	Thr	Gly	Leu	Leu	Ser	Phe	Ile	Arg	Arg	Val	Lys		1055	1060	1065	
Leu	Ser	Asn	Pro	Pro	Ser	Ala	Gly	Pro	Ile	Val	Val	His	Cys	Ser		1070	1075	1080	
Ala	Gly	Ala	Gly	Arg	Thr	Gly	Cys	Tyr	Ile	Val	Ile	Asp	Ile	Met		1085	1090	1095	
Leu	Asp	Met	Ala	Glu	Arg	Glu	Gly	Val	Val	Asp	Ile	Tyr	Asn	Cys		1100	1105	1110	
Val	Lys	Ala	Leu	Arg	Ser	Arg	Arg	Ile	Asn	Met	Val	Gln	Thr	Glu		1115	1120	1125	
Glu	Gln	Tyr	Ile	Phe	Ile	His	Asp	Ala	Ile	Leu	Glu	Ala	Cys	Leu		1130	1135	1140	
Cys	Gly	Glu	Thr	Ala	Ile	Pro	Val	Cys	Glu	Phe	Lys	Ala	Ala	Tyr		1145	1150	1155	
Phe	Asp	Met	Ile	Arg	Ile	Asp	Ser	Gln	Thr	Asn	Ser	Ser	His	Leu		1160	1165	1170	
Lys	Asp	Glu	Phe	Gln	Thr	Leu	Asn	Ser	Val	Thr	Pro	Arg	Leu	Gln		1175	1180	1185	

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Ala Glu Asp Cys Ser Ile	Ala Cys Leu Pro Arg Asn	His Asp Lys
1190	1195	1200
Asn Arg Phe Met Asp Met	Leu Pro Pro Asp Arg Cys	Leu Pro Phe
1205	1210	1215
Leu Ile Thr Ile Asp Gly	Glu Ser Ser Asn Tyr Ile	Asn Ala Ala
1220	1225	1230
Leu Met Asp Ser Tyr Arg	Gln Pro Ala Ala Phe Ile	Val Thr Gln
1235	1240	1245
Tyr Pro Leu Pro Asn Thr	Val Lys Asp Phe Trp Arg	Leu Val Tyr
1250	1255	1260
Asp Tyr Gly Cys Thr Ser	Ile Val Met Leu Asn Glu	Val Asp Leu
1265	1270	1275
Ser Gln Gly Cys Pro Gln	Tyr Trp Pro Glu Glu Gly	Met Leu Arg
1280	1285	1290
Tyr Gly Pro Ile Gln Val	Glu Cys Met Ser Cys Ser	Met Asp Cys
1295	1300	1305
Asp Val Ile Asn Arg Ile	Phe Arg Ile Cys Asn Leu	Thr Arg Pro
1310	1315	1320
Gln Glu Gly Tyr Leu Met	Val Gln Gln Phe Gln Tyr	Leu Gly Trp
1325	1330	1335
Ala Ser His Arg Glu Val	Pro Gly Ser Lys Arg Ser	Phe Leu Lys
1340	1345	1350
Leu Ile Leu Gln Val Glu	Lys Trp Gln Glu Glu Cys	Glu Glu Gly
1355	1360	1365
Glu Gly Arg Thr Ile Ile	His Cys Leu Asn Gly Gly	Gly Arg Ser
1370	1375	1380
Gly Met Phe Cys Ala Ile	Gly Ile Val Val Glu Met	Val Lys Arg
1385	1390	1395
Gln Asn Val Val Asp Val	Phe His Ala Val Lys Thr	Leu Arg Asn
1400	1405	1410
Ser Lys Pro Asn Met Val	Glu Ala Pro Glu Gln Tyr	Arg Phe Cys
1415	1420	1425
Tyr Asp Val Ala Leu Glu	Tyr Leu Glu Ser Ser	
1430	1435	

<210> SEQ ID NO 37

<211> LENGTH: 1272

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 37

Met Val Ala Ala Ala Ala Thr	Glu Ala Arg Leu Arg Arg Thr
1	15
Ala Ala Thr Ala Ala Leu Ala Gly	Arg Ser Gly Gly Pro His Trp Asp
20	30
Trp Asp Val Thr Arg Ala Gly Arg	Pro Gly Leu Gly Ala Gly Leu Arg
35	45
Leu Pro Arg Leu Leu Ser Pro Pro	Leu Arg Pro Arg Leu Leu Leu Leu
50	60
Leu Leu Leu Leu Ser Pro Pro	Leu Leu Leu Leu Pro Cys Glu
65	80
Ala Glu Ala Ala Ala Ala Ala Val	Ser Gly Ser Ala Ala Ala
85	95
Glu Ala Lys Glu Cys Asp Arg Pro	Cys Val Asn Gly Gly Arg Cys Asn
100	110

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Pro Gly Thr Gly Gln Cys Val Cys Pro Ala Gly Trp Val Gly Glu Gln		
115	120	125
Cys Gln His Cys Gly Gly Arg Phe Arg Leu Thr Gly Ser Ser Gly Phe		
130	135	140
Val Thr Asp Gly Pro Gly Asn Tyr Lys Tyr Lys Thr Lys Cys Thr Trp		
145	150	155
Leu Ile Glu Gly Gln Pro Asn Arg Ile Met Arg Leu Arg Phe Asn His		
165	170	175
Phe Ala Thr Glu Cys Ser Trp Asp His Leu Tyr Val Tyr Asp Gly Asp		
180	185	190
Ser Ile Tyr Ala Pro Leu Val Ala Ala Phe Ser Gly Leu Ile Val Pro		
195	200	205
Glu Arg Asp Gly Asn Glu Thr Val Pro Glu Val Val Ala Thr Ser Gly		
210	215	220
Tyr Ala Leu Leu His Phe Phe Ser Asp Ala Ala Tyr Asn Leu Thr Gly		
225	230	235
Phe Asn Ile Thr Tyr Ser Phe Asp Met Cys Pro Asn Asn Cys Ser Gly		
245	250	255
Arg Gly Glu Cys Lys Ile Ser Asn Ser Ser Asp Thr Val Glu Cys Glu		
260	265	270
Cys Ser Glu Asn Trp Lys Gly Glu Ala Cys Asp Ile Pro His Cys Thr		
275	280	285
Asp Asn Cys Gly Phe Pro His Arg Gly Ile Cys Asn Ser Ser Asp Val		
290	295	300
Arg Gly Cys Ser Cys Phe Ser Asp Trp Gln Gly Pro Gly Cys Ser Val		
305	310	315
Pro Val Pro Ala Asn Gln Ser Phe Trp Thr Arg Glu Glu Tyr Ser Asn		
325	330	335
Leu Lys Leu Pro Arg Ala Ser His Lys Ala Val Val Asn Gly Asn Ile		
340	345	350
Met Trp Val Val Gly Gly Tyr Met Phe Asn His Ser Asp Tyr Asn Met		
355	360	365
Val Leu Ala Tyr Asp Leu Ala Ser Arg Glu Trp Leu Pro Leu Asn Arg		
370	375	380
Ser Val Asn Asn Val Val Val Arg Tyr Gly His Ser Leu Ala Leu Tyr		
385	390	395
Lys Asp Lys Ile Tyr Met Tyr Gly Gly Lys Ile Asp Ser Thr Gly Asn		
405	410	415
Val Thr Asn Glu Leu Arg Val Phe His Ile His Asn Glu Ser Trp Val		
420	425	430
Leu Leu Thr Pro Lys Ala Lys Glu Gln Tyr Ala Val Val Gly His Ser		
435	440	445
Ala His Ile Val Thr Leu Lys Asn Gly Arg Val Val Met Leu Val Ile		
450	455	460
Phe Gly His Cys Pro Leu Tyr Gly Tyr Ile Ser Asn Val Gln Glu Tyr		
465	470	475
Asp Leu Asp Lys Asn Thr Trp Ser Ile Leu His Thr Gln Gly Ala Leu		
485	490	495
Val Gln Gly Gly Tyr Gly His Ser Ser Val Tyr Asp His Arg Thr Arg		
500	505	510
Ala Leu Tyr Val His Gly Gly Tyr Lys Ala Phe Ser Ala Asn Lys Tyr		
515	520	525

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Arg	Leu	Ala	Asp	Asp	Leu	Tyr	Arg	Tyr	Asp	Val	Asp	Thr	Gln	Met	Trp
530						535					540				
Thr	Ile	Leu	Lys	Asp	Ser	Arg	Phe	Phe	Arg	Tyr	Leu	His	Thr	Ala	Val
545					550					555					560
Ile	Val	Ser	Gly	Thr	Met	Leu	Val	Phe	Gly	Gly	Asn	Thr	His	Asn	Asp
				565					570					575	
Thr	Ser	Met	Ser	His	Gly	Ala	Lys	Cys	Phe	Ser	Ser	Asp	Phe	Met	Ala
			580					585					590		
Tyr	Asp	Ile	Ala	Cys	Asp	Arg	Trp	Ser	Val	Leu	Pro	Arg	Pro	Asp	Leu
	595						600					605			
His	His	Asp	Val	Asn	Arg	Phe	Gly	His	Ser	Ala	Val	Leu	His	Asn	Ser
610					615						620				
Thr	Met	Tyr	Val	Phe	Gly	Gly	Phe	Asn	Ser	Leu	Leu	Leu	Ser	Asp	Ile
625					630					635					640
Leu	Val	Phe	Thr	Ser	Glu	Gln	Cys	Asp	Ala	His	Arg	Ser	Glu	Ala	Ala
				645					650					655	
Cys	Leu	Ala	Ala	Gly	Pro	Gly	Ile	Arg	Cys	Val	Trp	Asn	Thr	Gly	Ser
			660					665					670		
Ser	Gln	Cys	Ile	Ser	Trp	Ala	Leu	Ala	Thr	Asp	Glu	Gln	Glu	Glu	Lys
		675					680					685			
Leu	Lys	Ser	Glu	Cys	Phe	Ser	Lys	Arg	Thr	Leu	Asp	His	Asp	Arg	Cys
	690					695					700				
Asp	Gln	His	Thr	Asp	Cys	Tyr	Ser	Cys	Thr	Ala	Asn	Thr	Asn	Asp	Cys
705					710					715					720
His	Trp	Cys	Asn	Asp	His	Cys	Val	Pro	Arg	Asn	His	Ser	Cys	Ser	Glu
			725						730					735	
Gly	Gln	Ile	Ser	Ile	Phe	Arg	Tyr	Glu	Asn	Cys	Pro	Lys	Asp	Asn	Pro
			740					745					750		
Met	Tyr	Tyr	Cys	Asn	Lys	Lys	Thr	Ser	Cys	Arg	Ser	Cys	Ala	Leu	Asp
	755						760					765			
Gln	Asn	Cys	Gln	Trp	Glu	Pro	Arg	Asn	Gln	Glu	Cys	Ile	Ala	Leu	Pro
	770					775					780				
Glu	Asn	Ile	Cys	Gly	Ile	Gly	Trp	His	Leu	Val	Gly	Asn	Ser	Cys	Leu
785					790					795					800
Lys	Ile	Thr	Thr	Ala	Lys	Glu	Asn	Tyr	Asp	Asn	Ala	Lys	Leu	Phe	Cys
				805					810					815	
Arg	Asn	His	Asn	Ala	Leu	Leu	Ala	Ser	Leu	Thr	Thr	Gln	Lys	Lys	Val
			820					825					830		
Glu	Phe	Val	Leu	Lys	Gln	Leu	Arg	Ile	Met	Gln	Ser	Ser	Gln	Ser	Met
		835					840					845			
Ser	Lys	Leu	Thr	Leu	Thr	Pro	Trp	Val	Gly	Leu	Arg	Lys	Ile	Asn	Val
	850					855					860				
Ser	Tyr	Trp	Cys	Trp	Glu	Asp	Met	Ser	Pro	Phe	Thr	Asn	Ser	Leu	Leu
865					870					875					880
Gln	Trp	Met	Pro	Ser	Glu	Pro	Ser	Asp	Ala	Gly	Phe	Cys	Gly	Ile	Leu
				885					890					895	
Ser	Glu	Pro	Ser	Thr	Arg	Gly	Leu	Lys	Ala	Ala	Thr	Cys	Ile	Asn	Pro
		900						905					910		
Leu	Asn	Gly	Ser	Val	Cys	Glu	Arg	Pro	Ala	Asn	His	Ser	Ala	Lys	Gln
		915					920					925			
Cys	Arg	Thr	Pro	Cys	Ala	Leu	Arg	Thr	Ala	Cys	Gly	Asp	Cys	Thr	Ser
	930					935						940			
Gly	Ser	Ser	Glu	Cys	Met	Trp	Cys	Ser	Asn	Met	Lys	Gln	Cys	Val	Asp

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945	950	955	960
Ser Asn Ala Tyr Val Ala Ser Phe Pro Phe Gly Gln Cys Met Glu Trp			
	965	970	975
Tyr Thr Met Ser Thr Cys Pro Pro Glu Asn Cys Ser Gly Tyr Cys Thr			
	980	985	990
Cys Ser His Cys Leu Glu Gln Pro Gly Cys Gly Trp Cys Thr Asp Pro			
	995	1000	1005
Ser Asn Thr Gly Lys Gly Lys Cys Ile Glu Gly Ser Tyr Lys Gly			
	1010	1015	1020
Pro Val Lys Met Pro Ser Gln Ala Pro Thr Gly Asn Phe Tyr Pro			
	1025	1030	1035
Gln Pro Leu Leu Asn Ser Ser Met Cys Leu Glu Asp Ser Arg Tyr			
	1040	1045	1050
Asn Trp Ser Phe Ile His Cys Pro Ala Cys Gln Cys Asn Gly His			
	1055	1060	1065
Ser Lys Cys Ile Asn Gln Ser Ile Cys Glu Lys Cys Glu Asn Leu			
	1070	1075	1080
Thr Thr Gly Lys His Cys Glu Thr Cys Ile Ser Gly Phe Tyr Gly			
	1085	1090	1095
Asp Pro Thr Asn Gly Gly Lys Cys Gln Pro Cys Lys Cys Asn Gly			
	1100	1105	1110
His Ala Ser Leu Cys Asn Thr Asn Thr Gly Lys Cys Phe Cys Thr			
	1115	1120	1125
Thr Lys Gly Val Lys Gly Asp Glu Cys Gln Leu Cys Glu Val Glu			
	1130	1135	1140
Asn Arg Tyr Gln Gly Asn Pro Leu Arg Gly Thr Cys Tyr Tyr Thr			
	1145	1150	1155
Leu Leu Ile Asp Tyr Gln Phe Thr Phe Ser Leu Ser Gln Glu Asp			
	1160	1165	1170
Asp Arg Tyr Tyr Thr Ala Ile Asn Phe Val Ala Thr Pro Asp Glu			
	1175	1180	1185
Gln Asn Arg Asp Leu Asp Met Phe Ile Asn Ala Ser Lys Asn Phe			
	1190	1195	1200
Asn Leu Asn Ile Thr Trp Ala Ala Ser Phe Ser Ala Gly Thr Gln			
	1205	1210	1215
Ala Gly Glu Glu Met Pro Val Val Ser Lys Thr Asn Ile Lys Glu			
	1220	1225	1230
Tyr Lys Asp Ser Phe Ser Asn Glu Lys Phe Asp Phe Arg Asn His			
	1235	1240	1245
Pro Asn Ile Thr Phe Phe Val Tyr Val Ser Asn Phe Thr Trp Pro			
	1250	1255	1260
Ile Lys Ile Gln Val Gln Thr Glu Gln			
	1265	1270	

<210> SEQ ID NO 38

<211> LENGTH: 289

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 38

Met Lys Asp Arg Leu Glu Gln Leu Lys Ala Lys Gln Leu Thr Gln Asp			
1	5	10	15
Asp Asp Thr Asp Ala Val Glu Ile Ala Ile Asp Asn Thr Ala Phe Met			
	20	25	30

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Asp Glu Phe Phe Ser Glu Ile Glu Glu Thr Arg Leu Asn Ile Asp Lys
   35                               40               45

Ile Ser Glu His Val Glu Glu Ala Lys Lys Leu Tyr Ser Ile Ile Leu
   50                               55               60

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

Thr Thr Glu Ile Lys Lys Arg Ala Asn Asn Val Arg Asn Lys Leu Lys
   85                               90               95

Ser Met Glu Lys His Ile Glu Glu Asp Glu Val Arg Ser Ser Ala Asp
  100                               105              110

Leu Arg Ile Arg Lys Ser Gln His Ser Val Leu Ser Arg Lys Phe Val
  115                               120              125

Glu Val Met Thr Lys Tyr Asn Glu Ala Gln Val Asp Phe Arg Glu Arg
  130                               135              140

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

Thr Asp Glu Glu Leu Glu Glu Met Leu Glu Ser Gly Asn Pro Ala Ile
  165                               170              175

Phe Thr Ser Gly Ile Ile Asp Ser Gln Ile Ser Lys Gln Ala Leu Ser
  180                               185              190

Glu Ile Glu Gly Arg His Lys Asp Ile Val Arg Leu Glu Ser Ser Ile
  195                               200              205

Lys Glu Leu His Asp Met Phe Met Asp Ile Ala Met Leu Val Glu Asn
  210                               215              220

Gln Gly Glu Met Leu Asp Asn Ile Glu Leu Asn Val Met His Thr Val
  225                               230              235              240

Asp His Val Glu Lys Ala Arg Asp Glu Thr Lys Lys Ala Val Lys Tyr
  245                               250              255

Gln Ser Gln Ala Arg Lys Lys Leu Ile Ile Ile Ile Val Leu Val Val
  260                               265              270

Val Leu Leu Gly Ile Leu Ala Leu Ile Ile Gly Leu Ser Val Gly Leu
  275                               280              285

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Asn

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<210> SEQ ID NO 39
<211> LENGTH: 666
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 39

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Met Arg Lys Val Arg Gly Pro Pro Val Ser Cys Ile Lys Arg Asp Ser
  1           5           10           15

Pro Ile Gln Cys Ile Gln Ala Ile Ala Glu Asn Arg Ala Asp Ala Val
  20           25           30

Thr Leu Asp Gly Gly Phe Ile Tyr Glu Ala Gly Leu Ala Pro Tyr Lys
  35           40           45

Leu Arg Pro Val Ala Ala Glu Val Tyr Gly Thr Glu Arg Gln Pro Arg
  50           55           60

Thr His Tyr Tyr Ala Val Ala Val Val Lys Lys Gly Gly Ser Phe Gln
  65           70           75           80

Leu Asn Glu Leu Gln Gly Leu Lys Ser Cys His Thr Gly Leu Arg Arg
  85           90           95

Thr Ala Gly Trp Asn Val Pro Ile Gly Thr Leu Arg Pro Phe Leu Asn
  100          105          110

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

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530	535	540
Asp Phe Ala Leu Leu Cys Leu Asp Gly Lys Arg Lys Pro Val Thr Glu		
545	550	555 560
Ala Arg Ser Cys His Leu Ala Met Ala Pro Asn His Ala Val Val Ser		
	565	570 575
Arg Met Asp Lys Val Glu Arg Leu Lys Gln Val Leu Leu His Gln Gln		
	580	585 590
Ala Lys Phe Gly Arg Asn Gly Ser Asp Cys Pro Asp Lys Phe Cys Leu		
	595	600 605
Phe Gln Ser Glu Thr Lys Asn Leu Leu Phe Asn Asp Asn Thr Glu Cys		
	610	615 620
Leu Ala Arg Leu His Gly Lys Thr Thr Tyr Glu Lys Tyr Leu Gly Pro		
	625	630 635 640
Gln Tyr Val Ala Gly Ile Thr Asn Leu Lys Lys Cys Ser Thr Ser Pro		
	645	650 655
Leu Leu Glu Ala Cys Glu Phe Leu Arg Lys		
	660	665

<210> SEQ ID NO 40
 <211> LENGTH: 4655
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens
 <400> SEQUENCE: 40

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

Cys	Asp	Gly	Glu	Asp	Asp	Cys	Lys	Asp	Asn	Gly	Asp	Glu	Asp	Gly	Cys	
				245					250					255		
Glu	Ser	Gly	Pro	His	Asp	Val	His	Lys	Cys	Ser	Pro	Arg	Glu	Trp	Ser	
				260					265					270		
Cys	Pro	Glu	Ser	Gly	Arg	Cys	Ile	Ser	Ile	Tyr	Lys	Val	Cys	Asp	Gly	
				275					280					285		
Ile	Leu	Asp	Cys	Pro	Gly	Arg	Glu	Asp	Glu	Asn	Asn	Thr	Ser	Thr	Gly	
				290					295					300		
Lys	Tyr	Cys	Ser	Met	Thr	Leu	Cys	Ser	Ala	Leu	Asn	Cys	Gln	Tyr	Gln	
				305					310					315		
Cys	His	Glu	Thr	Pro	Tyr	Gly	Gly	Ala	Cys	Phe	Cys	Pro	Pro	Gly	Tyr	
				325					330					335		
Ile	Ile	Asn	His	Asn	Asp	Ser	Arg	Thr	Cys	Val	Glu	Phe	Asp	Asp	Cys	
				340					345					350		
Gln	Ile	Trp	Gly	Ile	Cys	Asp	Gln	Lys	Cys	Glu	Ser	Arg	Pro	Gly	Arg	
				355					360					365		
His	Leu	Cys	His	Cys	Glu	Glu	Gly	Tyr	Ile	Leu	Glu	Arg	Gly	Gln	Tyr	
				370					375					380		
Cys	Lys	Ala	Asn	Asp	Ser	Phe	Gly	Glu	Ala	Ser	Ile	Ile	Phe	Ser	Asn	
				385					390					395		
Gly	Arg	Asp	Leu	Leu	Ile	Gly	Asp	Ile	His	Gly	Arg	Ser	Phe	Arg	Ile	
				405					410					415		
Leu	Val	Glu	Ser	Gln	Asn	Arg	Gly	Val	Ala	Val	Gly	Val	Ala	Phe	His	
				420					425					430		
Tyr	His	Leu	Gln	Arg	Val	Phe	Trp	Thr	Asp	Thr	Val	Gln	Asn	Lys	Val	
				435					440					445		
Phe	Ser	Val	Asp	Ile	Asn	Gly	Leu	Asn	Ile	Gln	Glu	Val	Leu	Asn	Val	
				450					455					460		
Ser	Val	Glu	Thr	Pro	Glu	Asn	Leu	Ala	Val	Asp	Trp	Val	Asn	Asn	Lys	
				465					470					475		
Ile	Tyr	Leu	Val	Glu	Thr	Lys	Val	Asn	Arg	Ile	Asp	Met	Val	Asn	Leu	
				485					490					495		
Asp	Gly	Ser	Tyr	Arg	Val	Thr	Leu	Ile	Thr	Glu	Asn	Leu	Gly	His	Pro	
				500					505					510		
Arg	Gly	Ile	Ala	Val	Asp	Pro	Thr	Val	Gly	Tyr	Leu	Phe	Phe	Ser	Asp	
				515					520					525		
Trp	Glu	Ser	Leu	Ser	Gly	Glu	Pro	Lys	Leu	Glu	Arg	Ala	Phe	Met	Asp	
				530					535					540		
Gly	Ser	Asn	Arg	Lys	Asp	Leu	Val	Lys	Thr	Lys	Leu	Gly	Trp	Pro	Ala	
				545					550					555		
Gly	Val	Thr	Leu	Asp	Met	Ile	Ser	Lys	Arg	Val	Tyr	Trp	Val	Asp	Ser	
				565					570					575		
Arg	Phe	Asp	Tyr	Ile	Glu	Thr	Val	Thr	Tyr	Asp	Gly	Ile	Gln	Arg	Lys	
				580					585					590		
Thr	Val	Val	His	Gly	Gly	Ser	Leu	Ile	Pro	His	Pro	Phe	Gly	Val	Ser	
				595					600					605		
Leu	Phe	Glu	Gly	Gln	Val	Phe	Phe	Thr	Asp	Trp	Thr	Lys	Met	Ala	Val	
				610					615					620		
Leu	Lys	Ala	Asn	Lys	Phe	Thr	Glu	Thr	Asn	Pro	Gln	Val	Tyr	Tyr	Gln	
				625					630					635		
Ala	Ser	Leu	Arg	Pro	Tyr	Gly	Val	Thr	Val	Tyr	His	Ser	Leu	Arg		

660										665										670									
Val	Cys	Val	Leu	Ser	His	Arg	Thr	Asp	Asn	Asp	Gly	Leu	Gly	Phe	Arg														
675										680										685									
Cys	Lys	Cys	Thr	Phe	Gly	Phe	Gln	Leu	Asp	Thr	Asp	Glu	Arg	His	Cys														
690										695										700									
Ile	Ala	Val	Gln	Asn	Phe	Leu	Ile	Phe	Ser	Ser	Gln	Val	Ala	Ile	Arg														
705										710										715									
Gly	Ile	Pro	Phe	Thr	Leu	Ser	Thr	Gln	Glu	Asp	Val	Met	Val	Pro	Val														
725										730										735									
Ser	Gly	Asn	Pro	Ser	Phe	Phe	Val	Gly	Ile	Asp	Phe	Asp	Ala	Gln	Asp														
740										745										750									
Ser	Thr	Ile	Phe	Phe	Ser	Asp	Met	Ser	Lys	His	Met	Ile	Phe	Lys	Gln														
755										760										765									
Lys	Ile	Asp	Gly	Thr	Gly	Arg	Glu	Ile	Leu	Ala	Ala	Asn	Arg	Val	Glu														
770										775										780									
Asn	Val	Glu	Ser	Leu	Ala	Phe	Asp	Trp	Ile	Ser	Lys	Asn	Leu	Tyr	Trp														
785										790										795									
Thr	Asp	Ser	His	Tyr	Lys	Ser	Ile	Ser	Val	Met	Arg	Leu	Ala	Asp	Lys														
805										810										815									
Thr	Arg	Arg	Thr	Val	Val	Gln	Tyr	Leu	Asn	Asn	Pro	Arg	Ser	Val	Val														
820										825										830									
Val	His	Pro	Phe	Ala	Gly	Tyr	Leu	Phe	Phe	Thr	Asp	Trp	Phe	Arg	Pro														
835										840										845									
Ala	Lys	Ile	Met	Arg	Ala	Trp	Ser	Asp	Gly	Ser	His	Leu	Leu	Pro	Val														
850										855										860									
Ile	Asn	Thr	Thr	Leu	Gly	Trp	Pro	Asn	Gly	Leu	Ala	Ile	Asp	Trp	Ala														
865										870										875									
Ala	Ser	Arg	Leu	Tyr	Trp	Val	Asp	Ala	Tyr	Phe	Asp	Lys	Ile	Glu	His														
885										890										895									
Ser	Thr	Phe	Asp	Gly	Leu	Asp	Arg	Arg	Arg	Leu	Gly	His	Ile	Glu	Gln														
900										905										910									
Met	Thr	His	Pro	Phe	Gly	Leu	Ala	Ile	Phe	Gly	Glu	His	Leu	Phe	Phe														
915										920										925									
Thr	Asp	Trp	Arg	Leu	Gly	Ala	Ile	Ile	Arg	Val	Arg	Lys	Ala	Asp	Gly														
930										935										940									
Gly	Glu	Met	Thr	Val	Ile	Arg	Ser	Gly	Ile	Ala	Tyr	Ile	Leu	His	Leu														
945										950										955									
Lys	Ser	Tyr	Asp	Val	Asn	Ile	Gln	Thr	Gly	Ser	Asn	Ala	Cys	Asn	Gln														
965										970										975									
Pro	Thr	His	Pro	Asn	Gly	Asp	Cys	Ser	His	Phe	Cys	Phe	Pro	Val	Pro														
980										985										990									
Asn	Phe	Gln	Arg	Val	Cys	Gly	Cys	Pro	Tyr	Gly	Met	Arg	Leu	Ala	Ser														
995										1000										1005									
Asn	His	Leu	Thr	Cys	Glu	Gly	Asp	Pro	Thr	Asn	Glu	Pro	Pro	Thr															
1010										1015										1020									
Glu	Gln	Cys	Gly	Leu	Phe	Ser	Phe	Pro	Cys	Lys	Asn	Gly	Arg	Cys															
1025										1030										1035									
Val	Pro	Asn	Tyr	Tyr	Leu	Cys	Asp	Gly	Val	Asp	Asp	Cys	His	Asp															
1040										1045										1050									
Asn	Ser	Asp	Glu	Gln	Leu	Cys	Gly	Thr	Leu	Asn	Asn	Thr	Cys	Ser															
1055										1060										1065									
Ser	Ser	Ala	Phe	Thr	Cys	Gly	His	Gly	Glu	Cys	Ile	Pro	Ala	His															
1070										1075										1080									

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Trp Arg Cys Asp Lys Arg Asn Asp Cys Val Asp Gly Ser Asp Glu		
1085	1090	1095
His Asn Cys Pro Thr His Ala Pro Ala Ser Cys Leu Asp Thr Gln		
1100	1105	1110
Tyr Thr Cys Asp Asn His Gln Cys Ile Ser Lys Asn Trp Val Cys		
1115	1120	1125
Asp Thr Asp Asn Asp Cys Gly Asp Gly Ser Asp Glu Lys Asn Cys		
1130	1135	1140
Asn Ser Thr Glu Thr Cys Gln Pro Ser Gln Phe Asn Cys Pro Asn		
1145	1150	1155
His Arg Cys Ile Asp Leu Ser Phe Val Cys Asp Gly Asp Lys Asp		
1160	1165	1170
Cys Val Asp Gly Ser Asp Glu Val Gly Cys Val Leu Asn Cys Thr		
1175	1180	1185
Ala Ser Gln Phe Lys Cys Ala Ser Gly Asp Lys Cys Ile Gly Val		
1190	1195	1200
Thr Asn Arg Cys Asp Gly Val Phe Asp Cys Ser Asp Asn Ser Asp		
1205	1210	1215
Glu Ala Gly Cys Pro Thr Arg Pro Pro Gly Met Cys His Ser Asp		
1220	1225	1230
Glu Phe Gln Cys Gln Glu Asp Gly Ile Cys Ile Pro Asn Phe Trp		
1235	1240	1245
Glu Cys Asp Gly His Pro Asp Cys Leu Tyr Gly Ser Asp Glu His		
1250	1255	1260
Asn Ala Cys Val Pro Lys Thr Cys Pro Ser Ser Tyr Phe His Cys		
1265	1270	1275
Asp Asn Gly Asn Cys Ile His Arg Ala Trp Leu Cys Asp Arg Asp		
1280	1285	1290
Asn Asp Cys Gly Asp Met Ser Asp Glu Lys Asp Cys Pro Thr Gln		
1295	1300	1305
Pro Phe Arg Cys Pro Ser Trp Gln Trp Gln Cys Leu Gly His Asn		
1310	1315	1320
Ile Cys Val Asn Leu Ser Val Val Cys Asp Gly Ile Phe Asp Cys		
1325	1330	1335
Pro Asn Gly Thr Asp Glu Ser Pro Leu Cys Asn Gly Asn Ser Cys		
1340	1345	1350
Ser Asp Phe Asn Gly Gly Cys Thr His Glu Cys Val Gln Glu Pro		
1355	1360	1365
Phe Gly Ala Lys Cys Leu Cys Pro Leu Gly Phe Leu Leu Ala Asn		
1370	1375	1380
Asp Ser Lys Thr Cys Glu Asp Ile Asp Glu Cys Asp Ile Leu Gly		
1385	1390	1395
Ser Cys Ser Gln His Cys Tyr Asn Met Arg Gly Ser Phe Arg Cys		
1400	1405	1410
Ser Cys Asp Thr Gly Tyr Met Leu Glu Ser Asp Gly Arg Thr Cys		
1415	1420	1425
Lys Val Thr Ala Ser Glu Ser Leu Leu Leu Leu Val Ala Ser Gln		
1430	1435	1440
Asn Lys Ile Ile Ala Asp Ser Val Thr Ser Gln Val His Asn Ile		
1445	1450	1455
Tyr Ser Leu Val Glu Asn Gly Ser Tyr Ile Val Ala Val Asp Phe		
1460	1465	1470

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Asp Ser Ile Ser Gly Arg Ile Phe Trp Ser Asp Ala Thr Gln Gly 1475 1480 1485	
Lys Thr Trp Ser Ala Phe Gln Asn Gly Thr Asp Arg Arg Val Val 1490 1495 1500	
Phe Asp Ser Ser Ile Ile Leu Thr Glu Thr Ile Ala Ile Asp Trp 1505 1510 1515	
Val Gly Arg Asn Leu Tyr Trp Thr Asp Tyr Ala Leu Glu Thr Ile 1520 1525 1530	
Glu Val Ser Lys Ile Asp Gly Ser His Arg Thr Val Leu Ile Ser 1535 1540 1545	
Lys Asn Leu Thr Asn Pro Arg Gly Leu Ala Leu Asp Pro Arg Met 1550 1555 1560	
Asn Glu His Leu Leu Phe Trp Ser Asp Trp Gly His His Pro Arg 1565 1570 1575	
Ile Glu Arg Ala Ser Met Asp Gly Ser Met Arg Thr Val Ile Val 1580 1585 1590	
Gln Asp Lys Ile Phe Trp Pro Cys Gly Leu Thr Ile Asp Tyr Pro 1595 1600 1605	
Asn Arg Leu Leu Tyr Phe Met Asp Ser Tyr Leu Asp Tyr Met Asp 1610 1615 1620	
Phe Cys Asp Tyr Asn Gly His His Arg Arg Gln Val Ile Ala Ser 1625 1630 1635	
Asp Leu Ile Ile Arg His Pro Tyr Ala Leu Thr Leu Phe Glu Asp 1640 1645 1650	
Ser Val Tyr Trp Thr Asp Arg Ala Thr Arg Arg Val Met Arg Ala 1655 1660 1665	
Asn Lys Trp His Gly Gly Asn Gln Ser Val Val Met Tyr Asn Ile 1670 1675 1680	
Gln Trp Pro Leu Gly Ile Val Ala Val His Pro Ser Lys Gln Pro 1685 1690 1695	
Asn Ser Val Asn Pro Cys Ala Phe Ser Arg Cys Ser His Leu Cys 1700 1705 1710	
Leu Leu Ser Ser Gln Gly Pro His Phe Tyr Ser Cys Val Cys Pro 1715 1720 1725	
Ser Gly Trp Ser Leu Ser Pro Asp Leu Leu Asn Cys Leu Arg Asp 1730 1735 1740	
Asp Gln Pro Phe Leu Ile Thr Val Arg Gln His Ile Ile Phe Gly 1745 1750 1755	
Ile Ser Leu Asn Pro Glu Val Lys Ser Asn Asp Ala Met Val Pro 1760 1765 1770	
Ile Ala Gly Ile Gln Asn Gly Leu Asp Val Glu Phe Asp Asp Ala 1775 1780 1785	
Glu Gln Tyr Ile Tyr Trp Val Glu Asn Pro Gly Glu Ile His Arg 1790 1795 1800	
Val Lys Thr Asp Gly Thr Asn Arg Thr Val Phe Ala Ser Ile Ser 1805 1810 1815	
Met Val Gly Pro Ser Met Asn Leu Ala Leu Asp Trp Ile Ser Arg 1820 1825 1830	
Asn Leu Tyr Ser Thr Asn Pro Arg Thr Gln Ser Ile Glu Val Leu 1835 1840 1845	
Thr Leu His Gly Asp Ile Arg Tyr Arg Lys Thr Leu Ile Ala Asn 1850 1855 1860	
Asp Gly Thr Ala Leu Gly Val Gly Phe Pro Ile Gly Ile Thr Val	

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1865	1870	1875
Asp Pro Ala Arg Gly Lys 1880	Leu Tyr Trp Ser Asp 1885	Gln Gly Thr Asp 1890
Ser Gly Val Pro Ala Lys 1895	Ile Ala Ser Ala Asn Met 1900	Asp Gly Thr 1905
Ser Val Lys Thr Leu Phe 1910	Thr Gly Asn Leu Glu His 1915	Leu Glu Cys 1920
Val Thr Leu Asp Ile Glu 1925	Glu Gln Lys Leu Tyr Trp 1930	Ala Val Thr 1935
Gly Arg Gly Val Ile Glu 1940	Arg Gly Asn Val Asp Gly 1945	Thr Asp Arg 1950
Met Ile Leu Val His Gln 1955	Leu Ser His Pro Trp Gly 1960	Ile Ala Val 1965
His Asp Ser Phe Leu Tyr 1970	Tyr Thr Asp Glu Gln Tyr 1975	Glu Val Ile 1980
Glu Arg Val Asp Lys Ala 1985	Thr Gly Ala Asn Lys Ile 1990	Val Leu Arg 1995
Asp Asn Val Pro Asn Leu 2000	Arg Gly Leu Gln Val Tyr 2005	His Arg Arg 2010
Asn Ala Ala Glu Ser Ser 2015	Asn Gly Cys Ser Asn Asn 2020	Met Asn Ala 2025
Cys Gln Gln Ile Cys Leu 2030	Pro Val Pro Gly Gly Leu 2035	Phe Ser Cys 2040
Ala Cys Ala Thr Gly Phe 2045	Lys Leu Asn Pro Asp Asn 2050	Arg Ser Cys 2055
Ser Pro Tyr Asn Ser Phe 2060	Ile Val Val Ser Met Leu 2065	Ser Ala Ile 2070
Arg Gly Phe Ser Leu Glu 2075	Leu Ser Asp His Ser Glu 2080	Thr Met Val 2085
Pro Val Ala Gly Gln Gly 2090	Arg Asn Ala Leu His Val 2095	Asp Val Asp 2100
Val Ser Ser Gly Phe Ile 2105	Tyr Trp Cys Asp Phe Ser 2110	Ser Ser Val 2115
Ala Ser Asp Asn Ala Ile 2120	Arg Arg Ile Lys Pro Asp 2125	Gly Ser Ser 2130
Leu Met Asn Ile Val Thr 2135	His Gly Ile Gly Glu Asn 2140	Gly Val Arg 2145
Gly Ile Ala Val Asp Trp 2150	Val Ala Gly Asn Leu Tyr 2155	Phe Thr Asn 2160
Ala Phe Val Ser Glu Thr 2165	Leu Ile Glu Val Leu Arg 2170	Ile Asn Thr 2175
Thr Tyr Arg Arg Val Leu 2180	Leu Lys Val Thr Val Asp 2185	Met Pro Arg 2190
His Ile Val Val Asp Pro 2195	Lys Asn Arg Tyr Leu Phe 2200	Trp Ala Asp 2205
Tyr Gly Gln Arg Pro Lys 2210	Ile Glu Arg Ser Phe Leu 2215	Asp Cys Thr 2220
Asn Arg Thr Val Leu Val 2225	Ser Glu Gly Ile Val Thr 2230	Pro Arg Gly 2235
Leu Ala Val Asp Arg Ser 2240	Asp Gly Tyr Val Tyr Trp 2245	Val Asp Asp 2250
Ser Leu Asp Ile Ile Ala 2255	Arg Ile Arg Ile Asn Gly 2260	Glu Asn Ser 2265

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Glu Val	Ile Arg Tyr Gly Ser	Arg Tyr Pro Thr Pro	Tyr Gly Ile
2270	2275	2280	
Thr Val	Phe Glu Asn Ser Ile	Ile Trp Val Asp Arg	Asn Leu Lys
2285	2290	2295	
Lys Ile	Phe Gln Ala Ser Lys	Glu Pro Glu Asn Thr	Glu Pro Pro
2300	2305	2310	
Thr Val	Ile Arg Asp Asn Ile	Asn Trp Leu Arg Asp	Val Thr Ile
2315	2320	2325	
Phe Asp	Lys Gln Val Gln Pro	Arg Ser Pro Ala Glu	Val Asn Asn
2330	2335	2340	
Asn Pro	Cys Leu Glu Asn Asn	Gly Gly Cys Ser His	Leu Cys Phe
2345	2350	2355	
Ala Leu	Pro Gly Leu His Thr	Pro Lys Cys Asp Cys	Ala Phe Gly
2360	2365	2370	
Thr Leu	Gln Ser Asp Gly Lys	Asn Cys Ala Ile Ser	Thr Glu Asn
2375	2380	2385	
Phe Leu	Ile Phe Ala Leu Ser	Asn Ser Leu Arg Ser	Leu His Leu
2390	2395	2400	
Asp Pro	Glu Asn His Ser Pro	Pro Phe Gln Thr Ile	Asn Val Glu
2405	2410	2415	
Arg Thr	Val Met Ser Leu Asp	Tyr Asp Ser Val Ser	Asp Arg Ile
2420	2425	2430	
Tyr Phe	Thr Gln Asn Leu Ala	Ser Gly Val Gly Gln	Ile Ser Tyr
2435	2440	2445	
Ala Thr	Leu Ser Ser Gly Ile	His Thr Pro Thr Val	Ile Ala Ser
2450	2455	2460	
Gly Ile	Gly Thr Ala Asp Gly	Ile Ala Phe Asp Trp	Ile Thr Arg
2465	2470	2475	
Arg Ile	Tyr Tyr Ser Asp Tyr	Leu Asn Gln Met Ile	Asn Ser Met
2480	2485	2490	
Ala Glu	Asp Gly Ser Asn Arg	Thr Val Ile Ala Arg	Val Pro Lys
2495	2500	2505	
Pro Arg	Ala Ile Val Leu Asp	Pro Cys Gln Gly Tyr	Leu Tyr Trp
2510	2515	2520	
Ala Asp	Trp Asp Thr His Ala	Lys Ile Glu Arg Ala	Thr Leu Gly
2525	2530	2535	
Gly Asn	Phe Arg Val Pro Ile	Val Asn Ser Ser Leu	Val Met Pro
2540	2545	2550	
Ser Gly	Leu Thr Leu Asp Tyr	Glu Glu Asp Leu Leu	Tyr Trp Val
2555	2560	2565	
Asp Ala	Ser Leu Gln Arg Ile	Glu Arg Ser Thr Leu	Thr Gly Val
2570	2575	2580	
Asp Arg	Glu Val Ile Val Asn	Ala Ala Val His Ala	Phe Gly Leu
2585	2590	2595	
Thr Leu	Tyr Gly Gln Tyr Ile	Tyr Trp Thr Asp Leu	Tyr Thr Gln
2600	2605	2610	
Arg Ile	Tyr Arg Ala Asn Lys	Tyr Asp Gly Ser Gly	Gln Ile Ala
2615	2620	2625	
Met Thr	Thr Asn Leu Leu Ser	Gln Pro Arg Gly Ile	Asn Thr Val
2630	2635	2640	
Val Lys	Asn Gln Lys Gln Gln	Cys Asn Asn Pro Cys	Glu Gln Phe
2645	2650	2655	

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Asn Gly 2660	Gly Cys Ser His 2665	Ile Cys Ala Pro Gly Pro 2670	Asn Gly Ala
Glu Cys 2675	Gln Cys Pro His 2680	Glu Gly Asn Trp Tyr Leu 2685	Ala Asn Asn
Arg Lys 2690	His Cys Ile Val 2695	Asn Gly Glu Arg Cys 2700	Gly Ala Ser
Ser Phe 2705	Thr Cys Ser Asn 2710	Arg Cys Ile Ser Glu 2715	Glu Trp Lys
Cys Asp 2720	Asn Asp Asn Asp 2725	Cys Gly Asp Gly Ser Asp 2730	Glu Met Glu
Ser Val 2735	Cys Ala Leu His 2740	Cys Ser Pro Thr Ala 2745	Phe Thr Cys
Ala Asn 2750	Gly Arg Cys Val 2755	Tyr Ser Tyr Arg Cys 2760	Asp Tyr Tyr
Asn Asp 2765	Cys Gly Asp Gly 2770	Asp Glu Ala Gly Cys 2775	Leu Phe Arg
Asp Cys 2780	Asn Ala Thr Thr 2785	Glu Phe Met Cys Asn Asn 2790	Arg Arg Cys
Ile Pro 2795	Arg Glu Phe Ile 2800	Asn Gly Val Asp Asn 2805	Cys His Asp
Asn Asn 2810	Thr Ser Asp Glu 2815	Lys Asn Cys Pro Asp Arg 2820	Thr Cys Gln
Ser Gly 2825	Tyr Thr Lys Cys 2830	His Asn Ser Asn Ile Cys 2835	Ile Pro Arg
Val Tyr 2840	Leu Cys Asp Gly 2845	Asn Asp Cys Gly Asp 2850	Asn Ser Asp
Glu Asn 2855	Pro Thr Tyr Cys 2860	Thr His Thr Cys Ser 2865	Ser Ser Glu
Phe Gln 2870	Cys Ala Ser Gly 2875	Arg Cys Ile Pro Gln His 2880	Trp Tyr Cys
Asp Gln 2885	Glu Thr Asp Cys 2890	Phe Asp Ala Ser Asp Glu 2895	Pro Ala Ser
Cys Gly 2900	His Ser Glu Arg 2905	Thr Cys Leu Ala Asp Glu 2910	Phe Lys Cys
Asp Gly 2915	Gly Arg Cys Ile 2920	Pro Ser Glu Trp Ile Cys 2925	Asp Gly Asp
Asn Asp 2930	Cys Gly Asp Met 2935	Ser Asp Glu Asp Lys Arg 2940	His Gln Cys
Gln Asn 2945	Gln Asn Cys Ser 2950	Asp Ser Glu Phe Leu Cys 2955	Val Asn Asp
Arg Pro 2960	Pro Asp Arg Arg 2965	Cys Ile Pro Gln Ser Trp 2970	Val Cys Asp
Gly Asp 2975	Val Asp Cys Thr 2980	Asp Gly Tyr Asp Glu Asn 2985	Gln Asn Cys
Thr Arg 2990	Arg Thr Cys Ser 2995	Glu Asn Glu Phe Thr Cys 3000	Gly Tyr Gly
Leu Cys 3005	Ile Pro Lys Ile 3010	Phe Arg Cys Asp Arg His 3015	Asn Asp Cys
Gly Asp 3020	Tyr Ser Asp Glu 3025	Arg Gly Cys Leu Tyr Gln 3030	Thr Cys Gln
Gln Asn 3035	Gln Phe Thr Cys 3040	Gln Asn Gly Arg Cys Ile 3045	Ser Lys Thr
Phe Val	Cys Asp Glu Asp Asn	Asp Cys Gly Asp Gly	Ser Asp Glu

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3050	3055	3060
Leu Met His Leu Cys His Thr Pro Glu Pro Thr Cys Pro Pro His 3065 3070 3075		
Glu Phe Lys Cys Asp Asn Gly Arg Cys Ile Glu Met Met Lys Leu 3080 3085 3090		
Cys Asn His Leu Asp Asp Cys Leu Asp Asn Ser Asp Glu Lys Gly 3095 3100 3105		
Cys Gly Ile Asn Glu Cys His Asp Pro Ser Ile Ser Gly Cys Asp 3110 3115 3120		
His Asn Cys Thr Asp Thr Leu Thr Ser Phe Tyr Cys Ser Cys Arg 3125 3130 3135		
Pro Gly Tyr Lys Leu Met Ser Asp Lys Arg Thr Cys Val Asp Ile 3140 3145 3150		
Asp Glu Cys Thr Glu Met Pro Phe Val Cys Ser Gln Lys Cys Glu 3155 3160 3165		
Asn Val Ile Gly Ser Tyr Ile Cys Lys Cys Ala Pro Gly Tyr Leu 3170 3175 3180		
Arg Glu Pro Asp Gly Lys Thr Cys Arg Gln Asn Ser Asn Ile Glu 3185 3190 3195		
Pro Tyr Leu Ile Phe Ser Asn Arg Tyr Tyr Leu Arg Asn Leu Thr 3200 3205 3210		
Ile Asp Gly Tyr Phe Tyr Ser Leu Ile Leu Glu Gly Leu Asp Asn 3215 3220 3225		
Val Val Ala Leu Asp Phe Asp Arg Val Glu Lys Arg Leu Tyr Trp 3230 3235 3240		
Ile Asp Thr Gln Arg Gln Val Ile Glu Arg Met Phe Leu Asn Lys 3245 3250 3255		
Thr Asn Lys Glu Thr Ile Ile Asn His Arg Leu Pro Ala Ala Glu 3260 3265 3270		
Ser Leu Ala Val Asp Trp Val Ser Arg Lys Leu Tyr Trp Leu Asp 3275 3280 3285		
Ala Arg Leu Asp Gly Leu Phe Val Ser Asp Leu Asn Gly Gly His 3290 3295 3300		
Arg Arg Met Leu Ala Gln His Cys Val Asp Ala Asn Asn Thr Phe 3305 3310 3315		
Cys Phe Asp Asn Pro Arg Gly Leu Ala Leu His Pro Gln Tyr Gly 3320 3325 3330		
Tyr Leu Tyr Trp Ala Asp Trp Gly His Arg Ala Tyr Ile Gly Arg 3335 3340 3345		
Val Gly Met Asp Gly Thr Asn Lys Ser Val Ile Ile Ser Thr Lys 3350 3355 3360		
Leu Glu Trp Pro Asn Gly Ile Thr Ile Asp Tyr Thr Asn Asp Leu 3365 3370 3375		
Leu Tyr Trp Ala Asp Ala His Leu Gly Tyr Ile Glu Tyr Ser Asp 3380 3385 3390		
Leu Glu Gly His His Arg His Thr Val Tyr Asp Gly Ala Leu Pro 3395 3400 3405		
His Pro Phe Ala Ile Thr Ile Phe Glu Asp Thr Ile Tyr Trp Thr 3410 3415 3420		
Asp Trp Asn Thr Arg Thr Val Glu Lys Gly Asn Lys Tyr Asp Gly 3425 3430 3435		
Ser Asn Arg Gln Thr Leu Val Asn Thr Thr His Arg Pro Phe Asp 3440 3445 3450		

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Ile His	Val Tyr His Pro	Tyr	Arg Gln Pro	Ile Val	Ser Asn Pro
3455		3460		3465	
Cys Gly	Thr Asn Asn Gly	Gly	Cys Ser His Leu	Cys	Leu Ile Lys
3470		3475		3480	
Pro Gly	Gly Lys Gly Phe	Thr	Cys Glu Cys Pro	Asp	Asp Phe Arg
3485		3490		3495	
Thr Leu	Gln Leu Ser Gly	Ser	Thr Tyr Cys Met	Pro	Met Cys Ser
3500		3505		3510	
Ser Thr	Gln Phe Leu Cys	Ala	Asn Asn Glu Lys	Cys	Ile Pro Ile
3515		3520		3525	
Trp Trp	Lys Cys Asp Gly	Gln	Lys Asp Cys Ser	Asp	Gly Ser Asp
3530		3535		3540	
Glu Leu	Ala Leu Cys Pro	Gln	Arg Phe Cys Arg	Leu	Gly Gln Phe
3545		3550		3555	
Gln Cys	Ser Asp Gly Asn	Cys	Thr Ser Pro Gln	Thr	Leu Cys Asn
3560		3565		3570	
Ala His	Gln Asn Cys Pro	Asp	Gly Ser Asp Glu	Asp	Arg Leu Leu
3575		3580		3585	
Cys Glu	Asn His His Cys	Asp	Ser Asn Glu Trp	Gln	Cys Ala Asn
3590		3595		3600	
Lys Arg	Cys Ile Pro Glu	Ser	Trp Gln Cys Asp	Thr	Phe Asn Asp
3605		3610		3615	
Cys Glu	Asp Asn Ser Asp	Glu	Asp Ser Ser His	Cys	Ala Ser Arg
3620		3625		3630	
Thr Cys	Arg Pro Gly Gln	Phe	Arg Cys Ala Asn	Gly	Arg Cys Ile
3635		3640		3645	
Pro Gln	Ala Trp Lys Cys	Asp	Val Asp Asn Asp	Cys	Gly Asp His
3650		3655		3660	
Ser Asp	Glu Pro Ile Glu	Glu	Cys Met Ser Ser	Ala	His Leu Cys
3665		3670		3675	
Asp Asn	Phe Thr Glu Phe	Ser	Cys Lys Thr Asn	Tyr	Arg Cys Ile
3680		3685		3690	
Pro Lys	Trp Ala Val Cys	Asn	Gly Val Asp Asp	Cys	Arg Asp Asn
3695		3700		3705	
Ser Asp	Glu Gln Gly Cys	Glu	Glu Arg Thr Cys	His	Pro Val Gly
3710		3715		3720	
Asp Phe	Arg Cys Lys Asn	His	His Cys Ile Pro	Leu	Arg Trp Gln
3725		3730		3735	
Cys Asp	Gly Gln Asn Asp	Cys	Gly Asp Asn Ser	Asp	Glu Glu Asn
3740		3745		3750	
Cys Ala	Pro Arg Glu Cys	Thr	Glu Ser Glu Phe	Arg	Cys Val Asn
3755		3760		3765	
Gln Gln	Cys Ile Pro Ser	Arg	Trp Ile Cys Asp	His	Tyr Asn Asp
3770		3775		3780	
Cys Gly	Asp Asn Ser Asp	Glu	Arg Asp Cys Glu	Met	Arg Thr Cys
3785		3790		3795	
His Pro	Glu Tyr Phe Gln	Cys	Thr Ser Gly His	Cys	Val His Ser
3800		3805		3810	
Glu Leu	Lys Cys Asp Gly	Ser	Ala Asp Cys Leu	Asp	Ala Ser Asp
3815		3820		3825	
Glu Ala	Asp Cys Pro Thr	Arg	Phe Pro Asp Gly	Ala	Tyr Cys Gln
3830		3835		3840	

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Ala Thr 3845	Met Phe Glu Cys Lys 3850	Asn His Val Cys Ile 3855	Pro Pro Tyr
Trp Lys 3860	Cys Asp Gly Asp Asp 3865	Asp Cys Gly Asp Gly 3870	Ser Asp Glu
Glu Leu 3875	His Leu Cys Leu Asp 3880	Val Pro Cys Asn Ser 3885	Pro Asn Arg
Phe Arg 3890	Cys Asp Asn Asn Arg 3895	Cys Ile Tyr Ser His 3900	Glu Val Cys
Asn Gly 3905	Val Asp Asp Cys Gly 3910	Asp Gly Thr Asp Glu 3915	Thr Glu Glu
His Cys 3920	Arg Lys Pro Thr Pro 3925	Lys Pro Cys Thr Glu 3930	Tyr Glu Tyr
Lys Cys 3935	Gly Asn Gly His Cys 3940	Ile Pro His Asp Asn 3945	Val Cys Asp
Asp Ala 3950	Asp Asp Cys Gly Asp 3955	Trp Ser Asp Glu Leu 3960	Gly Cys Asn
Lys Gly 3965	Lys Glu Arg Thr Cys 3970	Ala Glu Asn Ile Cys 3975	Glu Gln Asn
Cys Thr 3980	Gln Leu Asn Glu Gly 3985	Gly Phe Ile Cys Ser 3990	Cys Thr Ala
Gly Phe 3995	Glu Thr Asn Val Phe 4000	Asp Arg Thr Ser Cys 4005	Leu Asp Ile
Asn Glu 4010	Cys Glu Gln Phe Gly 4015	Thr Cys Pro Gln His 4020	Cys Arg Asn
Thr Lys 4025	Gly Ser Tyr Glu Cys 4030	Val Cys Ala Asp Gly 4035	Phe Thr Ser
Met Ser 4040	Asp Arg Pro Gly Lys 4045	Arg Cys Ala Ala Glu 4050	Gly Ser Ser
Pro Leu 4055	Leu Leu Leu Pro Asp 4060	Asn Val Arg Ile Arg 4065	Lys Tyr Asn
Leu Ser 4070	Ser Glu Arg Phe Ser 4075	Glu Tyr Leu Gln Asp 4080	Glu Glu Tyr
Ile Gln 4085	Ala Val Asp Tyr Asp 4090	Trp Asp Pro Lys Asp 4095	Ile Gly Leu
Ser Val 4100	Val Tyr Tyr Thr Val 4105	Arg Gly Glu Gly Ser 4110	Arg Phe Gly
Ala Ile 4115	Lys Arg Ala Tyr Ile 4120	Pro Asn Phe Glu Ser 4125	Gly Arg Asn
Asn Leu 4130	Val Gln Glu Val Asp 4135	Leu Lys Leu Lys Tyr 4140	Val Met Gln
Pro Asp 4145	Gly Ile Ala Val Asp 4150	Trp Val Gly Arg His 4155	Ile Tyr Trp
Ser Asp 4160	Val Lys Asn Lys Arg 4165	Ile Glu Val Ala Lys 4170	Leu Asp Gly
Arg Tyr 4175	Arg Lys Trp Leu Ile 4180	Ser Thr Asp Leu Asp 4185	Gln Pro Ala
Ala Ile 4190	Ala Val Asn Pro Lys 4195	Leu Gly Leu Met Phe 4200	Trp Thr Asp
Trp Gly 4205	Lys Glu Pro Lys Ile 4210	Glu Ser Ala Trp Met 4215	Asn Gly Glu
Asp Arg 4220	Asn Ile Leu Val Phe 4225	Glu Asp Leu Gly Trp 4230	Pro Thr Gly
Leu Ser	Ile Asp Tyr Leu Asn	Asn Asp Arg Ile Tyr	Trp Ser Asp

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4235	4240	4245
Phe Lys Glu Asp Val Ile 4250	Glu Thr Ile Lys Tyr 4255	Asp Gly Thr Asp 4260
Arg Arg Val Ile Ala Lys 4265	Glu Ala Met Asn Pro 4270	Tyr Ser Leu Asp 4275
Ile Phe Glu Asp Gln Leu 4280	Tyr Trp Ile Ser Lys 4285	Glu Lys Gly Glu 4290
Val Trp Lys Gln Asn Lys 4295	Phe Gly Gln Gly Lys 4300	Lys Glu Lys Thr 4305
Leu Val Val Asn Pro Trp 4310	Leu Thr Gln Val Arg 4315	Ile Phe His Gln 4320
Leu Arg Tyr Asn Lys Ser 4325	Val Pro Asn Leu Cys 4330	Lys Gln Ile Cys 4335
Ser His Leu Cys Leu Leu 4340	Arg Pro Gly Gly Tyr 4345	Ser Cys Ala Cys 4350
Pro Gln Gly Ser Ser Phe 4355	Ile Glu Gly Ser Thr 4360	Thr Glu Cys Asp 4365
Ala Ala Ile Glu Leu Pro 4370	Ile Asn Leu Pro Pro 4375	Pro Cys Arg Cys 4380
Met His Gly Gly Asn Cys 4385	Tyr Phe Asp Glu Thr 4390	Asp Leu Pro Lys 4395
Cys Lys Cys Pro Ser Gly 4400	Tyr Thr Gly Lys Tyr 4405	Cys Glu Met Ala 4410
Phe Ser Lys Gly Ile Ser 4415	Pro Gly Thr Thr Ala 4420	Val Ala Val Leu 4425
Leu Thr Ile Leu Leu Ile 4430	Val Val Ile Gly Ala 4435	Leu Ala Ile Ala 4440
Gly Phe Phe His Tyr Arg 4445	Arg Thr Gly Ser Leu 4450	Leu Pro Ala Leu 4455
Pro Lys Leu Pro Ser Leu 4460	Ser Ser Leu Val Lys 4465	Pro Ser Glu Asn 4470
Gly Asn Gly Val Thr Phe 4475	Arg Ser Gly Ala Asp 4480	Leu Asn Met Asp 4485
Ile Gly Val Ser Gly Phe 4490	Gly Pro Glu Thr Ala 4495	Ile Asp Arg Ser 4500
Met Ala Met Ser Glu Asp 4505	Phe Val Met Glu Met 4510	Gly Lys Gln Pro 4515
Ile Ile Phe Glu Asn Pro 4520	Met Tyr Ser Ala Arg 4525	Asp Ser Ala Val 4530
Lys Val Val Gln Pro Ile 4535	Gln Val Thr Val Ser 4540	Glu Asn Val Asp 4545
Asn Lys Asn Tyr Gly Ser 4550	Pro Ile Asn Pro Ser 4555	Glu Ile Val Pro 4560
Glu Thr Asn Pro Thr Ser 4565	Pro Ala Ala Asp Gly 4570	Thr Gln Val Thr 4575
Lys Trp Asn Leu Phe Lys 4580	Arg Lys Ser Lys Gln 4585	Thr Thr Asn Phe 4590
Glu Asn Pro Ile Tyr Ala 4595	Gln Met Glu Asn Glu 4600	Gln Lys Glu Ser 4605
Val Ala Ala Thr Pro Pro 4610	Pro Ser Pro Ser Leu 4615	Pro Ala Lys Pro 4620
Lys Pro Pro Ser Arg Arg 4625	Asp Pro Thr Pro Thr 4630	Tyr Ser Ala Thr 4635

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Glu Asp Thr Phe Lys Asp Thr Ala Asn Leu Val Lys Glu Asp Ser
 4640 4645 4650

Glu Val
 4655

<210> SEQ ID NO 41
 <211> LENGTH: 4544
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 41

Met Leu Thr Pro Pro 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
 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

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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		
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		

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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
 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

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Asp Gly 1175	Ser Asp Glu Gly 1180	Glu Leu Cys Asp Gln Cys 1185	Ser Leu Asn
Asn Gly 1190	Gly Cys Ser His 1195	Cys Ser Val Ala Pro 1200	Gly Glu Gly
Ile Val 1205	Cys Ser Cys Pro 1210	Leu Gly Met Glu Leu Gly 1215	Pro Asp Asn
His Thr 1220	Cys Gln Ile Gln Ser 1225	Tyr Cys Ala Lys His 1230	Leu Lys Cys
Ser Gln 1235	Lys Cys Asp Gln Asn 1240	Lys Phe Ser Val Lys 1245	Cys Ser Cys
Tyr Glu 1250	Gly Trp Val Leu Glu 1255	Pro Asp Gly Glu Ser 1260	Cys Arg Ser
Leu Asp 1265	Pro Phe Lys Pro Phe 1270	Ile Ile Phe Ser Asn 1275	Arg His Glu
Ile Arg 1280	Arg Ile Asp Leu His 1285	Lys Gly Asp Tyr Ser 1290	Val Leu Val
Pro Gly 1295	Leu Arg Asn Thr Ile 1300	Ala Leu Asp Phe His 1305	Leu Ser Gln
Ser Ala 1310	Leu Tyr Trp Thr Asp 1315	Val Val Glu Asp Lys 1320	Ile Tyr Arg
Gly Lys 1325	Leu Leu Asp Asn Gly 1330	Ala Leu Thr Ser Phe 1335	Glu Val Val
Ile Gln 1340	Tyr Gly Leu Ala Thr 1345	Pro Glu Gly Leu Ala 1350	Val Asp Trp
Ile Ala 1355	Gly Asn Ile Tyr Trp 1360	Val Glu Ser Asn Leu 1365	Asp Gln Ile
Glu Val 1370	Ala Lys Leu Asp Gly 1375	Thr Leu Arg Thr Thr 1380	Leu Leu Ala
Gly Asp 1385	Ile Glu His Pro Arg 1390	Ala Ile Ala Leu Asp 1395	Pro Arg Asp
Gly Ile 1400	Leu Phe Trp Thr Asp 1405	Trp Asp Ala Ser Leu 1410	Pro Arg Ile
Glu Ala 1415	Ala Ser Met Ser Gly 1420	Ala Gly Arg Arg Thr 1425	Val His Arg
Glu Thr 1430	Gly Ser Gly Gly Trp 1435	Pro Asn Gly Leu Thr 1440	Val Asp Tyr
Leu Glu 1445	Lys Arg Ile Leu Trp 1450	Ile Asp Ala Arg Ser 1455	Asp Ala Ile
Tyr Ser 1460	Ala Arg Tyr Asp Gly 1465	Ser Gly His Met Glu 1470	Val Leu Arg
Gly His 1475	Glu Phe Leu Ser His 1480	Pro Phe Ala Val Thr 1485	Leu Tyr Gly
Gly Glu 1490	Val Tyr Trp Thr Asp 1495	Trp Arg Thr Asn Thr 1500	Leu Ala Lys
Ala Asn 1505	Lys Trp Thr Gly His 1510	Asn Val Thr Val Val 1515	Gln Arg Thr
Asn Thr 1520	Gln Pro Phe Asp Leu 1525	Gln Val Tyr His Pro 1530	Ser Arg Gln
Pro Met 1535	Ala Pro Asn Pro Cys 1540	Glu Ala Asn Gly Gly 1545	Gln Gly Pro
Cys Ser 1550	His Leu Cys Leu Ile 1555	Asn Tyr Asn Arg Thr 1560	Val Ser Cys
Ala Cys	Pro His Leu Met Lys	Leu His Lys Asp Asn	Thr Thr Cys

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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
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

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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	
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			

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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
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

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2750	2755	2760
Asp Glu Ala Ala His Cys 2765	Glu Gly Lys Thr Cys 2770	Gly Pro Ser Ser 2775
Phe Ser Cys Pro Gly Thr 2780	His Val Cys Val Pro 2785	Glu Arg Trp Leu 2790
Cys Asp Gly Asp Lys Asp 2795	Cys Ala Asp Gly Ala 2800	Asp Glu Ser Ile 2805
Ala Ala Gly Cys Leu Tyr 2810	Asn Ser Thr Cys Asp 2815	Asp Arg Glu Phe 2820
Met Cys Gln Asn Arg Gln 2825	Cys Ile Pro Lys His 2830	Phe Val Cys Asp 2835
His Asp Arg Asp Cys Ala 2840	Asp Gly Ser Asp Glu 2845	Ser Pro Glu Cys 2850
Glu Tyr Pro Thr Cys Gly 2855	Pro Ser Glu Phe Arg 2860	Cys Ala Asn Gly 2865
Arg Cys Leu Ser Ser Arg 2870	Gln Trp Glu Cys Asp 2875	Gly Glu Asn Asp 2880
Cys His Asp Gln Ser Asp 2885	Glu Ala Pro Lys Asn 2890	Pro His Cys Thr 2895
Ser Pro Glu His Lys Cys 2900	Asn Ala Ser Ser Gln 2905	Phe Leu Cys Ser 2910
Ser Gly Arg Cys Val Ala 2915	Glu Ala Leu Leu Cys 2920	Asn Gly Gln Asp 2925
Asp Cys Gly Asp Ser Ser 2930	Asp Glu Arg Gly Cys 2935	His Ile Asn Glu 2940
Cys Leu Ser Arg Lys Leu 2945	Ser Gly Cys Ser Gln 2950	Asp Cys Glu Asp 2955
Leu Lys Ile Gly Phe Lys 2960	Cys Arg Cys Arg Pro 2965	Gly Phe Arg Leu 2970
Lys Asp Asp Gly Arg Thr 2975	Cys Ala Asp Val Asp 2980	Glu Cys Ser Thr 2985
Thr Phe Pro Cys Ser Gln 2990	Arg Cys Ile Asn Thr 2995	His Gly Ser Tyr 3000
Lys Cys Leu Cys Val Glu 3005	Gly Tyr Ala Pro Arg 3010	Gly Gly Asp Pro 3015
His Ser Cys Lys Ala Val 3020	Thr Asp Glu Glu Pro 3025	Phe Leu Ile Phe 3030
Ala Asn Arg Tyr Tyr Leu 3035	Arg Lys Leu Asn Leu 3040	Asp Gly Ser Asn 3045
Tyr Thr Leu Leu Lys Gln 3050	Gly Leu Asn Asn Ala 3055	Val Ala Leu Asp 3060
Phe Asp Tyr Arg Glu Gln 3065	Met Ile Tyr Trp Thr 3070	Asp Val Thr Thr 3075
Gln Gly Ser Met Ile Arg 3080	Arg Met His Leu Asn 3085	Gly Ser Asn Val 3090
Gln Val Leu His Arg Thr 3095	Gly Leu Ser Asn Pro 3100	Asp Gly Leu Ala 3105
Val Asp Trp Val Gly Gly 3110	Asn Leu Tyr Trp Cys 3115	Asp Lys Gly Arg 3120
Asp Thr Ile Glu Val Ser 3125	Lys Leu Asn Gly Ala 3130	Tyr Arg Thr Val 3135
Leu Val Ser Ser Gly Leu 3140	Arg Glu Pro Arg Ala 3145	Leu Val Val Asp 3150

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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
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	

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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
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	

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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		
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		

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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 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
 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 42
 <211> LENGTH: 375
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 42

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

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

<210> SEQ ID NO 43

<211> LENGTH: 198

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 43

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

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Asp Leu Pro Val Gly Arg Ser Val Asp Glu Ala Leu Arg Leu Val Gln
 145 150 155 160

Ala Phe Gln Tyr Thr Asp Glu His Gly Glu Val Cys Pro Ala Gly Trp
 165 170 175

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

Tyr Phe Ser Lys His Asn
 195

<210> SEQ ID NO 44
 <211> LENGTH: 124
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens
 <400> SEQUENCE: 44

Ser Phe Ser Ser Met Glu Ala Ser Ser Ala Leu Cys Trp Gly Val Met
 1 5 10 15

Ala Ser Ser Leu Leu Ala Ser Leu Ala Ile Glu Arg Val Met Arg Pro
 20 25 30

Leu Arg Leu Pro Trp Leu Leu Ala Val Leu Arg Pro Leu Glu Ala Thr
 35 40 45

Ala Ser Phe Ser Ser Leu Ser Ser Pro Glu Val Ser Ser Val Phe Ser
 50 55 60

Leu Arg Arg Ser Ser Leu Ser Phe Ser Thr Ser Gly Phe Ser Ser Ser
 65 70 75 80

Phe Ser Ala Ser Phe Ser Phe Ser Phe Ser Ser Phe Ser Ser Trp Leu
 85 90 95

Leu Arg Gly Met Gly Cys Cys Cys Cys Cys Cys Cys Cys Cys Cys
 100 105 110

Cys Cys Cys Cys Cys Trp Leu Leu Pro Arg Arg Arg
 115 120

We claim:

1. A kit for detecting the presence of myocardial ischemia in a subject, comprising reagents for detecting the amount of at least three of the following proteins:

- i) Lumican, and/or
- ii) Extracellular matrix protein 1, and/or
- iii) Carboxypeptidase N, and/or
- iv) Angiogenin, and/or
- v) Semenogelin, and/or
- vi) Long palate, lung and nasal epithelium carcinoma-associated protein 1, and/or
- vii) Peroxiredoxin isoform 2, and/or
- viii) Syntaxin 3, and/or
- ix) S100 isoform A7, and/or
- x) S100 isoform A8, and/or
- xi) S100 isoform A9, and/or
- xii) Sortilin-related receptor, and/or
- xiii) Catalase, and/or
- xiv) Low density lipoprotein receptor related protein 1, and/or
- xv) Low density lipoprotein receptor related protein 2.

2. The kit of claim 1, further comprising reagents for detecting the amount of at least one of the following proteins:

- xvi) Hepatocyte growth factor activator, and/or
- xvii) Alpha-2-HS-glycoprotein, and/or
- xviii) Insulin like growth factor protein 6, and/or
- xix) Galectin-7, and/or
- xx) Hornerin, and/or
- xxi) Proteoglycan-4, and/or
- xxii) Profilaggrin (also referred to as Filaggrin), and/or
- xxiii) Vitamin D binding protein, and/or
- xxiv) C4b-binding protein alpha chain, and/or
- xxv) Thyroxine binding globulin, and/or
- xxvi) Alpha-2-glycoprotein 1, zinc, and/or
- xxvii) Serine 3 protease, and/or
- xxviii) Caspase 14, and/or
- xxix) Desmogelin, and/or
- xxx) Kininogen -1, and/or
- xxxi) Hepatocyte growth factor like protein.

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专利名称(译)	用于心肌缺血的生物标志物		
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摘要(译)

本发明涉及例如确定受试者是否患有心肌缺血的方法，包括 (a) 提供从怀疑患有心肌缺血的受试者获得的血液样品; (b) 在样品中测定一种或多种下列蛋白质的量 : (i) Lumican和/或 (ii) 细胞外基质蛋白1和/或 (iii) 羧肽酶N; (c) 将蛋白质的量与基线值进行比较，该基线值表示受试者中没有心肌缺血的蛋白质的量，其中蛋白质的量在统计学上显著增加 (s)) 相比基线值表明心肌缺血。还描述了指示心肌缺血的其他蛋白质，以及基于本发明的诊断方法治疗受试者的方法，以及用于实施本发明方法的试剂盒。

MKRVLVLLAVAFGHALERGRDYEKNKVCKEFSHLGKEDFTSLSLVLY

SRKFPSGTFEQVSQVLKEVVSLEACCAEGADPDCTRTSALSACE

SNSFPVHPGTAECCCKEGLERKLCMAALKHQEQEFPTYVEPTNDEICE

AFKDPKEYANQFMWEYSTNYQAPLSLLVSYTKSYLSMVGSCCTSASP